

The Underwater Piano:

A Resonance Theory of Cochlear Mechanics

by James Andrew Bell

A thesis submitted for the degree of
Doctor of Philosophy of The Australian National University
July 2005



Visual Sciences Group
Research School of Biological Sciences
The Australian National University
Canberra, ACT 0200
Australia

This thesis is my original work and has not been submitted, in whole or in part, for a degree at this or any other university. Nor does it contain, to the best of my knowledge and belief, any material published or written by any other person, except as acknowledged in the text. In particular, I acknowledge the contribution of Professor Neville H. Fletcher who wrote Appendix A of Bell & Fletcher (2004) [§R 5.6 in this thesis] and who helped refine the text of that paper. Dr Ted Maddess provided the draft Matlab code used to perform the autocorrelation analysis reported in Chapter R7. Sharyn Wragg, RSBS Illustrator, drew some of the figures as noted.

Signed:

Date:

Acknowledgements

This thesis would not have appeared without the encouragement, support, and interest of many people. Yet, among them, the primary mainstay of this enterprise has been my wife, Libby, who has stayed by me on this long journey. I thank her for understanding and tolerance. Rachel, Sarah, Micah, Adam, Daniel, and Joshua have given their love and support, too, and that has been a source of strength.

My supervisors have contributed in large measure, and I am grateful to all of them. Professor Anthony W. Gummer of the University of Tübingen saw the potential of this work at an early stage, and I thank him for his initiative in opening the door to this PhD study and providing some support (a grant from the German Research Council, SFB 430, to A.W. Gummer). Professor Mandyam V. Srinivasan of this department immediately committed himself to supporting the enterprise and has not wavered in making it the best it could be. Professor Neville H. Fletcher of the Research School of Physical Sciences and Engineering at this university has contributed a depth of acoustic knowledge, quickly supplying prompts, questions, and criticisms which have all been aimed at making the thesis logically water-tight. Dr Ted Maddess, chair of the supervisory panel, has given freely of his time, interest, and programming skill and always kept the endpoint clearly in sight. Of course, my supervisors do not necessarily accept my assumptions, conclusions, and speculations. Indeed, it must be said that my efforts to pursue an unorthodox Helmholtz resonance model, rather than the standard Békésy traveling wave model, have not persuaded all of them; nevertheless, their constructive criticisms have served to sharpen my arguments and fill in some of the details.

My ideas have also been clarified by numerous email encounters with people in the field, and their time and perspectives are acknowledged. In particular, I thank members of the Auditory, Cochlea, and Blumschein discussion lists for their willingness to hear and discuss new approaches to how the ear works. Dr Paul Kolston has been a willing listener and persistent questioner. Along the way I have crossed paths with many others, and I am grateful for the leadings they have offered.

I regard experimentation on animals as ethically unsound, and in my view destroying living creatures is not a path to reliable knowledge. Francis Bacon saw the danger of “putting nature on the rack”, as Goethe expressed the scientific enterprise. Bacon thought that “intemperate experimentation might elicit misleading or distorted responses from nature [in the same way as] torture is futile because it tends to elicit false or garbled confessions”¹. My perspective is that hearing will only be understood by studying living, intact creatures, and in testing the ideas raised in this thesis I urge that experiments respect the lives of our kindred spirits, the animals.

I acknowledge the presence of the universal mind as a source of inspiration.

¹ As paraphrased by Pesic, P. (2000). *Labyrinth: A search for the hidden meaning of science*. (MIT Press: Cambridge, MA). [p. 27] Bacon, as Lord Chancellor, was qualified to judge.

Contents

Acknowledgements

Summary

Prologue and outline of the thesis

INTRODUCTION

- Chapter I 1** **The resonance principle in perspective**
- Chapter I 2** **What could be resonating? An historical survey**
- Chapter I 3** **Traveling wave theory, and some shortcomings**

MODEL

- Chapter M 4** **Cochlear fine-tuning: a surface acoustic wave resonator**

RESULTS

- Chapter R 5** **A squirting wave model of the cochlear amplifier**
- Chapter R 6** **Modeling wave interactions between outer hair cells**
- Chapter R 7** **Analysis of the outer hair cell unit lattice**

DISCUSSION

- Chapter D 8** **How outer hair cells could detect pressure**
- Chapter D 9** **Evidence and synthesis**
- Chapter D 10** **Evaluation, predictions, and conclusions**

References

Appendix

Summary

This thesis takes a fresh approach to cochlear mechanics. Over the last quarter of a century, we have learnt that the cochlea is active and highly tuned, observations suggesting that something may be resonating. Rather than accepting the standard traveling wave interpretation, here I investigate whether a resonance theory of some kind can be applied to this remarkable behaviour.

A historical survey of resonance theories is first conducted, and advantages and drawbacks examined. A corresponding look at the traveling wave theory includes a listing of its short-comings.

A new model of the cochlea is put forward that exhibits inherently high tuning. The surface acoustic wave (SAW) model suggests that the three rows of outer hair cells (OHCs) interact in a similar way to the interdigital transducers of an electronic SAW device. Analytic equations are developed to describe the conjectured interactions between rows of active OHCs in which each cell is treated as a point source of expanding wavefronts. Motion of a cell launches a wave that is sensed by the stereocilia of neighbouring cells, producing positive feedback. Numerical calculations confirm that this arrangement provides sharp tuning when the feedback gain is set just below oscillation threshold.

A major requirement of the SAW model is that the waves carrying the feedback have slow speed (5–200 mm/s) and high dispersion. A wave type with the required properties is identified – a symmetric Lloyd–Redwood wave (or squirting wave) – and the physical properties of the organ of Corti are shown to well match those required by theory.

The squirting wave mechanism may provide a second filter for a primary traveling wave stimulus, or stand-alone tuning in a pure resonance model. In both, cyclic activity of squirting waves leads to standing waves, and this provides a physical rendering of the cochlear amplifier.

In keeping with pure resonance, this thesis proposes that OHCs react to the fast pressure wave rather than to bending of stereocilia induced by a traveling wave. Investigation of literature on OHC ultrastructure reveals anatomical features consistent with them being pressure detectors: they possess a cuticular pore (a small

compliant spot in an otherwise rigid cell body) and a spherical body within (Hensens body) that could be compressible. I conclude that OHCs are dual detectors, sensing displacement at high intensities and pressure at low. Thus, the conventional traveling wave could operate at high levels and resonance at levels dominated by the cochlear amplifier. The latter picture accords with the description due to Gold (1987) that the cochlea is an ‘underwater piano’ – a bank of strings that are highly tuned despite immersion in liquid.

An autocorrelation analysis of the distinctive outer hair cell geometry shows trends that support the SAW model. In particular, it explains why maximum distortion occurs at a ratio of the two primaries of about 1.2. This ratio also produces near-integer ratios in certain hair-cell alignments, suggesting that music may have a cochlear basis.

The thesis concludes with an evaluation and proposals to experimentally test its validity.

Prologue and outline of the thesis²

Sitting in the enveloping quietness of an anechoic chamber, or other quiet spot, you soon become aware that the ear makes its own distinctive sounds. Whistling, buzzing, hissing, perhaps a chiming chorus of many tones – such continuous sounds seem remarkably nonbiological to my perception, more in the realm of the electronic.

Even more remarkable, put a sensitive microphone in the ear canal and you will usually pick up an objective counterpart of that subjective experience. Now known in auditory science as spontaneous otoacoustic emission, the sound registered by the microphone is a clear message that the cochlea uses active processes to detect the phenomenally faint sounds – measured in micropascals – our ears routinely hear. If the ear were more sensitive, we would need to contend with the sound of air molecules raining upon our eardrums.

What is that process – the mechanical or electrical scheme that Hallowell Davis in 1983 called the ‘cochlear amplifier’³ – which energises the hazelnut-sized hearing organ buried in the solid bone of our skull?

That question has engaged my curiosity since the late 1970s, when English auditory physicist David Kemp⁴ first put a microphone to an ear and discovered the telltale sounds of the cochlea at work. Siren-like, the sounds have drawn me into the theory and experiment of cochlear mechanics, first as a part-time MSc⁵ and now this PhD. This thesis is a study of the micromechanics of this process and its aim is to see whether a resonance picture of some kind can be applied to the faint but mysterious sounds most cochleas emit.

Kemp’s discoveries are rightly viewed as opening a fresh path to auditory science, and to the tools and techniques for diagnosing the functional status of the

² Based on Bell, A. (2004). Hearing: travelling wave or resonance? *PLoS Biology* 2: e337.

³ Davis, H. (1983). An active process in cochlear mechanics. *Hear. Res.* 9: 79-90.

⁴ Kemp, D. T. (1978). Stimulated acoustic emissions from within the human auditory system. *J. Acoust. Soc. Am.* 64: 1386-1391.

⁵ Bell, A. (1998). A study of frequency variations of spontaneous otoacoustic emissions from human ears. MSc thesis, Australian National University, Canberra.

cochlea. But in terms of fundamental understanding, I am indebted to a key paper by Thomas Gold more than half a century ago⁶. Still cited widely, this paper deals with the basic question of how the cochlea works to analyse sound into its component frequencies. Two prominent theories – sympathetic resonance, proposed by Hermann Helmholtz⁷ in 1885, and traveling waves, proposed by Georg von Békésy⁸ – need to be distinguished (Fig. 0.1). In brief, are there tiny, independently tuned elements in the cochlea, like the discrete strings of a piano, that are set into sympathetic vibration by incoming sound [**Chapters I 1 and I 2**], or is the continuously graded sensing surface of the cochlea hydrodynamically coupled so that, like flicking a rope, motion of the eardrum and middle ear bones causes a traveling wave to sweep from one end towards the other [**Chapter I 3**]?

The first option, sympathetic resonance, has the advantage of allowing vanishingly small energies to build up, cycle by cycle, into an appreciable motion – like boosting a child on a swing. The second, traveling wave, has the weight of von Békésy’s extensive experiments and a huge amount of theoretical analysis behind it. At the same time, one of the drawbacks of the traveling wave theory is the difficulty of accounting for the ear’s exquisite fine tuning: trained musicians can easily detect tuning differences of less than 0.2%. Even von Békésy himself notes that ‘the resonance theory of hearing is probably the most elegant of all theories of hearing’⁹.

Gold’s work, done in collaboration with R. J. Pumphrey¹⁰, was the first to consider that the ear cannot act passively, as both Helmholtz and von Békésy had thought, but must be an active detector. Gold was a physicist who had done wartime work on radar, and he brought his signal-processing knowledge to bear on how the cochlea works. He knew that, to preserve signal-to-noise ratio, a signal had to be amplified before the detector, and that ‘surely nature can’t be as stupid as to go and put a nerve fibre – that is a detector – right at the front end of the sensitivity of the

⁶ Gold, T. (1948). Hearing. II. The physical basis of the action of the cochlea. *Proc. Roy. Soc. Lond. B* 135: 492-498.

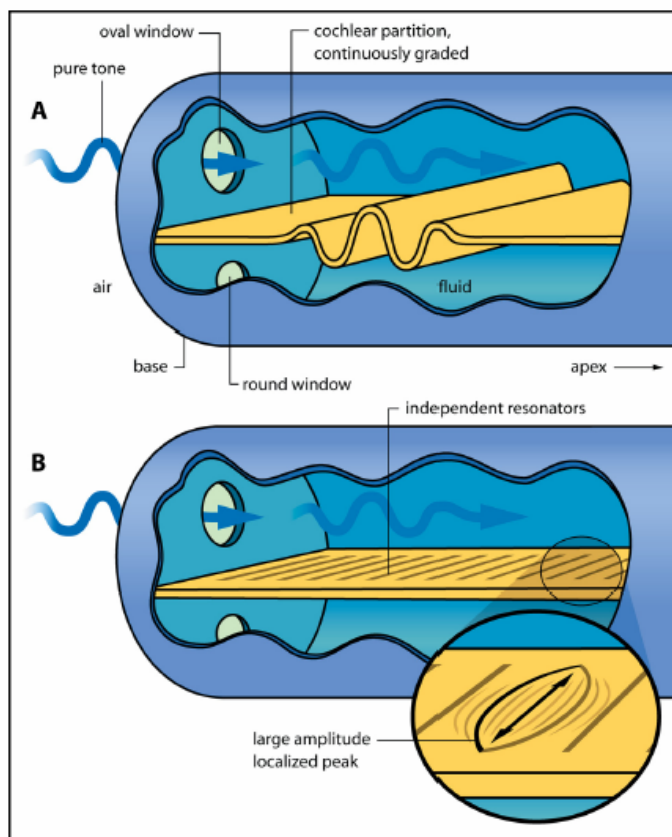
⁷ Helmholtz, H. L. F. v. (1875). *On the Sensations of Tone as a Physiological Basis for the Theory of Music*. (Longmans, Green: London).

⁸ Békésy, G. v. (1960). *Experiments in Hearing*. (McGraw-Hill: New York).

⁹ Ibid. p. 404.

¹⁰ Gold, T. and R. J. Pumphrey (1948). Hearing. I. The cochlea as a frequency analyzer. *Proc. Roy. Soc. Lond. B* 135: 462-491.

system'¹¹. He therefore proposed that the ear operated like a regenerative receiver, much like some radio receivers of the time that used positive feedback to amplify a signal before it was detected.



DOI: 10.1371/journal.pbio.0020337.g001

Fig. 0.1. Two Views of Cochlear Mechanics. The cochlea, shown uncoiled, is filled with liquid. In the accepted traveling wave picture (A), the partition vibrates up and down like a flicked rope, and a wave of displacement sweeps from base (high frequencies) to apex (low frequencies). Where the wave broadly peaks depends on frequency. An alternative resonance view (B) is that independent elements on the partition can vibrate side to side in sympathy with incoming sound. It remains open whether the resonant elements are set off by a traveling wave (giving a hybrid picture) or directly by sound pressure in the liquid (resonance alone).

Regenerative receivers were simple – one could be built with a single vacuum tube – and they provided high sensitivity and narrow bandwidth. A drawback, however, was that, if provoked, the circuit could ‘take off’, producing an unwanted whistle. Gold connected this with the perception of ringing in the ear (tinnitus), and daringly suggested that if a microphone were put next to the ear, a corresponding

¹¹ Gold, T. (1989). Historical background to the proposal, 40 years ago, of an active model for cochlear frequency analysis. In: *Cochlear Mechanisms: Structure, Function, and Models*, edited by J. P. Wilson and D. T. Kemp (Plenum: New York), 299-305.

sound might be picked up. He experimented, placing a microphone in his ear after inducing temporary tinnitus with overly loud sound. The technology wasn't up to the job – in 1948 microphones weren't sensitive enough – and the experiment, sadly, failed.

Gold's pioneering work is now acknowledged to be a harbinger of Kemp's discoveries. But there is one aspect of Gold's paper that is not so widely considered: The experiments of Gold and Pumphrey led them to favour a resonance theory of hearing. In fact, the abstract of their 1948 paper declares that 'previous theories of hearing are considered, and it is shown that only the resonance theory of Helmholtz... is consistent with observation'.

I think the resonance theory deserves reconsideration. The evidence of my ears tells me that the cochlea is very highly tuned, and an active resonance theory of some sort seems to provide the most satisfying explanation. Furthermore, as well as Gold's neglected experiment, we now know from studies of acoustic emissions that the relative bandwidth of spontaneously emitted sound from the cochlea can be 1/1000 of the emission's frequency, or less. This thesis, begun initially with Professor A. W. Gummer and continued under the guidance of Professors M. V. Srinivasan and N. H. Fletcher and Dr T. Maddess, has centred on finding an answer to that most fundamental question: if the cochlea is resonating, what are the resonant elements?

A point of inspiration for me is Gold's later discussion¹² of cochlear function – some nine years after Kemp's discoveries had been made. Gold draws a striking analogy for the problem confronting the cochlea, whose resonant elements – whatever they are – sit immersed in fluid (the aqueous lymph that fills the organ). To make these elements resonate is difficult, says Gold, because they are damped by surrounding fluid, just like the strings of a piano submerged in water would be. He concludes that, to make 'an underwater piano' work, we would have to add sensors and actuators to every string so that once a string is sounded the damping is counteracted by positive feedback. 'If we now supplied each string with a correctly designed feedback circuit,' he surmises, 'then the underwater piano would work again.'¹³

¹² Gold, T. (1987). The theory of hearing. In: *Highlights in Science*, edited by H. Messel (Pergamon: Sydney), 149-157.

¹³ Ibid, p.155.

This research includes an investigation of what Gold's underwater piano strings might be. A prime candidate has been found and its identity – squirting waves between rows of outer hair cells – put forward in a recent paper¹⁴ and elaborated in **Chapter R 5**. Outer hair cells are both effectors (they change length when stimulated) and sensors (their stereocilia detect minute displacements), so in this way a positive feedback network can form that sets up resonance between one row of cells and its neighbour. The key is to transmit the feedback with the correct phase delay, and the thesis describes how this can be done using the analogy of surface acoustic wave (SAW) resonators [**Chapter M 4**] in which squirting waves carry the wave energy in the gap occupied by the outer hair cell stereocilia [**Chapter R 5**]. The paper suggests that the outer hair cells create a standing wave resonance, from which energy is delivered to inner hair cells, a picture depicted schematically in Fig. 0.2 below. In this way, the input signal is amplified before it is detected – an active system functioning just like Gold's regenerative receiver – and which is modelled using Matlab in **Chapter R 6**.

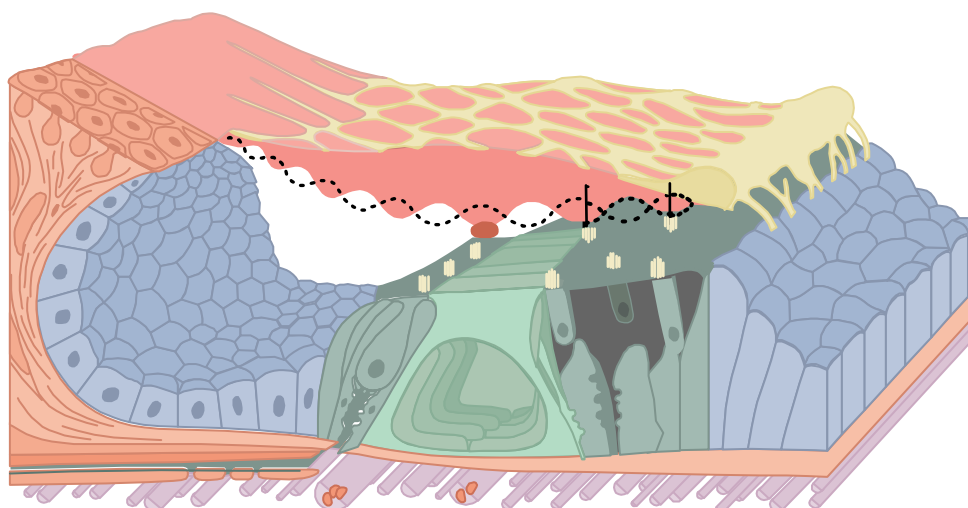


Fig. 0.2. A perspective view showing how a standing wave could form in the cochlea. The arrangement is similar to that of a surface acoustic wave (SAW) resonator, and is driven by positive feedback between rows of outer hair cells, which have both sensory and motor properties. [Adapted from Lim 1980, *J. Acoust. Soc. Am.* **67**, p. 1686, with permission of the author and the Acoustical Society of America]

¹⁴ Bell, A. and N. H. Fletcher (2004). The cochlear amplifier as a standing wave: "squirting" waves between rows of outer hair cells? *J. Acoust. Soc. Am.* **116**: 1016-1024.

With a prime candidate in place for the resonating elements, this should, I think, prompt us to re-evaluate resonance theories of hearing, which were first put forward by the ancient Greeks and which, irrepressibly, keep resurfacing. The best-known resonance theory was that formulated by Helmholtz, but at that time no satisfactory resonating elements could be identified, and it lapsed until Gold's attempt to revive it.

Chapter R 7 uses an autocorrelation technique to examine the distinctive pattern in which OHCs appear. It finds that the OHC unit cell has a geometry which may explain why distortion products in the ear reach a maximum at ratios of the primaries of about 1.2. Moreover, that same geometry produces distances between nearby cells that at times correspond to those produced by simple integer ratios of frequencies – that is, that the cochlear geometry may be designed for detection of harmonics. Here we find a possible cochlear basis for the origin of music. Pythagoras would be pleased.

There are other difficulties in reviving a resonance theory of hearing, and a major one is seeing how the outer hair cells can act as detectors of intracochlear pressure. **Chapter D 8** describes how this may occur by making use of a compressible element inside the body of the cell, a feature that also gives a natural explanation for kinocilia and the cuticular pore. **Chapter D 9** provides an electrophysiological basis for this detection scheme and suggests that the so-called 'silent current' in outer hair cells is, at sound pressure levels below about 60 dB SPL, modulated by intracochlear pressure.

It is conceivable that motion of the conventional traveling wave sets off the resonant elements, in which case we have an interesting hybrid of traveling wave and resonance. The other possibility, which this thesis argues the case for, is that outer hair cells are stimulated by the fast pressure wave that sweeps through all of the cochlear fluid at the speed of sound in water (1500 m/s). If that is so, and outer hair cells are sensitive pressure sensors, not displacement detectors, then the ear is a fully resonant, pressure-driven system, a conclusion set out in **Chapter D 10** along with predictions and suggestions for further investigation. The end point of the thesis is that it is not out of the question that the cochlea could function on resonance principles. Conceivably, Helmholtz, and Gold after him, could have been right.

The resonance principle in perspective¹

- 1.1 Introduction
- 1.2 History
- 1.3 Traveling wave theories
- 1.4 Gold's resonance ideas
- 1.5 Distinguishing traveling wave and resonance
- 1.6 Kemp and the active cochlea
- 1.7 Two signals in the cochlea
- 1.8 A new resonance model of the cochlea
- 1.9 Concluding remarks

This chapter provides an overview of how a powerful acoustical principle – sympathetic resonance – has been applied to our organ of hearing. It focuses on the principle's virtues, drawbacks, and varying fortunes. Why did Helmholtz's resonance theory of hearing in the 1850s fall from universal acceptance to near total disregard? What were the factors favouring traveling wave theories, most notably that of von Békésy in the mid 20th century? Post-Békésy, however, thinking on cochlear mechanics has been radically changed by findings that the cochlea is an active

¹ Based on Bell, A. (2004). Resonance theories of hearing: a history and a fresh approach. *Acoustics Australia* 32: 108-113.

transducer, not a passive one as previously thought. As Kemp demonstrated² in 1979, healthy cochleas are highly tuned and continuously emit narrow-band sound ... prompting the thought that something seems to be resonating. Maybe, then, it is worth re-examining resonance, even though traveling waves remain the centre-piece of the standard cochlear model. A fresh resonance formulation is described, and the way by which it appears to behave similarly to a traveling wave is pointed out.

1.1 Introduction

If the ear were more sensitive, we would have to contend with the noise of air molecules raining upon our ear drums³. The core of our multi-stage sound transducer is the cochlea, a spiral-shaped organ the size of a hazelnut buried in the solid bone of the skull.

Operating close to theoretical limits, the cochlea has a 10-octave frequency response, operates over a signal power range of a million million times (120 dB), and exhibits a noise floor close to thermal noise. Good frequency analysis is built in, with semitone (1/12-octave) precision as standard. It's electrically powered using supplies of a fraction of a volt, and operates underwater (the cochlea is filled with watery liquid). And while we have broad ideas of how it works, there's still a long way to go.

Because the cochlea is inaccessible and delicate, its experimental study is difficult, and so auditory science has relied heavily on theory, informed by anatomy, psychophysics, and sometimes inconclusive direct probing on animals (experiments which, from my ethical perspective, are regrettable). There have been a multitude of theories, and progress has often been slow.

But in 1978 a new window into the cochlea suddenly opened. English auditory scientist David Kemp discovered⁴ that the organ not only detects sound but

² Kemp, D. T. (1979). Evidence of mechanical nonlinearity and frequency selective wave amplification in the cochlea. *Arch. Otorhinolaryngol.* 224: 37-45.

³ Consider the performance of the B&K 4179 low-noise microphone which claims a noise floor of 2.6 dB SPL. At 1 kHz about half of this noise derives from thermal motion of air molecules [Fig. 2 of B&K 4179 data sheet at <http://www.bksv.com/pdf/Bp0389.pdf>]

⁴ Kemp, D. T. (1978). Stimulated acoustic emissions from within the human auditory system. *J. Acoust. Soc. Am.* 64: 1386-1391.

produces it. He placed a microphone in his ear and picked up the faint but distinct sounds of the cochlea at work.

His discovery of “otoacoustic emissions” has revolutionised the field and led to new diagnostic tools and methods. Most human cochleas produce an echo in response to a click and, more remarkably, constantly emit faint, narrow-band tones. We now know much about these energetic phenomena, but still remain largely ignorant of how they are produced and how they relate to the fundamental process of sound transduction.

In this chapter I give a broad outline of the two major theories of hearing – the accepted traveling wave theory and the now virtually outmoded resonance theory. A subsequent chapter more comprehensively documents attempts to construct resonance theories (Chapter I2). As a counterfoil, the next chapter (Chapter I3) deals with the traveling wave theory, but not in historical detail; rather, it sets out its broad principle of operation and then documents anomalies in the literature that the theory has difficulty explaining (and which a resonance theory could accommodate).

Following Kemp’s discoveries, the hearing field has generally been content to build active properties on top of the passive traveling wave, but I have misgivings. Because of anomalies in the traveling wave theory, a resonance picture presents certain highly attractive aspects. The question this thesis explores is whether it is possible to revive it. Starting at first principles, I have been endeavouring to construct a new resonance model of hearing. The following sections provide a historical perspective on the development of resonance theories, describe the general principles on which they operate, and argue for why resonance deserves reconsideration. As part of this, a summary is given of how the newly constructed model works, a model which receives elaboration in other parts of the thesis.

1.2 History

For most of recorded history, people have turned to resonance as an explanation of how we hear. The ancient Greeks held that “like is perceived by like” so, in order for the inner soul to perceive a sound, Empedocles (5th century BCE),

the person who probably first discovered and named the cochlea⁵ (κόχλοζ, meaning a snail), said there had to be direct contact. In other words, the ear must contain something of the same nature as the soul, and this was a highly refined substance particularly tenuous and pure called “implanted air”, and it was this that resonated to incoming sound. “Hearing is by means of the ears,” said Alcmaeon of Crotonia in 500 BCE, “because within them is an empty space, and this empty space resounds”⁶. Aristotle concurred and said that when we hear “the air inside us is moved concurrently with the air outside.”

Democritus described hearing as air rushing into the vacuum of the ear, producing a motion there. Heraclides expressed the idea of frequency: sound is composed of ‘beats’, he said, which can produce high or low tones depending on their number. We cannot distinguish the beats but perceive a sound as unbroken, with high tones consisting of more such beats and low tones fewer. Empedocles introduced the notion that in the same way as the eye contains a lantern, the ear contains a bell or gong that the sound from without causes to ring^{7,8}; perhaps he noticed the ringing sound in his own ears, an experience we now call tinnitus (Latin for “tinkling bell”).

Renaissance science recognised the importance of resonance and Galileo⁹ formally treated the phenomenon in 1638. He had noted the reverberation of hallways and domes and generalised this special behaviour to the acoustic properties of cavities and tubes of all sizes. Observation of stringed musical instruments showed that they readily picked up vibrations in the air around them. Importantly, they responded in a discriminating way, becoming alive only to like frequencies and remaining insensitive to others.

The first scientifically based resonance theory of hearing was that of Bauhin⁶ in 1605. It was successively refined by others, all considering air-filled spaces as the resonant elements. DuVerney¹⁰ in 1683 thought the cochlea’s bony but thin spiral

⁵ Hawkins, J. E. (2004). Sketches of otohistory. Part 1: otoprehistory, how it all began. *Audiol. Neurotol.* 9: 66-71.

⁶ Hunt, F. V. (1978). *Origins in Acoustics*. (Yale U. P.: New Haven, CT).

⁷ Békésy, G. v. and W. A. Rosenblith (1948). The early history of hearing – observations and theories. *J. Acoust. Soc. Am.* 20: 727–748. [p. 730]

⁸ Beare, J. I. (1906). *Greek Theories of Elementary Cognition*. (Clarendon Press: Oxford).

⁹ Wever, E. G. (1949). *Theory of Hearing*. (Dover: New York).

¹⁰ Wever (1949), p. 12-14. Békésy and Rosenblith (1948) see Duverney as standing at the head of a long series of scientists who based their hearing theory upon the concept of resonance (p. 741); they see Duverney and Valsalva as true precursors of Helmholtz’s resonance theory.

lamina vibrated – with high frequencies at one end and low at the other – and the notion of spectral analysis by sympathetic resonance had been born. Soon the idea of vibrating strings emerged, and by the 18th century people were using the analogy of the sensory membrane being composed of strings as in a stringed musical instrument.

All of this thinking culminated in the immensely influential work of Helmholtz which he put forth in his landmark *Sensations of Tone*¹¹. His resonance theory began as a public lecture in 1857 and within 20 years had gone on to become almost universally accepted. Helmholtz applied his scientific and mathematical skills to the simple analogy of the cochlea as a graded array of minute piano strings. Speak into a piano (with the dampers raised), said Helmholtz, and the strings will vibrate in sympathy, producing an audible echo; in like manner, the cochlea's arches of Corti will reverberate perceptibly in response to incoming sound. His presentation gave details of anatomy, number of resonators, and their degrees of coupling and damping, and it all seemed to fit nicely. He had to modify the theory to accommodate new anatomical findings, switching to the fibres of the basilar membrane as the preferred resonators, but the essence of his theory remained.

But then problems arose. The major one was a doubt that independently tuned stretched strings could exist in the basilar membrane. Anatomically, the structure shows a rather loose appearance and, since the fibres form a mesh, they must be closely coupled. It is therefore hard to see that the fibres could be finely tuned, that is, that they could have an appreciable quality factor, or Q , especially when the basilar membrane is immersed in liquid. And how could something no bigger than a nut have within it a structure able to resonate in sympathy with the throb of a double bass, for example?

The theory aims to explain how our keen pitch perception originates – we can easily detect changes in frequency of less than 1% – but if the Q of the fibres is low, this leads to the prediction that our pitch perception is correspondingly poor. On the other hand, if we nonetheless insist on retaining high Q , this invites another difficulty: a tone will take many cycles to build up and as many to decay, producing a hopeless blur of sound like a piano played with the sustain pedal always down. Something was amiss and the theory fell from favour, although its simple elegance meant that it continued to retain a few dogged adherents (see Chapter I2).

¹¹ Helmholtz, H. L. F. v. (1875). *On the Sensations of Tone as a Physiological Basis for the Theory of Music*. (Longmans, Green: London).

Moreover, there were new alternatives. With the invention of the telephone, theories appeared likening the cochlea to a vibrating diaphragm. Some thought that the diaphragm was the basilar membrane; others thought the tectorial membrane a better choice.

1.3 Traveling wave theories

Towards the end of the 19th century another novel theory arose: that of a traveling wave⁶. It came in a succession of forms, the first being that of Hurst in 1894, who suggested a wave of displacement traveling down the basilar membrane (hence the name). Variants were put forward by Bonnier (1895), ter Kuile (1900), and Watt (1914). These theories made a positive virtue out of their low Q , explaining how sound perceptions could start and stop instantly. They also gave a useful role for the cochlear fluids, using hydrodynamics to help with propagation of the wave.

The wave is considered to travel along the basilar membrane like a wave in a flicked rope. Traveling wave theories are built on the idea that the cochlea is a coarse frequency analyser, leaving it to the nervous system (or perhaps some mechanical “second filter” as discussed in the following chapter) to sharpen up the response.

The most famous traveling wave theory is due to György von Békésy who won a Nobel Prize for his decades-long efforts, beginning in 1928, to elucidate the mode of action of this wave. It is his name that we associate with the theory, for he was the first to actually observe a traveling wave in the cochlea, both in human cadavers and in animals, using intense sound stimulation and stroboscopic illumination¹². He also built water-filled boxes divided by rubber membranes, and saw similar behaviour. He started his experiments expecting¹³ to rule out the basic place principle of Helmholtz – that the sensing membrane in the cochlea maps frequency to distance along it – but was surprised to discover that, depending on the frequency of excitation, the peak of the wave shifted systematically from the base of the cochlea to its apex, offering a degree of frequency resolution. Again, the peak

¹² Békésy, G. v. (1960). *Experiments in Hearing*. (McGraw-Hill: New York).

¹³ Fay, R. R. (1992). Ernest Glen Wever: a brief biography and bibliography. In: *The Evolutionary Biology of Hearing*, edited by D. B. Webster et al. (Springer: New York), xliii–li.

was supposed to be fine-tuned neurally so that, to quote Békésy¹⁴ “very little mechanical frequency analysis is done by the inner ear.”

As well as suitably low Q , the other attractive feature of his traveling waves was that they showed, in accord with observations, several cycles of delay between input and response. This seemed to be decisive evidence against the Helmholtz theory, for a *simple resonator* can only give a phase delay between driving force and displacement of between 0 and 180°. By the 1940s the traveling wave theory seemed incontrovertible.

Békésy’s contributions to establishing the traveling wave model have been profound. Zwislocki made the comment¹⁵ that research into cochlear mechanics may be divided into three periods: before Békésy, during Békésy, and after Békésy. He set the direction of the entire field for a generation¹⁶. It inspired Zwislocki to formulate a mathematical model¹⁷ which provided physical understanding of the phenomenon. In 1951 Fletcher could say¹⁸ that “the dynamical behaviour of the hearing mechanism about which there has been so much speculation in the past is now placed on a very firm basis, both theoretically and experimentally, and leaves little room for further speculation.”

Perhaps, however, Békésy was too successful, in that his work focused attention in one direction at the expense of seeing any alternative^{19,20,21}. Later, Kemp

¹⁴ Békésy, G. v. (1961, 1999). *Concerning the pleasures of observing, and the mechanics of the inner ear*. In: *Nobel Lectures in Physiology or Medicine 1942–1962*. (World Scientific: Singapore). <http://www.nobel.se/medicine/laureates/1961/bekesy-lecture.pdf>

¹⁵ Zwislocki, J. J. (1973). Concluding remarks. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic Press: New York), 119–121. [p. 119] On the following page he relates that, during the Békésy era, “we learned that not the sound pressure but the motion of the basilar membrane excited the cochlear hair cells.”

¹⁶ Davis, H. (1973). Introduction: v. Békésy. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic Press: New York), 1–7. [p. 2]

¹⁷ Zwislocki, J. J. (1980). Five decades of research on cochlear mechanics. *J. Acoust. Soc. Am.* 67: 1679–1685. [p. 1680]

¹⁸ Fletcher, H. (1951). Acoustics. *Physics Today* 4(12): 12–18. [p. 18]

¹⁹ Patuzzi and Robertson, in discussing the work of Helmholtz and Gold, believe that (p. 1046) the “idea of a metabolically active, mechanical resonance was to be lost until relatively recently, however, and somewhat ironically it is likely that this was partly because of the impressive work of Georg von Békésy” [Patuzzi, R. B. and D. Robertson (1988). Tuning in the mammalian cochlea. *Physiol. Rev.* 68: 1009–1082.] Interestingly, they later (p. 1051) raise the possibility that “the transverse motion of the organ of Corti is no indication of the effective mechanical stimulus to the hair bundles of the receptor cells” but quickly dismiss it.

²⁰ Gold almost didn’t get his seminal 1948 papers published. According to Zwislocki, who was one of the referees, the papers contradicted Békésy’s direct observations, so as a reviewer he recommended rejection (p. 176, *Auditory Sound Transmission: An Autobiographical Perspective*). Noble, a collaborator of Gold’s at Cambridge, believes (pers. comm. 2004) that a later paper was probably submitted and rejected. Gold takes a philosophical look at factors promoting a ‘herd instinct’ and

observed that in the history of audiology important developments and concepts tend to be overlooked and resisted for a long time²².

At this point, two major difficulties associated with Békésy's observations are worth noting: one, "basilar membrane vibration may be non-linear... so that a broader tuning would have been observed at the high sound levels used by von Békésy", and two, "basilar membrane responses may change after death"^{23,24}. Davis says that although he built his thinking around the traveling wave, he continued to be concerned about the sharp analysis indicated by psychophysics²⁵.

"[H]ydrodynamics [is] a field in which plausible reasoning has quite commonly led to incorrect results" commented Békésy²⁶, and the observation of "eddies" on the basilar membrane²⁷⁻³⁰ is possibly a case in point. An aspect of traveling wave theory that has long concerned me is how it is possible for the auditory system to reconstitute an input signal that has been so blurred by dispersive traveling wave behaviour. Cooper stipulates³¹ that "the low-frequency components of

'communal judgement-clouding motivations' in Gold, T. (1989). New ideas in science. *Journal of Scientific Exploration* 3: 103-112. [www.amasci.com/freenrg/newideal.html]. See also Horrobin, D. F. (1990). The philosophical basis of peer review and the suppression of innovation. *Journal of the American Medical Association* 263: 1438-1441. This pattern was repeated with Naftalin and later Kemp, who had difficulty getting his discovery of sound emission from the ear accepted: "Back in 1978 when OAE were first reported the idea that the ear could generate sound seemed outrageous... the journal *Nature* rejected an article on the discovery on the advice of its referees who saw it as 'of limited significance' and needing to be 'first confirmed on laboratory animals rather than human ears' (pp. 47, 51) [Kemp, D. T. (2003). Twenty five years of OAEs. *ENT News* 12(5): 47-52.]

²¹ A review by Wilson sees that the persuasive effects of the Békésy model "probably stifled further research" [Wilson, J. P. (1992). Cochlear mechanics. *Adv. Biosci.* 83: 71-84. [p. 72]

²² When they do become accepted, "the oversimplified status quo becomes enshrined in dogma" so that new and apparently obscure or counterintuitive findings attract little interest. Kemp, D. T. (2002). Exploring cochlear status with otoacoustic emissions: the potential for new clinical applications. In: *Otoacoustic Emissions: clinical applications*, edited by M. S. Robinette and T. J. Glattke (Thieme: New York), 1-47. [p. 44]

²³ Moore, B. C. J. (1977). *Introduction to the Psychology of Hearing*. (Macmillan: London). [p. 32]

²⁴ Pickles later reiterated the same point. Pickles, J. O. (1988). *An Introduction to the Physiology of Hearing, Second edition*. (Academic Press: London). [p. 40] Pickles says that only Kohlöffel has repeated Békésy's experiments over a length of the cochlea; in this case [Kohlöffel 1972, p. 68] the sound pressures were so intense that cavitation noise became audible.

²⁵ Davis (1973), p. 4.

²⁶ Békésy, G. v. (1955). Paradoxical direction of wave travel along the cochlear partition. *J. Acoust. Soc. Am.* 27: 137-145. [p. 137]

²⁷ *EiH*, p. 420.

²⁸ Tonndorf, J. (1962). Time/frequency analysis along the partition of cochlear models: a modified place concept. *J. Acoust. Soc. Am.* 34: 1337-1350.

²⁹ Davis (1973), p. 4.

³⁰ Zwislocki (2002), pp. 168-172.

³¹ Cooper, N. P. (2004). Compression in the peripheral auditory system. In: *Compression: From Cochlea to Cochlear Implants*, edited by S. P. Bacon et al. (Springer: New York), 18-61. [p. 2 of ms copy]

the waves [travel] further and slightly faster than the high-frequency components, and the components of low-intensity sounds [travel] slightly further and slightly more slowly than those of higher intensity sounds”.

In comparison, Helmholtz’s key idea of one frequency, one resonator, is simple and direct. As we will see, it is not immune from difficulty, of course, and the major question – how the long build-up and decay is overcome – can still not be definitely answered, but a later chapter will attempt to provide an avenue (§D 9.1/k).

1.4 Gold’s resonance ideas

Nevertheless, putting aside these reservations, we return to 1946 and the clear success of traveling wave theory. In this year, a young Cambridge graduate accidentally landed into hearing research after doing war-time work on radar. Full of electronic signal-processing knowledge, Thomas Gold became focused on how the ear could attain such high sensitivity and frequency resolution. He was dissatisfied with the traveling wave picture because it cast an impossible burden onto the neural system: no matter how sharp its discrimination may be in theory, in practice noise enters all physical systems and will throw off attempts to precisely locate the peak. He became convinced that the basis of our acute frequency discrimination must reside in the ear. But how was that possible when cochlear fluids alone are sufficient to assure high damping?

During a boring seminar, inspiration hit: if the ear employed *positive feedback*, he realised, these problems could disappear³². He knew all about regenerative receivers, which were simple circuits that used positive feedback to amplify a radio signal before it was detected, thereby achieving high sensitivity and narrow bandwidth. He reasoned that “surely nature can’t be as stupid as to go and put a nerve fibre – that is a detector – right at the front end of the sensitivity of the system”, and so proposed that the ear must be an active system – not a passive one as everybody had previously thought – and that it worked like a regenerative receiver.

³² Gold, T. (1989). Historical background to the proposal, 40 years ago, of an active model for cochlear frequency analysis. In: *Cochlear Mechanisms: Structure, Function, and Models*, edited by J. P. Wilson and D. T. Kemp (Plenum: New York), 299–305.

In this way, damping could be counteracted by positive feedback, and, given just the right level of feedback gain, the bandwidth could be made arbitrarily narrow.

Gold later framed the problem confronting the cochlea in terms of an evocative analogy³³: the cochlea's strings – whatever they may be – are immersed in liquid, so making them resonate is as difficult as sounding a piano submerged in water. But if we were to add sensors and actuators to every string, and apply positive feedback, the “underwater piano” could work again.

He and Pumphrey, his colleague, designed experiments to test the hypothesis that there must be high- Q resonators in the ear, an idea they framed in terms of the ear's “phase memory” (how many cycles it could store and remember). There were two ground-breaking experiments^{34,35} in 1948, the first of which involved testing the hearing thresholds of listeners first to continuous tones and then to increasingly briefer versions. If hearing depends on resonators building up strength, like pushing a child on a swing, the threshold to a tone pulse should depend in a predictable way on the number of pushes, or cycles, in the pulse. Thus, the threshold to a short pulse should be measurably higher than to a long one of the same frequency and amplitude. Their results accorded satisfactorily with this picture, and they calculated that the Q of the resonators must be between 32 and 300, depending on frequency.

The second experiment was more ingenious, and used sequences of reversed phase stimuli to counter sequences of positive-phase ones. Listeners had to detect differences between the sound of repetitive tone pips (series one) and those same stimuli in which the phase of every second pip was inverted (series two, in which compressions replaced rarefactions and vice versa). Out-of-phase pips should counteract the action of in-phase pips and, following the child-on-swing analogy, rapidly bring swinging to a halt. Therefore, the argument goes, the two series should sound different. By increasing the silent interval between pips until the difference disappeared, the experimenters could infer how long the vibrations (or swinging)

³³ Gold, T. (1987). The theory of hearing. In: *Highlights in Science*, edited by H. Messel (Pergamon: Sydney), 149-157.

³⁴ Gold, T. and R. J. Pumphrey (1948). Hearing. I. The cochlea as a frequency analyzer. *Proc. Roy. Soc. Lond. B* 135: 462-491. See also: Pumphrey, R. J. and T. Gold (1947). Transient reception and the degree of resonance of the human ear. *Nature* 160: 124-125. ; Pumphrey, R. J. and T. Gold (1948). Phase memory of the ear: a proof of the resonance hypothesis. *Nature* 161: 640.

³⁵ Gold, T. (1948). Hearing. II. The physical basis of the action of the cochlea. *Proc. Roy. Soc. Lond. B* 135: 492-498.

appeared to persist and could then put a measure on the quality factor (Q) of the presumed underlying resonance.

The Q values inferred from the second experiment were comparable to those in the first. However, their resonance interpretation has been dismissed because of an apparent methodological flaw in the second experiment: the spectral signatures of the two series are not the same and may provide additional cues.

A clear exposition of the differences in the Fourier components of the two series is given by Hartmann³⁶, who says the experiment is just an example of ‘off-frequency listening’ and thus tends to discount the significance of the experiment. On the other hand, the presence of off-frequency detection does not mean that there is no such thing as resonating elements. I would emphasise that a physical system can be described *either* in the time domain *or* in the frequency domain; both domains are equivalent. If there actually is a harmonic oscillator tuned to a particular frequency and there is a sufficiently long time interval between the alternating pulses, then the time-domain description – of a phase memory – is a perfectly legitimate one that follows Gold and Pumphrey’s interpretation. The frequency-domain description just gives an alternative perspective on how differences might arise, but it is no way superior to the time-domain picture. Until we have a clearer picture of the actual cochlear resonators, I remain open on this point.

Flowing from Gold’s model was a startling prediction: if the ear were in fact using positive feedback, then if the gain were set a little too high, it would continuously squeal, as regenerative receivers (and PA systems) are prone to do. “If the ringing is due to actual mechanical oscillation in the ear, then we should expect a certain fraction of the acoustic energy to be radiated out. A sensitive instrument may be able to pick up these oscillations and so prove their mechanical origin.”³⁷ Daringly, he equated this state of affairs with the common phenomenon of ringing in the ear, or tinnitus. He caused his ears to ring by taking aspirin, placed a microphone in his ear, and tried to pick up a sound. The conditions and equipment weren’t right, and the experiment failed.

³⁶ Hartmann, W. M. (1998). *Signals, Sound, and Sensation*. (Springer: New York). pp. 312-314. The issue is also dealt with in: Hiesey, R. W. and E. D. Schubert (1972). Cochlear resonance and phase-reversed signals. *J. Acoust. Soc. Am.* 51: 518-519. Also: Green, D. M. and C. C. Wier (1975). Gold and Pumphrey revisited, again. *J. Acoust. Soc. Am.* 57: 935-938.

³⁷ Gold (1948), p. 497.

Gold and Pumphrey remained convinced that Helmholtz was correct, and the abstract of their 1948 paper declares³⁸ “previous theories of hearing are considered, and it is shown that only the resonance hypothesis of Helmholtz interpreted in accordance with the considerations enumerated in the first part of this paper is consistent with observation”. Gold paid a visit to Békésy in Harvard and tried to convince him of the impossibility of relying on neural discrimination. He also pointed out the scaling errors that Békésy introduced by building a cochlear model many times actual size, but each side stuck to their views, and for many years – until Kemp’s momentous discoveries – Békésy’s ideas prevailed.

There is one article³⁹ of Békésy’s that actually makes mention of Pumphrey and Gold. The context is Helmholtz’s resonance theory and the difficulty of ascertaining a time constant (or Q) for the cochlear resonators. Békésy ascribes the difficulty to the multiple time constants – physical, physiological, and psychological – underlying an auditory sensation. He appears to place the Pumphrey and Gold results under one of the latter two categories, for he proceeds to look at only the mechanical contributions to the time constant and says there are essentially but two: (1) the middle ear and (2) a damped traveling wave.

The factor that assured supremacy of the traveling wave picture was the introduction of mathematical models⁴⁰ that well described the traveling wave behaviour. These models took transmission line equations and applied them to the

³⁸ Gold and Pumphrey, op. cit., p. 462. From later comments of Gold, he may not have been as Helmholtzian as he professed. In a short 1953 paper [Gold, T. (1953). Hearing. *IEEE Transactions on Information Theory* 1: 125-127.] he talks of the analyser elements being ‘in series with the sonic signals’, and in Gold (1989) he describes his unpublished work on a transmission line model of the cochlea. Both these ideas reflect a traveling wave interpretation. In an attempt to shed light on his thinking here, the current whereabouts of his mathematician collaborator in 1948–49, Ben Noble, mentioned on pages 303–304 of Gold (1989), was sought. Gold says he and Noble wrote a paper saying that “instead of individual (resonant) elements we should look at it as a transmission line”, and my hope was that Noble may still possess that manuscript. A literature search established that a Cambridge-based Noble had published mathematical papers at that time and had moved to the University of Wisconsin–Madison. The University’s maths department has a link to a web site (www.genealogy.ams.org) listing Noble and his students. One of them, Kendall Atkinson, is still at the University of Iowa, and email to him established that he remains in regular contact with Noble and that Noble, now 82, is retired in the Lake District of England. A mailing address was supplied [25 Windermere Avenue, Barrow-in-Furness, Cumbria, England LA14 4LN], and Noble was delighted to reply to my letter of enquiry. Noble says he remembers Gold well, but that his role at Cambridge was a routine one, feeding equations into a mechanical differential analyser (transmission line equations, he presumes, derived by Gold and builder of the analyser, Hartree). He never saw even a draft of any joint paper. He guesses that Gold submitted a paper to a journal and it was rejected.

³⁹ Békésy, G. v. and W. A. Rosenblith (1951). The mechanical properties of the ear. In: *Experimental Psychology*, edited by S. S. Stevens (Wiley: New York), 1075-1115.

⁴⁰ Zwislocki, J. J. (2002). *Auditory Sound Transmission: An Autobiographical Perspective*. (Erlbaum: Mahwah, NJ).

cochlea (just like Gold and Noble set out to do), producing a good representation of what Békésy saw. They required that the basilar membrane have a graded stiffness from base to apex (grading in width and thickness could also contribute), and that the displacements of the basilar membrane are due to pressure differences across it. In this way, the motion induced in the base will be hydrodynamically coupled to neighbouring segments and cause a wave to propagate towards the apex. Békésy's measurements showed that the basilar membrane was graded in stiffness in the way required, he saw traveling waves in his models and in his surgically opened cochleas, so the theory was effectively proven.

With Gold's ideas falling on deaf ears⁴¹, he left the field and made a name in cosmology instead.

1.5 Distinguishing traveling wave and resonance

Békésy made many mechanical models demonstrating how a traveling wave works, and he did important work clarifying the fundamental differences between traveling waves and resonance. To model the cochlea he built arrays of pendulums – bobs on strings of varying length – suspended from a common rod⁴².

First he demonstrated that a bank of resonators (the pendulums) could behave like a traveling wave⁴³. If there were coupling between the resonators – such as by threading rubber strands between the strings – then after sharply exciting the shortest pendulum, a wave motion would be seen progressing from this pendulum to the longest. If the coupling is light, then the wave progresses very slowly, giving large delays. Stronger coupling gives a faster wave and shorter delays.

⁴¹ In Gold (1989) he describes giving a lecture to neurologists and otologists in London. Looking around the audience, he noticed (p. 301) two kinds of people in the audience: “those that had a twitch and those that had an ear trumpet!”

⁴² Békésy (1960), pp. 524-534. See also Békésy, G. v. (1956). Current status of theories of hearing. *Science* 123: 779-783. // Békésy, G. v. (1969). Resonance in the cochlea? *Sound* 3: 86-91. // Békésy, G. v. (1970). Travelling waves as frequency analysers in the cochlea. *Nature* 225: 1207-1209.

⁴³ “Any series of graded resonators, suitably coupled, can be made to have an apparent travelling wave.” p. 152, Johnstone, B. M., Patuzzi, R. B., and Yates, G. K. (1986). Basilar membrane measurements and the travelling wave. *Hear. Res.* 22: 147–153. Fig. 7 of this reference shows that the hearing organ of a frog, with no traveling wave, can show a similar phase response to a cat, which does.

The other way of exciting what looks like a traveling wave is to suddenly jerk the rod⁴⁴. Even with no coupling, an apparent wave will be seen to move from the shortest pendulum towards the longest. In this case the wave carries no energy; it is just an illusion, an epiphenomenon, reflecting the fact that the shortest pendulum will accumulate phase faster than the longer ones. It's rather like the blinking lights outside a theatre which give the impression of movement.

It is important for later discussion to recognise that although they can give a similar result, there are fundamentally different physical processes driving them. In terms of physical understanding, we need to clearly distinguish these two mechanisms, for one marks a traveling wave theory and the other a resonance theory. Much confusion has arisen about the actual physical processes that underlie the cochlea's traveling wave, for traveling wave theories still incorporate "resonant elements" (the pendulums, which are serially coupled).

Traveling wave. The essence of a traveling wave theory is that the signal passes through the resonators *in series*. That is, the input to the system is via the high frequency resonator and the energy is passed sequentially (via coupling) to lower frequency resonators. The Q of the individual resonators can be high or low, but the key is that the signal energy is injected into the high frequency end, just as what happens in a tapered transmission line. Likewise, the classic traveling wave theory of Békésy is that the input applied to the stapes causes an immediate deflection of the basilar membrane at the high frequency end and this is then coupled (hydrodynamically and materially) to neighbouring sections until a peak is reached at the characteristic place (after which motion quickly decays).

Resonance. By way of contrast, what distinguishes a resonance theory of excitation is that the signal energy is applied to the system *in parallel*. Thus, when we jerk the rod suspending the pendulums, or lift the lid on a piano and yell into it, the excitation is applied to all the resonant elements virtually simultaneously. In the

⁴⁴ A more sophisticated way is to simultaneously excite the tuned reeds of a Frahm frequency meter with a common electromagnetic frequency [see Békésy (1960), p. 494 and Wilson (1992).] Wilson points out (p. 74) that, contrary to Békésy's assertion, a traveling wave can still be seen when uncoupled reeds are excited *if frequency resolution is sufficient*. Both agree that a traveling wave becomes more pronounced as coupling of the reeds is increased (such as by threading rubber bands between them).

same way, Helmholtz called for an array of independent resonators that were excited by sound passing through the cochlear fluids. It is this idea that I want to reconsider.

The discussion above has considered simple pendulums, and although it shows the broad parallel, it only really works for sharp excitations. Moreover, in the cochlea there is another important difference. Rather than simple pendulums, the resonators in the cochlea occupy only a small portion of the basilar membrane and they vary in Q depending on their frequency. When the system is excited with a pulse train, there is complex coupling and the system is far from simple order. A better perspective on the system can be gained by considering the results of Shera and colleagues⁴⁵, who calculated the Q of the cochlear resonators using a combination of acoustic emission and psychophysical data. Importantly, they found that the Q (expressed as an equivalent rectangular fractional bandwidth) varied from about 12 at 1 kHz to about 28 at 10 kHz. Now the time for build up and decay of an oscillator is roughly Q cycles⁴⁶, so that in response to a simultaneously applied pulse train the base will approach maximum excitation after $28 \times 0.1 = 2.8$ ms while the apex will do so in $12 \times 1 = 12$ ms. Observing the basilar membrane from an external vantage point, the excitation will therefore *appear to travel from base to apex* – an epiphenomenal traveling wave⁴⁷.

The similarity in outcome between a traveling wave mechanism and a resonance one makes it important to maintain the distinction between the two theories on the basis of how energy reaches the sensing cells⁴⁸. If one abandons the distinction and simply calls a traveling wave anything that has a temporal sequence of events, then the difference between the two outlooks dissolves. People in both camps are then in verbal agreement, but the scientific question of *how* the cells are

⁴⁵ Shera, C. A., et al. (2002). Revised estimates of human cochlear tuning from otoacoustic and behavioural measurements. *Proc. Nat. Acad. Sci.* 99: 3318-3323.

⁴⁶ Fletcher, N. H. (1992). *Acoustic Systems in Biology*. (Oxford University Press: New York). [p. 26]

⁴⁷ The average speed will be about 30 mm per $(12-2.8)$ ms = 3.3 m/s, a figure comparable to typical traveling wave velocities [Donaldson, G. S. and R. A. Ruth (1993). Derived band auditory brain-stem response estimates of traveling wave velocity in humans. I: Normal-hearing subjects. *J. Acoust. Soc. Am.* 93: 940-951. Fig. 7]

⁴⁸ The distinction is discussed at some length by Licklider [Licklider, J. C. R. (1953). *Hearing. Annu. Rev. Psychol.* 4: 89-110. (pp. 92-94)], although not totally unambiguously. For a while there was a false distinction made about whether the energy traveled along the membrane (the “membrane hypothesis”) or through the fluid (the “fluid hypothesis”), and Licklider appears to buy into that; of course, we now clearly appreciate that the traveling wave is a hydrodynamic phenomenon that needs both: it results from the *interaction* between them.

stimulated has not been answered. If the distinction is dispensed with, then there is no difference between traveling wave theories and resonance theories, and that's not illuminating. At that point we would then need a new vocabulary to pick out the difference.

The above is written in reaction to a paper⁴⁹ Békésy wrote in collaboration with his long-standing antagonists, Wever and Lawrence, where they agreed to bury their differences⁵⁰. They agreed to mean by traveling wave any temporal sequence of motion along the partition “and nothing is implied about the underlying causes. It is in this sense that Békésy used the term ‘traveling wave’ in reference to his observations... Békésy did not consider that his visual observations gave any decisive evidence on the paths of energy flow in the cochlea, and therefore he has not taken any position on this issue” (pp. 511–512). But if he were alive today, I think he would want to take a position. Once the empty debate on membrane v. fluid is put to one side – and it was such a debate that motivated their paper – it makes an enormous difference whether passive basilar membrane displacements are stimulating the hair cells, or whether the compressional wave is stimulating them and they then produce a membrane displacement, even if the results look the same. Békésy's entire working life was concerned with demonstrating the adequacy of the *passive* traveling wave displacement (whether caused ‘by fluid’ or ‘by membrane’), and the notion of displacement being caused by *active* outer hair cell motility in reaction to the fast pressure wave would have caused him to take stock and form an opinion one way or the other. To reiterate, although the results may be the same, the causal chain and relevant equations are entirely different. Simply, one is what is best called a traveling wave theory (of hair cell excitation); the other is a resonance theory (of excitation).

The advantage of the pure resonance approach is that only that resonator with matching frequency receives energy (provided the Q is sufficiently high), making the governing equations simple. Moreover, weak signals can, cycle by cycle, cause a resonator to build up an appreciable in-phase motion, like a child pumping a swing. In this way the cochlea would be able to hear sounds just above thermal noise.

⁴⁹ Wever, E. G., Lawrence, M., and Békésy, G. v. (1954). A note on recent developments in auditory theory. *Proc. Nat. Acad. Sci.* 40: 508-512.

⁵⁰ Wever and Békésy became good friends in the 1950s following a period during which Wever was critical of Békésy's work [Fay (1992), p. xliv]

A major scientific question is whether the resonance mechanism is all that's needed. Or perhaps it operates in *conjunction with* the traveling wave? To optimise performance, the ear may use a hybrid of traveling wave and resonance. No one yet believes they have the perfect cochlear model, and maybe persistent anomalies in traveling wave models can be resolved by introducing resonance effects. Whatever the answer, it must accommodate the range of cellular-powered phenomena discovered by Kemp.

1.6 Kemp and the active cochlea

David Kemp's experiments gave a clear demonstration that Gold was heading in the right direction and have changed the face of auditory science. In the same way as faint radio signals have opened an unsuspected window on outer space, his otoacoustic emissions have limned a new horizon into inner space. In 1978 he placed a microphone in his ear and picked up the faint signal that Gold had been searching for 30 years earlier. His equipment was better, and you didn't need to induce tinnitus (as Gold did⁵¹) to pick up a ringing sound.

We now recognise broad classes of acoustic emissions⁵². As well as the striking spontaneous emissions, other continuous signals of cochlear origin can be detected: stimulus frequency emissions (where the sound coming out is at the same frequency as that going in) and distortion product emissions (where the modulation products of two input stimuli are detected). The most widely employed tools for diagnosis of cochlear function use transient stimuli: in response to a click, an echo will come back from the cochlea – Kemp's original experiment – and similarly a tone burst of a set frequency will lead to a similar answering echo.

These 'active' properties reflect the operation of a so-called 'cochlear amplifier'⁵³ and they fade away once sound intensities reach 60–80 dB SPL. The

⁵¹ Gold (1989) describes (p. 302) his use of aspirin to induce tinnitus, a drug that tends to suppress spontaneous emissions [McFadden, D. and H. S. Plattsmier (1984). Aspirin abolishes spontaneous oto-acoustic emissions. *J. Acoust. Soc. Am.* 76: 443-448.]

⁵² Robinette, M. S. and T. J. Glatke (2002). *Otoacoustic Emissions: Clinical Applications*. (Thieme: New York).

⁵³ Davis, H. (1983). An active process in cochlear mechanics. *Hear. Res.* 9: 79-90.

active cochlea is highly tuned, and the relative bandwidth of spontaneous emissions, which show very stable frequencies, can be less than 1 in 1000.

When I first read a report of Kemp's findings in 1979, I was astonished. Surely traveling wave theory couldn't be right: how could a membrane immersed in fluid sing? Helmholtz must be closer to the mark, I thought, and I have been intrigued by the cochlea and its micromechanics ever since. I have been searching for an explanation of spontaneous emissions: if something is constantly ringing, what are the resonating elements? Gathering clues to their origin, I studied the stability of these tones^{54,55}, work that laid the foundations for this thesis. The work demonstrated that the frequency of spontaneous emissions is affected by intracranial pressure, and the MSc thesis argues that this effect is more than can be accommodated by oval window stiffness. If outer hair cells are innately sensitive to static (dc) pressure, it seems reasonable to consider that they may be sensitive to ac pressure (sound) too.

The auditory community has interpreted Kemp's work in terms of a traveling wave but with additional parameters. People accept Gold's incisive idea of an active cochlear process, but resist his call to reinstate simple resonance. Thus, the delay of the cochlear echo has been seen as the delay of the traveling wave as it propagates from the stapes to its characteristic place and then, by means of a "reverse traveling wave"⁵⁶, returns to its place of origin. If the stimulus recirculates, the travel time for the loop defines the period of a spontaneous emission. To counter propagation losses, the basilar membrane has been ascribed negative resistance, a state of affairs presumed possible by some (unknown) sensing action of the outer hair cells – which are pretty certain to be the source of the mechanical activity detected by Kemp. We now know, for example, that when an outer hair cell is stimulated, it changes length cycle by cycle in step with the stimulus⁵⁷. In other words, these cells are effectors as well as sensors.

⁵⁴ Bell, A. (1992). Circadian and menstrual rhythms of spontaneous otoacoustic emissions from human ears. *Hear. Res.* 58: 91-100.

⁵⁵ Bell, A. (1998). A study of frequency variations of spontaneous otoacoustic emissions from human ears. MSc thesis, Australian National University, Canberra.

⁵⁶ Shera, C. A. (2003). Mammalian spontaneous otoacoustic emissions are amplitude-stabilized cochlear standing waves. *J. Acoust. Soc. Am.* 114: 244-262.

⁵⁷ Brownell, W. E., et al. (1985). Evoked mechanical responses of isolated cochlear outer hair cells. *Science* 227: 194-196.

1.7 Two signals in the cochlea

This all adds up to a system that can be described by traveling wave equations and which mimics what happens in a tapered transmission line (provided the line also contains a traveling wave amplifier and can operate in reverse). There is no doubt that this class of model comes close to describing the measured responses of the cochlea, and their workings are outlined in Chapter I3. However, I think a resonance mechanism may play a significant, if not dominant, part at low sound levels.

But first, one should realise that there are two different, although related, signals in the cochlea. Fig. 1.1 shows how they arise.

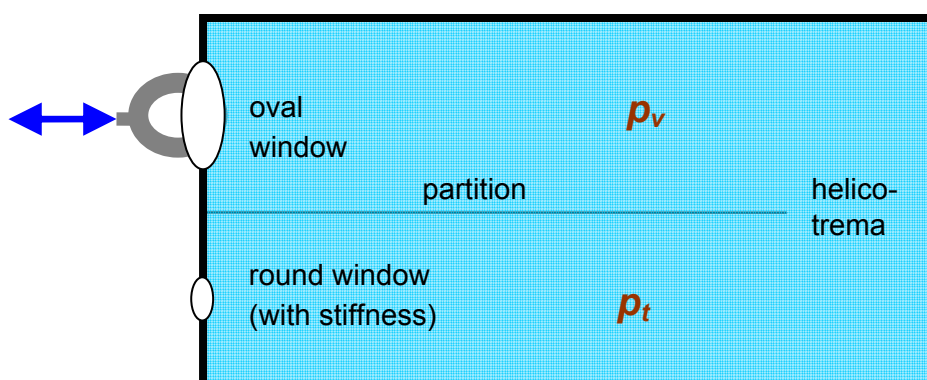


Fig. 1.1. In response to vibration of the stapes, a pressure wave fills the nearly incompressible cochlear fluids virtually instantly. The pressure in the upper gallery is taken to be p_v , while that in the lower is p_t . The common-mode pressure p_+ (common to both galleries) is $(p_v + p_t)/2$, while the differential pressure across the partition p_- is $(p_v - p_t)/2$.

The first is the usual acoustic pressure wave that, following back-and-forth vibration of the stapes, is communicated to the cochlear fluids at the speed of sound in water (1500 m/s). This wave creates, nearly instantaneously, a hydraulic pressure field, the size of the pressure depending crucially on the stiffness of the round window (which is the major point of pressure relief) since the rest of the cochlea, mostly water, is nearly incompressible. This hydraulic pressure, p_+ , is sometimes called common-mode pressure, for it occurs, in phase, on both sides of the sensory partition.

The second signal is the differential pressure, p_- , caused by the presence of the partition: it is the difference between p_v , the pressure in the upper gallery (scala vestibuli) and p_t , the pressure in the lower gallery (scala tympani).

Thus, the common mode pressure p_+ is given by $p_+ = (p_v + p_t) / 2$, whereas the differential pressure $p_- = (p_v - p_t) / 2$. The former is assumed to have no effect on cochlear mechanics whereas the latter gives rise to a slowly propagating traveling wave, a wave of displacement on the basilar membrane that propagates from base to apex and is presumed to stimulate hair cells by bending their stereocilia.

Because hair cells bear distinctive stereocilia, the common-mode pressure has been thought to have no sensible effect on them. One cell, one function. My idea is that outer hair cells may be dual detectors, able to sense the compressional wave and bending of their stereocilia. There are reasons to think (Chapter D8) that at low sound pressure levels, the pressure stimulus may be the primary one. This possibility fits in with how some water-dwelling animals hear: they need to detect the long-range (far-field) pressure component of an underwater sound, not the short-range (near-field) displacement component which rapidly fades. Sharks, for example, pick up distress calls over hundreds of metres (when displacements have shrunk to 10^{-12} m). Sharks have no swim bladder, and the auditory cells in their papilla neglecta carry no otoliths, so how do they detect long-range pressure? Anatomy gives a clue: their auditory cells house many ‘vacuities’ within the cell body itself⁵⁸, suggesting they use an enclosed bubble to perform ‘on the spot’ pressure-to-displacement conversion.

In a similar way, I suspect that mammalian outer hair cells detect acoustic pressure. The direct pressure signal is fast and phase coherent, making a clean, space-invariant signal for an organism to feed into a distributed set of cochlear amplifiers and into signal-processing circuits.

Such an arrangement may be able to explain behaviour that the traveling wave cannot. For example, cochlear echoes show a similar waveform as input signal strength is raised. Active traveling wave models have not yet replicated this behaviour and a recent paper announced in its abstract that this behaviour

⁵⁸ Corwin, J. T. (1977). Morphology of the macula neglecta in sharks of the genus *Carcharhinus*. *J. Morphol.* 152: 341-361.

“contradicts many, if not most, cochlear models”⁵⁹. De Boer⁶⁰ noted the difficulty of formulating a satisfactory time-domain model and suggested that “non-causal” factors must be at work. In addition, people with blocked round windows can still hear, as can those who have lost middle ears to disease – observations difficult to square with a traveling wave model. A wide-ranging critique of the model is presented in Chapter I3.

If a pressure wave is the exciting stimulus in these cases, it raises the possibility of parallel excitation of a resonant system. But what, then, are the resonating elements? As set out below, candidates for the piano strings can be identified and they appear to have the necessary pressure sensitivity⁶¹ (Chapter D8), allowing construction of a fully resonant model of the active cochlea.

1.8 A new resonance model of the cochlea

My conceptual resonance model takes as its starting point the special nature of spontaneous otoacoustic emissions. It sees these stable and narrow-band signals as the cochlea’s intrinsic resonant elements – its piano strings – and not as incidental by-products of over-active forward and reverse traveling waves in a recirculating loop. That implies we have an array of highly tuned generators, exquisitely sensitive to sound, disposed from base (high frequency) to apex (low). Each string has its distinct place on the membrane, as required by Helmholtz’s place principle.

We know that outer hair cells are the active elements responsible for the cochlear amplifier, so each string must somehow involve these cells. The inspiration for this work is that a string can form in the *space* between cells – each cell does not have to be individually tuned. Outer hair cells are typically arranged in three or more distinct rows, and because the cells are, as mentioned earlier, both sensors and effectors, it is possible for positive feedback to occur between the motor element of

⁵⁹ Shera, C. A. (2001). Intensity-invariance of fine-structure in basilar-membrane click responses: implications for cochlear mechanics. *J. Acoust. Soc. Am.* 110: 332-348.

⁶⁰ de Boer, E. and A. L. Nuttall (2003). Properties of amplifying elements in the cochlea. In: *Biophysics of the Cochlea: From Molecules to Models*, edited by A. W. Gummer (World Scientific: Singapore), 331-342.

⁶¹ Bell, A. (2003). Are outer hair cells pressure sensors? Basis of a SAW model of the cochlear amplifier. In: *Biophysics of the Cochlea: From Molecules to Models*, edited by A. W. Gummer (World Scientific: Singapore), 429-431.

one cell (its cell body) and the sensing element of a neighbour (its stereocilia). The result is stable oscillation, and this, I suggest, is the cochlea's elusive tuning element.

As suggested in Chapter R5, oscillation occurs in a direction across the partition, not up and down as the traveling wave theory supposes (see Fig. 0.1). This bypasses the requirement for the mechanics of the partition to be governed by differential pressures and traveling waves. However, it introduces its own tuning problem: how can the space between the rows be tuned over 3 decades of frequency? If we require a single wavelength between the rows – a distance of about 30 micrometres – this calls for a very slow wave. For example, a 1 kHz wave shuttling between the rows will need to travel 30 μm in 1 ms, or just 30 mm/s.

Happily, such waves do exist. They are known in ultrasonics as symmetric Lloyd–Redwood waves, or “squirting waves”, and propagate in the thin gap between two compliant plates immersed in water – just the arrangement we find in the space occupied by the hair cell stereocilia (Fig. 1.2). A recent paper⁶² (the basis for Chapter R5) shows how the slow speed and high dispersion of these waves allows the “strings” to be tuned over the full range of human hearing. The standing wave produced by the squirting wave provides a natural explanation for the cochlear amplifier: it is a positive feedback system that amplifies the input signal before passing it to the inner hair cells (which finally transduce the signal into nerve impulses). In other words we have a regenerative receiver performing amplification before detection, just as Gold required. The system is like his “underwater piano”: it uses a system of sensors and actuators in a positive feedback loop to overcome the effects of viscosity and produce high Q .

We have the piano strings, but for a true resonant system we need the bank of resonators to be excited in parallel (that is, simultaneously). How is this to be done? As foreshadowed, that could happen if outer hair cells are sensitive to the fast pressure wave. Outer hair cells are constructed like pressure sensors and are in continuous hydraulic connection with the cochlea's entire fluid contents – anatomically, they are, unlike inner hair cells, surrounded by fluid spaces, not other cells. Intracochlear fluid pressure could therefore be an important stimulus.

⁶² Bell, A. and N. H. Fletcher (2004). The cochlear amplifier as a standing wave: “squirting” waves between rows of outer hair cells? *J. Acoust. Soc. Am.* 116: 1016-1024.

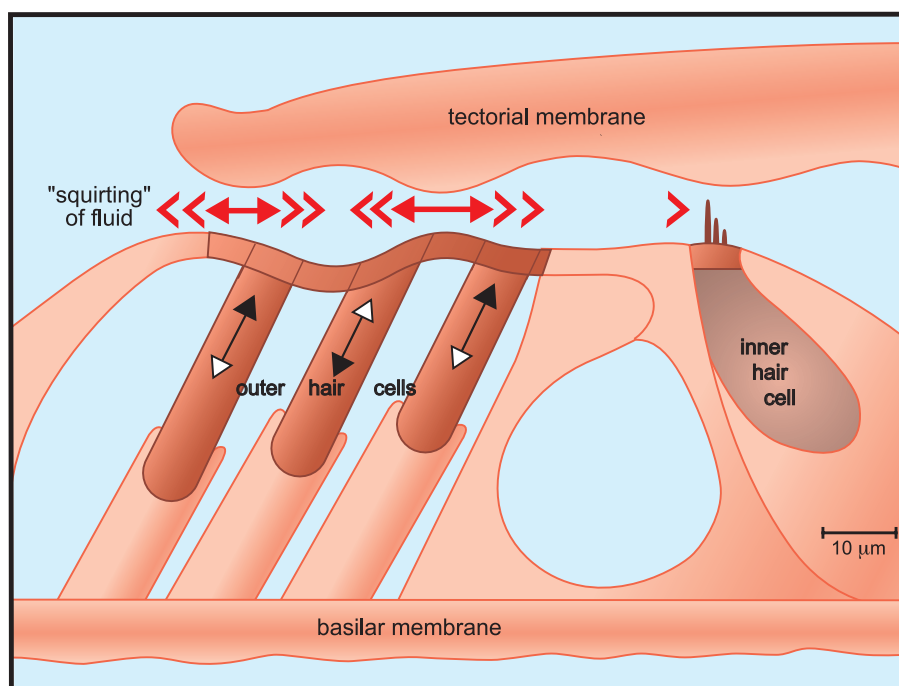


Fig. 1.2. Strings of an underwater piano? The cochlea's resonant elements could be tiny parcels of liquid oscillating in a positive feedback loop between rows of outer hair cells. Outer hair cells dancing up and down (in response to intracochlear pressure) could create 'squirting waves' in the fluid gap above. The waves could in turn bend stereocilia (for clarity, not shown), creating positive feedback and a standing wave. Wave energy escapes to the inner hair cell's stereocilia, and so we hear.

This new resonant scheme, unlike a bank of pendulums, is not limited to phase variations of 0–180°. This is because the wavelengths involved are small compared to the width of the basilar membrane, and so phase delays can accumulate in the supporting structure before they are communicated to the membrane where observations are finally made.

Like all pianos, the cochlear version has that essential component, dampers. The dampers are the efferent system, which is able to electrically adjust the gain of each of the outer hair cell triplets. The mechanical gain from positive feedback depends on having a differential response between the three rows, so by adjusting the resting membrane potentials between rows, efferent activity could quickly raise or lower the gain. Investigation of the way damping may operate in the resonant system formed between the rows of outer hair cells is explored in the cochlear model of Chapter R6.

The evidence that outer hair cells react to pressure stimuli⁶³ is scattered and indirect, but prevalent. Naturally, if the cells are pressure detectors, they will have some compressibility. Imagine what would happen if the stapes pushed in on the nearly incompressible fluids of a cochlea surrounded by solid bone: the energy would be funnelled directly to the most compressible parts – in particular, I suggest, the outer hair cells. These cells are seemingly well designed to be pressure sensors: they are constructed like rigid test tubes with a small compliant spot (the cuticular pore) at the top. Significantly, this pore is a vestige of where, during development, a sensory apparatus (the kinocilium) used to be. Thus, the original electrochemical signalling could still be in place to register movement of the cuticular pore created by pressure differences between the cell interior and the cochlear fluid.

For efficient operation, outer hair cells would need to contain a very compressible material. Air would be a good choice, and these cells do contain a peculiar spherically layered structure – Hensen's body – whose function could be to generate an air bubble, much like the swim bladder cells of fish do and, even more so, like the hearing cells of sharks and their 'vacuities'. The compressibility is possibly part of a positive feedback loop of its own in that when a cell changes length in response to stimulation it is difficult for it not to change volume too. If so, outer hair cells could appear much more compressible than air itself – rarefied air, if you will. This possibility will be discussed in detail in Chapter D8.

If this begins to sound like “implanted air”, one can only respect the insight of those ancient Greek philosophers and wonder again whether they, and Helmholtz and Gold, might have been right.

1.9 Concluding remarks

“The resonance theory of Helmholtz is probably the most elegant of all theories of hearing”, said Békésy⁶⁴, and I agree. The traveling wave theory strikes me as failing to meet the cochlea's requirement for utmost finesse. It is based on the assumption that up and down motion of the basilar membrane always drives the outer hair cells, when it could be that, at low sound levels, it's the other way round. In a

⁶³ By reciprocity, activity of the OHCs produces volume changes and generation of a fast pressure wave – Wilson's hair-cell swelling model of otoacoustic emissions.

⁶⁴ Békésy (1960), p. 404.

living system, common-mode pressure could resonantly stimulate outer hair cells to create standing waves across the partition; in this way we could escape the long-assumed need for differential pressure, and basilar membrane motion, to be the sole driving force in the cochlea.

The cochlea could make the best of both worlds, using resonance at low sound levels and a traveling wave at higher ones. This division of labour might underlie the cochlea's astounding dynamic range. Whatever the case, I think there must be a major role for resonance. Sympathetic resonance is a principle behind everything from quarks to quasars, and must surely have a place in the *raison d'être* of acoustics – the ear.

The next chapter will take a comprehensive look at the various resonance theories that have been proposed over the years. Their similarities and differences, and virtues and failings, provide a back-drop against which the present theory can be evaluated.

What could be resonating? An historical survey

2.1 Resonance post Helmholtz

2.1/a Resonating membranes

2.1/b Longitudinal standing waves

2.1/c The electronic era

2.2 Resonance post Gold

2.2/a Guelke

2.2/b Naftalin

2.2/c Huxley

2.2/d Offutt

2.2/e Styli

2.2/f Dancer

2.2/g Braun

2.2/h Flock and ITER

2.2/i Sohmer and Freeman

2.2/j Heerens

2.3 Second filters

2.3/a Evans and Wilson

2.3/b Davis

2.3/c Christiansen

2.3/d Tectorial membrane

2.4 Concluding remarks

The core idea of any resonance theory of hearing is that the ear contains a bank of thousands of independent resonators, one for every discernable pitch. This thesis identifies rows of outer hair cells operating in feedback resonance in the subtectorial space as the ear's resonant elements (Chapter R5). In gauging the credibility of such a proposal, it helps to look at past resonance theories and the resonating elements they chose, pointing out the associated virtues and drawbacks.

The broad brush strokes of the previous chapter should have given a sense of the long pedigree of resonance theories of hearing, beginning with the ancient Greeks. We focused principally on Helmholtz¹ as the founder of a science of hearing, and then skipped to Pumphrey and Gold² as modern interpreters of the resonance picture. Here I want to fill in the gaps and provide a fairly comprehensive, albeit nonexhaustive, account of the way that the idea has more or less persisted. The intention is to highlight the resonant elements involved.

Such a survey also makes clear that resonance theories have been the preferred explanation for many eminent auditory scientists, and have not just been the province of the misguided, as modern textbooks tend to convey. Resonance has simplicity and elegance; the overwhelming problem, as we will see, has been one of identifying the microscopic resonant elements – a problem which dates from its very beginnings, and one which has troubled every proponent from Helmholtz to Gold.

An overview of Helmholtz's work was given in the previous chapter. Details can be found in chapter 2 of Wever's comprehensive review³ and in chapter 11 of Boring's⁴, and will not be duplicated here. Rather, we will look at the reasons he chose the basilar membrane fibres as his preferred resonating elements. In so doing, we will come to appreciate the physical requirements for resonance to occur in the ear; as set out by Wever (*ibid.*, pp. 33–39 and pp. 97–117), the major requirements that any satisfactory resonance theory must fulfil are as follows.

1. *Independence of the resonators.* Whereas Helmholtz's original formulation specified the rods of Corti as the resonators, his revised version identified the fibres

¹ Helmholtz, H. L. F. v. (1875). *On the Sensations of Tone as a Physiological Basis for the Theory of Music*. (Longmans, Green: London).

² Gold, T. and R. J. Pumphrey (1948). Hearing. I. The cochlea as a frequency analyzer. *Proc. Roy. Soc. Lond. B* 135: 462-491.

³ Wever, E. G. (1949). *Theory of Hearing*. (Dover: New York).

⁴ Boring, E. G. (1942). *Sensation and Perception in the History of Experimental Psychology*. (Appleton-Century-Crofts: New York). pp.399-436.

of the basilar membrane. The advantage of the first choice is that the rods are independent entities; he abandoned them firstly because Hensen found they varied only by a factor of 2 in length, and secondly because Hasse found some years later that the arches were lacking in birds, which anatomically have in other respects very similar cochleas to ours. The basilar membrane fibres vary in length by an order of magnitude, and are common to birds and mammals. The drawback is that they are embedded in a matrix, so it is hard to see them acting independently⁵. To save the situation, Helmholtz assumed that the fibres had appreciable transverse tension but were weakly connected longitudinally⁶.

2. Number of resonators. We can discriminate 10–50 pitches per semitone, depending on musical training, meaning that there may be thousands of resonators. Since there are around 3000 inner hair cells lined up in a single column from one end of the tonotopically tuned cochlea to the other, it is not unreasonable to suppose that each cell may provide discrimination of a single pitch. The question is one of identifying what is the resonant element associated with each inner hair cell.

3. Tuning of the resonators. A real problem for a resonance theory is being able to tune the resonators, Helmholtz's piano strings, over the full range of human hearing, which encompasses 3 decades of frequency or 10 octaves. This range exceeds that of a piano's, and we need to squeeze the strings inside a tiny cochlea. The frequency, f , of a stretched string with zero stiffness is expressed by

$$f = \frac{1}{2l} \sqrt{\frac{T}{m}} \quad (2.1)$$

where l is its length, T its tension, and m its mass per unit length. The width of the basilar membrane increases more or less systematically from base to apex, but only by about an order of magnitude⁷. Moreover, it is not uncommon to see the membrane become narrower at certain points and in certain species (as with bats and guinea pigs), and wide variations between individual specimens are obvious. The conclusion is that length can only accommodate about 2 or 3 octaves and there must be substantial variations – by combined factors of 10^5 – in tension and mass to give the

⁵ Wever, in a review of traveling wave theories, speaks (p. 1319) of “the improbable nature of the assumption of isolated resonators in the cochlea” [Wever, E. G. (1962). Development of traveling-wave theories. *J. Acoust. Soc. Am.* 34: 1319–1324.]

⁶ Wever (1949), p. 34.

⁷ In humans, Wever (p. 100) shows it is about 5-fold.

appropriate gradation in tuning. Wever reviews many measurements and remains doubtful that there is any tension at all in the basilar membrane, and even granting there is, it is not sufficient, since mass (including fluid loading) can only contribute a factor of 10^2 if we are lucky. The conclusion is that the stretched-string idea does not fare well. Any candidate for a resonant element will have to be readily tuneable over 3 decades.

Traveling wave theory calls on mass and stiffness of the basilar membrane to vary systematically in order to provide its tonotopic tuning. This is a similar requirement to the stretched string except that differential fluid pressure is made to exert force on a stiffened membrane. With inherent stiffness, the frequency now depends on the length, l , of the ‘beam’, and varies as $1/l^2$, giving more readily achievable tuning. This aspect is looked at more closely in the next chapter (§I 3.2/b).

4. Selectivity (Q) of the resonators. The sharpness of a resonator can be expressed in terms of its quality factor, Q , taken as the bandwidth of the response of a resonator divided by its natural frequency. The bandwidth is usually taken at the upper and lower points where response is 3 dB down from the peak⁸. A high Q will therefore mean that the resonator is highly tuned, so that it responds strongly to its natural frequency but its response will drop off quickly when the frequency is changed even slightly. Damping is antithetical to high Q , so all sharply tuned resonators will have low damping.

A crucial property flowing from high Q is persistence. When excitation of a resonator ceases, it will keep vibrating for a time determined by its Q . Roughly, it will keep oscillating for Q cycles. The problem for the ear, as Helmholtz clearly saw, was that if each resonator has high Q , this will allow fine discrimination, but will mean that the resonator will take a long time to build up amplitude and will continue ringing for a comparable time after stimulation stops. Clearly, we do not hear sounds beginning and ending slowly, and Helmholtz’s observations allowed him to put a limit on the Q values of the ear’s resonators. He noted that the lower notes of a piano could continue to be discriminated when its keys were struck at a rate of 10 per second, and, with certain other assumptions, arrived at a Q of about 10 (compare this value with modern figures of 12 at 1 kHz and 28 at 10 kHz as mentioned on page

⁸ Fletcher, N. H. (1992). *Acoustic Systems in Biology*. (Oxford University Press: New York). §2.5.

11 [15]). This meant that a resonator could be set in motion by frequencies about a semitone above and below its natural frequency, and he therefore calculated that each note must excite a score or more resonators. A possible solution to the slow attack and decay problem in terms of a neurally adjustable Q of the cochlear resonators⁹ is portrayed in Chapter R6 (Fig. 6.33).

The problem now, as Wever points out (p. 109), is how do we discriminate pitch more accurately than a semitone? The difficulty can be overcome by assuming certain resolving abilities of the nervous system, but then the innate simplicity of the basic theory is lost. Essentially, we are no better off than we are with the traveling wave theory and its poor tuning. As Wever says, “Once the elementary and complete form of specificity [one resonator for each discriminable pitch] has been given up the theory is in difficulty” [ibid., p. 115].

5. *Dynamic range.* The vast dynamic range of the auditory system – a million million times in intensity – raises problems for any theory of hearing. For the resonance theory, it raises a particular problem: why does pitch discrimination not suffer as intensity is raised and more resonators are excited? The problem is noted, and the role of neural dynamics may play a part, but no ready solution is offered. A solution to the dynamic range problem is advanced in Chapter D8, but this does not automatically answer the pitch discrimination problem.

2.1 Resonance post Helmholtz

2.1/a *Resonating membranes*

Even before Helmholtz’s theory began to accumulate nagging doubts and suffer a steady decline, modifications to his central ‘one tone, one fibre’ idea had been made, mostly concerning alternative resonating structures. Wever (ibid., pp. 43–52) outlines several ‘membrane resonance’ theories which involved either the basilar or tectorial membranes.

⁹ That is, the system has high Q (and long build up and decay) at low sound pressure levels but a high Q and short time-constant at higher levels.

My knowledge of the tectorial membrane theory of Hasse (1867) is limited only to Wever's account, but a later development of it, by Shambaugh (1907), is worthy of mention because the work is still readily accessible¹⁰ and because it mounts strong arguments against any theory that proposes the basilar membrane as the locus of cochlear tuning. Instead, Shambaugh proposes that the tectorial membrane, with its "immense number of delicate lamellæ" act as the resonators.

He begins by pointing out that the basilar membrane is an inflexible meshwork of fibres, a construction making independent vibration impossible. Moreover, his well-illustrated studies of the pig showed some surprising anatomical variations that argue against the basilar membrane being a necessary component in hearing. Thus, he finds cases in this animal where the basilar membrane is thick and rigid, where it is absent altogether, and where in one case the entire intact organ of Corti rests upon solid bone (his Fig. 3). On the other hand, he found that the tectorial membrane was always coextensive with the sensory cells, leading him to adopt a resonance theory in which the "delicate film-like" tectorial membrane resonates.

He finds that the cross-sectional area of the tectorial membrane increases by a factor of hundreds from the base to the apex, an observation from which he infers a tuning role – exactly how is a question left to the physicist. I find his emphasis on the tectorial membrane compelling, and wonder why its impact has not been stronger.

Another early 20th-century anatomist impressed with the tectorial membrane was Hardesty. In 1908 and 1915 he published papers^{11,12} providing startlingly detailed drawings¹³ of the membrane, including of course the "accessory membrane" (which contacts the outer hair cell stereocilia) that we now call Hardesty's membrane. In considering how hearing happens and reviewing the work of a number of prior authors, Hardesty (1908) agreed with arguments that the basilar membrane is too coarse for the purposes of vibration – based on his own observations he likens it to a wooden board in comparison to the tissue paper or fine silk of the tectorial membrane – and hence favoured the latter in this role.

¹⁰ Shambaugh, G. E. (1907). A restudy of the minute anatomy of structures in the cochlea with conclusions bearing on the solution of the problem of tone perception. *Am. J. Anat.* 7: 245–257 (+ plates).

¹¹ Hardesty, I. (1908). On the nature of the tectorial membrane and its probable role in the anatomy of hearing. *Am. J. Anat.* 8: 109–179 (+ plates).

¹² Hardesty, I. (1915). On the proportions, development and attachment of the tectorial membrane. *Am. J. Anat.* 18: 1–73.

¹³ Pity about the crude labelling.

It should be quickly added that Hardesty rejected resonance (for a number of reasons, independence of the presumed resonating fibres being the main one) and, not wanting to set up yet another theory, favoured the telephone theory of Rutherford. In this theory, the partition's response was not graded in frequency but acted like the diaphragm of a telephone¹⁴. In supporting this idea, Hardesty thought (p. 117) the tectorial membrane suited it well as a diaphragm: it was “most inconceivably delicate and flexible” and “the readiness with which it bends when touched or even agitated is beyond description.”

Features well portrayed in his work were Hensens stripe and the multitude of fine parallel fibres embedded in the gelatinous matrix. Of interest, he describes (p. 167) the largely radial course of these fibres and, noting that vibrations tends to travel along fibres, suggests that the membrane may take up a radial vibration. An additional finding was the exceedingly thin transparent ribbon, the accessory tectorial membrane, on the underside of the membrane (Fig. 2.1), and Hardesty entertains the idea that it might take on independent vibration. If so, it would (p. 169) “undulate in accord with waves in the endolymph too faint to agitate the main body of the membrane at all”; and perhaps it would “act alone, only upon the outer and wider series of the auditory hairs.”

Hardesty's 1915 paper confirms the earlier descriptions and emphasises the fibrous nature of the membrane. He gives dimensions of the structure, again showing that, at least in the pig, it is largest at the apex and tapers towards the base. It appears about 7 times wider, and 3 times thicker, at the apex than at the base.

Another contemporary anatomist, Prentiss¹⁵, was convinced that the delicate tectorial membrane was better suited to act as a resonator than the basilar membrane, although he left it to physicists to decide if that were possible. He thought the membrane was divided into discrete honeycomb-like compartments, which may have provided the physical scientist with the basis of an interesting model. He noted that the cross-section of the apical membrane, again in the pig, was 30–40 times that at the base.

¹⁴ Wever (1949), pp. 77-79.

¹⁵ Prentiss, C. W. (1913). On the development of the membrana tectoria with reference to its structure and attachments. *Am. J. Anat.* 14: 425–457.

In evaluating these membrane resonance theories, Wever concludes by saying (p. 45) that “they are not taken very seriously at the present time.”

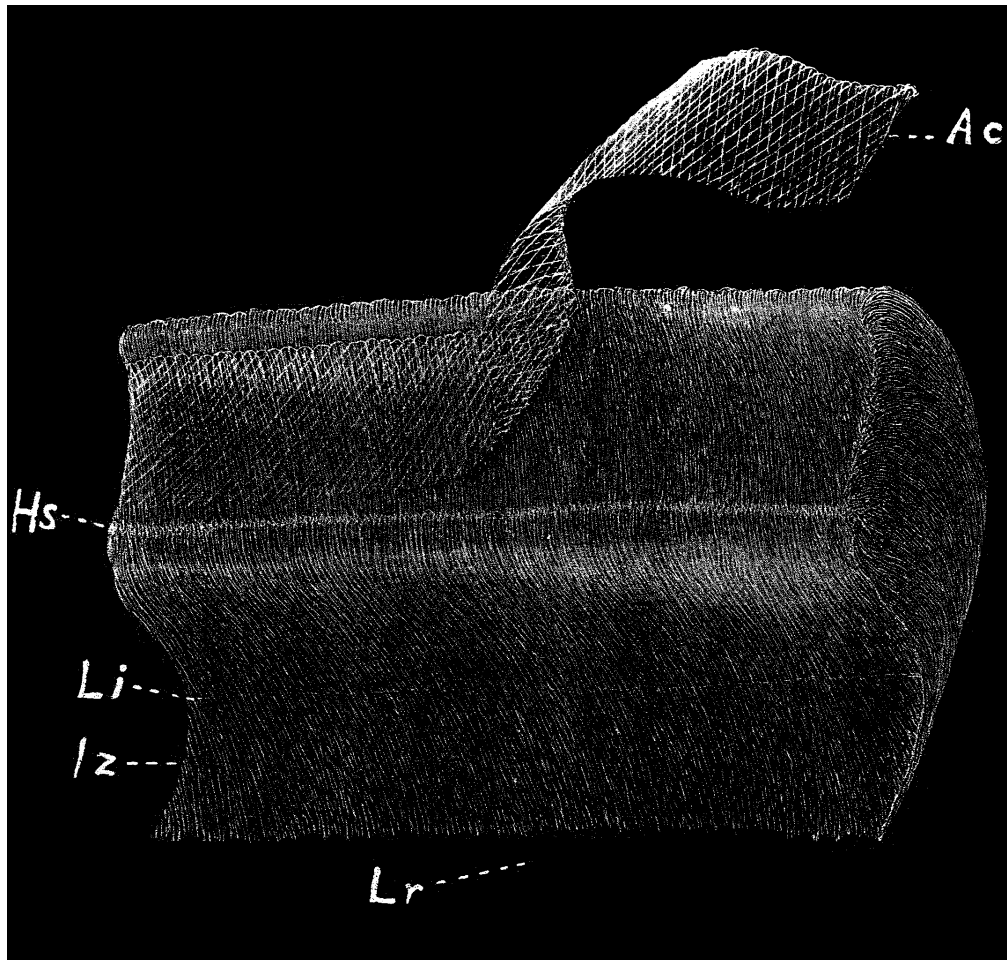


Fig. 2.1. Hardesty's illustration of the tectorial membrane (Fig. 3 of Hardesty, 1908), showing the many fibres and the delicate net of the accessory membrane (Ac) that lies above the outer hair cells and which he believed may be involved in independent vibration.

2.1/b Longitudinal standing waves

Instead of calling on a discrete physical structure to resonate, an alternative is to make use of the tube-like structure of the cochlea and create longitudinal standing waves, as in an organ pipe. In this way, the basilar membrane will be divided into nodes and antinodes, and the pattern of these will depend on the driving frequency. Wever (pp. 45–52) describes such a theory by Ewald (1898), who developed the theory mathematically. There will be a distinctly different pattern for each

discernable frequency, so auditory fibres will have to convey this *spatial pattern* to the brain for decoding. The higher the frequency, the smaller the spacing between antinodes. The idea of specific nerve energies – one fibre, one pitch – was abandoned, but this was not seen as an obstacle in the eyes of a number of subsequent followers. However, as Wever recounts, the theory encounters substantial difficulties in dealing with multiple simultaneous frequencies and in accounting for poorer pitch discrimination at higher frequencies than at low.

Later, variations on the longitudinal standing wave idea were presented by Ranke (1931) and Reboul (1937). The theories are set out in Wever pp. 68–75, but they appear complex and cut little ice, and I give them no further attention.

2.1/c The electronic era

The arrival of the electronic era opened up a whole new domain for resonance, and although the theory continued to decline in popularity in the 1920s as the traveling wave theory gained strength at the hands of Békésy, there were some adherents who kept the flame alive. There are two approaches worthy of mention, that of Hartridge and Hallpike (in the 1920s and 30s) and of Wilkinson and Gray (1920s).

“Hamilton Hartridge was a devoted, aggressive champion of resonance in the ear in the good old Helmholtz style” records Davis¹⁶. Hartridge did experiments with sirens^{17,18} (and also built pendulum models) and discovered a curious phenomenon: when the phase of the siren’s sound was rapidly changed by 180°, listeners reported that the sound died away momentarily before returning. Hartridge argued that this was evidence for a highly tuned resonator mechanism in the ear, one which took some time to decay and build up again. Davis (loc. cit.) seems to agree with this interpretation, acknowledging that the “Békésy envelope is not sharp enough and simply will not take care of all of the facts as we know them. Are there possibly little

¹⁶ Davis, H. (1973). The cocktail hour before the serious banquet. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic: New York), 259-271. [p. 263]

¹⁷ Hartridge, H. (1921). A vindication of the resonance hypothesis of audition. *Br. J. Psychol.* 11: 277-288.

¹⁸ Hartridge, H. (1921). A vindication of the resonance hypothesis of audition. II. *Br. J. Psychol.* 12: 142-146.

resonators which are loosely coupled to the basilar membrane as a whole or to one another that can continue to jingle after a transient stimulus?”

Békésy later (in 1928) repeated the experiment with an electrical circuit and an ear phone, and couldn't hear the effect, and therefore assumed that the cochlear resonators must be highly damped¹⁹. Yet Davis's concerns were not allayed, particularly when Hartridge and collaborators claimed to still hear the intervening silence with an electrical circuit and loudspeaker and, finally, showed that a correlate of it appeared in the auditory nerve²⁰. They thought the fibres of the basilar membrane were the resonating elements, although strangely they detected no silent period in the cochlear microphonic – it faithfully followed the stimulus waveform. Davis, in his own words²¹, brushed off the result with a vague explanation, but his conscience remained uneasy, and he made a point of raising this forgotten and neglected result in his 1973 account in case it turned out to be right.

In the 1920s, Wilkinson performed experiments with gelatin-coated brass wires and became another “convinced adherent of the resonance theory”²². He liked Hartridge's experiments and thought that the resonance theory alone could explain all the known facts. His favoured resonant elements were patches of basilar membrane, under tension, loaded on either side by the two fluid columns extending from each patch to the windows²³. An important insight presented in the Wilkinson and Gray book is “the astonishing fact” that sound perception can be quite good after loss of the ear drum and associated ossicles even though sound pressure must then act simultaneously on the round and oval windows (p. 133); moreover, in cases of fixation of the stapes (otosclerosis) some hearing persists and reception of bone-conducted sounds is actually enhanced (p. 135). These puzzling observations have continued to challenge both the resonance and the standard model²⁴.

¹⁹ Békésy (1960), pp. 411-413.

²⁰ Hallpike, C. S., Hartridge, H., and Rawdon-Smith, A. F. (1937). On the electrical responses of the cochlea and the auditory tract of the cat to a phase reversal produced in a continuous musical tone. *Proc. Roy. Soc. Lond. B* 122: 175-185.

²¹ Davis (1973), p. 264.

²² Wilkinson, G. (1927). Is the question of analysis of sound by resonance in the cochlea or by 'central analysis' in the brain still an open one? *Am. J. Psychol.* 38: 257-265.

²³ Wilkinson, G. and A. A. Gray (1924). *The Mechanism of the Cochlea: A Restatement of the Resonance Theory of Hearing*. (Macmillan: London).

²⁴ In Chapter 9 an attempt is made to reconcile these anomalies.

Fletcher's 1929 classic, *Speech and Hearing*²⁵, is positive towards the resonance or "Harp" theory, saying (p. 118) that the accumulation of evidence over the last few years has been overwhelmingly in favour of a modified Helmholtzian theory based on the fibres of the basilar membrane. And yet, at the same time, he emphasises fluid loading, so that in a structure as small as the cochlea, he thinks that damping will be so large that when a stimulating tone ceases, the 'hangover' will be minute and imperceptible. "For this reason when the ear mechanism is compared to a harp or a piano a wrong impression is usually created" (p. 125).

At this point the trail seems to run cold. Considerable interest developed in piezoelectricity, and Pohlman²⁶ in 1933 put forward the key idea, essential to this thesis, that auditory cells react directly to intracochlear pressure. However, his 'proposed mechanics', while arguing against the importance of differential pressures and traveling waves, does not directly relate to resonating structures, and so will not be discussed further here. Nevertheless, piezoelectricity was later incorporated into various resonance theories, Gold's included, so it is worth bearing in mind. But until Gold appeared, resonance faded from the scene, as far as I can tell, overshadowed by Békésy and his traveling wave.

2.2 Resonance post Gold

Gold's contributions have been treated in a broad context in the previous chapter. His work was groundbreaking because he reintroduced the notion of the ear's high Q , the hallmark of resonance, and proposed a way whereby the viscous damping could be overcome by positive (regenerative) feedback. Of course, at the time, the notion that the ear was active was heresy, and the psychophysical basis of his findings meant that physical resonance was able to be discounted – perhaps some neural process was responsible. The lacuna in his science was that no candidate for the resonators was nominated, greatly weakening his model. The only clues we find are a reference to "an oscillating fibre of the basilar membrane" (p. 495) and a

²⁵ Fletcher, H. (1929). *Speech and Hearing*. (Van Nostrand: New York). <http://auditorymodels.org>

²⁶ Pohlman, A. G. (1933). A reconsideration of the mechanics of the auditory apparatus. *J. Laryngol. Otol.* 48: 156-195.

calculation (p. 485) that there could be five rows of inner hair cells per frequency band, and hence “five resonant elements”.

2.2/a Guelke

A proposal in 1951 for an electromechanical damping mechanism²⁷ could be ignored as a curiosity except that it flags the author’s long-term quest for a satisfactory resonance theory of hearing. The magnetically controlled reed of Guelke’s model is portrayed as a way of overcoming the dilemma inherent in all resonance theories: whenever one has high Q , a sound will persist after excitation ceases. In contrast, his model is arranged so that when a resonator with high selectivity reaches a predetermined amplitude, an electrical damper comes into play, quickly reducing the vibration to zero. Guelke suggests the ear may possess something similar.

More than 30 years later, Guelke again returns to resonance²⁸, this time proposing that the resonators are like Helmholtz resonators (florence flasks) except that the resonance occurs not longitudinally in the neck of the flask but circumferentially. Guelke and Bunn suppose that a similar resonance may occur around the circular cross-section of the cochlea, but such an effect is hard to understand.

2.2/b Naftalin

Naftalin²⁹ began his crusade against the traveling wave orthodoxy in 1963 and continues it to this day. He is a biochemist with a drive to understand hearing, and his central idea is that the tectorial membrane must be resonating and, through some sort of electron–phonon interaction in its crystal-like structure, produce a piezoelectric voltage that is sensed by the hair cells. He deserves high praise for his

²⁷ Guelke, R. (1951). A theory of the action of the cochlear resonators. *J. Acoust. Soc. Am.* 23: 717-719.

²⁸ Guelke, R. W. and A. E. Bunn (1984). Resonance in theories of hearing. *J. Laryngol. Otol.* 98: 1177-1183.

²⁹ Naftalin, L. (1963). The transmission of acoustic energy from air to the receptor organ in the cochlea. *Life Sci.* 2: 101-106.

persistence and willingness to swim against the stream, although it is fair to say that his ideas are poorly received and he finds difficulty getting his latest work published. Some of his work has been mercilessly pilloried³⁰. Nevertheless, he seems undaunted, as I found in 2002 when I made a point of visiting him in Glasgow during a conference trip to Europe. Although officially retired, he is still active and regularly turns up at his lab bench at the University of Strathclyde.

His first paper on the subject (Naftalin 1963) is his most remarkable, as it simultaneously sets out major drawbacks in the traveling wave theory and offers a clear alternative – that the fast pressure wave stimulates the hair cells. He finds incredible that the traveling wave can stimulate a hair cell at threshold *when amplitudes have fallen to atomic dimensions* and, noting that people can hear without a tympanic membrane, suggests that a compression wave can do the job. Perhaps, he says, hair cells react to pressure like Pacinian corpuscles, or maybe the tectorial membrane senses the pressure piezoelectrically.

Naftalin's later publications were elaborations of that basic idea, and in so far as my thinking has gone in similar directions, I offer him due acknowledgement for the prescience set out in his 1963 paper. With an expertise in biochemistry and an appreciation of the peculiar physical properties of gels, Naftalin began to investigate the tectorial membrane. He was convinced, like the anatomists discussed above, that the tectorial membrane was a better candidate for resonance than the basilar membrane, and he began investigations of the tectorial membrane and of gels in general. A contribution³¹ in 1970 set out a table comparing the Young's moduli of various materials, including gelatine, from which he calculated that the speed of sound in the gel might be only 5 m/s, 2 orders of magnitude less than in water. His conclusion³² was that the tectorial membrane may alter the velocity of sound and support wavelengths of only 5 mm (at 1 kHz).

³⁰ In particular, see Tumarkin, A. (1964). Comment: Criticisms of Dr. Naftalin's theories. *J. Laryngol. Otol.* 78: 874-876. Gray, J. D. (1964). Comment: The transmission of acoustic energy from air to the receptor organ in the cochlea. *J. Laryngol. Otol.* 78: 877-878. But Naftalin took these "thunderbolts" with good grace: Naftalin, L. (1964). Comment: Reply to criticisms by Mr. A. Tumarkin and Mr. J. D. Gray. *J. Laryngol. Otol.* 78: 969-971., using the opportunity to once more point to inadequacies in traveling wave theory.

³¹ Naftalin, L. (1970). Biochemistry and biophysics of the tectorial membrane. In: *Biochemical Mechanisms in Hearing and Deafness*, edited by M. M. Paparella (Thomas: Springfield, ILL), 205-210; 290-293.

³² A conclusion that "upset" one participant, who proceeded to point out (p. 290-291) that an impedance discontinuity, such as an air bubble, is needed if sound is to interact with it [a notion

From his studies of the molecular composition of tectorial membranes, he came to the idea that there was some oscillating osmotic mechanism that was sensitive to pressure³³. This mechanism resonated with the incoming sound. Furthermore, because the tectorial membrane has a lattice-like structure that is graded in spacing from base to apex^{34,35}, the cochlea can perform frequency analysis. Another virtue of the pressure wave, Naftalin notes, is its speed, allowing simultaneous detection of transients and multiple frequencies³⁶.

Although the work can be faulted, in terms of insight into the fundamentals of hearing, Naftalin's theory forms a powerful and coherent option to the standard explanation. My own research has led me to an alternative resonator (parcels of fluid in the subtectorial space – Chapter R5), but in other respects similarities with Naftalin's picture are evident. I acknowledge his pioneering work, carried on when the traveling wave was the only game in town.

2.2/c Huxley

In 1969 Huxley gave an unexpected boost to the fortunes of the resonance idea. His mathematical analysis of a coiled cochlea³⁷ suggested that due to this peculiar geometry, ignored by most analyses, resonance was possible after all. His motivation was the extremely sharp tuning observed in auditory nerves, a sharpness standing in stark contrast to the broad tuning offered by traveling wave theory. However, he acknowledges (p. 935) that “most of the evidence which is accepted nowadays is against the existence in the cochlea of anything like true resonance, in the sense of incoming sound energy being stored over a considerable number of cycles in a mechanically oscillating structure.” Of course, this definition admits of

explored in detail in Chapter 7]. Naftalin acknowledged the point, but continued to maintain that some ability to ‘focus’ sound might be present.

³³ Naftalin, L. (1965). Some new proposals regarding acoustic transmission and transduction. *Symposia on Quantitative Biology* 30: 169–180.

³⁴ Naftalin, L. (1976). The peripheral hearing mechanism: a biochemical and biological approach. *Ann. Otol. Rhinol. Laryngol.* 85: 38–42.

³⁵ Naftalin, L. (1977). The peripheral hearing mechanism: new biophysical concepts for transduction of the acoustic signal to an electrochemical event. *Physiol. Chem. Phys.* 9: 337–382.

³⁶ Naftalin, L. (1981). Energy transduction in the cochlea. *Hear. Res.* 5: 307–315.

³⁷ Huxley, A. F. (1969). Is resonance possible in the cochlea after all? *Nature* 221: 935–940.

resonating second filters as well, whereas my concept of pure resonance requires that the stimulus energy be applied to all the resonators simultaneously (§I 1.5). Again, without this stipulation the distinction between traveling wave and resonance becomes merely a semantic one.

Huxley's analysis is complicated and involves tension in the basilar membrane. In the straight cochlea, the equations indicate that resonance is impossible; however, the effect of coiling the tensioned membrane is that it may act like a coiled spring and produce resonant oscillation. The key question, of course, is whether this possibility manifests in the real cochlea, and here Huxley calls for more work. He warns, though, that experiments on the cochlea can easily be misleading: opening the cochlea could alter the mechanical conditions and cause a resonant mode to disappear or perhaps even give the appearance of a traveling wave. In any event, Huxley's spiral spring has not been found, although some people have looked further into the effect of coiling^{38,39,40} and found it seems to make little difference.

2.2/d Offutt

Offutt was a marine biologist who did work on the hearing of fish and found, surprisingly, that the cod could hear underwater sounds nearly as well without its swim bladder as with it⁴¹. This led him to propose that they must be reacting directly to acoustic pressure. Cod do have otoliths in their sacculus, and the result could be explained in terms of the impedance discontinuity these masses offer to sound, but Offutt developed the idea that, for low-intensity stimuli, the otoliths were generating a piezoelectric signal⁴².

³⁸ Steele, C. R. and J. G. Zais (1985). Effect of coiling in a cochlear model. *J. Acoust. Soc. Am.* 77: 1849-1852.

³⁹ Viergever, M. A. (1978). Basilar membrane motion in a spiral-shaped cochlea. *J. Acoust. Soc. Am.* 64: 1048-1053.

⁴⁰ Manoussaki, D. and R. S. Chadwick (2000). Effects of geometry on fluid loading in a coiled cochlea. *SIAM J. Appl. Math.* 61: 369-386.

⁴¹ Offutt, G. (1974). Structures for the detection of acoustic stimuli in the Atlantic codfish, *Gadus morhua*. *J. Acoust. Soc. Am.* 56: 665-671.

⁴² Offutt, G. (1970). A proposed mechanism for the perception of acoustic stimuli near threshold. *J. Aud. Res.* 10: 226-228.

Some years later, Offutt issued a self-published book⁴³ that applied this unorthodox idea to the mammalian auditory system. In brief, he took the inner hair cells to be electroreceptors that responded to piezoelectric signals generated by the tectorial membrane, a structure analogous to fish otoliths. The outer hair cells remain as mechanoreceptors and provide a tuned amplifier. The action of the pressure wave is comparable to that of traveling wave (p. 146), both of which stimulate hair cells as they progress *slowly* (relative to the speed of sound) down the cochlea. This slow propagation of the pressure wave is one of a number of curious features of his theory. In what appear to be poorly controlled and fairly unconvincing experiments on chinchillas⁴⁴, he found that the compound action potential depended not on basilar membrane displacements but on acoustic pressure.

The theory, although interesting and covering a lot of material in a novel way, is opaque at many points and in the end is largely unconvincing. It has disappeared almost without trace.

2.2/e Stylis

In the early 1970s, Stylis put forward what he called a duplex theory of hearing⁴⁵ which was a hybrid of traveling wave and resonance. The traveling wave acted like a piano's damping pedal, its periodic motion at first freeing the stereocilia of the outer hair cells from their contact with the tectorial membrane and allowing them to resonate like xylophone rods to the incoming sound; half a cycle later, the wave reestablished contact and stereocilia motion was damped. Although it solved the problem of fast onset and offset of sounds, it failed in allowing sound energy to build up over many cycles, the intrinsic advantage of pure resonance theories. The theory did not gain currency. However one of its virtues was the way it highlighted two stimuli in the cochlea: the actual displacement of the traveling wave and the alternating pressure of the acoustic wave.

⁴³ Offutt, G. (1984). *The Electromodel of the Auditory System*. (GoLo Press: Shepherdstown, WV).

⁴⁴ No attempt was made to calibrate sound levels [p. 164].

⁴⁵ Stylis, S. C. (1973). The duplex theory of hearing. A new concept. *J. Laryngol. Otol.* 87: 727-738.

2.2/f Dancer

For more than 2 decades, Dancer has been attempting to dislodge the traveling wave theory, although without much success. Increasingly, his observations on guinea pigs led him to appreciate how crucial active processes were, so much so that he arrives at a point of seeing passive processes – the traveling wave – as irrelevant and disposable. His challenging 1989 paper⁴⁶ revives the idea of sharply tuned resonators inside the cochlea and he begins to analyse his cochlear microphonic data (from guinea pigs) in the context of a bank of resonators, of various degrees of damping, which are simultaneously excited. The measured delays in the cochlea, he surmises, could be due to cellular activity, not propagation delays, in which case the traveling wave becomes a non-causal side-effect, an epiphenomenon.

Dancer stimulated lively debate in 1992 when he published another paper⁴⁷ reinterpreting a whole range of data in the literature in the context of a pure resonance theory. He pointed out that Békésy used very high stimulation levels in dead cochleas, and these may not have a lot to do with what the live cochlea is doing. Dancer analysed cochlear microphonic data, intracochlear pressure measurements, and direct basilar membrane measurements. He concluded that “the cochlear partition appears to behave *in the same way as* a bank of resonators of which all the elements are excited simultaneously by the acoustic pressure”⁴⁸. It seemed that the cochlea registered responses much earlier than predicted by traveling wave theory, so that, for example, he saw in his own data delays in the second turn lower than 0.25 ms, less than half a period of the characteristic frequency (p. 305). This is a crucial point against the traveling wave theory, and is highlighted in §I 3.2/k.

The challenge was taken up by Ruggero⁴⁹, who proceeded to put forward evidence that the traveling wave is real. The issue is far from resolved, however, because Ruggero is prepared to entertain the idea that “traveling waves and cochlear

⁴⁶ Dancer, A. L. and R. B. Franke (1989). Mechanics in a "passive" cochlea: travelling wave or resonance? *Il Valsalva* 54 (Suppl. 1): 1-5.

⁴⁷ Dancer, A. (1992). Experimental look at cochlear mechanics. *Audiology* 31: 301-312.

⁴⁸ Ibid., p. 310, italics in original.

⁴⁹ Ruggero, M. A. (1994). Cochlear delays and traveling waves: comments on 'Experimental look at cochlear mechanics'. *Audiology* 33: 131-142.

resonance do not preclude each other” (p. 132), blurring the distinction possible in terms of energy flow and largely returning the argument to a semantic one (see §I 1.5). The really interesting thing is that the delays seen in a live cochlea (at low sound pressure levels) are remarkably longer than those obtained in a dead one⁵⁰ (or at high sound levels), and the question must be asked, how can that be? Clearly, the long delays are not due to traveling wave propagation delays, which, based on passive physical properties, one expects to be independent of intensity. Ruggero explains it as a “filtering” delay (p. 134), but the point is *what causes the narrow bandwidth filter*? If it’s the active process, then does energy reach it from adjoining filters (traveling wave) or from the simultaneous pressure stimulus (resonance)? The question can’t be decided on the evidence, although Ruggero does provide a Fig. 2 which, in contradistinction to his Fig. 1, appears to show a classic traveling wave signature – increasing lag with frequency – and *no difference* in response phase between live and dead, or between high and low level stimuli. That is because, as Ruggero explains (p. 139), the *group delay* is plotted, not the phase delay, and this tends to average out the effects of resonant peaks. But, I would say, the sharp tuning is precisely the feature to be emphasised rather than glossed over. In the end, I don’t think the issue, as portrayed, can be resolved either way on the evidence presented. What we need is to measure the time delays shown by outer hair cells, and the best way of doing this is with cochlear echoes. As the evidence shows (§I 3.2/k), the time delays can be exceedingly short.

Dancer was also taken to task by Ruggero and colleagues in a later paper⁵¹. Similar ground was covered (involving observations of response phases in live and dead animals), but the issue is not resolved in my mind, and questions can be raised about the effect of leaving the hole in the otic capsule open (see §D 9.3/d). As Dancer points out⁵², most work has focussed on measuring the velocity of the cochlear partition rather than intracochlear pressure.

⁵⁰ Ruggero (1994), Fig. 1.

⁵¹ Recio, A., Rich, N. C., Narayan, S. S., and Ruggero, M. A. (1998). Basilar-membrane responses to clicks at the base of the chinchilla cochlea. *J. Acoust. Soc. Am.* 103: 1972-1989. [p. 1985-1986]

⁵² Avan, P., Magnan, P., Smurzynski, J., Probst, R., and Dancer, A. (1998). Direct evidence of cubic difference tone propagation by intracochlear acoustic pressure measurements in the guinea-pig. *Eur. J. Neurosci.* 10: 1764-1770. [p. 1769]

2.2/g Braun

A persistent critic of the traveling wave theory, Braun's views have been mostly aired on the Cochlea⁵³ and Auditory⁵⁴ email lists, where they can be seen on the archives. In summary, he proposes that the ear operates by resonance, in particular by direct response of the hair cell stereocilia to sound and augmented by resonant connections to the tectorial membrane. He gives a nice explanation for the broad mechanical tuning of the basilar membrane⁵⁵: *it is an absorber of excess energy acquired by the sharply tuned resonant structures*. In a system with astounding sensitivity and dynamic range, protective mechanisms are essential.

Thus, Braun sees two resonant systems and two frequency maps in the ear, one originating in the organ of Corti and the other the basilar membrane. Importantly, for a given frequency, the peaks occur at slightly different locations, so that when a cochlea is damaged by destructively loud tone, stereocilia damage (due to excessive basilar membrane motion) occurs at a different location to where sensory function is impaired (presumably due to some other unobserved organ of Corti damage). This accords with the results of such experiments (see §I 3.2/l) and also explains why, in some bats, the thickness of the basilar membrane fails to correlate with the frequency map expected from traveling wave theory^{56,57} (so-called 'paradoxical' change in stiffness). A number of proponents of traveling waves have called for the action of a 'second filter' to provide additional selectivity, but in Braun's view (p. 106) there is really no need for the first filter and so the second filter is in fact the primary one.

By comparing the evidence from dolphins, bats, and desert rodents, Braun's 1994 paper gives good reasons for underplaying the role of the basilar membrane in hearing. It is difficult to offer conclusive proof that there are two mechanisms in the ear rather than one, but circumstantially the case builds weight.

⁵³ www.auditorymodels.org

⁵⁴ www.auditory.org

⁵⁵ Braun, M. (1994). Tuned hair cells for hearing, but tuned basilar membrane for overload protection: evidence from dolphins, bats, and desert rodents. *Hear. Res.* 78: 98-114.

⁵⁶ Kössl, M. and M. Vater (1985). The cochlear frequency map of the mustache bat, *Pteronotus parnelli*. *J. Comp. Physiol. A* 157: 687-697. [p. 696]

⁵⁷ Vater, M. (1988). Cochlear physiology and anatomy in bats. In: *Animal Sonar: Processes and Performance*, edited by P. E. Nachtigall and P. W. B. Moore (Plenum: New York), 225-241. [p. 235]

This thesis accepts there are two tonotopic maps in the cochlea and considers the proposal that the basilar membrane is for energy absorption a good one. The passive traveling wave (say in a dead cochlea) is merely a reflection of the motion of the basilar membrane system. The sensitive, sharply tuned system is not normally observable, except when it is able to set into motion the basilar membrane on which it sits. However, it does seem somewhat wasteful to throw away excess energy; perhaps, like the low-intensity rods and high-intensity cones in the eye, the high level system can be usefully harnessed, and in Chapter D8 this thesis proposes just such a system.

2.2/h Flock and ITER

‘Flock motility’ is a term current among hearing researchers, but you won’t find it in the literature. The term arose after observations made by Flock and his group that the body of outer hair cells could respond directly to imposed sound in a tuned manner^{58,59}. The idea is an important one for resonance theories of hearing, but the difficulty is that other researchers have not been able to reproduce it or aren’t willing to accept its radical implications. Lately, Flock himself appears to have been reticent in promoting the idea. So it remains in the shadows of hearing theory, but is very much worth noting here nonetheless.

The essentials of Flock motility can be seen in Fig. 3 of the Brundin et al. paper where tuning curves of seven outer hair cells isolated from guinea pigs are shown. When stimulated with an oscillating hydraulic system (a minishaker connected hydraulically to a holding pipette and supplying a force of 5×10^{-13} N), six of the cells whose tuning is plotted ended up becoming shorter whereas a seventh, inexplicably, became longer; values⁶⁰ of $Q_{10\text{dB}}$ ranged from 1.6 to 6.9, and the authors say such tuning could reflect the tip of the auditory tuning curve, tuning which is “independent from the basilar membrane travelling wave” (p. 815).

⁵⁸ Brundin, L., Flock, Å., and Canlon, B. (1989). Sound-induced motility of isolated cochlear outer hair cells is frequency-specific. *Nature* 342: 814–816.

⁵⁹ ITER [International Team for Ear Research] (1989). Cellular vibration and motility in the organ of Corti. *Acta Oto-Laryngologica, Supplement* 467: 1–279.

⁶⁰ $Q_{10\text{dB}}$ is the full width of the peak measured at –10 dB from the maximum.

Elsewhere, they comment that “long cells of the apical turn could either shorten or elongate” (ibid.), and show (Fig. 4) that the tuning depends on cell length according to a factor of about $-13 \mu\text{m}/\text{octave}$.

In Brundin and Russell (1994) they observe (Fig. 5) that a single OHC could change the phase of its response by 180° as stimulus intensity is raised.

The collection of ITER papers tells a similar story, and is notable for its wide-ranging list of eminent contributors (including Flock); however, it is unlikely all still hold to the views canvassed there. The summary (its Chapter 1) begins with a challenge: until now, it says, it was generally accepted that basilar membrane mechanics dominated inner ear tuning. By contrast, in this set of papers they present results that show that the response of the basilar membrane is considerably less than that of the outer hair cells themselves. Thus, at the apex of the isolated guinea pig temporal bone, they report (untuned) vibrations of the membrane hundreds of times less than of (tuned) outer hair cells; in the third turn, tuning of both was similar, but vibration amplitude of the membrane was an order of magnitude less than that of outer hair cells. Their conclusion (p. 12) is that “vibrations of the basilar membrane and the bony shelf may both be produced as a consequence of hair cell vibration... [so that] the concept that tuning arises from the mechanics of the basilar membrane.. is not consistent with measurements of cellular vibration in the organ of Corti.” That position essentially represents a resonance theory of hearing, although those words are not specifically used.

This thesis goes along with their conclusion, and also emphasises their cautionary note (p. 8) that simply opening the cochlea by removing the round window membrane causes damage to the sensory cells and alters the ear’s mechanical properties.

The Flock group makes a nice reference⁶¹ to Guild (1937), who appears to have been the first to put forward the view that outer hair cells – unlike inner hair cells – were stimulated directly by sound, not by movement of the basilar membrane. Noting that outer hair cells are surrounded by fluid (the space of Nuel), he says such an arrangement is ideal for permitting cell membranes to be deformed when sound passes through the intracochlear fluids. He seemed on the right track, but as it

⁶¹ Guild, S. R. (1937). Comments on the physiology of hearing and the anatomy of the inner ear. *Laryngoscope* 47: 365-372.

happened he was not prepared to take the idea further, saying he had no theory of hearing to propound or defend and wasn't even prepared to hazard a guess.

2.2/i *Sohmer and Freeman*

From their studies of bone conduction,^{62,63,64} Sohmer and Freeman have come to the conclusion that stimulation reaches the cochlea through the fluid pathways that connect it to the skull. They therefore see the outer hair cells being stimulated by the pressure wave, and not by a base-to-apex traveling wave⁶⁵.

2.2/j *Heerens*

Thanks to the power of the internet, Heerens has been able to broadcast his resonance theory of hearing⁶⁶ which involves the hair cells detecting a Bernoulli pressure associated with fluid displacement in the Venturi tubes of the cochlear ducts. Heerens is a retired physicist involved with ultrasensitive detectors, and became involved in the mystery of hearing after he became afflicted with Menieres disease. He has put considerable effort into developing his ideas, but has been unable to get them published.

Placing them on the web has allowed assessment of them to be made on the Cochlea list. They have not received a favourable reception, indeed sometimes attracting insults, mainly because the pressures to be detected are minute⁶⁷ and details of how the stimulus is transduced are unclear. Moreover, on my assessment, prime difficulties are that outer hair cell motility is not required and that Bernoulli

⁶² Freeman, S., et al. (2000). Bone conduction experiments in animals: evidence for a non-osseous mechanism. *Hear. Res.* 146: 72-80.

⁶³ Sohmer, H., et al. (2000). Bone conduction experiments in humans: a fluid pathway from bone to ear. *Hear. Res.* 146: 81-88.

⁶⁴ Sohmer, H. and S. Freeman (2004). Further evidence for a fluid pathway during bone conduction auditory stimulation. *Hear. Res.* 193: 105-110.

⁶⁵ Sohmer, H., et al. (2004). Semicircular canal fenestration: improvement of bone- but no air-conducted auditory thresholds. *Hear. Res.* 187: 105-110.

⁶⁶ www.slechthorend-plus.nl/fysica/en/heerens_en.htm (accessed January 2005)

⁶⁷ Christopher Shera calculated (Cochlea list, 2003/01/28) they would be about 2×10^{-14} Pa at threshold.

pressure oscillations occur at twice the stimulus frequency, a situation making detection and analysis of the stimulus by the auditory system more complex than it need be. Nevertheless, it is refreshing to see an alternative theory that questions the underlying assumptions of conventional theory and it is a pity that his work has not been formally published.

2.3 Second filters

We have made mention of how a traveling wave theory can incorporate resonant elements, adding to their selectivity until sharp resonant peaks appear. In this way, a highly tuned system – the second filter – sits on top of a broadly tuned one – the primary filter – like suspending a wind chime inside a moving car. Unfortunately, the distinction between traveling wave theories and resonance theories can then become blurred, as we have seen before (§I 1.5). This is unfortunate for understanding what is driving the system, and I would again like to emphasise the difference in terms of whether the excitation reaches the outer hair cells sequentially (traveling wave) or in parallel (resonance). Nevertheless, the fact remains that, as was the case with Dancer (§I 2.2/f), many second filter pictures can, with a change of adequate stimulus, be readily transformed into resonance theories, so here we will look at a range of them.

2.3/a *Evans and Wilson*

The notion of a second filter was first set out by Evans and Wilson⁶⁸ in 1981 in an effort to explain the sharp tips on neural tuning curves. At the time, acoustic nerve responses showed an order of magnitude better selectivity than basilar membrane measurements. Evidence was accumulating that the selectivity of the auditory system was already set at the level of the cochlea, so without recourse to the Békésy option (neural sharpening) they proposed that there was a second filter

⁶⁸ Evans, E. F. and J. P. Wilson (1973). The frequency selectivity of the cochlea. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic: New York), 519-551.

interposed between the basilar membrane and the inner hair cell. The second filter would be physiologically vulnerable and private to each nerve fibre. In addition, the filter had to be “not tightly coupled to the basilar membrane” (p. 545) to account for the striking disparity between measured basilar membrane responses and acoustic nerve responses (which they set out in their figures). Indeed, the disparity leads them to voice another “less likely” possibility: “that the motion of the basilar membrane does not represent the effective mechanical input to the hair cell transducer mechanism, but that other mechanical (more highly frequency selective) structures are involved” (p. 526).

They mention different ways of achieving sharpening, and that one might be an active filtering process involving positive feedback, but surprisingly no reference to Gold is made.

Of course, today we understand that the basilar membrane measurements were too crude, and as techniques improved the closer did the tuning of the basilar membrane approach that of the auditory nerve. We now take one to reflect the other⁶⁹, and so the question of the second filter seems to have faded away. And yet the fundamental question remains: if there is only one (sharp) filter, does the neural response reflect the motion of a highly tuned basilar membrane, or does, perhaps, the motion of the basilar membrane reflect the activity of that filter, as Evans and Wilson dared to suggest?

2.3/b Davis

When Davis first introduced his idea of the cochlear amplifier⁷⁰, he framed it in terms of a second filter, a sharp horn riding, like a unicorn's, on the front of the broad body of the traveling wave as it progresses from base to apex. The sensitive outer hair cells, with their active process, are responsible for the horn, while if the stimulus is strong enough, the passive movement of the basilar membrane stimulates the inner hair cells directly, just as the classical theory assumed. There is a half-

⁶⁹ Khanna, S. M. and D. G. B. Leonard (1982). Basilar membrane tuning in the cat cochlea. *Science* 215: 305-306.

⁷⁰ Davis, H. (1983). An active process in cochlear mechanics. *Hear. Res.* 9: 79-90.

octave separation between the tip of the horn and the peak of the traveling wave, explaining the fact that two separate processes seem to be operating in the cochlea.

The question of course, is whether the horn rides on the animal, or whether it might be an independent stimulus running ahead of it. Davis doesn't acknowledge the second possibility, but he does present again the sobering calculation that at threshold the traveling wave will give a displacement of 2×10^{-12} m, a sub-atomic motion that must feed into the cochlear amplifier and give a detectable output to the inner hair cells. Is that realistic? A seed of doubt is planted, but a possible answer could be, he suggests, the synchronous detection by multiple outer hair cells (perhaps that's why there's three rows of them).

Davis discusses possible candidates for the cochlear amplifier. Electrical feedback sources, perhaps involving the cochlear microphonic, are options, and here he mentions that piezoelectric effects could come into play. Another possibility is a mechanical feedback process, and two proposals are mentioned, one involving resonance of the tectorial membrane. A resonating tectorial membrane has long been associated with resonance theories of hearing, as we've already seen, and maybe this is why Davis generally prefers to speak of 'CA' (for the cochlear amplifier) instead. The interesting thing, therefore, is that in an earlier 1981 paper⁷¹ of Davis's (from which the 1983 paper evolved), he speaks freely of high-*Q* resonators and second filters. In physical terms, it is much easier to understand.

He describes a meeting with Kemp in 1977 at which a demonstration of cochlear echoes was given, and says (p. 154) he came away convinced that the second filter is real – and that it is a resonator. A resonator is the simplest form of acoustic amplifier, he reminds us, and that the amplifier must reside right where he said (many years earlier) it must reside: at the junction of the cilia and the reticular lamina. Further, he sets out how (and why) there are two receptor mechanisms in the ear – a high-level one with a short latency and a low-level one with a long latency – and associates the resonator mechanism with the latter. As above, he thinks the high-level sensor is the quick-acting inner hair cell and the low-level one a resonator, a highly tuned filter, formed from the outer hair cells. The resonator requires a number of cycles to build up strength before handing on their output to the inner hair cells.

⁷¹ Davis, H. (1981). The second filter is real, but how does it work? *Am. J. Otolaryngol.* 2: 153-158.

Now, as he says, comes the hard part: he can't figure out how the resonator works (p. 157). "The mechanism can't be simple or it would have been discovered long ago. We need a new idea of how it works." He points out that to get rid of high damping we need positive feedback, but Gold is neglected once more. He does want to keep with only one stimulus however – the Békésy tuning he calls it – and not introduce a second. Perhaps prophetically⁷², he refers to the outer hair cells once having kinocilia, and that "the metabolic system for doing work is probably still there, although with a different output system."

2.3/c Christiansen

Chronologically, Christiansen's second filter idea⁷³ should come first, as it dates from 1964. However, I only became aware of it from Davis's 1981 paper, and it conveniently sits here, given his consideration of it. Christiansen uses the piezoelectric properties of hyaluronate, present he thinks as long molecules projecting bristle-like from the stereocilia, to provide some sort of electromechanical resonance when they are bent by basilar membrane motion. Davis says it is an elaborate and unlikely speculation, but he likes the piezoelectric angle. Applying piezoelectric properties in reverse allows mechanical motion to emerge from the cochlear microphonic, and this could provide the necessary positive feedback (but still no reference to Gold, even though tinnitus and spontaneous emissions are alluded to).

2.3/d Tectorial membrane

The peculiar viscoelastic properties of the tectorial membrane have encouraged several researchers to attribute resonant properties to it. The membrane is envisaged to bounce up and down (or from side to side) on the hair cells and so create a second filter.

⁷² Albeit after the event so far as my thinking is concerned, as I only came across it late in the piece.

⁷³ Christiansen, J. A. (1964). On hyaluronate molecules in the labyrinth as mechano-electrical transducers, and as molecular motors acting as resonators. *Acta Otolaryngol.* 57: 33-49.

The first to put forward the idea was Zwislocki and Kletsy⁷⁴ in 1979, once again as a way of accounting for sharp tuning in the cochlea, a persistent feature that continued to defy explanation. They confidently put forward a transmission line model, which was “so obvious after the fact that it is difficult to understand how it could have remained undiscovered for so long” (p. 639), even though it assumed the mass of the membrane was negligible. Radial (side-to-side) resonance was stipulated and damping considered small. They later developed a mechanical model⁷⁵, an electrical vibrator on which was mounted a steel reed loaded at its tip with a small mass, the reed and mass mimicking the stereocilia and attached tectorial membrane. Driving the vibrator at various frequencies showed up an enhanced resonance when the reed and mass were in place. However, the physical properties of the real cochlea were not sufficiently well known to say whether the scheme would work as required.

A more sophisticated version of the scheme was put forward by Allen⁷⁶ in 1980 in which the tectorial membrane was allowed to vibrate independently of the basilar membrane and with a resonant frequency about half an octave below that of the basilar membrane. This allowed notches in the frequency response of the combined system to result, and a close match to the major features of neural tuning curves was demonstrated. According to a later review⁷⁷, an advantage of passive resonant tectorial membrane models is that they are simple and explicit; in contrast, active schemes relying on unspecified cochlear amplifiers are not. The possibility of an active tectorial membrane resonance was not considered.

Experimental evidence supporting tectorial membrane resonance⁷⁸ was reported by Gummer in the explanted temporal bones of guinea pigs. Laser doppler measurements showed differential vibration of the tectorial and basilar membranes, and confirmed a half-octave difference in the tuning of each of them. Given certain assumptions about the phase lag of outer hair cells to stimulation, Gummer suggests

⁷⁴ Zwislocki, J. J. and E. J. Kletsy (1979). Tectorial membrane: a possible effect on frequency analysis in the cochlea. *Science* 204: 639–641.

⁷⁵ Zwislocki, J. J. and E. J. Kletsy (1982). What basilar-membrane tuning says about cochlear micromechanics. *Am. J. Otolaryngol.* 3: 48–52.

⁷⁶ Allen, J. B. (1980). A cochlear micromechanic model of transduction. In: *Psychophysical, Physiological and Behavioural Studies in Hearing*, edited by G. van den Brink and F. A. Bilsen (Delft University Press: Delft), 85–95.

⁷⁷ Allen, J. B. and S. T. Neely (1992). Micromechanical models of the cochlea. *Physics Today* 45(7): 40–47.

⁷⁸ Gummer, A. W., et al. (1996). Resonant tectorial membrane motion in the inner ear: its crucial role in frequency tuning. *Proc. Nat. Acad. Sci.* 93: 8727–8732.

that relative motion of the tectorial membrane will, via bending of outer hair cell stereocilia, act to augment basilar membrane motion at certain frequencies and act as a brake at others.

2.4 Concluding remarks

Despite some ingenious proposals, some of which ventured close to the resonance mechanism proposed in this thesis, a convincing answer to the origin of the cochlea's sharp tuning has continued to elude researchers. It is a moot point as to whether pure resonance theories or second filter theories have come closer, particularly when the semantic distinction between them is often blurred.

Second filter theories often just assume an underlying traveling wave, perhaps unnecessarily, because in some cases the second filter by itself is perfectly adequate and the primary filter could well be dispensed with (the option chosen by Dancer, for example).

The key ideas that have emerged in this survey include

- the possibility of the cochlea reacting to intracochlear pressure instead of (or as well as) a traveling wave;
- that the selectivity of the auditory system is set by the cochlea;
- that positive feedback can overcome viscous damping;
- radial resonance;
- wave speed reduction by the tectorial membrane;
- that the resonator should reside in the subtectorial space;
- that the resonators be tuneable over a wide frequency range; and
- the choice of the tectorial membrane as a better candidate for resonance than the basilar membrane.

All of these ideas are taken on board in formulating a new model of the cochlea (Chapter M4).

In the following chapter, I take a closer look at the traveling wave. The main effort will be to document experimental findings that stand out as anomalies to the theory. In highlighting the limitations of the traveling wave theory, the aim will be to show that its explanatory (and causal) power has been exaggerated, a move which weakens its stranglehold on auditory theory and opens the door to another auditory stimulus, intracochlear pressure. As we will see, accepting intracochlear pressure as a companion stimulus allows certain anomalies to be explained; moreover, it lays the foundations for reviving a resonance theory of hearing.

Traveling wave theory, and some shortcomings

3.1 Formulation of the traveling wave equations

- 3.1/a The first transmission line model
- 3.1/b Differential pressure and common-mode pressure
- 3.1/c Discarding common mode pressure
- 3.1/d The modern standard model

3.2 Anomalies in traveling wave theory

- 3.2/a The peak is so sharp
- 3.2/b Doubts about the adequacy of the stiffness map
- 3.2/c The spiral lamina is flexible
- 3.2/d The basilar membrane rests on bone
- 3.2/e Holes in the basilar membrane
- 3.2/f Zero crossings
- 3.2/g Hear with no middle ear
- 3.2/h Hear with blocked round window
- 3.2/i Hear with no tectorial membrane
- 3.2/j The casing of the cochlea is exceptionally hard
- 3.2/k Fast responses
- 3.2/l A bootstrap problem
- 3.2/m No backward traveling wave

3.3 Summary

This chapter summarises the existing traveling wave model of the cochlea, looks at some shortcomings, and suggests that many of the documented anomalies can be explained by assuming that outer hair cells are responsive to the fast pressure wave. It does not try to present an historical account of the development of the theory nor offer a comprehensive account of every conceivable refinement that has been attempted – a vast task¹. Rather, it looks at the basic core of the theory and one modern account that is generally accepted as the standard picture. The modern version, due to Shera and Zweig (§I 3.1/d), adds two key elements – active properties and a reverse traveling wave – necessary to account for otoacoustic emissions. However, although generally successful, the modern version is still unable to account for the full range of cochlear phenomena, as we will see. Perhaps refinements can be made to overcome the shortcomings, but I want to suggest that the fault may lie in the basic reliance on differential pressure and that otoacoustic emissions could reflect a situation in which, at low sound pressure levels, the cochlea operates along pure local resonance principles and is responding to the fast pressure wave.

In some places the arguments I put forward rely on just sketching the outline of an alternative picture, as evidence is lacking to support what I admit is a non-conventional approach. Nevertheless, I have tried to make the alternative model as clear as I can, and I hope that others with more mathematical facility can place the model on a firmer footing if they see virtue in it. The intention is that by questioning the fundamentals of cochlear mechanics, progress in understanding may be made. I hope this sceptical approach will open up new avenues and therefore be more fruitful than simply accepting the textbook account on face value.

3.1 Formulation of the traveling wave equations

As described in §I 1.7, two different, but related, signals arise in the cochlea in response to sound stimulation. The first, p_+ , is the common-mode pressure and the second, p_- , the differential pressure.

¹ For two accounts, see Zwislocki, J. J. (2002). *Auditory Sound Transmission: An Autobiographical Perspective*. (Erlbaum: Mahwah, NJ). // de Boer, E. (1996). Mechanics of the cochlea: modeling efforts. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 258-317.

To recapitulate, p_+ is the acoustic pressure wave that is created by the stapes vibrating backwards and forwards in the oval window. It spreads throughout the cochlear fluids at the speed of sound in water (1500 m/s), creating, nearly instantaneously, a quasi-static hydraulic pressure field that is an exact analog of stapes motion (and ear-canal pressure). This pressure wave depends on the mass and compliance of the cochlear fluids; after the wave has traversed the cochlea a number of times, the magnitude of the residual common-mode pressure depends crucially on the compliance of the round window.

The second signal, p_- , is the difference in pressure between the upper and lower galleries caused by the presence of the partition. Depending on its acoustic impedance, a pressure difference will occur across the basilar membrane, leading to a pressure p_v in the upper gallery (scala vestibuli) and a pressure p_t in the lower (scala tympani).

Thus, the common mode pressure p_+ is given by $p_+ = (p_v + p_t) / 2$, whereas the differential pressure $p_- = (p_v - p_t) / 2$.

The standard view is that differential pressure is the sole stimulus in the system, and so a traveling wave mechanism excites the hair cells and thence auditory nerve fibres. As foreshadowed in Chapter II, I find this conclusion not fully justifiable, and here I want to put forward some reasons. I do not deny that a traveling wave mechanism may exist; but I think that the effects attributed to it have been exaggerated, and, at least at low sound pressure levels, are smaller than those due to excitation of the partition by outer hair cells in response to the fast pressure wave.

3.1/a *The first transmission line model*

Békésy provided no mathematical underpinning for his theory, leaving that to others. The first step towards a mathematical model was made by Wegel and Lane in 1924, who proposed that the cochlea operated like a tapered transmission line². Their electrical network model looked like Fig. 3.1, and this representation is the essence

² Here I follow Allen, J. B. (2001). Nonlinear cochlear signal processing. In: *Physiology of the Ear* (2nd ed.), edited by A. F. Jahn and J. Santos-Sacchi (Singular Thomson Learning: San Diego, CA), 393-442. Allen also points out (§1.1) that Fletcher deserves some credit too.

of the traveling wave formalism. Nearly the same arrangement is used today, albeit with additional serial and parallel elements; nowadays the mass (inductance) is usually taken to be more or less constant from base to apex³.

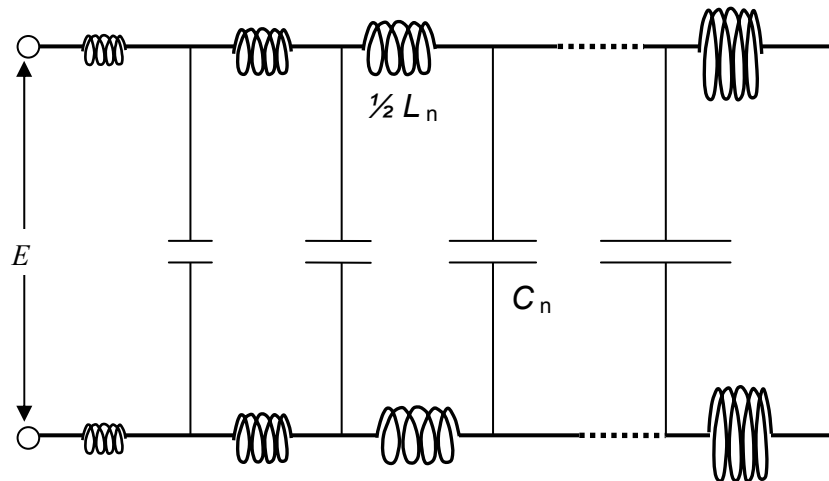


Fig. 3.1. An electrical network analog of the cochlea, the basis of all traveling wave models. The capacitances represent the compliances of the basilar membrane (the partition taken as a whole). The inductances represent masses of fluid in the upper and lower galleries.

A modern-day treatment⁴ of passive cochlear mechanics can be found in Fletcher (1992). A convenient analogue treatment giving a simple one-dimensional model is to take voltage to represent pressure and current to represent acoustic volume flow. Simplifying as much as possible, inductances represent the mechanical inertance, due to mass, of the fluid in the upper and lower galleries, which the stapes pressure encounters when the oval window pushes in and out; the capacitances represent the compliance of the basilar membrane, which tends to deflect in reaction to the pressure in the fluid moving along the galleries⁵. It is assumed that there is no mechanical coupling along the membrane itself, so that all coupling is due to the surrounding fluid. Dividing the cochlea into equal-length sections, the inductance, L_n , representing the mechanical impedance of each section is given approximately by

³ Geisler, C. D. (1976). Mathematical models of the mechanics of the inner ear. In: *Handbook of Sensory Physiology*, edited by W. D. Keidel and W. D. Neff (Springer: Berlin), vol. 5.3, 391-415.

⁴ Fletcher, N. H. (1992). *Acoustic Systems in Biology*. (Oxford University Press: New York). See Ch. 8 and Ch. 12.4.

⁵ The total volume of incompressible fluid displaced by the stapes has to move the round window, and in so doing it either moves along the upper gallery to the lower through the helicotrema or takes a short cut by deflecting the basilar membrane. By 'basilar membrane' is meant the whole partition – the organ of Corti and all its supporting structures.

$$\frac{1}{2} L_n \approx \frac{\text{density of fluid} \times \text{section length}}{1/2 \text{ cross-section area of channel}} \quad (3.1)$$

and the capacitance, C_n , is given by

$$C_n \approx \frac{\text{width of vibrating b.m.} \times \text{segment length}}{\text{stiffness of b.m.}} \quad (3.2)$$

As Fig. 3.1 illustrates schematically, both L_n and C_n increase as distance, x , from the base increases, in the first case because the cross-section of the channel decreases a little and in the second because the stiffness of the partition (essentially taken to be the basilar membrane) decreases and its width increases. The helicotrema (Fig. 3.7) is usually treated as a short circuit, although in practice there will be a small mechanical impedance associated with it.

The result is that the mechanical impedance, $Z(x, \omega)$, can be represented by an equation of the form

$$Z = i\omega m + K/(i\omega) + r \quad (3.3)$$

where⁶ m is the mass per unit length associated with each section (50 mg/cm² is typical), K is the stiffness (such that it decreases exponentially with distance like $K = 10^7 e^{-1.5x}$), and r is a damping term (in the manner of $r = 3000 e^{-1.5x}$).

At some angular frequency, ω , within the auditory range, the inertia and compliance of one section, taken to be the n th, will be in resonance so that $\omega = 1/(L_n C_n)^{1/2}$ and the section will have almost no impedance and look like a short circuit (a hole). The result is that all the flow passes through this section, causing large displacement of the partition, limited only by damping. On the apical side of this point, both L and C are large (large cross-section and low stiffness) and lie far from resonance so that the signal will, given the stiffness map, be attenuated about exponentially; very little will pass through the helicotrema. On the basal side, the two factors work together to produce a traveling wave which progresses along the partition, increasing gradually in amplitude to reach a broad peak, and dissipating

⁶ Typical values as used in Lesser and Berkley (1972).

before⁷ it reaches the resonant point. Each frequency will come to a peak at a particular point along the cochlea – its characteristic frequency: the lower the frequency, the further along the partition it will reach. At very low (subsonic) frequencies, ωL_n is very small and $1/\omega C_n$ very large, so fluid must then flow through the helicotrema.

Of course, this treatment is a simplification, and ignores active properties, but it gives a useful one-dimensional picture – the acoustic pressure is assumed to be a function of only the distance from the stapes – and provides an explanation of how tonotopic tuning can arise in the cochlea. It is the picture that naturally explains Békésy's stroboscopic observations on human cadavers at extreme sound levels and it remains the centre-piece of modern cochlear models.

More detailed treatments can be found in expositions by Lighthill⁸, Zwislocki⁹ and de Boer^{10–13}, and the accepted modern-day active model, due to Shera and Zweig, is outlined in §3.1/d below. Overall, none of these models deviate from the fundamental property that the stimulus travels through the network elements in series – a stimulus cannot reach its characteristic place on the partition without going through a cascade of circuit elements; thus for all audible sounds, there will be a significant time delay before a stimulus can reach a hair cell. The propagation speed of a traveling wave starts out at more than 100 m/s at the base and slows down to as low as 1 m/s at the apex. The time delay to the peak is typically 1 or 2 cycles, so that for a 1 kHz signal, the group delay will be 1 or 2 ms. A distinguishing feature of traveling waves is accumulating phase delay with frequency, until at the characteristic frequency many cycles of delay are apparent – the pivotal reason that resonance models, limited to $\pi/2$ delay, have been discarded¹⁴.

⁷ For discussion of this point, see Zwislocki (2002), Lighthill (1981, 1991), p. 9; Patuzzi (1996), p. 214; Withnell (2002), Fig. 3.

⁸ Lighthill, J. (1981). Energy flow in the cochlea. *J. Fluid Mech.* 106: 149-213.

⁹ Zwislocki, J. J. (1965). Analysis of some auditory characteristics. In: *Handbook of Mathematical Psychology*, edited by R. D. Luce et al. (Wiley: New York), 3, 1–97.

¹⁰ de Boer, E. (1980). Auditory physics. Physical principles in hearing theory. I. *Physics Reports* 62: 87-174.

¹¹ de Boer, E. (1984). Auditory physics. Physical principles in hearing theory. II. *Physics Reports* 105: 141-226.

¹² de Boer, E. (1991). Auditory physics. Physical principles in hearing theory. III. *Physics Reports* 203: 125-231.

¹³ de Boer (1995).

¹⁴ Patuzzi (1996), p. 199.

Some physically important insights into traveling wave behaviour are given by Lighthill (1981). First, he points out (his Fig. 1) that the system differs from a standard electrical waveguide in that the cut-off is a high-frequency one (not low-frequency); hence a propagating wave will not be reflected as it will in the standard electrical analogue. Thus, he prefers to make the analogy (his section 4) with an atmospheric wave phenomenon called critical-layer resonance. Secondly, he highlights (p. 193) that traveling wave mechanics entails that stapes pressure cannot remain perfectly in phase with volume flow – the wave is somewhat decoupled from its driving force – and so this reduces the ability of the stapes to efficiently drive the basilar membrane. This means that a purely resonant interaction between the two is not possible, particularly at low frequencies, where the phase relationship approaches 90° . Finally, he underlines the importance of the fast wave, which carries off half of the stapes energy according to his reckoning (pp. 150, 176), and which is necessary to explain why high-frequency limits in the cochlea often plateau at phases with integer multiples of π , behaviour which is “inconceivable” in a traveling wave system (pp. 153, 180).

3.1/b Differential pressure and common-mode pressure

In order to see how well the above description relates to the actual physics of the cochlea, we need to be sure that the equations we choose are comprehensive – as simple as possible, but no simpler, as Einstein expressed it. Fletcher (1992) provides a basic schema, but ignores common-mode pressure. In this thesis it is considered vital to set out a formalism that includes both differential and common-mode pressures. The first such approach was that due to Peterson and Bogert¹⁵ (1950), who in fact introduced the notation p_+ and p_- for what they called ‘longitudinal’ and ‘transverse’ modes of pressure (and similarly u_+ and u_- for the associated particle velocities). They give an equivalent circuit (Fig. 3.2 below) that generates both common-mode pressure ($p_v + p_t$) and a differential pressure ($p_v - p_t$). Given certain boundary conditions, a set of equations were developed that mirror this circuit.

¹⁵ Peterson, L. C. and B. P. Bogert (1950). A dynamical theory of the cochlea. *J. Acoust. Soc. Am.* 22: 369-381.

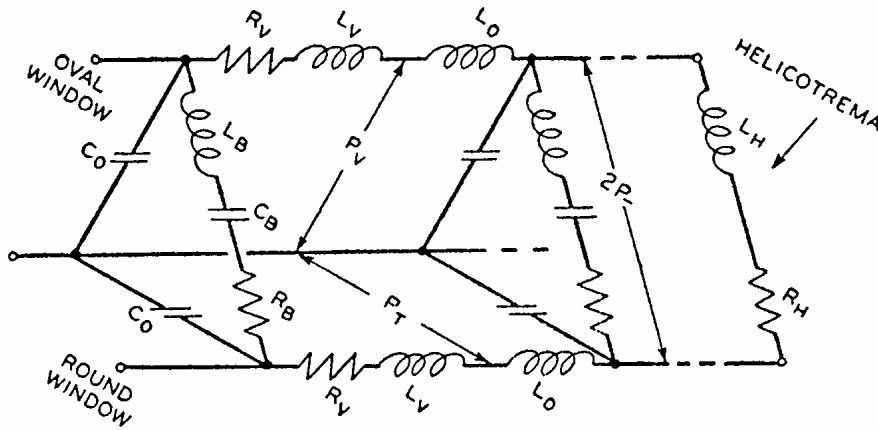


Fig. 3.2. The first equivalent circuit of the cochlea to include both common-mode and differential pressure. The three-terminal transmission line is from Fig. 22 of Peterson and Bogert (1950), and used with permission of the Acoustical Society of America.

The equations involving p_+ , the instantaneous pressure, were

$$p_+ = P_+ e^{i\omega t} \quad (3.4)$$

(where P_+ is the pressure amplitude at the stapes and ω its frequency)

$$\text{and} \quad \frac{1}{S(x)} \frac{\partial}{\partial x} \left(S(x) \frac{\partial p_+}{\partial x} \right) = \frac{1}{c^2} \frac{\partial^2 p_+}{\partial t^2} \quad (3.5)$$

where $S(x)$ is the cross-sectional area of each gallery at distance x from the base, and c is the velocity of sound in a free fluid. Given some simplifications, these equations, can be solved numerically. To do so, three boundary conditions are imposed: a fixed pressure of 2 dyne/cm² at the oval window; no pressure (but continuity of flow) across the helicotrema; and zero pressure at the round window. They therefore managed to derive a complex expression for $P_+(x, \omega)$ [their equation on bottom of p. 373)] which was independent of p_- and had a closed form solution involving Bessel functions. Another set of equations, independent of the first set, described the differential pressure, and these naturally lead to the standard traveling wave.

The numerical solutions provided a graph (their Fig. 4) of p_+ along the length of the cochlea. At low frequencies (some kilohertz), the average pressure is virtually constant along the partition at about 1 dyne/cm², but at higher frequencies a standing

wave begins to form¹⁶ and so at 10 kHz the average pressure ranges from 1 dyne/cm² at the stapes to nearly 4 dyne/cm² at the apex. Similarly, they calculate the differential pressure, which, for all frequencies, ranges from 1 dyne/cm² at the base to zero (as specified) at the apex. For progressively higher frequencies, zero differential pressure occurs closer to the base, so that at 10 kHz (shown in Fig. 3.3 below), all differential pressure vanishes 10 mm beyond the stapes. Calculations of transit times of impulses through the system (their Table 1) appear to broadly match those seen by Békésy.

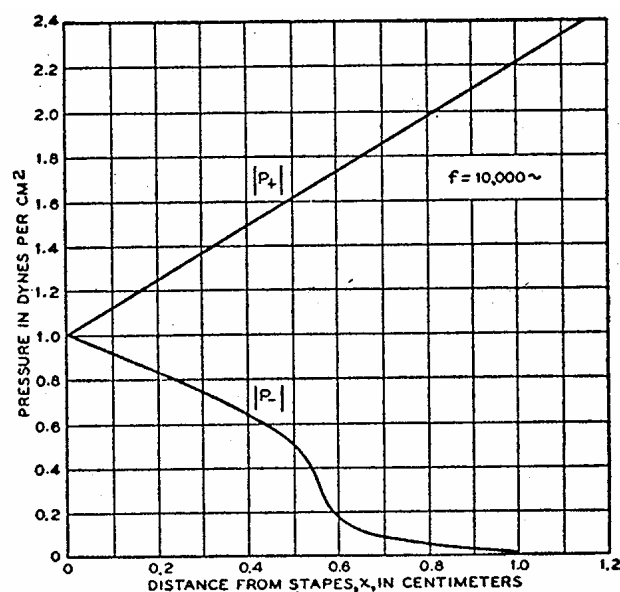


Fig. 3.3. Common-mode pressure p_+ and differential pressure p_- as calculated by Peterson and Bogert (1950) for a frequency of 10 kHz. Note that, given their boundary conditions, the magnitude of the former exceeds the latter. (Reproduced from their Fig. 9, and used with permission of the Acoustical Society of America)

Undoubtedly, the Peterson and Bogert paper is a major advance in understanding wave propagation in the cochlea. Given their consideration of common pressure, however, a peculiarity is that, in setting boundary conditions, they discard the round window membrane. “Since the round window membrane separates the fluid in the scala tympani from the air in the middle ear it is reasonable to assume that the acoustic impedance terminating the scala tympani is zero” they say (p. 373). But it is because of the round window’s stiffness that common-mode pressure arises in the first place. It almost produces a physical contradiction, for unless the cochlear channels are especially long and narrow, and the partition unusually stiff, there is no

¹⁶ Peterson and Bogert calculate (p. 373) that a quarter-wave resonance would appear at 12 kHz.

way that the pressure at the round window can remain zero when the stapes moves. Another consequence, of course, is that their formulation exaggerates the differential pressure, placing the full pressure generated at the stapes across the partition; it also has the effect of exaggerating the common mode pressure.

More than 20 years elapsed until Geisler and Hubbard (1972) appreciated the limitations of the Peterson and Bogert work and refined the analysis¹⁷ to specifically include round window stiffness. They called p_+ the ‘fast’ wave and p_- the ‘slow’ wave. They pointed out that the round window has a compliance of between 10^{-9} and 10^{-10} cm⁵/dyne (measured by Békésy [p. 435] and equivalent to 10^{-14} m³/Pa). It has an area of about 2 mm², so that it has an acoustic stiffness of 2×10^7 dyne/cm³ or (2×10^{-2} N/m³). Geisler and Hubbard used the same equation (3.5) as their starting point, but effected a considerable simplification by replacing $S(x)$ with a constant S . In justification, they remark that the cross-sectional area of the human cochlea is almost constant along its length (and as a side-effect making L_n about constant in Eq. 3.1); it also means that S in the numerator and denominator of Eq. 3.5 cancel, and we are left with a standard wave equation and its solution is

$$p_+(x) = \cos[\omega(l-x)c]e^{i\omega t} / \cos(\omega l/c) \quad (3.6)$$

which does not differ appreciably from the more complex Peterson and Bogert result. Introducing the round window stiffness, but eliminating the variation in S , gives the solution

$$p_+(x) = A \exp[i\omega(t-x/c)] + B \exp[i\omega(t+x/c)], \quad (3.7)$$

which is a familiar standing wave (two waves propagating in the $+x$ and $-x$ directions, with A and B complex constants). An interpretation is that the fast wave reflects multiple times in the cochlea and, since the cochlea is small and of irregular shape, forms a complex longitudinal pressure field.

Geisler and Hubbard show how the unknown constants can be found by applying boundary conditions. This results in a somewhat more complex expression for the fast wave, although still of the standing wave form:

¹⁷ Geisler, C. D. and A. E. Hubbard (1972). New boundary conditions and results for the Peterson–Bogert model of the cochlea. *J. Acoust. Soc. Am.* 52: 1629-1634.

$$p_+(x) = \frac{P_0 \{\rho\omega^2 c + Kc[P'_-(0)/P_-(0)]\} [e^{i\omega(t-x/c)} + e^{-2i\omega l/c} e^{i\omega(t+x/c)}]}{(1 + e^{-2i\omega l/c}) \{2\rho\omega^2 c + Kc[P'_-(0)/P_-(0)] + K\omega \tan(\omega l/c)\}}, \quad (3.8)$$

where P_0 is the sinusoidal pressure applied to the stapes, K is the acoustic stiffness of the round window membrane, l is the length of the cochlea, $P'_-(x)$ is the spatial derivative of $P_-(x)$ at $x = 0$, and the other symbols have their normal meaning.

For completeness, the corresponding slow (traveling) wave equation can be solved numerically¹⁸, but for the boundary conditions specified, the differential pressure at the stapes can be explicitly stated as

$$p_-(0) = \frac{P_0 [\rho\omega^2 c + K\omega \tan(\omega l/c)] e^{i\omega t}}{2\rho\omega^2 c + Kc[P'_-(0)/P_-(0)] + K\omega \tan(\omega l/c)}. \quad (3.9)$$

At any point x_0 in the cochlea, the pressure in the upper gallery will therefore be $p_+(x) + p_-(x)$, while the pressure in the lower will be $p_+(x) - p_-(x)$. In this case, the fast wave is no longer independent of the slow one, and the two waves are coupled. Notice that if $p_-(x)$ is small, the dominant signal in the cochlea will be $p_+(x)$, and vice versa. At the low frequency limit, $p_-(x)$ will be at its lowest and the pressure will be about constant throughout the whole cochlea. Thus, if we are looking for common-mode effects, they are more likely to be apparent at low frequencies. Geisler and Hubbard describe this situation as the cochlear fluids acting essentially as a tube of incompressible fluid, with the round window moving out when the stapes moves in, and vice versa.

Geisler and Hubbard conclude that at mid-frequencies the initial stapes stimulus is shared *about equally* between the two modes (not unlike Fig. 3.3), and just above 10 kHz a resonance occurs because at this frequency the length of the human cochlea is a quarter-wavelength of the pressure wave. The windows will usually act piston-like and 180° out of phase, but when the high frequency resonance is approached the relative phases of the windows will rapidly switch as the driving frequency passes through the resonance.

Geisler and Hubbard increased the stiffness by a factor of 5, and, apart from some frequency shifts, saw little change in the behaviour of their model. The input

¹⁸ Geisler (1972), p. 1630; for a broader perspective see also Geisler (1976).

impedance of their model cochlea was comparable at low frequencies to that measured by Békésy (*EiH*, p. 436) in a cadaver with the partition removed (leaving only the fluid and round window membrane). They also point out the similarity of their model to the results¹⁹ of Wever and Lawrence (1950) who measured the phase responses of the two windows in a cat and found resonance-like behaviour near 9 kHz. This important work will be discussed in more detail later (§D 8.1/b), since the observed antiphase motion of the windows, and the finding of a *minimum* in cochlear microphonic response when the windows are stimulated *in phase*²⁰, appears, *prima facie*, to contradict the idea that outer hair cells respond to common mode pressure.

In summary, the Geisler and Hubbard model gives a physically accurate insight into the mechanics of the actual cochlea. It describes both a fast wave and a slow wave, the first of which is associated with common mode pressure, and the second with differential pressure. A traveling wave emerges from the action of the differential pressure, and that slow wave has remained the focus of cochlear mechanics, generating more and more detailed models. *The surprise is the readiness with which the fast wave has been deemed irrelevant.*

3.1/c Discarding common mode pressure

Since consideration of common mode pressure is a major point of departure in this thesis, the literature's short treatment of the fast wave is worth documenting.

1. The first hint that the standard model may be inadequate came from reading the exposition²¹ of cochlear mechanics by Zwislocki (1980). He speaks of the Peterson and Bogert paper and claims (p. 173) that the pressure difference across the basilar membrane must be very small *and* that the pressure amplitude of the compressional waves must be small (because of the low impedance of the round window). Having both of these quantities small seems an ineffectual and unlikely outcome, so perhaps his other conclusion is open to question too: "Because hair cells

¹⁹ Wever, E. G. and M. Lawrence (1950). The acoustic pathways to the cochlea. *J. Acoust. Soc. Am.* 22: 460-467.

²⁰ In particular, Wever and Lawrence (1950) and subsequent work which is discussed in §D 8.1/b.

²¹ Zwislocki, J. J. (1980). Theory of cochlear mechanics. *Hear. Res.* 2: 171-182.

are excited as a result of deflection of their stereocilia rather than by pressure, compressional waves cannot be expected to play any direct role in the hearing process.” Note that direct pressure measurements may not answer the question satisfactorily because drilling a hole in the cochlea will disturb the pressure field.

2. Lighthill (1991) refers to the fast wave²² and says (p. 4) it is “uninteresting in another way as producing no motion of the cochlear partition. Accordingly, the fast wave becomes quite unimportant and I shall omit any further mention of it”.

3. Shera and Zweig²³ simply say (p. 1363) that “the inner ear responds only to the pressure difference $P_{ow} - P_{rw}$ between the oval and round windows and not the absolute pressure at either window.”

4. de Boer (1984) makes a one-sentence statement²⁴: “The mechanical impedance of the round window is assumed to be zero”. In his 1996 exposition, he devotes a paragraph to the “compressional wave”²⁵, but notes that the instantaneous pressure associated with it will be the same everywhere; thus, this component is considered “totally uninteresting” and not considered further.

5. Lindgren and Li (2003) began work with a double-sided transmission line model of the cochlea²⁶ that followed Peterson and Bogert’s original Fig. 22 and so specifically included the compliance of the round window (see Fig. 3.4a). However, they are soon led to say that the stiffness of the round window is small compared to other stiffnesses and so they considered the pressure at the round window to be zero (p. 6). Thus, the round window disappears (see Fig. 3.4b).

²² Lighthill, J. (1991). Biomechanics of hearing sensitivity. *Journal of Vibration and Acoustics* 113: 1-13.

²³ Shera, C. A. and G. Zweig (1992). Middle-ear phenomenology: the view from the three windows. *J. Acoust. Soc. Am.* 92: 1356-1370.

²⁴ de Boer (1984), p. 162.

²⁵ de Boer (1996), p. 263.

²⁶ Lindgren, A. G. and W. Li (2003). Analysis and simulation of a classic model of cochlea mechanics via a state-space realization. *unpublished manuscript*: <http://www.ele.uri.edu/SASGroup/cochlea.html>.

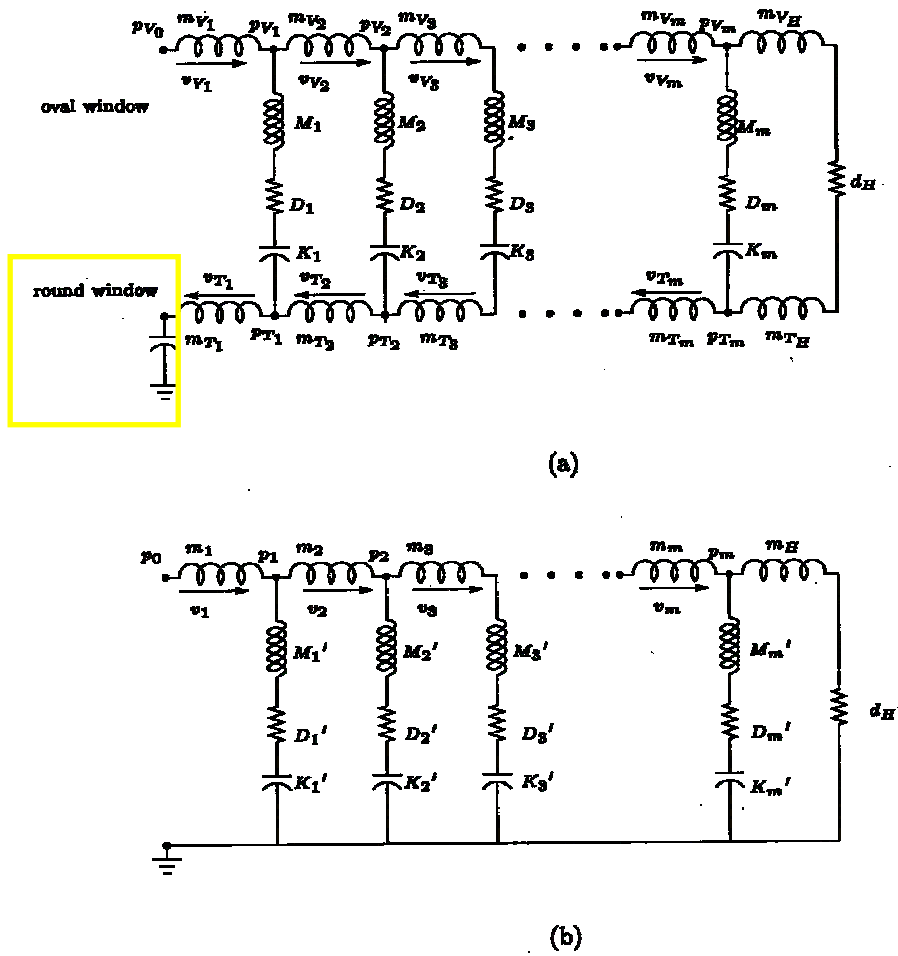


Fig. 3.4. A reasonably accurate model of the cochlea, the two-sided transmission line (top). Note the presence of a compliance (highlighted) representing the round window membrane which appears in series with the cochlear input. (Subscript V refers to scala vestibuli, T to scala tympani; the line is terminated by helicotrema mass m_H and damping d_H .) The authors also present an “equivalent” one-sided model (b) which, in omitting the round window, differs physically from (a). The diagrams are from Lindgren and Li (2003), and used with permission.

6. Baker (2000) sets out (his §3.3) to present²⁷ a mathematical development of the compressive wave. His aim is to develop piezoelectric amplification models of the cochlea. He notes that the compressive pressure field is symmetric about the partition, whereas the traveling wave of basilar membrane displacement is antisymmetric – thus “if one is interested in modelling basilar membrane motion, then one need not consider the compressive pressure wave. However, if one is interested in modelling fluid pressure measurement with the cochlear duct, then one must consider the compressive wave’s contributions as well” (p. 63). He proceeds to

²⁷ Baker, G. J. (2000). *Pressure-feedforward and piezoelectric amplification models for the cochlea*. PhD thesis, Department of Mechanical Engineering, Stanford University.

develop governing equations but sets a boundary condition that “At the round window, the total pressure should be zero or very nearly zero” (p. 65). Evidence for this is that “the round window membrane is relatively large and compliant, and that the cochlear fluids do not flow out when the round window membrane is carefully removed”. The first reason provides a useful simplifying assumption, but it tends to militate against the setting up of pressure fields. The round window’s stiffness is important in allowing common mode pressure to exist at all (and in some creatures the round window is remarkably small²⁸ or stiff²⁹). On the other hand, the mass of the cochlear fluids (and their small compliance) allows for pressure fields to establish at all frequencies above zero. The second reason has the limitation of applying only to static pressures and ignores surface tension effects. Overall, once it is acknowledged that outer hair cells may contribute significant amount of compressibility to the system, there are many possibilities for setting up a complex pressure field within the cochlea.

3.1/d *The modern standard model*

As said earlier, there is no intention of giving here a complete historical development of traveling wave theories. Allen (2001) provides a good perspective on the evolution of the field, and he discusses the way in which two- and three-dimensional models can improve the match between theory and experiment. However, to ward off complacency, he underlines (his §2.1) that “even a 3D model, no matter how much more frequency selective it was compared to the 1D model, would not be adequate to describe either the newly measured selectivity, or the neural tuning.”

de Boer also gives a wide-ranging summary³⁰ of cochlear modelling, prefaced with the warning “*How can we be sure that we are extracting the “true” information or drawing the “right” conclusions?* [p. 259, emphasis in original]. He discusses the

²⁸ Gulick, W. L., et al. (1989). *Hearing: Physiological Acoustics, Neural Coding, and Psychophysics*. (Oxford University Press: Oxford). [p. 115]

²⁹ In whales and bats it is funnel-shaped, like a loudspeaker cone [Reysenbach de Haan (1956), pp. 83, 89-90]

³⁰ de Boer (1996).

intricacies of long- and short-wave models of the cochlea³¹, as well as two- and three-dimensional models, second filters, active contributions from outer hair cells, and nonlinearity. Even so, longitudinal coupling, a real complication, needed to be ignored, and the chapter ends with a list of unsolved problems. The question posed again is (p. 307), “Haven’t we left out something essential?” The following section of this thesis (§I 3.2) takes this question seriously.

Nevertheless, despite acknowledged limitations, traveling wave models have captured major features of cochlear behaviour. If there is one accepted standard modern model it is probably the ‘coherent reflectance filtering’ (CRF) model due to Shera and Zweig^{32–35}. This model incorporates active elements and reverse traveling waves, for without both these features otoacoustic emissions could not arise within a traveling wave picture. The CRF model assumes that activity on the partition – mediated by outer hair cells – can cause a traveling wave to propagate in reverse towards the windows, where it is reflected at the stapes, and returns, via a traveling wave, to where it came. By multiple internal reflection, energy can in this way recirculate inside a longitudinally resonant cochlear cavity – and the end result is otoacoustic emissions.

Because of the appreciable length of the cochlear channels – some tens of millimeters – the theory establishes itself as a ‘global oscillator’ model, in contrast to the ‘local oscillator’ models of Gold and the like (included in which would be this thesis) where an oscillation emerging from the cochlea is traced back to a small group of outer hair cells on the partition. Because the traveling wave is broad, the CRF model cannot identify any single reflection point. It assumes that there is some ‘spatial corrugation’ or ‘distributed roughness’ inside the cochlea, so that scattering of a traveling wave occurs with a certain spatial regularity. The scattered wavefronts end up adding coherently in the opposite direction, and the result of this coherent reflection is acoustic emissions. The frequencies are not harmonically related, but there are an integer number of wavelengths in the round trip.

³¹ The former still stands on a pedestal (p. 270).

³² Shera, C. A. (2003). Mammalian spontaneous otoacoustic emissions are amplitude-stabilized cochlear standing waves. *J. Acoust. Soc. Am.* 114: 244-262.

³³ Zweig, G. and C. A. Shera (1995). The origin of periodicity in the spectrum of evoked otoacoustic emissions. *J. Acoust. Soc. Am.* 98: 2018-2047.

³⁴ Shera, C. A. and J. J. Guinan (2003). Stimulus-frequency-emission group delay: a test of coherent reflection filtering and a window on cochlear tuning. *J. Acoust. Soc. Am.* 113: 2762-2772.

³⁵ Shera, C. A. and J. J. Guinan (1999). Evoked otoacoustic emissions arise by two fundamentally different mechanisms: a taxonomy for mammalian OAEs. *J. Acoust. Soc. Am.* 105: 782-798.

The theory therefore places great emphasis on the relative phase of cochlear activity. A microphone in the ear canal measures regular peaks and valleys in pressure as frequency is swept, and CRF views these as an interference pattern produced by interaction of the forward and backward waves. Reflectance of waves at the stapes, R , will therefore have the form (Shera and Guinan, 1999, p. 795)

$$R \approx R_0 e^{-2\pi i f \tau} \quad (3.10)$$

where f is frequency and τ is a time constant. Experimentally, from investigation of stimulus frequency otoacoustic emissions (SFOAEs), τ appears to be about 10 ms at 1500 Hz. Since it has the form of a delay, “it is natural to associate that delay with wave travel to and from the site of generation of the re-emitted wave” (ibid., p. 785). The phase of the reflectance therefore rotates rapidly, going through one full period over the frequency interval $1/\tau$, which corresponds to the spacing between neighbouring otoacoustic emissions. That is, near 1500 Hz, the interval will be about 100 Hz, so that neighbouring emissions will occur in the frequency ratio $1600/1500 \approx 1.07$.

Another way of expressing τ is in terms of the number of periods of the traveling wave in the recirculating loop, so that $\tau(f) = N/f$, and experiment shows (Fig. 3 of Shera and Guinan, 2003) that in humans N ranges from about 5 (at 500 Hz) to near 30 (at 10 kHz). That is, the cochlea stores between 5 and 30 cycles of acoustic signal. The phase can also be expressed in the following way (Shera and Guinan, p. 785)

$$\angle R = \Delta\theta_{\text{forward-travel}} + \Delta\theta_{\text{re-emission}} + \Delta\theta_{\text{reverse-travel}} \quad (3.11)$$

in which $\angle R$, the phase unwrapped from 3.10, is taken to be the sum of three phase delays, the forward travel time of the traveling wave, a phase lag due to the signal passing through the cochlear filter, and a phase delay for the reverse traveling wave. Zweig and Shera (1995) have emphasised that the cochlea possesses scaling symmetry, so that the number of waves in any traveling wave is about constant: a low frequency wave will travel further along the cochlea than a high frequency one and will require a longer time to reach its peak, but in terms of total phase shift it is

about the same in the two cases. That means that the first and last terms on the right-hand side of 3.11 are about constant, and means that nearly all of the observed phase variation seen from the ear canal must derive from the second term. It is my contention that in fact the first and third terms are practically zero and that *nearly all* of the observed phase derives from the high Q of the cochlear resonators.

The same point can be approached from a different direction. Konrad-Martin and Keefe (2005) consider the Q of the cochlear filters³⁶ in terms of the ‘round-trip latency’³⁷ of Shera et al. (2002). Applied to SFOAEs, the latency amounts to Tf cycles of signal, where T is the measured latency and f is the frequency, and according to the Shera model, half of that latency ($Tf/2$) derives from the forward trip, and the other half (also $Tf/2$) from the reverse trip. Now the Q of the cochlear filters can be expressed as

$$Q = kTf/2 \quad (3.12)$$

where k is a dimensionless measure of the filter shape. Experimentally, k is found to be about 2 when the basilar membrane delay is assumed to be *half* the SFOAE delay, making $Q \approx Tf$, which is just what we expect from a simple resonating filter, since the Q is equivalent to the number of cycles of build up and decay³⁸. But the same result applies if we were to take k as 1 and the basilar membrane delay as simply *identical* to the filter delay. That is, the same results obtain whether k is set to be 1 (local oscillator model) or 2 (forward and reverse wave model).

Irrespective of what model one uses to interpret the results, the paper by Shera et al. (2002) is of interest in demonstrating that basilar membrane tuning in humans is appreciably sharper than previously thought. They used psychophysical studies conducted *near threshold* to show that the Q of the human cochlea is in the region of 15–20, values that are not as large as those calculated by Gold and Pumphrey, but indicative of high tuning nonetheless.

A large part of the argument for assuming that the traveling wave delay is not zero rests on showing that

³⁶ Konrad-Martin, D. and D. H. Keefe (2005). Transient-evoked stimulus-frequency and distortion-product otoacoustic emissions in normal and impaired ears. *J. Acoust. Soc. Am.* 117: 3799-3815.

³⁷ Shera, C. A., et al. (2002). Revised estimates of human cochlear tuning from otoacoustic and behavioural measurements. *Proc. Nat. Acad. Sci.* 99: 3318-3323.

³⁸ Fletcher, *Acoustic Systems in Biology*, p. 26.

$$\tau(f) = 2 \times \tau_{\text{BM}}(f) \quad (3.13)$$

where $\tau_{\text{BM}}(f)$ is the group delay of the basilar membrane. The factor of 2 is what one expects if the traveling wave carries the signal around the loop. The theory is open to the criticism that, experimentally, the appropriate factor is somewhat less than 2, with the weight of evidence pointing to an actual factor of 1.7 ± 0.2 (in the cat³⁹), 1.6 ± 0.3 (guinea pig⁴⁰), and 1.86 ± 0.22 (chinchilla and guinea pig⁴¹). However, a recent paper⁴² claims that the discrepancy can be accounted for by use of a more realistic two-dimensional model.

Finally, the CRF theory introduces one distinctive mechanical feature of the cochlea which is worthy of note. Phase measurements reveal that while SFOAEs show the expected rapid rotation with frequency, the behaviour of distortion product otoacoustic emissions (DPOAEs) is radically different⁴³. DPOAEs appear to be due to the interaction of the rapid rotation (slow time constant) with a very slow one (fast time constant). On this basis, Shera and Guinan identify two fundamentally different mechanisms: OAEs that arise by linear reflection and those that derive from nonlinear distortion. They set out a ‘taxonomy’ for acoustic emissions as set out in the table below.

³⁹ Shera and Guinan (2003), p. 2765.

⁴⁰ Shera and Guinan (2003).

⁴¹ Cooper, N. P. and C. A. Shera (2004). Backward-traveling waves in the cochlea? *Association for Research in Otolaryngology, Midwinter Meeting, Abstract 342*. This reference concludes that its results rule out the pressure wave hypothesis, but in this it only treats the hypothesis in its one-way guise: the DPOAEs travel from basilar membrane to ear canal via a pressure wave, but the traveling wave is still considered to take the signal back the other way. This is the original picture of Wilson (1980), but the model I want to promote is that the pressure wave acts in both directions, and that the “basilar membrane delay” is in fact all filter delay (see §I 3.2/k).

⁴² Shera, C. A., et al. (2005). Coherent reflection in a two-dimensional cochlea: short-wave versus long-wave scattering in the generation of reflection-source otoacoustic emissions. *J. Acoust. Soc. Am.* 118: 287-313. See also §D 10.1/b.

⁴³ Shera and Guinan (2003), p. 2764.

A taxonomy for mammalian acoustic emissions (Shera and Guinan, 1999)

Reflection source	Distortion source
Linear	Nonlinear
Rapid phase rotation	Slow wave rotation
SFOAEs, SOAEs, and TEOAEs	DPOAEs
Same frequency as stimulus (derive from near CF)	Frequency not in stimulus (require overlap of different TW peaks)
“place fixed”	“wave fixed”
High amplitude in humans, low in rodents	Maximum amplitude when $f_1/f_2 \approx 1.2$

Physically, the interpretation of the reflection source emissions (left column) is the one given above, in which there is one reverberating loop. By way of contrast, distortion sources (right column) arise, in the CRF view, from overlapping of the f_1 traveling wave peak and the f_2 peak, generating components at $2f_1 - f_2$ which travel to their own traveling wave maximum. The interactions become complicated, but the end result is a “wave fixed” emission that doesn’t depend on a single place on the partition in the way that “place fixed” emissions do. Importantly, the DPOAE emissions can be separated into a quickly rotating component (slow wave) and a slowly rotating one (fast wave).

The rapidity of the fast wave is highlighted in §I 3.2/k, and a ‘local’ model for generation of DPOAEs is put forward in Chapter R7. It seems much more straightforward to see practically all the phase delay as deriving from the filter delay of a local resonator.

At this point we bring discussion of traveling wave theories to an end. We have enough detail to convey a picture of the traveling wave running forth (and back) along the basilar membrane, generating responses in hair cells above. This background has been preparation for listing situations where traveling wave theories cannot give a comprehensive account of cochlear mechanics.

3.2 Anomalies in traveling wave theory

The traveling wave model has been the mainstay in interpreting the results of cochlear experiments. The model seems to fit, in the main, and there have been some notable achievements in matching theory and experiment. And yet, there are recurring disparities that suggest that our understanding is not quite right. By outlining these major points of departure, the hope is that the underlying root of the problem may come to the fore. As someone once remarked, “paradox is truth standing on its head in order to draw attention to itself.”⁴⁴ With that in mind, let us delve into the literature.

3.2/a *The peak is so sharp*

For a long time, the broad peak of the traveling wave was considered a virtue, for its associated low Q meant that hearing of transient sounds could begin and end quickly, without lag or overhang. But as improved experimental techniques showed increasingly sharp tuning of the basilar membrane⁴⁵, the problem became one of explaining how the traveling wave can give such a narrowly defined peak.

Some modern defining results include the following.

- Ren (2002) observed a traveling wave in a gerbil cochlea in response to 16 kHz tones and reported⁴⁶ that it occurred over a very restricted range (0.4–0.5 mm), even when the intensity varied from 10–90 dB SPL. Following death of the animal, response of the membrane was nearly undetectable and its tuning was lost.
- Nilsen and Russell (2000) saw sharp peaks in the tuning of a guinea pig basilar membrane⁴⁷ and evidence of radial phase differences.

⁴⁴ This saying is due, I believe, to Alan Watts (1916–1973).

⁴⁵ For quite some time mechanical tuning has been seen to be as sharp as neural tuning. Khanna, S. M. and D. G. B. Leonard (1982). Basilar membrane tuning in the cat cochlea. *Science* 215: 305–306.

⁴⁶ Ren, T. (2002). Longitudinal pattern of basilar membrane vibration in the sensitive cochlea. *Proc. Nat. Acad. Sci.* 99: 17101–17106.

⁴⁷ Nilsen, K. E. and I. J. Russell (2000). The spatial and temporal representation of a tone on the guinea pig basilar membrane. *Proc. Nat. Acad. Sci.* 97: 11751–11758.

When the animal died, responses dropped by up to 65 dB and phase gradients disappeared.

- Russell and Nilsen (1997) observed⁴⁸ in a similar investigation that the response to 15 kHz tones narrowed as intensity was reduced so that at 15 dB SPL, the peak was only 0.15 mm wide (the width of 14 inner hair cells). At 60 dB, the peak was more than a millimetre wide.
- Lonsbury-Martin et al. (1987) found histologically (Fig. 3.5) that the damage to a monkey's organ of Corti after exposure to loud pure tones was restricted to localised regions only 60–70 μm wide⁴⁹.

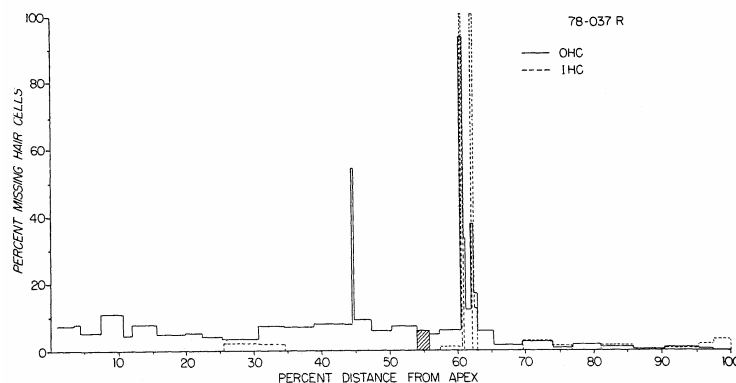


Fig. 3.5. Loss of inner and outer hair cells in the right ear of a monkey exposed long term to a wide range of pure tones at 100 dB SPL. Note the three sharp regions of high loss. The unexposed left ear showed no such peaks. [From Lonsbury-Martin et al. (1987) and used with the permission of the Acoustical Society of America]

- Lindgren and Li (2003) noted the discrepancy in the extent of excitation between their traveling wave model and the results of Ren (2002), but left it as inexplicable.
- Cody (1992) was puzzled⁵⁰ that neurally sharp tuning could remain in close proximity to regions damaged by overly loud sound. In one guinea pig, normal tuning and sensitivity were found within 0.5 mm of where 97% of outer hair cells were either missing or showed severe stereociliar damage.

⁴⁸ Russell, I. J. and K. E. Nilsen (1997). The location of the cochlear amplifier: spatial representation of single tone on the guinea pig basilar membrane. *Proc. Nat. Acad. Sci.* 94: 2660-2664.

⁴⁹ Lonsbury-Martin, B. L. and G. K. Martin (1987). Repeated TTS exposures in monkeys: alterations in hearing, cochlear structure, and single-unit thresholds. *J. Acoust. Soc. Am.* 81: 1507-1518.

⁵⁰ Cody, A. R. (1992). Acoustic lesions in the mammalian cochlea: implications for the spatial distribution of the 'active process'. *Hear. Res.* 62: 166-172.

In the opinion of Allen (2001), “The discrepancy in frequency selectivity between basilar membrane and neural responses has always been, and still is, the most serious problem for the cochlear modeling community. *In my view, this discrepancy is one of the most basic unsolved problems of cochlear modeling.*”⁵¹ While 2-D and 3-D models have improved matters, they have not narrowed tuning down to neural bandwidths. Active cochlear properties have opened the door to a gamut of signal processing strategies, but in Allen’s view, a theory and computational model are still desperately needed to tie it all together. He lists a number of anomalies between basilar membrane and neural responses (his §2.2.6) which we do not have the space to consider in detail. However, to mention an issue that relates to the resonance mechanism examined in this thesis, he calculates that, despite the best 3-D models, the deficiency in “excess gain” – the additional basilar membrane gain at the characteristic frequency (compared to its surrounding frequencies) – is out by a factor of between 10 and 100 (20 to 40 dB) when compared to nerve fibre data⁵².

de Boer (1996) also noted the poor match between models and experiment, even with short-wave 2-D and 3-D models. In no case does the response peak rise more than 10–15 dB above its surroundings. We might manipulate the parameters of the model, he observes (p. 281), but the dilemma is that either the amplitude of the peak remains too low or the phase variations in the peak region become too fast. He blames fluid damping, and makes a passing reference to the poor sound of an underwater piano (or carillon).

It is not often appreciated (or made clear by modelers) that there is flexibility in adjusting parameters to fit experimental data. Lesser and Berkley (1972) clearly spelt out that the process of matching experimental data to models is tricky⁵³. They pointed out (p. 509) that the resistance term in Eq. 3.3 is not readily amenable to independent measurement and so, following Zwislocki’s initial work, it is adjusted so as to yield agreement with the data. The mass term usually ends up larger than is physically plausible⁵⁴, even though some fluid will move with the partition.

⁵¹ §2.1, italics in original.

⁵² Last sentence of §2.2.6.

⁵³ Lesser, M. B. and D. A. Berkley (1972). Fluid mechanics of the cochlea. Part 1. *Journal of Fluid Mechanics* 51: 497-512.

⁵⁴ de Boer (1980), p. 166.

Similarly, Allen and Sondhi (1979) adjusted the damping term⁵⁵ until the best fit near CF was attained. Zwislocki (2002) adjusted parameters in an attempt to match his model to Békésy's narrow cochlear filter bandwidths; however, because the attempt failed (p. 156), Zwislocki was more inclined to suspect that the data was awry rather than consider his model wrong⁵⁶.

Active models provide even more adjustable parameters. Essentially, the active models allow for amplification stages between one transmission line stage and the next. This can work well in tuning frequency responses but it detracts from the physical realism of the model – in that the actual cochlea must make good use of all the signal energy available⁵⁷. It cannot afford, like the 120-section electronic analogue⁵⁸ of Lyon (1988), to employ a cascaded amplifier gain of 1800 just to prevent the traveling wave from dying out. Again, Hubbard and Mountain describe⁵⁹ an active model by Neely and Kim (1986) in which a power gain⁶⁰ of 30 000 is called for. Zweig and Shera⁶¹ have commented on the enormous gains typically required in active models to match theory with experiment. Gold, of course, would be quick to point out the danger of boosting a signal by 90 dB in the presence of unavoidable noise (§I 1.4).

3.2/b Doubts about the adequacy of the stiffness map

Even when the focus is kept on the stiffness of the embedded fibre, there are doubts that it can vary sufficiently between base and apex to tune the cochlea over 3

⁵⁵ Allen, J. B. and M. M. Sondhi (1979). Cochlear mechanics: time-domain solutions. *J. Acoust. Soc. Am.* 66: 123–132. [p. 128]

⁵⁶ Even though he gives the caveat (p. ix-x) that in auditory science “mathematical theory is often ignored or at least distrusted. In part, this is justified because the history of auditory research is full of examples of unrealistic mathematical and conceptual models that ignore existing experimental evidence” and contradict fundamental physical laws. Sentimentally, perhaps, he says (p. ix) that the simple classical picture of cochlear mechanics now has to be “reluctantly” abandoned in the light of Kemp's findings.

⁵⁷ Although in passive (linear) transmission line models, the primary wave suffers a power loss of about 15 dB before it reaches its best frequency [de Boer (1980), p. 160. See also de Boer, p. 267 of *Mechanics and Biophysics of Hearing*, edited by P. Dallos et al. (Springer: New York, 1990)].

⁵⁸ Lyon, R. F. and C. Mead (1988). An analog electronic cochlea. *IEEE Transactions on Acoustics, Speech, and Signal Processing* 36: 1119–1134.

⁵⁹ Hubbard, A. E. and D. C. Mountain (1996). Analysis and synthesis of cochlear mechanical function using models. In: *Auditory Computation*, edited by H. L. Hawkins et al. (Springer: New York), 62–120. [p. 97]

⁶⁰ The ratio of power entering the system at a given frequency to the power dissipated at the characteristic frequency.

⁶¹ Zweig and Shera (1995), p. 2039.

orders of magnitude. The issue was first raised in connection with the tuning range of resonating fibres⁶², and is summarised in Fig. 6.3 of de Boer (1980) and its associated discussion⁶³.

In general, a broad trend linking upper and lower hearing limits and cochlear width and thickness can be discerned across species, but the correlation is poor and is contradicted by certain specialised animals like horse-shoe bats and elephants⁶⁴. In a developmental study of gerbil cochleas, it was found that a region that codes for the same frequency can have basilar membranes of very different dimensions, depending on age⁶⁵. Treating the basilar membrane as having simple mass–spring resonance leads to difficulties. To vary the frequency by 10^3 means that the combined mass and stiffness needs to vary by a factor of 10^6 . Since the mass is generally accepted as more or less constant⁶⁶, this requires stiffness (measured in terms of resistance to displacement by a probe, the ‘point stiffness’, divided by the width of the membrane) to vary a million-fold.

Measurements show that the stiffness of the basilar membrane varies by less than this. Békésy, for example, measured a stiffness variation (using a fluid pressure of 1 cm water, which generated about 10 μm deflection) of only a hundred-fold⁶⁷. One possible avenue is to go beyond the simple two-dimensional picture and call on three-dimensional fluid–membrane interactions⁶⁸, although such a solution is by no means universally accepted.

The summary figure of de Boer (1980) shows stiffness variations (and characteristic frequency) plotted against distance from the stapes. Although the 100-fold variation of Békésy is depicted, his three data points obtained by pressing a hair on the membrane are also shown, and these are preferred because they show a 2.5 order of magnitude variation in stiffness over a similar variation in frequency – even

⁶² The discussion in Chapter 2 following Equation 2.1.

⁶³ de Boer (1980). Auditory physics. Physical principles in hearing theory. I. Physics Reports 62, 87-174. de Boer Auditory physics. Physical principles in hearing theory. I.

⁶⁴ Echteler, S. M., et al. (1994). Structure of the mammalian cochlea. In: *Comparative Hearing: Mammals*, edited by R. R. Fay and A. N. Popper (Springer: New York), 134–171.

⁶⁵ Schweitzer, L., et al. (1996). Anatomical correlates of the passive properties underlying the developmental shift in the frequency map of the mammalian cochlea. *Hear. Res.* 97: 84–94. With age, the position representing a given frequency (11.2 kHz) shifted along the cochlea, being 90% from the base (near birth) and shifting to 65% (adult). To preserve place coding in accordance with traveling wave theory, the authors suggest that the *stiffness* of the partition must have changed.

⁶⁶ de Boer (1980), p. 166; Naidu and Mountain (1998), p. 130; Allen (2001), §1.3.1.

⁶⁷ Békésy (1960), p. 476.

⁶⁸ Steele, C. R. (1999). Toward three-dimensional analysis of cochlear structure. *ORL – Journal for Oto-Rhino-Laryngology and Its Related Specialities* 61: 238–251.

though this data requires an assumption that the point stiffness, which varies by 1.7 orders, can be realistically converted into an area modulus. Extrapolating this limited data appears to give a mapping with a suitably steep slope.

Work after Békésy was largely confined to measurements at or near the base until a provocative paper⁶⁹ by Naidu and Mountain (1998) confirmed Békésy's original findings: in experiments on isolated gerbil cochleas, they could only measure a variation of 56 in the pectinate zone of the basilar membrane (below the outer hair cells) and a factor of 20 in its arcuate zone. Making allowance for variations in the width of the basilar membrane, they found a final volume compliance ratio of about 100 between base and apex. They conclude (p. 130) that “conventional theories that explain cochlear frequency analysis based on an enormous stiffness gradient and simplistic motion of the OC require substantial modification.”

One attempt at explaining cochlear tuning is due to Wada et al. (1998) who measured thickness and length along the whole of the guinea pig cochlea⁷⁰. Based on a computerised reconstruction and beam model, they found that the natural frequency at the basal turn was only 3.1 times that at the apical turn, assuming that the Young's modulus and diameter of the constituent fibres was constant. Given that the variation was inadequate to produce wide-range tuning, the authors conclude that the assumption must be wrong, and that the modulus must vary. Unfortunately, direct evidence (which they cite on p. 5) shows that the Young's modulus of human basilar membrane only varies by 50% between base and apex, so the question remains.

Inadequate variation in tuning also emerged from another finite-element model of the cochlea⁷¹. In this case, geometry alone gave a 2-fold change, and allowing for stiffness variations a 20-fold difference between base and apex resulted. A way around the limitation is, the authors suggest, to suppose – ad hoc – that hair cells in the apex respond to a first vibrational mode while hair cells in the apex respond to a second.

⁶⁹ Naidu, R. C. and D. C. Mountain (1998). Measurements of the stiffness map challenge a basic tenet of cochlear theories. *Hear. Res.* 124: 124–131.

⁷⁰ Wada, H., et al. (1998). Measurement of guinea pig basilar membrane using computer-aided three-dimensional reconstruction system. *Hear. Res.* 120: 1–6.

⁷¹ Zhang, L., et al. (1996). Shape and stiffness changes of the organ of Corti from base to apex cannot predict characteristic frequency changes: are multiple modes the answer? In: *Diversity in Auditory Mechanics*, edited by E. R. Lewis et al. (World Scientific: Singapore), 472–478.

An effort to meet Naidu and Mountain's challenge was made by Emadi et al. (2004), who used a vibrating stiffness probe on the basilar membrane of gerbils⁷² at various radial and longitudinal locations. In their unidirectional measurements, they focus on the minimum of the parabolic stiffness, values of which they took to reflect the basilar membrane fibres⁷³. Of the four radial positions at which they took readings, three of them gave a longitudinal gradient comparable to those of Naidu and Mountain. However, the fourth, measured at the mid-pectinate location, gave a steeper longitudinal gradient (-5.7 dB/mm) than Naidu and Mountain (-3.0 dB/mm), and the authors argue that this set of data is the most relevant⁷⁴. Putting this value into a simple resonance model and into a 3D fluid model, they calculate an excellent match between stiffness variation and frequency ratio between base and apex.

As a critique, I would argue that, since fluid pressure over the whole membrane is the physiological stimulus, an average of all positions would be more representative. Moreover, the statistics of the analysis are marginal, in that the gradient of the line through the three error-barred points in their Fig. 5D carries large uncertainties. The primary author says⁷⁵ that the 95% confidence limits on the gradient are -6.2 and -3.0 dB/mm, the last figure corresponding to the gradient they wish to dispute. Moreover, the figures derive from averaging, after 5-point ($5\text{-}\mu\text{m}$) smoothing, all data from $1\text{ }\mu\text{m}$ deflection to $17\text{ }\mu\text{m}$, and this processing may not yield the physiologically relevant value, particularly when most of the curves shown in Fig. 5B have non-linear slope (either less or more than 1 dB/dB , as shown in Fig. 5C). The non-linearity is a good reason to suspect that the statistical model applied to the data is not valid.

Nevertheless, it is true that fluid models do provide a way of expanding the tuning range for a given stiffness range. The model⁷⁶ used by Emadi et al., and its later form of development^{77,78}, do give wide-range tuning; the difficulty is accepting

⁷² The experiments were done both in vivo (base only) and in vitro (on a hemicochlea). As mentioned in §1 3.2/b, these authors used *unidirectional* probing of the basilar membrane.

⁷³ Although they acknowledge (p. 483) that the physiologically relevant stiffness may occur at smaller tissue deflections and be buried in the noise.

⁷⁴ The authors should not have expressed their findings in decibels, which applies to power, but their meaning, in terms of a ratio change of stiffness per millimetre, is clear enough.

⁷⁵ Personal communication to T. Maddess 2005/02/05.

⁷⁶ Steele, C. R. and J. G. Zais (1983). Basilar membrane properties and cochlear response. In: *Mechanics of Hearing*, edited by E. de Boer and M. A. Viergever (Delft University Press: Boston, MA), 29-36.

⁷⁷ Steele Toward three-dimensional analysis of cochlear structure.

the underlying finite-element model, which has some peculiar features. For example, the fluid pressure in the spiral sulcus is assumed central in stimulating inner hair cells, so that Steele argues (p. 241) that the whole purpose of the organ of Corti is to develop that pressure. He also uses (his Table 1) a Young's modulus of 1 GPa for *all* parts of the organ of Corti, including the tectorial membrane but excepting Hensen cells, which seems overly simplistic. For example, in Chapter 5 measurements of the stiffness of the tectorial membrane are examined and values in the region of some kilopascals seem most appropriate.

In conclusion, therefore, real doubts remain about being able to achieve a satisfactory range of tuning and, as Allen (2001) remarks, 3D models do not, without some radical assumptions, provide adequate sharpness.

3.2/c The spiral lamina is flexible

The basilar membrane is supported on its outer side by the spiral ligament and on its inner side by the (osseous) spiral lamina. While the width of the partition is about constant along its length, the basilar membrane is relatively wide at the apex and tapers to its narrowest at the base. This arrangement suggested to Helmholtz, and to many since, that the basilar membrane is tonotopically tuned via its width. The problem, as pointed out by Köhllöffel⁷⁹ (1983), is that the spiral lamina is in many animals as flexible as the basilar membrane. This author says (p. 215) that in unfixed human preparations the spiral lamina deflected as much as the basilar membrane (over the region 3–14 mm from the base when vibrated at frequencies up to 1 kHz). Using a hair probe, the human spiral lamina deflected nearly as much as the round window membrane.

Interestingly, the flexibility of the spiral lamina was noted as early as 1680 and formed the basis of DuVerney's cochlear frequency analysis idea in 1684. Its

⁷⁸ Steele, C. R. and K.-M. Lim (1999). Cochlear model with three-dimensional fluid, inner sulcus and feed-forward mechanism. *Audiol. Neurotol.* 4: 197-203.

⁷⁹ Köhllöffel, L. U. E. (1983). Problems in aural sound conduction. In: *Mechanisms of Hearing*, edited by E. de Boer and M. A. Viergever (Delft University Press: Delft), 211-217.

flexibility is confirmed by a recent study⁸⁰ in which the amplitude and tuning of the lamina in human cadavers was examined with a laser vibrometer. When exposed to air-conduction stimuli, the motion of the lamina (at 12 mm from the round window) was comparable to – and at some frequencies exceeded – the motion of the adjacent basilar membrane⁸¹.

If the whole partition is flexible (and nearly constant in width), it removes one more factor by which tonotopic tuning can be produced.

3.2/d The basilar membrane rests on bone

If the basilar membrane were essential for hearing, as the traveling wave theory supposes, then we would invariably find it present in a functioning cochlea. That is not always the case.

In some cases we find a well formed organ of Corti, but it rests on solid bone, not the basilar membrane. Fig. 3.6 shows a microscopic section made by Shambaugh (1907) of the organ of Corti of a pig⁸² sitting upon solid bone, one of several observations of the basilar membrane that made Shambaugh think that its “thick, inflexible character” makes it an unsuitable candidate as a vibrating structure. He thought the tectorial membrane, which was always associated with the organ, a much better candidate.

One may be tempted to argue that the pig was deaf. However, work in the 1930s by Crowe, Guild, and Polvogt (cited by Tonndorf⁸³ 1959) indicates otherwise. In a post mortem study of human temporal bones, Polvogt and colleagues compared the results with audiograms taken before death and found that the person with a similar bony projection could hear, at least for frequencies lower than those corresponding to the site of the abnormality.

⁸⁰ Stenfelt, S., et al. (2003). Basilar membrane and osseous spiral lamina motion in human cadavers with air and bone conduction stimuli. *Hear. Res.* 181: 131-143.

⁸¹ Stenfelt (2003), Fig. 5a.

⁸² Shambaugh, G. E. (1907). A restudy of the minute anatomy of structures in the cochlea with conclusions bearing on the solution of the problem of tone perception. *Am. J. Anat.* 7: 245–257 (+ plates).

⁸³ Tonndorf, J. (1959). The transfer of energy across the cochlea. *Acta Otolaryngol.* 50: 171–184. [p. 182]

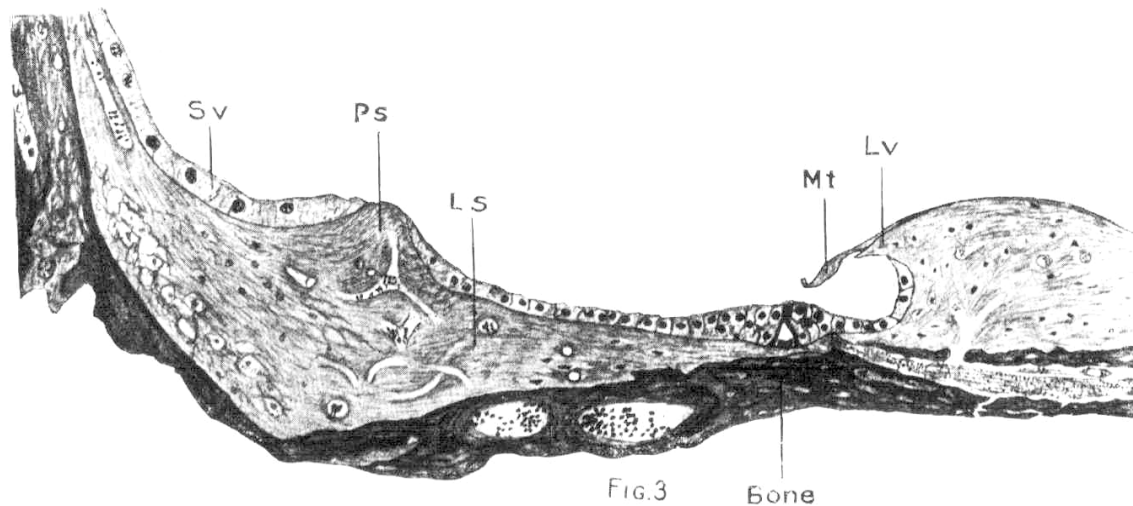


Fig. 3.6. A pig's organ of Corti, perfectly formed, sitting upon a solid bony plate. [From Fig. 3 of Shambaugh (1907)]

3.2/e Holes in the basilar membrane

1. That same temporal bone study⁸⁴ found other malformations in which there was either a hole in the basilar membrane or the bone separating one cochlear turn from another was lacking. In the first case there was open communication between the upper gallery of the first turn and the lower one of the second; in the second, two cochlear ducts stretched across one common channel. Again, the hearing thresholds of the affected ears were indistinguishable from those in the opposite, normally constructed, ears. One might predict that such holes would short-circuit a traveling wave, destroying sensitivity to all frequencies apical to the hole, but this did not happen. Another experiment reported by Tonndorf (loc. cit.) leads in a similar direction: Tasaki, Davis, and Legoux (1952) induced open communication between the adjacent turns of a guinea pig cochlea and found that cochlear microphonics apical to the injury site were unaffected.

2. In many species of birds there is a naturally occurring shunt through the basilar membrane called the ductus brevis^{85,86}. In contrast to the helicotrema, it connects the galleries *at the basal end*. According to Kohlöffel, it is variable in size

⁸⁴ Polvogt, L. M. and S. J. Crowe (1937). Anomalies of the cochlea in patients with normal hearing. *Ann. Otol. Rhinol. Laryngol.* 46: 579-591.

⁸⁵ Kohlöffel (1983)

⁸⁶ Kohlöffel, L. U. E. (1984). Notes on the comparative mechanics of hearing. II. On cochlear shunts in birds. *Hear. Res.* 13: 77-81.

and occurrence, being absent in owls and extremely narrow in turkey, pheasant, and quail; in contrast, it is present in pigeon, woodpecker, duck, and songbirds, and is especially wide in goose, reaching a diameter of 0.6 mm. The anatomy of birds forced Helmholtz to reconsider his theory, and it appears these creatures once more prompt us to re-examine our models.

3. Finally, let us look more closely at normal human anatomy. We tend to accept the presence of the helicotrema as a convenient way for pressure in the two galleries to be equalized. The hole, about 0.4 mm^2 in area, connects two ducts of about 1.2 mm^2 (*EiH*, p. 435).

But the form of the hole, as shown in Fig. 3.7, invites comment. There is no differential pressure at the helicotrema – it behaves hydraulically as a short circuit – and yet the organ of Corti retains the same form here as it does elsewhere in the cochlea: positioned near the apex of the triangular cochlear duct, but *without a basilar membrane underneath*. The question needs to be asked, are the hair cells at the helicotrema functional, because, if they are, they do not appear to be stimulated by motion of a basilar membrane.

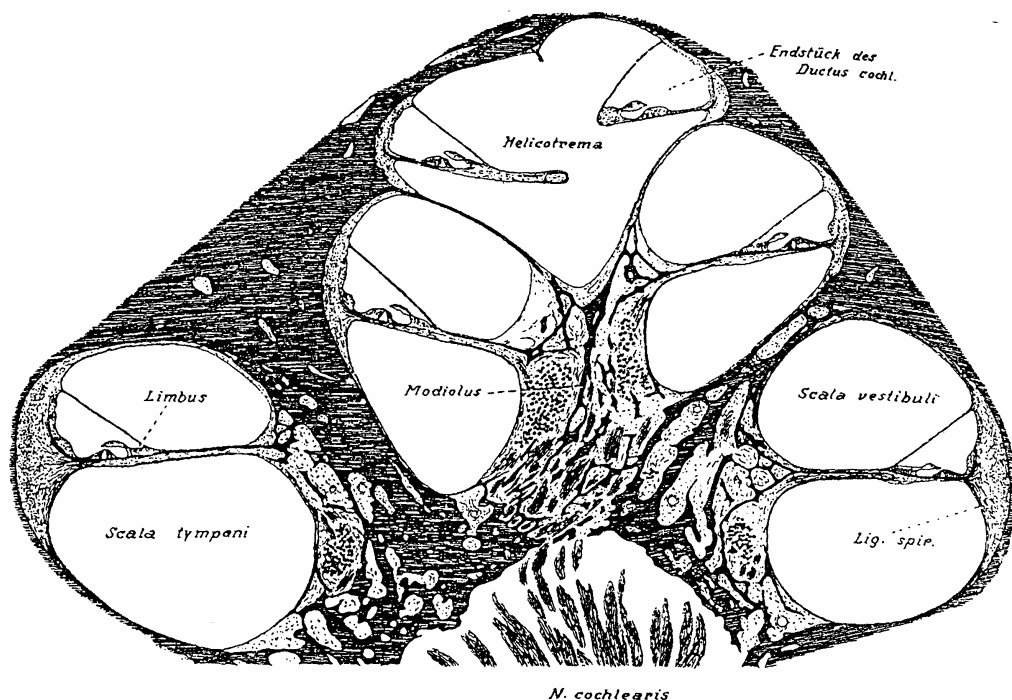


Fig. 3.7. Human cochlea, showing the form of the cochlear duct at the helicotrema⁸⁷. The organ of Corti retains its standard form, even though the differential pressure is zero. [From Fig. 9 of Neubert (1950) and reproduced with permission of Springer-Verlag]

⁸⁷ Neubert, K. (1950). Die Basilarmembran des Menschen und ihr Verankerungssystem: ein morphologischer Beitrag zur Theorie des Hörens. *Zeitschrift für Anatomie und Entwicklungsgeschichte* 114: 539-588. A similar picture is depicted in de Boer (1984), Fig. 3.1a.

3.2/f Zero crossings

As pointed out by Shera (2001), the cochlea possesses a remarkable symmetry⁸⁸. As the intensity of stimulation increases, the zero crossings of the basilar membrane response (and acoustic nerve firings) stay fixed. Although the waveform's centre of gravity moves to shorter times, the zero points stay put, as Fig. 3.8 makes plain. The phenomenon rules over nearly the entire dynamic range of the cochlea.

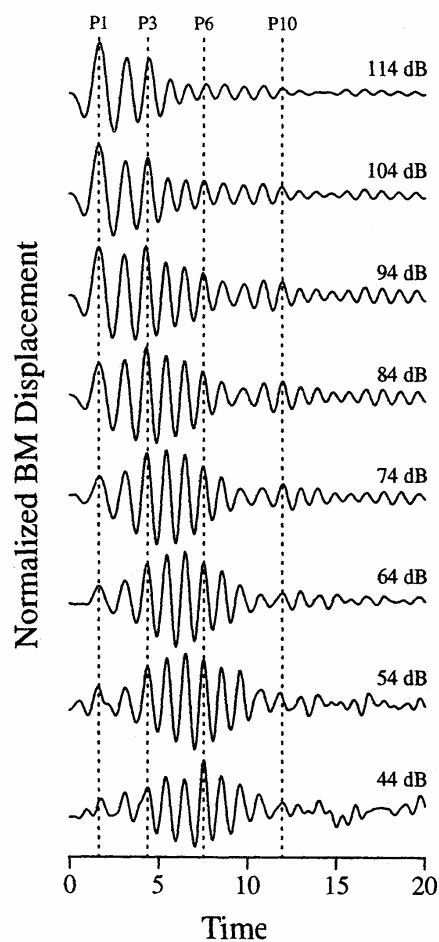


Fig. 3.8. Fixed zero crossings. As the intensity of a 1-kHz tone was raised from 44 to 114 dB, the basilar membrane motion of a chinchilla was monitored by a laser vibrometer. The time is in periods of 14.5 kHz (CF). The structure of the wave form in the time domain stays virtually constant. [From Recio and Rhode (2000) via Shera (2001), and used with permission of the Acoustical Society of America]

⁸⁸ Shera, C. A. (2001). Intensity-invariance of fine-structure in basilar-membrane click responses: implications for cochlear mechanics. *J. Acoust. Soc. Am.* 110: 332-348.

Physically, the effect only makes sense, says Shera, if the local resonant frequencies of the partition are nearly independent of intensity. This places strong constraints on the way that outer hair cells work, calling for the cochlear amplifier not to affect the natural resonant frequency of its surroundings as it works to supply feedback forces. In fact, *it contradicts many, if not most, cochlear models* (pp. 332, 345). In particular, it rules out all those models that require the outer hair cells to alter the stiffness (and impedance) of the partition.

Shera presents a detailed mathematical analysis of how a harmonic oscillator interacts with a traveling wave, and how the dispersion of the latter introduces time and frequency effects. He sets out certain conditions under which the oscillator's poles may stay fixed, but in general a traveling wave model will fail this requirement⁸⁹. On the other hand, it seems clear that a pure resonance model – such as the SAW model – will cope much better in meeting this condition: the independent oscillators will just gain strength as stimulus intensity is raised and the frequency (and time) structure will be preserved.

de Boer and Nuttall (2003) recognise the peculiarity of the zero crossings⁹⁰, but cannot suggest an answer. In fact, their active 'feed-forward' model doesn't help because it is 'non-causal', meaning that motion of the basilar membrane at one point would instantaneously affect points further away⁹¹. Chadwick (1997) saw the drawback of such non-causality⁹², and remarked that it would mean a non-unique, non-realizable, and less useful model. I agree that this way of refining traveling wave models strains understanding, although it may be useful to see that from a traveling wave perspective a fast pressure wave is in fact non-causal.

⁸⁹ Cooper (2004) explains how low-frequency components will travel further and slightly faster than the high-frequency components, and low-intensity sounds will travel slightly further and slightly more slowly than higher intensity ones. [Cooper, N. P. (2004). Compression in the peripheral auditory system. In: *Compression: From Cochlea to Cochlear Implants*, edited by S. P. Bacon et al. (Springer: New York), 18-61.] It makes one ask how the auditory system, on this basis, can disentangle the components.

⁹⁰ de Boer, E. and A. L. Nuttall (2003). Properties of amplifying elements in the cochlea. In: *Biophysics of the Cochlea: From Molecules to Models*, edited by A. W. Gummer (World Scientific: Singapore), 331-342.

⁹¹ A system is causal if it doesn't depend on future values of the input to determine its output. A non-causal system senses an input coming and gives an output before it does (Antoulas and Slavinsky, <http://cnx.rice.edu/content/m2102/latest/>)

⁹² Chadwick, R. S. (1997). What should be the goals of cochlear modeling? *J. Acoust. Soc. Am.* 102: 3054. Subsequently, de Boer defended his model [de Boer, E. (1999). Abstract exercises in cochlear modeling: reply. *J. Acoust. Soc. Am.* 105: 2984.]

3.2/g *Hear with no middle ear*

Before the days of antibiotics, it would be common for a middle ear infection to escalate to the point where there was total loss of the middle ear, including ear drum. The result was that the person was left only with oval and round windows, which opened directly to the ear canal. Surprisingly, such people do not suffer total hearing loss; they lose some 20–60 dB in sensitivity, but they can still hear, more so at low frequencies than high. In terms of the traveling wave theory, that is a major anomaly, because there should be no pressure difference across the partition to generate a stimulus, and any phase difference between the windows should virtually disappear at low frequency.

Békésy recognised the contradiction, and sought to explain it (*EiH*, p. 105–108). He suggested that the cochlea was not incompressible, so that even when sound impinged on the two windows in phase, the pressure could cause some movement of the windows. He imagined that some of the cochlear fluids could surge in and out of the cochlea through blood vessels or the “third windows” of the vestibular and cochlear aqueducts. If fluid flow is easier on the stapes side (it short-circuits stapes pressure), the round window pressure will force fluid to deflect the basilar membrane in a direction opposite to the usual – and hence the phase perception will be 180° different. Sound localisation experiments indeed show that, remarkably, people with only one middle ear hear sound 180° out of phase in that ear (*EiH*, Fig. 5-12), which tends to confirm Békésy’s conjecture⁹³.

Through introducing this mechanism, traveling wave theory can avoid an inherent contradiction. However, it is mentioned here as a signal that an alternative explanation is possible: that the outer hair cells can be stimulated directly by pressure.

No matter what model one chooses, the “middleless” ear configuration provides major constraints on the compressibility of the cochlea, as Shera (1992) calculated⁹⁴. He uses a network model and Békésy’s data to show that the degree of

⁹³ However, this fact is interpreted differently in Ch. 9 where it is used as evidence that the ear uses two detection systems: a pressure-detection one involving the outer hair cells, and a deflection mechanism involving the inner hair cells.

⁹⁴ Shera, C. A. and G. Zweig (1992). An empirical bound on the compressibility of the cochlea. *J. Acoust. Soc. Am.* 92: 1382-1388.

compressibility (ε , the ratio between the stiffness of the organ of Corti to the compressional stiffness of scala media) must be less than a few percent, but greater than zero (p. 1385). Similarly, Ravicz and colleagues⁹⁵ performed experiments on cochleas of human cadavers and expressed the compressibility as an upper bound on a parameter α , where α was the ratio of the motion of the stapes with the round window blocked to the motion normally. They found α to range from 0.015 (at 500 Hz) to 0.5 (at 30 Hz).

The result obviously depends on the model, but it is worth keeping in mind as we consider how compressible living outer hair cells might be (Ch. D8) and evidence advanced against any compressibility whatever (§I 3.3/c below).

3.2/h Hear with blocked round window

The traveling wave depends on a pressure difference between the oval window and the round window. Blocking the round window may then be expected to be a recipe for total loss of hearing. Again, that isn't the case.

The most startling and clear-cut instances are congenital, in which a person is born without a round window, an uncommon malformation called round window atresia⁹⁶. Instead, the round window niche is filled with bone and the person suffers a hearing loss of 30–40 dB.

Martin et al. (2002) confirmed the diagnosis in a bilateral case with high-resolution CT scans and found associated hearing losses of about 40 dB⁹⁷. They held back from surgery because they regard fenestration as likely to cause hearing loss rather than improvement. They mention (p. 801) that when round window absence is found in combination with stapes fixation, surgery is likely to lead to *hearing loss* (that is, they advise not interfering because the person is still able to hear). Linder et al. (2003) also did CT scans to confirm the condition in two cases and expressed puzzlement (p. 262) at the limited hearing deficit (40 dB or so), as they expected

⁹⁵ Ravicz, M. E., et al. (1996). An upper bound on the compressibility of the human cochlea. Midwinter Meeting, Association for Research in Otolaryngology (<http://www.mit.edu/~ajmiller/epl/RaviczARO1996.pdf>)

⁹⁶ Linder, T. E., et al. (2003). Round window atresia and its effect on sound transmission. *Otology and Neurotology* 24: 259-263.

⁹⁷ Martin, C., et al. (2002). Isolated congenital round window absence. *Ann. Otol. Rhinol. Laryngol.* 111: 799-801.

complete conductive hearing loss. They conclude that, instead of a traveling wave, the cochlea is sensitive to an alternative way of stimulation⁹⁸.

On the other hand, it is recognised that the pressure detection idea is not immune from criticism on this count either. If it were valid, then blocking the round window might be expected to increase hearing sensitivity, and this clearly does not happen. This problem is addressed in §D 8.2.

3.2/i Hear with no tectorial membrane

According to the standard model, motion of the basilar membrane causes shear between the stereocilia of the hair cells and the tectorial membrane. In a situation where the tectorial membrane is absent, one might reasonably conclude that all hearing would be absent, but again the real situation confounds this outlook.

It is possible to produce a knock-out gene in mice that leads to the loss of α -tectorin, an essential component of the tectorial membrane matrix⁹⁹. The result is that the affected mice have a completely detached tectorial membrane, and suffer a hearing loss of 35–40 dB. In terms of the standard model, however, we might expect to see total hearing loss, yet the authors report that outer hair cells still respond to sound with a reduced cochlear microphonic. How is that possible? One commentator¹⁰⁰ suggested that the stereocilia must be moved by fluid drag, which could happen if the hair cells were moving side to side as well as up and down.

However, in terms of the SAW model, a 40 dB loss is understandable because an essential feedback path is absent. However, it is still possible for the outer hair cells to provide an electrical response because they are reacting to the pressure wave, not a traveling wave. However, since the cells can no longer interact across rows,

⁹⁸ In the older literature, a mass of conflicting results on the role of the round window can be found, and not much ground can be gained by discussing it here. Many experimenters attempted to block the existing round windows of animals, but the problem is the extreme difficulty of achieving a true block, as even a minute air cavity would, given the vanishingly small displacements involved in hearing, provide sufficient compliance in the system. Nevertheless, they raise a real doubt about the necessity of a round window. One major doubt-raising paper [Hallpike, C. S. and P. Scott (1940). Observations on the function of the round window. *J. Physiol.* 99: 76-82.] favoured Pohlman's idea of pressure-sensitive cochlear receptors (p. 81).

⁹⁹ Legan, P. K., et al. (2000). A targeted deletion in α -tectorin reveals that the tectorial membrane is required for the gain and timing of cochlear feedback. *Neuron* 28: 273-285.

¹⁰⁰ Corey, D. P. (2000). Sound amplification in the inner ear: it takes TM to tango. *Neuron* 28: 7-9.

DPOAEs are impossible (see Chapter 7), and this is just what Legan et al. found (p. 276).

3.2/j *The casing of the cochlea is exceptionally hard*

The otic capsule in which the cochlea and its fluid contents are encased is noteworthy in its own right. The capsule is made of bone and, in humans, sits within the base of the skull. Remarkably, this bone is immensely hard, and this ivory-like bone is the hardest in the human body. Despite its small size, the otic capsule derives developmentally from 14 distinct ossification centres and the initial fetal architecture is maintained throughout adult life¹⁰¹.

In whales, the inner ear is separate from the skull, so that it forms a spherical mass, the os perioticum, that has been described as a very compact, stony-hard ‘glasslike’ bone¹⁰², the densest and hardest bone known in the animal kingdom. It is so solid that opening a specimen is a difficult and tedious job, often resulting in fracturing. When an animal dies, its soft spongy skeleton soon decays, but the os perioticum remains, littering the sea floor for millennia¹⁰³. The question therefore arises, why is the otic capsule so hard?

In terms of the standard model, this design effort is superfluous: all it has to do is contain the fluid contents and be adequately stiffer than the basilar membrane. Given the high compliance of the round window, the dense bone seems unnecessarily hard.

On the other hand, if the cochlea is designed to detect acoustic pressure, then the outlook changes considerably. In this case, the difference in acoustic impedance between the cochlear fluids and that of the capsule is crucial: acoustic energy will leak out of the cochlea unless there is a large ratio in acoustic impedance between the two. In terms of the proportion of energy reflected (R) at a boundary, Fletcher (1992) shows that (p. 98)

¹⁰¹ Jahn, A. F. (1988). Bone physiology of the temporal bone, otic capsule, and ossicles. In: *Physiology of the Ear*, edited by A. F. Jahn and J. Santos-Sacchi (Raven: New York), 143-158.

¹⁰² Reysenbach de Haan, F. W. (1956). Hearing in whales. *Acta Oto-Laryngologica Suppl.* 134: 1-114. [p. 44]

¹⁰³ Fossilised inner ear bones of whales, millions of years old, are therefore common [as a Google search confirms] and can be bought over the internet for a few dollars.

$$R = (z_2 - z_1)^2 / (z_1 + z_2)^2 \quad (3.14)$$

where z_1 and z_2 are the acoustic impedances of the two media. To prevent loss of acoustic energy from the cochlear fluids ($z = 1.5 \times 10^6$ rayl) into the skull, it therefore becomes important to make the acoustic impedance (ρc) of the surrounding bone as high as possible. The speed of sound in typical bone is about twice that in water, and its density greater by a similar factor, so that, using Eq. 3.14, we find that the energy reflected at the interface is only about a third. By making the density of cochlear bone double that of ordinary bone, the reflectance figure can be made to exceed 50%, which is then beginning to become a useful figure for containing the pressure wave. This is even more vital in the case of whales, because the loss will be not just to the skull, but to the surrounding water¹⁰⁴.

Interestingly, in guinea pigs and other rodents, the cochlea is encased only in thin bone and projects from the skull of the animal, a configuration greatly different to that in humans¹⁰⁵ and leading to the suspicion that the hearing process in these animals may differ in important respects from ours.

The issue of optimal design of the cochlea is a major one, and will be dealt with in the concluding chapter. Nevertheless, it is worth noting here that if the cochlea is configured to detect the fast pressure wave, then the presence of a round window nearby to an oval window appears counterproductive: if the windows move out of phase to each other, then the pressure waves generated by each would tend to cancel, leaving an evanescent wave which should decay rapidly with increasing distance from the windows. To avoid cancellation, a better design for pressure detection would be to have the round window at the far (apical) end of the cochlea, but the possibility is nonetheless worth exploring.

3.2/k *Fast responses*

Traveling waves progress relatively slowly, starting at the base at about 100 m/s and slowing down until at the apex their speed is more like 1 m/s. The slow

¹⁰⁴ Whale hearing is discussed in more detail in §3.3, where the special arrangement of their round window is outlined.

¹⁰⁵ Wysocki, J. (2005). Topographical anatomy of the guinea pig temporal bone. *Hear. Res.* 199: 103-110.

speed is understood as the basis of the time delay in Kemp echoes, where the travel time to a tuned place on the partition and its return to the stapes underlies the long delays observed¹⁰⁶. Here we note cases where the cochlear responses are too fast to be mediated by a traveling wave, and instead a fast pressure wave must be carrying them.

1. *Wilson hair-cell swelling model.* The credit for seeing an association between outer hair cells and fast pressure waves must, in modern times, go to Wilson. Although he kept to the idea of traveling waves exciting the cells, he proposed that the activity of outer hair cells produced a change in volume, so that in this way a pressure wave could be *generated* and return almost instantly to the ear canal, thereby explaining Kemp echoes. This *hair-cell swelling model* was presented in a 1980 paper¹⁰⁷ as a way of explaining why the cochlear microphonic recorded at the round window in response to a low-level 800-Hz tone burst appeared to occur simultaneously with the ear canal pressure recorded with a microphone.

Since the electrical signal was instantaneous, so too must have been the acoustic signal conveyed from the outer hair cell, and a pressure wave is the only signal carrier fast enough. The data in the paper are not convincing by themselves, but the idea is an engaging one. However, in going against the mainstream it has not caught on¹⁰⁸.

If there is a negligible reverse travel time, where do long response times come from? Wilson still retained the idea that acoustic stimulation reached the outer hair cells via the traveling wave, but, even allowing for that forward propagation path, the long total echo delay meant an extra source of delay must be sought. He attributed this to the delay inherent in building up oscillation in a narrowly tuned filter – the ‘second filter’ delay. Noting that such an extended delay means the corresponding tuning would be uncommonly narrow – narrower than observed inner hair cell tuning – he suggested that the outer hair cells are actually more sharply tuned than inner hair cells. We are back into Gold territory.

¹⁰⁶ Even though making the time delay equal to twice the travel time is not as straightforward as it seems. For example, Shera and Guinan (2003) find that the delay is about 1.3–1.9 times the one-way travel time.

¹⁰⁷ Wilson, J. P. (1980). Model for cochlear echoes and tinnitus based on an observed electrical correlate. *Hear. Res.* 2: 527-532.

¹⁰⁸ It was considered briefly on pp. 522-523 of de Boer, E. (1980). Nonlinear interactions and the ‘Kemp echo’. *Hear. Res.* 2: 519-526. Wilson’s name was not attached to it, but the idea was considered unlikely and not considered further.

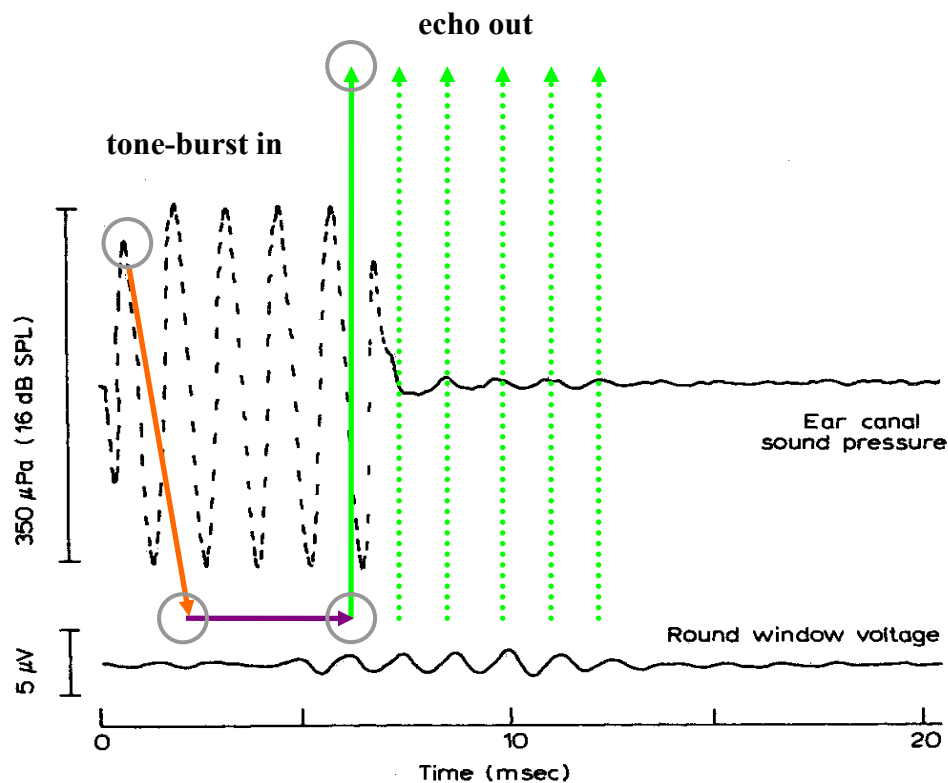


Fig. 3.9. In response to a tone-burst stimulus, the ear canal pressure of the echo (recorded with a microphone) occurred simultaneously with the voltage due to the cochlear microphonic (recorded with an electrode). This suggested to Wilson that a fast pressure pulse (nearly as fast as the electrical correlate) was conveying the echo from the 800-Hz position on the basilar membrane to the ear canal. Stimulus enters cochlea as traveling wave (orange), builds up oscillation in second filter (maroon), and exits cochlea as pressure wave (green). [Adapted from Fig. 2 of Wilson (1980), with permission of Elsevier Science]

In earlier chapters the suggestion was made that Wilson's model be modified so as to introduce a simple symmetry: not only do outer hair cells produce a fast pressure wave but in addition the fast pressure wave directly stimulates the outer hair cells, in this way bypassing the traveling wave (at least at low sound pressure levels). Consequently, all the delays we see are now due to filter delay (the orange line in Fig. 3.9 becomes vertical, and the maroon line doubles in length), but given what we know about the sharpness of cochlear tuning, the additional factor of 2 should be able to be accommodated with a suitably high Q filter. Wilson calculates (the basis of which is not given) that the volume change necessary to produce an ear canal

pressure of 20 dB SPL would require less than a 0.01% volume change in 300 outer hair cells (p. 530) and my own calculations suggest that this may be reasonable¹⁰⁹.

All the remaining material in this section is consistent with a two-way fast pressure wave and a slow build up in a highly tuned resonator. The filter could equally be considered a first filter as a second one. A reinterpretation of Shera and Zweig along these lines was given in §I 3.1/d.

2. Fast distortion products. It has been known for a long time that cochlear distortion products can occur remarkably quickly. In 1985, Brown and Kemp measured distortion products in gerbils, both acoustically in the ear canal and electrically via the cochlear microphonic¹¹⁰. They found several instances of delays at a small fraction of a millisecond (their Fig. 2), but in the main the delays were between 0.5 and 1.3 ms, slightly shorter than a two-way traveling wave. They were more puzzled that the delays in upper sideband distortion products ($2f_2 - f_1$) were shorter than for upper ($2f_1 - f_2$), and suggested that the acoustic distortion product may reach the base as ‘fluid borne sound waves’ (p. 197), in accordance with Wilson’s proposal. Even so, the extremely short delays they measured were not highlighted.

A reason too much store has not been placed on distortion product measurements is that the mechanism is not well understood¹¹¹. It is generally supposed that the interaction of the two primary frequencies takes place where the two traveling wave envelopes overlap on the partition. The observed result is an extended series of peaks and troughs, including much fine structure. The rapid phase and amplitude variations make data collection difficult and it has been easier to ignore discordant data.

¹⁰⁹ An OHC 50 μm long and 10 μm in diameter occupies a volume of $4 \times 10^{-15} \text{ m}^3$. When 300 of them change volume by 0.01%, the volume change is 10^{-16} m^3 . The cochlear fluid is incompressible, so this volume will displace the stapes and round window (about equally) and cause $15\times$ this volume change at the ear drum. If the ear canal occupies a microphone-sealed volume of 1 cm^3 , the ear canal volume will change by about 1 part in 10^8 . Changing the ear canal pressure of 10^5 Pa by 1 in 10^8 gives a pressure of 10^{-3} Pa , and this is an SPL of 34 dB.

A change of 0.01% in volume could be effected by tilting the hinged cuticular plate by 0.1° . The cuticular plate can tilt by up to 15° [Zenner et al. (1988), p. 234].

¹¹⁰ Brown, A. M. and D. T. Kemp (1985). Intermodulation distortion in the cochlea: could basal vibration be the major cause of round window CM distortion? *Hear. Res.* 19: 191-198.

¹¹¹ A proposal is made in Chapter D7.

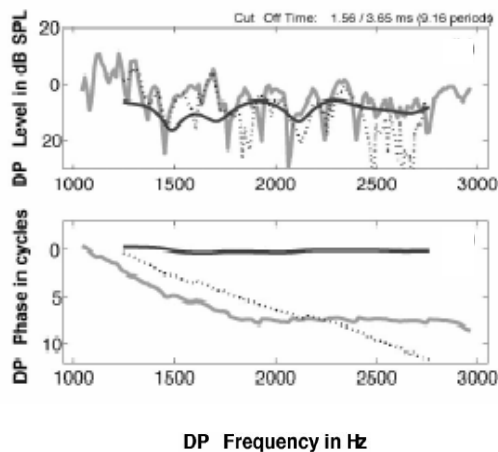


Fig. 3.10. Grey = black + dotted. How an actual DPOAE (grey line) can be separated into two components, a low-latency contribution (black line) and a high-latency one (dotted line). [Data is for a $2f_1 - f_2$ DPOAE with $f_2/f_1 = 1.2$ and $f_1 = 51$ dB and $f_2 = 30$ dB SPL. From Fig. 1 of Mauermann and Kollmeier (2004) with permission of the Acoustical Society of America]

The whole picture has recently been brought into sharp focus by a trio of papers^{112,113,114} that demonstrate that a given DPOAE signal can be separated into two discrete components. Goodman et al. (2003) used an inverse FFT method on guinea pig data, Shera used a suppressor tone near the $2f_1 - f_2$ frequency in a human, and Mauermann and Kollmeier (2004) employed a time-windowing procedure, again with human data. In such ways, the experimenters were able to separate DPOAEs into (using the most recent paper's terminology) a long-latency 'reflection' component (RCOAE, almost equivalent to an SFOAE) and a short-latency distortion component (DCOAE). The analyses reveal that a DPOAE is actually due to the interference of two components arising from two separate mechanisms, a conclusion that is not entirely new but which had not before been clearly demonstrated. As Fig. 3.10 illustrates, the separation provides a simpler picture of what may be going on.

¹¹² Goodman, S. S., et al. (2003). The origin of SFOAE microstructure in the guinea pig. *Hear. Res.* 183: 7-17.

¹¹³ Shera, C. A. (2004). Mechanisms of mammalian otoacoustic emission and their implications for the clinical utility of otoacoustic emissions. *Ear Hear.* 25: 86-97. See also Fig. 9 of Shera and Guinan (1999).

¹¹⁴ Mauermann, M. and B. Kollmeier (2004). Distortion product otoacoustic emission (DPOAE) input/output functions and the influence of the second DPOAE source. *J. Acoust. Soc. Am.* 116: 2199-2212.

In terms of amplitude variations, we see that instead of wide-ranging peaks and nulls the amplitude excursions are generally less. More dramatically, we see that the DPOAE phase curve is decomposed into two almost linear components: an RCOAE plot with a slope of about -1 cycle per 138 Hz, and a DCOAE plot, *almost horizontal*, with a slope of no more than about -1 cycle per 10 000 Hz. A major conclusion for the discussion here is that the horizontal component corresponds to a delay of no more than 0.1 ms and possibly much less, whereas the slow component corresponds to a delay of about 7.2 ms. The Shera paper shows a phase lag of less than 30° over the frequency range 2.6–7 kHz, corresponding to a time delay of about 34 μ s, whereas the Goodman et al. paper show an average phase slope of -55° over 2–10 kHz, equivalent to a lag of some 19 μ s. These are extremely small delays, suggestive of a fast mechanism – perhaps, I would venture, a compression wave. Shera has argued¹¹⁵ against any naïve equivalence between DPOAE phase gradients and wave travel times, but there is reason to think¹¹⁶ that the low phase gradient in fact represents the action of the pressure wave. The complete inference (drawn in more detail in Chapter R7) is that DPOAEs are due to the interaction of two tones at a single place on the partition where there are two highly tuned resonators; the tones enter and exit the cochlea via fast compression waves, and in between they interact through the slow build-up of highly tuned resonators.

Such a picture may be disputed, but it does at least suggest that further examination of the phase slope of DCOAEs is warranted, as it certainly looks like a fast wave underlies them¹¹⁷. A recent paper¹¹⁸ confirms such an interpretation: it observed SFOAE latencies and found that “many of the latencies were too short to be considered valid” and were “apparently inconsistent with the reflection source hypothesis” (p. 3811). One of the explanations considered for the recurring “invalid” data is the reverse transmission path through the fluid, although the authors underline the need to reconcile this with long-latency observations, which are consistent with the conventional round-trip concept. The model in the preceding paragraph does this.

¹¹⁵ Footnote 27 of Shera and Guinan (1999).

¹¹⁶ Fuller, R. B. (1975). *Synergetics: Explorations in the Geometry of Thinking*. (Macmillan: New York). [p. xix]

¹¹⁷ In all the papers showing a near-horizontal phase plot, none has sought to provide a physical interpretation.

¹¹⁸ Konrad-Martin and Keefe Transient-evoked stimulus-frequency and distortion-product otoacoustic emissions in normal and impaired ears.

3. Fast suppression. The amplitude and frequency of a spontaneous emission can be disturbed by projecting a suppressing tone into the cochlea, and recording the time course of the process gives useful information about the oscillator dynamics. In one such study, the experimenters found that just prior to release from suppression, a prominent short-lived dip appeared¹¹⁹. The time-constant of the dip was found (p. 3718) to be 0.03 ms, a lag which strains an explanation based on interactions of traveling waves but matches the figures derived from the DPOAE phase measurements.

3.2/I A bootstrap problem

An interesting perspective on the traveling wave theory is given¹²⁰ by Fukazawa (2002). If the fundamental stimulus to the outer hair cells is differential pressure – that is, pressure across the partition – how can the outer hair cells, embedded *in* the membrane, cause any change in that differential pressure? That is, the outer hair cells have nothing to push against: any force generated by them will pull down on the plateau of Corti at the same time as they push against the basilar membrane and the forces will cancel. It is the classic bootstrap problem in which internal forces can never change the momentum of a system. Fukazawa concludes that the cochlear amplifier can never get off the ground.

3.2/m No backward traveling wave

Kemp introduced the idea of a backward traveling wave in order to explain cochlear echoes, and the concept is now a standard part of the modern traveling wave model (see §I 3.1/d), even though a backward traveling wave has never been directly observed. Wilson queried the concept¹²¹ in 1988, but it has persisted because without it active cochlear mechanics is left high and dry. A provocative discussion on the

¹¹⁹ Fig. 2c (p. 3714) of Murphy, W. J., et al. (1995). Relaxation dynamics of spontaneous otoacoustic emissions perturbed by external tones. II. Suppression of interacting emissions. *J. Acoust. Soc. Am.* 97: 3711-3720.

¹²⁰ Fukazawa, T. (2002). How can the cochlear amplifier be realized by the outer hair cells which have nothing to push against? *Hear. Res.* 172: 53–61.

¹²¹ p. 114 of *Basic Issues in Hearing*, ed. Duifhuis, Horst, Wit (Academic, London, 1988).

issue can be found on pp. 583–586 of *Biophysics of the Cochlea*¹²² in which Dallos concurs that “there is absolutely no experimental evidence that shows there is a backward travelling wave.”¹²³

It is impossible to prove a negative, since lack of evidence is not evidence of lack. Perhaps the traveling wave is at such a low level it is beyond observation. Nevertheless, the longer it remains unobserved, the more doubts grow. The latest observations to draw a blank¹²⁴ were done on the gerbil cochlea by Ren (2004) using a scanning laser interferometer to detect vibration of the stapes and of the partition. He projected two tones into the cochlea and detected the DPOAE at $2f_1-f_2$. Significantly, the interaction generated a forward traveling wave – he could see the stapes vibrate at the $2f_1-f_2$ frequency 50 μ s before the basilar membrane at its best frequency did – but he could not see any motion on the basilar membrane before that stapes vibration. So what caused the stapes to vibrate? There didn’t seem to be any backward traveling wave, so Ren proposes a compression wave, even though he acknowledges it contradicts current theory. In supplementary material on the *Nature* web site, Ren discusses similar work by Narayan et al. (1998) and concludes that “This unambiguous finding in different species of experimental animals by two independent laboratories clearly demonstrates that the stapes vibration at the emission frequency and the consequent resulting otoacoustic emission in the ear canal are not mediated by the hypothetical backward travelling wave.”

The problem of anomalous round trip travel times was raised in §I 3.1/d, and this also strengthens doubts about the existence of backward traveling waves.

In brief, there are certain difficulties underlying traveling wave theory, and these are magnified when trying to sustain the case for a backward-traveling version.

¹²² Ed. A. W. Gummer (World Scientific, Singapore, 2003).

¹²³ Gummer (2003) p. 584. Long candidly admits that “I think it goes back to most published experiments – they only show the beautiful and simple results. Every time I have done transient-evoked emissions and even in some of our distortion-product emissions, although the major returning wave has a two-times travel-time, there are indications of a one-time travel-time, and [even though] Pat Wilson talked about it [and] other people have talked about it, it is not talked about much, we can’t explain it, so we don’t tend to stress it, but I am sure that it is there.” [ibid., p. 585]

¹²⁴ Ren, T. (2004). Reverse propagation of sound in the gerbil cochlea. *Nat. Neurosci.* 7: 333-334.

3.3 Summary

This wide-ranging discussion has highlighted the major limitations of the traveling wave theory and has shown how these may have to do with neglecting the round window membrane and its generation of common-mode pressure. A later part of this thesis (Chapter D8) sets out evidence that outer hair cells do in fact appear to act as pressure detectors, and a mechanism is described whereby this could happen. However, at this point the hypothesis that outer hair cells detect acoustic pressure is taken as a viable theory, and a model of how this process – likened to a surface acoustic wave (SAW) resonator – could operate in the cochlea is presented in the following chapter. We will return to considerations of pressure detection in the cochlea in an assessment of supporting evidence for the model in Chapter D9.

Cochlear fine-tuning: a surface acoustic wave resonator

- 4.1 Introduction
- 4.2 Basic description of the model
- 4.3 Parallels between SAW devices and the cochlea
- 4.4 Prima facie validity
- 4.5 What is the wave propagation mode?

This chapter introduces the idea that the cochlea analyses sound in a way resembling electronic surface acoustic wave (SAW) devices. The outer hair cells (OHCs) of our cochlea typically occur in three distinct rows¹, and it is suggested the rows act like the interdigital electrodes of a single-port SAW resonator. Frequency analysis occurs through sympathetic resonance of a graded bank of these resonators. This active process relies on the motor properties of OHCs: as well as being sensors, OHCs undergo cycle-by-cycle length changes in response to stimulation. The SAW analogy works if the motility of one row of cells can be communicated to a neighbouring row, allowing positive feedback between one cell's body (an effector) and another's stereocilia (a sensor). If the wavelength of the disturbance were comparable to the row spacing then inter-row reverberation could occur. A candidate wave possessing the required properties has been identified – a ‘squirting wave’ known in ultrasonics – and this wave, operating in the subtectorial space between the tectorial membrane and the plateau of Corti, is described in Chapter R5.

¹ As we will see in Chapter R6, occasional extra rows are not a problem.

Standing-wave resonance between the rows could thus provide amplification and high Q , characteristics underlying the ‘cochlear amplifier’ – the device whose action is evident to auditory science but the identity of which has not yet been established. Also emerging naturally from such a local interaction on the partition are spontaneous, evoked, and distortion-product emissions (Chapter R7).

The SAW mechanism, as outlined in this chapter, may provide a second filter for a primary traveling wave stimulus, and this cannot be ruled out without further experiments. The advantage of taking this approach is conformity with the standard model. The drive of this thesis, however, is towards a simple resonance theory of hearing along the lines of Helmholtz, in which case we require that the input to the SAW is the fast pressure wave stimulus. The advantage here is simplification of cochlear mechanics. A later chapter (Chapter D8) strengthens the supposition about pressure sensitivity.

4.1 Introduction

Earlier chapters have focused on the cochlea’s behaviour as an active transducer, a necessary consideration flowing from Kemp’s seminal discovery² of sound emerging from the ear. An essential element of the auditory organ is therefore a ‘cochlear amplifier’ whose action improves gain and tuning. If the gain is excessive at some frequency, the cochlea will spontaneously oscillate, a possible source of ‘spontaneous otoacoustic emissions’ – soft, pure tones – that may be detected with a microphone placed in the ear canal. Most human ears continuously emit such tones at frequencies of 1–4 kHz and with bandwidths ranging down to 1 Hz or less. A detailed review³ of these developments was given by Robinette and Glatcke in 2002.

What sort of biological structure could produce such pure tones? The outer hair cells (OHCs) must be intimately involved, for these sensing cells are active, possessing a property known as ‘electromotility’. When an audio-frequency voltage

² Kemp, D. T. (1979). Evidence of mechanical nonlinearity and frequency selective wave amplification in the cochlea. *Arch. Otorhinolaryngol.* 224: 37-45.

³ Robinette, M. S. and T. J. Glatcke (2002). *Otoacoustic Emissions: Clinical Applications*. (Thieme: New York).

is applied to an isolated cell, it synchronously changes length⁴. Nevertheless, how the cochlear amplifier harnesses electromotility is unknown. This thesis offers a possible solution.

The standard cochlear model assumes that stimulation of hair cells occurs by a hydrodynamic *traveling wave* moving along the partition. The difficulty has been to understand how the response of such an intrinsically broad-tuned system can be sharpened to give the fine frequency resolution it displays⁵. This chapter puts forward a proposal whereby the unique structure of the sensing surface of the cochlea can achieve narrow-band frequency analysis. It conjectures that the cochlear amplifier is based upon the cooperative activity of neighbouring OHCs, which work together like the interdigital electrodes of the SAW resonator^{6,7}.

4.2 Basic description of the model

The SAW model builds on a remarkable fact: in all higher animals, including humans, OHCs lie in three (or more) well-defined rows (Fig. 4.1), hitherto unexplained.

SAW devices are signal-processing modules in which finger-like electrodes are interleaved on the surface of a piezoelectric substrate to create slowly propagating electromechanical ripples of wavelength equal to the periodicity of the interdigital electrodes^{8,9}. The minimum number of electrode fingers is three (Fig. 4.2), an arrangement giving the widest bandwidth response¹⁰.

⁴ Brownell, W. E., et al. (1985). Evoked mechanical responses of isolated cochlear outer hair cells. *Science* 227: 194-196.

⁵ Patuzzi, R. B. (1996). Cochlear micromechanics and macromechanics. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 186–257.

⁶ Campbell, C. K. (1998). *Surface Acoustic Wave Devices for Mobile and Wireless Communications*. (Academic Press: San Diego).

⁷ Ballantine, D. S., et al. (1997). *Acoustic Wave Sensors: Theory, Design, and Physico-Chemical Applications*. (Academic: San Diego).

⁸ Bell, D. T. and R. C. Li (1976). Surface-acoustic-wave resonators. *Proc. IEEE* 64: 711-721.

⁹ Smith, W. R. (1981). Circuit-model analysis and design of interdigital transducers for surface acoustic wave devices. In: *Physical Acoustics*, edited by W. P. Mason and R. N. Thurston (Academic: New York), 15, 99-189.

¹⁰ Campbell (1998), p. 501.

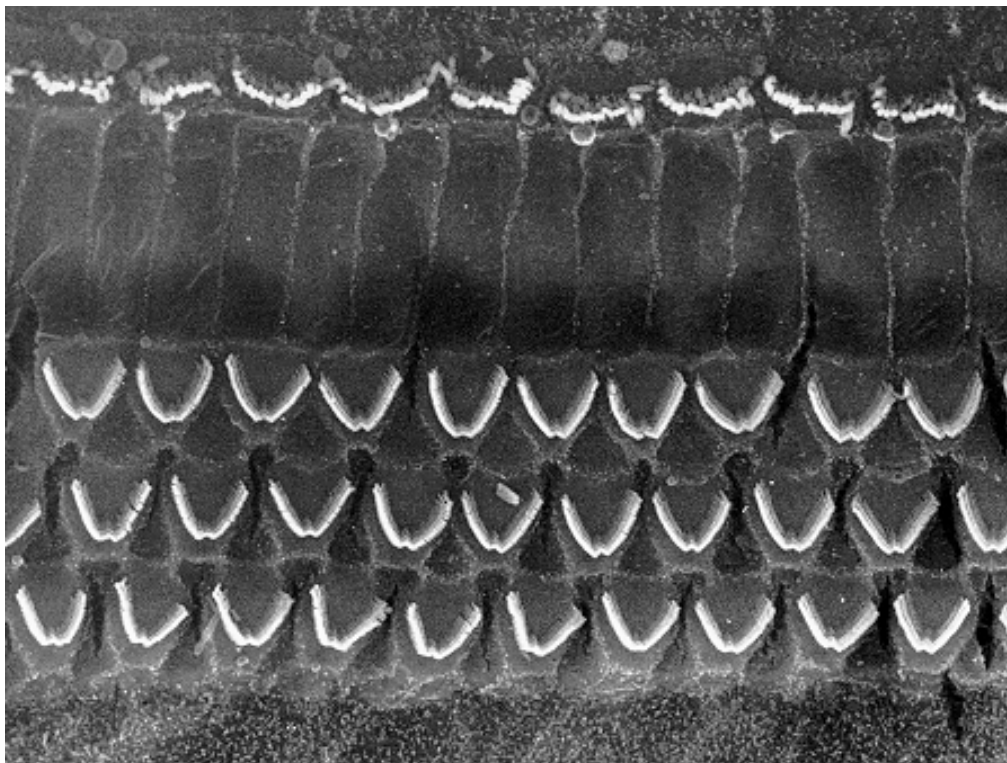


Fig. 4.1. Three rows of outer hair cells (bottom) and one row of inner hair cells (top) in the cochlea of a rabbit. Spacing between OHC rows is about 15 μm . [From Counter et al. (1993)¹¹ with permission of S. A. Counter (Karolinska Institute) and Elsevier Science]

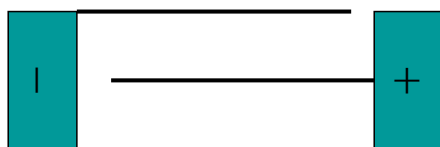


Fig. 4.2. The simplest interdigital electrode has three fingers.

The SAW resonator (Fig. 4.3) has a topology in which the electromechanical waves on the surface are arranged in a feedback loop between two sets of electrodes – a ‘two-port’ system, normally operated as a delay line, in which one set of electrodes launches the ripples and a similar set some distance away detects them.

¹¹ Counter, S. A. (1993). Electromagnetic stimulation of the auditory system: effects and side-effects. *Scand. Audiol. Suppl.* 37: 1-32.

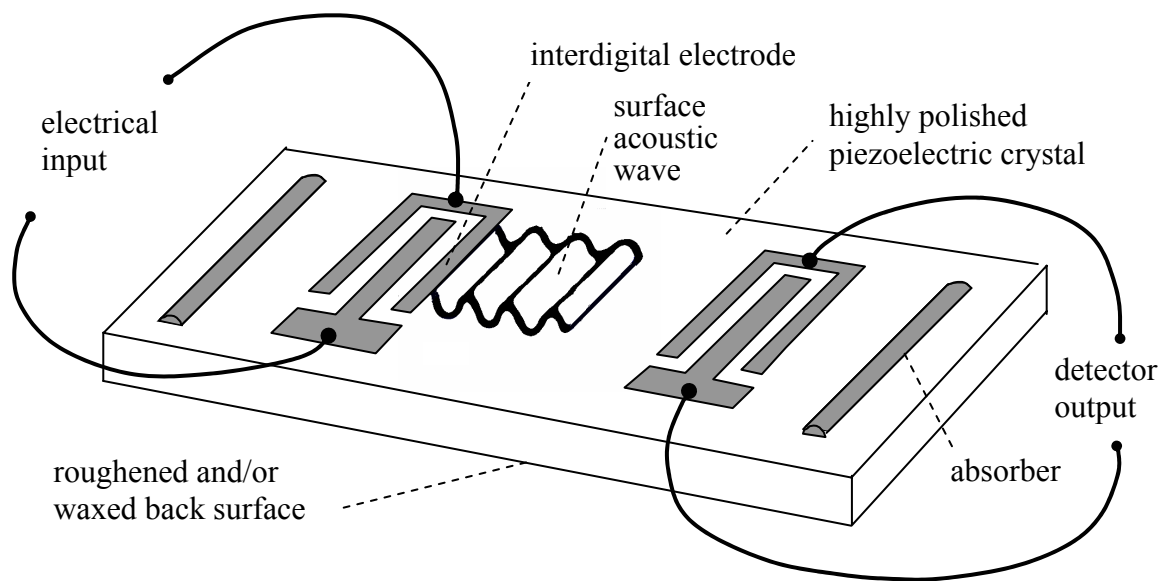


Fig. 4.3. Schematic of surface acoustic wave delay line (after Maines and Paige, 1976). Electromechanical ripples are generated and detected by two sets of interdigital electrodes on a piezoelectric substrate to give a delay line. Driving and sensing functions can be combined into a single set of electrodes with resonance between the fingers.

SAW modules are used whenever a number of cycles of signal need to be stored and operated on. Feeding the output of the second set of electrodes back to the input set creates a highly tuned resonance ($Q \approx 10^3\text{--}10^4$) typically in the megahertz range. Resonance can also occur when the two sets of electrodes are merged into a ‘single-port’ resonator¹²; in this degenerate case, ripples now reverberate back and forth between the fingers instead of between the two electrode sets. The present hypothesis is that audiofrequency resonances arise in the cochlea in a similar way (Fig. 4.4).

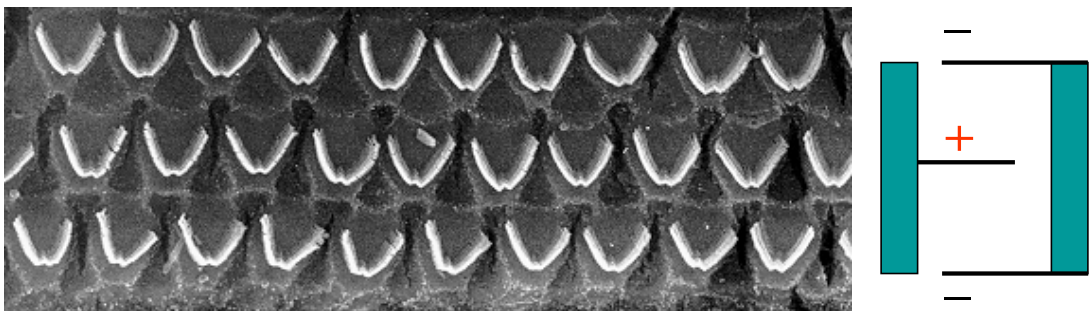


Fig. 4.4. The rows of outer hair cells are assumed to act like the 3 fingers of an interdigital transducer.

¹² Bell and Li (1976); Campbell (1998), Ch. 11.3.

M 4 [6]

The model is most easily conveyed by reference to Fig. 4.5, which shows a cross-section of the cochlear partition. The key components are the three rows of OHCs overlain by the soft gel¹³ of the tectorial membrane (TM) in which the tips of the hair-like stereocilia are embedded. Forced oscillation of an OHC could send out waves that, if sufficiently slow, will have wavelengths comparable to the OHC row spacing.

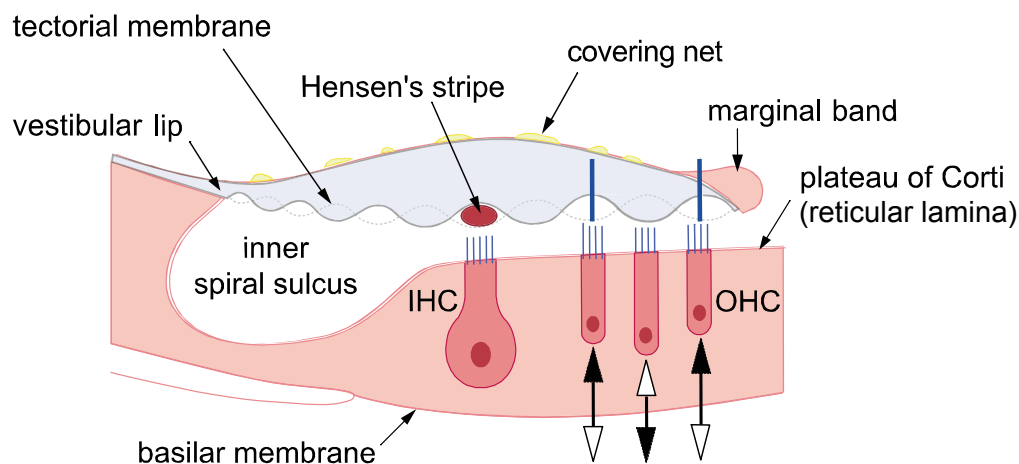


Fig. 4.5. Because outer hair cells are both sensors and effectors, ripples could reverberate between them to produce a standing wave. Double-headed arrows indicate contraction/elongation of cells (electromotility) in response to a common stimulus.

As described later on (§M 4.5), a literature search into wave propagation at liquid–solid interfaces revealed a prime candidate for such a wave: a slow, highly dispersive wave known in ultrasonics as a symmetric Lloyd–Redwood wave or ‘squirting’ wave¹⁴. These waves can arise when a thin fluid layer is sandwiched between two deformable plates, as occurs in the cochlea (Fig. 4.5). Because squirting waves rely on the interaction between the mass of the fluid and the elastic restoring force of the plates, they are characteristically slow – measured in the cochlear case in millimetres per second.

Squirting waves provide a ready basis for positive mechanical feedback and amplification in the partition (Chapter R5). The proximity of motors – OHC bodies – to sensors – OHC stereocilia – invites feedback, and if the phase delay of the wave

¹³ Steel, K. P. (1983). The tectorial membrane of mammals. *Hear. Res.* 9: 327–359.

¹⁴ Bell, A. and N. H. Fletcher (2004). The cochlear amplifier as a standing wave: "squirting" waves between rows of outer hair cells? *J. Acoust. Soc. Am.* 116: 1016–1024.

reaches 360° , oscillation between the rows of OHCs will occur. Modeling (Chapter R6) shows that after applying an input signal to the rows of OHCs, a standing wave appears between the outermost rows (OHC1 and OHC3). The standing wave can occur either in a whole wavelength mode (if the polarity of the input to all rows is the same) or half-wavelength mode (if the polarity of OHC1 is the inverse of that of OHC3). At the same time, a progressive, but attenuating, wave will move towards the inner hair cells (IHCs), the ear's detectors. We now have a SAW resonator amplifying an input signal and passing it to a detector.

This scheme meets Gold's prescription for a 'regenerative receiver' in the cochlea where, to avoid compromising signal-to-noise ratio, positive feedback is used to amplify a signal before its detection. Later (Gold, 1987), he drew an analogy to the functioning of an 'underwater piano': only by introducing a sensor onto each string and supplying positive feedback could such a viscously loaded instrument be made to operate, and this is what the SAW model achieves. The SAW resonator can be identified with the cochlear amplifier and would explain spontaneous emissions and other active aspects of cochlear mechanics.

The arrangement also fits the description by Hudspeth¹⁵ of a distributed amplifier. Reinterpreting Hudspeth, the separate OHCs could be likened to a pendulum clock (a distributed mechanical amplifier in which a pendulum is driven by a coiled spring through an escapement); thus, their oscillation frequencies would be determined by one physical property (the length of the SAW cavity, equivalent to the length of a pendulum), while the timed release of energy (from the OHC motor – the escapement) overcomes damping and sustains activity.

The key assumptions of the SAW hypothesis are set out below.

1. *The OHCs and their surroundings have properties conducive to the propagation of a slow wave – probably a squirting wave – communicating the motion of one row to the next.*

2. *The speed of the waves varies from base to apex in a systematic way, thereby supplying the cochlea's tonotopic tuning.* Halfway along the cochlea, where the spacing between OHC1 and OHC3 is about $30\ \mu\text{m}$ and a characteristic frequency (CF) of 1 kHz is typical, the wave will need to have a propagation speed of

¹⁵ Hudspeth, A. J. (1997). Mechanical amplification of stimuli by hair cells. *Curr. Opin. Neurobiol.* 7: 480-486.

M 4 [8]

30 $\mu\text{m}/\text{ms}$ (= 30 mm/s) to establish whole-wavelength resonance. Near the base, with a CF of say 10 kHz and spacing is 20 μm , the necessary speed is 200 mm/s; in contrast, near the apex where CF may be 0.1 kHz and the spacing 50 μm , the corresponding speed would fall to 5 mm/s. Chapter R5 shows that the dispersive properties of a squirting wave allow the human cochlea to be tuned over its full frequency range (20–20 000 Hz) based largely on the spacing of OHC rows.

3. Rows 1 and 3 respond with the same phase to a stimulus, while row 2 probably responds in anti-phase. Modeling in Chapter R6 shows two likely modes: a full wavelength mode, like the first overtone of an organ pipe open at both ends, in which the response of OHC2 is in antiphase to OHC1 and OHC3; and a half-wavelength mode, like the fundamental mode of the open-ended organ pipe, in which the responses of OHC1 are in antiphase to OHC3 (and OHC2 is a displacement node)¹⁶. Evidence for bi-phasic activity in OHCs is presented in §R 9.1.

The result of the interaction is a standing wave, a mechanical cochlear amplifier. That is, IHCs respond to wave energy delivered to them by a squirting wave generated by the combined activity of the outer hair cells.

4.3 Parallels between SAW devices and the cochlea

There are strong analogies between a SAW resonator and the anatomy of the cochlea. Comparison is aided by reference to Fig. 4.5 and anatomical texts¹⁷.

1. The three rows of OHCs are the interdigital electrodes. It is significant that the required minimum number of fingers for an electronic SAW device is three, and in all vertebrate animals there are three or more OHC rows¹⁸. Additional rows, sometimes present, would supply extra gain.

2. Wave energy propagating on the surface of a SAW resonator can be absorbed or reflected by impedance discontinuities, and, when required, this is

¹⁶ A dynamic display of organ pipe modes can be found at http://www.cord.edu/dept/physics/p128/lecture99_35.html

¹⁷ Such as Slepecky, N. B. (1996). Structure of the mammalian cochlea. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 44–129.

¹⁸ Bredberg, G. (1968). Cellular pattern and nerve supply of the human organ of Corti. *Acta Otolaryngol. Suppl.* 236: 1-135.

normally achieved by etching grooves or placing strips of material on the surface of the device¹⁹. The TM possesses Hensen's stripe²⁰, a rounded feature located above the IHC stereocilia (see Fig. 4.5) which may act as a mechanical impedance discontinuity: this might redirect wave energy emerging from the OHC cavity and send it to this detector.

3. Energy escaping the OHC cavity towards the outer edge of the TM is a potential problem and needs to be reflected so as to re-enter the cavity with appropriate phase delay. At the outer edge of the TM another aggregation of material is found, a rounded thickening known as the marginal band²¹, which may act this way (Fig. 4.5).

4. To absorb and disperse unwanted bulk propagation modes (multiple fast compressional waves that propagate throughout the substrate of the device), the back of a SAW resonator is either roughened or waxed²². In the cochlea the top of the TM is criss-crossed with a covering net²³.

5. Towards the inner edge of the TM we find a sharp discontinuity – the vestibular lip (Fig. 4.5) – and here reflections could occur, possibly acting to return wave energy back into the amplifying cavity and allowing real-time convolution and autocorrelation of the signal to take place^{23,24,25}. The key idea here is that the IHC would then sit as a central detector between the signal source (the OHC cavity) and its reflected image. As explained by Fergason and Newhouse (1973), when two surface waves pass through each other from opposite directions and interact nonlinearly (to produce sum and difference frequencies), a centrally placed detector integrates the sum frequency to form the convolution and the difference frequency supplies the correlation²⁶.

6. The speed of electromechanical ripples in a solid-state SAW resonator is about 5 orders of magnitude lower than the speed of the electrical signal in its input

¹⁹ Smith (1981), p. 102.

²⁰ Hardesty, I. (1908). On the nature of the tectorial membrane and its probable role in the anatomy of hearing. *Am. J. Anat.* 8: 109–179 (+ plates).

²¹ Edge, R. M., et al. (1998). Morphology of the unfixed cochlea. *Hear. Res.* 124: 1-16.

²² Smith (1981), p. 130.

²³ Campbell 1998, Ch. 17.3.

²⁴ Quate, C. F. and R. B. Thompson (1970). Convolution and correlation in real time with nonlinear acoustics. *Appl. Phys. Lett.* 16: 494-496.

²⁵ Kino, G. S. (1976). Acoustoelectric interactions in acoustic-surface-wave devices. *Proc. IEEE* 64: 724-748. (p. 728 and Fig. 6)

²⁶ Fergason, E. S. and V. L. Newhouse (1973). Convolution and correlation using nonlinear interactions of Lamb waves. *IEEE Transactions on Sonics and Ultrasonics* SU-20: 360-364.

leads, a reduction that makes it possible to compactly store many cycles for signal analysis²⁷. Thus, it is possible to store in an inch of crystal the information that would otherwise fill a mile-long cable²⁸. In a similar way, the speed of the hypothetical squirting wave is 4–5 orders of magnitude lower than the speed of a sonic pressure wave in the surrounding cochlear fluids, some 1500 m/s. In the width of the tectorial membrane, then, may be stored up to a dozen cycles of acoustic signal. One experiment involving a microphone in a human ear canal²⁹ observed a 1280-Hz tone continually waxing and waning every 5.8 ms— that is, an envelope repeating every 7.4 waves.

4.4 *Prima facie* validity

The structural parallels are suggestive, but by themselves they are not conclusive. A number of lines of evidence can be found in the literature, and a more detailed presentation of some of them is set out in Chapter D9. However, in order to justify the modeling that forms the core of this thesis (Chapter R6), it is worth noting two main predictions of the SAW model and the major evidence supporting them.

A. Inverted response of different rows. A distinctive feature of SAW devices is the alternating polarity of the interdigital electrodes. Translated to the cochlea, this means that the response polarity of one or more rows of OHCs should be inverted compared to the others. One key finding here is that the cochlear microphonic, an electrical potential recordable from outside the cochlea, exhibits ‘dual’ polarities³⁰, as if it were composed of two potentials of opposite polarity (which could in turn derive from two populations of OHCs of opposite polarity). Moreover, isolated OHCs can either lengthen *or shorten* in a tuned manner in response to oscillating pressure³¹, and

²⁷ Maines, J. D. and E. G. S. Paige (1976). Surface-acoustic-wave devices for signal processing applications. *Proc. IEEE* 64: 639-652.

²⁸ Claiborne, L. T., et al. (1976). Scanning the issue. *Proc. IEEE* 64: 579-580.

²⁹ Wit, H. P. and R. J. Ritsma (1980). Evoked acoustical responses from the human ear: some experimental results. *Hear. Res.* 2: 253-261. The wave continued for more than 280 ms.

³⁰ Pierson, M. and A. R. Møller (1980). Some dualistic properties of the cochlear microphonic. *Hear. Res.* 2: 135-149.

³¹ Brundin, L., Flock, Å., and Canlon, B. (1989). Sound-induced motility of isolated cochlear outer hair cells is frequency-specific. *Nature* 342: 814-816.

direct antiphasic activity of OHC rows has been observed, even (surprisingly) in an explant³².

B. Radial wave motion. If the SAW model is valid, we would expect closely spaced phase changes across the partition. Indeed, relative phase changes of up to 180° between locations only 10 µm apart radially have been observed on the basilar membrane of a guinea pig³³. Nilsen and Russell drilled a hole in the cochlea and measured, in a profile across the basilar membrane, the motion of the membrane in response to sound stimulation. By using a beam from a self-mixing laser diode, focused to a 5-µm spot, they avoided having to place reflective beads on the membrane, a routine practice that conceivably might interfere with normal cochlear activity. The unique Nilsen and Russell results are highly suggestive, even though several other workers have only seen smaller phase gradients and others have not seen any (see §D 9.3/b). Rapid phase variations strongly support the SAW model, and are otherwise difficult to explain.

4.5 What is the wave propagation mode?

SAW devices can, in principle, operate using a wide range of wave propagation modes: Rayleigh waves are the most common, but Lamb, Love, Bleustein–Gulyaev–Shimizu, Stonely, Sezawa, and other wave modes are employed^{34,35}. Deciding which mode operates in the cochlea is difficult due to complex structure and little-explored physical properties of the layers bounding the OHC stereocilia – the tectorial membrane (TM) at the top (in which the tips of the longest stereocilia are embedded) and the plateau of Corti (reticular lamina, or RL) underneath. The TM is a fibre-reinforced viscoelastic gel covered with surface layers (Hardesty’s membrane and covering net) and immersed in electrolytes and an electrical field; the RL, for its part, is a very thin (~1 µm) membrane composed of

³² Scherer, M. P. and A. W. Gummer (2004). Vibration pattern of the organ of Corti up to 50 kHz: evidence for resonant electromechanical force. *Proc. Nat. Acad. Sci.* 101: 17652-17657.

³³ Nilsen, K. E. and I. J. Russell (1999). Timing of cochlear feedback: spatial and temporal representation of a tone across the basilar membrane. *Nat. Neurosci.* 2: 642-648.

³⁴ Ballantine, et al. *Acoustic Wave Sensors: Theory, Design, and Physico-Chemical Applications*. Chapters 2 and 3.

³⁵ Campbell (1998), Chapter 2.

the interlocking flattened heads of phalangeal processes that in turn originate from Deiters cells (see §R7).

Wave modes can be categorised in two main ways: longitudinal, in which the particles move back and forth in the direction of wave propagation; and transverse, in which they move at right angles to this direction. In geophysics, the first are known as *P*-waves whereas the second are *S*-waves. *P*-waves depend on compressional moduli, and hence are relatively fast compared to *S*-waves which rely on shear moduli and can be much slower in gel-like materials. In seeking a remarkably slow wave in the cochlea, shear waves appear the better candidates.

Simple capillary (surface tension) waves, with their characteristically slow speed, are also worth consideration since surface tension effects have been observed in the cochlea³⁶. The speed, c , of a surface tension wave³⁷ of wavelength λ on the surface between a liquid and a gas is:

$$c = (2\pi T/\lambda\rho)^{1/2} \quad (5.1)$$

where T is the surface tension and ρ is the density of the underlying liquid. Surface tension may have a role in the cochlea, but it is difficult to see how this parameter can be made to vary systematically from base to apex by a factor of 10^4 or more in order to tune the partition over a frequency range of at least 2 decades. Note from Eq. 5.1 that capillary waves are dispersive, with speed varying as $\omega^{0.5}$.

A shear wave of some type is a strong possibility because the shear moduli of gels are small, much less than their compressional (Youngs) moduli. In its most basic form, the speed, v , of a bulk shear wave is given by

$$v = (G/\rho)^{1/2} \quad (5.2)$$

where G is the shear modulus and ρ is the density. These waves are non-dispersive (speed independent of frequency); a Rayleigh wave, a shear wave on the surface of a solid that is thick compared with the wavelength involved, travels at about 90% of this speed. Acoustic measurements^{38,39} of soft ‘ringing gels’ (showing the peculiar

³⁶ Olson, E. S. and D. C. Mountain (1990). In vivo measurement of basilar membrane stiffness. In: *Mechanics and Biophysics of Hearing*, edited by P. Dallos et al. (Springer: Berlin), 296-303. The attraction between the basilar membrane and a probe only occurred pre-mortem; it was also noted by Olson in subsequent work.

³⁷ Lighthill, J. (1978). *Waves in Fluids*. (Cambridge University Press: Cambridge).

³⁸ Sinn, C. (2000). Acoustic spectroscopy of aerogel precursors. *Progr. Colloid Polym. Sci* 115: 325-328.

property of ringing like a bell when struck), give shear moduli as low as 14 kPa and a corresponding shear-wave velocity of 4.1 m/s, which is not low enough for audio-frequency SAW operation in the cochlea – some millimetres per second (point 2 on page M 4 [8]).

Measurements of the shear modulus (elasticity) of the actual TM have returned a remarkably wide range, as Table 4.1 shows. The table includes values of the less precise ‘point stiffness’, which earlier experimenters used, a measure that depends on the sharpness of the probe (elasticity of 1 kPa $\approx$ point stiffness of 0.01 N/m). Values vary from as low as 0.0004 N/m to as high as 10 N/m, but even the lowest value ($G \approx 0.2$ kPa) is, after using equation 5.2, still too high for our purposes (giving a c of 800 mm/s).

For comparison, measurements on the elasticity of the gel covering the otoliths in an amphibian are also given in Table 4.1. These values are very low, and the unsupported gel would probably collapse under its own weight in air, but even this material gives a shear wave speed no lower than 50 mm/s. Experiments with a vibrating magnetic bead inside a cell⁴⁰ give a shear modulus of the cell contents as 20–735 Pa, and one cannot hope to go lower than that. Taken together, the evidence suggests that a shear wave does not seem to be the answer.

A more likely avenue is to look at bending or flexural waves in plates, which in general have lower velocities than waves based on shear. These waves also tend to be highly dispersive. The basic surface wave is a Lamb wave, and they come in symmetric and antisymmetric forms^{41,42}. SAW devices based on Lamb waves can be lowered further in frequency by immersing them in liquid or loading them with a layer of high density and lower shear modulus, which retards the wave speed and tends to trap wave energy at the surface. As a result, other interface modes such as Stoneley, Sezawa, and Scholte waves begin to appear⁴³. In this connection, we note that the TM is not a homogeneous layer, but has its underside covered with a very thin layer about 1 μm thick⁴⁴ called Hardesty’s membrane.

³⁹ Sinn, C. (2004). When jelly gets the blues: audible sound generation with gels and its origins. *Journal of Non-Crystalline Solids* 347: 11-17.

⁴⁰ Bausch, A. R., et al. (1999). Measurement of local viscoelasticity and forces in living cells by magnetic tweezers. *Biophys. J.* 76: 573-579.

⁴¹ Wenzel, S. W. and R. M. White (1988). A multisensor employing an ultrasonic Lamb-wave oscillator. *IEEE Transactions on Electron Devices* 35: 735-743.

⁴² White, R. M. (1970). Surface elastic waves. *Proc. IEEE* 58: 1238-1277.

⁴³ Ballantine et al. (1997), Ch. 3, pp. 89 ff.

⁴⁴ Hardesty (1908).

Table 4.1. Measurements of tectorial membrane stiffness

Experimenter	Point stiffness (N/m)	Elasticity (kPa)
Békésy (1960) ⁴⁵	0.1–10	
Zwislocki & Cefaratti (1989) ⁴⁶	0.13	0.6
Hemmert et al. (2000) ⁴⁷	0.1–0.6	
Abnet & Freeman (2000) ⁴⁸	0.07–1	7–100
Freeman et al. (2003) ⁴⁹	0.06–0.34	
Shoelson et al. (2003) ⁵⁰	0.0004–0.003	0.7–3.9
Shoelson et al. (2004) ⁵¹		3–20
Measurements of otolith gel		
Kondrachuk (1991) ⁵²		1
Kondrachuk (2002) ⁵³		0.01

The way in which liquid and gel layers combine to form low propagation-speed layers prompts further investigation. Ballantine et al. (1997) discuss lossless Scholte waves (their p. 124) and they mention that its phase velocity approaches *zero* for very thin layers (which they show in their Fig. 3.46). A literature search on Scholte waves returned a most astonishing reference – Hassan and Nagy (1997) – the abstract of which describes the experimental finding of “a mode slower than the slowest-order bending mode of the plates and [which] asymptotically approaches the

⁴⁵ Békésy, G. v. (1960). *Experiments in Hearing*. (McGraw-Hill: New York).

⁴⁶ Zwislocki, J. J. and L. K. Cefaratti (1989). Tectorial membrane II: stiffness measurements in vivo. *Hear. Res.* 42: 211-228.

⁴⁷ Hemmert, W., et al. (2000). Mechanical impedance of the tectorial membrane. Midwinter Meeting, Florida, Association for Research on Otolaryngology <http://www.aro.org/archives/2000/4838.html>.

⁴⁸ Abnet, C. C. and D. M. Freeman (2000). Deformations of the isolated mouse tectorial membrane produced by oscillatory forces. *Hear. Res.* 144: 29-46.

⁴⁹ Freeman, D. M., et al. (2003). Dynamic material properties of the tectorial membrane: a summary. *Hear. Res.* 180: 1-10.

⁵⁰ Shoelson, B., et al. (2003). Theoretical and experimental considerations for the study of anisotropic elastic moduli of the mammalian tectorial membrane. Mid-Winter Meeting, Florida, Association for Research in Otolaryngology

⁵¹ Shoelson, B., et al. (2004). Evidence and implications of inhomogeneity in tectorial membrane elasticity. *Biophys. J.* 87: 2768-2777.

⁵² Kondrachuk, A. V., et al. (1991). Mathematical simulation of the gravity receptor. *The Physiologist* 34: S212-S213.

⁵³ Kondrachuk, A. V. (2002). Models of otolithic membrane–hair cell bundle interaction. *Hear. Res.* 166: 96-112.

Stonely–Scholte mode” of a solid–liquid interface⁵⁴. The mode, which involves the motion of fluid in the gap between two symmetrically flexing plates, was first predicted in 1965 by Lloyd and Redwood, and they called it a ‘squirting wave’ after the way in which fluid squeezed between two closely spaced plates behaves. This wave, which I call a symmetric Lloyd–Redwood (SLR) wave, applies well to the anatomy of the cochlea’s sensing surface. Moreover, the predicted wave speed – based on the dimensions and properties of the subtectorial space – gives a good match to the speeds required to operate the SAW resonator. This prime candidate is described in detail in the next chapter.

⁵⁴ Hassan, W. and P. B. Nagy (1997). On the low-frequency oscillation of a fluid layer between two elastic plates. *J. Acoust. Soc. Am.* 102: 3343-3348. (p. 3343).

A squirting wave model of the cochlear amplifier¹

- 5.1 Introduction
- 5.2 Squirting waves
- 5.3 SLR wave in the cochlea
- 5.4 Dispersion and tonotopic tuning
- 5.5 The cochlear amplifier as a standing wave
- 5.6 Derivation of equations governing squirting waves
- 5.7 Viscosity and the effects of hydrophobicity
- 5.8 Conclusions

This chapter investigates the distinctive properties of symmetric Lloyd–Redwood (SLR) waves – known in ultrasonics as squirting waves – and describes how their unique characteristics make them well-suited for carrying positive feedback between rows of outer hair cells. This could provide standing-wave resonance – in essence a narrow-band cochlear amplifier. Based on known physical properties of the cochlea, such an amplifier can be readily tuned to match the full 10-octave range of human hearing.

SLR waves propagate in a thin liquid layer enclosed between two thin compliant plates or between a single such plate and a rigid wall, conditions found in the subtectorial space of the cochlea, and rely on the mass of the inter-plate fluid

¹ Based on Bell, A. and N. H. Fletcher (2004). The cochlear amplifier as a standing wave: "squirting" waves between rows of outer hair cells? *J. Acoust. Soc. Am.* 116: 1016-1024.

interacting with the stiffness of the plates to provide extremely low phase velocity and high dispersion. The first property means SLR wavelengths can be as short as the distance between rows of outer hair cells, allowing standing wave formation; the second permits wide-range tuning using only an order-of-magnitude variation in cochlear physical properties, most importantly the inter-row spacing.

Theoretically, viscous drag at the two surfaces should hinder SLR wave propagation at low frequencies, but by invoking hydrophobic effects this limitation might be overcome.

5.1 Introduction

A major unresolved problem in cochlear mechanics is a basic one: how is it physically possible to finely tune the human cochlea over three decades of frequency? The conventional model involving traveling waves propagating lengthwise along the basilar membrane (BM) certainly gives broad tuning, with the local resonance frequency being determined largely by the plate-stiffness and width of the BM², but a local-resonance theory, in some way involving the active outer hair cells (OHCs), appears necessary to provide the observed sharp tuning³. The nature of this active tuning has been a matter for speculation and debate, since the identified material properties of the cochlear structures do not vary along the partition by the large factor required in order to cover the large frequency range involved⁴.

Here a solution is proposed involving standing-wave resonance between the rows of OHCs. The resulting wave direction is across the partition (radially) in a direction at right angles to the standard lengthwise (longitudinal) direction of propagation of the traveling wave. If the OHCs are excited by such a wave, then their mechanical responses will deflect the membrane to which they are attached and launch a secondary wave from each cell. These secondary waves will interact with the other OHCs, causing them to respond with further waves, and so on. Because the phase change of the primary exciting wave along the rows is small, many OHCs will

² See §I 3.1.

³ See §I 3.2/a.

⁴ Naidu, R. C. and D. C. Mountain (1998). Measurements of the stiffness map challenge a basic tenet of cochlear theories. *Hear. Res.* 124: 124–131. A broader discussion of this issue was made in §3.2/b.

respond in unison. Furthermore, since the OHCs are arranged in three parallel rows, positive feedback at a resonance frequency related to the OHC spacing will occur and, as a result, will launch a ‘radial’ wave in a direction normal to the rows. This mechanism would operate effectively if the response sensitivity of the individual cells were adjusted neurally to be just below the threshold of oscillation.

A major difficulty confronting this radial wave hypothesis, however, is the extremely low wave velocity and high dispersion required in order to have the wavelength match the separation between OHC rows over the full frequency range of the human cochlea. In this paper a wave type is identified that meets these requirements: a symmetric Lloyd–Redwood (SLR) wave, known in ultrasonics as a ‘squirting’ wave. This mechanism would provide the ‘self-tuned critical oscillators’ by which amplification of small signals takes place at a frequency where there is a dynamic instability (Hopf bifurcation)^{5–9}. A feature of Hopf resonance (§D 9.2/c) when applied to this system is that the tuning is governed by the frequencies of the oscillators, not the stiffness or inertia of the partition, and the oscillators will act as sharply tuned high-gain amplifiers for weak stimuli and as low-gain filters for strong ones. Around a Hopf bifurcation there is a range of frequency and amplitude where a stimulus is able to entrain the resonance, a distinctive feature of SOAEs¹⁰.

5.2 Squirting waves

SLR waves arise when a thin fluid layer is sandwiched between two deformable plates. They were predicted by Lloyd and Redwood¹¹ in 1965 and first

⁵ Duke, T. and F. Jülicher (2003). Active traveling wave in the cochlea. *Physical Review Letters* 90: 158101.

⁶ Camalet, S., et al. (2000). Auditory sensitivity provided by self-tuned critical oscillations of hair cells. *Proc. Nat. Acad. Sci.* 97: 3183–3188.

⁷ Ospeck, M., et al. (2001). Evidence of a Hopf bifurcation in frog hair cells. *Biophys. J.* 80: 2597–2607.

⁸ Eguíluz, V. M., et al. (2000). Essential nonlinearities in hearing. *Physical Review Letters* 84: 5232–5235.

⁹ Stoop, R., et al. (2004). Limit cycles, noise, and chaos in hearing. *Microsc. Res. Tech.* 63: 400–412.

¹⁰ Wilson, J. P. and G. J. Sutton (1981). Acoustic correlates of tonal tinnitus. In: *Tinnitus*, edited by D. Evered and G. Lawrenson (Pitman: London), 82–107.

¹¹ Lloyd, P. and M. Redwood (1965). Wave propagation in a layered plate composed of two solids with perfect contact, slip, or a fluid layer at their interface. *Acustica* 16: 224–232.

experimentally verified in the ultrasonic regime by Hassan and Nagy¹² in 1997. Unlike normal flexural or shear waves in a plate¹³, the SLR wave relies primarily upon interaction between the inertia of the fluid and the elastic restoring force of the plates. While the original analysis of Lloyd and Redwood assumed that the plates deformed by shear, plates thinner than about one-sixth of the wavelength will deform by bending, the case considered by Coulouvrat et al.¹⁴ and by Hassan and Nagy. Both these cases are treated in §R 5.6 below [due to N. H. Fletcher], and certain variations are also discussed there.

To visualise liquid displacement patterns, Lloyd and Redwood solved the equations of motion numerically for two modes, one antisymmetric and the other symmetric with respect to a plane along the centre of the fluid layer (Fig. 5.4). In the antisymmetric mode, discussed in more detail in §R 5.6, the upper and lower layers, and the fluid, move up and down together in a sinuous fashion, so that the width of the fluid layer is constant and no enhanced motion of fluid occurs. Applied to the cochlea, the lack of such fluid motion implies that the stereocilia would not be deflected. Moreover, this mode does not give appropriately low propagation speeds or such high dispersion (see equation A13 in §R 5.6), so we conclude it is not auditorily relevant.

The symmetric mode, however, in which the two facing solid layers vibrate in mirror symmetry to give a varicose wave, which we call the SLR mode, is of considerably greater interest. This mode¹⁵ involves squeezing of the intervening fluid backwards and forwards in the direction of propagation. Hassan and Nagy called it a ‘squirting’ mode because horizontal displacements of the fluid become magnified when the gap is narrow relative to the wavelength, as is the case in the typical cochlear configuration shown in Fig. 5.1. Maximum horizontal velocity of fluid occurs one-quarter of a wavelength away from the place where the plates undergo maximum vertical displacement.

¹² Hassan, W. and P. B. Nagy (1997). On the low-frequency oscillation of a fluid layer between two elastic plates. *J. Acoust. Soc. Am.* 102: 3343-3348.

¹³ Junger, M. C. and D. Feit (1993). *Sound, Structures, and Their Interaction*. (Acoust. Soc. Am.: New York). [pp. 236–239]

¹⁴ Coulouvrat, F., et al. (1998). Lamb-type waves in a symmetric solid-fluid-solid trilayer. *Acustica* 84: 12-20.

¹⁵ The mode is similar to the undulation modes (bending and squeezing) in soap films, which were treated in Sens, P., et al. (1993). Hydrodynamic modes of viscoelastic soap films. *Langmuir* 9: 3212-3218.

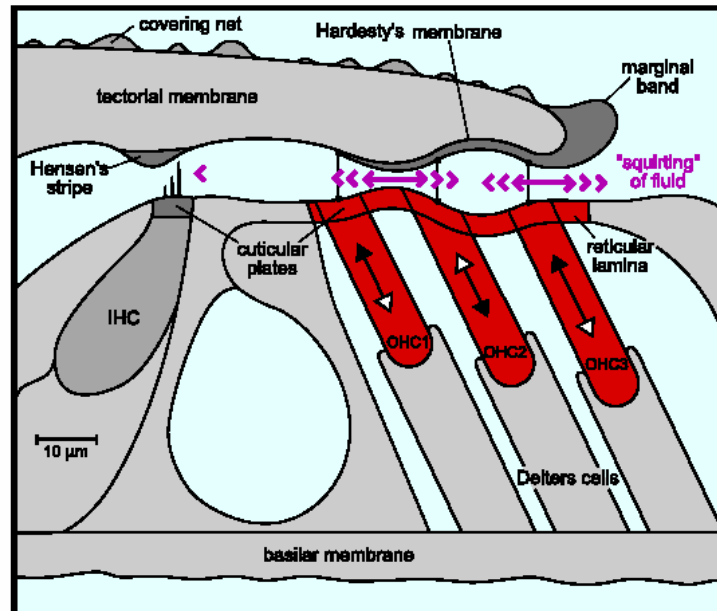


Fig. 5.1. Simplified diagram of the anatomy of the human cochlea in cross section. Radial SLR waves (squirting waves) could be generated by cyclic length changes of OHCs. Symmetric undulations induced in the facing surfaces of the TM and the RL squeeze the intervening fluid and produce a squirting action (horizontal arrows). The wave will continue to the IHCs, where squirting will tilt the free-standing IHC stereocilia. Shorter OHC stereocilia (unattached to TM and also subject to squirting effects) are, for clarity, not shown. Light-blue areas are occupied by fluid; the space surrounding the body of the OHCs is called the spaces of Nuel, and is in continuous hydraulic connection with the rest of the cochlear fluids.

Hassan and Nagy studied the waves at ultrasonic frequencies (15–150 kHz) with a liquid film approaching 1 mm in thickness. At audio frequencies, however, the effect of viscosity becomes increasingly pronounced (see Sections 6 and 7), a factor that, acting in the subtectorial space, would tend to damp the wave and prevent its propagation unless some other mechanism intervenes. As it happens, there appears to be just such a possibility deriving from the properties of hydrophobic surfaces, as will be discussed later.

Anatomically, the cochlea has a thin layer of fluid (aqueous endolymph) enclosed between the gelatinous tectorial membrane (TM) and the thin reticular

lamina (RL), perhaps more accurately called a reticular membrane¹⁶, as shown in Fig. 5.1. The two surfaces are held apart by the stereocilia of the OHCs, with the tips of the tallest stereocilia embedded in the lower surface of the TM. From the analysis of Lloyd and Redwood and of Hassan and Nagy, the phase velocity c of the symmetric Lloyd–Redwood wave for two identical plates of half-thickness h , Young’s modulus E , and Poisson’s ratio σ , separated by a liquid layer of thickness d and density ρ , is given approximately by

$$c \approx \left[\frac{Eh^3d}{3(1-\sigma^2)\rho} \right]^{1/6} \omega^{2/3}, \quad (1)$$

provided the plates are thin compared with the wavelength so that they deform by bending. The wavelength $\lambda = 2\pi c/\omega$ is then given by

$$\lambda \approx 2\pi \left[\frac{Eh^3d}{3(1-\sigma^2)\rho} \right]^{1/6} \omega^{-1/3}, \quad (2)$$

which more readily illustrates the dispersive properties of the wave. A doubling of wavelength, for example, is accompanied by an eightfold change in frequency.

Plates thicker than about one-sixth of the wavelength undergo shear instead of bending, and the approximate result for the case where the plates are still thinner than the enclosed liquid layer is

$$c \approx \left[\frac{Ehd\omega^2}{(1+\sigma)\rho} \right]^{1/4}. \quad (3)$$

The corresponding expression for wavelength λ is

$$\lambda \approx 2\pi \left[\frac{Ehd}{(1+\sigma)\rho} \right]^{1/4} \omega^{-1/2}. \quad (4)$$

As shown in §R 5.6, both (1) and (3) can be simply derived by neglecting the mass of the plates and equating the kinetic energy of the ‘squirting’ liquid to the elastic strain energy of the plates. Inclusion of the mass of the plates is simple, but complicates the resulting expressions unnecessarily.

¹⁶ A name used, for example, in Wilkinson, G. and A. A. Gray (1924). *The Mechanism of the Cochlea: A Restatement of the Resonance Theory of Hearing*. (Macmillan: London).

When one of the plates is much thicker, stiffer, or denser than the other, then it moves very little and the motion reduces essentially to that of the original model with the immobile plate located along the centre-plane of the original fluid layer. Section R5.6 shows that this does not change the form of the dispersion relations (1) and (3), except that d is now equal to twice the thickness of the liquid layer. The wave of relevance is therefore that involving bending and with a dispersion relation of the form (1), provided at least one of the plates is sufficiently thin.

In the case of the cochlea, there is liquid on the outer side of each plate as well as between them, and the wave motion extends some distance into this liquid. But again, Section R5.6 shows that the effect of this surrounding liquid is small in the case of a structure with dimensions typical of the cochlea.

An important property of Eqs. (1) and (3) is that the SLR wave velocity increases markedly with frequency, as $\omega^{2/3}$ in the first case and as $\omega^{1/2}$ in the second. The wave is thus highly dispersive and, as given by (2) or (4), the wavelength range for a given frequency range is greatly compressed, varying as $\omega^{-1/3}$ and $\omega^{-1/2}$, respectively, for the two cases discussed, rather than as ω^{-1} for nondispersive propagation. It is this feature that potentially allows SLR waves to provide a way of tuning an active cochlear amplifier over a 3-decade (10-octave) frequency range by requiring only an order of magnitude variation in other physical parameters.

5.3 SLR wave in the cochlea

As §R 5.6 makes clear, the primary requirement for generating SLR waves in accordance with (1) is that at least one of the two enclosing plates is thin enough to deform by bending. Given the extreme thinness of the RL (1–3 μm), this condition appears likely to be met in the cochlea, although no direct measurements of this structure's stiffness have been made. Prior work has assumed that the reticular laminar is stiff, an approach that simplifies the treatment (e.g., Raftenberg, 1990).

It is known, however, that this articulated mesh of interlocking plates appears more flexible than the basilar membrane¹⁷ and there is some indication¹⁸ that it is

¹⁷ Mammano, F. and J. F. Ashmore (1993). Reverse transduction measured in the isolated cochlea by laser Michelson interferometry. *Nature* 365: 838-841.

more compliant than the TM. In what follows, therefore, it is assumed that deformation is by bending of at least one of the plate structures involved, so that the dispersion relation is given by (1). A difficulty, however, is that no individual data set provides all the required values, so it is necessary to use data compiled from measurements on several different species of mammal.

The most comprehensive data in the literature relates to the water buffalo¹⁹; here the thicknesses of the TM (3–8 μm) and RL (1.8–2.9 μm) are tabulated along the cochlea. It is immediately apparent that, in this case, both of these key structures are appreciably thinner than a wavelength, suggesting that both undergo bending. Because Naidu (2001) found that the RL appeared to have an elastic modulus comparable to that of the TM, it seems appropriate to use RL dimensions and to combine these with a representative Young's modulus of 2 kPa, as derived from recent measurements²⁰ on the guinea pig TM in which figures of 0.7–3.9 kPa were reported. (Note, however, that the exact value of the modulus is not important because it only affects wave speed according to the one-sixth power.) The gap width, d , reflects the height of the tallest stereocilia, and here there is no water buffalo data; instead, human data²¹, showing a gradation of 3–7 μm from base to apex, are used.

For the mid-region of the cochlea where frequencies near 1000 Hz ($\omega \approx 6000$ rad/s) are detected, the assumed values are thus, $E \approx 2$ kPa, $h \approx 1$ μm , $d \approx 3$ μm , and $\rho \approx 1000$ kg/m³. Equation (1) then gives a wave speed $c \approx 40$ mm/s and a wavelength, c/f , of about 40 μm . A plot of wave speed against frequency over the length of the cochlea is shown as the full line in Fig. 5.2 and shows values ranging from 3 mm/s at the apex (20 Hz) to 300 mm/s at the base (20 kHz). Extremely slow wave speeds and short wavelengths thus appear possible in the cochlear structure. According to LePage²², the tonotopic mapping (for humans) of frequency f to

¹⁸ Naidu, R. C. (2001). Mechanical properties of the organ of corti and their significance in cochlear mechanics, PhD thesis, Boston University. [pp.117–134]

¹⁹ Tiedemann, H. (1970). A new approach to theory of hearing. *Acta Oto-Laryngologica Suppl.* 277: 1-50.

²⁰ Shoelson, B., et al. (2003). Theoretical and experimental considerations for the study of anisotropic elastic moduli of the mammalian tectorial membrane. Mid-Winter Meeting, Florida, Association for Research in Otolaryngology.

²¹ Wright, A. (1984). Dimensions of the cochlear stereocilia in man and the guinea pig. *Hear. Res.* 13: 89-98.

²² LePage, E. L. (2003). The mammalian cochlear map is optimally warped. *J. Acoust. Soc. Am.* 114: 896-906.

fractional distance x from the apex is well-approximated by the function $f = 165.4(102.1^x - 0.88)$, and this expression is used in the following calculations.

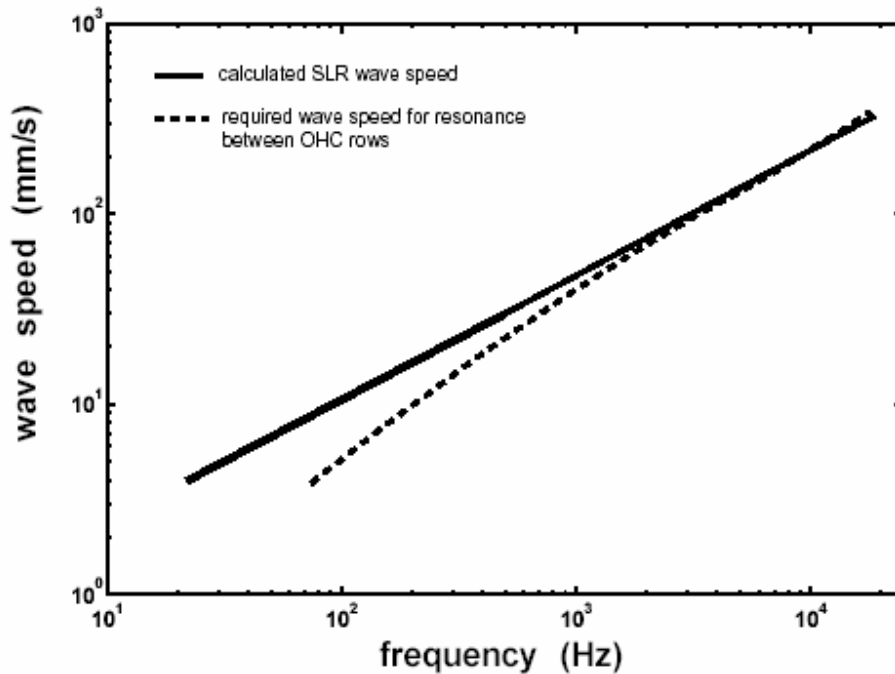


Fig. 5.2. Calculated speeds of SLR waves (full line) based on measured RL dimensions of the water buffalo (Tiedemann 1970) and assuming that the RL has an elastic modulus similar to that of the TM (~ 2 kPa, Shoelson et al. 2003). The gap width is that for human stereociliar height (Wright 1984) and a human frequency–place map (LePage 2003) is used. These speeds agree well with wave speeds inferred (dotted line) from assuming one wavelength of a standing wave to form between the experimentally determined spacing OHC1–OHC3 (Bredberg 1968) for humans.

Since Fig. 5.2 reflects a mixture of cochlear properties from water buffalo, guinea pig, and human, one may question the aptness of the values derived from (1) to human hearing. In general, micrographs show that the differences between these species are not major, and most cross sections appear similar. Although detailed measurements of human TM dimensions are lacking, it does seem, however, that the thickness of the human TM is, at least at the apex, appreciably greater than in the water buffalo, and its overall structure thus appears as in Fig. 5.1. The analysis in §R 5.6 then shows that SLR waves will propagate by bending of the RL with the TM remaining nearly inactive. Since the speed of an SLR wave varies only as the sixth-root of the Young’s modulus, errors introduced by assuming values of RL stiffness about equal to those of the TM (2 kPa) should not be serious.

As well as the subtectorial space in the cochlea being well-configured for propagation of SLR waves, it is important to note that OHCs appear strategically positioned to generate these waves, as shown in Fig. 5.1. A key property of OHCs is that they are electromotile, with the ability to change length, cycle by cycle, in response to variations in cell potential^{23,24}, such as might be caused by stereocilia deflection. Thus, changes in length of OHCs could excite SLR waves.

OHCs are mechanically clamped at the bottom by Deiters cells, which rest on the basilar membrane, and are firmly connected at the top to the interlocking platelike network of the RL. When OHCs are electrically stimulated *in vivo*, the RL at the top moves 5–10 times more²⁵ than does the basilar membrane at the bottom, a key indicator that the RL is highly flexible and could readily respond to elongation and contraction of OHCs.

From this numerical analysis, supported by the theoretical results in §R 5.6, it can be concluded that audio-frequency SLR waves with speeds as low as tens to hundreds of millimeters per second and wavelengths of tens to hundreds of micrometers could occur in many, if not all, mammalian cochleas. The wave speed will be governed by the bending of the thinnest membrane, usually the RL, although deformation of the TM may also contribute in some cases.

The possible existence of such radial waves prompts the question of how they may interact with a longitudinal travelling wave. Some kind of direct coupling of excitation from the longitudinal direction to the radial would presumably help in funnelling energy of a particular frequency to its appropriate location on the partition, at which point the OHCs could then begin actively fine-tuning the response via SLR waves.

The precise micromechanics of this interaction is beyond the scope of this thesis. It is reasonable, however, to treat the radial wave as an independent entity because its wavelength is generally very small – tens of micrometers – compared to that of a travelling wave, which is typically in the range of millimetres. In turn this means that the input stimulus to the OHCs is essentially in phase over reasonably large OHC aggregates. Of course, in the case of spontaneous emissions where, with

²³ Brownell, W. E., et al. (1985). Evoked mechanical responses of isolated cochlear outer hair cells. *Science* 227: 194-196.

²⁴ Evans, B. N. and P. Dallos (1993). Stereocilia displacement induced somatic motility of cochlear outer hair cells. *Proc. Nat. Acad. Sci.* 90: 8347-8351.

²⁵ Mammano and Ashmore (1993) [ibid.]

no external sound input, the active process dominates, the situation could be rather different.

A simple interpretation, then, broadly in keeping with existing traveling wave theory, might be that the traveling wave is the primary filter and the SLR wave the second filter. However, the SLR mechanism proposed here does leave open the nature of the primary input to the OHCs, which is not certain. In particular, the possible role of the fast pressure wave in stimulating OHCs requires careful consideration²⁶. In this case, the so-called second filter may be all that is necessary for frequency analysis (that is, there is no need for a primary filter). This aspect is discussed in Chapter D10.

5.4 Dispersion and tonotopic tuning

It was noted earlier that SLR waves are highly dispersive ($c \propto \omega^{2/3}$), so that in order to vary tuning 1000-fold, dispersion will provide a factor of 100, leaving only a factor of 10 to be contributed by other variables. This means that if inter-row spacing of OHCs were constant between base and apex, physical and geometrical characteristics of the cochlea would only be called on to alter wave speed by tenfold in order to maintain a full wavelength between OHC1 and OHC3. In reality, the spacing of OHC rows in humans²⁷ widens by a factor of 2.5 from base to apex, meaning that wave speed need only vary by a factor of 4 through the other parameters in Eq. 1.

The same equation indicates that possible graded variations of the elasticity E and gap thickness d along the basilar membrane are of little consequence in tuning, as phase velocity only varies as their sixth-root. The most likely parameter leading to tuning is the membrane half-thickness h , since $c \propto h^{1/2}$. A systematic variation in h from base to apex might therefore be expected, with h smaller at the apex (low frequencies). The detailed water buffalo data confirms this expectation. For this

²⁶ Bell, A. (2003). Are outer hair cells pressure sensors? Basis of a *SAW* model of the cochlear amplifier. In: *Biophysics of the Cochlea: From Molecules to Models*, edited by A. W. Gummer (World Scientific: Singapore), 429-431.

²⁷ Bredberg, G. (1968). Cellular pattern and nerve supply of the human organ of Corti. *Acta Otolaryngol. Suppl.* 236: 1-135.

animal, the thickness of the TM decreases from 26 μm at the base to 10 μm at the apex (2.6-fold); similarly, the RL thins out from 2.9 μm to 1.8 μm (1.6-fold).

5.5 The cochlear amplifier as a standing wave

Distinctive features of SLR waves are their low speeds and correspondingly short wavelengths. At the same time, a system in which motile elements (OHC cell bodies) are in close proximity to sensory elements (OHC stereocilia) immediately raises the possibility of feedback. Over the span of a single SLR wavelength the phase of a propagating wave changes by 360° , a situation inviting positive feedback and, given a suitable two-way interaction, standing waves. It appears significant that OHCs typically lie in three well-defined rows and are graded in their separation along the cochlea so as to span a distance ranging from 20 to 50 μm , dimensions comparable to calculated SLR wavelengths. It is also of some reassurance for our previous pooling of data that the graded spacings of OHC rows for both human and water buffalo are nearly identical.

A real possibility, therefore, is that positive feedback may occur between OHC rows. In response to a sound stimulus, the OHCs will undergo movement, launching an SLR wave, and the distinctive squirting motion of the wave will then initiate positive feedback through bending of neighbouring OHC stereocilia, creating a standing wave. Here we consider that it is the shorter OHC stereocilia, which are freestanding, that are bent and contribute most to feedback. At the same time, the tallest stereocilia, which are firmly attached to the TM may still contribute feedback as they must tilt with respect to their bases when the reticular lamina, on which they rest, undulates underneath. The important result is that in the end some of the oscillating fluid flow associated with the standing wave will escape the OHC region and propagate towards the IHCs, where the squirting fluid will bend stereocilia (which here are all free-standing) and greatly enhance the responses of the cells at the standing-wave resonance frequency.

Mention of nonradial propagation of SLR waves is also called for. Because OHCs are regularly arranged longitudinally as well as radially, cell interaction may launch lengthwise SLR waves, too. We note, however, that the longitudinal cell spacing is smaller than the radial spacing, so the corresponding resonance frequency

would be much higher, perhaps making the initial tuned stimulus from a travelling wave ineffective. Moreover, these waves would travel in directions that would not strongly affect the IHCs. While subtle effects due to nonradial waves cannot therefore be immediately ruled out, they do not constitute the major mechanism investigated here.

The location of the maxima and minima of the standing wave relative to the OHC rows will depend upon the mechanical impedance of the OHCs relative to the wave impedance of the surrounding plate. Since the cells are large in diameter relative to the thickness of the plate, it is likely that their mechanical impedance (force divided by displacement velocity) is also relatively large, which means that the standing wave will be excited in such a way that the OHCs lie close to, but not coincident with, the displacement nodes of the plate. Furthermore, because these plate displacement nodes are also the regions of maximum squirting wave fluid velocity (and maximum tilt of stereocilia with respect to their bases), this location also provides optimal feedback to the OHCs through displacement of their stereocilia (Fig. 5.3).

Although each OHC acts as a circular wave source, their linear arrangement effectively produces a nearly linear wavefront parallel to the OHC rows, and in this way an escaping wave propagates at right angles to the rows and towards the IHCs. This behaviour is modeled in Chapter R6.

Some experiments have seen large phase variations across the partition (up to 180° between points $10\text{ }\mu\text{m}$ apart²⁸), which can be interpreted as good evidence for short wavelength radial wave motion; however others²⁹ have seen no radial phase variability, so that more work is needed to clarify this behaviour. Conflicting reports of phase variability across the partition are discussed in §D 9.3/b.

²⁸ Nilsen, K. E. and I. J. Russell (1999). Timing of cochlear feedback: spatial and temporal representation of a tone across the basilar membrane. *Nat. Neurosci.* 2: 642-648.

²⁹ Ren, T., et al. (2003). Measurements of basilar membrane vibration using a scanning laser interferometer. In: *Biophysics of the Cochlea*, edited by A. W. Gummer (World Scientific: Singapore), 211-219.

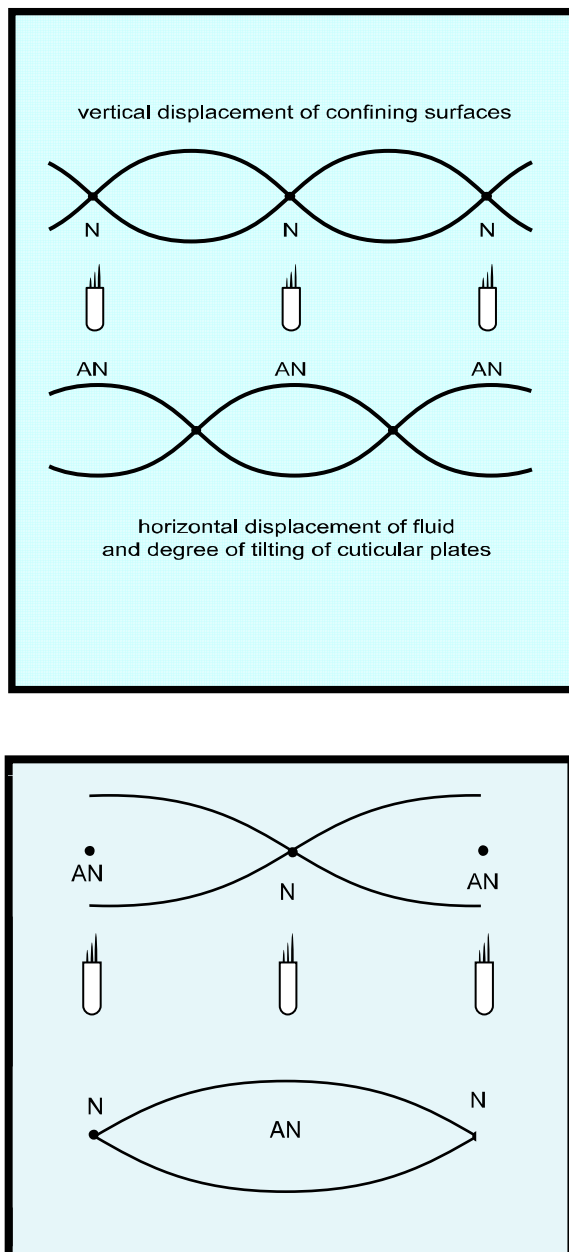


Fig. 5.3. Nodes and antinodes. Location of outer hair cells in terms of vertical displacement of confining plates and horizontal displacement of fluid. The top diagram represents the full wavelength mode and the bottom one the half-wavelength mode.

The dotted line in Fig. 5.2 shows the phase velocity required to create feedback resonance between rows of OHCs in the human cochlea, placed next to a line showing the wave velocities expected from an SLR wave based on composite cochlear data. To calculate the dotted line, the speed needed to make the OHC1–OHC3 distance a full-wavelength standing wave cavity was used; as Bredberg 1968

showed³⁰, this distance is continuously graded from base (20 μm) to apex (50 μm) in humans, and the same frequency–place map as before was again used to convert location to frequency. The general trend and proximity of the lines support the possibility that resonance between OHC rows may occur via SLR waves. An SLR wave thus makes an ideal candidate for tuning standing waves between OHC rows. Modeling of this process is presented in the following chapter.

Since OHC stereocilia are particularly sensitive to lateral jets of fluid³¹, the postulated reverberating activity between rows of OHCs could provide a physical realisation of the cochlear amplifier, the device proposed by Davis^{32,33} to explain the active nature of the cochlea at low sound pressures. It also has strong parallels with the regenerative receiver described by Gold³⁴ (Chapters I1 and I2) and with surface acoustic wave resonator devices³⁵ (Chapter M4). If SLR waves do operate in the cochlea as supposed here, it would confirm some long-standing conjectures that fluid flow in the subtectorial space was crucial for IHC stimulation^{36,37} and would relate to a recent speculation³⁸ that the cochlear amplifier was a fluid pump. An analysis of fluid flow in the subtectorial space³⁹, driven by basilar membrane motion, was performed by Raftenberg in 1990, and he found that appreciable “second filter” tuning was possible in this gap, even though he set the boundaries of this space to be rigid. Interestingly, he mentions at least eight times the limitation of assuming no outer hair cell motion, whereas in reality there is the “possibility of boundary

³⁰ *ibid*, Fig. 92.

³¹ Canlon, B. and L. Brundin (1991). Mechanically induced length changes of isolated outer hair cells are metabolically dependent. *Hear. Res.* 53: 7–16.

³² Davis, H. (1981). The second filter is real, but how does it work? *Am. J. Otolaryngol.* 2: 153–158.

³³ Davis, H. (1983). An active process in cochlear mechanics. *Hear. Res.* 9: 79–90.

³⁴ Gold, T. (1948). Hearing. II. The physical basis of the action of the cochlea. *Proc. Roy. Soc. Lond. B* 135: 492–498.

³⁵ Campbell, C. K. (1998). *Surface Acoustic Wave Devices for Mobile and Wireless Communications*. (Academic Press: San Diego).

³⁶ Steele, C. R. (1973). A possibility for sub-tectorial membrane fluid motion. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic: New York), 69–93.

³⁷ Frommer, G. H. and C. R. Steele (1979). Permeability of fluid flow through hair cell cilia. *J. Acoust. Soc. Am.* 65: 759–764.

³⁸ Karavitaki, K. D. and D. C. Mountain (2003). Is the cochlear amplifier a fluid pump? In: *Biophysics of the Cochlea: From Molecules to Models*, edited by A. W. Gummer (World Scientific: Singapore), 310–311.

³⁹ Raftenberg, M. N. (1990). Flow of endolymph in the inner spiral sulcus and the subtectorial space. *J. Acoust. Soc. Am.* 87: 2606–2620.

oscillations driven by outer cell motions that occur independently of basilar membrane motion” [p. 2620].

The work here assumes that the boundaries are not rigid and that outer hair cell motion can generate fluid flow in the form of squirting waves. However, N. H. Fletcher has drawn attention to a major problem with the SLR wave hypothesis: his analysis in §R 5.6 shows that propagation of SLR waves in the narrow subtektorial space might be expected to be strongly damped by viscous forces, particularly at low frequencies as indicated in Eq. (A15).

The problem is clearly evident in recent modeling work. One recent paper⁴⁰ modeled the cochlea as three linked subpartitions – the basilar membrane, the plateau of Corti (reticular lamina), and the tectorial membrane – in which the dynamics of the fluid in the subtektorial space was explicitly analysed. They used standard lubrication theory, including the no-slip assumption, and found that the viscosity of fluid in the gap effectively prevented squeezing motion. Interestingly, however, they noted that the small residual degree of gap squeezing, although three orders of magnitude smaller than the motion of the basilar membrane, was sharply tuned. They do, however, point to Steele’s earlier work (ref. 36) and suggest [p. 2568] the mechanism “could provide some amplification and sharpening”.

The authors also refer to an analysis by Lighthill⁴¹, which examined the problem of whether the traveling wave, as it approaches its characteristic place and rapidly slows down, might lead to fluid flow (“acoustic streaming”) in the gap at that point. Lighthill notes the apparent paradox [p. 556] that the biomechanics of a living cochlea is notably different from the mechanics of a cochlea immediately after death, even while the cochlear fluids exhibit the same mechanical properties. He then proceeds to examine just the fluid mechanics alone and postpones consideration of physiological questions for a later paper [p. 551] – which, so far as I can ascertain, never appeared. He imagines that if flow were channelled through the gap in which the inner hair cells reside, perhaps a “jet-like” motion could be produced, although in the end endolymph viscosity would make this small.

⁴⁰ Chadwick, R. S., et al. (1996). Active control of waves in a cochlear model with subpartitions. *Proc. Natl. Acad. Sci. U. S. A.* 93: 2564-2569.

⁴¹ Lighthill, J. (1992). Acoustic streaming in the ear itself. *J. Fluid Mech.* 239: 551-606.

An early abstract⁴² referred to by Chadwick and colleagues is intriguing because it specifically examined possible wave interactions in the fluid gap, including effects of dispersion. Mention is made of the gap presenting a complex impedance to traveling waves, and that “insights [were] sought into the allowed wave types, their localization along the cochlea, and the nature of the vibration modes.” It would appear they came close to uncovering squirting waves.

In a later implementation of their numerical model^{43,44}, Chadwick’s group allowed the subpartitions to flex and incorporated explicit fluid–solid coupling. Again, the no-slip assumption suppressed fluid motion in the gap, but they did find a complex vibrational mode in the gap at the base (11 kHz), while at the apex (1 kHz) some radial motion is evident in an animation (viewable at www.pnas.org).

Underlying all of this previous work is the assumption that viscosity hinders fluid flow in the subreticular gap and that the reticular lamina is stiff and does not bend. Given recent measurements of the stiffness of cochlear structures, the no-bending condition can be readily relaxed. There are two ways to deal with the viscosity obstacle. One approach is not to see it as insuperable but just an inherent property of the system. This is the approach taken by Elliott et al. in a recent conference contribution⁴⁵, and here they find that by including viscosity in the initial wave equation the wave still propagates but with reduced velocity. Viscosity reduces the wave speed by a factor of about 2, they find, and inspection of Fig. 5.2 shows that the difference between the theoretical wave speed and that required to tune the cavity between the outer hair cells is out by approximately this factor at low frequencies. Thus, viscosity naturally explains the divergence between the two lines. The second way of overcoming viscosity limitations is to question the no slip assumption in the presence of surface tension effects. Of course, a combination of both approaches may be valid.

Recent experiments in surface physics have shown that the effects of viscosity in narrow channels can be greatly diminished when hydrophobic surfaces

⁴² Dimitriadis, E. K. and R. S. Chadwick (1994). Local wave dispersion in the cochlea [abstract]. *J. Acoust. Soc. Am.* 95: 2840.

⁴³ Cai, H. and R. S. Chadwick (2003). Radial structure of traveling waves in the inner ear. *SIAM J. Appl. Math.* 63: 1105-1120.

⁴⁴ Cai, H., et al. (2004). Evidence of tectorial membrane radial motion in a propagating mode of a complex cochlear model. *Proc. Nat. Acad. Sci.* 101: 6243-6248.

⁴⁵ Elliott, S. J., et al. (2005). Incorporation of an active feedback loop into the "squirting wave" model of the cochlear amplifier. Twelfth International Congress on Sound and Vibration, Lisbon, Portugal.

are involved, and this thesis incorporates the phenomenon into how the cochlea functions. As described in more detail in Section 7, slippage between a polar liquid and its bounding surfaces can be considerably enhanced if the surfaces are made hydrophobic by coating them with a thin layer of oil. The relevance here is that *lipid droplets are secreted by Hensen cells*, immediately next to the subtectorial space (see Fig. 5.1), and my hypothesis is that the function of these droplets is to coat both TM and RL surfaces (but presumably not the stereocilia) and so reduce their viscous drag upon the squirting fluid in the subtectorial space.

5.6 Derivation of equations governing squirting waves⁴⁶

Suppose that, to conform to the notation of previous investigators, the system consists of two identical parallel plates, each of thickness $2h$, density ρ_1 , Young's modulus E , and Poisson's ratio σ , separated by a layer of liquid of thickness d , and density ρ , as shown in Fig. 5.4.

The simplest way to determine the phase velocity c of a wave of angular frequency ω that is symmetric about the center plane AB, which we have called an SLR wave, is to equate the maximum values of the potential and kinetic energies of the wave. This procedure is clearly appropriate in the case of standing waves, where displacement and velocity are 90° out of phase with each other, but can also be shown to be correct for propagating waves. In the derivations below, some factors of order unity are neglected in the interests of simplicity of presentation. The final results are therefore only approximate but, since fourth or sixth roots are involved, this is of little practical consequence.

⁴⁶ Due to N. H. Fletcher.

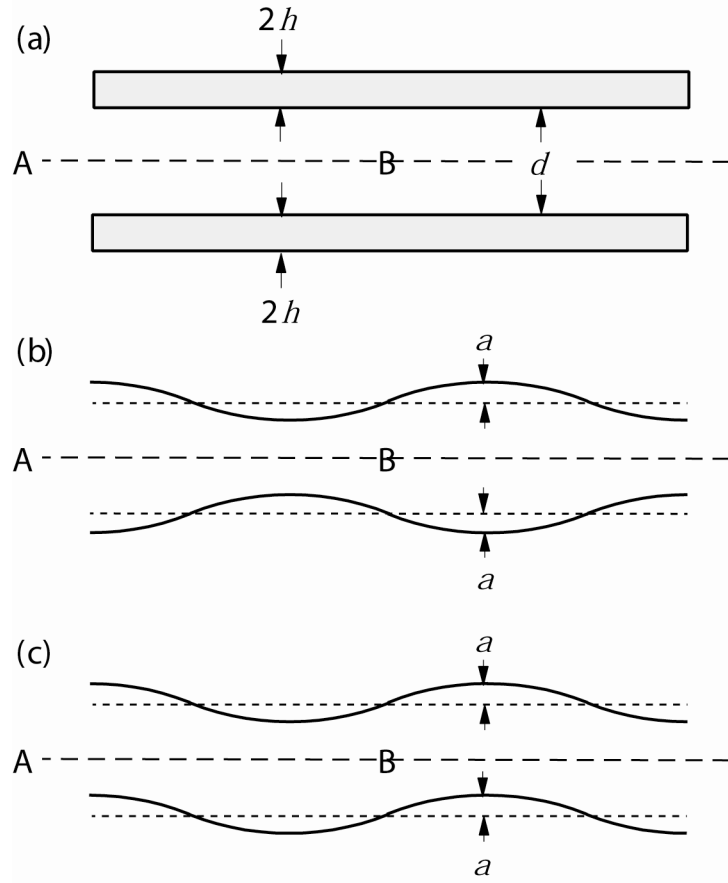


Fig. 5.4. (a) Section of two parallel plates surrounded by liquid. (b) Geometry of the symmetric Lloyd-Redwood (SLR) wave, the motion of which gives rise to the squirting of liquid between the plates. (c) The antisymmetric wave, displayed here for completeness. It is considered to play no functional role in the cochlea.

In what follows, we consider the behaviour on only one side of the symmetry plane AB, and assume a standing wave of the form

$$y(x,t) = a \cos kx \sin \omega t, \quad (\text{A1})$$

where $k = \omega/c$. If λ is the wavelength at angular frequency ω , and the plates are sufficiently thin that $h \ll \lambda$, then their elastic distortion occurs through bending, and the peak elastic potential energy P_{bend} per unit area is

$$P_{\text{bend}} = \frac{Eh^3 k^4 a^2}{3(1-\sigma^2)} = \frac{Eh^3 \omega^4 a^2}{3(1-\sigma^2)c^4}. \quad (\text{A2})$$

If, however, the plates are thicker so that h is greater than about λ/π , then the plates distort predominantly by shear rather than bending, and the corresponding result is

$$P_{shear} = \frac{Ehk^2a^2}{2(1+\sigma)} = \frac{Eh\omega^2a^2}{2(1+\sigma)c^2}. \quad (A3)$$

The difference in structure between (A2) and (A3) is accounted for partly by the fact that the bending modulus is involved in (A2) while the shear modulus is involved in (A3), and partly by the fact that the wave equation for a bending wave involves the operator $\partial^4 z/\partial x^4$ while that for a shear wave involves only $\partial^2 z/\partial x^2$.

The kinetic energy in the simple system considered involves two contributions, one from the moving mass of the plates, and one from that of the liquid between them. The kinetic energy K_{plate} per unit area of the single plate has the simple form

$$K_{plate} = \rho_1 h \omega^2 a^2, \quad (A4)$$

but the liquid motion requires more analysis.

From (A1), if it is assumed that the plates are close enough together that $d \ll 1$, the fluid flow velocity in the space between the plates is essentially parallel to AB and has the form

$$v(x, z, t) = \frac{2f(z)}{d} \int_0^x \frac{\partial y}{\partial x} dx = \frac{2a\omega}{kd} f(z) \sin kx \cos \omega t, \quad (A5)$$

where z is the coordinate normal to the plates and the function $f(z)$ is approximately parabolic and becomes zero at the plane of contact with the plates, so that $\int_0^d f(z) dz = 1$. Since $f(z)$ contributes a factor of order unity, it will be neglected in the following analysis. The mean square velocity amplitude averaged over the x -direction is

$$\langle v^2 \rangle \approx \frac{2a^2\omega^2}{k^2 d^2} = \frac{2a^2 c^2}{d^2}, \quad (A6)$$

and the peak kinetic energy of the flow is

$$K_{liq} \approx \frac{\rho a^2 c^2}{d}. \quad (A7)$$

Finally, because in the case of the cochlea the plates are immersed in a surrounding liquid, account must be taken of the kinetic energy associated with flow in this liquid. Consideration of the wave equation for a liquid with a standing or propagating wave disturbance imposed upon its surface shows that this wave is exponentially attenuated with distance y from the surface by a factor e^{-ky} . To evaluate, to an adequate approximation, the kinetic energy associated with this motion, the quantity d in (A7) can simply be replaced by $k^{-1} = c/\omega$, giving a kinetic energy contribution

$$K_{outer} = \frac{1}{2} \rho a^2 c \omega, \quad (A8)$$

and the total kinetic energy is

$$K_{total} = K_{plate} + K_{liq} + K_{outer}. \quad (A9)$$

The total symmetric propagation problem can now be solved by choosing either P_{bend} or P_{shear} , depending upon the thickness of the plates, and setting this equal to K_{total} . For the standard SLR-wave situation, the plates are taken to be thin enough that $h \ll \lambda/2\pi$ so that P_{bend} is the appropriate choice, and they are close enough together that $d \ll \lambda/2\pi$, so that K_{plate} and K_{outer} can be neglected relative to K_{liq} . Setting $P_{bend} = K_{liq}$ then leads to the Hassan–Nagy result

$$c \approx \left[\frac{Eh^3 d \omega^4}{3(1-\sigma^2)\rho} \right]^{1/6} \propto \omega^{2/3}. \quad (A10)$$

If the thickness of the plates is comparable to or greater than the wavelength, however, then distortion is by shear and, provided the plates are close enough together that K_{liq} is still greater than K_{plate} and K_{outer} , the equation $P_{shear} = K_{liq}$ leads to the result

$$c \approx \left[\frac{Ehd\omega^2}{(1+\sigma)\rho} \right]^{1/4} \propto \omega^{1/2}. \quad (\text{A11})$$

For intermediate cases, an appropriate interpolation between (A2) and (A3) for the potential energy must be used, and the full expression (A9) may be required for the kinetic energy.

One further important implication of the model is also worth noting. The squirting-wave motions considered above are mirror-symmetric about the central plane AB of Fig. 5.4. This means that exactly the same results will be obtained if a rigid plate is set along this plane, so that there is only a single thin plate separated from it by a liquid-filled space of width $d/2$. Indeed, the elastic stiffness of a thin plate increases so rapidly with its thickness, as indicated by (A2), that in most asymmetric situations an assumption that the thicker plate is essentially rigid will provide a good approximation, provided the thinner plate can distort by bending rather than shear. Of course, the relative elastic moduli of the two plates must also be taken into account.

A similar approach to that above can be applied to the antisymmetric case. Since there is no squirting motion, the enclosed fluid simply moves up and down with the enclosing plates, and its mass is added to the combined plate mass. For plates thinner than about $\lambda/6$, so that they deform by bending, the result is

$$c \approx \left[\frac{2Eh^3}{3(\rho d + 4\rho_1 h)(1-\sigma^2)} \right]^{1/4} \omega^{1/2}, \quad (\text{A12})$$

where $2h$ is the thickness and ρ_1 the density of each of the plates. If the plate sandwich is taken to be much thinner than $\lambda/6$ and immersed in surrounding liquid, as discussed above for the symmetric case, then the loading effect of the surrounding evanescent waves must be taken into account. The result is a propagation law of the form

$$c \approx \left[\frac{Eh^3}{3(1-\sigma^2)\rho} \right]^{1/5} \omega^{3/5}. \quad (\text{A13})$$

These equations imply much faster speed and rather less dispersion than in the symmetric case. Another point of interest is that, in the case discussed above in which one of the plates is essentially rigid and the other flexible, antisymmetric waves do not exist, as can be seen from simple symmetry considerations.

There is, however, an apparent major obstacle to this cochlear model, namely the viscosity of the liquid in the narrow region between the two plates. These viscous losses will generally exceed all other losses in the system and thus provide the primary wave damping. The viscosity η of water at body temperature is about 7×10^{-4} Pa s, and measurements of endolymph and perilymph return similar values⁴⁷, so that the diffusion length $L \approx (\eta/\rho\omega)^{1/2}$ at a frequency of 1 kHz is about 10 μ m and essentially all of the inter-plate liquid will be within the boundary layer. Viscosity will therefore provide a nearly frequency-independent damping force $\kappa v \approx (\eta/d)v$ per unit area, where v is the flow velocity. Inserting this viscous damping term, an equation describing the behavior of an SLR standing wave has the form

$$\rho d \frac{\partial^2 y}{\partial t^2} + \frac{\eta}{d} \frac{\partial y}{\partial t} + Ky = 0, \quad (\text{A14})$$

where y measures the longitudinal displacement of the fluid between the plates and K is the elastic stiffness of these plates, expressed in terms of y . If a standing-wave resonance for this oscillation is considered, then the quality factor Q is given by

$$Q = \frac{\rho d^2 \omega}{\eta}, \quad (\text{A15})$$

where ω is the frequency of the standing-wave resonance. Inserting numerical values for the human cochlea into (A15) gives $Q \approx 10^{-5} \omega$, so that at 1 kHz Q is only about 0.1 and about 1 at 10 kHz. Any such standing-wave resonance is therefore virtually nonexistent under these simple assumptions. While active resonant feedback between cells would contribute negative resistance that could help reduce the effect of this

⁴⁷ See review in Tsang, P. T. S. K. (1997). *Laser interferometric flow measurements in the lateral line organ. PhD thesis*. (Rijksuniversiteit: Groningen). www.ub.rug.nl/eldoc/dis/science/p.t.s.k.tsang/

R 5 [24]

damping, this would not overcome the damping between OHC1 and the IHCs, so the waves could not then propagate effectively.

Propagating SLR waves of frequency ω in the system are attenuated in amplitude as $\exp(-\omega x/2cQ)$, which amounts to $\exp(-\pi/Q)$ per wavelength. Clearly we require that $Q > 1$ for propagating waves to have any significance. Since Q increases nearly linearly with frequency while the viscous barrier-layer thickness is greater than the liquid film thickness, as assumed above (and actually as the square root of frequency above this limit), this explains why SLR waves have been studied mainly at megahertz frequencies and for much thicker liquid layers than found in the cochlea.

As suggested in §R 5.5, however, the existence of a hydrophobic film on each of the two surfaces involved could induce slip between the endolymph and its bounding surfaces in the subreticular space, thereby overcoming this limitation. The basis of viscosity calculations is the classical ‘no slip’ assumption, and for narrow channels and hydrophobic surfaces this is not always correct. Instead, the interface may give rise to relative slip⁴⁸, and this will make the liquid more slippery than its bulk viscosity would predict. In laboratory experiments⁴⁹ the effective viscous drag was reduced by a measured factor of about 5 for films of the thickness found in the cochlea and a single treated surface, using simple laboratory chemicals to produce the film. Such a film applied to both surfaces might be expected to increase the resonant Q value by a factor of about 10, and thus to about 1 at 1 kHz and 10 at 10 kHz, which begins to allow significant propagation of SLR waves. Indeed, when more is known about the molecular and hydrodynamic mechanisms involved, the increase might prove to be larger than this.

5.7 Viscosity and the effects of hydrophobicity

As outlined above, the viscosity of the waterlike endolymph between the reticular lamina and the tectorial membrane appears at first to offer an insurmountable barrier to the propagation of SLR waves below about 10 kHz.

⁴⁸ Granick, S., et al. (2003). Slippery questions about complex fluids flowing past solids. *Nature Materials* 2: 221-227.

⁴⁹ Hild, W., et al. (2003). The effect of wetting on the microhydrodynamics of surfaces lubricated with water and oil. *Wear* 254: 871-875.

However, the classical ‘no slip’ assumption underlying high viscous forces in narrow channels may be unwarranted. Helmholtz in 1860 published an analysis of experiments by Piotrowski on a water–gold interface and concluded there was appreciable slip⁵⁰. More recent experiments using atomic force microscopy⁵¹ have confirmed these long-held suspicions and shown that in some situations the solid surface and liquid may slip relative to each other, a phenomenon describable in terms of a ‘slip length’.⁵² The present focus of much surface physics is on understanding the unique properties of water, and it is now known that water near boundaries is more ‘slippery’ than its bulk viscosity value would predict.

The physics underlying slippage is still uncertain, but it is clear that the effect is one involving surface tension and is greatest for hydrophobic surfaces⁵³. It is therefore significant for the configuration of the cochlea that Hensen cells are located immediately adjacent to the subreticular space and that these cells are characterised by abundant production of lipid droplets^{54–58} which, at least in the case of guinea pigs, accumulate on their surface. Lipids are oily organic compounds insoluble in water; the molecules are amphiphilic: they have a polar (hydrophilic) head and a nonpolar (hydrophobic) tail.

The function of the droplets is puzzling, but one could suppose that this substance might be readily conveyed by capillary effects to the nearby reticular lamina and, via the marginal net, to the underside of the tectorial membrane. How the molecules group together in the cochlea is unknown, but if they made the

⁵⁰ Goldstein, S. (1965). Note on the conditions at the surface of contact of a fluid with a solid body. In: *Modern Developments in Fluid Dynamics [reprint of 1938 edition]*, edited by S. Goldstein (Dover: New York), 676-680. The reappearance of Helmholtz in this new context is startling, so his original text was examined; however, no further connections with hearing were obvious.

⁵¹ Craig, V. S. J., et al. (2001). Shear-dependent boundary slip in an aqueous Newtonian liquid. *Physical Review Letters* 87: 054504.

⁵² See Granick et al. (2003).

⁵³ Cottin-Bizonne, C., et al. (2003). Low-friction flows of liquid at nanopattern interfaces. *Nature Materials* 2: 237-240.

⁵⁴ Merchan, M. A., et al. (1980). Morphology of Hensen's cells. *J. Anat.* 131: 519-523.

⁵⁵ Vinnikov, Y. A. and L. K. Titova (1964). *The Organ of Corti*. (Consultants Bureau: New York). p.24.

⁵⁶ Brundin, L., et al. (1992). Sound induced displacement response of the guinea pig hearing organ and its relation to the cochlear potentials. *Hear. Res.* 58: 175-184.

⁵⁷ Flock, Å., et al. (1998). Vital staining of the hearing organ: visualization of cellular structure with confocal microscopy. *Neuroscience* 83: 215-228.

⁵⁸ Santos-Sacchi, J. (1991). Isolated supporting cells from the organ of Corti: some whole cell electrical characteristics and estimates of gap junctional conductance. *Hear. Res.* 52: 89-98.

subtectorial space hydrophobic, the cochlea could overcome the limitations imposed by the bulk viscosity of water and be able to support a full range of audiofrequency SLR waves. Significantly, Hensen cells are larger and the lipid droplets more abundant at the low-frequency apex where, as (A15) indicates, viscosity reduction is most needed. The droplets reflect light and make the Hensen cells glisten (Brundin et al., 1992), as one might expect from an oily substance. When the cochlea is immunostained for 8-isoprostane (a lipid peroxidation product), cross-sections show, after intense noise, a continuous band of staining encompassing the surface of Hensen cells, the plateau of Corti, and hair cells⁵⁹. Another factor helping to reduce viscous drag at low frequencies is that the height of the tallest OHC stereocilia (and hence the width of the subtectorial gap) increases from about 3 μm at the base to 7 μm at the apex.

The evidence for hydrophobic surfaces reducing viscous forces is widespread, but it has been collected using varying apparatus under disparate conditions. Perhaps most relevant to the subtectorial space is the finding⁶⁰ that the force between a spherical surface vibrating underwater within several micrometers of a plane surface was reduced by a factor of about 5 when one of the surfaces was made hydrophobic (and suggesting a factor of 10 if both surfaces were treated). Another experiment⁶¹ involving a sphere and a plane vibrating relative to each other underwater found a slip length of up to 2 μm under some conditions; in this case hydrodynamic forces were 2–4 orders of magnitude less than those expected from the no-slip condition. More indirectly, observations of water droplets sandwiched between hydrophobically treated glass plates⁶² have measured flow resistances 95% less than when the plates were untreated.

Much current work in surface physics is aimed at enhancing slippage between water and adjacent surfaces, either to increase water repellency or reduce hydrodynamic drag. Of particular interest, one way of increasing a surface's

⁵⁹ Ohinata, Y., et al. (2000). Intense noise induces formation of vasoactive lipid peroxidation products in the cochlea. *Brain Res.* 878: 163-173. Fig. 4b.

⁶⁰ Hild et al. (2003)

⁶¹ Zhu, Y. and S. Granick (2001). Rate-dependent slip of Newtonian liquid at smooth surfaces. *Physical Review Letters* 87: 096105.

⁶² Kim, J. and C.-J. Kim (2002). Nanostructured surfaces for dramatic reduction of flow resistance in droplet-based microfluidics. Proc. 2002 IEEE Conf. MEMS, Las Vegas, 479-482

hydrophobicity is to increase the surface roughness⁶³, leading to ‘superhydrophobic states’ with contact angles approaching 180°. Thus, counterintuitively, a rough surface with high surface area can exhibit appreciably less hydrodynamic drag. A standard method of increasing surface roughness is to create tiny fingerlike protrusions from a surface⁶⁴, in this way making the surface resemble that of a lotus leaf, off which water droplets effortlessly roll. In the cochlea we note that the reticular lamina^{65,66}, and Hensen cells^{67,68}, are decorated with similarly shaped microvilli whose large surface area would act to increase the hydrophobicity of the surfaces from which they protrude.

These considerations suggest that the ear may use hydrophobic properties to increase slippage and escape the standard limitations imposed by viscosity. Measurements of the contact angle of endolymph on the reticular lamina would be of great interest, as would modern assessments of the chemical make up and physical properties of the lipids secreted by Hensen cells, which, as far as now known, are made up of cholesterol esters, triglycerides, and phospholipids⁶⁹. These substances may provide a more effective slip than the standard materials used in surface film experiments.

5.8 Conclusions

This chapter, together with the one preceding, has constructed an attractively simple model for sharp tuning in the cochlea by assuming that SLR waves are generated by interaction between rows of motile outer hair cells, the reticular lamina, and the fluid lying between it and the tectorial membrane. In turn, these squirting waves create, through stereocilia-mediated positive feedback, a standing wave

⁶³ Lafuma, A. and D. Quéré (2003). Superhydrophobic states. *Nature Materials* 2: 457-460.

⁶⁴ Feng, L., et al. (2002). Super-hydrophobic surfaces: from natural to artificial. *Advanced Materials* 14: 1857-1860.

⁶⁵ Engström, H. and J. Wersäll (1958). Structure and innervation of the inner ear: sensory epithelia. *Int. Rev. Cytol.* 7: 535-583.

⁶⁶ Krstic, R. V. (1979). *Ultrastructure of the mammalian cell: an atlas*. (Springer: Berlin). pp. 220–221.

⁶⁷ Merchan et al. (1980)

⁶⁸ Kimura, R. S. (1975). The ultrastructure of the organ of Corti. *Int. Rev. Cytol.* 42: 173–222.

⁶⁹ Schiff, M. and H. Christiansen-Lou (1967). The nature of lipid globules in Hensen's cells. *Ann. Otol. Rhinol. Laryngol.* 76: 624-637.

between the rows. The gain of the reverberating system – operating broadly like a solid-state surface acoustic wave device (Chapter M4) – is presumably neurally adjusted so as to be close to the oscillation threshold in order to provide high gain and narrow frequency response. Squirting waves generated in the OHC region could propagate radially across the space to the inner hair cells and there initiate a strong and sharply tuned neural response.

This model also displays other interesting features. For example, it assigns a role to Hensen cell lipids in overcoming limitations imposed by viscosity. Whether this is the case, or whether viscosity is an inherent feature that helps lower wave speed at low frequencies (as assumed by Elliott et al.), is a question that is left for further work. The model also points to a highly localised basis for the cochlear amplifier, suggesting for example that spontaneous otoacoustic emissions could arise from a small group of OHCs with positive feedback gain exceeding the oscillation threshold for SLR waves.

Modeling wave interactions between outer hair cells

6.1 The basics of wave propagation

6.1/a Effects of changes in standard parameters

6.2 Feedback between outer hair cells

6.2/a Feedback topology

6.2/b Response of three rows of cells

6.3 Modeling squirting wave excitation of the OHC array

6.3/a Explicit solution of the many-cell problem: full wavelength resonance

Results and derivations

6.3/b Explicit solution of the many-cell problem: half-wavelength resonance

The picture set out in the introduction represents the organ of Corti as an array of compressible and pressure-sensitive outer hair cells immersed in incompressible cochlear liquids. This arrangement is favourable for conveying inward and outward motion of the stapes directly and almost simultaneously to the outer hair cells via the fast pressure wave. The pressure signal is therefore applied to the 12 000 OHCs in parallel.

For pure tone input, modeling can be simplified enormously for only a limited number of cells near the resonance frequency need to be considered – there is no need to consider the progressive (serial) motion of a traveling wave along the whole partition. To illustrate the point, in a recent (2003) attempt to model a

traveling wave¹, Givelberg and Bunn ran a supercomputer for some days in a cochlea model divided into a 20- μm grid of more than 8 million points at 30-ns intervals. The authors took fluid–structure interactions into account, and assumed a viscous fluid interacting with a simple elastic membrane under no-slip conditions. However, the mechanics was limited to passive interactions and the pressure at the round window was taken to be zero. It took 20 hours on a 32-processor, 64-GB machine to calculate the response of the basilar membrane to a 10 kHz tone for 0.9 ms, and even then the results were coarse: the envelope was erratic, and the authors conclude that “more data must be collected from numerical experiments before further conclusions about the shape of the traveling wave envelope can be drawn” [p. 388]. The authors note that improving the mesh to 10 μm would require 16 times more computing power.

By way of contrast, when we limit our attention to a circumscribed patch of cells undergoing resonance, we can ignore most of the other, unresponsive, cells. The modeling work described below was done on a standard personal computer (1.2 GHz, 256 Mb RAM). If the response to a click were sought, however, calculations would become difficult – all frequencies, and all cells, are then involved, and individually addressing the time-domain response of 12 000 outer hair cells is not so straightforward. The numerical modeling study described below (using Matlab: The MathWorks, Natick MA) was therefore largely limited to examining frequency-domain responses of a small collection of outer hair cells in response to steady-state tonal input. To maintain generality, wave motion was taken to radiate from each cell in a circular fashion; in terms of a mental picture, the wave energy can be considered to be expanding ripples on a semi-infinite, uniform tectorial membrane.

For tractability, an assembly of 62 cells was studied: basically 3 rows of OHCs extending 10 cells on either side of a chosen IHC. At this place on the partition, the characteristic frequency was arbitrarily set at 1 kHz, meaning, in terms of the SAW model, that the distance from OHC1 to OHC3 (30 μm) was 1 wavelength of a 1-kHz tone. In addition, calculations were done for steady-state conditions of pure-tone input using analytic equations describing the inputs and outputs of all the OHCs. Once the output of each cell is known, numerically summing the outputs of the 62 cells gives the output of the system at the location of the nearby IHC – and hence, the input to this sensing cell.

¹ Givelberg, E. and J. Bunn (2003). A comprehensive three-dimensional model of the cochlea. *J. Comp. Phys.* 191: 377-391.

The key variable was frequency, and by calculating the steady-state response of the system over a range of 0.1–10 kHz at 10-Hz intervals, the frequency response of the system could be graphed.

Outline

The first section, §R 6.1, begins at first principles and sets out the situation governing expansion of a wave from a single oscillating point on a membrane. The treatment is quite general in that no particular wave propagation mode is specified; however, it is initially assumed that the wave is non-dispersive – that is, phase velocity does not depend on frequency. Another simplification is that when wavefronts meet (from opposite directions), their amplitudes were considered to add, implying that the amplitude is essentially a scalar quantity, not a vector.

The modeling looks at the outcome when the number of cells is progressively increased, although initially no feedback between cells is considered. This situation reflects that which may occur when all the cells are driven hard and operating close to their maximum output, say at 60 dB SPL when the cochlear amplifier is close to saturation.

The second section, §R 6.2, investigates a more realistic scenario in which feedback interaction between the OHCs is considered, although still under steady-state conditions of continuous tones.

Finally, the last section, §R 6.3, takes the prime candidate for the wavefront – the squirting wave described in Chapter R5 – and examines how the OHC array may behave when this highly dispersive wave ($c \propto \omega^{2/3}$) operates in the system.

6.1 The basics of wave propagation

1. Assumptions

The assumptions used are:

1. That OHCs detect intracochlear pressure and react with a change in length. That is, the vertical movement of the cells follows, cycle by cycle, the pressure in the cochlea imposed by the stapes.

This is a key assumption for this thesis², and means that OHCs are dual sensors, being able to sense displacement via their stereocilia as well as pressure via their cuticular pore. Chapters D8 and D9 are devoted to justifying this assumption. The arrangement initiates a feedback loop, with ripples emanating from one cell being sensed by the stereocilia of others nearby. The primary stimulus, at least for sound intensities below 60 dB SPL, is taken to be pressure, producing a parallel, simultaneous input to all cells – in accordance with a resonant system (§I 1.5). The engine of the system is electromotility, with the pressure changing membrane potential via the cuticular pore in the same way as deflection of stereocilia does. In this low-intensity regime, stereocilia act as feedback sensors, detecting the ripples emanating from neighbouring cells and again creating another set of circularly expanding ripples. This positive feedback loop underlies the cochlear amplifier. Briefly, then,

- (a) The stereocilia mode of detection is less sensitive than the pressure mode, so that near threshold the pressure response initiates the causal chain. This supposition may be wrong, of course, and the alternative could be that the initial excitation may come from a traveling-wave induced bending of stereocilia. In such a case, the same feedback loop is activated and similar amplification results. However, the process then becomes second filter, not a stand-alone primary filter, and it is not pure resonance.
- (b) The cell's stereocilia do not respond to its own pressure response because the pressure response is vertically directed whereas bending of the stereocilia requires shear.
- (c) The gain of the system is $A\beta$, where A is the electromotility gain and β is the stereociliar gain. The feedback loop will be described in more detail below, but when a ripple of unity amplitude bends the stereocilia, the hair cell elongates by a fractional amount $A\beta$.

2. We assume that the OHCs are laid out in three rows with a regular geometric arrangement (Fig. 6.1) reflecting the pattern seen in micrographs

² While this is true in terms of motivation and the establishment of a resonance theory of hearing, most of the treatment in this chapter can be carried across to a second-filter picture, since an assembly of cells at a given point on the partition can be considered to act simultaneously (effectively in phase) under a traveling wave stimulus.

(Fig. 4.1). The typical geometry has cells separated by a regular distance a in the longitudinal direction and $b/2$ radially. In accordance with most micrographs, cells in OHC1 and OHC3 are aligned in the radial direction, whereas OHC2 is offset by $a/2$. This arrangement gives a face-centered rectangular lattice with the diagonal forming an angle $\arctan a/b$ of about 0.35 (that is, some 19°). That is, the distance b from row OHC1 to row OHC3 is defined to be unity and the distance a between cells longitudinally then appears at a distance 0.35.

As Chapter R7 makes clear, the unit cell becomes shorter and wider as the characteristic frequency increases (that is, a/b becomes larger), and Fig. 7.10 shows the ratio (for a monkey) rising from 0.3 to 0.4 over the mid-frequency range³. A face-centred rectangular lattice of 5 cells can also be described as a face-centered hexagonal lattice of 7 cells, a case in which two of the three OHC2 cells overlap each other. As well as the radial alignment L_0 , note the oblique alignments $L_1, L_2, L_3 \dots$

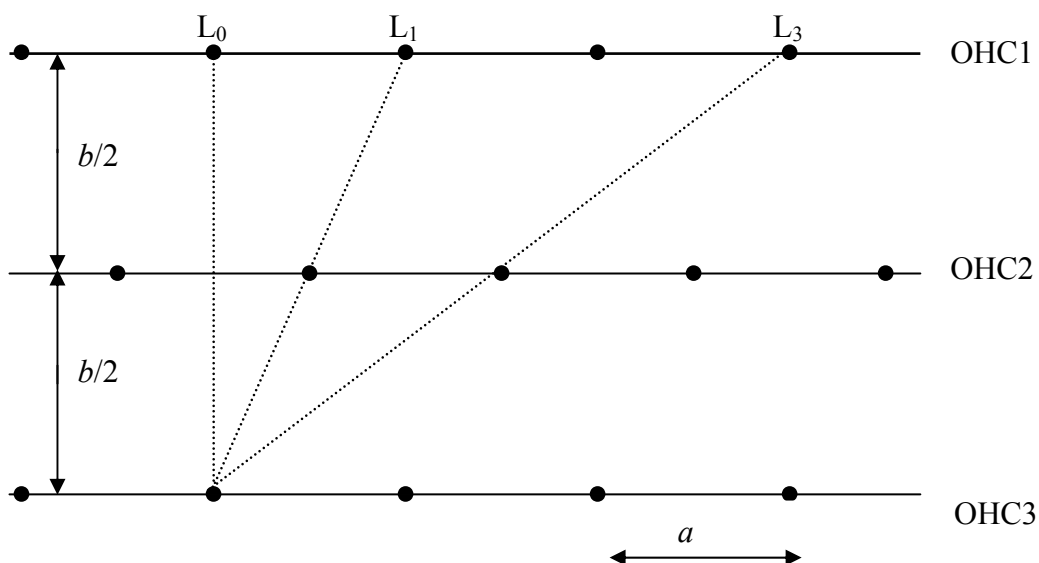


Fig. 6.1. Arrangement of the OHC lattice.

3. In keeping with the SAW analogy, we assume that OHC2 reacts in antiphase to OHC1 and OHC3. That is, when OHC1 and OHC3 lengthen, OHC shortens, and vice versa. (To jump ahead, this assumption was tested and was not seen to be as crucial for excitation and tuning as originally thought; specifically, the

³ Chapter R7 also finds that, for the monkey, the lattice exhibits a small, but systematic, amount of tilt, but this factor has not been included in the modeling.

initial excitation of all three rows can be in phase and still lead to feedback resonance.)

4. It is assumed that the stereocilia of the OHCs are inserted into a uniform, viscoelastic tectorial membrane, so that movement of the cells creates circular ripples on the undersurface of the membrane and these expand at constant velocity in a nondispersive manner. That is, the wave speed is independent of frequency and at a given point on the partition depends only on the mass and elasticity of the membrane. The wave motion is transverse⁴, in the sense that the components of the TM move largely perpendicularly to its surface – although the possibility of a to-and-fro⁵ component in the evolution of the wavefront is retained (that is, each particle on the surface of the TM may, like particles in an ocean wave, trace out an elliptical locus). We assume initially that the stereocilia sense the transverse component of the wavefront, so that where waves combine the displacements simply add and the stereocilia sense the net response. This assumption obviously depends on the type of wave involved, and now that a prime candidate for the wave has been identified (the squirting wave of Chapter R5), it will need to be examined more critically.

In this picture, circular waves keep expanding uniformly and no reflections occur either at the outer edge of the TM (the marginal net) or at its inner edge, the vestibular lip. Clearly, this is not realistic, but the intent of the modeling is to set up the simplest scheme and establish whether feedback resonance is possible.

5. We assume that the propagating wavefront undergoes attenuation (attenuation coefficient γ) with distance, so that amplitude $A = A_0 e^{i\gamma x}$, where A_0 is the initial amplitude and x is distance.

The equations governing this system can be found in Morse's classic textbook⁶. In section 20 of chapter 5, Morse describes the case of forced motion of a membrane. His aim is to analyse the response of a condenser microphone's diaphragm to a point disturbance, but the case applies equally well to the OHC/TM

⁴ *Transverse* in cochlear mechanics is a term used for up-and-down motion of the partition; here it also means at right angles to the direction of wave propagation.

⁵ To prevent confusion, we avoid the usual term *longitudinal* for vibration in the direction of wave propagation because in the cochlea this word means motion along the partition from base to apex.

⁶ Morse, P. M. (1991). *Vibration and Sound*. (Acoustical Society of America: New York).

system considered here where the OHC impresses circular waves onto the compliant surface of the TM.

The speed c of a wave of frequency f hertz and wavelength λ is given by

$$c = f \times \lambda \quad (1)$$

from which it is helpful to define $k = 2\pi f/c = \omega/c = 2\pi/\lambda$, where ω is the angular frequency in radians per second.

The displacement, z , at distance r due to a periodic force $F e^{-2\pi i f t}$ acting at $r = 0$ on a membrane of tension T is given by:

$$z = i \left(\frac{\pi F}{T} \right) [H_0(kr)] e^{-i\omega t} \quad (2)$$

where H_0 is the Hankel function (Bessel function of the third kind) of order 0. The Hankel function may be expressed in terms of the familiar Bessel functions by

$$H_0 = J_0 + iN_0 \quad (3)$$

where J_0 is the Bessel function of the first kind and N_0 (sometimes designated Y_0) is the Bessel function of the second kind, often called the Neumann function. In this way, we can alternatively express z as

$$z = i \left(\frac{\pi F}{T} \right) [J_0(kr) + iN_0(kr)] e^{-i\omega t}. \quad (4)$$

As Morse shows (p.196), when r is large, z approximates to the function

$$i \left(\frac{F}{T} \right) \sqrt{\frac{1}{2\pi kr}} e^{ik(r-ct) - i\pi/4} \quad (5)$$

the real part of which is

$$z \xrightarrow{r \rightarrow \infty} \left(\frac{F}{T} \right) \sqrt{\frac{2\pi}{kr}} \cos \left[k(r-ct) + \frac{\pi}{4} \right]. \quad (6)$$

This shows that the wave is sinusoidal with time, but only approximately sinusoidal with distance owing to the $r^{-1/2}$ factor. Note also that the displacement lags what would be expected from the displacement at the origin by $\pi/4$. This carries

some significance for achieving resonance between cells for it means that a ripple can achieve the necessary 2π phase change by traveling less than a wavelength (i.e., by traveling a distance 0.875λ) because of the additional $\pi/4$ built in to the system⁷. In other words the wave appears to be traveling $8/7$ times faster than it really is to achieve resonance conditions between two points, or, equivalently, that the cavity need only be $7/8$ as long as it otherwise would be. Despite this effect, however, the resonance properties of the OHC lattice are not changed because each resonant cavity is equally affected.

The $\pi/4$ phase change reflects the special conditions of wave propagation near the origin ($r \rightarrow 0$), and that is where virtually all that phase change occurs. Not only does the wave front possess high curvature, but, as an examination of the Hankel function shows, the amplitude approaches infinity. That is, $N_0(z) \rightarrow (2/\pi) \ln(0.8905z) = (2/\pi) \ln z - 0.1159$. As r increases, the wavefront loses its curvature and its amplitude decreases and the phase evolution of the system becomes linear with distance.

The reason for the infinite values is that a membrane cannot support a force concentrated at a point (Morse, p.176). Of course, the OHC has a finite diameter, and its force is conveyed to the TM via a V-shaped stereocilia bundle. The TM displacement will not therefore be infinite, even if the OHC were capable of unlimited extension. Nevertheless, the physical behaviour is reflected by the Hankel function so long as we take care to truncate it at small r , effectively taking the driving force to be applied to a finite area.

In the modeling calculations an arbitrary phase term φ is used, and this accommodates all phase changes in the system including those introduced by transduction delays. However, these delays will in general be small, as outer hair cells are noted for their fast response. Frequency responses have been seen to extend beyond 60 kHz in a guinea pig⁸, and in bats⁹ spontaneous emission has been observed at about the same frequency.

⁷ Assuming, of course, that the OHC response time is zero.

⁸ Frank, G., et al. (1999). Limiting dynamics of high-frequency electromechanical transduction of outer hair cells. *Proc. Nat. Acad. Sci.* 96: 4420-4425.

⁹ Drexler, M., et al. (2004). Isoflurane increases amplitude and incidence of evoked and spontaneous otoacoustic emissions. *Hear. Res.* 194: 135-142.

2. Hankel functions and their approximations

We have set down equations for the wave motion on a membrane emanating from a sinusoidally driven point. Before modeling of a set of points can begin, it is helpful to know what the wave motion looks like and what are the limits of the “large r ” approximation.

The Hankel function can have real or complex arguments. When plotted as function of $x + iy$, the function presents the following form.

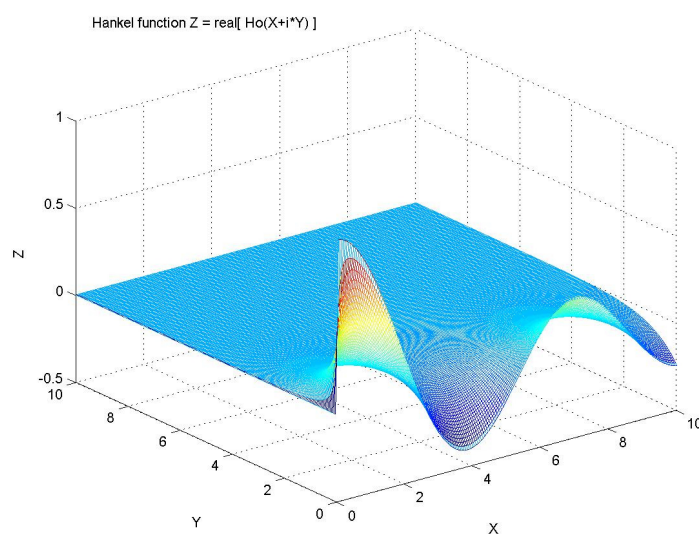


Fig. 6.2. Plot of real part of Hankel function H_0 .

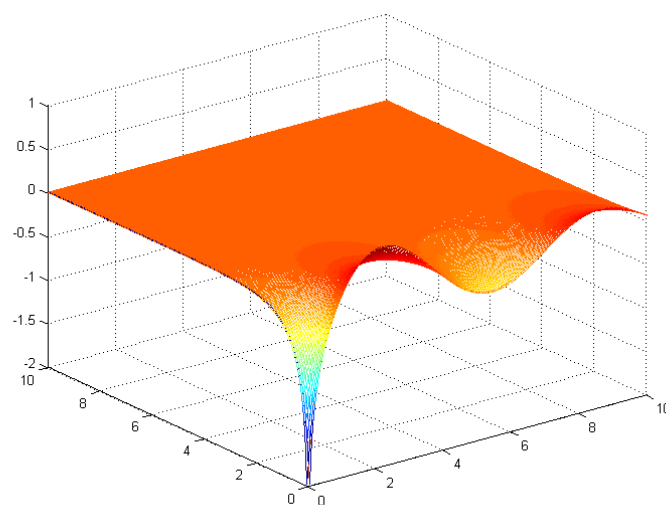


Fig. 6.3. Plot of imaginary part of Hankel function H_0 .

The sinusoidal approximation derives from the imaginary part of H_0 , reversed in sign, and is shown in Fig. 6.4.

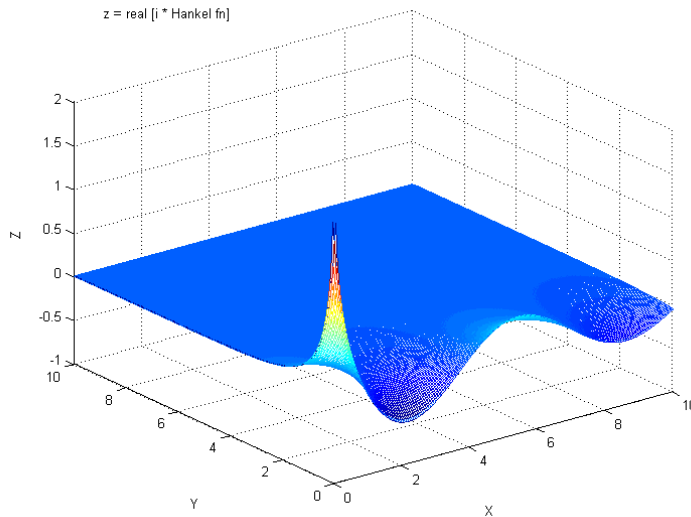


Fig. 6.4. Plot of imaginary part of H_0 , reversed in sign.

The plot shows the oscillating behaviour with x , which is what we require physically. By making the function circularly symmetric, we obtain a picture of how ripples emanate from an oscillating point source on a membrane (Fig. 6.5).

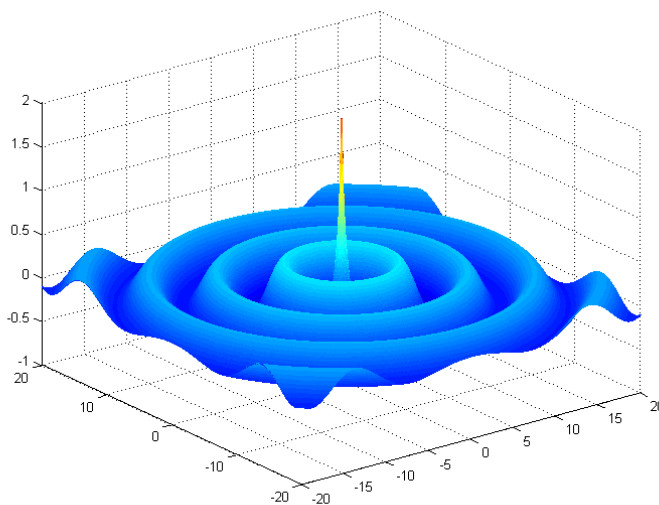


Fig. 6.5. Plot of radially symmetric function $z = \text{Re}[i \times H_0(r)]$. This is the wave displacement at the moment when the displacement is a maximum at $r = 0$. The imaginary part, $\text{Im}[H_0(r)]$, will show the wave when the displacement at the origin is zero.

Whereas Fig. 6.5 gives an exact picture of the behaviour of a tensioned membrane when subject to an oscillating point force, Hankel functions are more complicated than cosine functions, and it is interesting to see how closely the approximation given by Morse represents the exact solution. The exact and approximate solutions are both plotted on the following graph (Fig. 6.6).

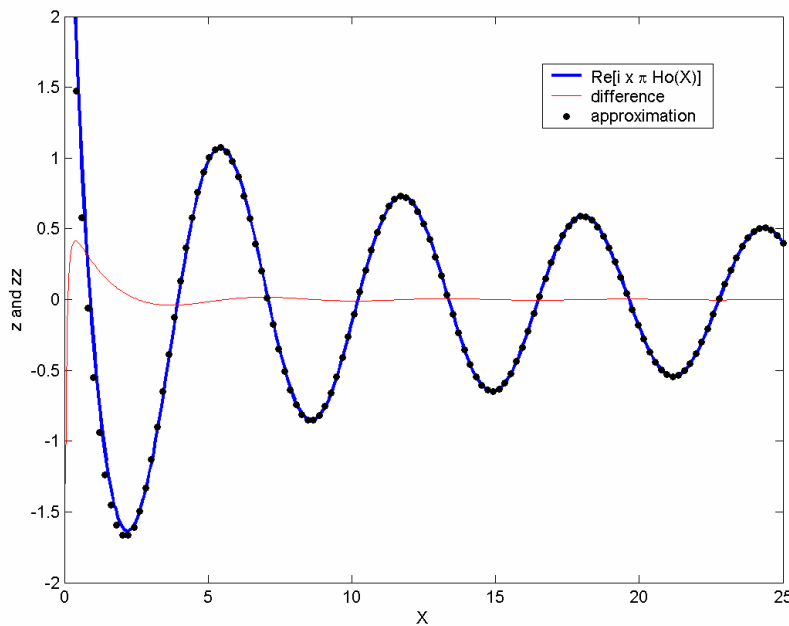


Fig. 6.6. Comparison of $z = \text{Re}[i \pi H_0(x)]$, plotted as blue line, and $zz = \sqrt{2\pi/x} \cos(x + \pi/4)$, plotted as points. The difference is shown in red.

It is clear that the approximation is very good for all values of x greater than about 3 (half a wavelength). Since OHCs are normally situated more than half a wavelength apart, the approximation is used from hereon.

3. Ripples emanating from 3 rows of cells

The ultimate aim of modeling is to see how, through mutual interaction, the OHCs can confer frequency-selective properties to the cochlea. Before we get to this point, a simple first stage of modeling is to look at what happens when all the OHCs give out circular ripples: how do those ripples sum at an IHC position? The geometric arrangement follows the standard arrangement as set out earlier, with the position of IHC set at a distance d from OHC1 (Fig. 6.7).

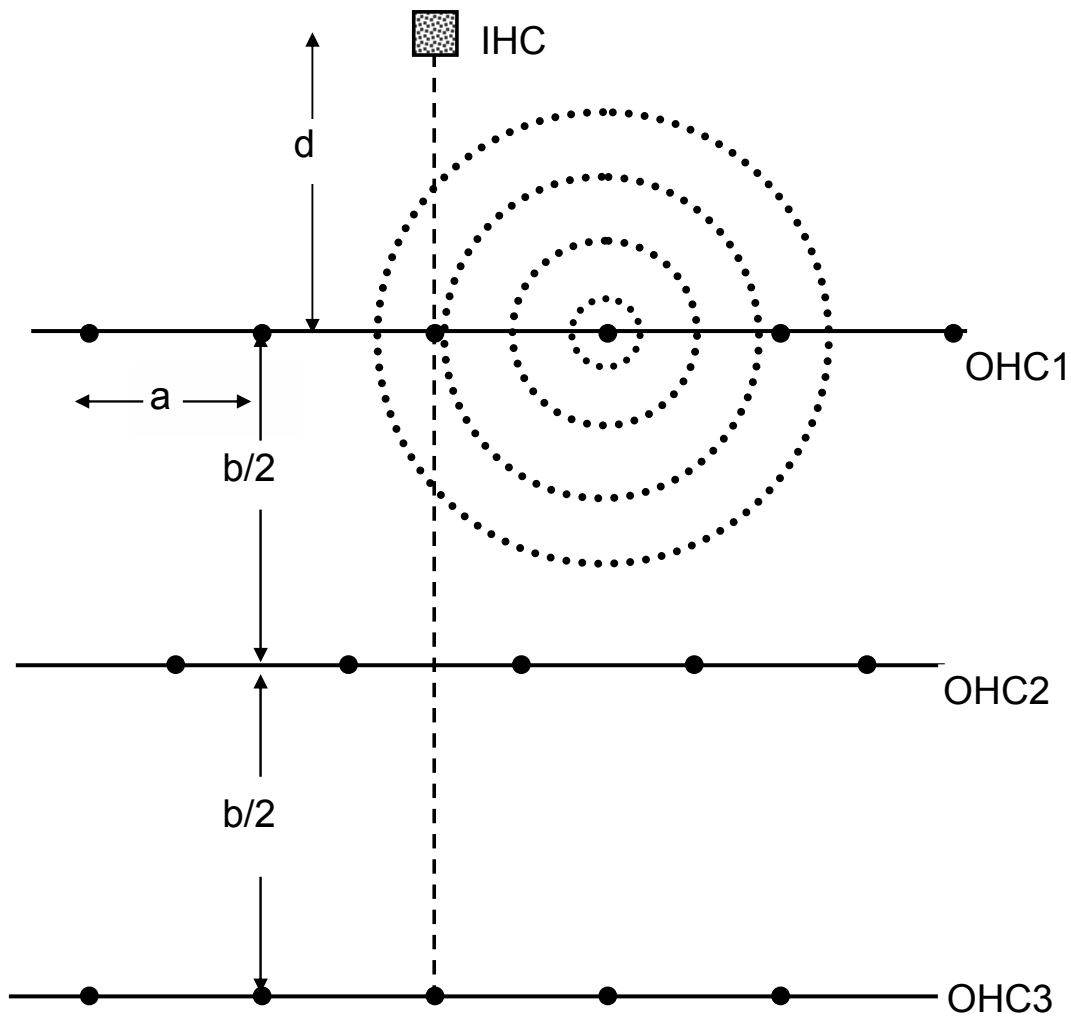


Fig. 6.7. Idealised geometrical arrangement of the OHC lattice, showing positions of three rows of OHCs. The position of an inner hair cell is marked at a distance d from OHC1.

From observation of micrographs (Chapter R7), d is numerically close to b (i.e., about 1 wavelength away from OHC1 when 1 wavelength is OHC1–OHC3). Typically, at cochlear positions where mid-frequencies of about 1 kHz are detected, b is observed to be about $30\ \mu\text{m}$ and a is about 0.35 times this, giving a first oblique alignment of about 19° . In the following calculations, a was therefore taken to be $10.5\ \mu\text{m}$ ¹⁰. As a point of reference, the speed of wave propagation is taken to be

¹⁰ This value was chosen to make L_3 precisely $2b$ since this double spacing may have special significance in the cochlea in that it might allow – if oblique interactions can act independently of

30 mm/sec, so that for a wavelength of 30 μm , the frequency is 1000 Hz. This speeds accords with that calculated on page M 4 [8] as giving resonance at the 1 kHz position in the cochlea.

Assuming that all cells are giving out the same amplitude is one way of looking at the situation in which there is no feedback between cells. The arrangement represents the situation of a saturated cochlear amplifier when all the cells generate their maximum amplitude. The result is shown in Fig. 6.8.

A broad peak in IHC amplitude is evident at about 800 Hz, somewhat below the frequency of 1000 Hz corresponding to 1 wavelength separation of OHC1–OHC3. The amplitude steadily rises at low frequencies due to the ripple amplitude decaying with a $\sqrt{\lambda/d}$ factor, so that the amplitude is high when the frequency is low (λ is long). At higher frequencies, the amplitude decreases with a number of peaks and dips. The maxima and minima generally correspond to simple fractions of a wavelength (i.e. at multiples of 1000 Hz). Fig. 6.8 also demonstrates that the $\pi/4$ factor has no effect on the wave amplitude at the IHC, for calculations in which the phase was set to zero gave identical results.

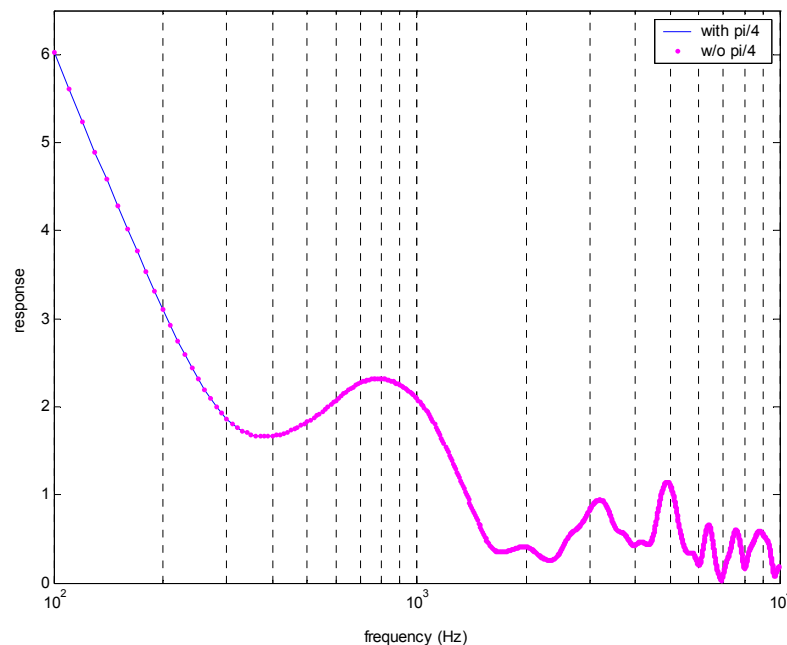


Fig. 6.8. The amplitude of waves generated by 62 OHCs at IHC when all cells are giving equal output. The output of OHC2 is in antiphase to the others. IHC is 30 μm from OHC1.

adjacent interactions – resonance an octave lower. One of the aims of the modeling was to see whether this circumstance is physically possible.

The calculations were also done for lesser and greater number of cells; no perceptible difference in the summation was evident when cell numbers increased beyond about 16 per row (see Fig. 6.13 below). Consequently, the number of cells was set at 20 per row as a number that was amenable to calculation without compromising accuracy of the results.

Changing the distance of the IHC from the array naturally affects the amplitude, but not in a way that drastically alters the frequency response of the system (Fig. 6.9). A linear frequency scale is used to show the regularity of the peaks and dips.

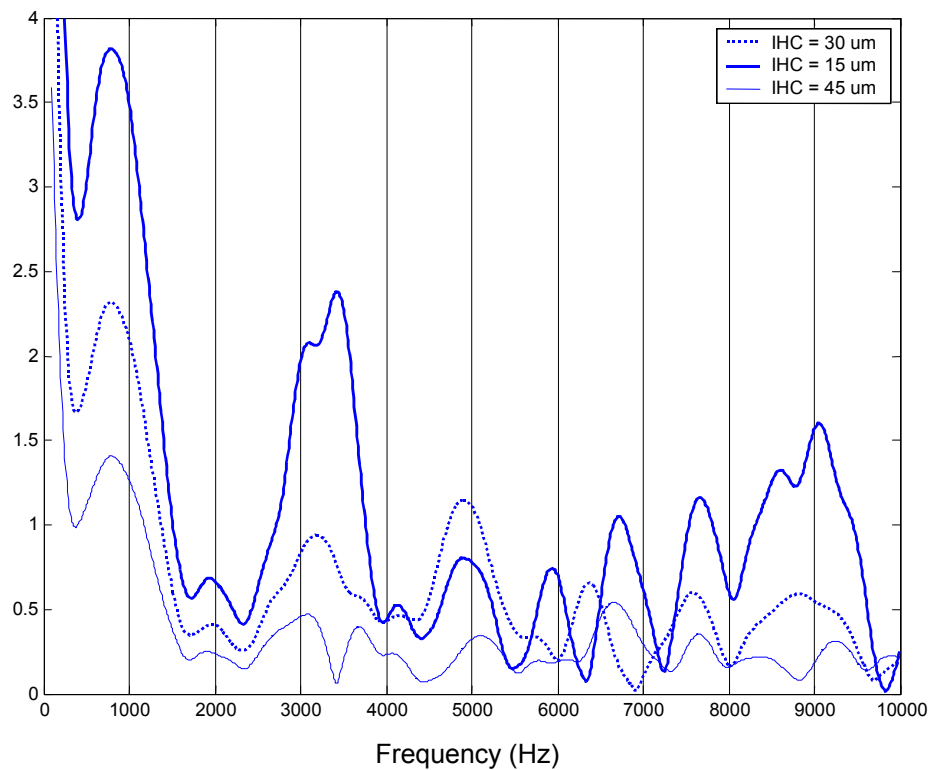


Fig. 6.9. Sum of the wavefronts at various positions (15, 30, and 45 μm) away from OHC1, representing possible positions of the IHCs.

One could reasonably conclude that the exact radial placement of the IHC is not crucial so far as the frequency range 0.5–2 kHz is concerned. Given the repetitive OHC cell geometry in the longitudinal direction, one also expects that the longitudinal placement of the IHC should not alter the situation appreciably either. Two distinct arrangements can be discerned: one in which IHC is aligned with a cell

in OHC2 and another where the IHC is shifted longitudinally by a distance $a/2$. Fig. 6.10 shows that there are some higher-frequency differences between the two arrangements, but at the tuned (characteristic) frequency near 1 kHz the responses are similar.

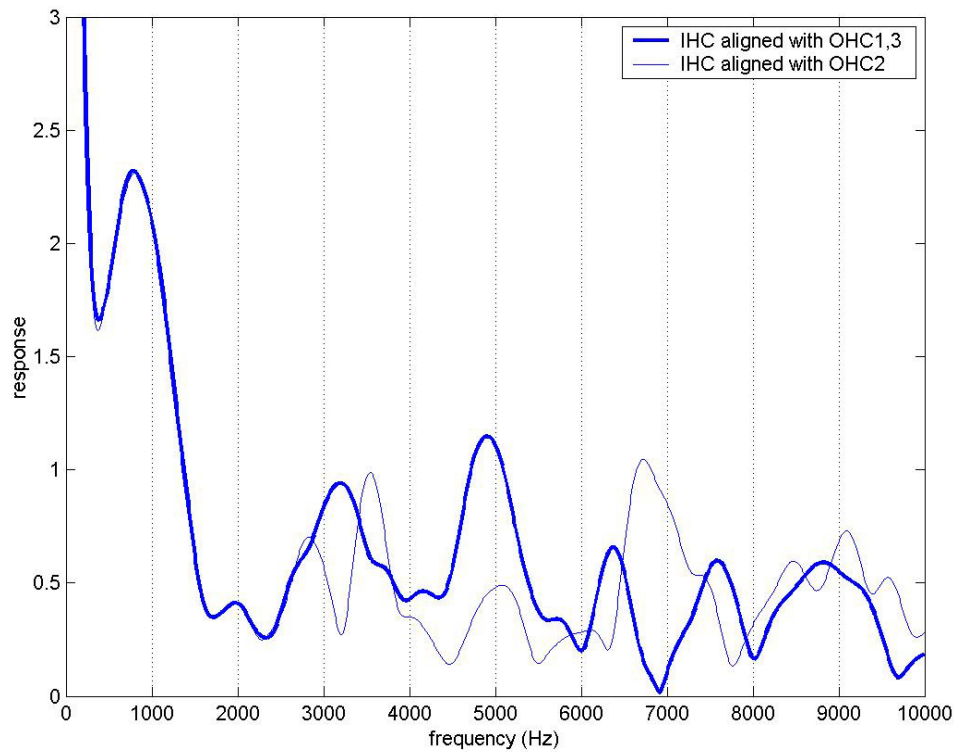


Fig. 6.10. Sum at IHC when IHC aligned radially with a cell in OHC1 and a corresponding cell in OHC3. For comparison, the response is shown when it is aligned radially with a cell in OHC2.

The differences between the two are negligible below 2.7 kHz. At higher frequencies there are some distinct differences, the most significant being the disappearance of the null just below 7 kHz in one case and its replacement with a substantial peak. However, given that the IHC stereocilia are spread out over more than the lateral separation studied ($a/2$), and so will presumably integrate the response of all its stereocilia, the difference is assumed to have no practical effect. Since the two chosen positions are limiting cases, the integrated effect will fall somewhere between the two curves.

6.1/a Effects of changes in standard parameters

1. Magnitude of OHC2 response

The model was changed in two different ways: one where the output of the antiphase OHC2 cells was made 3 times normal, and another where it was reduced to 1/3 of the output of the other two rows.

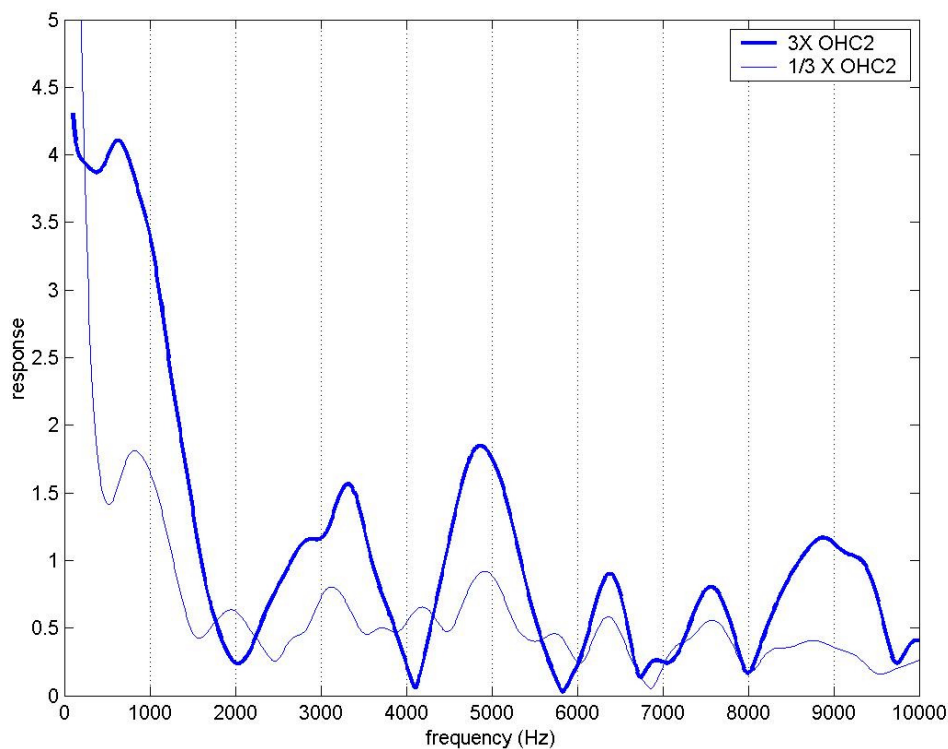


Fig. 6.11. Difference in the sum at IHC when the antiphase output of OHC2 is either greater than or less than normal.

The results (Fig. 6.11) show that the output of the system increases as OHC2 increases. The position of the main peak near 800 Hz is moved down in frequency and the peak near 2 kHz has been eliminated; other higher frequency peaks are affected in different ways, although the major peaks remain.

2. Damping coefficient enhanced or diminished

One of our basic assumptions (page R6 [6]) was that the propagating wavefront suffered intrinsic propagation losses with distance, so that with attenuation coefficient γ the amplitude diminished as $A = A_0 e^{i\gamma x}$, where A_0 was the initial amplitude and x the distance. The coefficient γ was initially set at 1 so that it gave a $1/e$ decrease in amplitude for every 30 μm ; this is in addition to the intrinsic $\sqrt{(\lambda/d)}$ factor by which the amplitude of a ripple decreases with distance (simply because energy must be conserved as the circular wavefront expands). The standard damping coefficient was at first increased, and then decreased by a factor of 3.

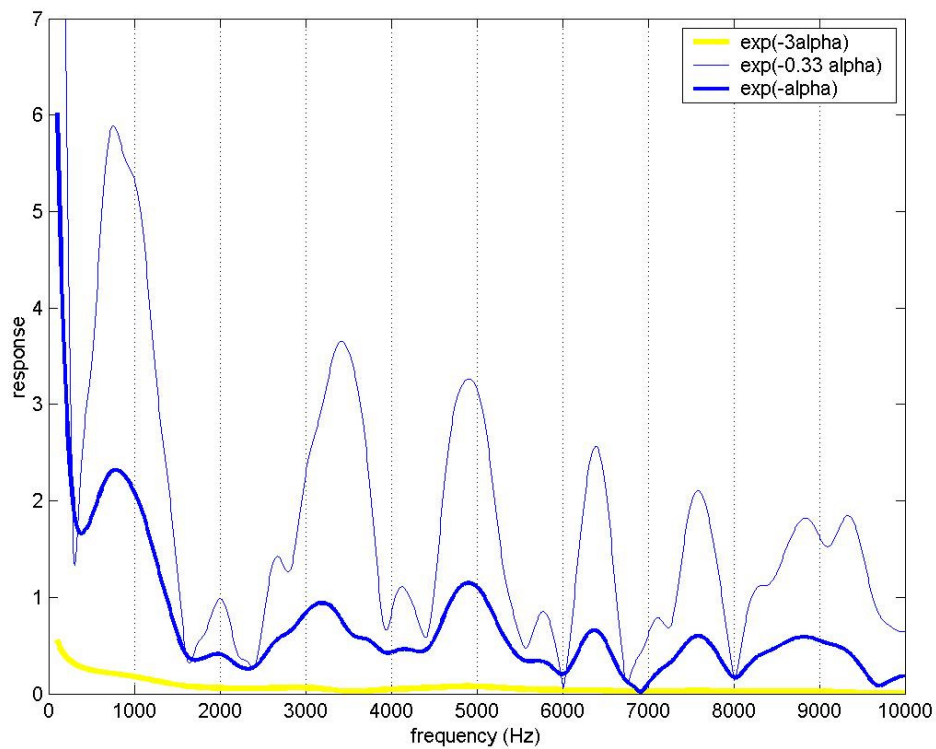


Fig. 6.12. Sum at IHC when damping is higher than, or less than, normal.

It is seen (Fig. 6.12) that with attenuation significantly greater than the reference of $1/e$ per 30 μm , the peaks disappear, whereas under undamped conditions they are enhanced, with a number of previously weak or nonexistent peaks becoming evident. However, where peaks are apparent in both, their frequency does not appear to be appreciably altered by the change in damping.

3. Number of contributing cells

When the number of contributing cells per row is altered from 10 (± 5 from the reference position) to 16 (± 8), the fine structure of the sum at the IHC alters somewhat (Fig. 6.13), but there is little change once the number of cells is increased beyond 20 (± 10). For purposes of calculation, the number of cells is kept at 20 per row, a number that gives accurate results without excessive computational effort.

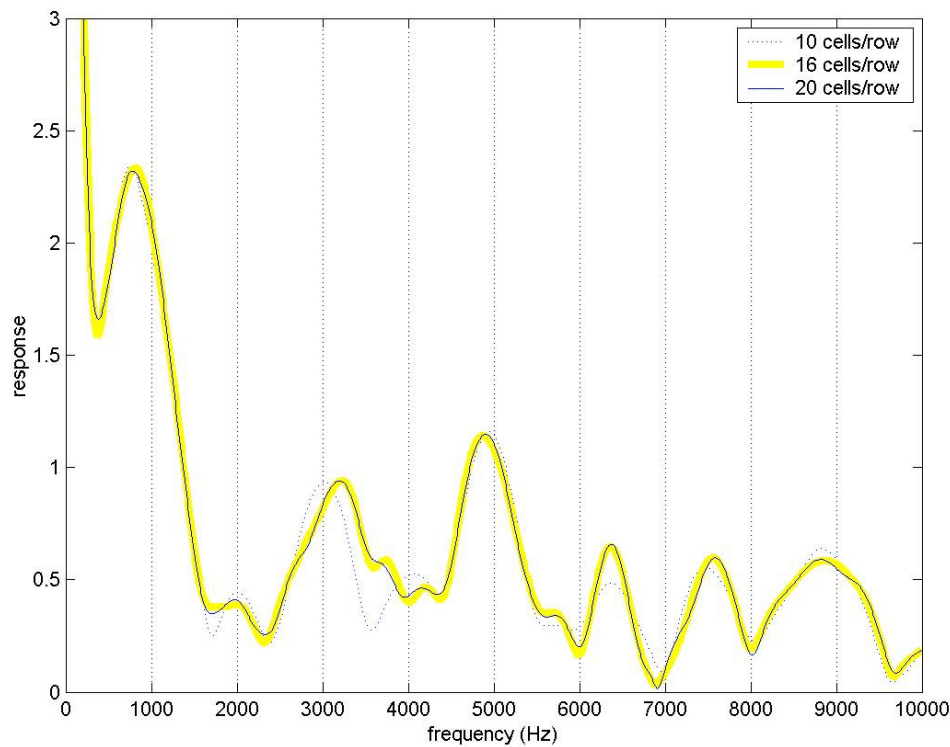


Fig. 6.13. Sum at IHC when the number of contributing cells per row is varied from 10 to 20.

To conclude this section, the main result to be noted is that the OHC array has inherent strong tuning properties, even without considering feedback. The dominant frequency is that of the fundamental, corresponding to a single wavelength between OHC1 and OHC3. Higher harmonics may have some effect, but are probably less important given that OHCs can be expected to have electrical tuning properties broadly matching the characteristic frequency of the partition at that location.

In the next section we will consider what happens when feedback between the cells is introduced.

6.2 Feedback between outer hair cells

So far we have only considered the situation of each OHC responding directly to imposed oscillating pressure (detected by the body of the cell) with synchronous expansion and contraction, a motion which causes ripples of some kind to spread out from each cell. As we have seen, when the individual wavefronts from a number of OHCs add up at the IHC position, distinct peaks and dips in the steady-state frequency response of the system are produced.

Here we consider the effect of adding feedback to the system. That is, let us examine what happens when the stereocilia of each OHC respond to the wave amplitude produced by neighbouring OHCs. The expectation is that this process will lead to enhanced tuning in the system whenever there is a phase change of 2π in the feedback loop.

1. The OHC and its feedback system

As described earlier (§R 6.1), we hypothesise that the OHC is a dual detection system, able to respond to both intracochlear pressure (via its cuticular pore sensor) and to displacement (via bending of its stereocilia). The first system is the more sensitive and gives rise to ripples which are sensed by stereocilia of neighbouring cells. In turn, the receiving cells give out ripples that can return to their source, thereby providing a positive feedback pathway. The system is illustrated below (Fig. 6.14).

The primary stimulus for the OHC is intracochlear pressure, P , which is sensed by the cuticular pore system. As discussed in detail elsewhere (§D 8.4/f), the pore is a hole in the cuticular plate covered only by the cell's plasma membrane. It is therefore extremely thin and has high compliance; moreover, because the rest of the cell is relatively rigid, it will readily respond to pressure differences between the interior of the cell and the cochlear fluids. Water is virtually incompressible, so an efficient way to move the cuticular pore and thereby detect pressure is for the cell to

contain a compressible material; for the highest efficiency, a gas (air) is favoured, and the possibility that Hensens bodies enclose air bubbles is also set out in §D 8.4/e.

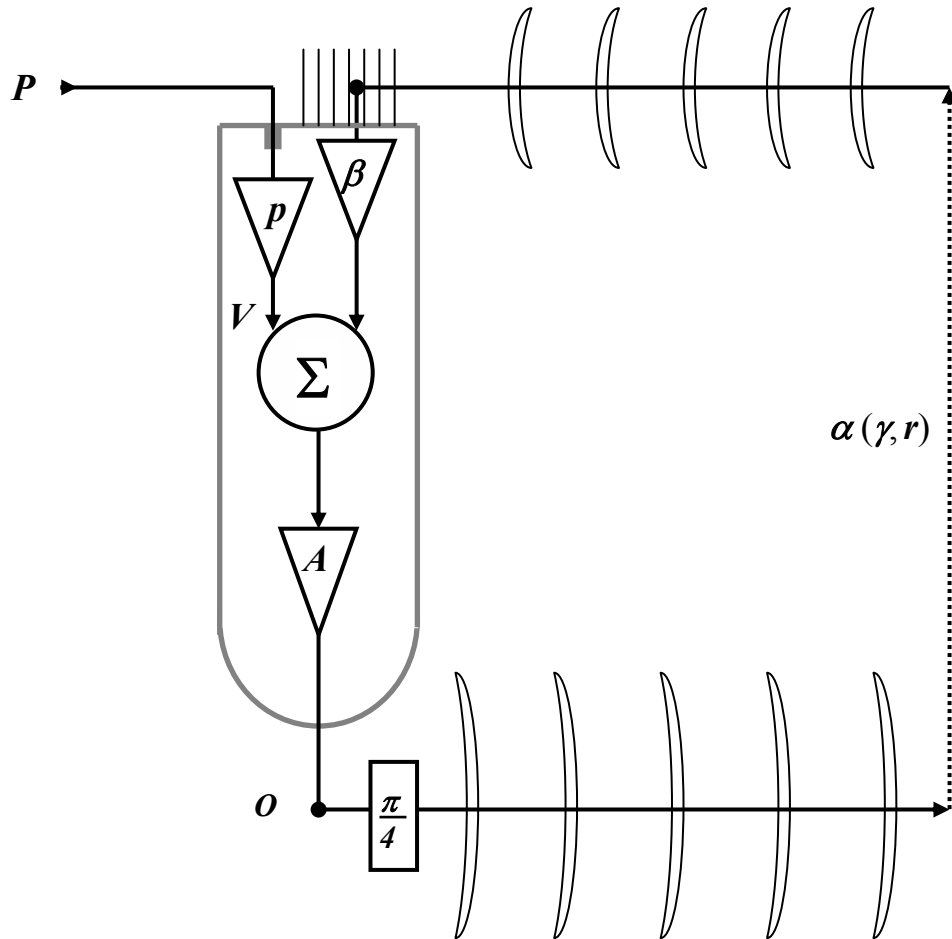


Fig. 6.14. Signal pathway in the OHC. P is the intracochlear pressure (pascal); p the piezoelectric transducer constant in mV/Pa; V the transduced pressure signal (receptor potential) in mV; A the electromotility gain (nm/mV); O the output (nm); $\pi/4$ the intrinsic phase delay between OHC displacement and propagating wave; $\alpha(\gamma, r)$ the attenuation in ripple amplitude between the output of one cell and stereociliar input of another (both amplitude and phase delay will depend on the path length); β is the stereociliar efficiency in converting ripple amplitude into receptor potential (mV/nm). The summing point Σ denotes the (in phase) input to the cell's voltage-to-length converter.

A full description of the presumed mechanism is given in Chapters D8 and D9, but at this point a summary would appear useful. The cuticular pore is a remnant of the kinocilium, a motile cilium which disappears before or shortly after birth. This is unusual, and the explanation offered here is not that an intricate cell mechanism has been lost but rather that the mechanism has been elaborated so as to detect pressure directly. That is, the cellular electromechanical machinery which once

moved the kinocilium might still be in place and, by working in reverse, produce a change in the receptor potential of the cell in response to movement of the cuticular pore. The transduction channels for this pressure transducer modulate the cell's "silent current"¹¹ and have been appropriated for low-level detection of sound. The system is reminiscent of the two-level system in vision, where less-sensitive cones are responsible for detection of bright light whereas much more sensitive rods are used for low light levels. The OHCs have combined two detection systems into one, so that the cuticular pore is involved in low-level sound detection, whereas bending of stereocilia is used for high-level sound detection.

The pressure-detection function of OHCs is a feature that has not yet been confirmed experimentally, and is subject to verification. Nevertheless, as discussed elsewhere (§I 2.2/h), it makes sense of "Flock motility" – a feature of a collection of papers from Flock's group in which OHCs were observed to undergo motile responses in response to direct sound pressure. Therefore, at low sound levels, it is hypothesised that, V , the receptor potential of the cell, is given by

$$V = p P \quad (7)$$

where p , in mV/Pa, is the conversion factor between intracochlear pressure P and receptor potential, V . Effectively, p is the piezoelectric coefficient of the cell.

The receptor potential is the input to the cell's electromotile apparatus. The system has been called a voltage-to-movement converter¹², and involves the action of a voltage-sensitive protein, prestin¹³, in the cell wall. The system is fast, and can respond, cycle by cycle, to at least 50 kHz¹⁴. The output of the system, O , is therefore given by

$$O = A V \quad (8)$$

¹¹ Brownell, W. E. (1982). Cochlear transduction: an integrative model and review. *Hear. Res.* 6: 335-360.

¹² Evans, B. N., et al. (1991). Outer hair cell electromotility: the sensitivity and vulnerability of the DC component. *Hear. Res.* 52: 288–304.

¹³ Zheng, J., et al. (2000). Prestin is the motor protein of cochlear outer hair cells. *Nature* 405: 149-155.

¹⁴ Scherer, M. P. and A. W. Gummer (2004). Vibration pattern of the organ of Corti up to 50 kHz: evidence for resonant electromechanical force. *Proc. Nat. Acad. Sci.* 101: 17652-17657.

where O is the amplitude of the cell's length oscillation and A is the conversion factor, in nm/mV, between receptor potential and cell length.

The output creates circular ripples (Fig. 6.5) on the smooth isotropic surface of the TM, and these propagate with attenuation, α , towards neighbouring cells where they cause deflection of the stereocilia. This opens conduction channels which add to the receptor potential of the cell. The efficiency of this stereociliar process is denoted β , and is expressed in terms of mV/nm. The two detection processes add together at a point designated Σ , the return point of the feedback loop and the input to the electromotile apparatus.

The feedback loop thus involves two key parameters, a loss factor α and gain factors A and β , and these are now examined more closely.

First, α is the attenuation of a ripple as it passes from one cell to the next. It therefore depends on distance and expresses the ratio of the amplitude of the wave as emitted by one cell to the amplitude of the wave at the point where it is detected by the second. The amplitude reduction involves two factors.

(1) Expansion of the circular wavefront. Here the amplitude falls as $\sqrt{(2\pi/kr)}$ or $\sqrt{(\lambda/r)}$, where r is the distance, which means that, when the distance is expressed in wavelengths, the amplitude will fall by 0.7 for each doubling of distance. By itself, this attenuation factor is relatively small, and long-range propagation would appear possible. A difficulty in specifying α numerically is that the amplitude theoretically goes to infinity at zero distance, so that to define a reasonable measure for the output of a cell we need to introduce a finite source size. This can conveniently (and realistically) be the radius of the cell, which is typically about 4 μm . For a given frequency, the amplitude will fall as $\sqrt{(4 \cdot 10^{-6}/r)}$, where r is the distance in micrometres. Inserting values, we see that the amplitude will reduce to one-half at a distance of 16 μm , approximately the inter-row distance, and about one-third at a distance of 32 μm , the distance between OHC1 and OHC3.

(2) Intrinsic propagation losses in the medium on which the ripple travels will introduce additional attenuation of the form $e^{-\gamma r}$, where γ is the attenuation factor. The value of γ can only be roughly specified, with in vitro experiments¹⁵ indicating a 'space constant' ($1/e$ attenuation) of about 25 μm . When r is expressed in

¹⁵ Abnet, C. C. and D. M. Freeman (2000). Deformations of the isolated mouse tectorial membrane produced by oscillatory forces. *Hear. Res.* 144: 29-46.

micrometres, this means that γ is about 0.04. In modeling the system, γ will be taken to range from about 0.01 to 0.1.

Therefore, with both factors at work, the reduction in amplitude of a wave in progressing a distance r micrometres from one cell to its neighbour can be taken to be

$$\alpha = \sqrt[3]{(4 \cdot 10^{-6}/r)} e^{-\gamma r}. \quad (9)$$

As a point of reference, for the standard 30- μm distance from OHC1 to OHC3 and a loss-factor in the medium of 0.04, the total attenuation will be ≈ 0.1 . Note that α will always be less than 1.

The parameter β represents the gain of the conventional stereociliar detection system in converting ripple amplitude into receptor potential and is expressed in mV/nm. The other circuit gain is provided by the electromotility gain, A , so that both together give a gain of $A\beta$. The circuit gain of the whole system will therefore be $\alpha A\beta$, a dimensionless number, and when this exceeds unity the whole system undergoes spontaneous oscillation.

2. Two detection systems

The two detection systems, body-sensing of pressure and stereocilia detection of ripple amplitude, are both able to generate a receptor potential, and the net effect is simply the sum of the two individually. We assume the sum is in-phase (additive) and linear. They act independently and instantaneously, a statement that requires clarification.

The stereocilia of the OHC act essentially as feedback elements, at least at sound intensities less than 60 dB SPL, returning the ripples that were originally broadcast by the cell as output, O , back to the cell's input. The primary input stimulus at these sound pressures is the pressure signal, while stereocilia deflection is an auxiliary system necessary for the cochlear amplifier to function. The feedback path is completed at the level of the receptor potential, and this summation point is designated Σ in Fig. 6.14.

The requirement of independence means that the stereocilia must respond (instantly) only to bending, and the body of the cell must respond (instantly) only to intracochlear pressure. The bending will be produced by the component of the wave in the tectorial membrane that deflects the stereocilia. For any type of wave, the movement it produces at each point on the surface of the TM can be considered as tracing out a locus. For a Rayleigh wave (and most other wave types), that locus will be an ellipse (in the vertical plane). The elliptical locus will resemble the path that a small object floating on the sea surface undergoes. The ellipse can be considered to be composed of a backward-and-forward component superimposed on an up-and-down or “transverse” component. The vertical component is not sensed by the stereocilia; this means that the cell does not respond to its own vertical movement (which it executes in response to imposed pressure and stereociliar deflection) and makes calculations tractable. This assumption is unrealistic in that vertical motion of the cell is likely to produce bending of stereocilia and change of membrane potential. Nevertheless, because this action is fast (virtually instantaneous), we can consider it as part of a tight (positive) feedback loop that improves sensitivity of the system. Put another way, p is the closed loop feedback gain of a system that converts intracochlear pressure to receptor potential.

The OHC’s double-detection system makes sense of the V-shape of the stereociliar arms, for this arrangement gives stability against bending when vertical forces are applied, but allows each arm to deflect under the influence of a passing ripple. The angle enclosed by the arms of the V is small (30° or less) at the cochlear apex and large, almost collinear (180°), at the base. This arrangement may account for the different shape of the cochlear tuning curve at base and apex (see conference abstract of Bell, 2002), but modeling here has not progressed far enough to confirm this supposition. Geometrically, the arrangement points to possible oblique (relatively long-distance) interactions between widely separated OHCs at the apex, while only short (nearest neighbour) interactions are possible at the base. Further work is needed here.

To complete the story, it may also be worth considering that the cuticular plate bearing the OHC stereocilia can actively tilt¹⁶. Actin filaments¹⁷ have also been

¹⁶ Zenner, H. P., et al. (1988). Active movements of the cuticular plate induce sensory hair motion in mammalian outer hair cells. *Hear. Res.* 34: 233-240.

detected beneath the plate. These observations suggest that the OHC probably actively controls the set point and gain of the stereocilia-bending and the pressure-detection systems, as hinge-like movement of the cuticular plate will affect both processes. However, these possible complications are set aside. An adequate explanation for the tilting is that it allows long-term adaptation of the cell, either increasing or decreasing sensitivity as required. Cuticular plate tilting is probably behind the observed ‘slow motility’¹⁸ of OHCs. For now, we will focus on the fast electromotile system as the key component of our modeling. In summary, instantaneous self-interaction of the two detection systems has not been explored and for simplicity has been ignored.

6.2/a *Feedback topology*

Given the feedback paths described in Fig. 6.14, the steady-state response of the system can be analysed by treating it as a circuit and applying feedback equations.

1. Two interacting cells, fixed distance

Take first the simplest case: two interacting OHCs separated by a distance a , which in the first instance will be taken to be 1 wavelength. They are both simultaneously excited by a pressure signal of strength P pascal which gives rise to a receptor potential V mV which in turn creates a ripple on the tectorial membrane of amplitude AV nm (where, as before, A is the conversion efficiency in nm/Pa between input pressure and the resulting OHC vibrational amplitude. The ripple, which is the output O of the cell, propagates from one cell to its neighbour with amplitude reduction α and is detected by the second cell’s stereocilia to give a receptor potential $\alpha\beta$ mV. The system can be described with the following circuit diagram (Fig. 6.15) in which triangles denote amplifiers and squares represent resistors.

¹⁷ Slepecky, N. B. and S. C. Chamberlain (1982). Distribution and polarity of actin in the sensory hair cells of the chinchilla cochlea. *Cell Tissue Res.* 224: 15-24.

¹⁸ Schacht, J., et al. (1995). Slow motility of outer hair cells. In: *Active Hearing*, edited by Å. Flock et al. (Pergamon: Oxford), 209-220.

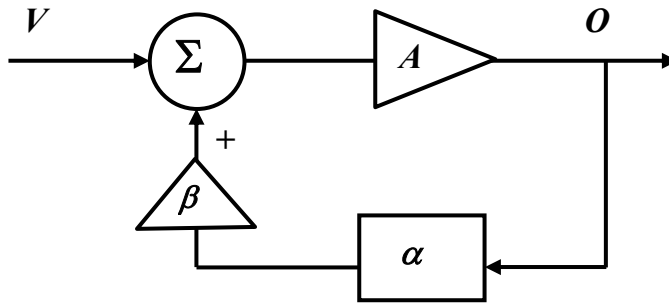


Fig. 6.15. Equivalent circuit diagram of the two-hair-cell system.

With input potential V and positive feedback factor $\alpha\beta$, the input to the electromotile system is $V + O\alpha\beta$. The output O is A times the input, where A is the gain of the amplifier stage. Therefore, the steady-state output of the system is $A(V + O\alpha\beta)$. That is,

$$O = A(V + O\alpha\beta)$$

$$\therefore O = \frac{AV}{1 - A\alpha\beta} \quad (10)$$

We see that the stand-alone output of the cell, AV , has through positive feedback been amplified by a factor $1/(1-A\alpha\beta)$. O can be very large if $A\alpha\beta \rightarrow 1$, which it will be if the gain ($A\beta > 1$) is sufficient to counteract the attenuation ($\alpha < 1$). The system will break into oscillation if $A\beta \geq 1/\alpha$. Here is the cochlear amplifier at work, and one of the side-effects is spontaneous oscillation if the gain is not kept below well-defined limits.

Using Equation 10 it is possible to calculate the output of the cell. The value of α can be calculated provided the distance between the cells is known and γ is specified. The effect of a range of values of the cochlear amplifier gain $A\beta$ will be examined in the following calculations. If we know the output of each cell, the total steady-state output of the two cells can be added at any point – and in particular at an IHC position, as done before.

Let us assume that the IHC lies at distances of 0–100 μm from the line joining the two cells (and, for simplicity, at the centre-point of the line, Fig. 6.16).

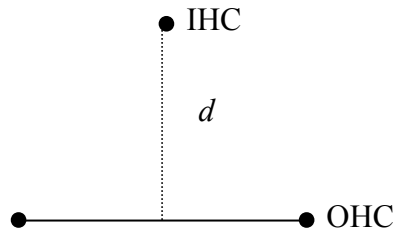


Fig. 6.16. Location of IHC with respect to two OHCs separated by 26.25 μm (resonance condition at 1 kHz).

The sum at IHC was computed for distances d of 0 to 100 μm . For a separation of the OHCs of 26.25 μm (7/8 times 30 μm , resonance conditions at 1 kHz after allowing for a $\pi/4$ phase lag), the attenuation, α , between the two cells was 0.15. The result for various values of $A\beta$ is shown in Fig. 6.17.

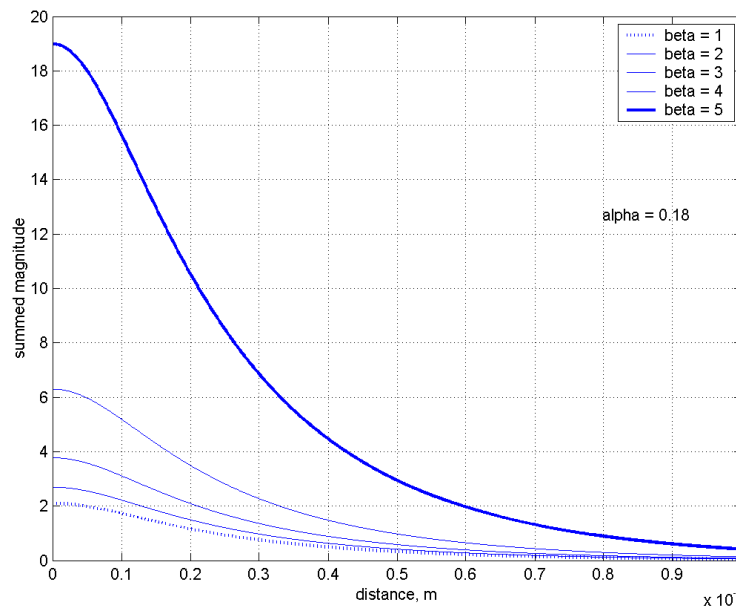


Fig. 6.17. Summed wave amplitudes at the IHC position computed for various distances from the axis of the OHCs. The attenuation α was 0.18 and values of β ranged from 1 to 5.

The plot shows how the output of the system increases markedly as the gain of the cochlear amplifier increases from 1 to 5. The system would break into oscillation if $A\beta$ reached 5.5.

Similarly, the output of the system for an arrangement in which the cells are collinear (Fig. 6.18) is shown in Fig. 6.19. This arrangement simulates the conditions where the IHC lines up with a cell from OHC1 and another from OHC3.

- IHC
- OHC
- OHC

Fig. 6.18. The same three cells as before, but all cells are now in line.

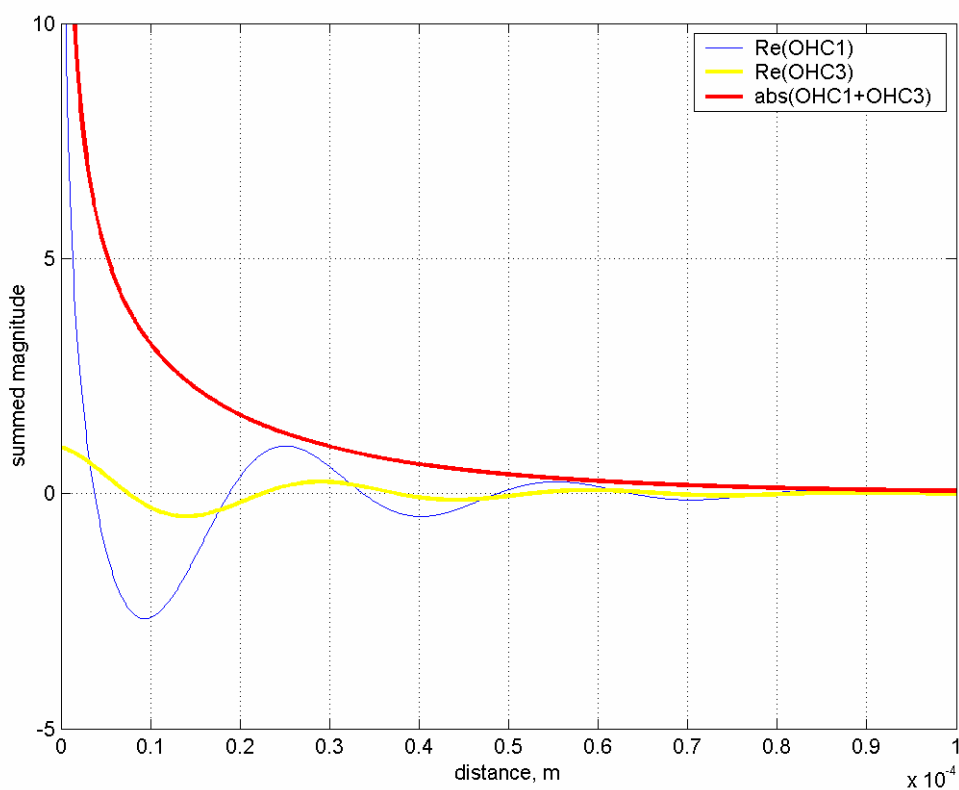


Fig. 6.19. Summed magnitude of the response at IHC due to two OHCs when all cells are collinear.

2. Two interacting cells, arbitrary separation

In the previous section it was assumed that the separation between the cells was such that a phase change of precisely 2π occurred between the cells. Let us now look at a system where the distance between the cells is arbitrary. In this case, the mathematics is as before except that the attenuation factor, α , includes a phase shift so that

$$\alpha = \sqrt{\frac{4 \cdot 10^{-6}}{r}} e^{-\gamma r} e^{-i(kr + \pi/4)} \quad (11)$$

and so the output of the cell, now complex and frequency-dependent, is

$$O(\omega) = \frac{AV}{1 - A\alpha\beta} \quad (12)$$

where α is defined according to Equation 11.

The output of each cell is amplified when waves traverse the feedback loop with phase delays of multiples of 2π . Taking a distance of $30 \mu\text{m}$ and a circuit gain ($A\beta$) around the feedback loop of 5, the following responses were calculated (Fig. 6.20).

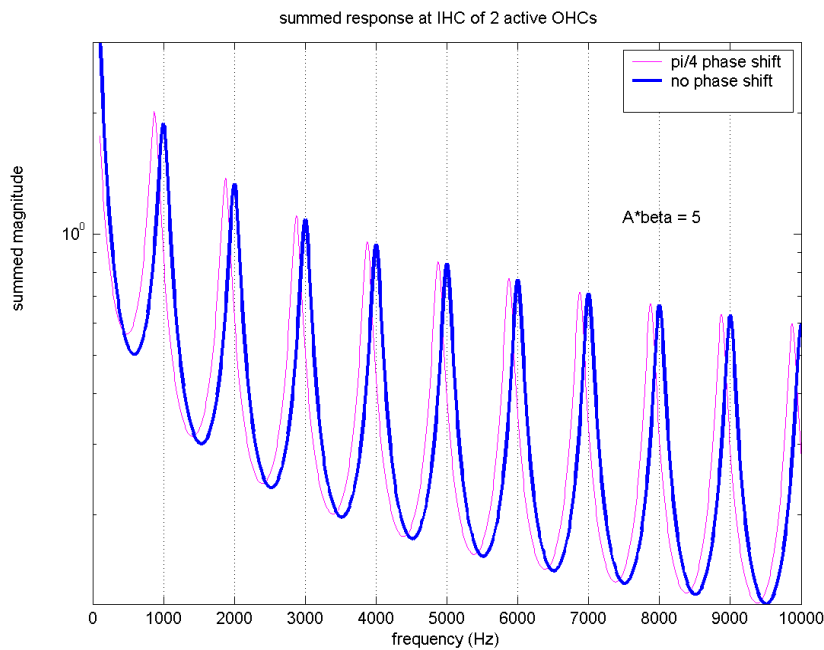


Fig 6.20. Frequency response of 2 interacting OHCs calculated at an IHC position $30 \mu\text{m}$ from the midpoint of the line joining the two cells.

Note that the recurring peaks at multiples of 1000 Hz when in-phase conditions occur. The insertion of the $\pi/4$ phase shift simply lowers the frequency of these peaks by a small amount.

3. Single row of cells

Let us now analyse the response of a single row of OHCs which extends indefinitely in each direction (Fig. 6.21). Because of attenuation (arising from outwards expansion of ripples and intrinsic losses), in practice it is sufficient to consider just 20 cells participating in the interaction. With every cell having the same inputs and outputs, each will behave identically. Consider the inputs and outputs passing through the grey box enclosing a typical cell.

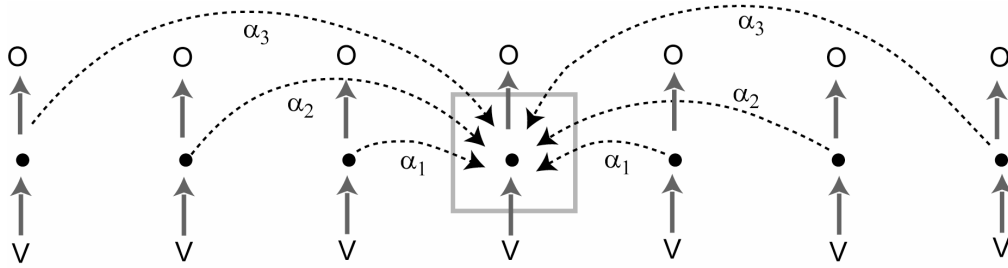


Fig. 6.21. Feedback between cells in a row of identical cells.

The same feedback network as before is applicable, except there are more inputs, not just feedback $\alpha_1\beta$ from the neighbouring cell, but also two contributors from two cells away, $\alpha_2\beta$, two from 3 cells away, $\alpha_3\beta$, and so on. Therefore, output of the typical cell, O , is

$$O = A [V + 2\alpha_1\beta O + 2\alpha_2\beta O + 2\alpha_3\beta O + \dots]$$

which means that

$$O = \frac{AV}{1 - 2A\beta(\alpha_1 + \alpha_2 + \alpha_3 + \dots)}$$

which we write as

$$O = \frac{AV}{1 - 2A\beta\alpha} \quad (13)$$

where $\alpha = \sum_1^{10} \alpha_n$, a complex quantity (carrying both amplitude and phase).

To model a row of cells, a line of 21 cells separated by $10\text{ }\mu\text{m}$ was placed in the Matlab simulation. The spacing is typical of OHCs in the cochlea. Because of the closer proximity of the OHCs in this direction, attenuation is less than before; moreover, feedback gain is doubled because of cells on both sides of each cell. For these reasons, system gain $A\beta$ needed to be kept below 2 and attenuation factor γ kept at 0.12 or above to prevent oscillation. An example with $A\beta$ of 1.5 and attenuation factor 3 is shown below (Fig. 6.22).

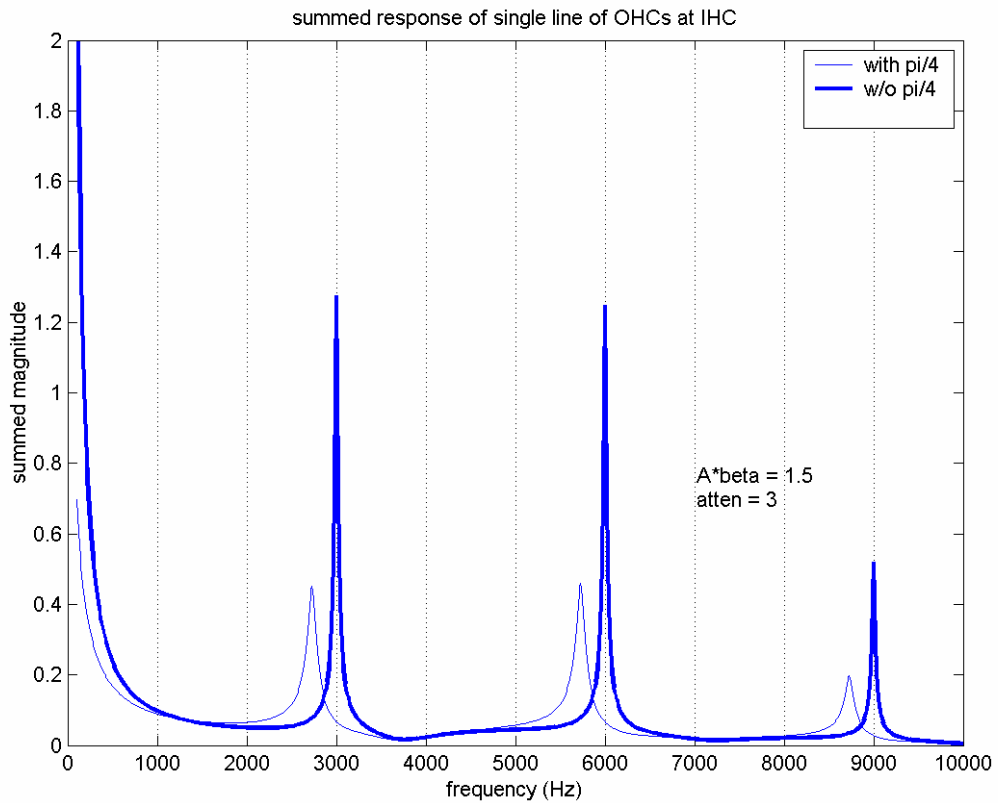


Fig. 6.22. Response of a line of cells spaced $10\text{ }\mu\text{m}$ apart (wave velocity is 30 mm/s).

Note that resonance occurs when the feedback is in phase, which happens whenever there is a 1-wavelength spacing between cells (that is, every 3000 Hz).

6.2/b Response of three rows of cells

The next stage is to introduce three rows of OHCs. Taking rows of 20 and 21 cells per row as before, we now consider the mutual interaction of 62 cells. Fortunately, there are certain symmetries which make the problem tractable.

First, the response of each cell within a row is again identical, and the response of a cell in row 1 will be the same as a cell in row 3. However, the output of a cell in row 2 will not be the same as cells in the other rows because it is surrounded by more cells and hence receives more positive feedback.

We can therefore write the output of cells in row 1 and row 3 as

$$O_1 = O_3 \quad (14)$$

and the output of a cell in row 2 as

$$O_2 = s O_1 \quad (15)$$

where s is a complex quantity that expresses the ratio of the output of a cell in row 2 to the output of a cell in row 1 (or row 3).

Let us now focus attention on a single cell in row 1. Its input is a pressure signal pP which generates receptor potential V and output O_1 . The arrangement of cells and the feedback paths between them are shown in Fig. 6.23, which also shows the equivalent circuit. From consideration of the equivalent circuit, we note that

$$\begin{aligned} O_1 = A [& V + 2\alpha_1\beta O_1 + 2\alpha_2\beta O_1 + 2\alpha_3\beta O_1 + \dots \\ & + 2\kappa_1\beta O_2 + 2\kappa_2\beta O_2 + 2\kappa_3\beta O_2 + \dots \\ & + \tau_0\beta O_3 \\ & + 2\tau_1\beta O_3 + 2\tau_2\beta O_3 + 2\tau_3\beta O_3 + \dots] \end{aligned}$$

Writing all the outputs in terms of O_1 using equations 14 and 15, we derive

$$O_1 = \frac{AV}{1 - 2A\beta(\alpha_1 + \alpha_2 + \alpha_3 + \dots + 0.5\tau_0 + \tau_1 + \tau_2 + \tau_3 + \dots + s(\kappa_1 + \kappa_2 + \kappa_3 + \dots))}$$

which, using the shorthand set out earlier, we write as

$$O_1 = \frac{AV}{1 - 2A\beta(\alpha + \tau + s\kappa)}. \quad (16)$$

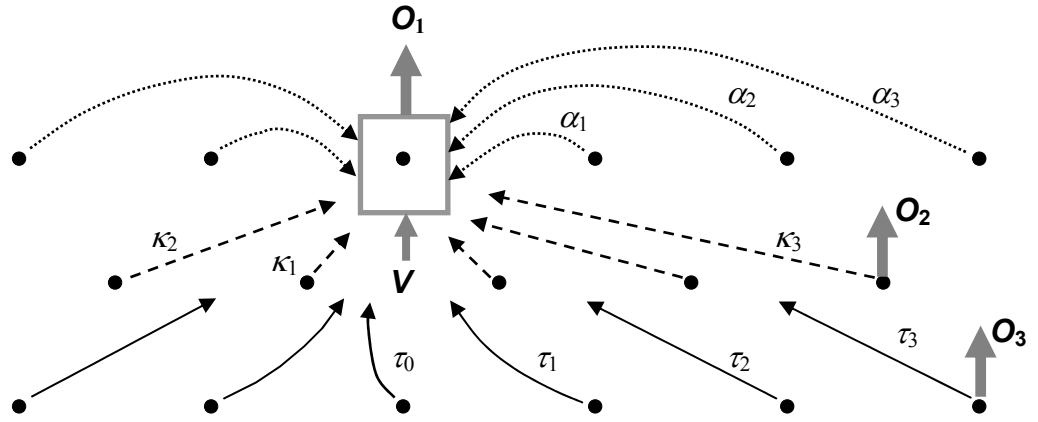


Fig. 6.23. Feedback paths between a cell in OHC1.

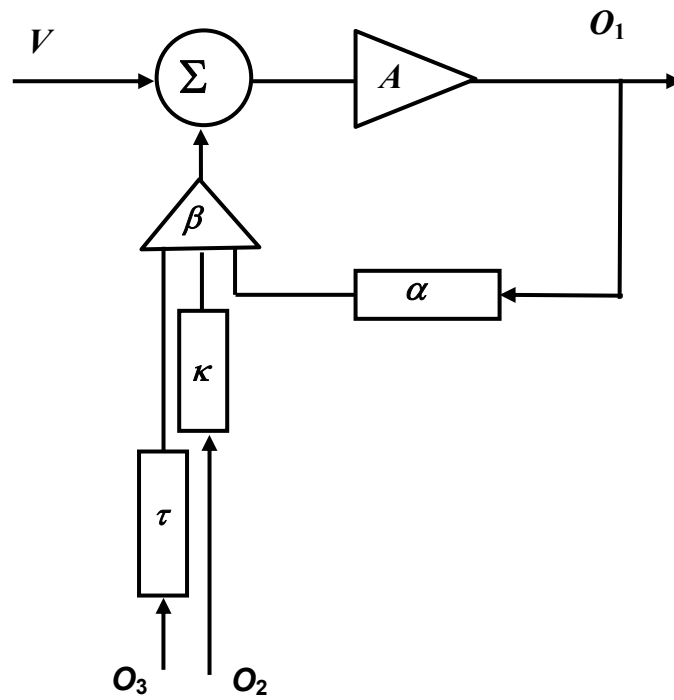


Fig. 6.24. Equivalent circuit of a cell in OHC1.

Now consider a cell in row 2. Its input signal is again V but its output is O_2 . The gain is B (probably the same as A for the other rows, but kept distinct for modeling purposes), and in keeping with the analogy with surface acoustic wave

devices we take it to be negative in the first instance. The stereocilia gain is β^* (again probably the same as β for the other rows), and the within-row attenuation α^* . The feedback paths and equivalent circuit are set out in Fig. 6.25.

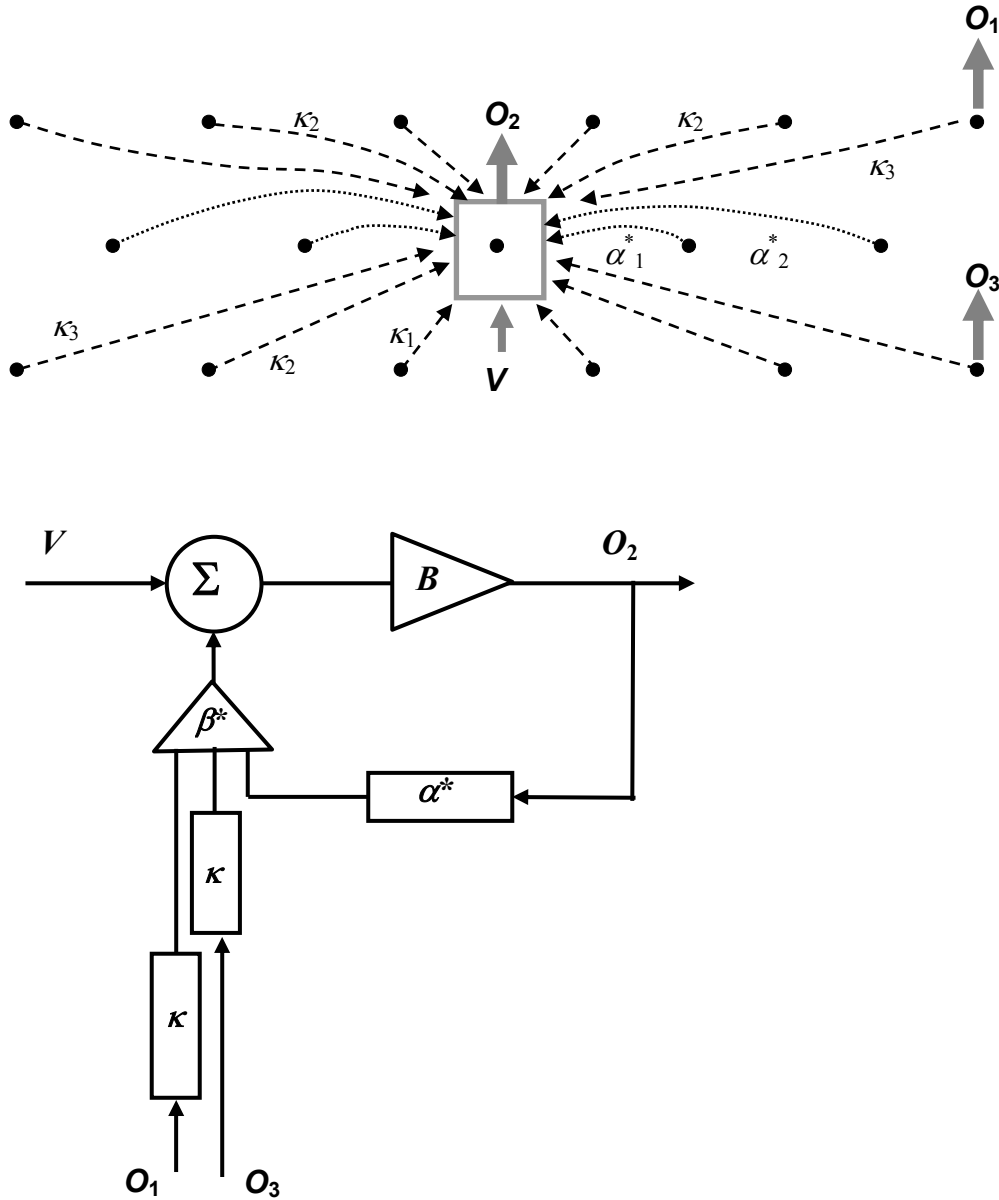


Fig. 6.25. Feedback paths and equivalent circuit for a cell in row 2.

Circuit analysis (output = gain $\times$ input) shows that

$$O_2 = B(V + 2O_2\alpha^*\beta^* + 4O_1\kappa\beta^*),$$

from which we derive, using Equation 15,

$$O_2 = \frac{BV}{1 - 2B\beta^*(\alpha^* + \frac{2\kappa}{s})}. \quad (17)$$

From Equations 16 and 17, we get

$$\frac{O_2}{O_1} = s = \frac{BV}{1 - 2B\beta^*(\alpha^* + \frac{2\kappa}{s})} \cdot \frac{1 - 2A\beta(\alpha + \lambda + s\kappa)}{AV}, \text{ which allows us to}$$

solve for s . Thus,

$$s = \frac{B(1 - 2A\beta(\alpha + \tau) + 4A\beta^*\kappa)}{A(1 - 2B(\beta^*\alpha^* - \beta\kappa))}. \quad (18)$$

Equation 18 now makes it possible to calculate the output of O_1 , O_2 , and O_3 through use of Equations 16, 17, and 14. Knowing the output of each cell in the system, we can find the wave output at the IHC position by summing the output of the 62 cells. In practice, we take the gain and attenuation of the middle row to be the same as the other rows, so that $B = A$, $\alpha^* = \alpha$, and $\beta^* = \beta$. Fig. 6.26 shows the result.

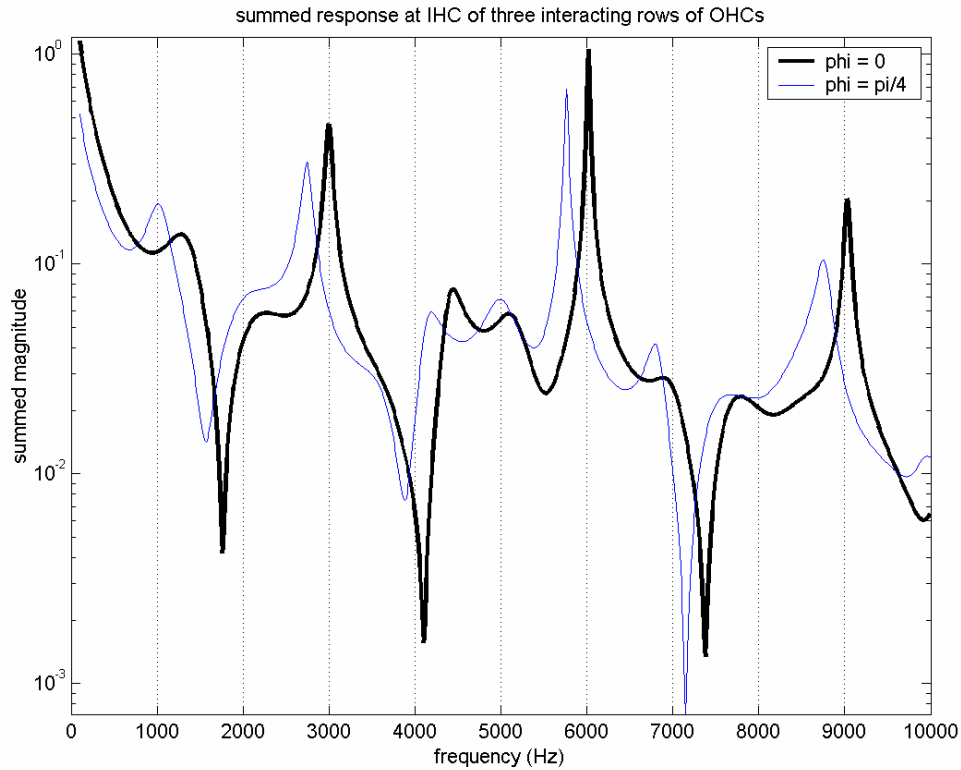


Fig. 6.26. Summed response at the IHC position (30 μm from OHC1) of an array of 3 rows of OHCs. Spacing along row = 10 μm ; spacing between rows = 15 μm . Wave velocity = 30 mm/s. Stereocilia gain $\beta = 1.5$; attenuation factor = 0.128 per 30 μm .

The response is dominated by peaks at 3000, 6000, and 9000 Hz, which represents resonance conditions in along-row positive feedback between the cells. Feedback between the rows makes a lesser contribution, so that the peak at 1000 Hz from this is weaker.

Comments

Once again we have seen that, given comparable OHC spacings and wavelengths, the OHC system displays tuning. The introduction of positive feedback can make the tuning arbitrarily narrow provided the feedback gain is adjusted to be just below the oscillation threshold.

One of the instructive results of the modeling is that the feedback terms are part of a “phase averaged” system. What I mean here is that the feedback terms α , κ , and τ are sums of amplitudes and phases from a series of cells arrayed at increasing distances from the cell under investigation. In the feedback circuit, the amplitudes and phases are summed algebraically, so that so far as a particular cell is concerned, it ‘sees’ a single feedback term – the same as if all its neighbours were replaced by a single cell giving the same amplitude and phase. The modeling shows this in terms of generating a single resonance peak whose frequency is slightly less than the resonance frequency between three collinear cells, one in each row. In other words, the additional cells have altered the feedback term by a small amount, as if the three rows were slightly further apart. Thus, instead of a resonance frequency of 1000 Hz resulting from an array in which OHC1 is separated one wavelength from OHC3, the resonance frequency is about 700 Hz (using the assumed parameters).

The lesson to be extracted here is that oblique interactions between cells do not occur via discrete ‘channels’. The term ‘phase averaging’ describes the situation in which the phases from oblique alignments add together linearly so that the individual components cannot be distinguished from one another. This means, on the point-source assumptions, that a discrete resonance cannot occur at an oblique distance of two wavelengths (for example, along an oblique designated L_3 in Fig. 6.1 when the angle reaches 60°).

The only way in which this could happen is if there were favoured channels that protected the oblique interaction from interference from neighbouring phase

contributors. In this regard, the direction in which the stereocilia arms face might allow some degree of beam steering, and physical or electrical connections between OHCs in various rows could also play a part. The way in which the phalanges of Deiters cells (which support the OHCs) stretch obliquely from row to row¹⁹, for example, could produce favoured channels and allow secondary resonances to arise. These possibilities are discussed more in Chapter R7, but are beyond the capabilities of the present modeling to demonstrate.

Another issue that the modeling is able to settle is the polarity of the middle row of cells. In terms of the SAW analogy, the polarity of OHC2 should be in antiphase to that of the other rows. Modeling shows that while the output of OHC2 is in antiphase to the other rows, this does not translate to a requirement that the initial pressure stimulus to this row give an antiphase output. The initial stimulus can give identical outputs in all three rows; subsequently, however, feedback interactions produce an antiphase output of the middle row. Indeed, it appears that the initial polarity of OHC2 is not critical. While this has been demonstrated using graphical output of the equations developed so far, the matter will be deferred to the next section because, as we will see, the equations in this section are not as simple and transparent as they actually can be.

Looking at both the system without feedback (Figs 6.9–6.13) and with feedback (Fig. 6.26), we see that the shortest, and hence strongest, feedback path has the dominant effect in producing response peaks. The 3-kHz peak spacing corresponds to the short, along-row cell spacing. This result reflects our assumption that wave amplitudes from opposite directions will add. This is the case where stereocilia react simply to displacement amplitude, but of course other sensing schemes are possible, including some where the responses may instead cancel. Intuitively, it doesn't seem as if the OHCs are placed so as to detect longitudinal interactions. In the next section, we will be examining the response of the system when a prime candidate for wave interaction – squirting waves – is introduced. In this case, fluid motions from opposite sides will in fact cancel (although we should keep in mind that pressures might add).

The along-row feedback resonances shown in Fig. 6.26 may therefore be spurious. Nevertheless, depending on the sensing scheme invoked, these longitudinal

¹⁹ Ulfendahl, M. (1997). Mechanical responses of the mammalian cochlea. *Prog. Neurobiol.* 53: 331–380.

interactions could play a role and cannot be dismissed without further investigation. The modeling approach outlined here could be useful in suggesting possibilities for wave interactions in the cochlea.

The next section aims for greater realism in setting up a model of the OHC system using what is thought to be the prime candidate for wave interaction in the cochlea, squirting waves.

6.3 Modeling squirting wave excitation of the OHC array

Previous sections have considered a generalised form of wave excitation in which circular ripples spread out nondispersively from each OHC in response to their electromotility. The effective stimulus has been taken to be the simultaneous and instantaneous response of OHCs to intracochlear pressure. Where paths of individual wavefronts cross, their amplitudes have been summed.

This section aims to revise the modeling so as to reflect the properties of squirting waves. There are three outstanding differences:

1. Wavefronts that meet from opposite directions will cancel, not add. This is because we assume that the effective action of the squirting wave is its fluid motion and motion from opposite directions will cancel. In particular, this means that there will be no within-row interaction because, by symmetry, motion generated on one side of a hair cell (by an adjacent cell in the row) will be cancelled by equivalent motion by the neighbour on its opposite side.
2. Similar symmetry considerations lead to the expectation that OHC2 will only contribute an initial excitation via a pressure response; any ensuing motion generated from OHC1 will be cancelled by an equal and oppositely directed motion from OHC3, so there will be no additional feedback-driven interaction. Obviously, this is not realistic because OHC2 cells, identical in their V shape to other OHCs, should function in a broadly similar way (in nature, form reflects function). We will therefore, in the first instance, allow

OHC2 to sense some of the *difference* between activity in OHC1 and OHC3, noting that the V will allow the cell to more strongly sense fluid moving from the direction of OHC1 than fluid moving from OHC3. In a subsequent section we examine a half-wavelength mode in which the difference-sensing function finds a more natural explanation.

3. Squirting waves are strongly dispersive. The phase velocity, c , of a squirting wave is given by^{20,21}

$$c = \left[\frac{Eh^3d}{3(1-\sigma^2)\rho} \right]^{1/6} \omega^{2/3}, \quad (19)$$

where E is Young's modulus, h is the half-thickness of the plates, σ is Poisson's ratio, ρ is the density of the fluid, and ω is the angular frequency.

Writing this as $c = Z \omega^{2/3}$, where Z is, for purposes of modeling, an adjustable term (used to give the standard one wavelength between the outer-most rows at 1000 Hz), we have $k = \omega/c = \omega^{1/3}/Z$.

As an illustration of the SLR wave's dispersive properties, we now see that, with $k = 2\pi/\lambda$,

$$\lambda = 2\pi Z \omega^{-1/3}, \quad (20)$$

meaning that a doubling of the wavelength is accompanied by an eight-fold (3-octave) decrease in frequency.

We can now write the wave equation for an expanding squirting wave produced by an oscillating point on a membrane in the same way as before, except that k is no longer a linear function of ω , as it was for the nondispersive case considered earlier (in which $k = \omega/c$ and c was constant). Instead, k is now a function of $\omega^{1/3}$ (that is, $k = \omega/c = \omega^{1/3}/Z$).

²⁰ Lloyd, P. and M. Redwood (1965). Wave propagation in a layered plate composed of two solids with perfect contact, slip, or a fluid layer at their interface. *Acustica* 16: 224-232.

²¹ Bell, A. and N. H. Fletcher (2004). The cochlear amplifier as a standing wave: "squirting" waves between rows of outer hair cells? *J. Acoust. Soc. Am.* 116: 1016-1024.

Thus, the amplitude A of the circular squirting wave at distance D from the oscillating point is

$$A = \sqrt{\frac{2\pi}{kD}} e^{-\gamma D} e^{-i(kD + \phi)} \quad (21)$$

where γ is the attenuation coefficient per unit distance and ϕ is the phase. As we have seen earlier (Morse, 1981), the far-field displacement of a wave produced by an oscillating point on a membrane lags the displacement of the point with a phase lag of $\pi/4$. However, for a squirting wave, the phase of fluid squirting (that is, the horizontal displacement of the fluid and the effective stimulus for the hair cell stereocilia) leads the membrane displacement by $\pi/4$. Simplistically, then, the two phases should cancel and for most purposes $\phi \approx 0$. However, additional phase delays will be introduced by the transduction speed of the OHC. This is a fast process, in that we know that mammalian OHCs can produce electromotile responses of 50 kHz or more (essential in a bat). If stereocilia deflection closely followed fluid displacement, ϕ might be close to zero, but if stereocilia deflection depended on fluid velocity, this would introduce a phase term of $\pi/2$. In the following simulations ϕ is varied from 0 to $\pi/2$ to see what effects transduction speed and sensitivity to displacement or velocity might introduce.

The OHC is again presumed to have dual inputs: a sensitivity to pressure via its cell body and a sensitivity to displacement of its stereocilia (Fig. 6.14). As mentioned earlier (Chapter M4), this scheme allows the cochlear amplifier to be driven by a fast, clean signal that is a good replica of the stapes motion, and hence of the ear-canal pressure. This signal, which is invariant from one part of the cochlea to another, is in marked contrast to the traveling wave waveform which embodies large phase lags and which varies from place to place. Nevertheless, should a second-filter scheme prove more attractive, the mathematics will follow through in much the same way for a single-frequency input; the difficulties will only emerge when two or more tones are considered (such as when investigating DPOAEs).

To recapitulate, Fig. 6.23 shows the dual-input nature of OHCs. They respond to both intracochlear pressure P (in μPa) and deflection of stereocilia d (in nm). Both of these inputs produce an electrical signal, V , a change in membrane potential, via conversion factors p (mV/ μPa) and β (mV/nm), respectively. This receptor potential

drives the cell's electromotility mechanism with efficiency A nm/mV to give an output deflection of O nm. It is this movement which creates squirting waves that can feed back to neighbouring OHC stereocilia.

The feedback loop we model only involves a feedback path via the stereocilia. This is not strictly true, for we know that OHC activity generates pressure in the ear canal. Our explanation for this follows the haircell-swelling model of Wilson (see §D 8.3/b) who assumed that OHC activity causes a change in cell volume, and this creates intracochlear pressure changes which move the middle ear system. This is the exact reciprocal of that process by which OHCs detect incoming sound pressure. Thus, there is another possible feedback path via pressure: the pressure generated by OHCs could feed back to other OHCs. However, for simplicity, this effect is not considered here.

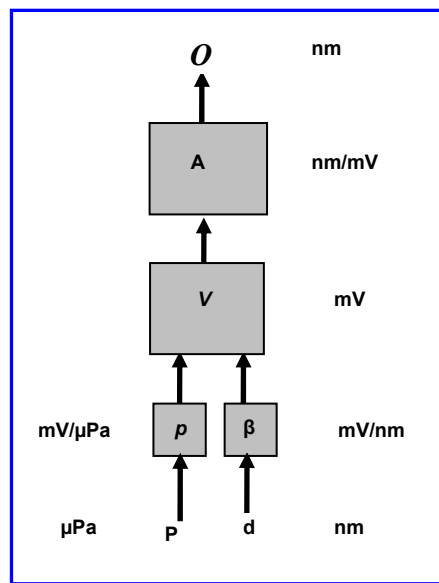


Fig. 6.23. Transduction stages in an outer hair cell.

For numerical simplicity, we assume that a standard pressure input to the system gives a unit change in receptor potential (that is, $P \cdot p = V = 1$), in which case gain adjustment in the system can be accommodated by adjusting the other feedback parameters β and A . In all of the simulations to follow, we adjust the value of the combined gain $A \beta$. The actual individual values are not important for our purposes.

6.3/a Explicit solution of the many-cell problem: full wavelength resonance

In the previous section (§R 6.2), we examined the feedback interactions between three rows of OHCs and derived equations by which the output of the array could be calculated. These equations involved calculating s , the ratio between the output of the middle row, OHC2, to the others (Eq. 15). After calculating s numerically in Matlab (Eq. 18), this value was inserted into Eqs 16 and 17 to give the required result. Although workable, and giving some insight into the relative behaviour of the rows, this scheme is inefficient. It is possible to eliminate the intermediate calculation of s and derive equations that explicitly give the output of the system. The derivation is set out below and follows Fig. 6.24.

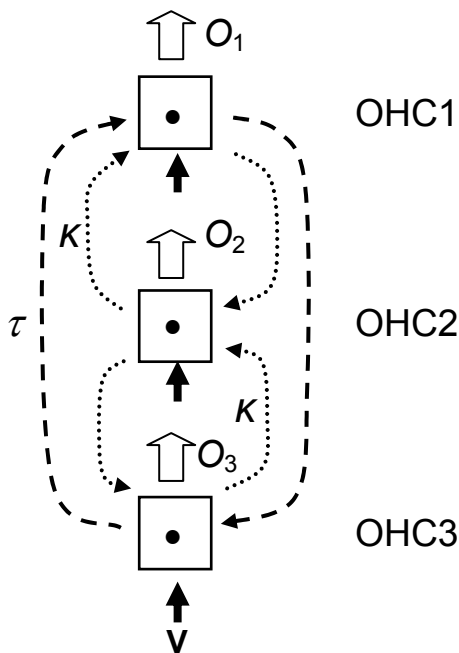


Fig. 6.24. Interactions between three outer hair cells.

The formulation uses the notation adopted earlier. O_1 , O_2 , and O_3 are the outputs of cells in OHC1, OHC2, and OHC3, respectively, in response to common input stimulus V (presumed here to be a pressure stimulus). Further stimuli to the cells are the waves emanating from neighbouring cells, so that the output from O_1 is attenuated by a factor κ (that is, $\kappa < 1$) in traveling across a single row. As before, $\kappa = \kappa_1 + \kappa_2 + \kappa_3 + \dots$. In addition, there will be an attenuation factor τ (again < 1) as wave energy travels across two rows

(and τ is likewise a sum of contributions from all cells two rows across). Roughly, $\tau \approx \kappa^2$, although the two quantities are always calculated exactly. The system responds in accord with expected squirting wave behaviour (points 1, 2, and 3 at the beginning of §R 6.3). The consequence of point 1 is that, with no within-row interactions, $\alpha = 0$.

We introduce a new parameter, δ , that represents the asymmetry of the stereocilia. Because of the V shape, it is expected that, like an anemometer cup, fluid moving from OHC1 will be more effective in deflecting stereocilia than fluid from OHC3, even though the amplitudes of motion of OHC1 and 3 are equal. Thus, $\delta = (\kappa' - \kappa'')/(\kappa' + \kappa'')$, where κ' and κ'' are the effective attenuation factors ($\approx \kappa$) for waves progressing from OHC1 to OHC2 and OHC3 to OHC2, respectively. If there were perfect cancellation, δ would be zero; if there is a residual response due to anemometer-like asymmetry, then OHC2 will respond as δ times κ . Thus, in the following work, we take δ to be some factor between 0 and ± 0.2 .

First we consider a typical cell in OHC2, which is assumed to be a line of cells extending indefinitely in both directions. Drawing on Fig. 6.24 and examining its inputs and outputs, we see that the equivalent circuit for a typical cell in this row is as follows (Fig. 6.25).

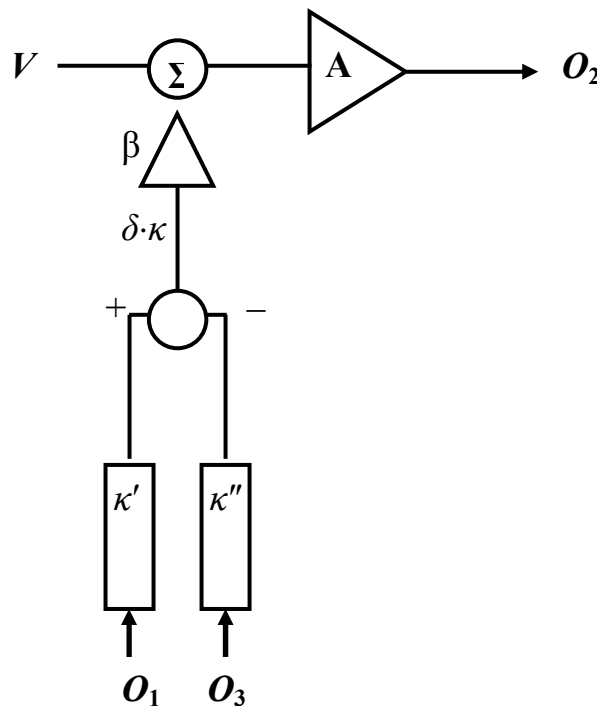


Fig. 6.25. The equivalent circuit for a cell in OHC2.

We take the output of OHC1 to be the same as that of OHC3, so that $O_1 = O_3$, and putting the output equal to gain $\times$ inputs we get

$$O_2 = A(V + \beta\delta\kappa O_1) \quad (22)$$

Now consider the inputs and outputs of a typical cell in OHC1. Again referring to Fig. 6.24, we see that its equivalent circuit is as follows.

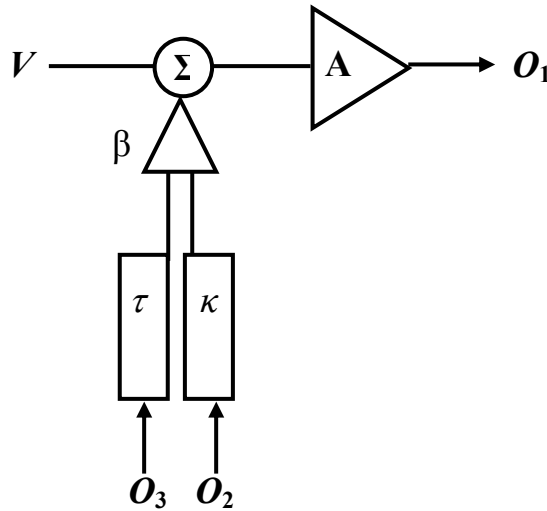


Fig. 6.26. Equivalent circuit for a cell in OHC1.

Consideration of inputs and outputs this time yields

$$O_1 = A(V + \kappa\beta O_2 + \tau\beta O_3) \quad (23)$$

Substituting for O_2 in (23) using (22), we find that

$$O_1 = \frac{AV(1 + A\beta\kappa)}{1 - A\beta\tau - A^2\beta^2\kappa^2\delta}, \quad (24)$$

which is also the output of O_3 .

Substituting for O_1 in (22) using (24) then gives

$$O_2 = \frac{AV(1 + A\beta(\kappa\delta - \tau))}{1 - A\beta\tau - A^2\beta^2\kappa^2\delta}. \quad (25)$$

Results and derivations

Using equations (24) and (25) it is now possible to calculate the output of each cell in an outer hair cell array. Then, by adding up the amplitudes of waves generated from each point in the array, the amplitude at any point – most usefully at the IHC position – can be calculated.

Matlab code was written to compute this over a frequency range of 0.1 to 10 kHz. The standard reference frequency was set at 1 kHz, a frequency at which the squirting wave occupied one wavelength from OHC1 to OHC3. The IHC position was taken to be 30 μm inwards from OHC1. A representative result is shown in Fig. 6.27.

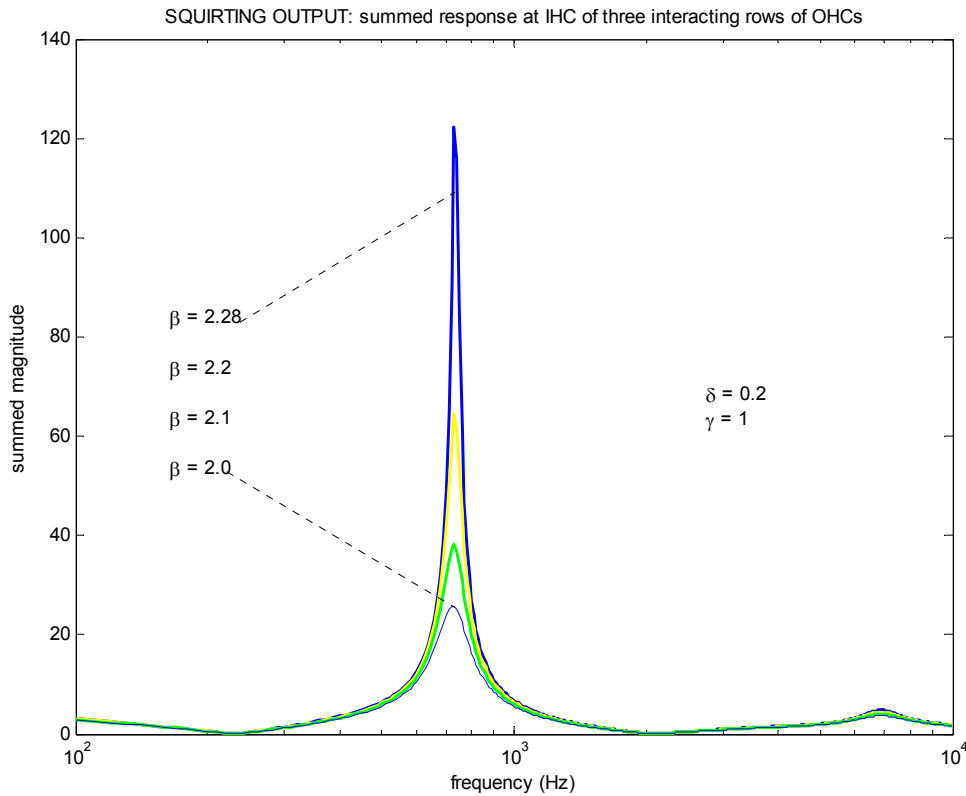


Fig. 6.27. Resonant peak due to squirting waves in an OHC array.

This graph shows how the resonant peak just below 1 kHz increases in height and sharpness as the gain is increased. For an attenuation factor γ of 0.04 (amplitude reduction of $1/e$ per 30 μm), the peak reaches a maximum of several hundred at a frequency of about 700 Hz when the gain $A\beta$ was 2.3. The value of δ was 0.2.

Increasing the gain beyond this figure produces a negative denominator in Eqs (24) and (25), a physically unreal situation which the code guarded against.

Note also the minimum at about 2 kHz and a second peak, broader and lower, at about 6.8 kHz. This secondary peak occurs about 3 octaves above the first, as expected for a dispersive system in which halving the wavelength is accompanied by an 8-fold increase in frequency. Unlike the nondispersive system examined in §R 6.2, the secondary peak is much less prominent.

1. Swelling output

Using equations (24) and (25), the simultaneous output of all cells over the small length of partition containing the 62 cells – which is the pressure output according to the Wilson haircell-swelling model (§§3.2/k, 8.3/b) – can be explicitly calculated. In Wilson's model, the activity of an OHC is accompanied by a volume change. Hence, the total output, O , of the length of partition we are considering will be

$$\begin{aligned} O &\propto O_1 + O_2 + O_3 \\ &= W(2O_1 + O_2), \end{aligned}$$

where W is a constant, so that

$$O = WAV \left[\frac{3 + A\beta(2\kappa + \delta\kappa - \tau)}{1 - A\beta\tau - A^2\beta^2\kappa^2\delta} \right]. \quad (26)$$

Fig. 6.28 shows the hair-cell swelling output for 62 cells. Reducing the number of cells to only 5 had little effect, indicating that, with sharp tuning, the contributing cells are, in the main, those at the resonant location.

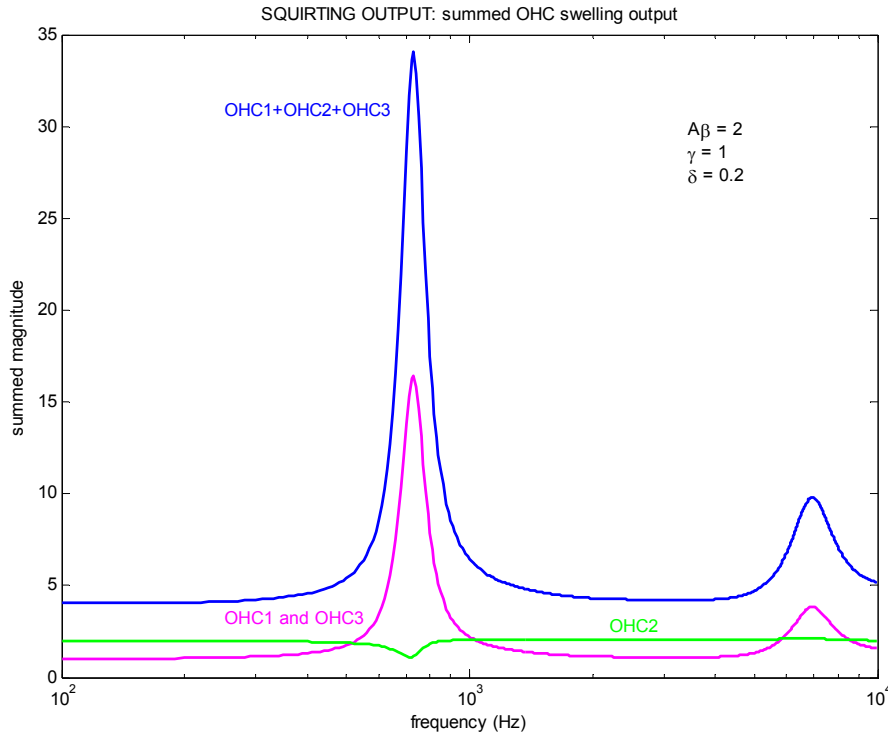


Fig. 6.28. Combined output of 62 cells assuming volume of each cell is proportional to its activity (Wilson's haircell-swelling model).

2. Effect of OHC2 in-phase or antiphase

When initially formulating the SAW model, it was considered, to preserve the SAW analogy, that OHC2 would need to act in antiphase to the other rows. However, equations (24) and (25) demonstrate that this is not necessary. Consider the situation when V in Eq. 22 is replaced by $-V$. Then we see that

$$O_1 = \frac{-AV(1 + \kappa\beta)}{1 - A\beta\tau - A^2\beta^2\kappa^2\delta}, \quad (27)$$

which is identical to Eq. (24) except for the leading minus sign. In other words, the gain of the middle row is unchanged. Similarly, it follows that the output of O_2 is

$$O_2 = \frac{-AV(1 + A\beta(\kappa\delta - \tau))}{1 - A\beta\tau - A^2\beta^2\kappa^2\delta} \quad (28)$$

which is the same, apart from the sign, of Eq. 25.

It is true that when the system is in resonance, and OHC1 and OHC3 are giving maximum output, the distance between these cells will be close to a wavelength and OHC2 will be moving in antiphase to them. However, the final antiphase motion of OHC2 does not mean that the initial stimulus to OHC2 has to be inverted. It would appear that the feedback interactions of the three rows automatically lead to the inverted motion of OHC2, even when the initial stimulus to all rows is identical.

Another way of seeing the relative unimportance of the initial OHC2 response phase is to recognise that δ can approach zero, or go negative, without a sudden effect on the response of the system, as inspection of Eq. 25 shows.

3. Effect of different values of δ

Fig. 6.29 shows the effect of changing δ from 0.2 to 0 and then to -0.2 . The effect is small, which suggests that OHC2 may be involved more in sensing the activity of the system. The supposition is made that OHC2 may be able to apply sudden damping to the system, acting as the cochlea's 'brakes' or 'dampers', preventing continued oscillation of the otherwise high- Q resonance. However, the details of such a scheme are presently left unspecified, although it could involve the efferent system. An alternative half-wavelength mode is considered later and this system shows a much greater change in response when the gain of the middle row is altered (Fig. 6.33).

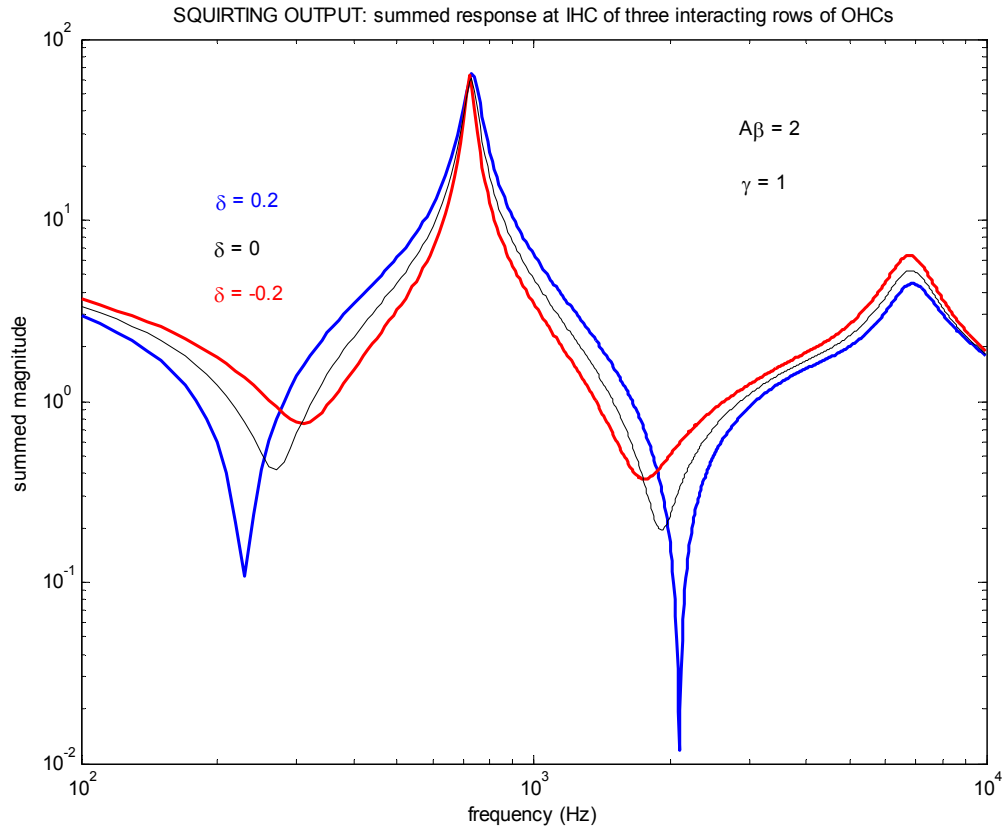


Fig. 6.29. Effect of changing the relative sensitivity of OHC2 from $\delta = 0.2$ (OHC1 favoured) to $\delta = -0.2$ (OHC3 favoured). When $\delta = 0$, cells in OHC2 do not respond.

4. Effect of variations in electromotility response phase

Fig. 6.30 shows the effect of increasing the magnitude of the phase delay in OHC electromotility – that is, between OHC voltage and wave displacement – from 0 to $\pi/2$. As discussed earlier (§R 6.3), the phase could be as low as 0 if the squirting wave phase advance of $\pi/4$ cancelled the inherent phase delay associated with motion of point on a membrane. We see that the resonance frequency progressively reduces as phase delay is introduced, but the system-wide behaviour is otherwise similar.

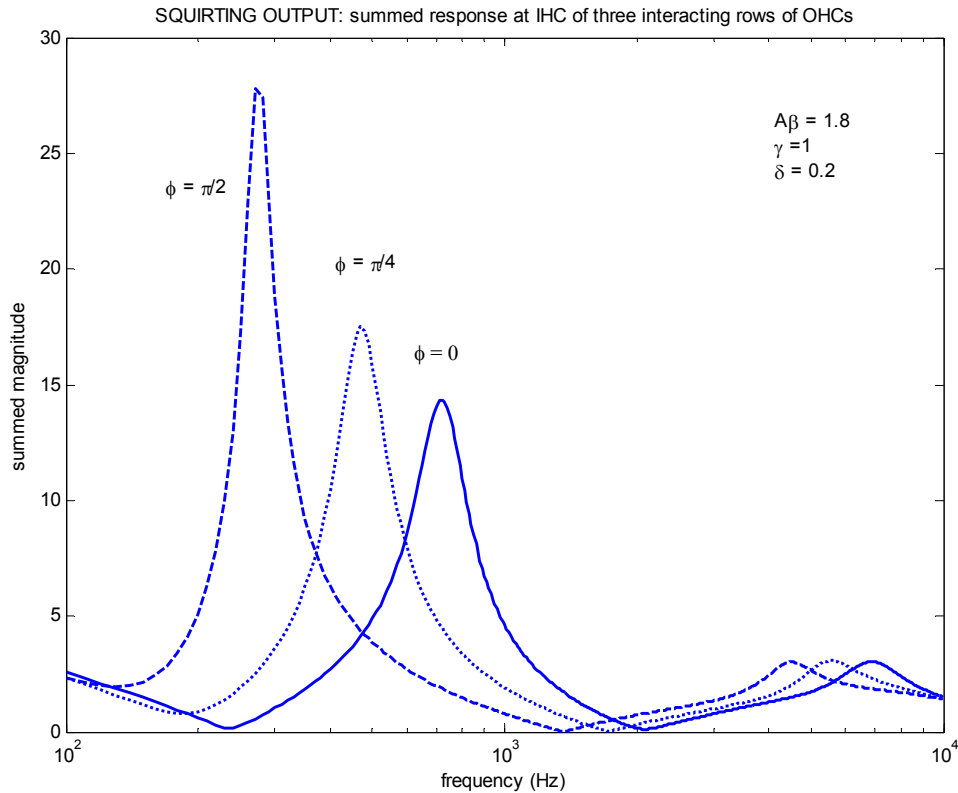


Fig. 6.30. Effect of phase delays in cell response.

6.3/b *Explicit solution of the many-cell problem: half-wavelength resonance*

The whole of the preceding work has considered a resonance scheme for the outer hair cells that reflected the behaviour of surface acoustic wave resonators. While the analogy does seem to carry through, when we try to mesh it with a squirting wave engine, we are left with two aspects which I find not totally satisfying.

The first has to do with the way in which the role for OHC2 has been nearly squeezed out of existence. If OHC1 and OHC3 both launch squirting waves equally, then the stereocilia of OHC2 will not be deflected. The situation has only been saved by calling on the anemometer-cupped asymmetry of the V-shaped stereociliar arms; in this way some stereociliar motion might result.

The second major concern centres around the way in which the stereocilia of OHC1 and OHC3 are deflected. Originally, we used the notion that stereocilia may

follow the scalar amplitude of a wave, a scheme that allowed two waves to meet head on and sum algebraically in amplitude. It is difficult to carry this notion over to squirting waves, when waves meeting head on should cancel their displacement (although not their pressure). It seems more realistic for squirting waves meeting head on to subtract not add. That is, not only should OHC2 stereocilia sense the *difference* between fluid motion on one side and the other, but so too should OHC1 and OHC3.

What may resolve the situation is to see that OHC1 and OHC3 are acting in a reciprocal relationship to each other, as illustrated in Fig. 6.31.

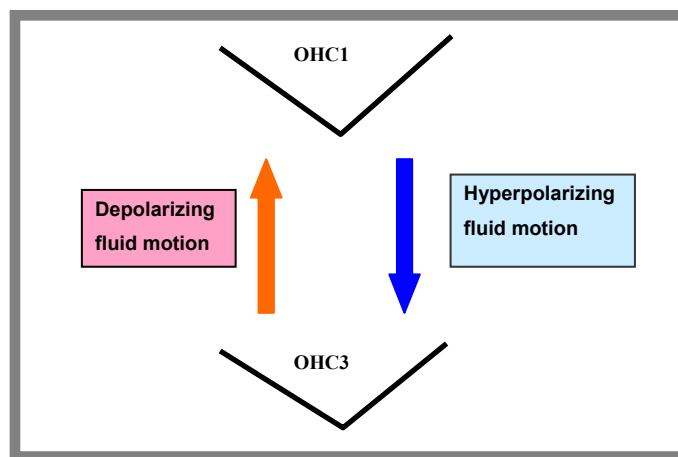


Fig. 6.31. Antisymmetry between OHC1 and OHC3.

When OHC1 moves upwards, say, and produces a squirting wave that propagates towards OHC3, this will bend the latter's stereocilia in a direction towards its kinocilium, that is, it will have a hyperpolarizing and inhibitory effect. In contrast, when OHC3 moves upward and produces a squirting wave that propagates towards OHC1, this motion will bend stereocilia away from the kinocilium, producing a depolarizing and excitatory effect. In summary, the antisymmetrical responses of the stereocilia lead to an antisymmetrical relationship between OHC1 and OHC3.

This difference is reflected in the feedback paths. Whereas the attenuation constant from OHC3 to OHC1 may be represented as τ , that from OHC1 to OHC3 should be represented as $-\tau$, for it will have an effect 180° different – as if it were coming from the opposite direction. Another way of expressing the difference would be to have the β term in OHC3 the reverse ($-\beta$) of that in OHC1 so that the

R 6 [52]

stereociliar transducer is wired in with opposite polarity. Examination of circuit diagrams (Figs 6.25 and 6.26) shows that it makes no difference which formalism is adopted, and here we will use the convention of $+\tau$ for an ‘upward’-moving (radially inwards) path and $-\tau$ for a ‘downward’-moving (radially outwards) one.

Similarly, with the stereocilia of OHC2 depolarizing for fluid motion from OHC1 and hyperpolarizing from fluid motion from OHC3, we also need to use $+\kappa$ for feedback paths from OHC3 and $-\kappa$ for feedback paths from OHC1.

Referring back to Fig. 6.24, and taking note of the necessary changes in sign, we now have the following equations.

$$O_1 = A [V + \kappa\beta O_2 + \tau\beta O_3] . \quad (29)$$

Similarly, the equation for O_3 may be

$$O_3 = A [V - \kappa\beta O_2 - \tau\beta O_1] . \quad (30)$$

Adding (29) and (30), we eliminate O_2 and get an expression for O_3 in terms of O_1 . That is,

$$O_3 = [2AV - O_1(1 + A\tau\beta)] / (1 - A\tau\beta) \quad (31)$$

This expression has a satisfying symmetry if the $2AV$ term is dropped. This term is small when the gain is high, and only provides a kind of offset. Moreover, our experience earlier has shown that the polarity of the initial stimulation does not seem to be crucial in the system. Later calculations also become substantially simpler without it. Dropping this term is equivalent to changing the sign of V in equation 30, so that it now becomes

$$O_3 = A [-V - \kappa\beta O_2 - \tau\beta O_1] . \quad (32)$$

Adding (29) and (32) now produces

$$O_1 = \frac{-(1 - A\tau\beta)O_3}{1 + A\tau\beta} \quad (33)$$

From Fig. 6.24, the corresponding expression for O_2 is

$$O_2 = A [V + \kappa\beta O_3 - \kappa\beta O_1] . \quad (34)$$

Solving these equations, we find the following explicit solutions.

$$O_1 = \frac{AV(1 + A\kappa\beta)(1 - A\tau\beta)}{1 + A^2\beta^2(2\kappa^2 + \tau^2)} \quad (35)$$

$$O_3 = \frac{-AV(1 + A\kappa\beta)(1 + A\tau\beta)}{1 + A^2\beta^2(2\kappa^2 + \tau^2)} \quad (36)$$

$$O_2 = AV \left[1 - \frac{2A\kappa\beta(1 + A\kappa\beta)}{1 + A^2\beta^2(2\kappa^2 + \tau^2)} \right] \quad (37)$$

Again, we note the constant offset term in (37), and, purely on the basis of simplicity and symmetry, are led to drop it. This time it means that for OHC2 only, $V=0$, or in words, that OHC2 does not receive initial stimulation, only feedback from OHC1 and OHC3. Equation 37 then becomes

$$O_2 = \frac{-2A^2V\kappa\beta(1 + A\kappa\beta)}{1 + A^2\beta^2(2\kappa^2 + \tau^2)} . \quad (38)$$

These compact equations are appealing, but whether the organ of Corti operates in a half-wavelength mode, as they imply, is a question left for further investigation. We see immediately (Eqs 33, 35, 36) that the outputs of OHC1 and OHC3 are in antiphase – one row is moving up at the same time as the other is moving down, so that there is a *half-wavelength* standing wave between them. OHC2 is in the middle of this push–pull arrangement, so that its stereocilia are being driven

backwards and forwards by these flanking cells. It doesn't need a direct input signal to drive it.

Placing these equations into Matlab (Fig. 6.32) confirms this half-wavelength mode. The resonance now occurs near 2 kHz when the wave speed is, as before, configured to have a full wavelength at 1 kHz.

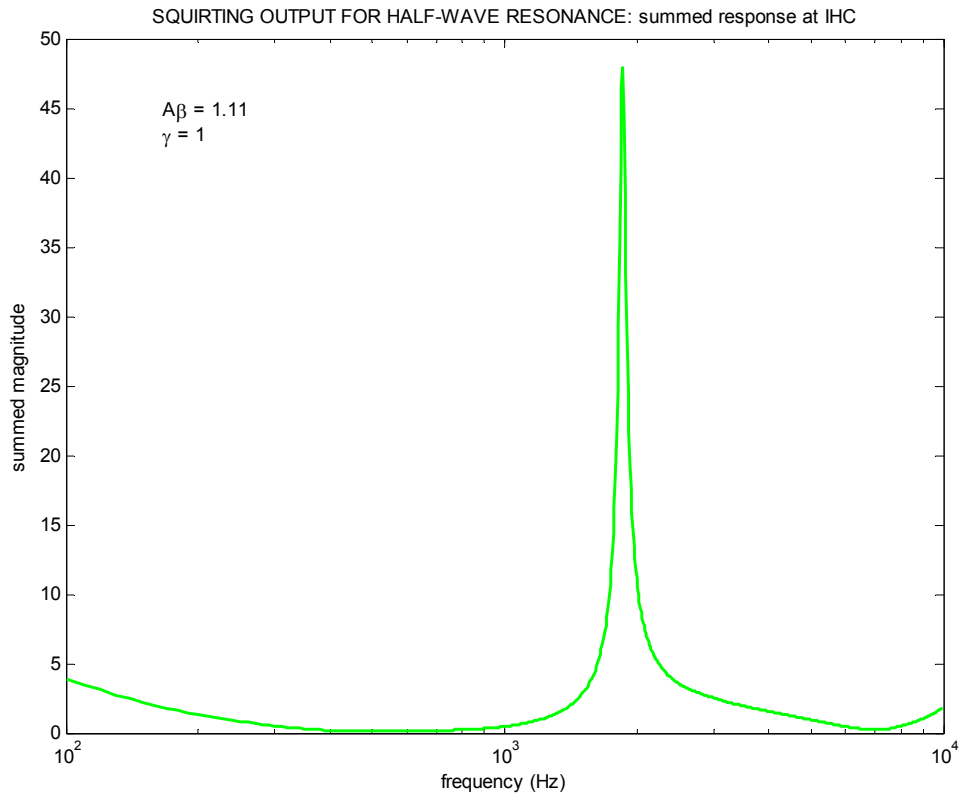


Fig. 6.32. Resonance of the OHC array in its half-wavelength mode.

Flowing from the insight provided by the half-wavelength model, the prediction is that OHC1 would have opposite response phase to OHC3. This could result from the membrane potential of OHC1 being significantly different to OHC3, causing certain cellular currents (probably a fast potassium current) to be turned on or off. OHC2 may be expected to have more of a coasting and sensing function, and could also operate as the dampers.

To investigate this possibility, we take the system as before, with OHC2 having no pressure-sensing function (it only senses the output of OHC1 and OHC3 using its stereocilia, and gives electromotility output accordingly), but now the gain of the stereociliar transducer in OHC2 is represented by a variable β^* . We will look at the response of the system when β^* is varied from high to low values while β

(OHC1 and OHC3 gain) is held high; this might be expected to reflect the situation when OHC2 changes from sustaining the oscillation (gain ≈ 1) to active brake (fractional gain, with $\beta < 1$).

The equations now are:

$$O_2 = A\kappa\beta^*(O_3 - O_1) \quad (39)$$

$$O_1 = A(V + \kappa\beta O_2 + \tau\beta O_3) \quad (40)$$

$$O_3 = A(-V - \kappa\beta O_2 - \tau\beta O_1) \quad (41)$$

So that, as before,

$$O_3 = \frac{-(1 + A\tau\beta) O_1}{(1 - A\tau\beta)}, \quad (42)$$

but now we find that

$$O_1 = \frac{AV(1 - A\tau\beta)}{1 + A^2\beta(2\kappa^2\beta^* + \tau^2\beta)} \quad (43)$$

$$O_3 = \frac{-AV(1 + A\tau\beta)}{1 + A^2\beta(2\kappa^2\beta^* + \tau^2\beta)} \quad (44)$$

$$O_2 = \frac{-2A^2\kappa\beta^*V}{1 + A^2\beta^2[\tau^2 + 2\kappa^2(\beta^*/\beta)]} \quad (45)$$

Evaluating these equations in Matlab, we set β and $\beta^* = 1.1$, a value that gives good gain and tuning in the system. Keeping β the same, we drop β^* to 0.3, and observe (Fig. 6.33) that the response of all rows falls considerably and tuning almost disappears. This scheme provides a simple and rapid way of providing damping, allowing the resonance of the three rows to be effectively curtailed by altering the membrane potential (through efferent control) of a single row. It has the virtue of

having separate drivers and dampers, which seems desirable from the point of view of control.

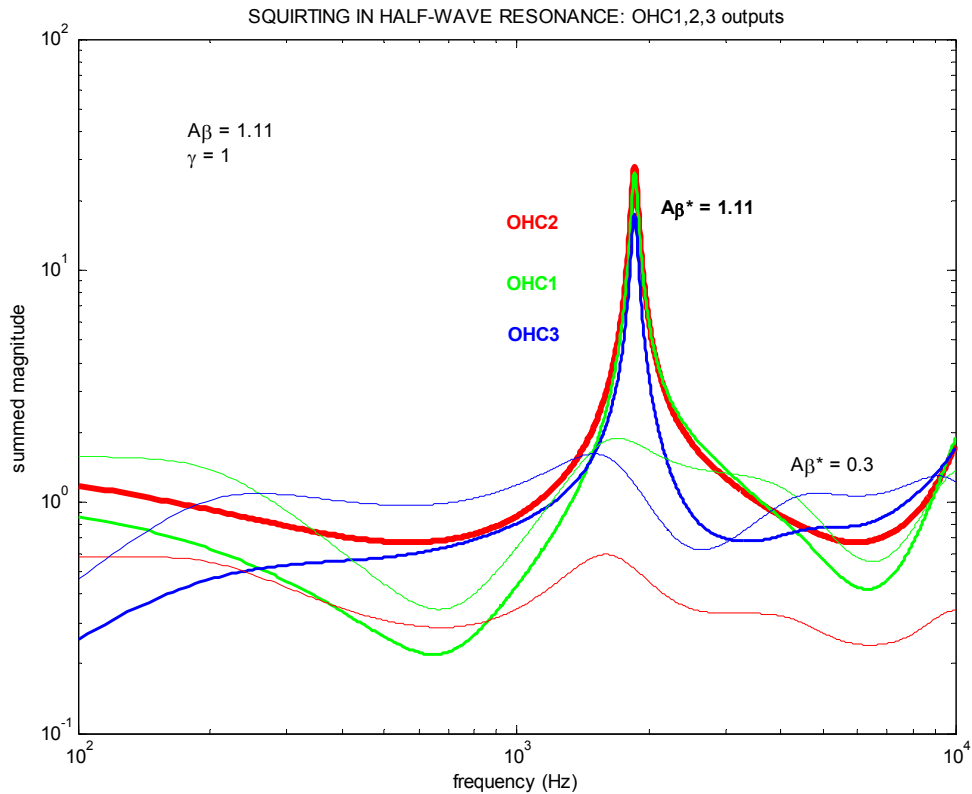


Fig. 6.33. Response of individual rows of OHCs when gain of OHC2 is dropped from 1.1 to 0.3.

In conclusion, there is a certain simplicity in the half-wavelength mode. On the other hand, the full-wavelength mode provides a more equal sharing of effort between the rows. The full-wavelength mode, although it calls for a lower phase velocity, still provides a good numerical fit to the data (Fig. 5.2). The frequent appearance of a fourth row of outer hair cells in primate cochleas (see the next chapter) would not appear to be very useful on the half-wavelength picture (we would need 5 rows for this scheme to be useful), but in the full wavelength mode 4 rows would provide additional gain over 3, since the polarity of the rows simply alternates. The general preference is therefore for the full wavelength mode, but the question cannot be unequivocally decided here and is left open for further investigation.

Analysis of the outer hair cell lattice

7.1 Introduction

7.2 Comparison of lattice parameters between species

7.3 The OHC lattice of the rhesus monkey

7.3/a The regular unit cell (L-M Figure 8)

7.3/b A second look at the lattice (L-M Figure 7)

7.3/c Extending the range of results (L-M Figure 3)

7.3/d Confirmatory results (L-M Figure 12)

7.4 Discussion

7.4/a Implications of tilt for DPOAEs

7.4/b Support for the tilted unit cell model

7.4/c Relating the model to the literature

7.4/d Oblique interactions and Deiters cell processes

7.5 Conclusion

Supposing that squirting waves are active between rows of outer hair cells, confirmatory evidence could come by analysing the distinctive pattern in which outer hair cells lie and seeing whether the expected micromechanical properties of such a system fit with known cochlear behaviour. This chapter takes this approach and finds that the outer hair cell lattice has properties consistent with the tonotopic properties of the cochlea; moreover, this lattice is expected to produce distortion products that

reach a maximum for a ratio of the primary frequencies of about 1.2^{1,2,3}, which is a key property of DPOAEs that requires a fairly complex explanation in terms of current cochlear mechanics.

7.1 Introduction

The uniform arrangement of three or more rows in which outer hair cells array themselves (Fig. 4.1) was the initial stimulus for the SAW model. The modelling in the previous chapter treated the outer hair cells as point sources, and showed that the three rows could interact via slow wave propagation to form a positive feedback loop, the net result being sharp tuning and high sensitivity provided the gain of the system was set just below oscillation threshold. We have already seen (§R 5) that squirting waves fulfil the requirement for slow phase velocity, and their high dispersion also allows the cochlea to be tuned over 10 octaves based on the properties of the subreticular space, notably the inter-row spacing. The human row-spacing data of Bredberg (1968), supplemented with physical data for other species, was used for this calculation.

This initial evaluation was sufficient to show that the squirting wave model is feasible. In order to strengthen the model, a search was made for surface views of the plateau of Corti (the reticular lamina) showing the distinctive outer hair cell pattern. Some hundreds of micrographs were acquired from the literature, and they derived from mammals as diverse as human, monkey, cat, tiger, guinea pig, chinchilla, mouse, mole rat, rabbit, dolphin, and bat. All showed the distinctive pattern of regularly spaced rows, resembling that in Fig. 4.1, although sometimes there are more rows and in some cases the pattern is rather irregular (particularly in humans). The OHC rows become closer at high frequency, as the Bredberg data⁴ used in §R5

¹ Kemp, D. T. (2002). Exploring cochlear status with otoacoustic emissions: the potential for new clinical applications. In: *Otoacoustic Emissions: clinical applications*, edited by M. S. Robinette and T. J. Glatke (Thieme: New York), 1-47. Fig. 1-12.

² Lonsbury-Martin, B. L., et al. (1990). Distortion product emissions in humans I. Basic properties in normally hearing subjects. *Ann. Otol. Rhinol. Laryngol.* 99: 3-29.

³ Furst, M., et al. (1988). Ear canal acoustic distortion at 2f₁-f₂ from human ears: relation to other emissions and perceived combination tones. *J. Acoust. Soc. Am.* 84: 215-221.

⁴ Bredberg, G. (1968). Cellular pattern and nerve supply of the human organ of Corti. *Acta Otolaryngol. Suppl.* 236: 1-135.

show clearly. A similar picture emerges from a study of the chinchilla cochlea⁵ by Santi et al. (1986), and the data here have the advantage of measuring the position of the inner hair cells as well. This data is plotted below (Fig. 7.0).

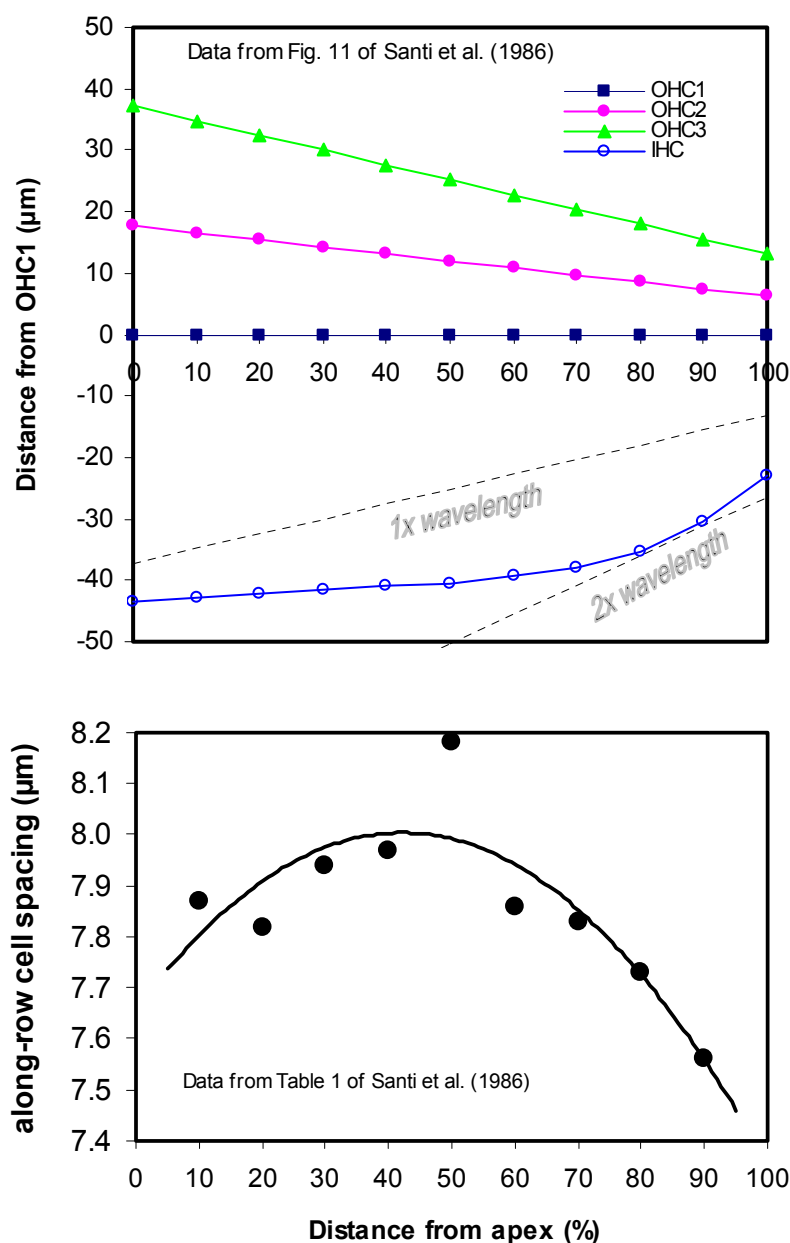


Fig. 7.0. Distances between hair cells in the chinchilla. Spacing between rows (top) and along-row spacing (below). Data from Santi et al. (1986).

It is of interest to see that the spacing between OHC rows varies more than 3-fold from 12 μm at the base to 37 μm at the apex. The row of inner hair cells comes

⁵ Santi, P. A., et al. (1986). A computer-assisted morphometric analysis of the organ of Corti. *Hear. Res.* 24: 189-201.

progressively closer to OHC1 as frequency increases, although in terms of presumed squirting wave wavelengths it varies between 1 and 2. The bottom part of the figure shows the along-row spacing, and although fairly constant, there may be a trend to closer spacing towards the base and apex.

Expressed in terms of the parameters a (along-row spacing) and b (spacing of OHC1 and OHC3), in all the micrographs I have examined the most common a/b ratio averaged about 0.35; it ranged from as low as 0.22 in a human to 0.64 in a dolphin. Data on this will be the subject of a separate paper.

All species show that the stereocilia form a distinctive V, whose enclosed angle widens from apex to base, and so treating each cell as a point source and detector of squirting waves is not strictly true. The implications of the V require further examination, although this thesis did not reach a point where the complex mathematical modelling of this feature was accomplished. At this stage, it may be enough to consider that the V will allow a certain amount of ‘beam steering’ to occur, in which the squirting wave is preferentially propagated in a direction at right angles to each arm of the V, and further implications are discussed in §R 7.3.

The micrographs also showed that the outer hair cells arrange themselves in a typical unit cell. This unit cell was described in §R 6.1 as face-centered rhombic, where a cell in OHC2 sits surrounded by four others, two from OHC1 and two from OHC3. The rhombus is nearly a rectangle (orthorhombic) and has spacing a along the row of cells and spacing b from OHC1 to OHC3; however, the rhombus is sometimes found tilted by several degrees, as the following analysis will illustrate. The unit cell can therefore be described by three parameters: a , b , and θ , the latter being the tilt of the lattice away from the normal⁶ (the radial direction).

The micrographs collected typically show about a dozen cells, and frequently the position in the cochlea from where the specimen was taken is not given. A mapping of every outer hair cell in a human cochlea would be ideal, but a range of enquiries showed that no such data sets were available⁷. For my purposes, the most

⁶ The tilt will be measured in degrees, with positive values considered to derive from a ‘slash’-like configuration for a right cochlea (when the lattice is viewed from the stereocilia side with IHC at the top). Negative values of tilt therefore describe a ‘backslash’ under the same conditions. For mirror-symmetric left cochleas, a backslash configuration will carry a positive tilt value, and a slash a negative one.

⁷ Ulfendahl suggested that Bredberg’s extensive collection of human specimens may reside in a collection at the Karolinska Institute, but this could not be confirmed.

extensive data set appears to be that from several rhesus monkeys^{8,9} and this published set is also accompanied by audiological data. With the kind permission of the author, Dr Lonsbury-Martin, this data set was made the subject of this thesis chapter. As we will see, the data provides a valuable perspective on cochlear function, and indirectly gives confirmatory evidence that squirting waves (or similar short-wavelength waves) are active between rows of outer hair cells. Interpreted this way, the outer hair cell pattern gives a physical model for how distortion product emissions are generated. As I aim to show below, this new perspective gives a possible explanation for why DPOAEs reach maximum strength when the two primary frequencies are separated by a ratio of about 1.2.

7.2 The OHC lattice of the rhesus monkey

The published data originated from four rhesus monkeys, who had their cochleas fixed for microscopy after one of them, designated 84-098, had a set of audiological measures conducted. The auditory data included recording of spontaneous and stimulus-frequency otoacoustic emissions. Surface microscopy (in the plane of the plateau of Corti) was conducted after extensive preparation procedures which included fixation, alcohol drying, embedding in plastic, and baking. The possibility of distortion arising from this treatment needs to be noted. More details of the procedures are provided in Martin et al. (1988) and Lonsbury-Martin et al. (1988). After embedding, the cochlea was broken into sections and the outline of outer hair cell stereocilia (the V shapes) traced. The data derived from segments which were extracted from portions of the cochlea located between 24% and 60% of the distance from the apex.

The fullest data set comes from monkey 84-098 (who was also audiotically tested) and is given in Figures 7 and 8 of the Lonsbury-Martin et al. (1988). It shows every stereocilia bundle from 24–59% from the apex in the left ear (Fig. 7) and every bundle from 24–60% in the right ear (Fig. 8). A more fragmentary set of data – giving spot data at three locations (at 26–32%, 41–47%, and 56–60%) from the left

⁸ Martin, G. K., et al. (1988). Spontaneous otoacoustic emissions in a nonhuman primate. I. Basic features and relations to other emissions. *Hear. Res.* 33: 49-68.

⁹ Lonsbury-Martin, B. L., et al. (1988). Spontaneous otoacoustic emissions in a nonhuman primate. II. Cochlear anatomy. *Hear. Res.* 33: 69-94.

and right ears of three other monkeys – was presented in their Fig. 12. All the data from these three figures is analysed in the following three sections.

Because the pattern of the right ear of monkey 84-098R appeared more regular (and was presented in straighter strips¹⁰) it is here examined first. It is notable that the right ear was, in terms of spontaneous emissions, only weakly emitting, whereas the left ear was more irregular and strongly emitting.

7.2/a The regular unit cell (L-M Figure 8)

To examine the underlying geometric pattern of the stereocilia bundles, a spatial autocorrelation analysis of the outer hair cell pattern of the monkey's right ear (reproduced below as Fig. 7.1) was performed. To make sure that the frequency–position map was correctly presented here, it was first ascertained that the distance between rows was measurably greater for the right-hand end of the strips than the left. This must mean that the characteristic frequency of the right end is lower than the left, and so the right is closer to the apex. Hence, to avoid confusion, the labeling of the strips should read 27-24%, 30-27%, etc. (instead of, as published, 24-27%, 27-30%, etc.) to accord with standard left-to-right reading convention, and this has been applied in Fig. 7.1. Of course, since the two cochleas are mirror symmetric, strips from the left ear (such as the whole of Fig. 7 and parts of Fig. 12) are, as is, labeled with the correct convention, so that the end representing lower frequencies is at the left of the figure.

¹⁰ The cochlea is a spiral, and it is not surprising that a number of the strips in the figures appear curved. However, the tracings were done in small segments and in the course of this process most of the strips appear to have been straightened. The extent of distortion arising from this is unknown. Note that the autocorrelation analysis here looks at about 20 cells at a time, a distance over which the cochlea is effectively straight, so in practice there should be little difference between the results from curved and straightened segments.

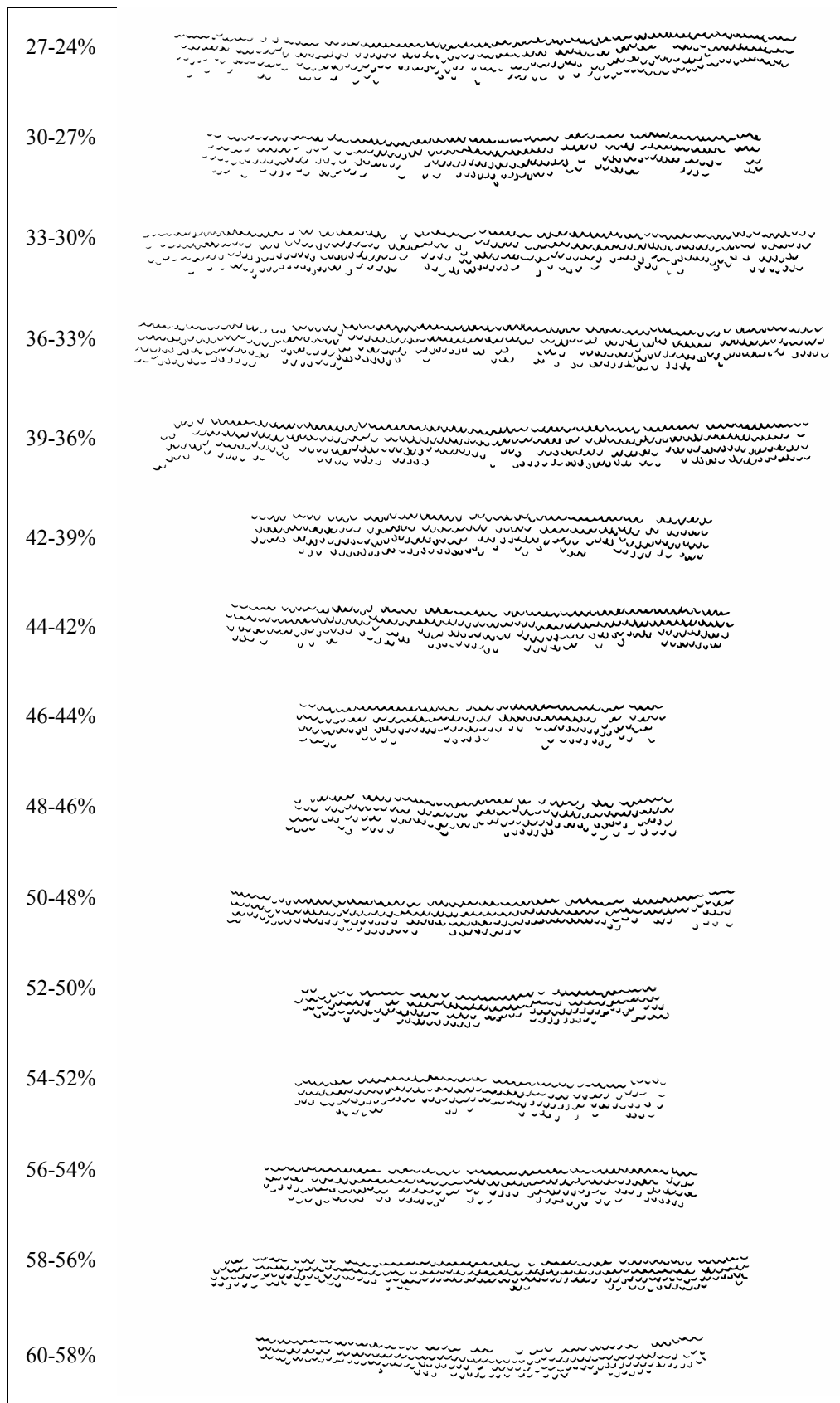


Fig. 7.1. The stereocilia pattern of outer hair cells from the right ear of rhesus monkey 84-098. All cells from 24% of the distance from the apex (top right) to 60% of the distance (bottom left) are shown. [From Fig. 8 of Lonsbury-Martin et al. (1988) and used with the permission of the author and Elsevier Science]

To analyse the cell pattern, a Matlab program, a draft version of which was written by Dr T. Maddess, was adapted to the task, and it operated on the image scanned at 600 dpi or 1200 dpi (depending on original size) from the published black-and-white figures. It performed fast autocorrelation analysis by creating a power spectrum, using a fast two-dimensional Fourier transform, and then created an autocorrelation image by performing a subsequent inverse Fourier transform on the real part of the power spectrum. This method is hundreds of times faster than directly computing the autocorrelation function (but gives the same result, as a cross-check demonstrated). The program divided each of the 15 segments into equal steps of about 10 cells across, thereby giving 6 steps for the shortest segment and 10 for the longest¹¹. Importantly, equal-sized steps were used for all segments so that the distance units in the resulting autocorrelation functions were directly comparable. An average autocorrelation for the whole strip was then computed and displayed. Fig. 7.2 shows the average autocorrelation function for the middle strip (46-44%) representing a characteristic frequency of around 1700 Hz. Below it (Fig. 7.3) is a contour plot of the same data which clearly shows the repeating cell pattern. A surface plot of the same data (Fig. 7.4) and two cross-sectional plots (Fig. 7.5) portray the difference in heights between the peaks.

¹¹ Because the steps are equal, sometimes a small amount of data was lost at the right-hand end of the strip. The program kept to this lost data to a calculated minimum. The number of cells selected for each step seemed about optimum in terms of balancing the contradictory requirements of spatial resolving power, signal-to-noise ratio, and the (unknown and variable) effects of segment straightening that was part of the original histology.

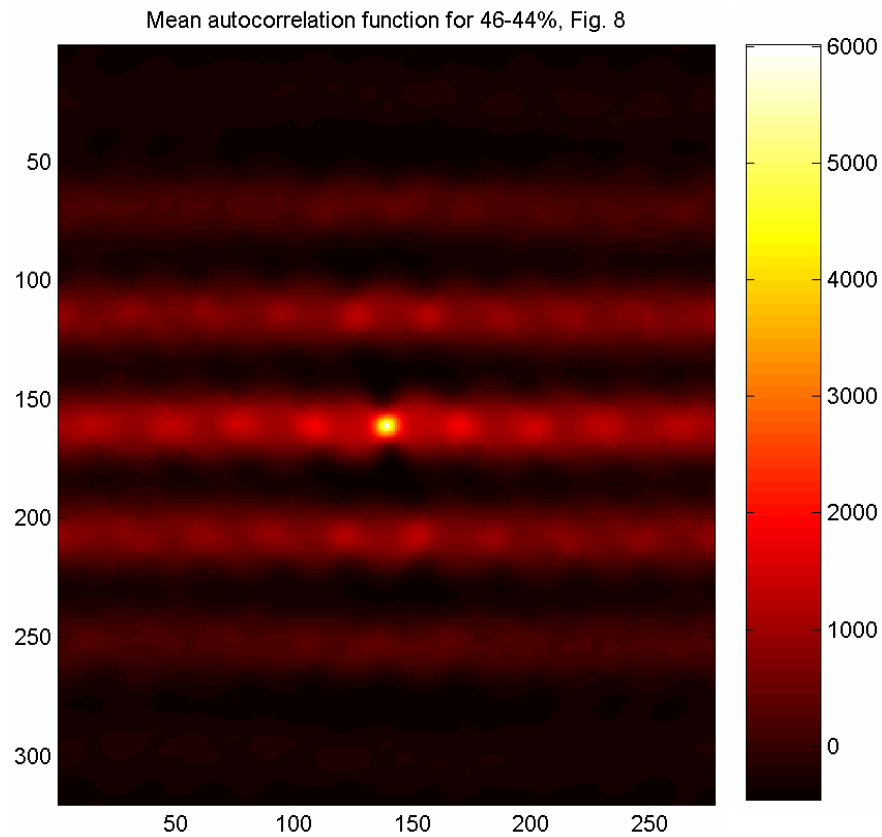


Fig. 7.2. Mean autocorrelation function for strip 8 of Fig. 7.1 (Fig. 8 of Lonsbury-Martin et al. (1988)). The x and y scales are in pixels; the colour scale is in relative units.

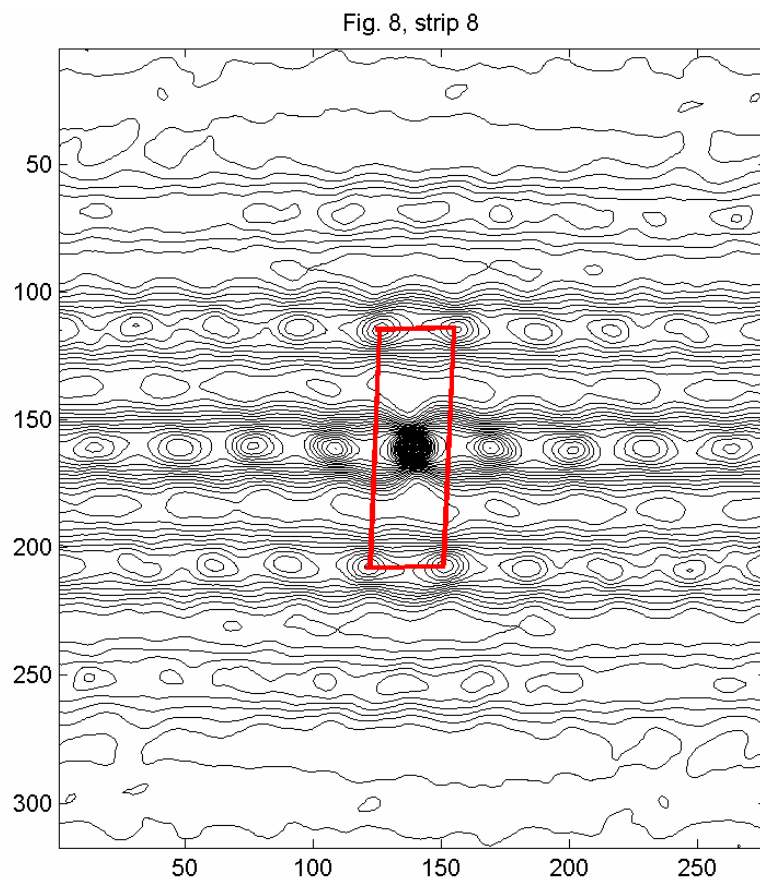


Fig. 7.3. The same data as the previous figure plotted as a contour map. The unit cell is outlined in red.

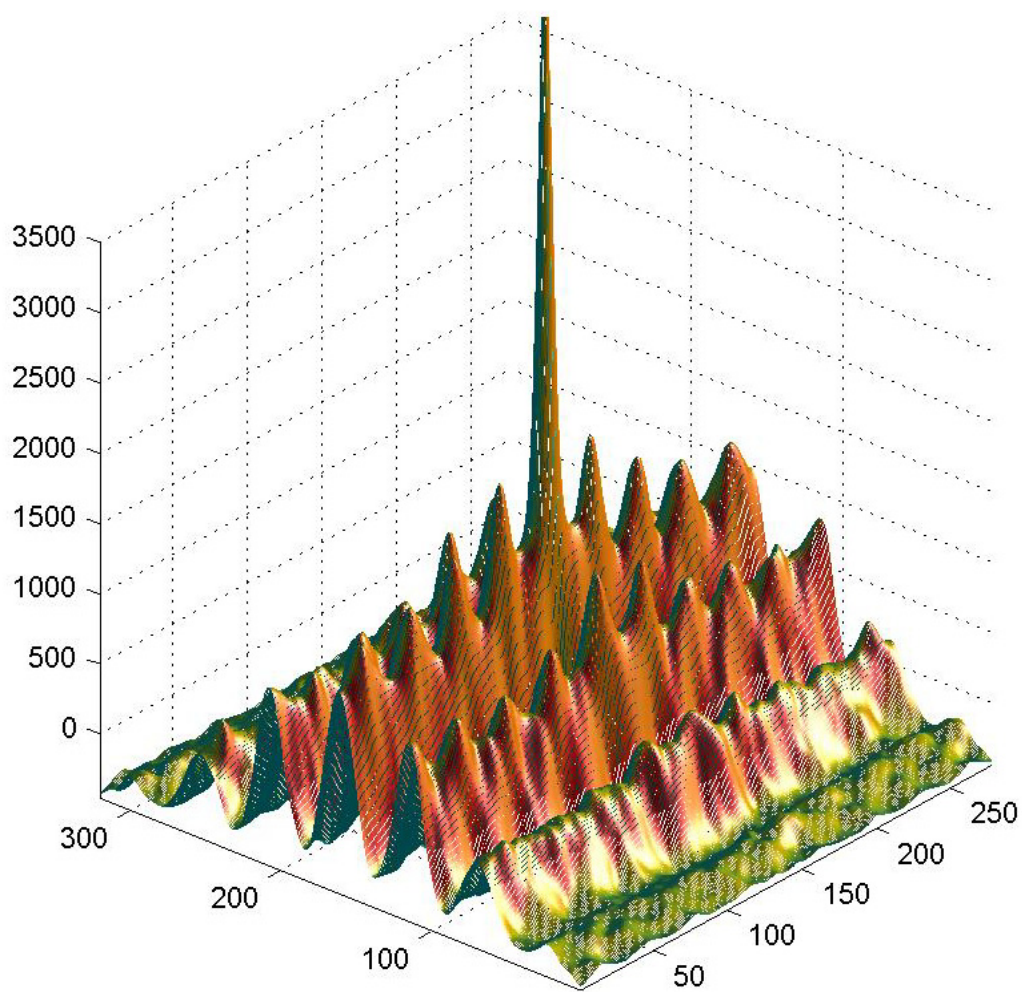


Fig. 7.4. Autocorrelation image, same data as Fig. 7.2, plotted as a perspective view of a surface to more readily convey the relative height of peaks.

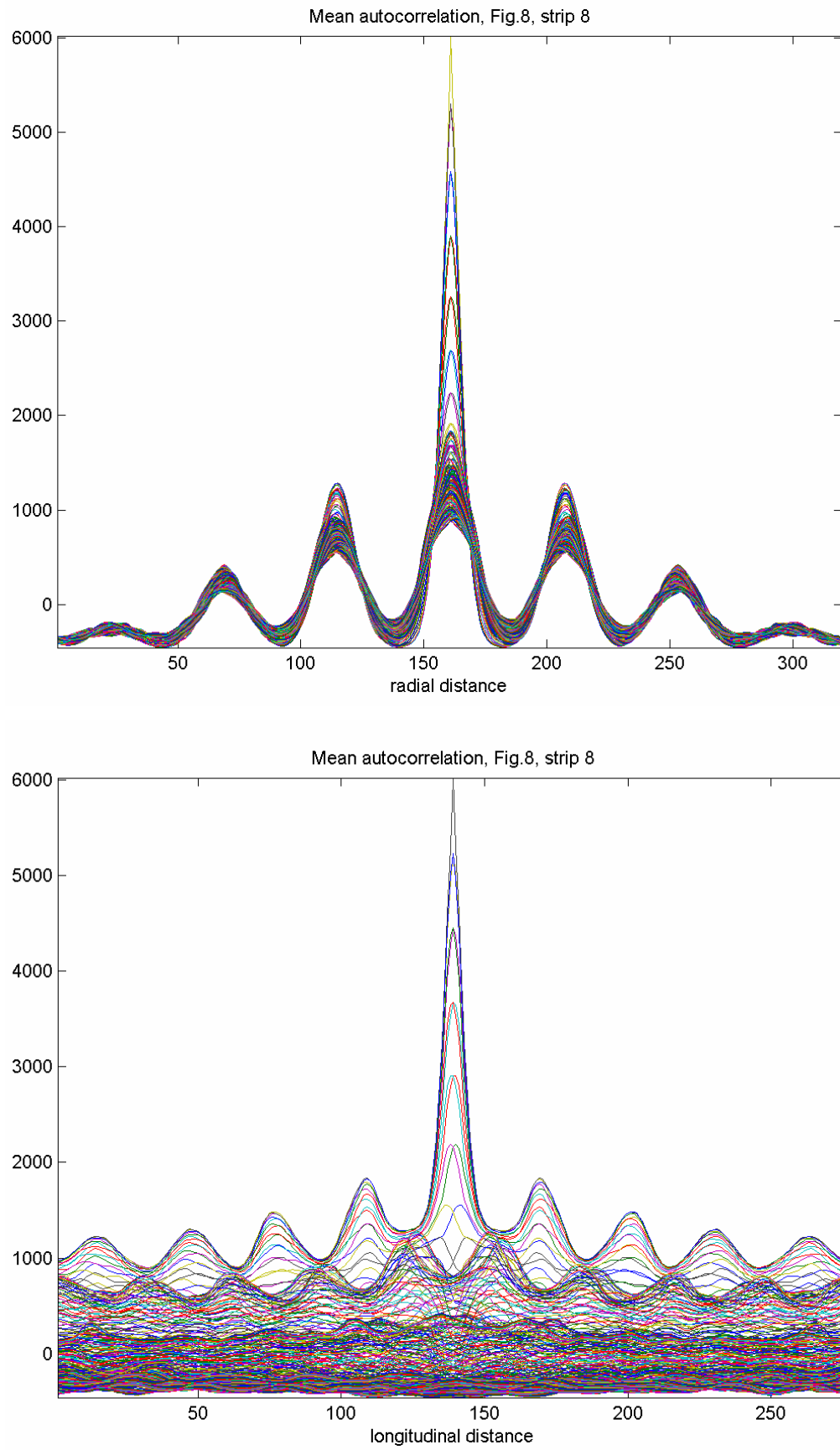
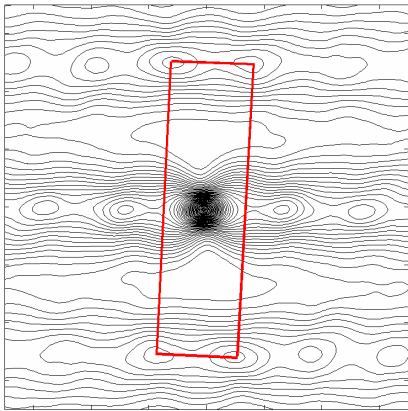
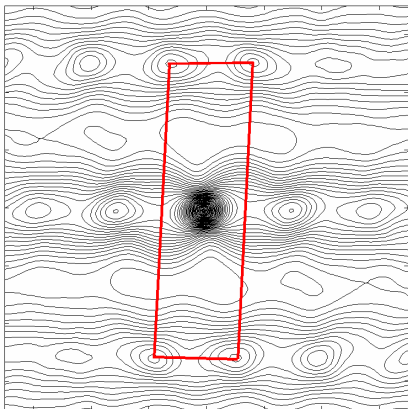
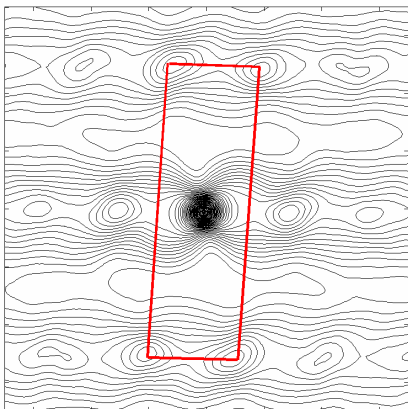
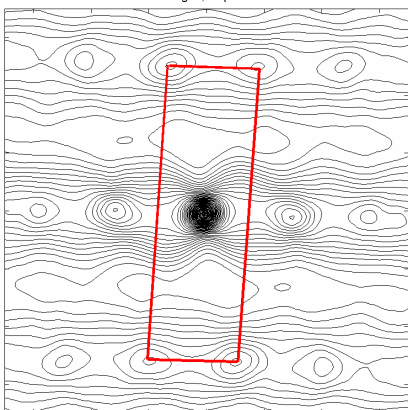
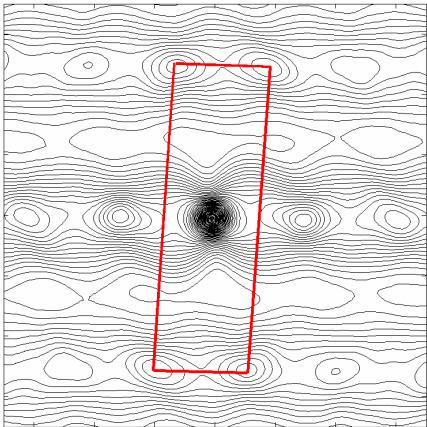
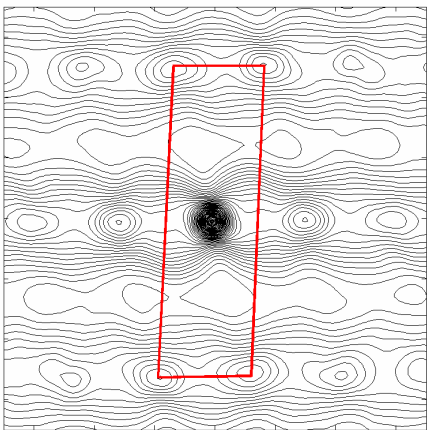
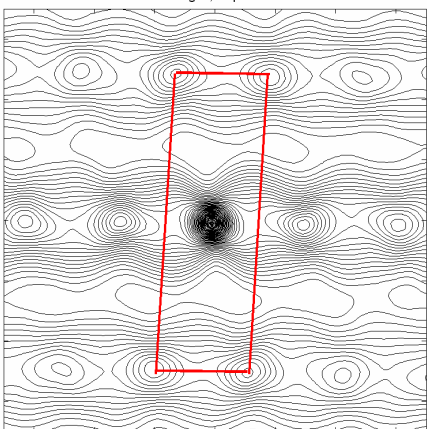
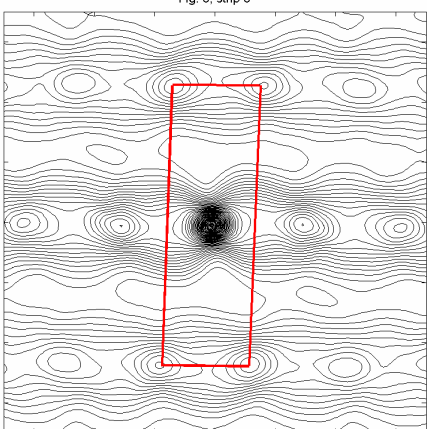


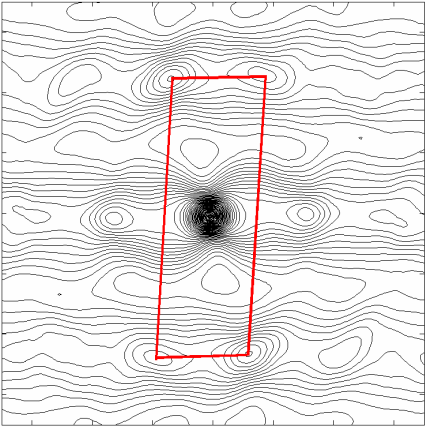
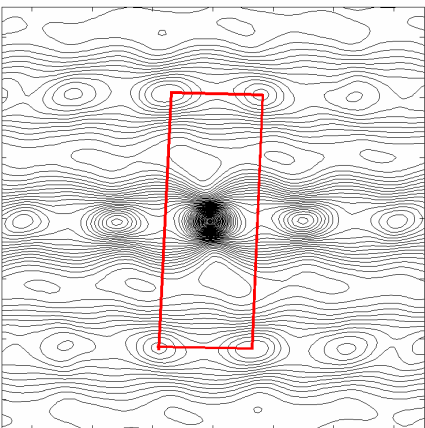
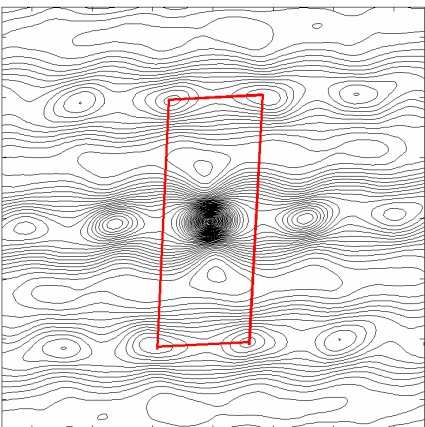
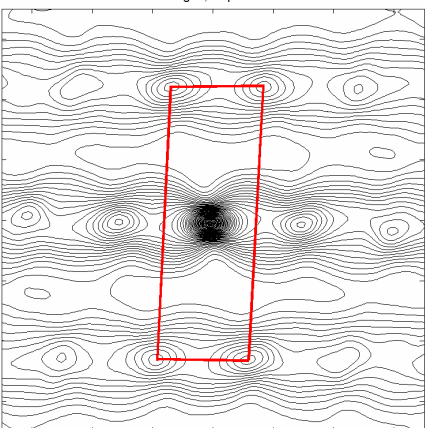
Fig. 7.5. Radial and longitudinal slices through the perspective view of Fig. 7.4.

Once the autocorrelation image was obtained, the next stage was to extract the dimensions of the unit cell in each image (outlined in red in Fig. 7.3). One approach is to find the coordinates of each of the corners of the unit cell, but in practice it is more accurate to determine the horizontal spacing a by measuring the distance between the two major peaks immediately flanking the central peak and dividing this dimension by two. (These peaks are higher and sharper than those vertically displaced from the centre line, and by dividing by two the parameter a can be extracted to within half a pixel). Using this approach on each strip, unit cell dimensions for each of the mean autocorrelation images were found. The images, and corresponding dimensions of each strip's average unit cell (again marked in red), are shown in Fig. 7.5.

Fig. 7.5 shows that the autocorrelation values can go negative at places where it is unlikely for an outer hair cell to appear. Another feature is that the standard deviation of the nearest-neighbour distances is around 20% of the mean value, indicating that there is considerable scatter around the mean. This in turn implies that the squirting wave tuning would not be very sharp. The reason for the scatter in the primate is not clearly understood, although handling, fixation, and tracing artefacts will contribute; by way of contrast, the placement of outer hair cell in rodent species is particularly regular, so there must be a good reason for the apparent irregularity in primates. Nevertheless, this chapter aims to see how far the frequency resolution of the system can be extended, and we will be particularly concerned with the *mean* values of a and b , which can be determined to within about 2%.

Strip of L-M FIG. 8 [see Fig. 7.1] (nr steps)	mean autocorrelation image	dimensions a , b , $tilt$ (pixels) [degrees]
27-24% (10)	Fig. 8, strip 1 	27 ± 0.5 102 ± 1 6 ± 1 [$3.4^\circ \pm 0.6^\circ$]
30-27% (8)	Fig. 8, strip 2 	30.5 ± 0.5 102 ± 1 6 ± 1 [$3.4^\circ \pm 0.6^\circ$]
33-30% (10)	Fig. 8, strip 3 	29.5 ± 0.5 101 ± 1 8 ± 1 [$4.5^\circ \pm 0.5^\circ$]
36-33% (10)	Fig. 8, strip 4 	30.5 ± 0.5 102 ± 1 5 ± 1 [$2.8^\circ \pm 0.6^\circ$]

39-36% (10)	Fig. 8, strip 5 	30.5 ± 0.5 101 ± 1 6 ± 1 [$3.4^\circ \pm 0.6^\circ$]
42-39% (6)	Fig. 8, strip 6 	31 ± 0.5 102 ± 1 5 ± 1 [$2.8^\circ \pm 0.6^\circ$]
44-42% (8)	Fig. 8, strip 7 	30.5 ± 0.5 99 ± 1 6 ± 1 [$3.5^\circ \pm 0.6^\circ$]
46-44% (6)	Fig. 8, strip 8 	30 ± 1 93 ± 1 5 ± 1 [$3.1^\circ \pm 0.6^\circ$]

48-46% (6)	Fig. 8, strip 9 	32 ± 1 92 ± 1 5 ± 1 [$3.1^\circ \pm 0.6^\circ$]
50-48% (8)	Fig. 8, strip 10 	31 ± 1 84 ± 1 3 ± 1 [$2.0^\circ \pm 0.6^\circ$]
52-50% (6)	Fig. 8, strip 11 	31.5 ± 0.5 81 ± 1 8 ± 1 [$5.6^\circ \pm 0.7^\circ$]
54-52% (6)	Fig. 8, strip 12 	30 ± 0.5 91 ± 1 3 ± 1 [$1.9^\circ \pm 0.6^\circ$]

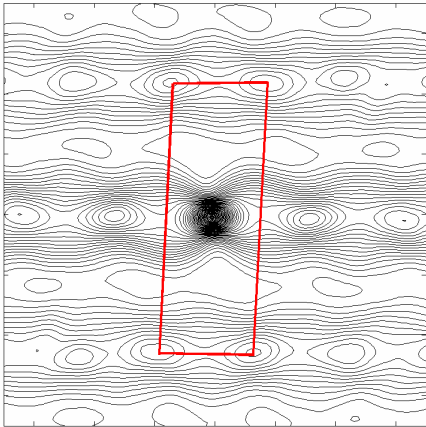
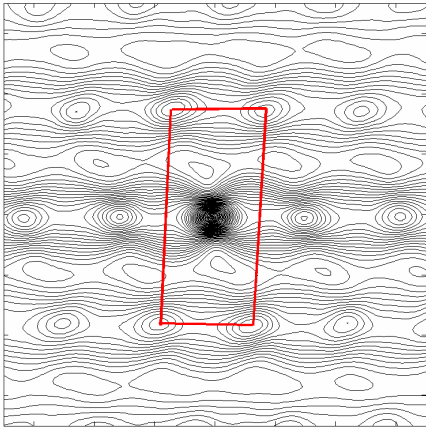
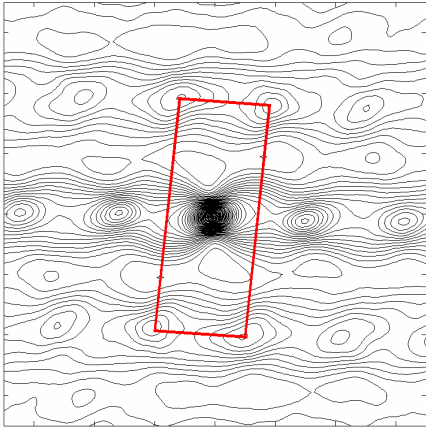
56-54% (6)	Fig. 8, strip 13 	32.5 ± 0.5 89 ± 1 3 ± 1 [$1.9^\circ \pm 0.6^\circ$]
58-56% (8)	Fig. 8, strip 14 	30.5 ± 0.5 71 ± 1 5 ± 1 [$4.0^\circ \pm 0.8^\circ$]
60-58% (6)	Fig. 8, strip 15 	31 ± 0.5 77 ± 1 8 ± 1 [$5.9^\circ \pm 0.7^\circ$]

Fig. 7.5. Mean autocorrelation functions of the strips shown in Fig. 7.1, plotted as contour maps. The peaks defining the unit cell are outlined in red. Lattice dimensions are given at right (horizontal cell spacing in pixels; OHC1–OHC3 spacing in pixels; offset of OHC1 relative to OHC3 in both pixels and degrees). Note that, for clarity, the images are cropped from originals like those of Fig. 7.3. Stated errors apply to precision of inter-peak distances in each image; standard deviations computed from multiple steps in a strip are typically 2–4 times larger (that is, there is more variation in the component steps than shows up in the averaged image). As a point of clarification, the contour circles that sometimes appear half way between the central peak and the peaks defining the unit cell represent minima, not maxima (that is, hair cells tend *not* to be located at those intermediate locations).

The systematic way in which the unit cell varies from base to apex is a key characteristic, and the three defining variables, a , b , and tilt (converted to an angle, θ) are shown in Fig. 7.6.

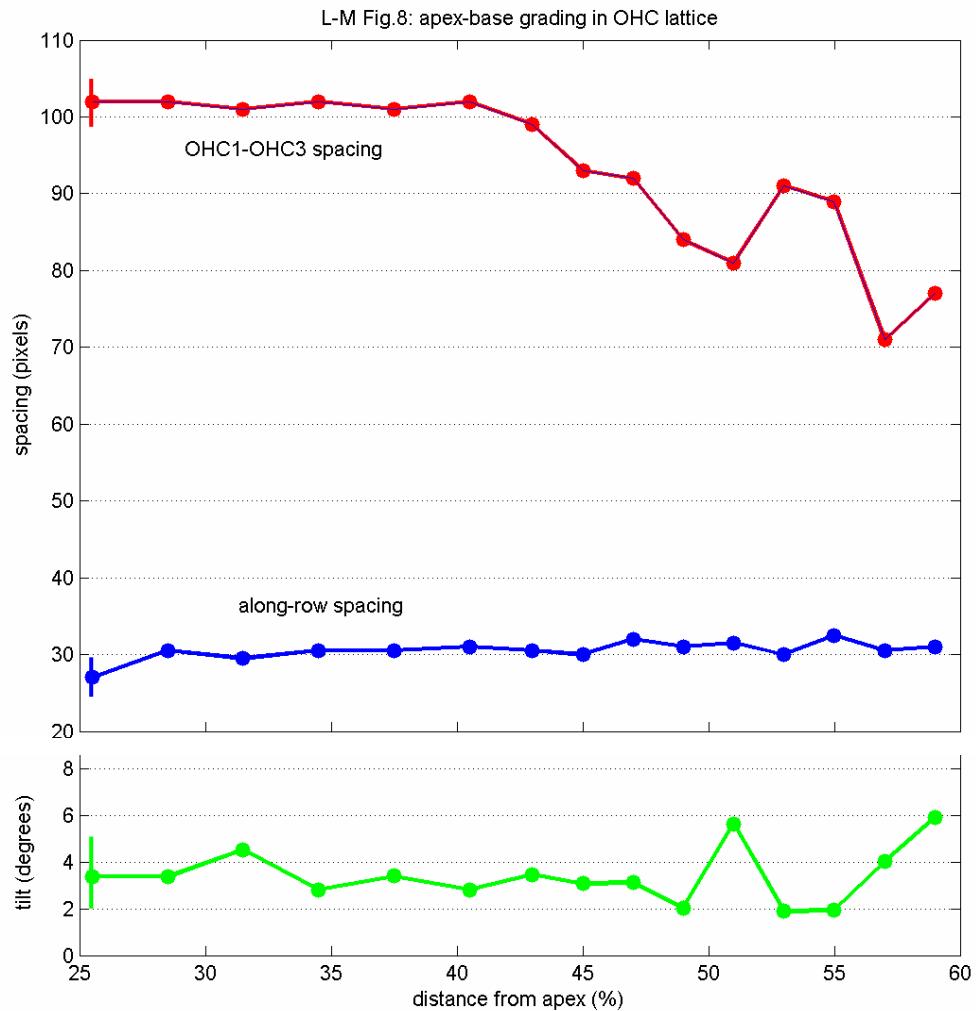


Fig. 7.6. Variation in unit cell parameters (a , b , θ) as a function of distance from the apex for the right ear. Error bars (on left-most symbols) represent the standard deviations derived from measuring component steps of a typical strip. [Based on Fig. 8 of Lonsbury-Martin et al. (1988)].

7.2/b A second look at the lattice (L-M Figure 7)

A similar analysis to that given above was performed on the monkey data of Figure 7 of Lonsbury-Martin et al. (1988). This is the strongly emitting left ear of monkey 84-098, and it ranges in 11 strips from 24-26% to 54-59% of the distance

from the apex (Fig. 7.7). Since this is a left ear, the characteristic frequency in the maps increases from left to right. It is of interest to see if there are any distinctive differences with the weakly emitting right ear. The autocorrelation images are shown in Fig. 7.8.

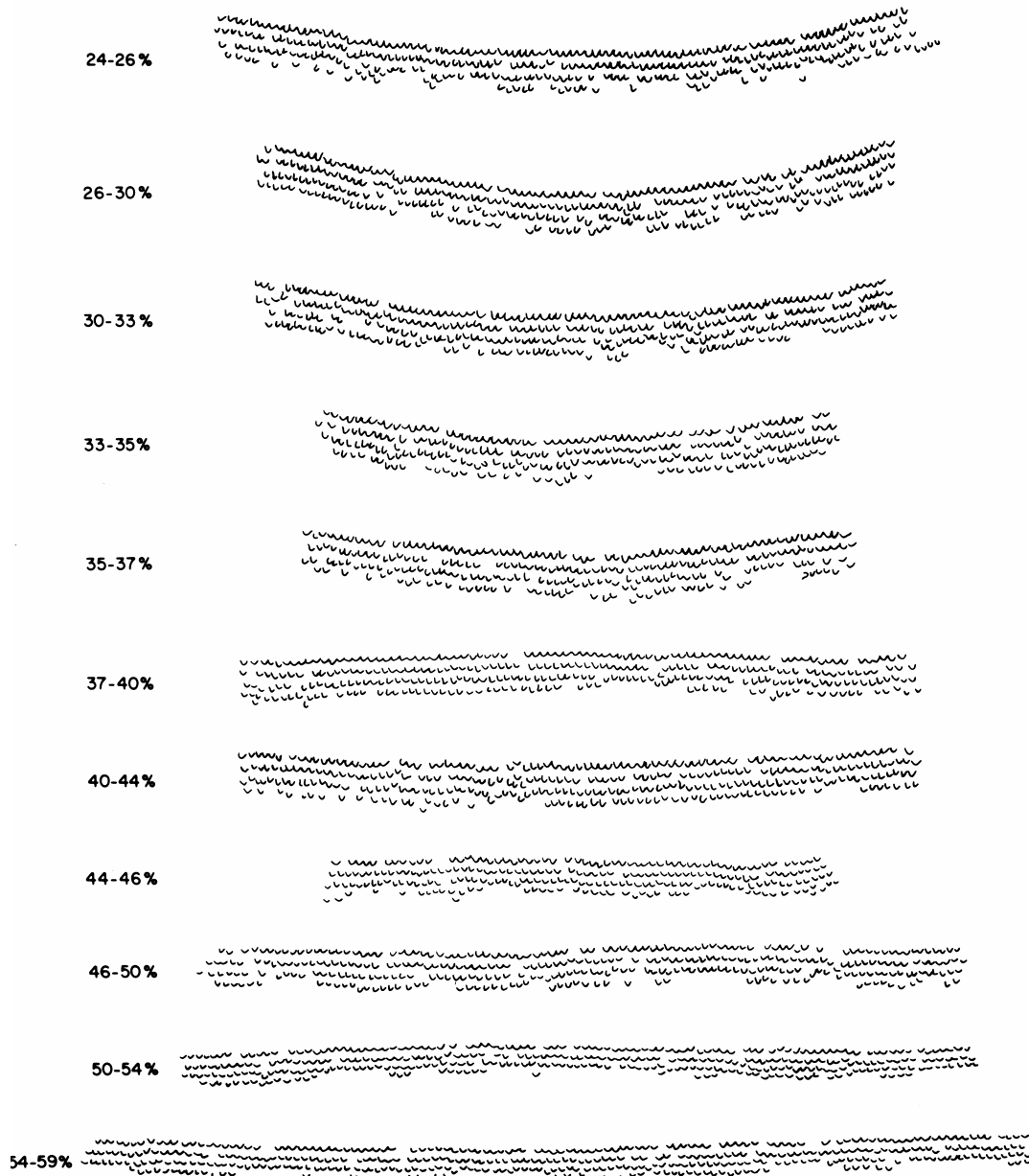
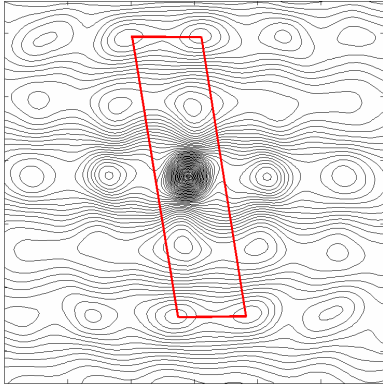
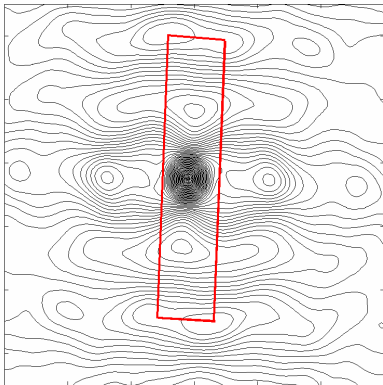
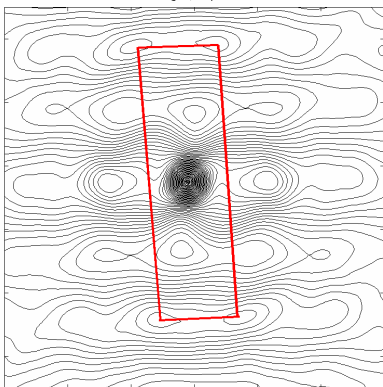
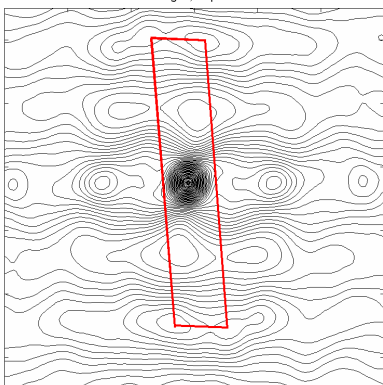
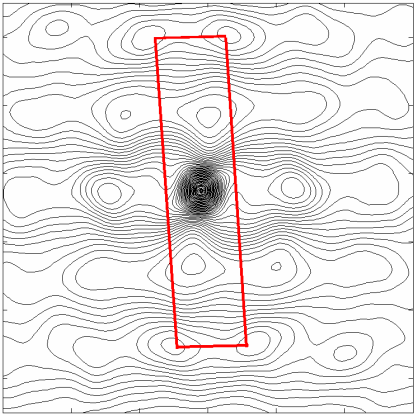
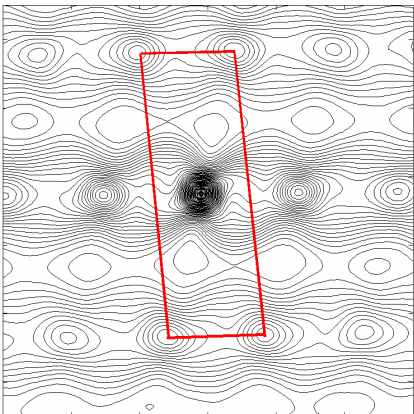
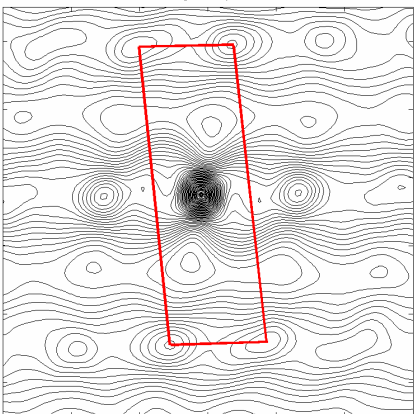
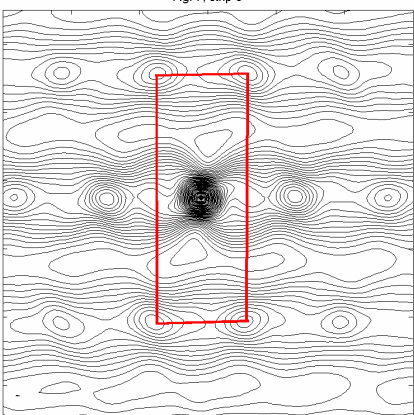


Fig. 7.7. The stereocilia positions of all the outer hair cells for the strongly emitting left ear of monkey 84-098. [From Fig. 7 of Lonsbury-Martin et al. (1988) and reproduced with the permission of the author and Elsevier Science]

Strip L-M FIG. 7 [see Fig. 7.7] (and nr of steps)	mean autocorrelation image (contour plot)	dimensions a , b , $tilt$ (pixels) [degrees]
24-26% (10)	Fig. 7, strip 1 	24.5 ± 0.5 88 ± 1 15 ± 1 [$9.7^\circ \pm 0.3^\circ$]
26-30% (10)	Fig. 7, strip 2 	25.5 ± 0.5 89 ± 1 0 ± 1 [$0^\circ \pm 0.6^\circ$]
30-33% (10)	Fig. 7, strip 3 	24.5 ± 0.5 86 ± 1 6 ± 1 [$4.0^\circ \pm 0.7^\circ$]
33-35% (8)	Fig. 7, strip 4 	27 ± 0.5 90 ± 1 6 ± 1 [$3.8^\circ \pm 0.6^\circ$]

R 7 [20]

35-37% (8)	Fig. 7, strip 5 	27 ± 0.5 91 ± 1 $5 \pm 1 \quad [3.1^\circ \pm 0.6^\circ]$
37-40% (10)	Fig. 7, strip 6 	28.5 ± 0.5 83 ± 1 $8 \pm 1 \quad [5.5^\circ \pm 0.7^\circ]$
40-44% (10)	Fig. 7, strip 7 	28.5 ± 0.5 88 ± 1 $8 \pm 1 \quad [5.2^\circ \pm 0.6^\circ]$
44-46% (8)	Fig. 7, strip 8 	27.5 ± 0.5 73 ± 1 $0 \pm 1 \quad [0^\circ \pm 0.8^\circ]$

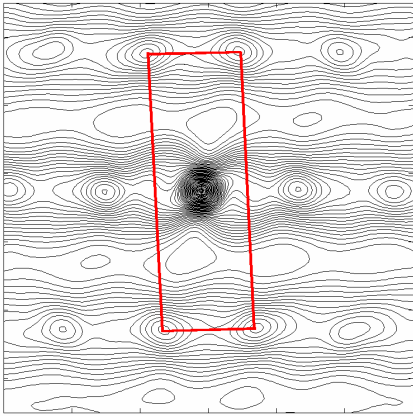
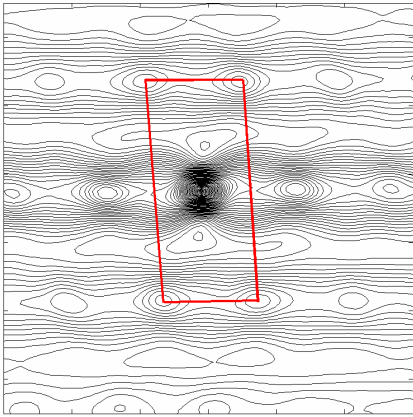
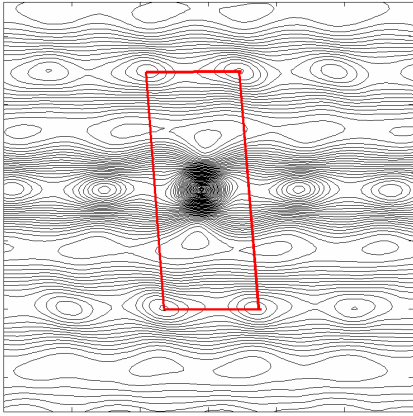
46-50% (12)	Fig. 7, strip 9 	28.5 ± 0.5 81 ± 1 4 ± 1 [$2.8^\circ \pm 0.7^\circ$]
50-54% (12)	Fig. 7, strip 10 	27.5 ± 0.5 64 ± 1 4 ± 1 [$3.6 \pm 0.9^\circ$]
54-59% (14)	Fig. 7, strip 11 	28.5 ± 0.5 70 ± 1 5 ± 1 [$4.1^\circ \pm 0.8^\circ$]

Fig. 7.8. Autocorrelation images (shown as contour maps) of the hair cell pattern of Fig. 7 of Lonsbury-Martin et al. (1988), [Fig. 7.7 here], the left strongly emitting ear of monkey 84-098. Again, the images shown are cropped versions of larger originals. Superimposed in red is the unit cell. The cell dimensions are shown as before.

Immediately it can be seen that the unit cell for the left ear tilts consistently to the left, whereas for the right ear the tilt was to the right. However, in terms of the direction of increasing characteristic frequency, the tilt is the same (that is, OHC1 consistently tilts towards the apex relative to OHC3).

Proceeding in the same way as before, the unit cell dimensions were plotted as a function of distance along the cochlea (in percentage distance from apex). The results are shown in Fig. 7.9. For comparison, the data are shown alongside that for the previous right ear. Note that since the scale of the two original figures differed, the number of pixels per unit distance was slightly different. Nevertheless, it is clear that the trends are similar.

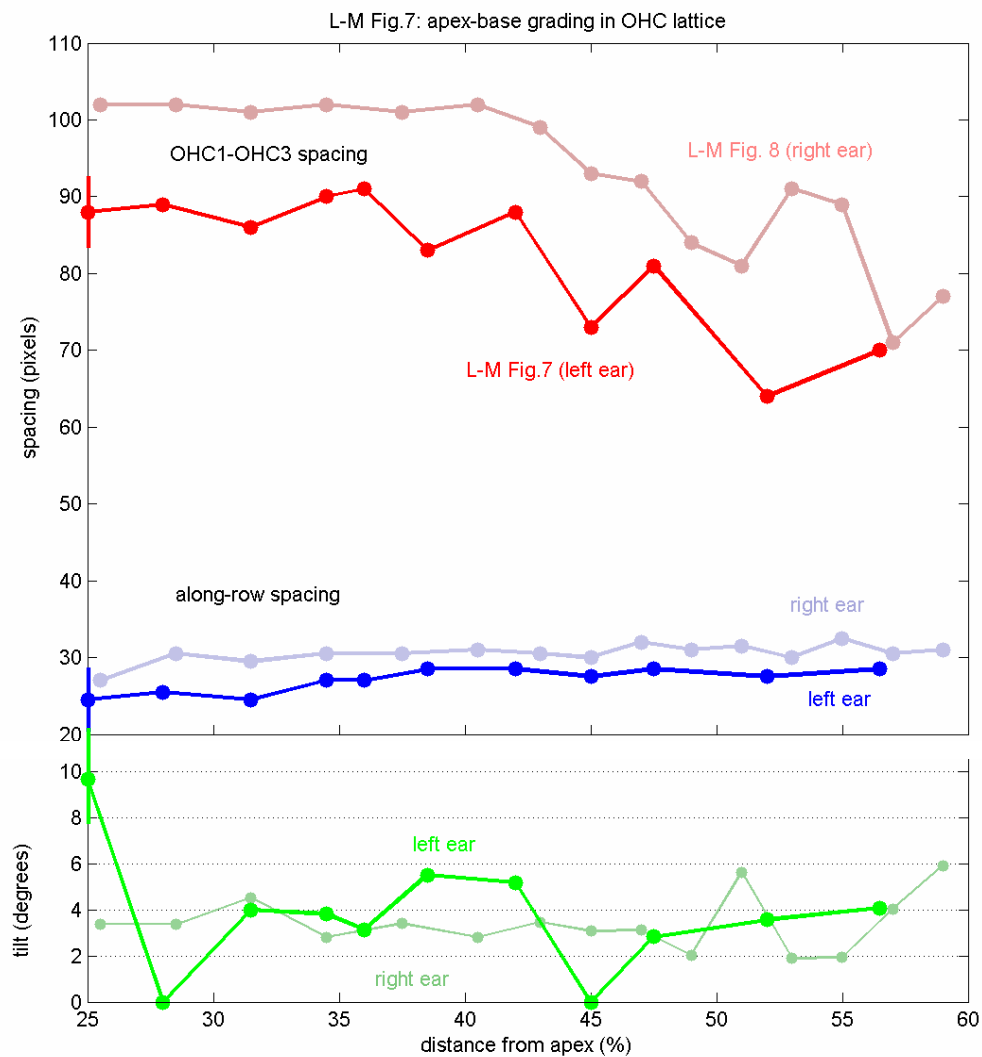


Fig. 7.9. Variation in unit cell parameters (a , b , θ) as a function of distance from the apex for the left ear [Fig. 7 of Lonsbury-Martin et al. (1988)]. For comparison, the matching data for the right ear (from Fig. 7.6, but in lighter colour) are also shown. (In reading the top graph, note that the pixel unit differs in size for the left and right ears because of a scale difference. Fig. 7.11B shows left and right images at the same scale, allowing cross-calibration to be done; the pixel scale for the left should be multiplied by 1.18 in order to correspond to the pixel scale for the right.)

To compare the relative size of the unit cell, the following figure (Fig. 7.10) shows the ratio of a/b plotted along the cochlea. The scatter of the figures appears to overlap, suggesting that the unit cell is similar between ears, and that the differences are probably due to shrinkage of the specimens. Note that the shrinkage appears to occur only in the radial direction, while the spacing between the cells along the length of the cochlea stays remarkably constant. It therefore seems reasonable to pool scaled data between the left and right ears, and Fig. 7.10 shows a quadratic fit to all the data.

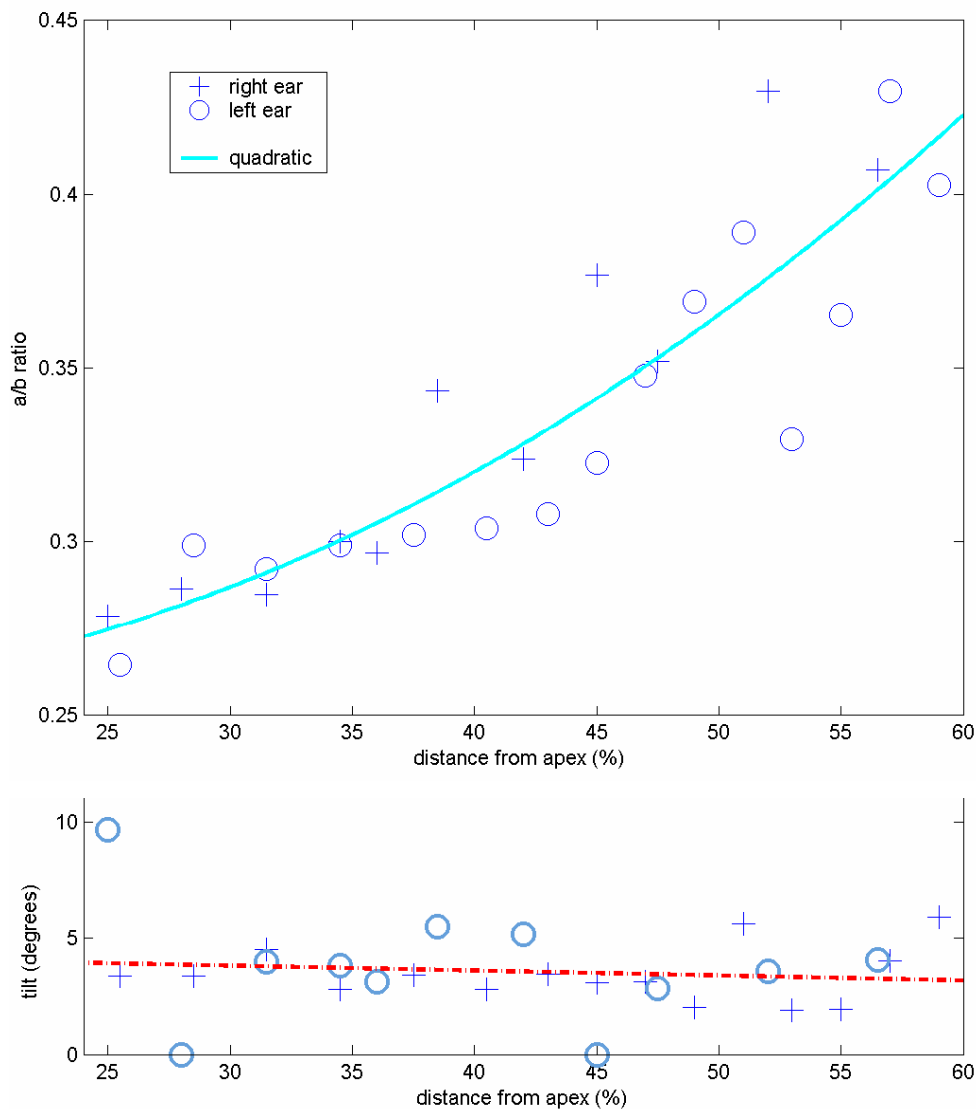


Fig. 7.10. Pooled data for the right and left ears. The a/b ratio of the unit cell (top) follows a quadratic term fairly closely. The tilt of the unit cell (below) appears fairly constant as the linear fit shows. The mean $\pm$ SD of the left ear is $3.8^\circ \pm 2.5^\circ$ while that of the right ear is $3.4^\circ \pm 1.2^\circ$.

The curve reflects a fairly strong relationship between distance along the cochlea and row spacing. This relationship reinforces the outlook, which the SAW model suggests, that the separation between the first and third rows of outer hair cells is a key parameters determining the characteristic frequency of the partition. (Other key factors – as set out in §R 5 – are the thickness of the reticular lamina and the width of the gap determined by the height of the stereocilia.)

The tilt of the unit cell is shown once more in the bottom part of Fig. 7.10 with a line of best fit inserted. This line is almost horizontal, indicating that the tilt is virtually constant along the cochlea. As we will demonstrate later, this is an important result. The mean tilt of the left ear is 3.8° with a large standard deviation of 2.5° ; for the right ear the comparable figures are $3.4^\circ \pm 1.2^\circ$. We take the tilt of the living cochlea to lie closely to the overall mean of $3.6^\circ \pm 1.9^\circ$. The median is 3.8° for the left and 3.4° for the right, with an overall median of 3.4° . For want of a single figure of the tilt of the in vivo cochlea we will use a figure of 3.5° in later discussion.

7.2/c *Extending the range of results (L-M Figure 3)*

The data so far examined can be extended to regions of higher and lower frequencies. In Fig. 3 of Lonsbury-Martin et al. (1988) are presented mappings of outer hair cells for regions of monkey 94-098's cochleas 20% from the apex, representing a characteristic frequency of about 400 Hz, and 80% from the apex, a region with CFs of about 13 kHz. For comparison, the region 46% from the apex is also presented; although this data is the same as already examined, it provides a useful cross-check and calibration.

The outer hair cell pattern is reproduced in Fig. 7.11 and the autocorrelation pattern in Fig. 7.12.

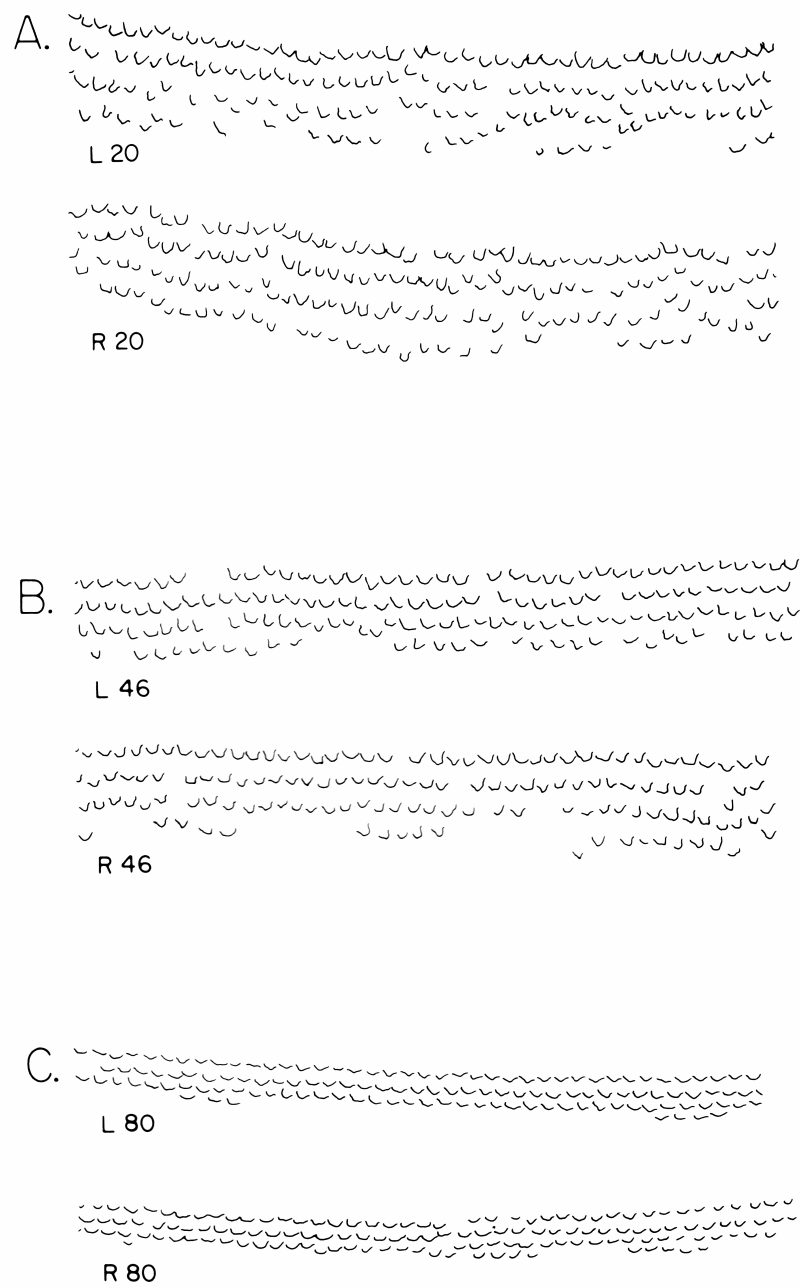


Fig. 7.11. Outer hair cell pattern in three diverse regions of the cochleas of monkey 84-098. The regions come from 20%, 46%, and 80% of the distance from the apex. (Note that the strips at 46% appear at the same scale, allowing one to calibrate the differing pixel scale in Fig. 7.9.) [Reproduced from Lonsbury-Martin et al. (1988) with permission of the author and Elsevier Science]

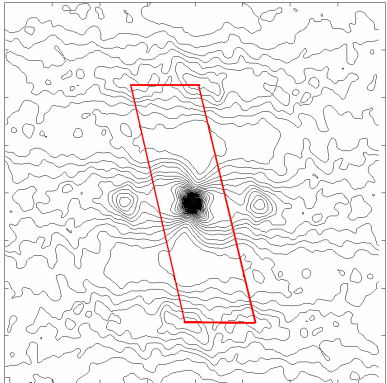
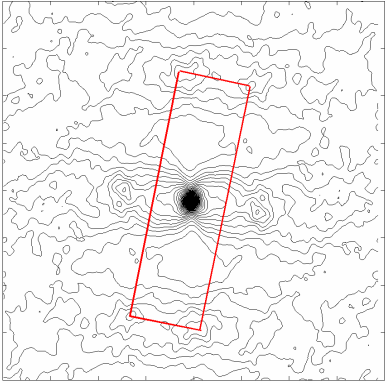
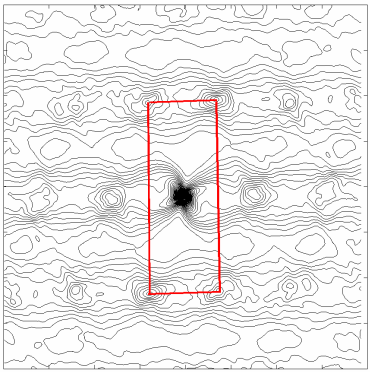
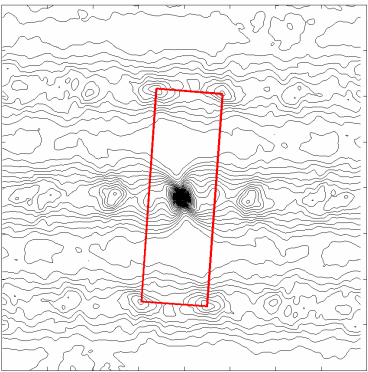
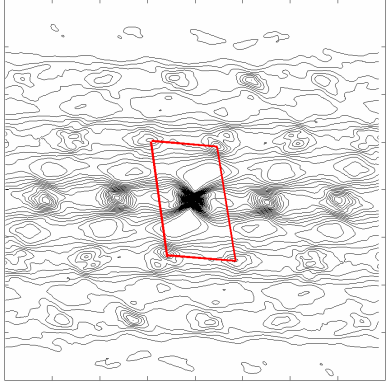
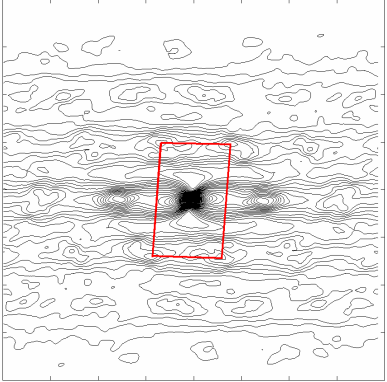
	LEFT	$a, b,$ tilt	RIGHT	$a, b,$ tilt
20 %		71 249 62		71 262 7
47 %		79 210 -2		73 232 11
80 %		79 119 22		75.5 120 7

Fig. 7.12. Mean autocorrelation images for the regions depicted in Fig. 7.11. Each image is the result of dividing each strip into 8 segments and averaging the autocorrelation images of the segments. The unit cell is outlined in red and the dimensions are in pixels (note that they are of different size to before). In all images the contour levels are 50% closer (to better locate the peaks in the 20% region, which are low and relatively noisy).

The form of the unit cell is generally the same as found previously. The a dimension is still constant to $\pm 5\%$, and the b dimension decreases as the characteristic frequency becomes higher; the a/b ratio therefore increase from about 0.27 at the 20% region to 0.66 at the 80% region. The values are set out in Table 7.1.

Distance from apex	LEFT a/b , tilt	RIGHT a/b , tilt	Mean a/b Mean tilt
20%	0.285 14.0°	0.271 1.5°	0.278 $\pm$ 0.007 7.8° $\pm$ 6°
46%	0.376 −0.5°	0.315 2.7°	0.346 $\pm$ 0.04 1.1° $\pm$ 1.6°
44–46% (Fig. 7.8, strip 8; Fig. 7.5, strip 8)	0.377 0°	0.323 3.1°	0.350 $\pm$ 0.03 1.6° $\pm$ 1.5°
80%	0.664 10.5°	0.629 3.3°	0.647 $\pm$ 0.02 6.9° $\pm$ 4°
Average of new data (20% and 80%)	12.3° $\pm$ 2°	2.4° $\pm$ 1°	5.3° $\pm$ 3° (all non-grey) 7.4° $\pm$ 5° (20% + 80%)

Table 7.1. Summary of data in Fig. 7.12. The row in grey is the equivalent data from Figs 7.8 and 7.5, and shows close agreement with the row above. Based on the two new data points (20% and 80%), the average tilt appears greater in the left ear.

Comparison of this data with Fig. 7.10 shows that the two points at 20% and 80% extend the graph to higher and lower frequencies and sit well with an extrapolation of the line of best fit. The generalisation holds true that the tilt is to the left for the left ear and to the right for the right ears¹². It may be significant that the two additional points show considerably more tilt in the left ear (12.3° $\pm$ 2°) than in the right (2.4° $\pm$ 1°), and inspection of Fig. 7.10 shows that the only other large tilt measurement (9.7°, strip 1 of Fig. 7.8) originates from the left ear too.

¹² The tilt for the 47% region of the left ear is effectively zero (−0.5° $\pm$ 0.2°), a result in line with that (0° $\pm$ 0.8°) observed for the 44–46% region of Fig. 7.8, a satisfying cross-check on the method of analysis.

7.2/d Confirmatory results (L-M Figure 12)

To show that the results derived from the left and right ears of monkey 84-098 are indeed representative, autocorrelation analysis of data (Lonsbury-Martin et al. 1988, Fig. 12) for three other monkeys at three cochlear distances (26–32%, 41–47%, and 56–60%) was also performed. The results confirmed the previous trends, as the following summary data show. Figure 7.13 illustrates the traced hair cell pattern and Fig. 7.14 gives the autocorrelation images. The numerical values of the unit cells are given in Table 7.2.

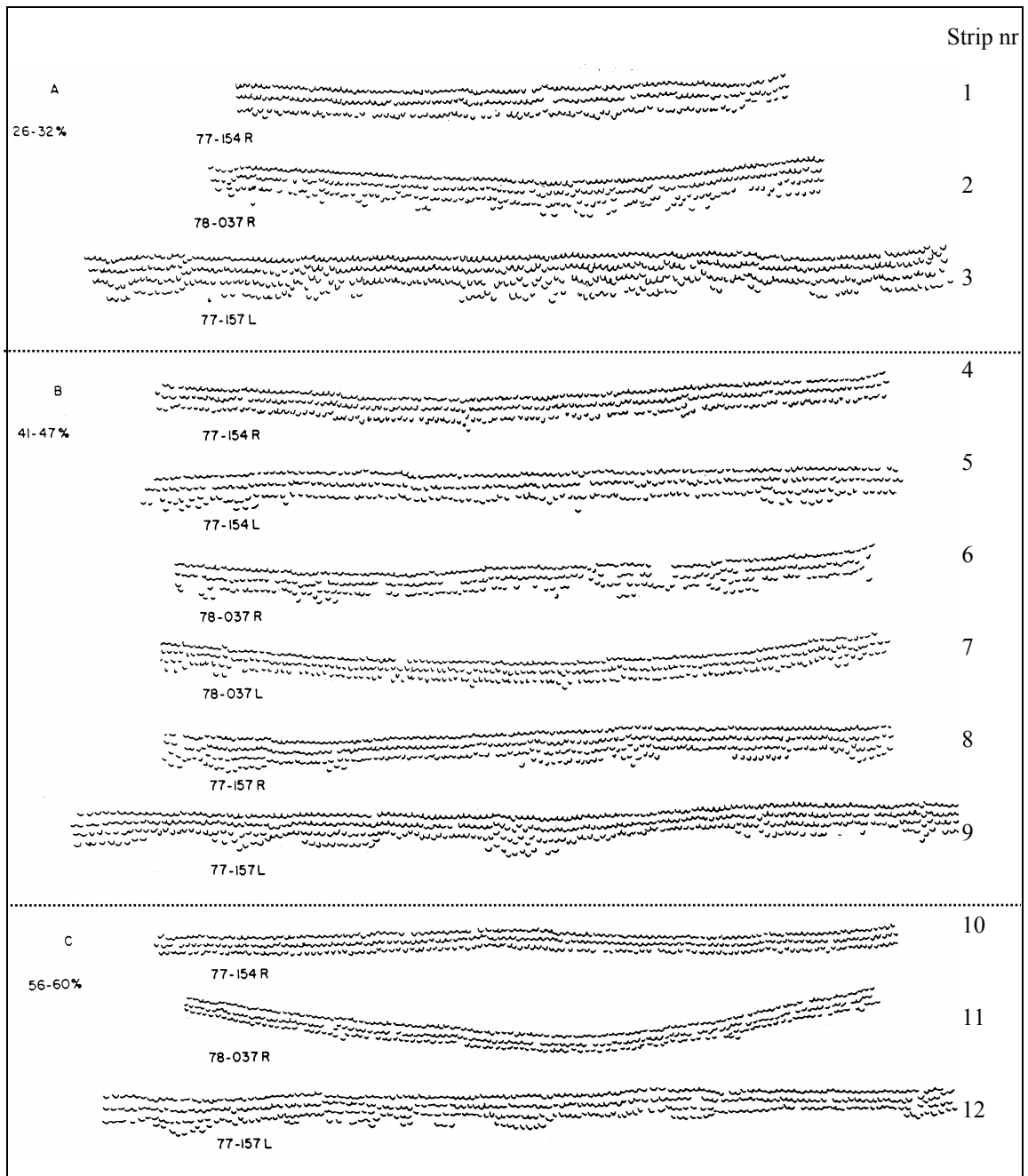


Fig. 7.13. The outer hair cell pattern for three other monkeys (Fig. 12 of Lonsbury-Martin et al. 1988). The 12 strips (numbered at right) have been taken from the left and right ears at three cochlear locations, marked A, B, and C on the figure and representing 26–32%, 41–47%, and 56–60% of the distance from the apex. Note that in right-ear strips the characteristic frequency increases from right to left, whereas in left ear ones it increases from left to right. [Reproduced with the permission of the author and Elsevier Science]

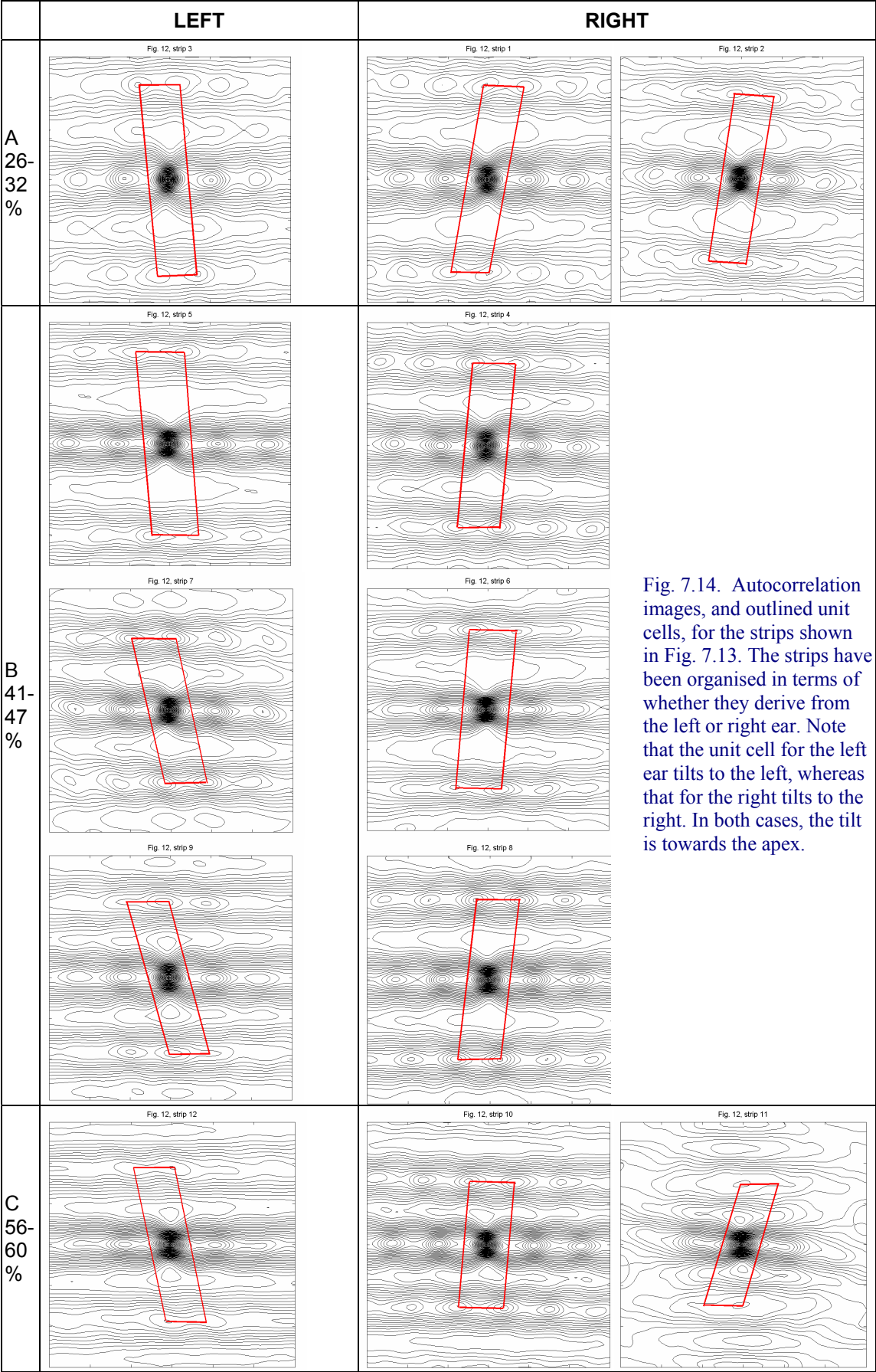


Fig. 7.14. Autocorrelation images, and outlined unit cells, for the strips shown in Fig. 7.13. The strips have been organised in terms of whether they derive from the left or right ear. Note that the unit cell for the left ear tilts to the left, whereas that for the right tilts to the right. In both cases, the tilt is towards the apex.

Following is a table summarising the unit cell dimensions derived from the foregoing contour maps. Before examining them, it is worth noting that the consistent direction of tilt of the unit cell: the cell tilts to the right for right ears and to the left for left ears, in both cases towards the apex.

Distance from apex (and strip nr)	LEFT	RIGHT		Mean <i>a/b</i>	Mean tilt (degrees)
26–32% (strips 3,1,2)	21.5 ±0.5 92 ±1 12 ±1	20.5 91 16	20.5 83 12	0.235 ±0.005	8.5° ±1.3°
41–47%					
77-154 (strips 5,4)	25 91 8	22.5 80 7		0.278 ±0.003	5.0° ±0.6
78-037 (strips 7,6)	23 71 18	22 78 8		0.302 ±0.020	10.0° ±4.2°
77-157 (strips 9,8)	22 74 21	22.5 77 9		0.295 ±0.002	11.3° ±4.6°
56–60% (strips 12,10,11)	22 75 17	23.5 62 4	21 59 15	0.339 ± 0.046	10.3° ±6.6°
Average ±s.d.	11.0° ±4.1°	7.7° ±3.3°			
	9.1° ±4.0°; <i>a</i> = 22.2 ±1.3				

Table 7.2. Unit cell dimensions and tilt for the 12 strips, from 3 monkeys, shown in Fig. 7.13 (from Fig. 12 of Lonsbury-Martin et al. 1988). In columns 2 and 3 of the table, the order is a , b , and tilt, all measured in pixels. Columns 4 and 5 give the derived values of the ratio a/b and of the tilt in degrees. The errors on the pixel measurements are the same as before, and are only given explicitly in the top row for the left ear. Again, the data are organised to allow comparison of left and right ears. Of particular value, the 41–47% strips allow, in three cases, for the direct comparison of the left and right ears of the same monkey.

The data shown in the table can be compared with the more extensive data for monkey 84-098 set out previously. Little appeared to be gained by plotting this

sparse data on a separate graph¹³; however, comparison with Fig. 7.10 shows that the a/b ratio falls roughly in the same range as before, indicating the same progression in unit cell dimensions between base and apex. The along-row spacing was again about constant, reinforcing the idea that the a/b ratio changes via variation of OHC1–OHC3 spacing. Once more we note a considerable degree of noisiness in the b parameter.

One major difference between this data for the 3 monkeys and that examined previously for monkey 84-098 is the figure for tilt of the lattice (last column of the table). Even though the *direction* of tilt exhibited the same consistent pattern for the left and right ears, the *size* of the tilt was considerably larger, with a mean value of $9.1^\circ \pm 4.0$, compared to the $3.6^\circ \pm 1.9^\circ$ before. Interestingly, though, we see that the average tilt for the right ear ($7.7^\circ \pm 3.3^\circ$) is about a standard deviation less than the tilt for the left ($11.0^\circ \pm 4.1^\circ$), which could be significant, especially given the greater tilt for the left ear shown in Table 7.1.

Again, no systematic trend in tilt angle between base and apex is evident. One possible explanation for the difference might be greater handling and shrinkage effects for these specimens. Another possibility – that the lattice geometry adjusts so as to produce distinctive geometrical ratios – is raised in the discussion below (§7.3).

In summary, the data for the 4 monkeys has revealed the following patterns.

1. The along-row spacing of the outer hair cells (a) is practically constant from base to apex.
2. The spacing between rows ($b/2$) increases from base to apex. The a/b ratio increases in a curvilinear fashion from 0.27 ± 0.01 at a distance of 20–25% from the apex to 0.42 ± 0.02 at a distance of 60% (the corresponding frequency range is about 500 Hz to 4 kHz). At 80% from the apex (14 kHz), the ratio approaches 0.65 ± 0.02 .
3. The b parameter exhibits considerable local variation, so that the trend is not always monotonic.

¹³ Given that the table only gives values for three locations along the cochlea and given that each location is less accurately specified (in the percentage units given, a range of 4–6% rather than 2–5% previously – that is, the strips are about twice as long).

4. There is a distinct tilting of the unit cell, to the right for right ears and to the left for left ears. In both cases this corresponds to the apical direction.
5. The tilt varies considerably from point to point and from one monkey to another, although there appears to be no trend with cochlear location. In one monkey (84-098) the average tilt amounted to about 3.5° , whereas in the other three monkeys it was larger, reaching up to 16° , almost the maximum of what can be accommodated within the lattice dimensions.
6. There is an indication that the tilt may be larger and more variable in left ears than in right.

7.3 Discussion

In general, these results are consistent with the SAW model. A major feature is that the consistent increase in row spacing from base to apex allows the characteristic tuning of the cochlea to be progressively lowered in accordance with squirting wave propagation speed. The increase in row spacing over the closely studied middle third of the cochlea amounted to about 1.6 times, and this parameter alone allows the tuning to vary by about $(1.6)^3$ (that is, 4-fold or 2 octaves) in accordance with squirting wave dispersion (see §R5 and Eq. 2). Of course, in addition to row spacing, the other factor of importance is the reticular lamina thickness. Except for the water buffalo, no data on this parameter are available, but using this unique data and pooling it with other parameters from various species (as was done in §R 5.3), shows that both factors together can accommodate the range of tuning typical of primates. The cochlear data analysed (26–60% from the apex) represented a range of characteristic frequency of 3 octaves (0.5–4 kHz, Fig. 1 of Lonsbury-Martin et al. 1988), so that additional parameters only needs to contribute an additional octave. For example, an RL thickness variation of 4 times could achieve this (§R5, Eq. 1).

Against this consideration needs to be placed the finding that the a/b ratio was subject to local fluctuations, and did not monotonically increase. The characteristic frequency is expected to systematically increase along the partition, so the ratio fluctuations constitute something of an anomaly. It means one of two things.

R 7 [34]

Firstly, it could mean that factors apart from row spacing, like RL thickness, are at work to counteract the spacing anomaly. Secondly, it could mean that the published data are not a fair reflection of in vivo conditions, because of inevitable handling and fixation effects.

A remarkable feature is the tilt of the unit cell, and this is a consistent observation which was not expected at the time that the earlier modeling work (§R6) was done. The modeling assumed that the unit cell was orthorhombic, so that tilt was not considered. It is apparent that the tilt can be considerable, reaching in exceptional cases up to 16° (L-M Fig.12, strip 9, set out in Fig. 7.14 here). In such a situation, the tilt is almost as large as the unit cell diagonal, meaning that the diagonal is lined up almost in the radial direction. Thus, all three rows are almost perfectly aligned (there is no offset as in the standard arrangement), and the squirting wave will be carried directly in the radial direction. Some differences in behaviour might be expected from this, and this is a situation where more work needs to be done.

Given the presence of tilt, large or small, the main interest at this point is outlining one possible implication. The focus of the next section is setting out the proposition that the tilt is the cause of distortion product otoacoustic emissions (DPOAEs).

7.3/a Implications of tilt for DPOAEs

The squirting wave model envisages feedback between rows of outer hair cells. In particular, it sees each hair cell launching a squirting wave that is communicated to a neighbouring cell and its response is another squirting wave that is sent back to its source, creating positive feedback and, if the gain is sufficient, oscillation. Each cell is a partner in this process, and the net result will be radial wave motion. The cells are exchanging wavefronts with neighbours over a specific feedback path. The favoured feedback path will be that between closest cells, but there will be some contributions from all of them. In the modeling done in §R6, for example, we saw that ‘phase averaging’ meant that a resonance set to occur at 1 kHz between a single cell in OHC1 and another in OHC3, will, through signal contributions by neighbouring cells, occur at a lower frequency, perhaps 0.7 kHz. In

other words, the along-row contributions have effectively widened the gap between OHC1 and OHC3.

Nevertheless, the process still hinges critically on exchange of wavefronts between closest cells. If there is more than one signal path, multiple feedback loops become possible, and here is where tilt has a large impact, as the following diagram (Fig. 7.15) should make clear.

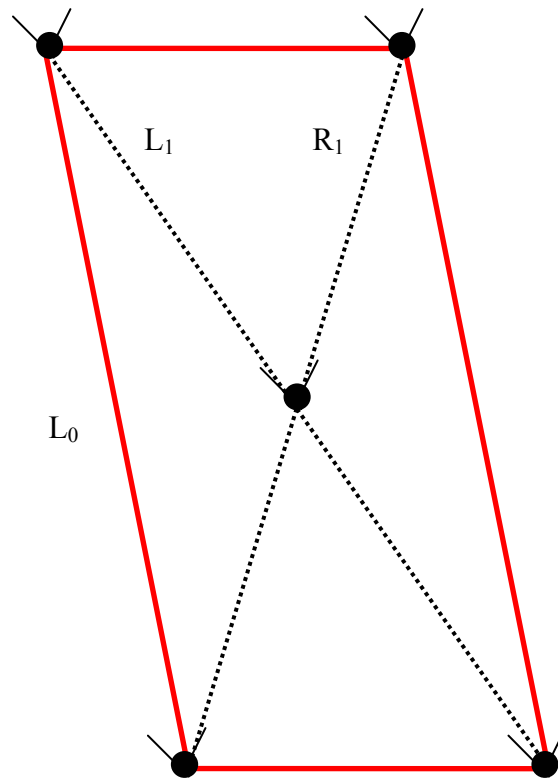


Fig. 7.15. A diagrammatic representation of the outer hair cell lattice showing horizontal, vertical, and diagonal interactions between the cells.

The diagram illustrates that horizontal, vertical and diagonal interactions are possible between hair cells. Modeling in §R6, and considerations of symmetry between cells in the same row, suggested that horizontal interactions were not likely. In this situation, we see that leaves vertical and diagonal interactions. For small values of tilt, the shortest diagonal, R_1 , will not be appreciably different from the spacing between OHC1 and OHC3, L_0 . However, there will be an appreciable difference in length of the diagonals R_1 and L_1 . Should there be a mechanism for discriminating between these signal paths, then they might have independent

existence. The implication then is that distortion could result from interaction at the paths have points in common, and this is how I propose DPOAEs arise. I point out that OHC2 lies precisely at the intersection between R_1 and L_1 , and that it bears stereocilia that more or less point at right angles to the direction of each path. Other cells in OHC1 and OHC3, in adjoining unit cells, also share in sustaining these particular paths¹⁴.

Perhaps the geometrical arrangement of stereocilia arms acts to ‘beam steer’ squirting waves. This would involve the stereocilia preferentially reacting to, and countering attenuation of, squirting waves proceeding in a direction at right angles to the arms. A second way, involving Deiters cell processes, by which the paths may be discriminated for is presented later (§R 7.3/d). At this stage, the idea is put forward as a hypothesis, and further experimentation and refined modeling will be needed to confirm it. It certainly goes beyond the simple point source modeling used in Chapter R6. However, it is worth presenting at this point because, firstly, it explains why the stereocilia display a V configuration¹⁵ and, secondly, it gives, as we will see, a numerical rationale for why DPOAEs peak at a maximum of the primaries of about 1.225. Thirdly, and most speculatively, it provides a way by which the outer hair cell array may be configured to detect specific frequency intervals, in particular those represented by small integer ratios.

Connecting tilt with distortion requires two steps. First, we have already demonstrated (§R5) that squirting wave dispersion means that the frequency is inversely proportional to the *cube* of the wavelength. Secondly, it is easy to appreciate that the ratio of the diagonals depends directly on the degree of tilt. Thus, assuming a typical a/b ratio of 0.3, the following graph (Fig. 7.16) shows the connection between the cube of the ratio of the diagonals and tilt. Clearly, in cases where the frequency of two tones is able to resonate in the two cavities defined by the diagonals, the distortion of the participating cells will be at a maximum. Hence, for a tilt of 7° , the cube of the ratio of the diagonals, and hence the relative frequencies of wavelengths filling these diagonals, will be in the ratio of 1.225. Distortion will therefore reach a maximum at those frequencies.

¹⁴ The symbols R and L have been used throughout this thesis to label the diagonals, but now that the mirror symmetry between ears has been clearly portrayed, a better notation would be F and B (for forward tilt and backward tilt, irrespective of left or right ear).

¹⁵ It may also explain why the V, upon closer examination, often appears as a W (see Fig. 4.1), providing an articulated joint that could promote independent operation of each arm.

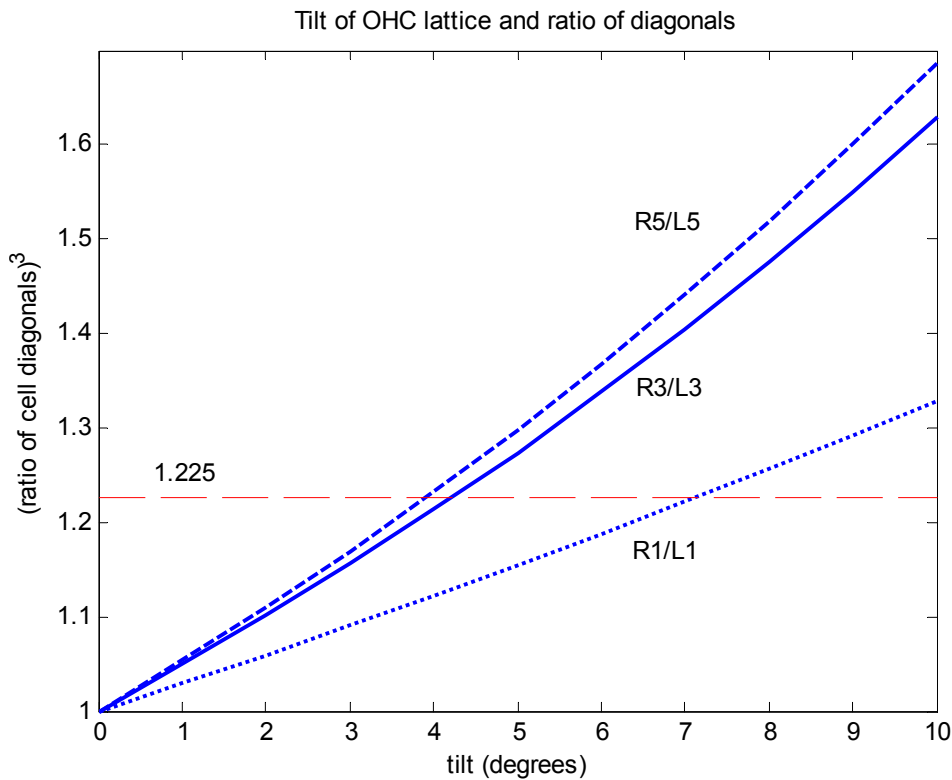


Fig. 7.16. Cube of the ratio of the diagonals of a unit cell with a/b of 0.3. The calculation is based on a unit cell with ratio $a/b = 1/3$ and tilt t (in offset of OHC3 re OHC1). Simple trigonometry shows that $(R_n/L_n)^3$ can be evaluated as $R_n = [(n*a + t)^2 + b^2]^{1/2}$ and $L_n = [(n*a - t)^2 + b^2]^{1/2}$. Interpreted as a ratio of underlying resonant wavelengths (or frequencies), the ordinate increases almost linearly with tilt. Note that at 7° the maximum distortion due to R_1 and L_1 interactions will occur at a ratio of primary frequencies of 1.225. The model has here been extrapolated to include ratios between the longer diagonals R_3 and L_3 and R_5 and L_5 (as defined in Fig. 6.1).

One refinement given in Fig. 7.16 is to include interactions due to longer diagonals. Modeling in §R6 has shown that squirting wave interactions become progressively weaker with distance, but given the potential, but unexplored, beam steering property of outer hair cells the longer diagonals have been included. Their importance relates to an unproved speculation I wish to raise about the detection of musical ratios. If these longer interactions occur, and the outer hair cell is able to discriminate wavefronts impinging upon it from different directions (in particular the two directions at right angles to the stereociliar arms) then detection of frequency ratios may be possible¹⁶. Data are presently insufficient to establish the case, and I

¹⁶ This idea was presented earlier [Bell, A. (2002). Musical ratios in geometrical spacing of outer hair cells in the cochlea: strings of an underwater piano? 7th Intl Conference on Music Perception and Cognition, Sydney, Causal Productions, Adelaide], but at that stage the system was considered non-dispersive and so the length–wavelength relationship was assumed linear. With squirting wave dispersion, the resonant frequencies involved must be compared in terms of the *cube* of their lengths.

will not dwell on the idea in detail here, but there are some results, perhaps fortuitous, that suggest further investigation may be worthwhile¹⁷.

We now proceed to see if, given this basic model, the data can provide a degree of support.

7.3/b Support for the tilted unit cell model

From Fig. 7.10 we saw that for monkey 84-098 the mean tilt of the left ear was $3.8^\circ \pm 2.5^\circ$ over the range 25–60%, while for the right ear the comparable figure was $3.4^\circ \pm 1.2^\circ$. These figures are almost the same, although adding the two data points from Table 7.1 gives weight to the idea that the left ear generally exhibits more tilt (or more variability). For the other three monkeys, Table 7.2 shows that the tilt was $11.0^\circ \pm 4.1^\circ$ (left ear) and $7.7^\circ \pm 3.3^\circ$ (right). These figures are consistent with the suggestion that distortion arises between the unit cell diagonals, although more detailed examination of the hypothesis is needed. Martin et al. (1988) records (p. 53) that the distortion products from monkey 84-098 were detected using an f_1/f_2 ratio of 1.25, a ratio not far removed from the optimum values suggested by these tilts and Fig. 7.16. It would have been particularly informative if the optimum ratio had been determined as a function of frequency (e.g., in the manner determined by Moulin for human subjects¹⁸) because a parallel movement between (a) optimum ratio for a given geometric ratio of the primaries and (b) tilt at a particular cochlear location known to closely represent those frequencies would carry significant weight. For example, the trend between tilt and frequency in Fig. 7.17 (below) seems to show tilt

¹⁷ For example, taking the unit cell geometries of Fig. 7.5, we find that the ratio $(R2/L1)^3$ is 1.50 ± 0.01 (strip 1 and 6) and 1.99 ± 0.01 (strip 11); further, $(L2/R1)^3$ is 1.53 ± 0.01 (strip 10) and 1.49 ± 0.01 (strip 14). Other musically significant intervals appear in other cavity ratios, but a difficulty is that other, apparently non-musical, ratios appear too. Another problem is that we have averaged first over about 20 unit cells and then over an entire strip, and yet we might expect to find a *mixture* of different ratio-detection geometries within that length. Indeed, that is a possible explanation of why the OHC pattern *appears* irregular. Disentangling such a mixture might not be easy (for the outside observer, that is – for the animal concerned, neural wiring simply picks out the appropriate ratio). Nevertheless, the small-integer ratios that do appear are intriguing and, given their potential importance for musical perception, call for further investigation.

¹⁸ Moulin, A. (2000). Influence of primary frequencies ratio on distortion product otoacoustic emissions amplitude. II. Interrelations between multicomponent DPOAEs, tone-burst-evoked OAEs, and spontaneous OAEs. *J. Acoust. Soc. Am.* 107: 1471-1486. Fig. 4.

increasing with distance from the apex, so that we might expect optimum distortion ratio to increase with frequency.

Notwithstanding this specific lack of comparable data, there is some other audiological evidence that is relevant and which can help decide whether tilt is the key parameter underlying distortion. As well as the anatomical evidence of Lonsbury-Martin et al. (1988), Martin et al. (1988) present audiological measurements made on the same monkey 84-098 whose hair cell patterns we have analysed. Some of this data gives support for the unit cell model in which the ratio of its diagonals indicates the ratio of the two frequencies that are interacting in the cochlea. Before presenting this evidence, it will be helpful to directly plot the ratio of the diagonals of the unit cell for monkey 84-098's left and right ears. These are the unit cells revealed in Fig. 7.5 and 7.8, and are plotted in Fig. 7.17 below.

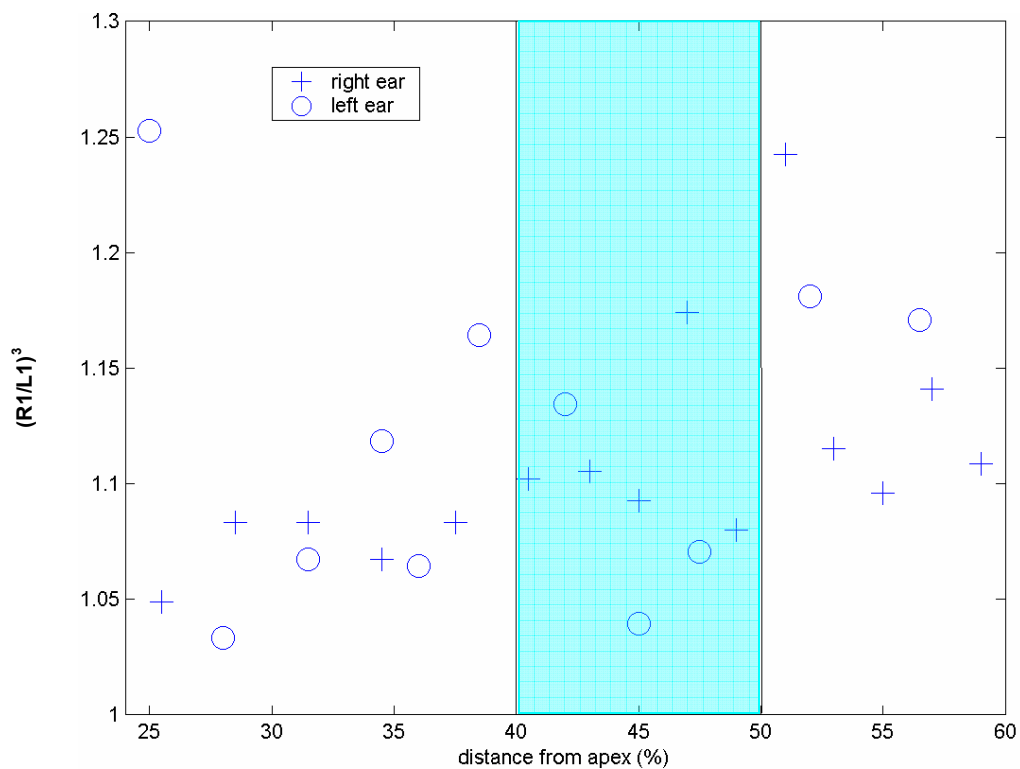


Fig. 7.17. Cube of the ratio of the unit cell diagonals for left and right ears of monkey 84-098 as measured directly from Figs 7.5 and 7.8. This monkey had diagonal ratios lower than the other 3 monkeys, but the values near the middle of the cochlea (40–50%) represent a region of 1200–2400 Hz that was audiologicaly probed. The average values of $(R1/L1)^3$ in this shaded region are 1.10 ± 0.04 (1.11 ± 0.03 for the left ear and 1.08 ± 0.03 for the right).

There are three figures in Martin et al. (1988) which provide interesting parallels.

1. The authors recorded stimulus frequency otoacoustic emissions (SFOAEs) from the left and right ears of monkey 84-098 between 0.8 and 2.8 kHz, producing the characteristic record of peaks and troughs in the ear canal pressure as the external tone interacted with the cochlea's own inherent acoustic output. Peaks of pressure correspond nicely, as their Fig. 4 shows, to frequencies of spontaneous otoacoustic emissions (SOAEs). The regular occurrence of the peaks and troughs is intriguing, and the numerical value of the spacing is of considerable interest, as it reflects basic cochlear mechanics. From the work of Gaskill and Brown (1990), it is known that the peak frequencies of SFOAEs generally correspond to the peaks in the fine structure of DPOAE sweeps¹⁹. That is, SFOAEs, although generated by a single tone interacting with an internally generated cochlear signal, somehow reflect the way in which two external tones interact in the cochlea.

The CRF model of Shera and Zweig see the peaks as corresponding to longitudinal standing waves, but I regard them as resulting from radial standing waves, and so the difference between peaks derives from how closely neighbouring unit cells can be tuned to different frequencies. At the same time, a unit cell (or group of neighbouring unit cells) will have a finite bandwidth limited by the squirting wave tuning. The interaction of these factors will require careful modeling, but the implication I want to emphasise is that each local cell cluster reacts to at least two sharply tuned frequency components corresponding to radial and diagonal cell interactions.

Whether the resonators are longitudinal (Shera and Zweig) or radial (this thesis), let us examine the spacing of the peaks and troughs as presented in Fig. 6 of Martin et al., which I will interpret, following Gaskill and Brown (1990), in terms of the optimum frequency ratios of two interacting tones. I will aim to show that the data in Martin et al.'s Fig. 6 show the tuning bandwidth of the cochlear resonators. The data were originally plotted as absolute bandwidths, but these values have been converted to relative bandwidths and are plotted in Fig. 7.18 below.

¹⁹ Gaskill, S. A. and A. M. Brown (1990). The behavior of the acoustic distortion product, $2f_1-f_2$, from the human ear and its relation to auditory sensitivity. *J. Acoust. Soc. Am.* 88: 821-839. Fig. 13.

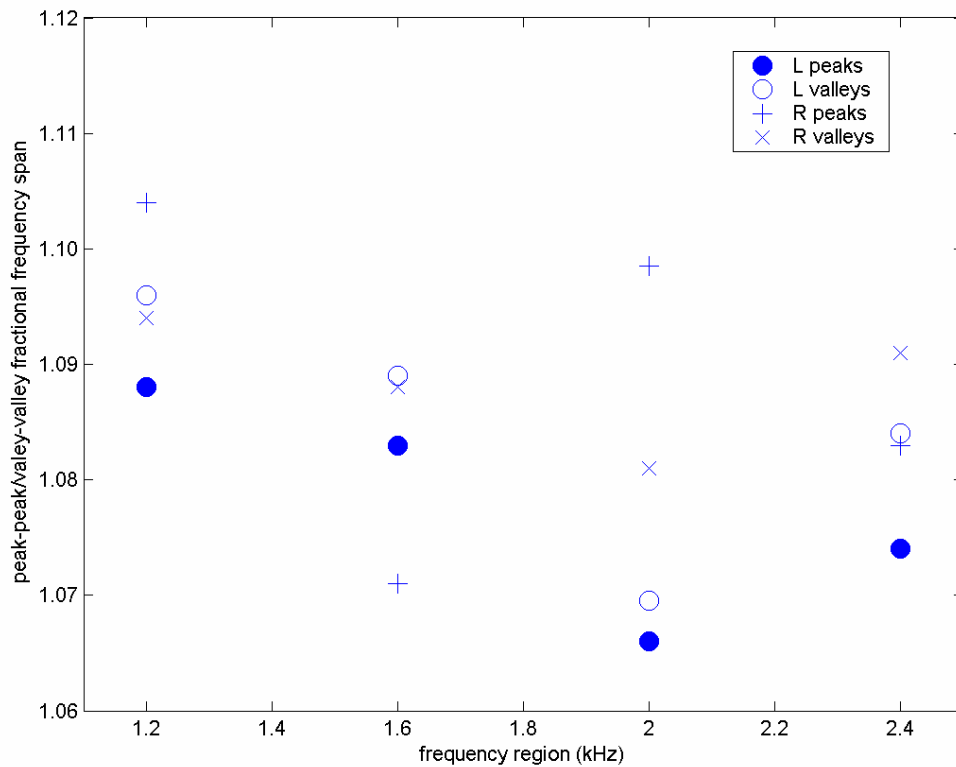


Fig. 7.18. Spacing between peaks and valleys of SFOAEs in both ears of monkey 84-098, expressed as a ratio of the span to the mean frequency. Data from Fig. 6 of Martin et al. (1988).

The distinctive feature of Fig. 7.18 is that the relative frequency span between SFOAE peaks (expressed as a fraction of the centre frequency) covers the same range as the shaded area in Fig. 7.17. In the first case, the mean and standard deviation is 1.081 ± 0.01 for the left ear and 1.089 ± 0.01 for the right; for comparison, the average shaded region values were 1.11 ± 0.03 for the left ear and 1.08 ± 0.03 for the right). That is, the SFOAEs display the same spacing ratio that one might expect if the unit cell had diagonals with length ratios just as we have measured. As a first approximation (and more modeling will need to be done here) the tuning of the cochlea in this region appears to match the tuning inherent in a set of outer hair cells arranged in a rhombus tilted at about 4° . Certainly, it makes sense to consider that an untilted, symmetrical lattice will have limited opportunity to generate distortion whereas a tilted one gives an immediate asymmetry supportive of two co-localised frequencies, which is just what is required to generate distortion. Of course, the close agreement could be fortuitous, but there is more evidence supporting this interpretation.

2. Data on the frequency (and amplitude) of the strongly emitting left ear of monkey 84-098 is presented in Figs 1 and 2 of Martin et al. (1988) and is reproduced below as Fig. 7.19 and Fig. 7.20.

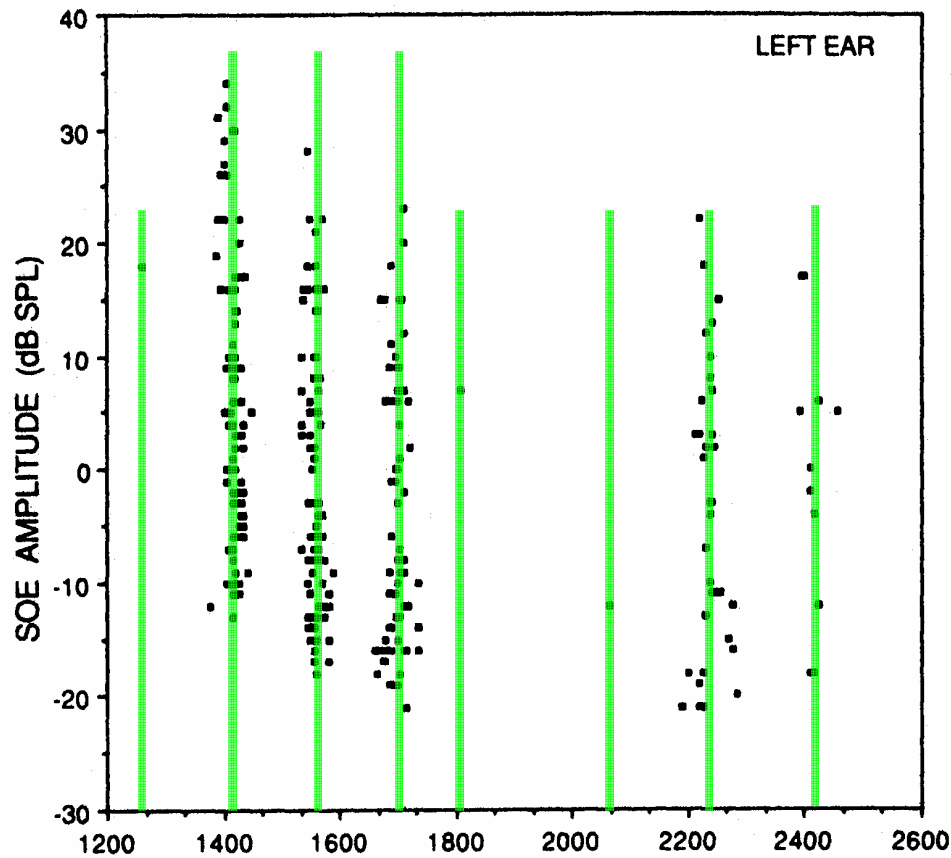


Fig. 7.19. Frequencies and amplitudes of 7 SOAEs recorded over 1 year from the left ear of monkey 84-098, and reproduced with permission from Fig. 1 of Martin et al. (1988). Reading off this data, the mean frequency of each of the 7 emissions was computed (added green bars) and presented in Table 7.3.

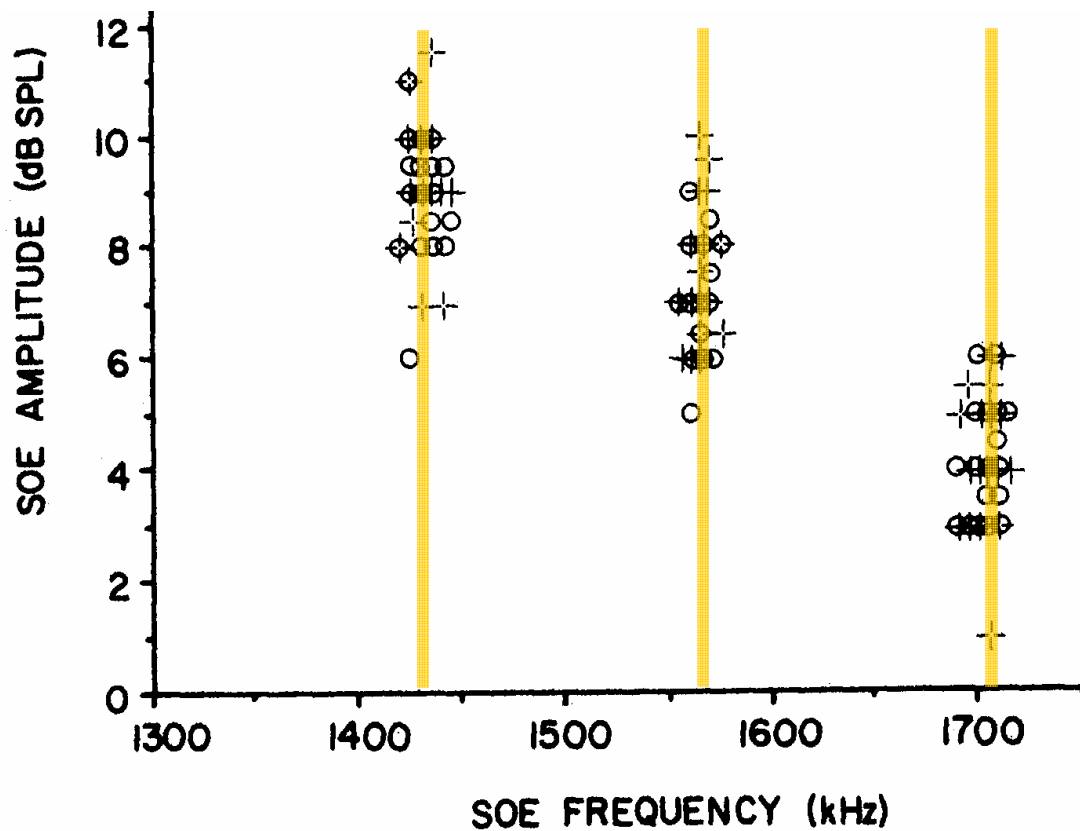


Fig. 7.20. As for Fig. 7.19 except 3 SOAEs recorded at 3-minute intervals over a single 3-h test period. Again, the frequencies were read off, and the averages presented as orange bars and in Table 7.3.

SOAE nr	Mean frequency (Hz) ± 5 (green bars except where noted)	Ratio to next highest frequency (± 0.005)
1	1260	
2	1418 1436 (orange)	1.125
3	1562 1567 (orange)	1.102 1.091
4	1700 1705 (orange)	1.088 1.088
5	1814	1.067
6	2066	1.139 ($=1.067^2$)
7	2239	1.084
8	2412	1.077

Table 7.3. Ratios between SOAEs in monkey 84-098 as derived from Fig. 7.19 and Fig. 7.20.

Once again, the ratios between the SOAEs are remarkably regular, and the numerical value corresponds closely to those derived from unit cell diagonals. The suggestion seems to be that SOAEs could arise in two different ways: as oscillation between the shortest diagonal and between the longest. The observation of linked bistable emissions – SOAEs that spontaneously switch between one frequency and another – would fit in with this picture. The most commonly observed ratio between the two frequencies, for humans, is about 1.06 (1/12 octave), a figure that matches the preferred ratio between SOAEs. This is somewhat smaller than the ratio for the monkey – about 1.09 (1/8 octave).

3. An SOAE can be suppressed by an external tone, and isosuppression contours for three strong SOAEs are given in Fig. 7 of Martin et al. (1988). Potentially, the data might reveal the ratios between an SOAE frequency and one differing by 1.09, as the unit cell model suggests; however, the data were collected at too coarse a resolution (100 Hz) for this to be clearly evident. Nevertheless, we see a suggestion of this in Fig. 7C of this reference where we see an SOAE at 2235 Hz being maximally suppressed by a tone at 2400 Hz, a ratio of 1.07. In parts A and B of the figure the data spacing is too coarse²⁰. Martin et al. speak of a ‘trilobed’ appearance of the suppression curves, and indeed there are consistent patterns and ratios between the points of maximum suppression. It would seem though that there are many more than three interactions going on and very fine frequency sweeps could resolve many more.

7.3/c Relating the model to the literature

The unit cell model suggested here has the potential to explain an extensive range of known cochlear properties. There is not room here to consider the implications in detail, but there are some major features that deserve pointing out.

One is the insight into why the human (or primate) cochlea so readily generates distortion. The strange thing is that rodents, who have cochleas that look very much like ours, exhibit remarkably little distortion and it is difficult to

²⁰ Although it may be significant that the next major dips appear at a ratio of $1700/1413 = 1.20$ in A and at a ratio of $1900/1560 = 1.22$ in B. The square root of 1.21 is 1.10.

understand why that should be so²¹. For distortion to occur, two simultaneously acting frequencies need to operate *at the same point*. The standard explanation of cochlear distortion is that it is due to overlap of two traveling wave envelopes^{22,23}. Why should the traveling wave envelopes of rodents be so different? By way of contrast, the unit cell model gives a ready explanation of why primate cochleas are different: our unit cell is tilted, whereas that of rodents is presumably not. Brief inspection of some human micrographs indicates that this may be so²⁴, but more extensive research is needed to establish it convincingly.

Martin et al. (1988) emphasise how similar the human cochlea is, in general terms, to that of the monkey, and so it will be of interest to see if the tilt of unit cells in human cochleas is also of similar magnitude. Distortion product studies should be able to reveal this key quantity. Given that distortion for humans peaks at about 1.225²⁵, the implication, based on Fig. 7.16, is that our unit cells have a tilt of about 7°. Variability of this parameter might explain why our left cochlea is more likely to be active, in the acoustic emission sense, than the right. Similarly, it might explain why monkey 84-098 had stronger emissions in its left ear, since the tilt in this ear tended to be larger (and more variable). It also relates to why female ears (and female hormones) are more likely to produce spontaneous emissions than male ones^{26,27}.

Some human DPOAE data suggest that the optimum f_2/f_1 ratio tends to decrease systematically with rising frequency^{28,29}. If this is so, then we might expect

²¹ Lonsbury-Martin, B. L., et al. (1997). Distortion product otoacoustic emissions. In: *Otoacoustic Emissions: Clinical Applications*, edited by M. S. Robinette and T. J. Glatke (Thieme: New York), 83-109. [p. 103]

²² Moulin, A. and D. T. Kemp (1996). Multicomponent acoustic distortion product otoacoustic emission phase in humans. II. Implications for distortion product otoacoustic emissions generation. *J. Acoust. Soc. Am.* 100: 1640-1662.

²³ Konrad-Martin, D., et al. (2001). Sources of distortion product otoacoustic emissions revealed by suppression experiments and inverse fast Fourier transforms in normal ears. *J. Acoust. Soc. Am.* 109: 2862-2879.

²⁴ For example, Fig. 39 of Bredberg (1968) shows a tilt of about 10°; Fig. 3B of Kimura et al. (1964) shows a tilt of about 11°; even two drawings of Retzius (1881, 1884) show a tilt of some 5°.

²⁵ Gaskill and Brown (1990)

²⁶ McFadden, D. and E. G. Pasanen (1999). Spontaneous otoacoustic emissions in heterosexuals, homosexuals, and bisexuals. *J. Acoust. Soc. Am.* 105: 2403-2413.

²⁷ McFadden, D. (1993). A speculation about the parallel ear asymmetries and sex differences in hearing sensitivity and otoacoustic emissions. *Hear. Res.* 68: 143-151.

²⁸ Moulin (2000), Fig. 4 // Brown, D. K., et al. (2000). The effects of maturation and stimulus parameters on the optimal f_2/f_1 ratio of the $2f_1-f_2$ distortion product otoacoustic emission in neonates. *Hear. Res.* 145: 17-24. Fig. 3.

²⁹ Brown et al. (2000), Fig. 3.

the tilt of the unit cell to decrease steadily with distance from the apex. However, other data show considerable scatter, and a clear trend is not apparent^{30,31}. Moulin (2000) established that the optimum ratio depended on the order of the distortion product. With multiple factors at work, confirming a possible tilt–distance relationship will require careful investigation.

A long-standing puzzle relating to cochlear distortion is that lower side-bands are much more prominent than upper side-bands, even though simple physical theory suggests they should be equal³². In the cochlea, the characteristic frequency will be effectively controlled by the unit cell spacing. If distortion arises at that point, the lower side-bands (lower frequencies) will readily find longer (oblique) cavities in which to resonate, whereas upper sidebands (higher frequencies) will fail to find any cavity shorter than the radial. In the same way, the unit cell model begins to provide some understanding of the typical cochlear tuning curve, which has a very steep high-frequency slope – up to 1000 dB/octave – and a more gentle low-frequency slope. The longer (oblique) cavities provide for some response at low frequencies, but no cavity shorter than the CF one is available for high frequencies. Again, these are general insights that will require further work to quantify.

Distortion can arise whenever two frequencies non-linearly interact at a common site. In the cochlea, there are many non-linear active processes, and of course there is more going on than can be explained just using unit cell diagonals. The literature on DPOAEs provides evidence of additional interactions at higher intensities³³, which led Mills and Rubel (1994)³⁴ to postulate that there were two sources of DPOAEs: one due to an active source at low sound pressure levels and another due to a passive one at high levels³⁵. This could explain the notch in DPOAE amplitudes which become apparent at about 65 dB SPL³⁶. Recently, however, the

³⁰ Londero, A., et al. (2002). Magnitudes and phases of human distortion-product otoacoustic emissions at $2f_1-f_2$ against f_2/f_1 : effects of an audiometric notch. *Hear. Res.* 167: 46-56. Fig. 2.

³¹ Vento, B. A., et al. (2004). Development of f_2/f_1 ratio in humans. *J. Acoust. Soc. Am.* 115: 2138-2147. Fig. 4.

³² de Boer, E. (1984). Auditory physics. Physical principles in hearing theory. II. *Physics Reports* 105: 141-226. [p. 146]

³³ Lonsbury-Martin et al. (1997).

³⁴ Mills, D. M. and E. W. Rubel (1994). Variation of distortion product otoacoustic emissions with furosemide injection. *Hear. Res.* 77: 183-199.

³⁵ Mills, D. M. (1998). Origin and implications of two "components" in distortion product otoacoustic emissions. In: *Otoacoustic Emissions: Basic Science and Clinical Applications*, edited by C. I. Berlin (Singular: San Diego), 85–104.

³⁶ Talmadge, C. L., et al. (1999). Experimental confirmation of the two-source interference model for the fine structure of distortion product otoacoustic emissions. *J. Acoust. Soc. Am.* 105: 275-292.

two-source model has been disputed, with a model being presented^{37,38,39} that showed how a single non-linear amplifier with saturating input–output characteristics could produce notches at intermediate sound pressure levels.

The diagonal interaction model presented here is mainly concerned with explaining how distortion arises in the mechanics of the active, low-level cochlea. However, in terms of the broader SAW model we see that complex interactions might arise at higher levels where the local SAW resonator becomes affected by passive, traveling wave mechanisms (that is, bending of stereocilia rather than pressure stimuli). At this point the detailed ramifications of higher level mechanics are left for further investigation. The simple diagonal interaction model should be amenable to further experimental test using a combination of audiology and post-mortem anatomy. In terms of understanding human hearing, a study using human volunteers who have given informed consent would be the most ethically sound and the most informative scientifically.

7.3/d Oblique interactions and Deiters cell processes

In the discussion above, it was suggested that the orientation of the stereociliar arms could allow discrimination between squirting waves traveling in different directions and hence produce two distinct feedback paths between the rows of hair cells. While this mechanism may suffice, there is a second feature of cochlear anatomy that immediately suggests the possibility of oblique interactions. This feature is the phalangeal process of the Deiters cell that holds neighbouring outer hair cells in place. Detailed discussion is not warranted at this point, but I present two diagrams (Figs 7.21 and 7.22) that well illustrate how the long process of the arm could launch and perhaps sustain oblique wave propagation in directions specified by the oblique reach of the arm. The arm often extends over two or more cells,

³⁷ Lukashkin, A. N., et al. (2002). One source for distortion product otoacoustic emissions generated by low- and high-level primaries. *J. Acoust. Soc. Am.* 111: 2740-2748.

³⁸ Lukashkin, A. N. and I. J. Russell (2005). Dependence of the DPOAE amplitude pattern on acoustical biasing of the cochlear partition. *Hear. Res.* 203: 45-53.

³⁹ For context, see also: Liberman, M. C., et al. (2004). Otoacoustic emissions without somatic motility: can stereocilia mechanics drive the mammalian cochlea? *J. Acoust. Soc. Am.* 116: 1649-1655.//Avan, P., et al. (2003). Physiopathological significance of distortion-product otoacoustic emissions at $2f_1-f_2$ produced by high- versus low-level stimuli. *J. Acoust. Soc. Am.* 113: 430-441.

permitting mechanical or perhaps electrical interactions to propagate in that direction. The fact that the processes contain myosin⁴⁰ gives a hint that the position of outer hair cells, and hence the tuning of the cavities they form, may be actively controlled. The cells appear to lie somewhat erratically, but in fact they may be disposed to move to a position that optimises the tuning of a certain cavity or pair of cavities.

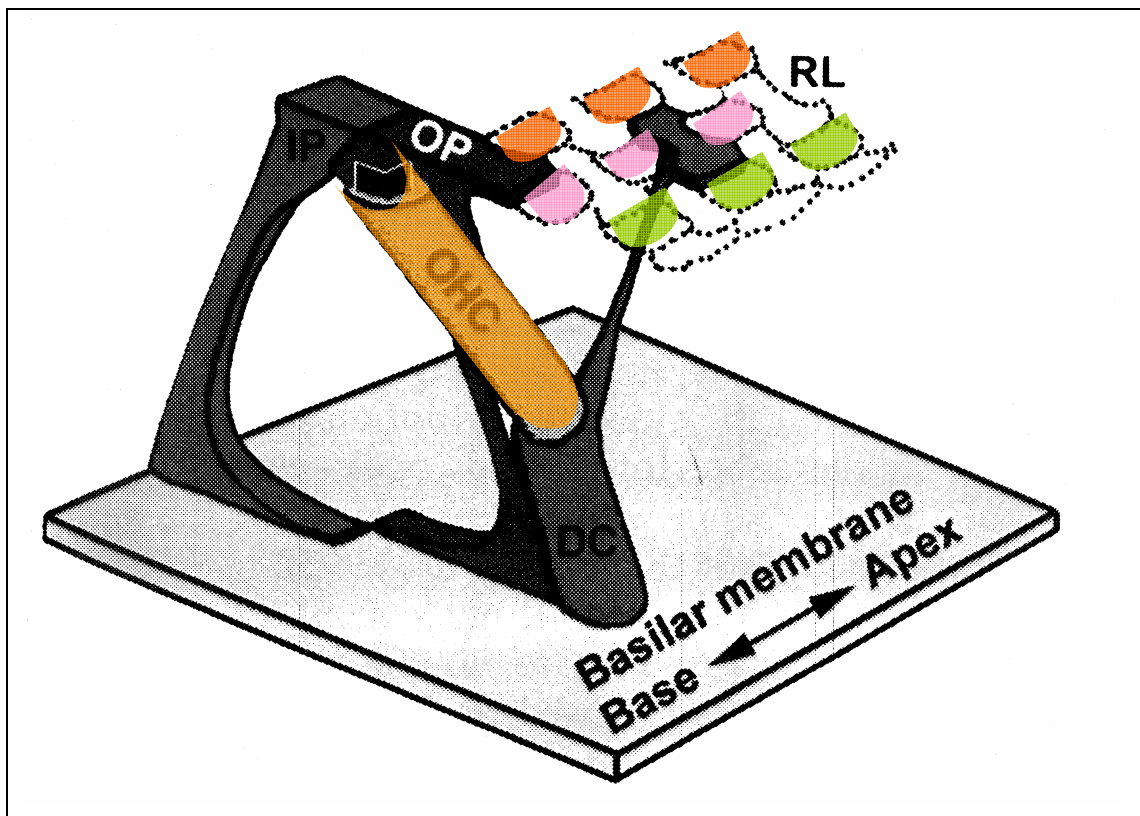


Fig. 7.21. A schematic view of the way outer hair cells (OHC) sit within the cup of a Deiters cell (DC) and are connected physically, and electrically, with outer hair cells in a neighbouring row. OHC1 are shaded orange, OHC2 pink, and OHC3 green. RL is the reticular lamina and OP the outer pillar, abutting the inner pillar (IP). The resulting arrangement could promote oblique interactions. [Adapted from Fig. 1C of Ulfendahl (1997)⁴¹ and reproduced with permission]

⁴⁰ Slepecky, N. B. (1995). Sensory and supporting cells in the organ of Corti: cytoskeletal organization related to cellular function. In: *Active Hearing*, edited by Å. Flock et al. (Pergamon: Oxford), 87-101. Fig. 6.

⁴¹ Ulfendahl, M. (1997). Mechanical responses of the mammalian cochlea. *Prog. Neurobiol.* 53: 331–380.

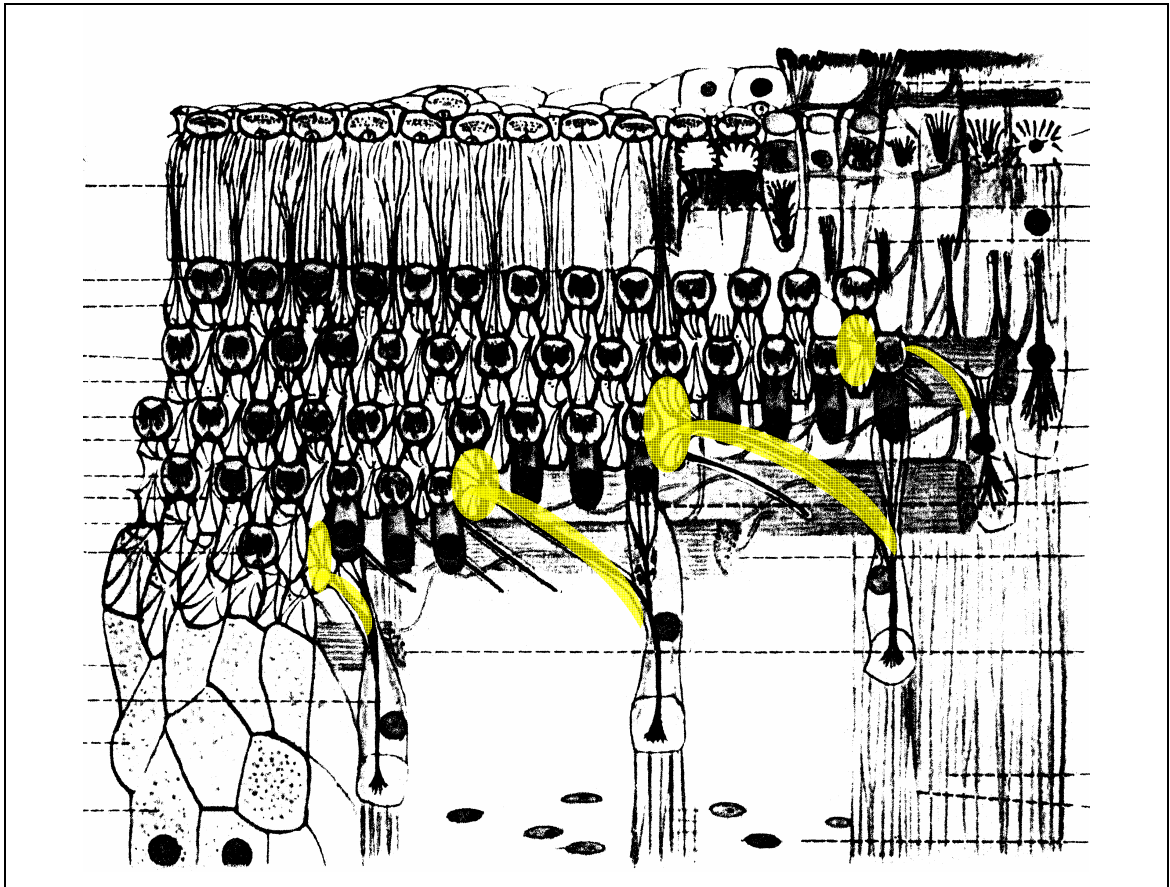


Fig. 7.22. An anatomist's view of the Deiters cells which again nicely portrays the diagonal reach of the phalangeal processes (yellow) holding the outer hair cells in place. In addition to the oblique angle of the stereociliar arms (the V), this arrangement could promote oblique wave propagation. [Adapted from von Eggeling et al. (1927)⁴²]

7.4 Conclusion

This analysis has provided strong circumstantial evidence that cochlear mechanics can be described in terms of a unit cell of outer hair cells. It provides a consistent picture in which the a dimension of the lattice is approximately constant and the b dimension is a major factor in determining, via squirting wave interactions, the characteristic frequency of the partition at that point. Potentially, the unit cell picture gives a fundamental insight into the way by which the cochlea analyses sound. It reinforces a local resonance picture and need not rely on a traveling wave

⁴² von Eggeling, H., et al. (1927). *Haut und Sinnesorgane*. (Springer: Berlin).

for its operation. The difference between pure resonance mechanisms and traveling waves with added second-filter is discussed in §D 10.1/a.

The unit cell model, mediated by squirting waves, gives a fairly complete account of cochlear mechanics, explaining the operation of the cochlear amplifier and the generation of otoacoustic emissions. It unifies spontaneous, click-evoked, stimulus frequency, and distortion product emissions, explaining them in terms of the properties of a well-defined, place specific, lattice of outer hair cells. The interaction is local, and we do not need to consider longitudinal wave propagation as required by the CRF model. Of course, we do need to consider fast wave propagation, which is probably constitutes the effective stimulus to the outer hair cells.

The model suggests that the two arms of the outer hair cell enable it to work as a detector of specific frequency ratios – at least those two frequencies resonant in the short and long diagonals of the tilted unit cell – and this bears directly on the question of how the ear might detect the harmonic structure of sound and therefore musical ratios. This exploration is reserved for further work.

Given this interpretation, the model calls for multiple frequencies to be able to interact at the same place on the partition – in particular, the two frequencies that constitute the diagonals of the unit cell. No standard traveling wave excitation can produce two resonances at different frequencies at the same point on the partition; however, the omnipresent pressure signal, which operates throughout the entire fluid contents of the cochlea almost simultaneously, has the advantage of being able to deliver the signal to all places where resonance conditions occur. This means there instead of a single cochlear frequency–place map, there are several positions along the cochlea where a tone of a given frequency (say 1 kHz) can resonate: there is its characteristic place, of course, but there are also other shorter cavities (with higher frequency characteristic places) where an oblique cavity can have that same frequency. At this stage, the number of oblique resonances that are possible will need to be the subject of experiment.

In considering squirting wave resonance between OHCs, the broad peaks in the autocorrelations presented here might work against the establishment of strong resonance in the lattice structure, at least in primates. That is a question left unresolved for now. It should be said that the original tracings were done in a way to straighten the segments, and this may have compromised correlations. We also do not know the effects of shrinkage due to histological preparation. Finally, the

possible effect of the V shape in enhancing interactions is not known. For the moment we must be content with the data as presented and recognise that it indicates a way forward. The cochlea appears to have a remarkably intricate micromechanics.

The cochlea and its response to pressure

8.1 Evidence that the ear detects common-mode pressure

8.1/a Cochlear sensitivity to pressure

8.1/b Phase of the two windows and compressibility of the cochlea

8.1/c Input impedance of the live cochlea

8.1/d Summary

8.2 The cochlea as a loudspeaker enclosure

8.2/a Perceptible effects of the round window

8.2/b Effects of cochlear compressibility

8.3 Are outer hair cells pressure sensors?

8.3/a Evidence for OHC pressure sensitivity

8.3/b Revisiting the Wilson hair-cell swelling model

8.4 Detecting sound underwater

8.4/a Detecting pressure and displacement

8.4/b The revealing case of shark hearing

8.4/c Bubbles and underwater acoustics

8.4/d Cells containing air

8.4/e An air bubble in outer hair cells?

8.4/f The fontanelle as a pressure sensor

8.4/g Kinocilia, basal bodies, and centrioles

8.5 Towards a functional integration

In order to provide a resonance model of the cochlea, this thesis has been postulating simultaneous (parallel) excitation of the cochlear resonators. As set out in Chapter I1, this translates to a requirement that the resonant elements react to the fast pressure wave (common-mode or hydrostatic pressure) rather than to differential pressure. Chapter I3 sought to show that the traveling wave fails to give a full account of cochlear mechanics – there are anomalies, and most of them appear to centre around extremely fast responses. In this context, it seems a reasonable hypothesis to assume that the compressional wave is the missing element and that it is in fact a major force in the mechanics of the active cochlea. This chapter investigates the hypothesis.

Chapter R5 has proposed that the resonant elements are the regular rows of outer hair cells coupled by squirting waves. In order for these elements to be simultaneously excited, we require that outer hair cells react directly to intracochlear pressure. Expressed simply, the hypothesis amounts to OHCs being pressure sensors.

The sequence of this chapter is first to look for evidence that the ear reacts to common-mode pressure. If it does, this leads to the corollary that, like all pressure sensors, it must display some compressibility, and evidence is assembled to show that indeed this is the case. A functional model for the pressure sensor is put forward, and an examination made of how it could operate within a cochlea possessing a large ‘hole’: a compliant round window.

A starting point is to consider some underwater acoustics and recognise that the problem of detecting pressure in the cochlear liquids is the same as that confronting some marine creatures in detecting underwater sound. The answer, as found by a number of aquatic animals, is to use compressible materials in order to transform pressure signals into displacements. This analogy leads us to suspect that mammalian outer hair cells also use this strategy. The hypothesis is therefore made that their characteristic Hensen bodies (and perhaps the accompanying cisternal system) enclose compressible material, most likely air, just like cells in the macula neglecta of sharks appear to do. Finally, we propose how compression of the cell leads to its excitation. The hypothesis is made that the kinocilium (and its degenerate form, the cuticular pore) are important in this process, as they contain the actual sensory apparatus: the basal body. In the light of this model, some confirmatory evidence is presented.

8.1 Evidence that the ear detects common-mode pressure

The unifying idea is that the compressional wave is the major stimulus for outer hair cells (at least at sound pressure levels below about 60 dB SPL) and that their excitation causes a squirting wave which drives the sharply tuned elements of a SAW resonator. It is proposed that outer hair cells can detect pressure because they are compressible, and their excitation leads in turn to volume changes, and pressure waves, that are detectable in the ear canal. The effect of the excitation of a bank of highly tuned resonators is, of course, an *apparent* traveling wave (§I 1.5), and it is a mistake to consider this traveling wave as having causal properties. The traveling wave produced by outer hair cell excitation might just be an epiphenomenon.

It is possible our understanding of the cochlea went awry when the common-mode pressure, p_+ , was seen to be of no consequence and discarded. Just because outer hair cells bear stereocilia is not sufficient reason to ignore their potential pressure-detection capability. According to this thesis, outer hair cell stereocilia are primarily feedback devices, not sensors (although a sensory function is exhibited at high sound levels).

In this section, we will see how an active (low-level) cochlear mechanics can be constructed in which common-mode pressure takes the principal role.

8.1/a Cochlear sensitivity to pressure

The idea that hearing might result from direct detection of sound has had a long history. In the 20th century the idea was considered by Pohlman in 1933 who reviewed various opposing theories at the time¹ and was not averse to the idea that “the auditory cells react directly to the vibrations in the liquid in which they are immersed” [p. 193] rather than to transverse vibrations in the cochlear duct. The

¹ Pohlman, A. G. (1933). A reconsideration of the mechanics of the auditory apparatus. *J. Laryngol. Otol.* 48: 156-195.

advantage of this “piezo-electrical” concept, he said, is that it simplifies matters enormously and does not confuse the issue by employing mechanical structures extrinsic to the auditory cells. He cites literature that accords with this concept, some of which, like human temporal bone studies, we have already referred to (§I 3.2/e).

In the previous chapter we referred to the insights of Guild (1937), who was the first to suggest, albeit diffidently, that the outer hair cells may be directly stimulated by sound². He made the leap (p. 370) from the purely anatomical observation that outer hair cells are surrounded by large fluid-filled spaces – the spaces of Nuel – to the physical interpretation that this is an ideal arrangement for detecting pressure changes in the cochlear fluids. In recent times, the peculiarity of the spaces of Nuel have also been noted, and in a popular review³ Brownell reminds us that in no other organ of the body does one find cells surrounded on all sides by large fluid spaces. Other cells, inner hair cells included, are surrounded by supporting cells. Brownell, however, presents a different interpretation: the spaces are there to permit the outer hair cells to change length – which of course is equally true, but misses a possibility I wish to propose.

Davis and colleagues in 1934 addressed the pressure-sensitivity question when considering the origin of the cochlear microphonic⁴. They suggested that the cochlear microphonic arose from the body of hair cells being squeezed. “We venture the hypothesis that the electrical potential arises from the sensory cells themselves as a result of mechanical deformation ... [and that] the difference of potential is developed between the upper and lower ends of these cells.” [p. 329]. Crucially, though, they thought that the out-of-phase responses of the oval and round windows “definitely rules out the possibility that the potential is generated merely by increased or diminished pressure within the cavity of the inner ear” [loc. cit.].

The underlying idea is that if the cochlear contents are incompressible and the windows move out of phase in a shuttle-like motion, then differential pressure must be the way by which the cochlea is excited. What is wrong with that? The sections below attempt to uncover a flaw in that thinking.

² Guild, S. R. (1937). Comments on the physiology of hearing and the anatomy of the inner ear. *Laryngoscope* 47: 365-372.

³ Brownell, W. E. (1998). How the ear works: Nature's solutions for listening. *Volta Review* 99: 9–28. §12: The Organ of Corti – The Temple of Hearing.

⁴ Davis, H., et al. (1934). The electric response of the cochlea. *Am. J. Physiol.* 107: 311-332.

8.1/b Phase of the two windows and compressibility of the cochlea

If the cochlea were a detector of common-mode pressure, then it would have to exhibit some compressibility. This is because any hydrophone needs to have some compressibility in order to react physically to the pressure and convert energy from one form (acoustic) into another (electrical). For optimum signal-to-noise ratio, that conversion needs to be done efficiently, with well-matched impedances. One way of measuring the compressibility of the cochlea is to measure the relative phases – or better, the volume velocities – of the oval and round windows. If the volume velocities are equal and the windows move precisely out of phase, then the cochlea is incompressible. If so, the inference is that it cannot be a hydrophone, rather it is simply responding to shear of the partition generated by differential forces.

Experiments have attempted to show that differential pressure is the effective stimulus in the cochlea in two ways. The first is to directly measure the phase of motion of the two windows. The second is to apply stimuli to the two windows precisely in phase and show that the cochlea fails to respond (electrically) to this condition.

1. In Wever and Lawrence (1950), a paper⁵ alluded to earlier (§D 3.1/b), sounds of independently adjustable phase were conducted (via two rubber tubes) to each of the round and oval windows of cats and, to gauge cochlear responses, an electrode picked up cochlear microphonics. They sought to dispel an ‘alternative’ view of cochlear mechanics – which they regarded not as a popular one but which in the absence of evidence had to be entertained as a possibility – in which the basilar membrane only served as a suspension for the hair cells and cochlear fluid pressure served as the stimulus. On this view, maximum stimulation would occur when the sounds to the two windows are in phase. Significantly, they found that the electrode response was near a minimum at this condition. Common-mode pressure did not appear to be an effective stimulus.

⁵ Wever, E. G. and M. Lawrence (1950). The acoustic pathways to the cochlea. *J. Acoust. Soc. Am.* 22: 460-467.

A major limitation⁶ of this experiment now needs to be made plain: Wever and Lawrence used sound intensities well above 60 dB SPL. Intensities were not calibrated, but they set levels to give a cochlear microphonic of 10 μ V, which corresponds to about 65–70 dB SPL. It is possible that at low intensities the windows moved in phase and the majority of the electrode response would then derive from the common mode signal (which drives the cochlear amplifier and which saturates at 60–80 dB SPL).

2. Offutt later^{7,8} tried to replicate the Wever and Lawrence work in chinchillas and provided an interesting new dimension to the story. He measured the cochlear microphonic due to two phase-adjustable sound sources: one in the ear canal and another through a hole drilled in the cochlea⁹. He found that at times when the cochlear microphonic due to the two tone-pips was nulled, the compound action potential – the electrical signature from the acoustic nerve – reached a *maximum*. A major limitation of this work was that, again, sound stimuli were not calibrated and drilling a hole in the cochlea is likely to have disturbed the natural situation (see §D 10.1/d). Nevertheless, given a lack of data on the question, the work deserves some consideration.

3. Kringelbotn (1995) measured the volume displacements through the round and oval windows in 34 isolated inner ears of pigs and one human temporal bone¹⁰. The volume displacements for the pigs were “within 1 dB”¹¹ of being equal, whereas for the human specimen, the round window displacement was some 3 dB *smaller* than the oval window’s. Inferred ratios, derived from related measurements on 20 other human temporal bones, also gave a comparable figure of 3.4 dB. Although his text stresses the *equality* of the two displacements, given the large variance in the

⁶ Another limitation is that at low frequencies – a few hundred hertz – minimum response differed considerably from the in-phase condition. According to their Fig. 5, phase offsets reached about 45° at these frequencies, meaning that a secondary response may be contributing at only several decibels below the main one. However, not too much store can be taken by these phase anomalies since it is unrealistic to expect the round window and oval window to contribute identical sound pressure.

⁷ Offutt, G. (1984). *The Electromodel of the Auditory System*. (GoLo Press: Shepherdstown, WV). [pp. 162-169]

⁸ Offutt, G. (1986). Wever and Lawrence revisited: effects of nulling basilar membrane movement on concomitant whole-nerve action potential. *J. Aud. Res.* 26: 43-54.

⁹ *ibid.*, Appendix 1, p. 162-169.

¹⁰ Kringelbotn, M. (1995). The equality of volume displacements in the inner ear windows. *J. Acoust. Soc. Am.* 98: 192-196.

¹¹ Strictly, it is incorrect to use decibels when powers are not involved. I presume he means “within 10%”.

measurements this conclusion cannot be strongly sustained¹². He acknowledges (p. 195) that the deviation admits for a compliance¹³ in the inner ear, but then only 0.2 dB inequality was sufficient for Shera and Zweig (1992) to explain the puzzling residual hearing in Békésy's "middleless" ears (§D 9.3/e). Calculations by Ravicz et al. (1996) show that Kringelbotn's inequality translates to a large inner ear compressibility: a figure for α (the ratio of stapes motion with the round window blocked to normal stapes motion) of 0.3. Perhaps it is obvious, but the comment needs to be made that these experiments are only relevant to the compressibility of dead cochleas.

4. Voss et al. (1996) approached the problem¹⁴ by bringing modern technology to bear on the Wever and Lawrence experiments. They applied two independent sounds of controlled amplitude and phase to the round window and oval window of cats and looked at the effect on the cochlear microphonic. They expressed their results in terms of common-mode rejection ratio (CMRR) – the ratio between the cochlear microphonic in response to the out-of-phase condition compared to the response in the in-phase condition. They found that the minimum CMRR (for up to seven cats) ranged from 15 to 28 dB, while the maximum was 22 to 78 dB. Before one concludes that the results show responses to common-mode pressure can be neglected, the following factors need to be appreciated.

(i) Despite the findings of Offutt that the compound action potential (CAP), generated by the auditory nerve, could behave differently to the cochlear microphonic (CM), generated by the outer hair cells, the researchers applied tetrodotoxin (TTX) to most of the cats to eliminate CAP. This was meant to get rid of possible interference with the CM, which they focused on. While that no doubt happened, perhaps they were also eliminating a physiologically important signal. In this context, we learn (p. 1605) that TTX eliminates voltage-gated sodium channels, and these could well be the channels that are involved in generating a response between the outer hair cell rows – that is, the pressure-related signal which drives the

¹² He also quotes (p. 192) data from Nedzelnitsky (a 1974 thesis), who found that the volume flows were only equal to within ± 10 dB.

¹³ He uses the adjective 'small', but that is inappropriate.

¹⁴ Voss, S. E., et al. (1996). Is the pressure difference between the oval and round windows the effective acoustic stimulus for the cochlea? *J. Acoust. Soc. Am.* 100: 1602-1616.

cochlear amplifier (see §D 9.1/j). In partial confirmation of this, we see that the CMRR values become perhaps 5 dB higher after TTX administration (their Fig. 9).

(ii) The sound pressure levels used by the experimenters were high, largely in the range 60–120 dB. Of particular interest, the linearity of the CMs (amplitude v. sound intensity) disappears and becomes quite erratic below 80 dB (their Fig. 4). This is especially noticeable for animals before TTX treatment.

My conclusion is that the Voss et al. experiments do not rule out the possibility that the ear is sensitive to common-mode pressure below about 60 dB. That is, that the cochlea is pressure-sensitive at low levels, but the sensitivity saturates at about 60 dB SPL and becomes swamped by displacement sensitivity at high levels.

5. As mentioned previously (§I 3.2/g), Ravicz et al. (1996) measured the compressibility of the cochlea of cadavers and expressed it in terms of α , the ratio between the motion of the stapes with the round window blocked to normal stapes motion. If $\alpha = 0$, then the cochlea is incompressible and no stapes motion is possible when the round window is blocked; if $\alpha = 1$, the contents are so compressible that stapes motion produces no round window motion. Values of α found by their work, and applied to the work of others, form a useful comparison, and are shown in the table below.

author	value of α	comments
Ravicz et al. (1996)	0.015–0.5	Human cadavers. Upper bound is within an order of magnitude of the compressibility of water
Shera and Zweig (1992)	0.04	Based on hearing thresholds of live humans without middle ear as measured by Békésy (1960)
Kringlebotn (1995)	0.3	Isolated temporal bones of human cadaver and pigs
Tonndorf and Tabor (1962)	0.1	Blocked round window of live cats
Harrison et al. (1964)	Not specified, but between 0.015 and 0.5	Patient with congenitally blocked round window. Hearing improved by 20–40 dB when surgically corrected

The main point to be derived from this comparison is that it only requires minute compressibility to allow a significant amount of hearing to develop (even with a poor matching of sound input to the cochlea – a missing middle ear or blocked round window). The input impedance of the cochlea is large (more than $20\text{ M}\Omega$ ¹⁵), and consequently the volume changes we are trying to detect are minute. So the cochlear fluids may be shuttling back and forth at *close to* 180° to each other, but at the same time the primary input to the cochlea may be the common-mode pressure generated by stapes motion. The other thing to notice is that according to the transduction model presented in this thesis, live cochleas will have a different compressibility to dead ones. Anomalies in the input impedance of the live cochlea suggest this is the case (see following section).

5. Stenfelt and colleagues examined the vibration of the temporal bones of human cadavers¹⁶ and found that, with stimulation with air-borne sound, the volume displacement of the round window was comparable with, but generally less than, that of the oval window (some decibels less) and the phase about 180° ($\pm 20^\circ$ depending on frequency). Particularly interesting was their finding¹⁷ that the round window only moved as a whole below 1.5 kHz; at higher frequencies the vibration was multimodal, with portions moving in at the same time as others moved out. Clearly, the motion of the round window is complex, even in dead cochleas, and some compressibility of the *live* cochlear contents is compatible with current measurements (made either at high sound pressure levels or on dead specimens).

8.1/c Input impedance of the live cochlea

The input impedance of the live human ear differs from that of a non-living one¹⁸, and there are a number of reasons that may account for that. One factor I

¹⁵ Aibara, R., et al. (2001). Human middle-ear sound transfer function and cochlear input impedance. *Hear. Res.* 152: 100–109.

¹⁶ Stenfelt, S., et al. (2004). Round window membrane motion with air conduction and bone conduction stimulation. *Hear. Res.* 198: 10-24.

¹⁷ Stenfelt, S., et al. (2004). Fluid volume displacement at the oval and round windows with air and bone conduction stimulation. *J. Acoust. Soc. Am.* 115: 797-812.

¹⁸ Goode, R. L., et al. (1993). Measurement of umbo vibration in human subjects: method and possible clinical applications. *Am. J. Otol.* 14: 247-251. See also Zwislocki (2002), Fig. 3.35.

would like to suggest is a difference in compressibility. The measurements are difficult and the scatter of data points is high, but it appears that (Goode et al., Fig. 6) a live cochlea has, beyond a few thousand hertz, a 5–10 dB smaller input impedance than a dead one¹⁹.

In general, the live ear has a negative reactance, behaving²⁰ at low frequencies as if it were a volume of air of 1.4 cm³. Beyond a couple of thousand hertz, however, the reactance goes positive (Zwislocki, p. 47), suggesting resonance at the crossover point and a more complicated process. Compliance values rise (p. 50–51) and approach infinite values – just like they would if lossless mass and spring elements were resonating. The associated acoustic resistance is the tell-tale sign: at these frequencies the resistance of the live ear falls to the resistance of air and even approaches *zero* (Zwislocki, p. 47). Zwislocki is puzzled by this result, which contrasts with the measurements on cadavers, and he suggests it is an artefact. However, it is a long-standing result, and is mentioned by Békésy (*EiH*, p. 312). It is well portrayed in Fig. 10 of Zwislocki²¹ (1957), where results by a number of different experimenters are plotted on a scale where the resistance of air is unity. Data points converge towards, and even fall below, the unity line. Understanding this apparent paradox may be helped by recognising that measurements of cochlear impedance in frequency bands encompassing spontaneous emissions can return negative values²².

8.1/d Summary

The orthodox view that the cochlear contents are incompressible is possibly incorrect, and only a small amount of compressibility is needed to allow hearing to happen. The reported experiments on animals are misleading in that they have not

¹⁹ At 10 kHz, the gap can be as large as 17 dB [Fig. 3.35 of Zwislocki, J. J. (2002). *Auditory Sound Transmission: An Autobiographical Perspective*. (Erlbaum: Mahwah, NJ).]

²⁰ Zwislocki (2002), Ch. 3.

²¹ Zwislocki, J. J. (1957). Some measurements of the impedance at the eardrum. *J. Acoust. Soc. Am.* 29: 349-356. See also Kosteljik, P. J. (1950). *Theories of Hearing*. (Universitaire Pers Leiden: Leiden). [pp. 141, 144]

²² Burns, E. M., et al. (1998). Energy reflectance in the ear canal can exceed unity near spontaneous otoacoustic emission frequencies. *J. Acoust. Soc. Am.* 103: 462-474.

been done at low sound pressure levels where pressure sensitivity is highest; they reflect measurements of passive cochlear mechanics rather than active. A similar comment applies of course to measurements on non-living specimens. Finally, there are doubts that measuring the cochlear microphonic is a suitable test of hearing acuity, and the compound action potential might be a better indicator.

It therefore remains an open question as to whether outer hair cells are pressure sensors and whether intracochlear pressure drives the cochlear amplifier. The natural inclination is to suppose that the active process works with the same stimulus as the passive²³, but I suspect the effective stimulus could be different in each case. In the next section, it is shown how the presence of a compliant round window (a ‘hole’) is compatible with a system that senses intracochlear pressure.

8.2 The cochlea as a loudspeaker enclosure

At this point, I set out a model of how the pressure wave at the oval window may be coupled to the outer hair cells. Rather than transverse vibration of the basilar membrane, which is the standard picture, the model suggests that it is the compressibility (compliance) of the outer hair cells that form a major input impedance of the cochlea. Thus, the propagating wave in the cochlear fluids, with pressure and displacement components, interacts with a compressible element within the outer hair cell, and it is supposed that it is the *pressure* component that is the key parameter.

The effect of the round window also needs to be considered²⁴, since at first sight it seems inappropriate to contain the pressure sensors within an enclosure that possesses a large compliant membrane – effectively, a hole. However, consideration of the *mass* of the cochlear fluids allows for the presence of this hole to be accommodated, as we will see.

²³ Chapter 4 of Zwislocki (2002) is headed “The Cochlea Simplified by Death” and he claims that the fundamental mode of its mechanical operation is retained post mortem, but this is not necessarily true.

²⁴ Anatomy suggests “compliant capabilities” (p. 44 of Goycoolea, M. V. (1992). The round window membrane under normal and pathological conditions. *Acta Otolaryngol.* 493: 43-55.)

To sketch the basic interaction, Fig. 8.1 shows the simple mechanical picture and Fig. 8.2 shows a circuit analog. Encased in bone and filled with 100–200 μL of incompressible water, the input pressure to the cochlea is applied through the oval window. This launches a wave front, with pressure p and particle velocity v , that reverberates around the cochlea and becomes absorbed by the compressible outer hair cells (maroon). Unabsorbed pressure also distends the round window and raises the intracochlear pressure.

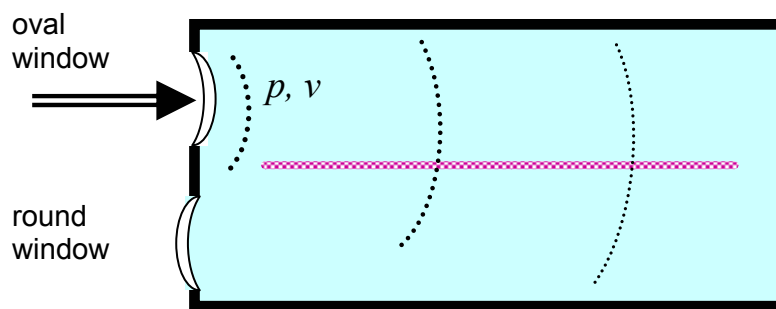


Fig. 8.1. How the pressure signal, launched from the oval window, interacts with compressible outer hair cells (maroon), becoming absorbed as it reverberates around the cochlea. Because of compressibility, the round window volume displacement need not be equal and opposite to that of the oval window. The cochlea is not a box, but a spiral, a shape that tends to prevent the formation of standing waves.

The description is complicated because the pressure sensors – the outer hair cells – are close to the pressure-forming stapes. Hence, the acoustics is near-field and we cannot properly use standard far-field equations. Nevertheless, the propagating pressure signal will encounter compressible elements and undergo many reflections in the spiral cochlea before returning to the stapes, so there should be an appreciable propagating component to the signal. It will not just form a standing wave, although there will inevitably be some. To signify the complicated mixture of propagating and standing waves we use the term propagating *signal*.

To give this propagating signal a physical underpinning, we follow the fundamentals of section 6.2 of Fletcher (1992). If any wave of frequency ω propagates through a medium of density ρ (here considered water) with amplitude ξ , then $v = j\omega \xi$ and $p = j\rho c^2 k \xi$ where c is the phase velocity and k is ω/c . This means

that the wave impedance, p/v , is simply ρc . If we consider the wave to be propagating in a pipe (a simplified cochlea), then its impedance will be $\rho c/A$, where A is its cross-sectional area. The acoustic inductance, L , of a unit length of pipe (associated with its mass) is ρ/A , and its capacitance, C (from its compressibility), is $A/\rho c^2$. Using electrical analogs of these quantities, we draw a circuit diagram, as follows (Fig. 8.2).

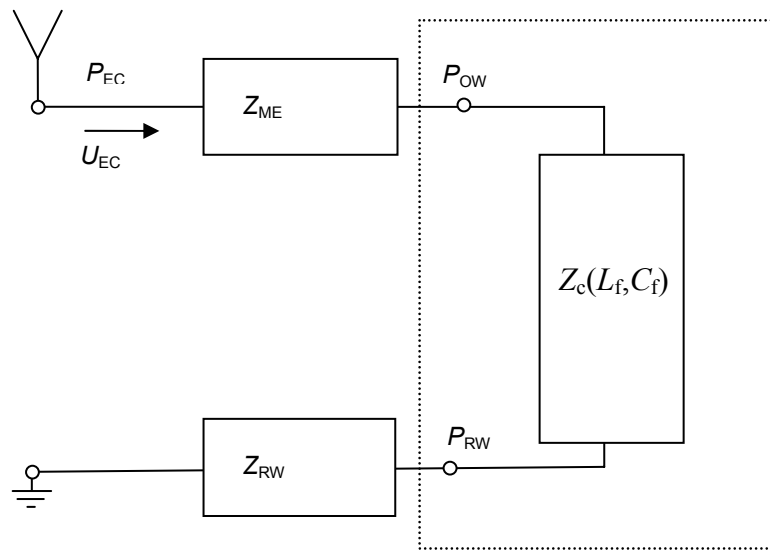


Fig. 8.2. A simplified network model of the cochlea. As well as lumped acoustic impedances, there are distributed elements (within dotted box) associated with the individual outer hair cells and their interaction, through a pressure wave, with the cochlear fluids. The lumped sections comprise outer ear (an antenna); middle ear impedance, Z_{ME} (effectively a transformer); cochlear impedance, Z_C , essentially the compressibility of all the outer hair cells (a compliance); and round window impedance Z_{RW} , a simple compliance. Z_C is comprised of distributed masses and compliances of the cochlear fluids, L_f and C_f , which interact in a complex way as the pressure signal traverses the cochlea through multiple reflections. In essence, the ear-canal pressure P_{EC} (and associated volume velocity U_{EC}) create pressure waves in the cochlear fluids, which are detected by the outer hair cells.

This circuit diagram provides a way of seeing the crucial importance of the mass and compliance of the cochlear fluids in cochlear mechanics. In effect, the system is working together like a reflex loudspeaker enclosure: the oval window is the loudspeaker driver and the round window is the port or drone cone (Fig. 8.3). In such a system, the compressibility of the enclosure interacts with the mass and

compliance of the port, and the system must be tuned for optimum performance²⁵. If the resonance is placed at a suitably low frequency, the bass performance of the enclosure can be enhanced, with the radiation from the rear of the driver used to augment²⁶ the output of the system.

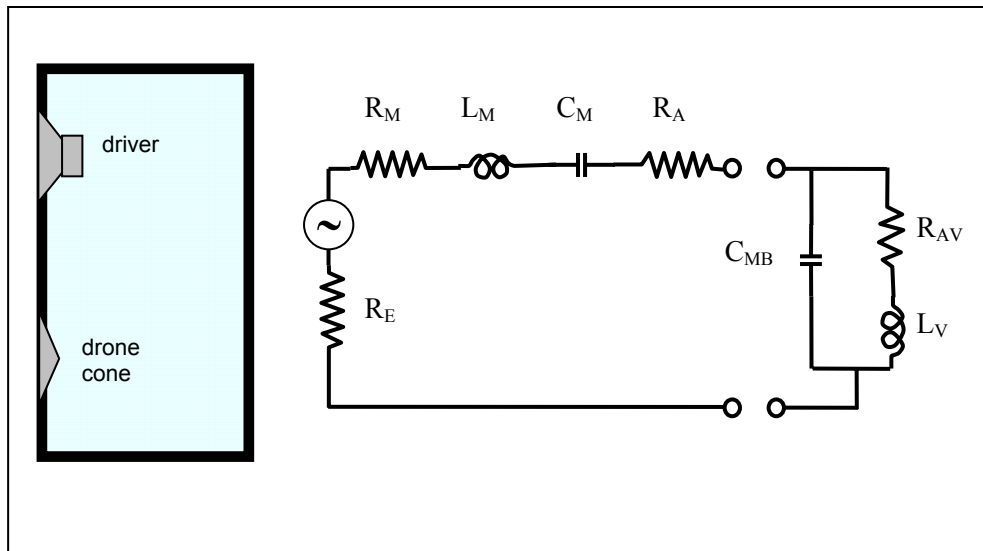


Fig. 8.3. The reflex loudspeaker enclosure. It houses an active driver (top) and a vent (below) which can comprise either a duct or passive driver. The mass of the air in the duct (or of the drone cone) creates a resonance when it bounces against the compliance of the enclosed air, extending the frequency response and output of the system at low frequencies. The circuit impedance of the system, as seen by the air – or a pressure sensor in the box – is given at right, in which the components to the left of the terminals apply to the driver and those to the far right to the enclosure and vent. R_E is the source resistance of the driver, R_M its mechanical resistance, L_M the mass of the cone, C_M its compliance, R_A the radiation resistance, C_{MB} the combined compliance of the air and vent, R_{AV} the vent resistance, and L_V the mass of the air in the vent. [Adapted from Jordan (1970, 1971)^{27,28}]

Similarly, the cochlea can be considered a reflex enclosure in which the stapes is the driver and the round window the vent. Pressure sensors are located inside the enclosure, and the system is arranged so that excitation of the driver will deliver maximum pressure to the sensors inside. It seems clear that, in general, this situation will correspond with maximum amplitude of vibration of the speaker cone

²⁵ The system is described in terms of the Thiele–Small parameters. An overview and list of references can be found in Thiele, A. N. (2004). The Thiele–Small parameters for measuring, specifying and designing loudspeakers. *Address to Singapore Engineering Society, July 2004*: www.aes-singapore.org/LSPRMTRS604.doc.

²⁶ Although at certain frequencies there will also inevitably be cancellation.

²⁷ Jordan, E. J. (1971). Loudspeaker enclosures. Types of baffle and the acoustical laws governing their application. *Wireless World* Jan: 2-6.

²⁸ Jordan, E. J. (1970). The design and use of moving-coil loudspeaker units. *Wireless World* Nov: 533-537.

(the stapes); on the other hand, the presence of a nearby hole, the port or round window, need not diminish the power output (or sensitivity) of the system if the masses and compliances are chosen correctly. Hence, although the presence of the round window seems at first glance to suggest that pressure detection is not involved (see §D 9.4/b), the analogy with the speaker enclosure says this need not be the case. The resonance is expected to be at the lowest audible frequency, about 20 Hz.

In vivo, the compressibility (compliance) of the outer hair cells will be of primary importance. However, the difficulty in analysing the cochlea in terms of its equivalent circuit is that the compressibility will be frequency dependent – because outer hair cells vary systematically in length from base to apex. No single lumped circuit parameter will suffice. Another difficulty in trying to calculate the system response using the equivalent circuit is that data are insufficient. A major reason is that data that might be useful was derived from dead specimens, whereas compressibility of live outer hair cells is the crucial factor. Clearly, measurements of the impedance of live ears (§D 8.1/c) should prove useful in overcoming this lack.

Nevertheless, it is possible to make a few broad conclusions. One is that the oval and round windows will not ordinarily move out of phase with each other at equal amplitudes. Post mortem, when outer hair cells have died and lost their actively maintained compressibility, antiphase motion is almost inevitable, and in this case the radiation from the oval window is expected to be equal and opposite to that of the round window – only a small evanescent wave would then penetrate a limited distance into the cochlea.

The action of the middle ear also deserves mention. The transformer ratio of the middle ear (about 25 times) acts so as to lower the impedance of the inner ear as seen by the tympanic membrane by a factor of 500 (Zwislocki, p. 60) and in this way only about two-thirds of the acoustic energy incident on the ear drum is reflected away. The impedance of the cochlea is about the same as that of the air in the ear canal, and this impedance matching makes for efficient energy transfer. The issue has been discussed by Kosteljik²⁹ in 1950 and summarised by Schubert³⁰ in his 1978 review [pp. 46–47].

²⁹ Ch. VII.2.

This leads us towards a consideration of the whole of the middle ear, including the middle ear muscles, which is beyond the scope of this thesis. It is enough for now to see that if the middle ear muscles push the stapes into the cochlea, the round window membrane will be stretched and the *static pressure* in the fluid contents will rise. Thus, the protective action of the middle ear muscles comes about not through increasing the stiffness and sound transmission of the ossicles, which is the textbook account, but by increasing intracochlear pressure, a d.c. signal that turns down the a.c. gain of the cochlear amplifier. That is, we have returned to the old *intralabyrinthine pressure theory* of middle ear muscle action, put forward by Gellé in 1885. There is evidence in its favour, but it tends to be overlooked because it does not fit in with traveling wave theory. To present just one such piece of evidence, Fig. 10 of Lynch (1982) shows the cochlear microphonic varying by 10 dB as the intracochlear pressure is varied by 7 cm of water. A synthesis of evidence supporting the intralabyrinthine pressure theory will be the subject of future work.

8.2/a Perceptible effects of the round window

The previous section sketched a simple picture of the cochlea (Fig. 8.1) in which the fast wave and the pressure it conveys was taken into account and contrasted it with the traveling wave view where the opposite is the case. In this section I will set out to show how the revised picture might explain findings that the latter view cannot.

A difficulty in trying to examine the effect of the round window is that it cannot be simply isolated from the rest of the system. For a start, the compliance of the round window is in series with the compliance of the oval window (as well as the rest of the middle ear system), so that their values cannot be determined separately by simple impedance measurements. However, we know that with bone stimulation of the cochlea³⁰, the volume displacement of the round window is 5–15 dB greater (say 10 dB) than that of the oval window, so we can assume that the compliance of

³⁰ Schubert, E. D. (1978). History of research on hearing. In: *Handbook of Perception, vol. IV, Hearing*, edited by E. C. Carterette and M. P. Friedman (Academic: New York), 41-80.

³¹ Stenfelt, S. et al. (2004). Fluid volume displacement at the oval and round windows with air and bone conduction stimulation. *JASA* 115: 797-812.

the round window is about 3 times greater. This is confirmed by other studies³², although the compliances vary from one experiment to another.

Nevertheless, it is generally agreed^{33,34} that the round window membrane is a major component of cochlear input impedance at low frequencies (several hundred hertz). As shown in Fig. 10 of Lynch et al. (1982), the input impedance was approximately halved at low frequencies when the round window was removed. At higher frequencies, the magnitude of the cochlear impedance itself tends to dominate and the effect of removal is not clear. However, it is still the case that increasing pressure in the cochlea (Lynch, 1982, p. 115) reduces the cochlear microphonic to a 1 kHz tone³⁵, suggesting that the round window is still having an effect, but less obviously.

At higher frequencies, the round window impedance will dwindle in comparison with that of the cochlea (refs. 33, 34), but it should be pointed out the sound pressure levels used (105–130 dB) were so intense that active outer hair cell properties would have been swamped. In any case, it is noted that the input impedance of the cochlea is largely resistive at most frequencies³⁶.

8.2/b Effects of cochlear compressibility

Evidence put forward in §I 3.3/b was consistent with the idea that the cochlea is compressible, although probably much more so in a live cochlea – with its outer hair cell bubble – than in a dead one. There have been a handful of studies in which the effect of compressibility was considered, although the motivation was to examine the effect on the cochlea of inadvertently introduced air bubbles rather than in its natural condition, but the same physical principles apply nevertheless and the conclusions reached are useful.

³² Zwislocki (2002), p. 73. Stenfelt et al. (2004) report Kirikae's 1959 result that the oval window is about 20 times stiffer than the round window (p. 809).

³³ Nedzelnitsky, V. (1980). Sound pressures in the basal turn of the cat cochlea. *J. Acoust. Soc. Am.* 68: 1676-1689.

³⁴ Lynch, T. J., et al. (1982). Input impedance of the cochlea in cat. *J. Acoust. Soc. Am.* 72: 108-130.

³⁵ The reduction is less than 3 dB, which is not as much as the 10 dB at 100 Hz, but still appreciable.

³⁶ Zwislocki (2002), p. 128.

Merchant et al. (1996) studied the input impedance of human temporal bones by measuring the volume displacements of the two windows³⁷. In this way they could obtain a direct measure of the compressibility of their inner ears. They separate the impedance effects of any introduced bubble from those of the existing cochlea³⁸. They calculate (p. 37) that any air bubble must have been less than 0.2 μL ($2 \times 10^{-10} \text{ m}^3$), which is about 500 smaller than the volume of the cochlear fluids (100 μL). Such a bubble would be comparable to the total volume of outer hair cell cisterns³⁹, although of course the specimen they measured was far from alive. They found several anomalies between their impedance figures and those of previous workers, particularly below several hundred hertz and above 4 kHz, and conclude (p. 44) that the combined impedance of the stapes and cochlea may be higher than previously thought. I surmise there may be large differences between the impedances of live and dead cochleas, a position supported by Ruggero and Temchin (2003) who surveyed the disparity between live and dead measurements and concluded that there were substantial differences⁴⁰. Most post mortem studies of temporal bones are flawed, they suggest, and the inner ear is more wide-band and sensitive than these studies imply.

Puria et al. (1997) also studied human temporal bones and devoted some effort to looking at the effect of air bubbles⁴¹. First they degassed their specimens in a vacuum chamber and found that the input impedance increased, typically by a factor of about 2 (their Fig. 6). Then they introduced air bubbles of 8–20 μL and found inexplicably variable effects (Figs 7 and 8). Sometimes the effects were large (a factor of 30 or more at some frequencies) and sometimes small (negligible), but almost invariably a bubble will decrease input impedance. The authors develop a circuit model of bubble inclusion (Fig. 10) that differs depending on whether the

³⁷ Merchant, S. N., et al. (1996). Acoustic input impedance of the stapes and cochlea in human temporal bones. *Hear. Res.* 97: 30-45.

³⁸ A bubble impedance Z_B would be in series with the stapes impedance Z_S but in parallel with the existing cochlear impedance Z_C . Therefore, effective $Z = Z_S + [Z_C \cdot Z_B / (Z_C + Z_B)]$. I think that most of Z_C is due to bubble compressibility anyway, which supports this equation.

³⁹ In §D 8.4/d, we calculate that the cisternal system of each outer hair cell may contain about $5 \times 10^{-16} \text{ m}^3$ of air. For a total of 12 000 outer hair cells, this means a volume of about $6 \times 10^{-12} \text{ m}^3$.

⁴⁰ Ruggero, M. A. and A. N. Temchin (2003). Middle-ear transmission in humans: wide-band, not frequency-tuned? *Acoustics Research Letters Online* 4: 53-58. Persistent efforts to derive live cochlea properties from dead specimens is no doubt underlain by the thought that the basilar membrane provides the tuning. See footnote 144.

⁴¹ Puria, S., et al. (1997). Sound-pressure measurements in the cochlear vestibule of human-cadaver ears. *J. Acoust. Soc. Am.* 101: 2754-2770.

bubble is in the upper or lower gallery. They note that intracochlear pressure should depend on the cochlear and round window impedances (p. 2762), but when an air bubble is introduced into the upper gallery it will act as a shunt across the cochlear impedance, whereas one in the lower gallery will shunt the round window impedance. On my interpretation, the effect should be equivalent, but the impedances are so high that measurement errors may be responsible. In any case, the authors agree that, in general, significant volume velocity can be lost in compressing the air within a bubble (p. 2762).

Most recently, Ravicz et al. (2004) performed a study on the middle ears of human temporal bones and found some puzzling effects⁴². They were looking at the effects of otitis media with effusion (when infection causes the middle ear to fill with fluid) and could not understand why, when the middle ear (minus mastoid air cells) was filled with fluid, the tympanic membrane could still move. It was as if (p. 121) the middle ear had a hidden air bubble of between 25 and 270 μL . The authors considered compressibility in the cochlea, but dismissed it because of previous studies. They left the findings as a mystery, on a par with the curious fact (p. 127) that patients with middle ears completely filled with fluid lose only 20–30 dB of hearing sensitivity.

Whether the answer lies in cochlear compressibility or small hidden compliances in the middle ear, this work highlights how crucial small bubbles can be to the cochlea's input impedance – and thus to our hearing sensitivity.

8.3 Are outer hair cells pressure sensors?⁴³

Because outer hair cells bear stereocilia, it is natural to assume that, like inner hair cells, the unique stimulus to which they react is bending of the stereocilia. But is this long-standing assumption necessarily true?

⁴² Ravicz, M. E., et al. (2004). Mechanisms of hearing loss resulting from middle-ear fluid. *Hear. Res.* 195: 103-130.

⁴³ This and the following section based on Bell, A. (2003). Are outer hair cells pressure sensors? Basis of a SAW model of the cochlear amplifier. In: *Biophysics of the Cochlea: From Molecules to Models*, edited by A. W. Gummer (World Scientific: Singapore), 429-431.

Textbooks usually refer back to an experiment of Hudspeth and Corey⁴⁴ on which to justify their statement that hair cells are displacement detectors. Whereas a glass probe bending a group of stereocilia will indeed give rise to a receptor potential, this experiment does not rule out the possibility that the cell body is also being subject to pressure. Of course, I would agree that in the investigated case (a hair cell in the bull-frog's sacculus) the stimulus is likely to be stereocilia bending alone, but to generalise this experiment to include adult mammalian outer hair cells, which lack kinocilia, is perhaps an unjustifiably large leap.

The text that follows considers a number of recurring anomalies which have appeared in the literature over the years and concludes that their common underlying feature is an OHC response to pressure. Section D 8.4/e (below) examines the hypothesis that OHCs have dual sensitivity, responding not only to displacement – via deflection of the stereocilia – but, through their cell body, reacting directly to imposed pressure as well. A later section (§D 9.1) describes how this cooperative arrangement could work, but the key proposition is that OHCs react predominantly to intracochlear pressure at levels of less than about 60 dB SPL.

Of course, the stereocilia still function at these low levels, but most of the receptor potential they generate comes from responding to the standing wave of the cochlear amplifier – which is primarily initiated, it is proposed, by the pressure signal. The implication is that the traveling wave is not well suited to stimulating OHCs: up and down movement of the basilar membrane does not easily translate into bending fairly rigid V-shaped stereocilia bundles. At higher intensities, the cochlear amplifier saturates, and has no major role in IHC stimulation⁴⁵. At these elevated levels, direct displacement of the IHC stereocilia may be the important process, and this could be a role for the traveling wave.

By using two mechanisms, one operating at low levels and the other at high, the cochlea can split its working range into two⁴⁶. Interestingly, cancellation effects

⁴⁴ Hudspeth, A. J. and D. P. Corey (1977). Sensitivity, polarity, and conductance change in the response of vertebrate hair cells to controlled mechanical stimuli. *Proc. Nat. Acad. Sci.* 74: 2407-2411.

⁴⁵ When people lose OHCs, their hearing threshold rises by about 60 dB. The idea that OHCs are mechanical preamplifiers that send their output to the IHCs was put forward in §M 4.2.

⁴⁶ Davis originally made the suggestion that the cochlea was composed of two sensory systems side by side. He said that the outer hair cells were sensitive and fragile while the inner hair cells were less sensitive but rugged [Davis, H. (1960). Mechanism of excitation of auditory nerve impulses. In: *Neural Mechanisms of the Auditory and Vestibular Systems*, edited by G. L. Rasmussen and W. F. Windle (Thomas: Springfield, IL), 21–39. p. 36.

become evident at about 60 dB, as we will see in Chapter D9. Range-splitting is an important way by which the ear can increase its dynamic range to 120 dB, a range which, for a single transducer, is extremely challenging. As explained later, the two systems operate independently; perhaps as protection against overload, they are even separately tuned (by half an octave or more: §D 9.1/l).

The unifying hypothesis is that there are two detection systems in the cochlea, each arranged to detect a different signal: the OHCs detect the common-mode pressure signal between 0 and 60 dB SPL (and pass it on to the IHCs); from 60 to 120 dB, the IHCs directly detect traveling wave motion. That our perception of sound is seamless, irrespective of level, is remarkable, but the cochlea is a detection system refined over millions of years of evolution. A comparison may be made with the visual system, where the rods and cones operate at low and high light levels respectively. With that perspective, let us now turn our attention to how the novel pressure-detection mechanism can work as claimed.

8.3/a Evidence for OHC pressure sensitivity

We have set out a *prima facie* case in Chapter I3 that outer hair cells were sensitive to oscillating hydrostatic pressure. The following sections draw parallels with other sensory systems and provide a detailed account of how this sensitivity could arise. To recap and expand the case, the following lines of evidence are set out. Additional evidence will be presented in Chapter D9.

A. Motility of OHCs is driven by the electrical potential of the cell^{47,48}, and this is usually thought to derive from bending of stereocilia. This is not always the case, however, and in one study⁴⁹ when the stereocilia were directly stimulated no length changes could be elicited.

B. If stereocilia are meant to detect relative shear between the basilar membrane and the tectorial membrane, their V-shaped arrangement on the cuticular

⁴⁷ Brownell, W. E., et al. (1985). Evoked mechanical responses of isolated cochlear outer hair cells. *Science* 227: 194-196.

⁴⁸ Evans, B. N. and P. Dallos (1993). Stereocilia displacement induced somatic motility of cochlear outer hair cells. *Proc. Nat. Acad. Sci.* 90: 8347-8351.

⁴⁹ Canlon, B. and L. Brundin (1991). Mechanically induced length changes of isolated outer hair cells are metabolically dependent. *Hear. Res.* 53: 7-16.

plate seems far from optimum. The resistance of the V to deformation would appear to make bending in a radial direction more difficult.

C. OHCs give strong responses to oscillating water jets placed near the cell body^{50–55}. Responses are seen both in membrane potential and length changes, and the length changes, which can be either positive or negative, depend on cell length. The ground-breaking study of Brundin et al. (1989) found that the cells were inherently tuned, with best frequency varying systematically with cell length⁵⁶. The cells could *either lengthen or shorten* and the researchers conclude that “each outer hair cell is a tuned detector of mechanical vibrations...” (p. 816) “independent from the basilar membrane travelling wave” (p. 815). A number of reports explicitly note how difficult it is to bend stereocilia directly (which is the prime reason that water jets are used). However, in using a water jet, the observed response could be seen as deriving from the oscillating pressure component of the jet rather than its movement, although there is as yet no direct evidence for this.

D. The responses persist when the apical end of the cell is held in a pipette^{57,58}, so that the stereocilia are completely protected (Fig. 8.4).

⁵⁰ *ibid.*

⁵¹ Canlon, B., et al. (1988). Acoustic stimulation causes tonotopic alterations in the length of isolated outer hair cells from guinea pig hearing organ. *Proc. Nat. Acad. Sci.* 85: 7033–7035.

⁵² Brundin, L., Flock, Å., and Canlon, B. (1989). Sound-induced motility of isolated cochlear outer hair cells is frequency-specific. *Nature* 342: 814–816.

⁵³ Brundin, L. and I. J. Russell (1993). Sound-induced movements and frequency tuning in outer hair cells isolated from the guinea pig cochlea. In: *Biophysics of Hair Cell Sensory Systems*, edited by H. Duifhuis et al. (World Scientific: Singapore), 182–191.

⁵⁴ Brundin, L. and I. J. Russell (1994). Tuned phasic and tonic motile responses of isolated outer hair cells to direct mechanical stimulation of the cell body. *Hear. Res.* 73: 35–45.

⁵⁵ Preyer, S., et al. (1995). Abolition of the receptor potential response of isolated mammalian outer hair cells by hair-bundle treatment with elastase: a test of the tip-link hypothesis. *Hear. Res.* 89: 187–193.

⁵⁶ Brundin et al. (1989), Fig. 4. The frequency increased by about an octave for every 13 μm decrease in cell length.

⁵⁷ Brundin and Russell (1993).

⁵⁸ Brundin and Russell (1994).

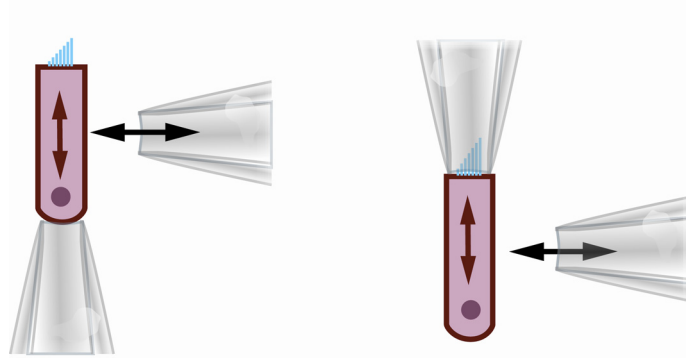


Fig. 8.4. Identical responses. Experiments by Brundin and Russell (1994) showed that an OHC responded identically whether held from above or below. [Drawing by Sharyn Wragg, RSBS Illustration]

E. Similar responses are observed when a vibrating probe is placed against the cuticular plate or on the side of the cell⁵⁹. The vibrating probe would cause the interior pressure of the cell to vary (Fig. 8.5).

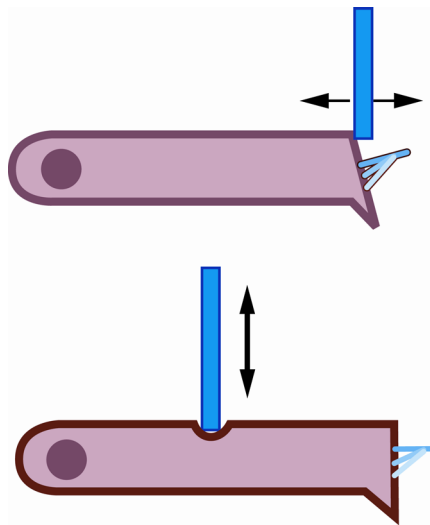


Fig. 8.5. Responses to a vibrating probe were the same irrespective of whether Chan and Ulfendahl (1999) stimulated them from the top or the side. [Drawing by Sharyn Wragg]

F. OHCs are constructed like pressure vessels: they are shaped like a test-tube with rigid walls reinforced with cross-ply belting (Fig. 8.12), and maintain an internal turgor pressure of about 1 kPa.

G. The bodies of OHCs are surrounded by perilymph, and this watery incompressible liquid is in continuous hydraulic connection with the entire fluid

⁵⁹ Chan, E. and M. Ulfendahl (1999). Mechanically evoked shortening of outer hair cells isolated from the guinea pig organ of Corti. *Hear. Res.* 128: 166–174.

contents of the cochlea via the spaces of Nuel (see Fig. 5.1). The otic capsule is comprised of ivory-like bone, the hardest bone in the body. Such a design would allow a compressible OHC to directly and efficiently sense intracochlear pressure.

H. OHCs display piezoelectric-like properties – an electric response to pressure. In terms of length change per millivolt, the sensitivity of OHCs is more than 10 000 times greater than Rochelle salt, a common piezoelectric material⁶⁰.

Taken together, these results suggest that pressure may be the key stimulus to OHCs, not bending of their stereocilia. Of course, the above experiments were done without thought that the water jet's pressure was itself causing the observed effects, and so experimental set-up and control was far from ideal for deciding the question. It is difficult to separate a pressure stimulus from a displacement one because they go hand in hand. Ideally, we would like an experiment where the two possible stimuli were well isolated, say with the cells enclosed in a container holding a large volume of liquid and pressure applied to the container. Then we could clearly determine whether outer hair cells do respond to imposed pressure.

Nevertheless, one of the above experiments did provide a suggestive numerical result. Brundin and Russell (1993) observed that water-jet responses of OHCs could be seen down to a (roughly) calculated pressure equivalent to 49–64 dB SPL. Allowing for middle-ear gain of 30 dB, this equates to a situation of 19–34 dB SPL in the ear canal. But this measurement is on a single OHC, and so represents an open-loop gain. In the cochlea, positive feedback between the rows (the basis of the cochlear amplifier according to the SAW model) will amplify the pressure-induced signal by 40–60 dB (§M 4.3, §R 6.2). That is, the closed-loop gain of the system in response to a pressure stimulus of 0 dB SPL (threshold of hearing) would be sufficient to produce a detectable response. In other words, to evoke responses at threshold, no travelling wave and no bending of stereocilia is required.

⁶⁰ Dong, X., et al. (2002). Piezoelectric reciprocal relationship of the membrane motor in the cochlear outer hair cell. *Biophys. J.* 82: 1254-1259.

8.3/b Revisiting the Wilson hair-cell swelling model

The Wilson hair-cell swelling model was constructed to explain how acoustic emissions could travel from outer hair cells to the ear canal (§I 3.2/k). It follows that if outer hair cells change volume and create fast pressure waves, then simple reciprocity would see fast pressure waves causing volume changes. Thus, instead of restricting the Wilson model to one-way signal travel, it is suggested that signals (at least at low levels) travel into, and out of, the cochlea via fast waves.

If that is so, then delays measured in active cochlear mechanics must nearly all be due to filter delays – that is the time required for a sharply tuned filter to build up its oscillation. That is a simple but strong statement, and can be directly tested. The fast time constants mentioned in the second part of §I 3.2/k provide some credence that travel times in and out can be very short. The drawback with basilar membrane measurements is that they do not automatically give a measure of the cochlear oscillators; rather, they give the averaged response of many such oscillators (which, in the main, act radially). Isolating SAW oscillator behaviour from basilar membrane behaviour may not be straightforward, but it could in theory be done.

8.4 Detecting sound underwater

This section goes back to first principles. Immersed as they are in liquid, OHCs are effectively hydrophones, detecting sound propagating through water. It therefore pays to take a look at underwater acoustics and the approaches that marine creatures use to detect sound in water. In this context it is worth remembering that our hearing sense first evolved in water and only later became adapted to life in air.

A creature living in water faces a major problem in detecting sound in its environment. As pointed out by Pumphrey⁶¹, its tissues are largely composed of water, and so it will have nearly the same compressibility and density as the medium in which it lives. In other words, sound will pass straight through it without interacting; effectively, the animal is acoustically transparent. The way around this is

⁶¹ Pumphrey, R. J. (1950). Hearing. *Symp. Soc. Exp. Biol.* 4: 3-18.

to introduce an impedance discontinuity, but first we need to be clear in our terminology.

A basic starting point⁶² is to understand that all plane propagating waves carry two different, but intimately related properties: particle displacement and sound pressure. Thus, a plane wave moving through a medium of density ρ at phase velocity c will have an rms particle velocity u and rms sound pressure p . The characteristic impedance of the medium, p/u , is given by $p/u = \rho c$. In air the acoustic impedance is close to 415 Pa s/m (rayls), whereas in water the corresponding figure is 1.5×10^6 , about 3600 times greater. Since the sound intensity, I , the acoustic power per unit area, is given by the product of pressure and particle velocity, $p \times p/\rho c = p^2/\rho c$, this means that for the same acoustic power, the pressure in water is 60 times greater than it is in air and the particle velocity 60 times less. Rephrased, *in detecting sound underwater, sensing the pressure component of a wave is easier than extracting its displacement component* – provided, of course, that you have a way of introducing a compressible element to detect the pressure.

This situation, however, only applies to plane waves, far from the source. As described by van Bergeijk⁶³, when we are close to the source, as well as the propagated pressure wave there is an important near-field displacement effect to take into account. Van Bergeijk considers as source the case of an oscillating air bubble. As the bubble expands and contracts, it displaces water away from, and towards, itself. Because water is virtually incompressible, this radial displacement is passed on from one concentric layer to the next. The displacement amplitude will fall off as $1/r^2$, where r is the distance from the source.

If water were completely incompressible, this displacement would be, van Bergeijk observes, the only detectable phenomenon. But due to water's small compressibility, the vibrating bubble will also generate an acoustic wave, the familiar pressure wave. This wave will decrease in amplitude as $1/r$.

Therefore, close to the source, in the near-field, the displacement amplitudes are greater than expected from a plane wave; in the far-field, the displacement amplitudes are virtually all contributed by the pressure wave. The boundary between

⁶² Wartzok, D. and D. R. Ketten (1999). Marine mammal sensory systems. In: *Biology of Marine Mammals*, edited by J. E. Reynolds and S. A. Rommel (Smithsonian: Washington), 117-175.

⁶³ van Bergeijk, W. A. (1964). Directional and nondirectional hearing in fish. In: *Marine Bio-Acoustics*, edited by W. N. Tavolga (Pergamon: Oxford), 1, 281-299.

the two regimes, where the two displacement amplitudes are about equal, is generally taken to be one-sixth of a wavelength⁶⁴. In water at 1 kHz, this is about 25 cm.

A radially oscillating bubble gives the strongest near-field effect. Other oscillating bodies, such as solid spheres vibrating side to side, will also produce near-field effects, but the displacements will fall off faster ($1/r^3$ for the sphere) and there will be directional effects as well. A wriggling worm will only make its presence felt very close by⁶⁵.

The major conclusion to this discussion is to see that in detecting sound underwater we are better off, in the near field, with using a displacement-sensitive detector, whereas in the far field both pressure and displacement detectors are equally effective.

8.4/a Detecting pressure and displacement

The classic displacement detector is the hair cell (Fig. 8.6A), and it is usually considered that all hair cells of the acoustico-lateralis system (from which mammalian ears evolved) are displacement detectors. On the other hand, if we are to detect pressure, an impedance discontinuity is needed, and a common implementation is a diaphragm across an enclosed space so as to detect the force generated across it, as shown in Fig. 8.6B. The distinction is spelt out⁶⁶ in Ewing (1989).

⁶⁴ In the case of a source that is very much smaller than the sound wavelength. A more rigorous treatment is given in Section 6.2 of Rossing, T. D. and N. H. Fletcher (1995). *Principles of Vibration and Sound*. (Springer: New York).

⁶⁵ For analysis see Section 7.1 of Rossing and Fletcher (1995).

⁶⁶ Ewing, A. W. (1989). *Arthropod Bioacoustics: Neurobiology and Behaviour*. (Edinburgh University Press: Edinburgh). [pp. 58 ff.]

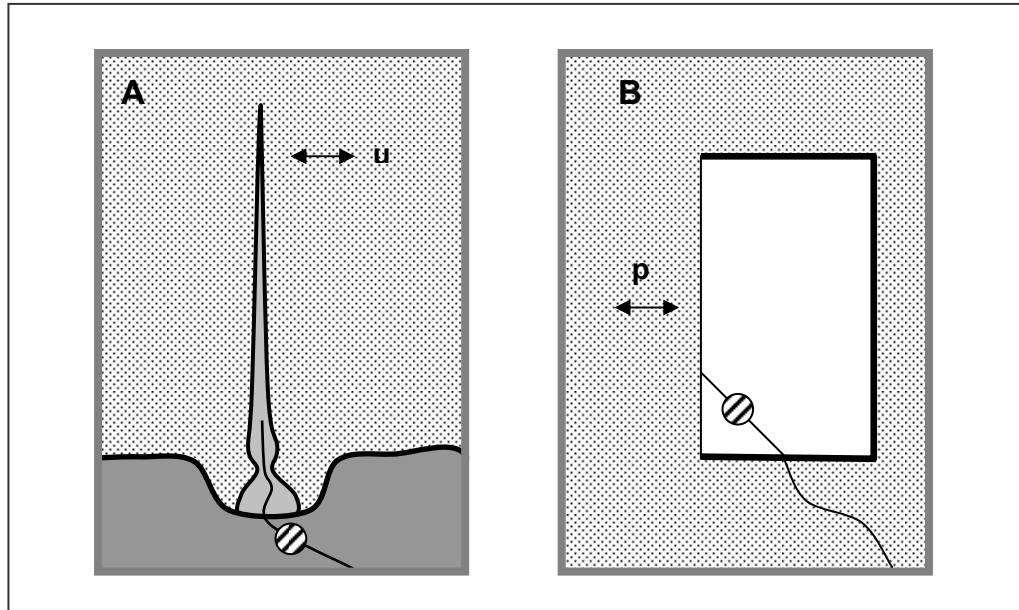


Fig. 8.6. Detecting displacement (A) and pressure (B). A hair on a hair cell responds to water displacement u by bending; a sensor mechanism (striped) responds neurally. To respond to a pressure wave, p , in the water, a diaphragm across an impedance discontinuity is required; the sensor is set to detect movement of the diaphragm. Air is commonly used to fill the space. Adapted from Ewing (1989).

Fish use both these mechanisms. Firstly, the hair cells in the lateral line organ respond to movement of fluid as the fish swims, giving important information about its nearby environment and relative motion. Secondly, most fish also detect pressure waves – they hear – by using an impedance discontinuity. One way is to introduce a material with density greater than water, such as calcium carbonate; this is the option taken by cod which have calcite otoliths sitting on top of hair cells⁶⁷. The second way is to use a light or compressible material, and many fish species use a gas bladder filled with air⁶⁸. The bladder is useful for buoyancy, but it also oscillates in volume and displacement as pressure waves pass through. By coupling the surface of the bladder to the ear via special bones (the Weberian ossicles), the fish can hear long-distance pressure waves⁶⁹.

The following demonstration from Békésy⁷⁰ well illustrates how a compressible volume can be very efficient in allowing vibration to be detected within nearly incompressible water. He placed his finger inside a cavity formed out of a

⁶⁷ See Ch. 4 of Fletcher (1992).

⁶⁸ Fletcher (1992), section 9.2.

⁶⁹ van Bergeijk (1964).

⁷⁰ Békésy, G. v. (1967). Some similarities in sensory perception of fish and man. In: *Lateral Line Detectors*, edited by P. H. Cahn (Indiana University Press: Bloomington), 417-435.

heavy block of lead and filled the cavity with paraffin oil (Fig. 8.7). On one face of the cavity was a flexible membrane driven by a vibrator, in this way supplying oscillating pressure to the oil.

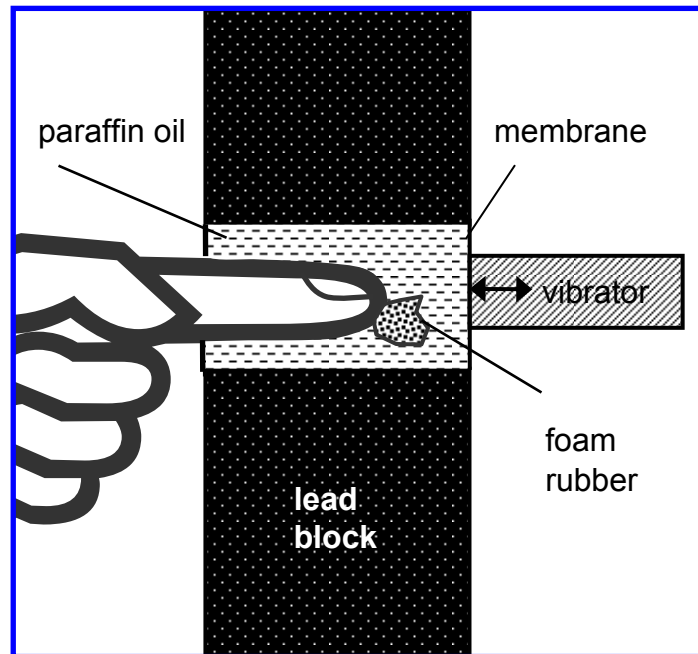


Fig. 8.7. Békésy's demonstration of an efficient way to hear underwater. Touching the foam rubber produced "the sensation of strong vibrations".

When he placed a small piece of foam rubber inside the cavity, he reported that touching the foam rubber "produced the sensation of strong vibrations" [p. 424]. His experiment was done in the context of a discussion of whether we hear by sensing pressure or displacement. Anatomy seems to suggest that with the mammalian cochlea containing hair cells, as in Fig. 8.6A, it is designed to respond to fluid displacements. If that is so, then the middle ear can be regarded as a device, like the swim bladder, for converting sound pressures into volume displacements. Such an account accords with the travelling wave theory – in which displacement of the basilar membrane is the focal stimulus. But I want to look closer at anatomy and point out that *there appears to be another pressure-to-displacement converter, Békésy's piece of foam rubber, strategically located inside the hair cell itself* – an ideal arrangement for detecting underwater sound directly which has so far been overlooked.

The material to follow therefore presents a novel extension of the underwater acoustics story. It describes a situation that neatly reflects Békésy's revealing experiment. We note that Fig. 8.7 is an arrangement in which a compressible material is completely enveloped by incompressible surrounds to create a pressure-to-displacement converter. In the ear the otic capsule is made of material even harder than a lead block – ivory-like bone, the hardest in the human body – and is filled with nearly incompressible water. Helmholtz elaborates on this arrangement by noting that “An incompressible fluid... contained between solid walls is distinguishable from a compressible one in this: that every impulse [however minute] which reaches any part of its surface communicates itself immediately throughout the whole fluid...”⁷¹. Now, if we introduce compressible hair cells into the system, this permits efficient detection of vibration. This possibility is explored by first considering sharks and other creatures who, without swim bladders, hear remarkably well underwater.

8.4/b The revealing case of shark hearing

How sharks hear has been a long-standing puzzle. As with all elasmobranchs – sharks, rays, and skates – they lack bone and make do with cartilage instead. Unlike the bony fish, they also lack swim bladders. While some of the cells in their labyrinth bear otoconia, others, particularly those most sensitive to vibration, do not. The standard conclusion⁷² is that sharks must rely on detecting water displacement directly.

The problem is that these motions are extremely minute far from the source, and amount to molecular dimensions. Some authors have even doubted that sharks could hear over large distances, and that they converge on prey through the use of smell, but Corwin's review mentions observed acoustic responses over 250 m in some sharks. At such distances, particle displacements, he calculates, must be as small as 5×10^{-10} m, and the signal-to-noise ratio must therefore be low. If shark

⁷¹ Helmholtz, H. L. F. v. (1874). *The Mechanism of the Ossicles and the Membrana Tympani* [translated by J. Hinton]. (New Sydenham Society: London). [p. 106]

⁷² Corwin, J. T. (1981). Audition in elasmobranchs. In: *Hearing and Sound Communication in Fishes*, edited by W. N. Tavolga et al. (Springer: New York), 81-105. His Fig. 5-1 provides a good summary.

hearing is comparable to that of fish, then another perspective on the problem⁷³ suggests that the displacements are about 2×10^{-12} m, about 1/100th the diameter of the hydrogen atom. But the real problem is not the size of these motions but that they are theoretically undetectable because any small sensor will move in step with its surroundings as an acoustic pressure wave passes through. There is no *relative motion* to sense, a situation aggravated by wavelengths underwater being so long.

In order to hear the shark must somehow introduce an impedance discontinuity so that the pressure wave will produce differential forces. The shark has two populations of cells in its labyrinth that are involved in vibration responses: the sacculus, covered in otoliths, and the well-named macula (or papilla) neglecta^{74,75} which is covered only with a gel (Fig. 8.8).

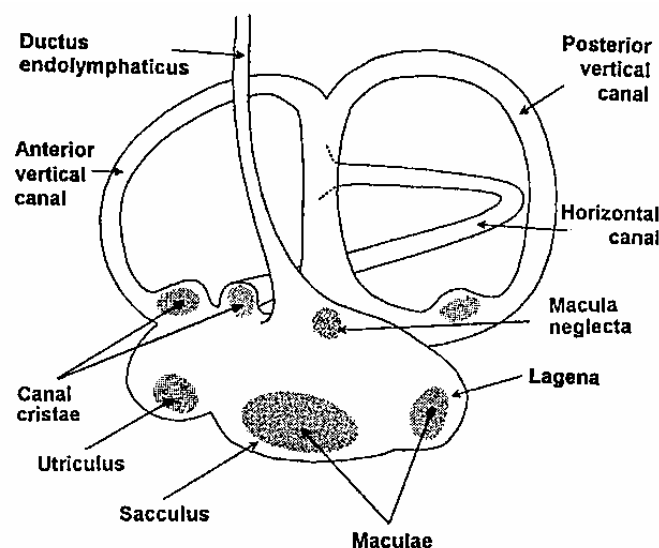


Fig. 8.8. In sharks, the macula neglecta is strongly sensitive to vibration. This extensive patch of hair cells sits inside the labyrinth but unlike the other maculae it is not covered with otoliths, only gel. What is its mode of stimulation? [From Myrberg (2001) and used with permission of Kluwer]

The otoliths, with a density some 3 times higher than water, will undergo a relative displacement of about four-sevenths that of the surrounding water, and perhaps this motion is detected. The outstanding problem relates to the neglecta and

⁷³ Rogers, P. H. and M. Cox (1988). Underwater sound as a biological stimulus. In: *Sensory Biology of Aquatic Animals*, edited by J. Atema et al. (Springer: New York), 131-149.

⁷⁴ Lewis, E. R., et al. (1985). *The Vertebrate Inner Ear*. (CRC Press: Boca Raton, FL). pp. 58-62.

⁷⁵ Myrberg, A. A. (2001). The acoustical biology of elasmobranchs. *Environmental Biology of Fishes* 60: 31-45.

its 200 000 or so cells, which are highly sensitive to vibration^{76,77}. There should be no relative difference between the motion of the water and the motion of the covering gel (which is mainly water). One suggestion⁷⁸ has been that this sensory patch of cells may react to some pressure-to-displacement conversion in the labyrinth, but such a process seems physically unrealistic and has been criticised⁷⁹.

The answer lies, I think, in a closer study of the anatomy of the macula neglecta⁸⁰. The microscopic study of Corwin (1981) showed that the cells of this sensory region contained both ‘dark’ and ‘light’ types, and that the light cells contained many distinctive ‘vacuities’ of unknown function⁸¹. I suggest that if these vacuities were filled with air, then, finger-like, the detection problem would be solved⁸².

8.4/c Bubbles and underwater acoustics

A clear example of what I have in mind is the mechanosensor of a primitive marine polyp⁸³ which reacts to vibration near its tentacles by shooting out spikes (nematocysts) at high speed. Microscopic anatomy of the sensor reveals that it comprises a kinocilium, surrounded at its base by a bell-shaped basal body, sitting directly on top of a large clear vesicle (Fig. 8.9). The function of the vesicle is unknown, and its contents could not be ascertained, but the authors say it may have

⁷⁶ Lewis (1985).

⁷⁷ Corwin, J. T. (1981). Peripheral auditory physiology in the lemon shark: evidence of parallel otolithic and non-otolithic sound detection. *J. Comp. Physiol.* 142: 379-390.

⁷⁸ van den Berg, A. V. and A. Schuijf (1983). Discrimination of sounds based on the phase difference between particle motion and acoustic pressure in the shark *Chiloscyllium griseum*. *Proc. Roy. Soc. Lond. B* 218: 127-134.

⁷⁹ Kalmijn, A. J. (1988). Hydrodynamic and acoustic field detection. In: *Sensory Biology of Aquatic Animals*, edited by J. Atema et al. (Springer: New York), 83-130.

⁸⁰ Corwin, J. T. (1977). Morphology of the macula neglecta in sharks of the genus *Carcharhinus*. *J. Morphol.* 152: 341-361.

⁸¹ Like outer hair cells, the light cells appeared turgid, as if under pressure.

⁸² Even though a review thought it ‘highly unlikely’ that, in fish at least, the inner ear could act as a pressure transducer independent of the swimbladder [p. 581 of Tavolga, W. N. (1981). Retrospect and prospect: listening through a wet filter. In: *Hearing and Sound Communication in Fishes*, edited by W. N. Tavolga et al. (Springer: New York), 573-587.] Of relevance, Wever (1978) points out that “the papilla neglecta is responsive to vibratory stimuli...” although “... it does not lie in a path of vibratory fluid flow and can be expected to be insensitive to aerial and aquatic sounds” (p. 974). A logical inference is that the cells are sensitive to pressure.

⁸³ Tardent, P. and V. Schmid (1972). Ultrastructure of mechanoreceptors of the polyp *Coryne pintneri* (Hydrozoa, Athecata). *Exp. Cell Res.* 72: 265-275.

functional significance. Given that the purpose of the cell is detection of vibration, it is a reasonable speculation that the vesicle is an example of a pressure-to-displacement converter and that its contents are probably air. Another candidate might be a compressible lipid⁸⁴ which is able to change phase (and volume) under pressure.

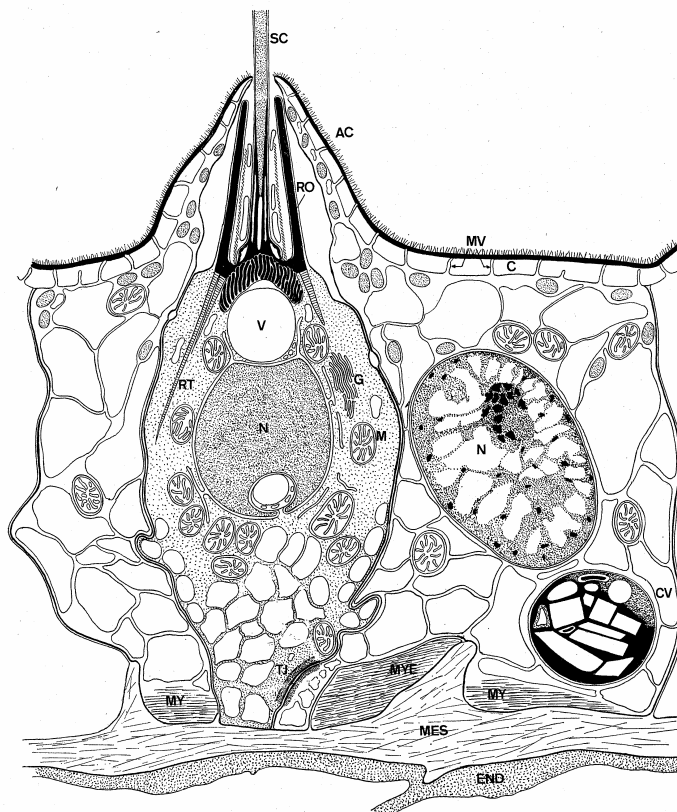


Fig. 8.9. A vibration sensor on a marine polyp. A kinocilium (SC), surrounded at its base with a basal body (black wavy vertical lines), sits on top of a vesicle (V). The contents of the vesicle are not known, but it makes sense to presume it contains air or other compressible material. [Reproduced from Tardent and Schmid (1972) with permission of Elsevier Science]

There is a distinct advantage in having an ‘on-the-spot’ pressure-to-displacement converter. First, it is a simple scheme, not requiring complicated anatomical structures such as the Weberian ossicles. It is also direct and robust, and each cell operates independently of the others. The problem with the swim bladder is that there’s only one, an arrangement that compromises direction-finding, as each ear senses the same signal; some researchers have therefore doubted that bony fish can localise sound sources⁸⁵, a proposition which, if true, would have enormous

⁸⁴ Some biological materials are even known to have negative compressibilities: Kornblatt, J. A. (1998). Materials with negative compressibilities. *Science* 281: 143a. See also §D 8.5

⁸⁵ van Bergeijk (1964), p. 290.

evolutionary disadvantages. The suggestion made here is that many marine creatures – polyps, at least some species of fish, and sharks – have learnt to use air bubbles enclosed within hair cells as detectors of underwater sound.

Air bubbles have dramatic effects on underwater acoustics, and recognition of this opens the door to a fast-growing literature⁸⁶. Although we do not have the space to consider the details, we note that “Gas bubbles are the most potent naturally-occurring entities that influence the acoustic environment in liquids” [Leighton (2004), p. 3267] and there is “exceptionally efficient coupling between bubbles and acoustic waves” [p. 3272], properties that nature has probably exploited in more ways than we currently appreciate. Ultrasound technologists makes use of the phenomenon to increase the contrast of the bloodstream by injecting saline in which microscopic air bubbles are suspended⁸⁷. Whales and dolphins use it by surrounding schools of fish with cylindrical “bubble nets” into which they project intense sounds, generating a reverberating wall of sound through which the fish cannot or will not swim⁸⁸; once corralled, the cetaceans enter for the feed.

When bubbles interact with an underwater sound field they can undergo strong resonances, or “ringing”, with the stiffness coming from the bubble’s compliance and the inertia from the surrounding liquid. The Q varies between about 5 and 30, depending on whether the bubble’s radius is micrometres or millimetres (Leighton, 2004, p. 3278) and attenuations can exceed 200 dB/m (ibid., p. 3291). The resonance frequency, f_r , depends approximately on the inverse of the bubble radius, r , so that⁸⁹

$$f_r = \frac{1}{2\pi r \sqrt{\rho}} \left(3\kappa \left(p_0 - p_v + \frac{2\sigma}{r} \right) - \frac{2\sigma}{r} + p_v - \frac{4\eta^2}{\rho r^2} \right)^{1/2} \quad (8.3)$$

where ρ is the density of the liquid, κ is an index between 1 and 1.4 depending on the thermodynamic properties of the gas, p_0 is the static pressure surrounding the bubble, p_v is the vapour pressure inside the bubble, σ is the surface tension, and η is the viscosity. This equation holds for free-field conditions, and does not include thermal losses, acoustic radiation losses, or bubble–bubble interactions, which appreciably

⁸⁶ Leighton, T. G. (2004). From seas to surgeries, from babbling brooks to baby scans: the acoustics of gas bubbles in liquids. *Int. J. Modern Phys. B* 18: 3267-3314.

⁸⁷ Stewart, M. J. (2003). Contrast echocardiography. *Heart* 89: 342-348.

⁸⁸ Leighton (2004), pp. 3284-3289.

⁸⁹ Eq. 1 of Leighton (2004)

lower the natural frequency. This equation was first derived in simplified form by Minnaert in 1933 by equating the kinetic and potential energies in a linear oscillating system. Then $f_r = (1/2\pi r) \cdot (3\gamma p_0/\rho)^{1/2}$, and we see that spherical bubbles will resonate in the audio range when of millimetre dimensions and in the ultrasonic range when of micrometre size. Of course, as Leighton points out, real bubbles are non-linear and the system is difficult to treat analytically. Nevertheless, the point is the strong interaction between sound and bubbles, whether by resonant or non-resonant means, and this can provide the basis of a sensitive acoustic detector.

8.4/d Cells containing air

When cells contain air bubbles, microscopically identifying the fact is difficult. Tiny bubbles tend to dissolve rapidly in water, and fixation techniques involving various stages of dehydration are bound to give unpredictable results⁹⁰. Examining cells that most definitely contain air bubbles therefore gives some insight.

We mentioned the swim bladder of fish, which they employ for hearing, converting pressure into displacement. Fish also use their gas bladders for buoyancy control, saving them much energy by providing neutral buoyancy. The bladders are filled by a gas gland, which takes molecules of gas, mostly oxygen, out of solution from the blood. The process sounds simple, but it is physically remarkable and incompletely understood⁹¹. Somehow a metabolic process concentrates gas against an increasing tendency for it to dissolve in water as the pressure increases (Henry's law). Since even chemically inert gases like argon are concentrated, some physical process must be harnessed. The partial pressure of gas dissolved in sea water stays constant at about the level present at the surface (that is, about 0.2 atmosphere for oxygen). A fish living at 100 m will therefore need to concentrate oxygen from 0.2 atmospheres in the blood to 2 atmospheres in the swim bladder⁹². Nitrogen (and argon) are concentrated in a similar way and presumably by a similar mechanism.

⁹⁰ Dr Sally Stowe, ANU Electron Microscopy Unit (personal communication).

⁹¹ Phleger, C. F. (1991). Biochemical aspects of buoyancy in fishes. In: *Biochemistry and Molecular Biology of Fishes, Vol. 1*, edited by P. W. Hochachka and T. P. Mommsen (Elsevier: Amsterdam), 209-247.

⁹² Wittenberg, J. B. (1958). The secretion of inert gas into the swim-bladder of fish. *J. Gen. Physiol.* 41: 783-804.

Even some fish that live at a depth of more than 7000 m are able fill their swim bladders with gas⁹³. At that depth, the pressure is 630 atmospheres and the density of air is close to that of water, suggesting that the function of the bladder is for hearing (using its contents' compressibility) rather than for buoyancy. On the other hand, many fish species^{94,95} – such as lantern fish, which migrate daily over a depth of 500 m – have their swim bladders filled with wax esters, which provides buoyancy independent of depth (a drawback of gas is that its buoyancy is a function of depth, which is not ideal for fish ranging hundreds of metres vertically). Other fish species have a swim bladder filled with gas while they are juvenile, but progressively fill it with lipids as they mature until it is completely full. In both these cases, the standard interpretation would be that these fish have compromised their hearing – an unlikely situation from an evolutionary standpoint; *alternatively, if they were to have other sites of compressibility, such as in the body of their hearing cells, the problem would not exist.*

At this point it is appropriate to draw attention to one remarkable facet of fish hearing: in contrast to the early literature that gives the hearing limit of fish at a few kilohertz, recent research shows that a number of species – notably those in a family that include the herring – can hear well into the ultrasonic range⁹⁶, up to 180 kHz. The probable reason is to enable detection, and avoidance, of predatory whales and dolphins which emit strong ultrasound signals for echolocation. The observed sensitivity is sufficient to detect cetaceans at a distance of more than 1 km. But the facility raises the question of how these fish do it, as mechanically their auditory system appears ill-suited to high-frequency operation. A simple answer may come from noting that a 10- μ m air bubble possesses a resonance frequency in water of about 170 kHz, and this resonance can increase the amplitude of vibration by orders of magnitude as the mass of the water interacts with the springiness of the air.

The prediction is that the hair cells of these fish, like sharks, contain microscopic air bubbles. In terms of the SAW model, it is also noteworthy that the

⁹³ Nielsen, J. G. and O. Munk (1964). A hadal fish (*Bassogigas profundissimus*) with a functional swimbladder. *Nature* 204: 594-595.

⁹⁴ Nevenzel, J. C., et al. (1969). The lipids of some lantern fishes (family Myctophidae). *Comp. Biochem. Physiol.* 31: 25-36.

⁹⁵ Nevenzel, J. C., et al. (1966). Lipids of the living coelacanth, *Latimeria chalumnae*. *Science* 152: 1753-1755.

⁹⁶ Higgs, D. M. (2004). Neuroethology and sensory ecology of teleost ultrasound detection. In: *The Senses of Fish*, edited by G. von der Emde et al. (Kluwer: Boston, MA), 173-188.

utricle of herring-like fish contains “bands of hair cells of alternating polarity” [Higgs (2004), p. 180], just like the supposed pattern of outer hair cells in the mammalian cochlea.

A prime reason for introducing a discussion of swim bladders is to look more closely at the gas gland itself. Somehow cells of the gland, typically 10–100 μm in diameter, must create tiny gas bubbles and release them into the swim bladder. Bubble formation is a tricky process in that it has to overcome surface tension between the gas and the liquid in which it forms. Because the pressure inside a gas bubble depends directly on the surface tension and inversely on the radius ($p \propto T/r$, Laplace’s law), a minute bubble faces immediate extinction because the pressure will be so high as to dissolve it away again⁹⁷. For a 0.1 μm diameter air bubble in water, the pressure due to surface tension will be nearly 30 atmospheres. Nevertheless, it is a fact that bubbles do appear out of liquids (beer, for example) and it seems that indents in a surface (such as scratches in a glass) offer some protection from collapsing pressures. Another way of assisting bubble formation is to modify the surface tension, and so it seems no coincidence that gas glands are associated with various kinds of oily lipids. An oil will allow gas to spread on its surface at the same time as repelling water, which explains why lipid droplets are often pearly white (as are the lipid droplets secreted by Hensen’s cells). In the same way, the swimbladder wall of freshly captured specimens is often observed to be brilliantly white⁹⁸ and reflective due to a lipid coating.

Microscopic examination of gas gland cells confirms this picture. A general feature is the presence of vacuoles and lipid droplets⁹⁹. Somehow the hydrophobic lipids allow the cell to generate gas bubbles. A difficulty for the microscopist is that it is hard to tell whether the observed vacuoles contain gas or lipid^{100,101}, due the fact that bubbles quickly dissolve once the cell dies, and preparation for microscopy induces further changes. Nevertheless, inspection of published gas gland micrographs (Fig. 8.10) shows such a profusion of vacuoles that, given the cell’s function,

⁹⁷ Vogel, S. (2003). *Comparative Biomechanics*. (Princeton University Press: Princeton). pp. 110–111.

⁹⁸ Phleger (1991), p. 217.

⁹⁹ Pelster, B. (1995). Metabolism of the swimbladder tissue. In: *Biochemistry and Molecular Biology of Fishes*, vol. 4, edited by P. W. Hochachka and T. P. Mommsen (Elsevier: Amsterdam), 101–118. Fig. 2.

¹⁰⁰ Fänge, R. (1953). The mechanisms of gas transport in the euphysoclist swimbladder. *Acta Physiologica Scandinavica Suppl.* 110: 1–133. [p. 34]

¹⁰¹ Fänge, R. (1966). Physiology of the swimbladder. *Physiol. Rev.* 46: 299–322. [p. 315]

there is little doubt some of the vacuoles must be air bubbles¹⁰². Coincidentally, in Dorn's work he identifies two types of neighbouring cells – “helle” (light, left of Fig. 8.10) and “dunkle” (dark, right), the same terminology that Corwin uses to describe the two types of interleaving cells in the neglecta of the shark.

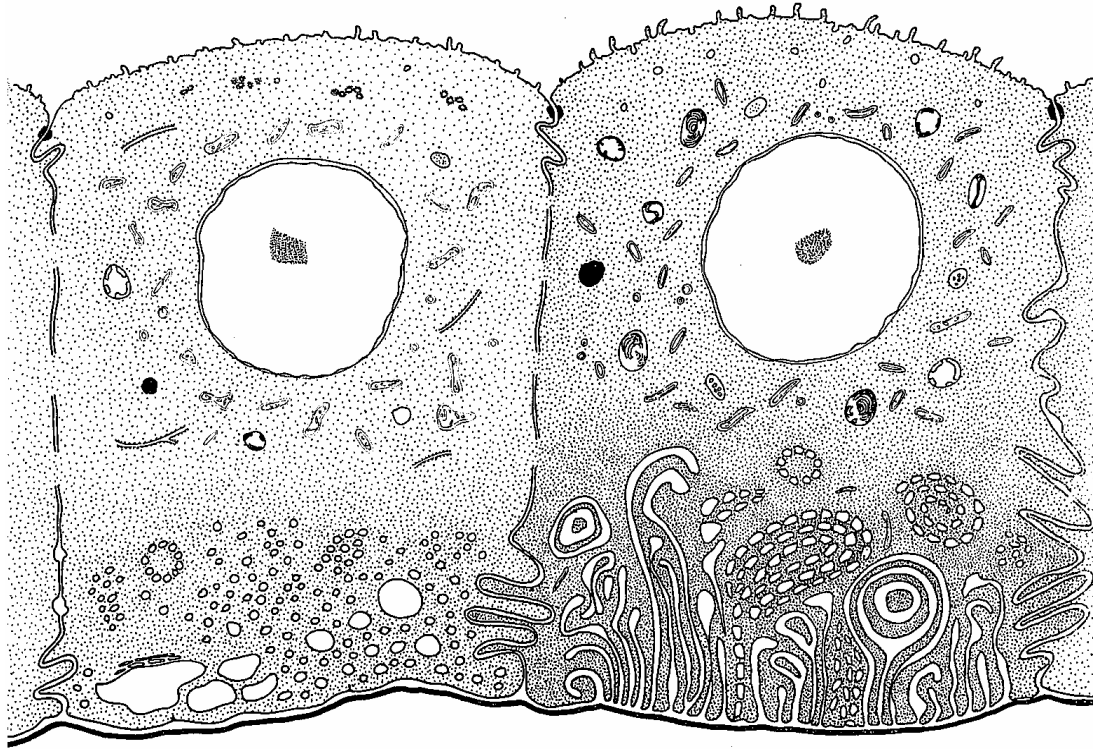


Fig. 8.10. Two types of gas gland cell, which take dissolved oxygen and other gases from the blood and pump them into the swim bladder (here, the cavity below the thick line). The cells contain many vacuoles and it is unclear whether, in vivo, they are filled with gas or lipid, since preparation for microscopy will compromise their natural appearance. Given the cells' function, it is hard to resist the conclusion that some of these vacuoles are air bubbles. [From Dorn (1961) and used with the permission of Springer Verlag]

Before concluding, it is worth noting a recent review¹⁰³ of how marine animals, including those without an obvious gas phase, are able to accurately sense depth. The field is full of uncertainties and few definite conclusions can be reached, prompting the authors to suggest that such organisms “may still contain a small gas pocket which would... [enable] stretch receptors to transduce micro-hydrostatic pressure changes” [ibid., p. 27].

¹⁰² Dorn, E. (1961). Über den Feinbau der Schwimmblase von *Anguilla vulgaris* L. *Zeitschrift für Zellforschung* 55: 849-912.

¹⁰³ Macdonald, A. G. and P. J. Fraser (1999). The transduction of very small hydrostatic pressures. *Comp. Biochem. Physiol.* 122A: 13-36.

The conclusion is that, despite obstacles, it is possible for living cells to produce, and sustain, tiny gas bubbles within.

8.4/e *An air bubble in outer hair cells?*

If outer hair cells are pressure detectors, there must be some compressible material within. There are non-aqueous materials inside cells that may have compressibility higher than that of water (45 Mbar^{-1}), but the obvious candidates – conventional lipids and proteins¹⁰⁴ – have compressibility coefficients about the same as water (22–130 and 10–25 Mbar^{-1} , respectively). When seeking responses to micropascal pressures, it is hard to escape the conclusion that the compressible material is a gas, and air, or a component of air, is the logical choice, as consideration of §D 8.4/c, and our underwater heritage, suggests. Following Boyle's law, a gas will halve its volume for doubling of pressure, so that a threshold pressure elevation of 0.5 mPa in the cochlear liquids¹⁰⁵ will cause the volume of a bubble at atmospheric pressure to decrease by a factor of 1 part in $100 \text{ kPa}/0.5 \text{ mPa} = 2 \times 10^8$. Below I will outline a scheme by which it appears physically possible to detect such a small change.

Outer hair cells contain two distinctive multilayered structures that appear unique to these cells: Hensen's body and subsurface cisternae (Fig. 8.11). These features, of unknown function, are closely related anatomically, and my suggestion is that Hensen's body is a generator of gas which is distributed to the subsurface cisternae, filling the cell with a proportion of air and making it compressible. These features are now examined.

¹⁰⁴ Kharakoz, D. P. (2000). Protein compressibility, dynamics, and pressure. *Biophys. J.* 79: 511-525.

¹⁰⁵ A 20 μPa threshold pressure in air $\times$ 25 middle ear gain.

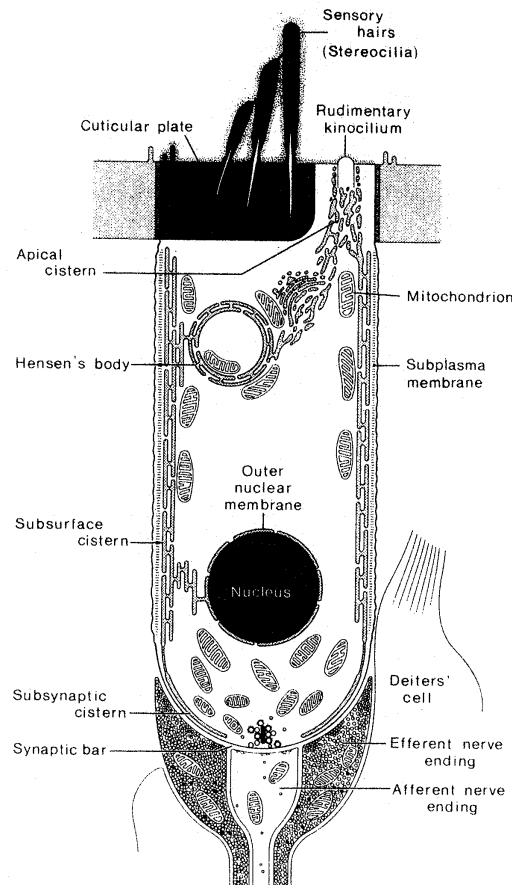


Fig. 8.11. Major organelles in an outer hair cell. Note in particular Hensen's body beneath the cuticular plate and the subsurface cisterns lining the lateral cell walls. [From Lim (1986) with permission of Elsevier Science]

As described in a review by Lim (1986)¹⁰⁶, Hensen's body is a spherical whorl of endoplasmic reticulum just below the cuticular plate connected to an elaborate cisternal system residing largely on the walls of the cell. Mitochondria lie nearby. Both organelles show a multilayered but fenestrated structure. The subsynaptic portion of the cisterns is close to efferent terminals, suggesting a susceptibility to efferent control. The number of layers and abundance of discrete bodies increases after acoustic stimulation and toxic treatments; distinct vacuoles also become more common¹⁰⁷. Aspirin is one agent particularly effective in causing blistering and vacuolisation of the cisterns (and of course in reducing hearing sensitivity).

¹⁰⁶ Lim, D. J. (1986). Functional structure of the organ of Corti: a review. *Hear. Res.* 22: 117-146.

¹⁰⁷ Leonova, E. V. and Y. Raphael (1998). Alteration of membranous structures in ototoxically damaged outer hair cells of the organ of Corti. Midwinter Meeting, Florida, Association for Research in Otolaryngology [abstract 791]

The body is named after Hensen, who first described it in 1863; it appeared to him to have a spiral arrangement¹⁰⁸. The appearance of Hensens body varies from worker to worker, but clear renderings of the layered structure are seen in a TEM¹⁰⁹ by Engström and Ades and a freeze-fracture micrograph¹¹⁰ by Mammano et al. (1999). Some revealing micrographs¹¹¹ can also be found in Harada et al. (1990). Using a different staining method¹¹², Spicer et al. (1998) find that the bodies appear as a cluster of vesicles and there is an abundance, and diversity of appearance, not seen before.

An ultrastructural study of the cistern system¹¹³ of guinea pigs showed that each cell usually had between two and four Hensens bodies. Their concentric layers were connected to the cisternal system that typically had 4–7 parallel stacks, but sometimes up to 12. The lumens of the bodies and the cisterns were found to be filled with an electron opaque material, suggestive of neither water nor air; on the other hand, empty areas (caveolae) were found next to bulging and dilated cisterns (their Figs 8 and 9), and these look like remnants of aggregated air bubbles. I suspect that in vivo a thin layer of air exists next to the electron-dense generating apparatus.

Studies of the subcisternal layers with certain vital fluorescent dyes are also revealing. When the lipophilic dyes CTC and DiOC6 are applied^{114–116}, the whole cisternal system lights up. It appears to occupy an appreciable fraction of the cell's contents, particularly in the region of Hensens body, but also below the nucleus. A

¹⁰⁸ Engström, H. and J. Wersäll (1958). The ultrastructural organization of the organ of Corti and of the vestibular sensory epithelia. *Exp. Cell Res. Suppl.* 5: 460-492. [p. 464]

¹⁰⁹ Engström, H. and H. W. Ades (1973). The ultrastructure of the organ of Corti. In: *The Ultrastructure of Sensory Organs*, edited by I. Friedman (North-Holland: Amsterdam), 83-151.

¹¹⁰ Mammano, F., et al. (1999). ATP-induced Ca^{2+} release in cochlear outer hair cells: localization of an isositol triphosphate-gated Ca^{2+} store to the base of the sensory hair bundle. *J. Neurosci.* 19: 6918-6929. Fig. 6B.

¹¹¹ Harada, Y., et al. (1990). Three-dimensional ultrastructure of cochlea: a review. In: *Inner Ear Pathobiology (Adv. Otorhinolaryngol. v. 45)*, edited by M. Ciges and A. Campos (Karger: Basel), 49-68. Figs 5–7.

¹¹² Spicer, S. S., et al. (1998). Cytologic evidence for mechanisms of K^{+} transport and genesis of Hensen bodies and subsurface cisternae in outer hair cells. *Anat. Rec.* 251: 97-113.

¹¹³ Saito, K. (1983). Fine structure of the sensory epithelium of guinea-pig organ of Corti: subsurface cisternae and lamellar bodies in the outer hair cells. *Cell Tissue Res.* 229: 467-481.

¹¹⁴ Forge, A., et al. (1993). Structural variability of the sub-surface cisternae in intact, isolated outer hair cells shown by fluorescent labelling of intracellular membranes and freeze-fracture. *Hear. Res.* 64: 175-183.

¹¹⁵ Pollice, P. A. and W. E. Brownell (1993). Characterization of the outer hair cell's lateral wall membrane. *Hear. Res.* 70: 187-196.

¹¹⁶ Ikeda, K. and T. Takasaka (1993). Confocal laser microscopical images of calcium distribution and intracellular organelles in the outer hair cell isolated from the guinea pig cochlea. *Hear. Res.* 66: 169-176.

feature revealed by these dyes is that the cisternal system is lipophilic, implying some associated lipids; in turn this suggests a role for the lipids in separating a gas from its aqueous substrate via surface tension effects, as they do in the swim bladder¹¹⁷. The lipids could originate from within the cell itself (outer hair cells are able to synthesise lipids¹¹⁸) or from the nearby lipid-rich Hensen cells.

Another fluorescent lipophilic dye, FM1-43, is indicative of cell membrane turnover, and Meyer et al. (2001) found that it strongly stained Hensen's body¹¹⁹ in a guinea pig OHC. The dye cannot penetrate passive cell membranes, but when turnover (endocytosis) of membrane occurs, FM1-43 can be readily taken through into the interior of the cell. In an OHC, dye molecules enter the cell through its apical end, suggesting that the dye penetrates the cuticular pore (shown as the 'rudimentary kinocilium' in Fig. 8.12) and is carried to Hensen's body. This fits in with the authors' finding that the dye does not penetrate through the other possible route – the MET or mechanoelectric transducer channels of the stereocilia (at least when the MET channels are blocked)¹²⁰. The work by Meyer et al. therefore reveals a close association between Hensen's body and the cuticular pore, a relationship that will be detailed further below.

An important finding is that the cisternal system is essential for electromotility, and hence hearing. When the system is disrupted by high doses of salicylate¹²¹, motility disappears, along with hearing sensitivity, only to return when the drug is rinsed away. Salicylate enlarged the distances between the cisternal layers, and led to increased numbers of vesicles next to them.

¹¹⁷ Pelster (1995), p. 104.

¹¹⁸ Schacht, J. and H. P. Zenner (1987). Evidence that phosphoinositides mediate motility in cochlear outer hair cells. *Hear. Res.* 31: 155-160.

¹¹⁹ Meyer, J., et al. (2001). Pronounced infracuticular endocytosis in mammalian outer hair cells. *Hear. Res.* 161: 10-22.

¹²⁰ The entry of FM1-43 into hair cells has been investigated by a number of workers recently, and their somewhat contradictory results can be better understood once the presumed high permeability of the cuticular pore (and low permeability of the kinocilium) is taken into account. Thus, when MET channels were blocked [Meyer et al. (2001); Griesinger, C. B., et al. (2002). FM1-43 reveals membrane recycling in adult inner hair cells of the mammalian cochlea. *J. Neurosci.* 22: 3939-3952.], these workers concluded that FM1-43 does not enter via the stereocilia because blocking did not prevent dye entry; in contrast, other work concluded the opposite [Meyers, J. R., et al. (2003). Lighting up the senses: FM1-43 loading of sensory cells through nonselective ion channels. *J. Neurosci.* 23: 4054-4065.] because blocking did stop dye entry. The anomaly is resolved when one sees that the first workers used guinea pig cochleas – that have no kinocilia – so that blocking the MET channels still leaves the fontanelle route open, whereas the later work used frogs and mice, animals that have kinocilia instead.

¹²¹ Dieler, R., et al. (1991). Concomitant salicylate-induced alterations of outer hair cell subsurface cisternae and electromotility. *J. Neurocytol.* 20: 637-653.

A number of authors have noted the importance of the cisternal system and speculated on its function. As long back as 1955, Engström noted the distinctive regular layers, or lamellæ, beneath the outer membrane (and in Hensens body) and suggested that polarized molecules aligned within them might produce potentials when distorted, in this way explaining the origin of the cochlear microphonic. More recently, Brownell^{122,123} has tried to relate the ultrastructure of the cisterns to the necessary expansions and contractions of the cell wall, and mentioned electrostatic and electroosmotic mechanisms.

While these ideas have merit in understanding electromotility, they are secondary to the main point of this thesis: what is the key initial (or ‘adequate’) stimulus – bending of stereocilia or compression of a bubble within the cell body? If it is the latter, then the outstanding role of the cisternal system is providing compressibility. Let us calculate the volume of the cisternal system. A single Hensens body, with a diameter of 3 μm , has a volume of $1.5 \times 10^{-17} \text{ m}^3$, and there may be a handful of such organelles, but probably amounting to no more than 10^{-16} m^3 . Cisterns have a typical thickness of 0.5 μm , so the volume they occupy in a cell 10 μm in diameter and 50 μm long is about $5 \times 10^{-16} \text{ m}^3$. Take the volume of enclosed air to be half that, about $2 \times 10^{-16} \text{ m}^3$. If threshold sound pressure causes a reduction in volume of 2×10^{-8} , as calculated above, then this will produce a change in the volume of the cell of 10^{-24} m^3 (which, in terms of cell-sized units, is $10^{-6} \mu\text{m}^3$ or a cube with edges of 1/100th of micrometre – small, but not vanishingly so).

Do outer hair cells show compressibility? The common assumption is that they possess no compressibility^{124,125}, a move predicated on the idea that the cells are filled with water. When the cells expand and contract at acoustic frequencies, there is not enough time for water to pass in and out across the cell membrane, so the shape change must be isovolumetric – when the cell lengthens, its diameter narrows

¹²² Brownell, W. E. (1986). Outer hair cell motility and cochlear frequency selectivity. In: *Auditory Frequency Selectivity*, edited by B. C. J. Moore and R. D. Patterson (Plenum: New York).

¹²³ Brownell, W. E. and A. S. Popel (1998). Electrical and mechanical anatomy of the outer hair cell. In: *Psychophysical and Physiological Advances in Hearing*, edited by A. R. Palmer et al. (Whurr: London), 89-96.

¹²⁴ Iwasa, K. H. and R. S. Chadwick (1992). Elasticity and active force generation of cochlear outer hair cells. *J. Acoust. Soc. Am.* 92: 3169-3173. The measurements were made over timescales that allowed diffusion of water in and out of the cell, so they cannot be used to calculate compressibility, but they do indicate that the cell's geometry is such that volume changes will accompany length changes.

¹²⁵ Steele, C. R. (1990). Elastic behaviour of the outer hair cell wall. In: *Mechanics and Biophysics of Hearing*, edited by P. Dallos et al. (Springer: Berlin), 76-83.

accordingly. This can be expressed in terms of the Poisson ratio, σ , the ratio of the radius strain to the length strain. For an incompressible material, $\sigma = 0.5$ (so that for a cylinder the length must change twice as much as the radius), and we would expect measurements on individual OHCs to return such a value. Actual measurements¹²⁶ on an OHC gave a value of σ between 1.85 and 2.3, implying that the incompressibility assumption is wrong¹²⁷ (and that length changes must be accompanied by appreciable changes in axial and circumferential stresses and internal pressure¹²⁸). In actual fact, not too much credence can be put on reported measurements since the in vivo changes we are looking for are, as calculated above, in the region of parts in 10^8 , way below the levels detectable by standard measurement techniques. However, there are measurements on the whole cochlea which bear on the question, and these were discussed in §D 8.2/b. In §D 8.5 we look at the functional implications of a Poisson's ratio larger than 0.5.

How can an OHC detect an internal volume change of 10^{-24} m^3 ? There are two important features.

A. The first is that the outer hair cell, test-tube like, is constructed so as to resist pressure deformations. Brownell aptly describes the OHC as a pressure vessel^{129,130} or cylindrical hydrostat¹³¹, capped by a solid plate (the cuticular plate) and encircled by strong helically wound fibres that cross clockwise and anticlockwise like a reinforced garden hose. The actin fibres are set at an angle of 9–15° to the circumference, forming a cytoskeletal spring that, together with a rippled outside plasma membrane, makes it possible for the cell to undergo length

¹²⁶ Iwasa and Chadwick (1992).

¹²⁷ Allen, J. B. (2001). Nonlinear cochlear signal processing. In: *Physiology of the Ear (2nd ed.)*, edited by A. F. Jahn and J. Santos-Sacchi (Singular Thomson Learning: San Diego, CA), 393-442. [§3.2.2].

¹²⁸ Allen calculates, for example, that the observed cyclic length changes mean that internal fluid pressure must increase and decrease by a factor of about 3 during the cycle [his Eq. 30]. Interpreted at face value, the high Poisson's ratio implies that the cell is hypercompressible and has a negative elastic modulus. This possibility is discussed further in §§D 8.4/f and 8.5.

¹²⁹ Brownell, W. E. (1990). Outer hair cell electromotility and otoacoustic emissions. *Ear Hear.* 11: 82–92.

¹³⁰ Brownell, W. E. and W. E. Shehata (1990). The effect of cytoplasmic turgor pressure on the static and dynamic mechanical properties of outer hair cells. In: *Mechanics and Biophysics of Hearing*, edited by P. Dallos et al. (Springer: Berlin), 52–59.

¹³¹ Brownell and Popel (1998), *ibid.*, p. 89.

changes¹³². To increase rigidity, the cells are inflated to a hydrostatic pressure (turgor pressure) of about 1 kPa¹³³. This arrangement is shown in Fig. 8.12.

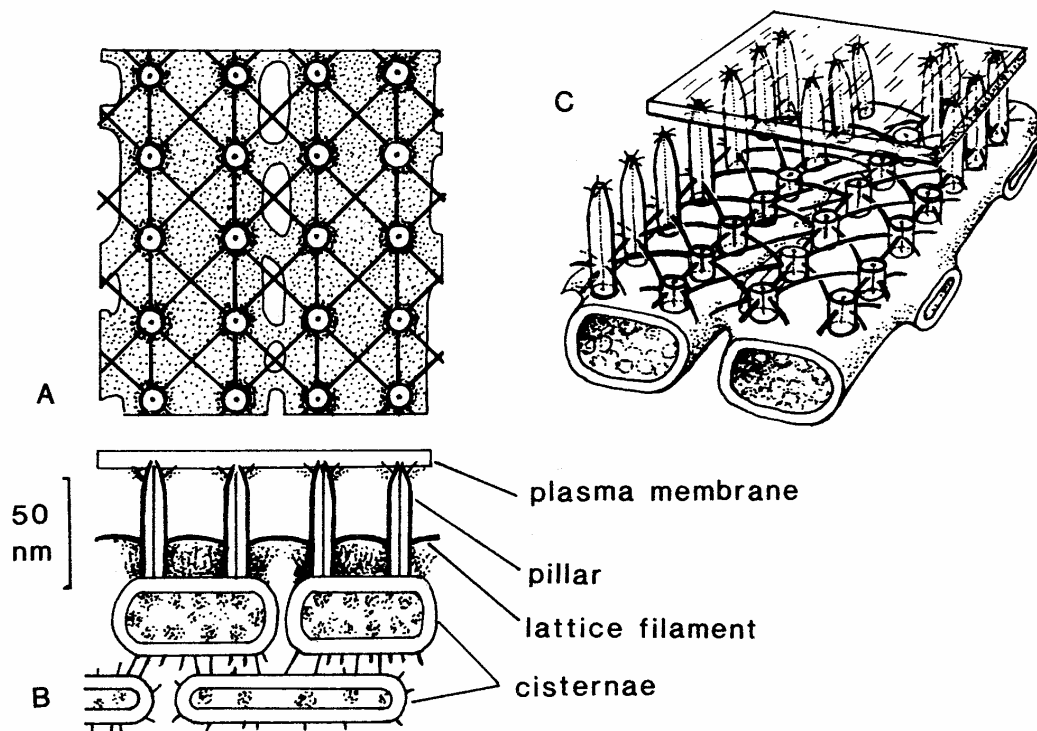


Fig. 8.12. The structure of the cell wall of an outer hair cell. The cross-ply structure, like a garden hose, adds rigidity when the cell is inflated with an internal pressure (of about 1 kPa). One place where the cell cannot resist external pressure is at the cuticular pore, which is covered only by the plasma membrane, and this is where intracochlear pressure is sensed. The unusual cisterns connect with Hensens body (both organelles are unique to outer hair cells) and may contain compressible material. [From Fig. 7 of Bannister et al. (1988)¹³⁴ and used with the permission of Elsevier]

B. The second is the presence of a small compliant spot on top of the cell, a hole in the cuticular plate anatomically associated with sensory capabilities. I suggest that this strategically placed organelle – the cuticular pore or fontanelle – is the pressure sensor.

¹³² Brownell and Popel (1998).

¹³³ Ratnanather, J. T., et al. (1993). Mechanical properties of the outer hair cell. In: *Biophysics of Hair Cell Sensory Systems*, edited by H. Duifhuis et al. (World Scientific: Singapore), 199–206. The pressure is metabolically controlled, and, because σ is greater than 0.5, an increase in pressure leads to a radial expansion and an axial contraction (Steele, 1990).

¹³⁴ Bannister, L. H., et al. (1988). The cortical lattice: a highly ordered system of subsurface filaments in guinea pig cochlear outer hair cells. *Prog. Brain Res.* 74: 213-219.

8.4/f *The fontanelle as a pressure sensor*

Whereas Fig. 8.11 shows the cuticular pore (the rudimentary kinocilium) in vertical section, a cross-section through the cuticular plate shows that it as a tiny circular hole. The cylindrical pore was first observed by Held early in the 20th century, and has been consistently seen by others^{135–139}, but its function is unclear. An image from Flock et al. (1962), traced in Fig. 8.13 below, shows the familiar array of stereocilia and a distinct hole, about 0.1 μm in diameter, near the vertex of the V. Flock calls it a cuticular pore; Hawkins calls it, rather aptly, a fonticulus or fontanelle¹⁴⁰.

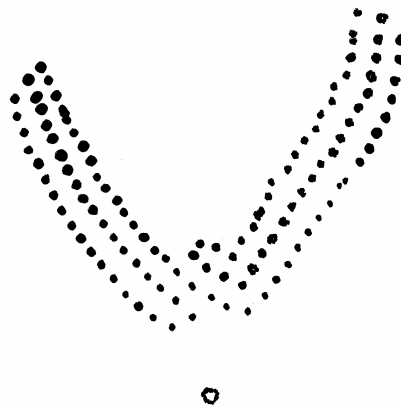


Fig. 8.13. Stereocilia and cuticular pore of an OHC (guinea pig) traced from Fig. 1 of Flock et al. (1962).

Flock and colleagues identify it as a basal body through its obvious similarity at high magnification (their Fig. 3a and shown below in Fig. 8.14A here) to the characteristic 9-fold symmetry of that familiar organelle, the basal body, at the base

¹³⁵ Engström, H., et al. (1962). Structure and functions of the sensory hairs of the inner ear. *J. Acoust. Soc. Am.* 34: 1356–1363.

¹³⁶ Hawkins, J. E. (1965). Cytoarchitectural basis of the cochlear transducer. *Symposia on Quantitative Biology* 30: 147–157.

¹³⁷ Flock, Å., et al. (1962). Morphological basis of directional sensitivity of the outer hair cells in the organ of Corti. *J. Acoust. Soc. Am.* 34: 1351–1355. Fig. 1.

¹³⁸ Wersäll, J. and P.-G. Lundquist (1966). Morphological polarization of the mechanoreceptors of the vestibular and acoustic systems. Second Symposium on the Role of the Vestibular Organs in Space Exploration, Washington, DC, NASA, SP-115, 57-72

¹³⁹ Sobkowicz, H. M., et al. (1995). The kinocilium of auditory hair cells and evidence for its morphogenetic role during the regeneration of stereocilia and cuticular plates. *J. Neurocytol.* 24: 633–653.

¹⁴⁰ Hawkins, J. E. (1976). Drug ototoxicity. In: *Handbook of Sensory Physiology*, vol. 5.3, edited by W. D. Keidel and W. D. Neff (Springer: Berlin), 707–748.

of kinocilia¹⁴¹. It is significant that most mammals, humans included, have a kinocilium during gestation, but it disappears at or shortly after birth, apparently becoming functionless. As its name implies, the kinocilium is a true cilium, with the well-known ‘9 + 2’ arrangement of 9 filaments arranged around 2 central ones. (Many researchers have noted that *stereocilia* are inappropriately named, as they are not cilia at all but modified microvilli, but the name seems too well established¹⁴².) Kinocilia have a clear motile function in certain animals in certain places – allowing unicellular animals to move about and allowing wax-laden dirt to be transported out of the ear canal, for example – but their association with stereocilia is unclear and in any event widely considered unimportant.

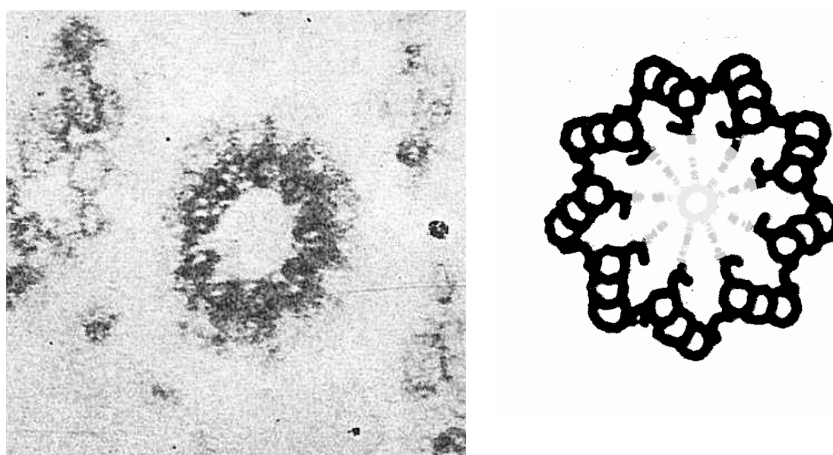


Fig. 8.14. Left: the cuticular pore, showing its 9-fold rotational symmetry; its inside diameter is about 0.1 μm . Right: image of a centriole, of similar size, enhanced to show detail. The hooks are dynein arms. [Cuticular pore from Fig. 3a of Flock et al. (1962) and reproduced with permission of the Acoustical Society of America; centriole from frontispiece of Wheatley (1982) and used with permission of Elsevier Science]

Engström, Ades, and Hawkins¹⁴³ seem to have been the only researchers who have taken the cuticular pore seriously. They point out its connection with the basal bodies of kinocilia, which in turn derive from the distinctive centrioles that all animal cells – from amoeba to human – display. Because of the major organising influence of centrioles in the growth and maintenance of cells, they suggest that the basal body

¹⁴¹ Clear views of the basal body in vertical section are depicted in Engstrom and Ades (1973), Figs 21 and 24.

¹⁴² Some have suggested the name *stereovilli* (Santi, P. A. (1988). Cochlear microanatomy and ultrastructure. In: *Physiology of the Ear*, edited by A. F. Jahn and J. Santos-Sacchi (Raven Press: New York), 173–199. p. 182).

¹⁴³ Engström et al. (1962).

“should be regarded as the essential excitable structure of the hair cell.” (ibid., p. 1363). Indeed, since they thought that stereocilia deflection was the adequate stimulus, the stereocilia must therefore not bend but act as stiff levers, transmitting force to the cuticular place and thereby excite the basal body. The idea received support in a review by Fex¹⁴⁴.

Engström and colleagues also pointed out that the pore is covered only by the plasma membrane of the cell and tends to bulge out, sometimes forming balloon-like protuberances during fixation¹⁴⁵. This indicates “a high degree of compliance”, and, if not artefactual, “must represent structures of great physiological importance.” The basal body is surrounded by a radiating pattern of many organelles – mitochondria, small vesicles, granules, and vacuoles – suggestive of a close functional and metabolic relationship; immunolabeling for tubulin, the major component of microtubules, gives an intense fluorescent spot at this point¹⁴⁶. Hillman noted the pliability of the membrane at the base of the kinocilium¹⁴⁷, and suggested that tilting of the kinocilium excited the cell by its plunger-like action at this point.

My proposal follows Engström and colleagues in accepting the essential importance of the basal body, but rather than having it stimulated by bending of stereocilia, I suggest it could be stimulated directly by intracochlear pressure. Although the kinocilium may be absent in humans after birth, it seems reasonable to suppose that all the machinery for operating it is still in place. That is, the cell has remodelled and refined an existing structure, not wantonly thrown one away. Specifically, I suggest this machinery has been adapted to operate in reverse, allowing it to act as a sensor. A subsequent literature search indicated a close approach to this idea, perhaps even the same: Hillman, pursuing the plunger analogy, concluded a 1971 study (with Lewis) of kinocilia movement at the cell surface of the

¹⁴⁴ Fex, J. (1974). Neural excitatory processes of the inner ear. In: *Handbook of Sensory Physiology*, vol 5.1, edited by W. D. Keidel and W. D. Neff (Springer: Berlin), 585-646. “For evolutionary reasons, it would seem more likely that the site of the mechano-transducer of mammalian cochlear hair cells would be in the membrane of the cuticle free region of the hair cell top, or very close to this membrane, rather than anywhere else” [p. 596].

¹⁴⁵ Lavigne-Rebillard, M. and R. Pujol (1986). Development of the auditory hair cell surface in human fetuses. *Anat. Embryol.* 174: 369–377.

¹⁴⁶ Steyger, P. S., et al. (1989). Tubulin and microtubules in cochlear hair cells: comparative immunocytochemistry and ultrastructure. *Hear. Res.* 42: 1-16.

¹⁴⁷ Hillman, D. E. (1969). New ultrastructural findings regarding a vestibular ciliary apparatus and its possible functional significance. *Brain Res.* 13: 407–412.

frog labyrinth¹⁴⁸ by referring to the mammalian auditory system and speculating (ibid., p. 418) that the “basal kinociliary remnant” could be a “diaphragm-like, pressure-sensitive spot”. The authors do not specify exactly what the cause of such a deformation might be, and the idea was not taken further. A subsequent major review¹⁴⁹ by one of the pair gives only passing reference to this work and fails to even mention the speculation.

Let us revisit the figure of 10^{-24} m^3 for the volume change inside an OHC at threshold. We see in Fig. 8.15 that the bore of the cuticular pore has a diameter of $0.1 \text{ }\mu\text{m}$, which means its area is about 10^{-14} m^2 . At threshold pressure, therefore, that volume change of 10^{-24} m^3 inside the cell will be accomplished by fluid flowing through this pore a distance of 10^{-10} m . Detecting such a threshold displacement seems relatively easy, as mammalian stereocilia are called on to sense a deflection of 10^{-10} to 10^{-11} m at threshold¹⁵⁰, and, even in crickets¹⁵¹, nerve impulses are produced when their *kinocilia* are deflected *at their base* by 10^{-12} m .

The reference to crickets provides a good example that kinocilia can act as sensors as well as motors. To understand how this can happen, and to give a clearer insight into the mechanism proposed here, we need to take a general survey of kinocilia and the basal bodies at their base.

8.4/g *Kinocilia, basal bodies, and centrioles*

A good starting point is a wide-ranging review¹⁵² by Flock in which he discusses sensory transduction in hair cells with a focus on the inner ear. Both

¹⁴⁸ Hillman, D. E. and E. R. Lewis (1971). Morphological basis for a mechanical linkage in otolithic receptor transduction in the frog. *Science* 174: 416–419.

¹⁴⁹ Lewis et al. *The Vertebrate Inner Ear* (1985).

¹⁵⁰ When extrapolations are made from much higher levels. Dallos, P. (1996). Overview: cochlear neurobiology. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 1–43. I would maintain that stereocilia are part of the cochlea’s high-level sound detection system and cannot respond to deflections of 10^{-11} m and tilts of 0.01° .

¹⁵¹ Thurm, U., et al. (1983). Cilia specialized for mechanoreception. *J. Submicrosc. Cytol.* 15: 151–155.

¹⁵² Flock, Å. (1971). Sensory transduction in hair cells. In: *Handbook of Sensory Physiology*, edited by W. R. Loewenstein (Springer: Berlin), vol. 5.1, 396–441. For the reader unfamiliar with the anatomical arrangement of kinocilia and stereocilia, reference to Fig. A2 may be helpful. Stereocilia are really modified microvilli and emerge in distinct arrays from the hair cell’s solid cuticular plate. Each hair cell usually has a single kinocilium that is strategically placed next to the stereocilia. The kinocilium is a true cilium, with a complex internal structure which in some cases allows it to move (hence the name). Both OHCs and IHCs bear them. The kinocilium is a complex, distinct system that does not emerge from the cuticular plate. In mammals, the kinocilium is lost at birth, inviting the question, *what does it do?*

stereocilia and kinocilia are given treatment. He considers what the adequate stimulus may be, and comes to the conclusion that the hair cell, in all organs, is basically a directionally sensitive displacement detector. Static pressure is considered as a stimulus at one point (*ibid.*, p. 400), but with no direct evidence in its favour, is put to one side. Engström's lever-action of stiff hairs, and excitation at the basal body, are mentioned as possibilities but a decision on the validity of these ideas must await improved knowledge of cellular mechanics since "the final mechanical transformer is probably of molecular dimensions" (p. 408). The 9-fold symmetry of the kinocilium and its basal body is set out, and its strange disappearance in adult mammals stated. The key question of the role of the kinocilia in transduction is tackled, and among some possibilities the best answer, to my mind, provided (p. 424): *that a kinocilium can act as a motile cilium in reverse*.

This idea was first proposed in 1958 by Gray and Pumphrey¹⁵³ after study of the tympanic organ of a locust¹⁵⁴. A micrograph of its sensory unit shows the distinctive '9 + 2' pattern seen in kinocilia, and Gray and Pumphrey suggested that a kinocilium can, through a reversed sense, play the part of a receptor. Lowenstein and Wersäll echoed the reverse transduction idea after examining the arrangement of kinocilia in the labyrinths of guinea pigs and rays¹⁵⁵. If cellular electricity can drive a motor, then all the parts exist for motion of the motor to generate an electrical signal^{156,157}.

Experiments leave no doubt that kinocilia can act as sensors, although this work has largely been confined to insects and molluscs. Thurm describes¹⁵⁸ how by slight modification of the ciliary shaft – removing dynein arms and adding some extra components – the cell can become sensory. In this way a stimulus can modulate the receptor current and depolarise the cell (producing excitation), or hyperpolarise it (producing inhibition). The outstanding common feature of this work is that the final stimulus is not bending of the hair, per se, but *pressure* (or force) exerted *at the base* of the hair, in the region of the basal body.

¹⁵³ Pumphrey being the same person whom Gold worked with earlier.

¹⁵⁴ Gray, E. G. and R. J. Pumphrey (1958). Ultra-structure of the insect ear. *Nature* 181: 618.

¹⁵⁵ Lowenstein, O. and J. Wersäll (1959). A functional interpretation of the electron-microscopic structure of the sensory hairs in the cristæ of the elasmobranch *Raja clavata* in terms of directional sensitivity. *Nature* 184: 1807–1808.

¹⁵⁶ Lewis et al. (1985) p. 126.

¹⁵⁷ Wiederhold, M. L. (1976). Mechanosensory transduction in "sensory" and "motile" cilia. *Annu. Rev. Biophys. Bioeng.* 5: 39–62.

¹⁵⁸ Thurm (1983).

Thus^{159,160}, if a cilium is made completely pliable, by application of a drug (chloral hydrate), they collapse and lie flat; nevertheless, pressure on the cell surface still produces a generator potential. Conversely, making the cilium completely rigid – so it is unable to bend – still allows potentials to be generated. Another relevant observation is that paramecium, who swim, and sense, using motile cilia, still show depolarising and hyperpolarising responses after removal of their cilia.

The focus therefore falls on the basal body. How can this organelle make the test-tube-like entity shown in Fig. 8.11 into a pressure transducer? There are no definite answers, but by assembling a few clues the following intriguing picture takes shape.

All cilia have at their base a characteristic 9-fold structure, the basal body, from which they grow. Unique among cell organelles, they have a constant size, shape, and ultrastructure¹⁶¹. The mystery comes from their close similarity, if not identity, to the other vital but enigmatic cell organelle, the centriole¹⁶². Centrioles, which come in matched pairs usually at right angles to each other, spring from the nucleus and play a major part in organisation, structure, polarity, growth, division, and death of cells¹⁶³. They are ubiquitous throughout the animal kingdom, indicating they have some vital function to perform. A suggestive image is that, like a spider in a web, centrioles sit at microtubular centres of the cell¹⁶⁴, surveying activity. Both sensory and non-sensory cells have centrioles, but in a sensory cell one centriole will migrate to its surface and grow a cilium, its partner usually nearby¹⁶⁵. Theories about centriole function, and the significance of the 9 arms, abound^{166,167}, but here I will briefly set out one model that provides a meaningful picture of what the sensory fontanelle could be doing.

¹⁵⁹ Alkon, D. L. (1983). The role of statocyst sensory cilia in mechanotransduction. *J. Submicrosc. Cytol.* 15: 145-150.

¹⁶⁰ Alkon, D. L. (1983). Sensory function of cilia. *J. Submicrosc. Cytol.* 15: 173-176.

¹⁶¹ Afzelius, B. A. (1983). Basal bodies in the immotile-cilia syndrome. *J. Submicrosc. Cytol.* 15: 111-114.

¹⁶² Wheatley, D. N. (1982). *The Centriole: a central enigma of cell biology*. (Elsevier: Amsterdam).

¹⁶³ Impressively, so-called killer cells use miniature spears to kill target cells, and the latter can survive such barbs until struck in the centriolar region (Afzelius, 1983, p. 112).

¹⁶⁴ Schliwa, M. (1992). Cell polarity and centrosomes. In: *The Centrosome*, edited by V. I. Kalnins (Academic: San Diego), 331-351.

¹⁶⁵ Wersäll, J., et al. (1965). Structural basis for directional sensitivity in cochlear and vestibular sensory receptors. *Symposia on Quantitative Biology* 30: 115-132. Fig. 31.

¹⁶⁶ Albrecht-Buehler, G. (1992). Function and formation of centrioles and basal bodies. In: *The Centrosome*, edited by V. I. Kalnins (Academic: San Diego), 69-102.

¹⁶⁷ Wheatly highlights one scientist as saying “Biologists have long been haunted by the possibility that the primary significance of centrioles has escaped them” (p. 185).

According to Brinkley and Stubblefield¹⁶⁸, the entity we see in Fig. 8.14 is a motor with rotating blades. The blades are angled from one end of the centriole to the other, to give the simplified turbine-like structure seen in Fig. 8.15. In this figure, the inner dynein arms (Fig. 8.14) that presumably drive the turbine have been omitted. An attractive feature of the turbine model is the straightforward way by which flow through the core of the system might cause the blades to rotate.

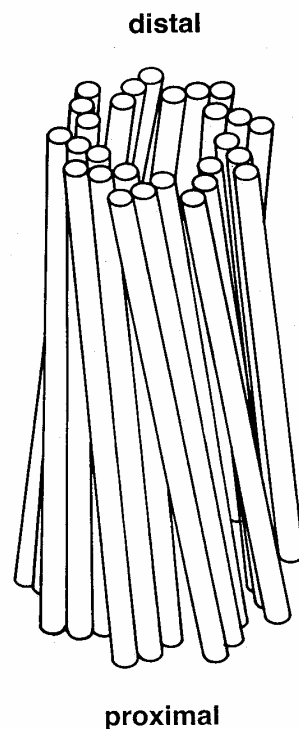


Fig. 8.15. Simplified structure of a centriole or basal body showing the turbine-like arrangement of the blades. [From Albrecht-Buehler (1992) and used with the permission of Academic Press]

A slightly different formulation was put forward by Bornens¹⁶⁹, who considered that the centriole may act more like a stepper motor so that portions of the device either (a) rotated or (b) oscillated backwards and forwards a number of degrees in an electrical field between the triplets. In either way, a torsional oscillator of fixed vibrational frequency might result, allowing the centriole to act as a pacemaker for the rest of the cell. Any slight change in the device's mechanical environment could affect its oscillation frequency and be detected by comparison

¹⁶⁸ Brinkley, B. R. and E. Stubblefield (1970). Ultrastructure and interaction of the kinetochore and centriole in mitosis and meiosis. *Adv. Cell Biol.* 1: 119-185.

¹⁶⁹ Bornens, M. (1979). The centriole as a gyroscopic oscillator. Implications for cell organization and some other consequences. *Biol. Cellulaire* 35: 115-132.

with the frequency of the companion centriole¹⁷⁰. The unexpected finding of silicon in centrioles may be coincidental but it highlights the possibility of electrical interactions.

The idea that the basal body of outer hair cells could be an electrical motor or, acting in reverse, a rotational sensor is given credence by consideration of a comparable structure in motile bacteria. These microorganisms propel themselves using a rotating flagellum, and ultrastructural studies show it is a miniature electric motor, complete with stator, rotor, drive shaft, bushing, universal joint, and helical propeller^{171,172}. Notably, the motor can rotate well into the auditory range, at up to 1700 revolutions per second¹⁷³. Unifying the picture we have been constructing, the rotary motor originates from the cell's basal body. A micrograph and diagram of such a rotational motor are shown in Fig. 8.16.

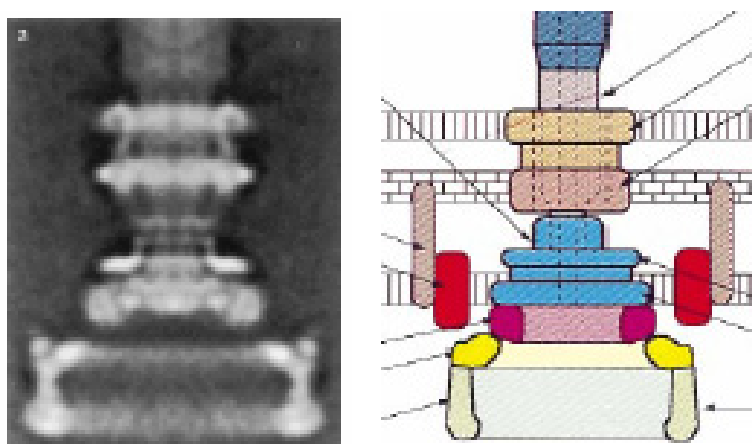


Fig. 8.16. A rotary motor, 45 nm in diameter, located at the basal body of a bacterium's flagellum. At left is a micrograph of the basal body in cross-section, showing the multiple rings of the stepper motor. At right is a schematic diagram (labels omitted) illustrating the major molecular components. A similar motor, minus the flagellum, could occur at the basal body of an outer hair cell, and might operate in reverse as a sensor of pressure: fluid flow through the pore might induce rotation. [From Thomas et al. (1999) and Namba and Vonderviszt (1997), with permission of the National Academy of Sciences USA and Cambridge University Press]

If we identify the centriole of the outer hair cell as a flagellum-less version of this motor, configured to act as a sensor, then the forces acting on it are minute. If the

¹⁷⁰ In this connection, we may even consider quantum mechanical effects, as in paired detectors set at right angles which sense electron spin (Stern–Gerlach effect).

¹⁷¹ Namba, K. and F. Vonderviszt (1997). Molecular architecture of bacterial flagellum. *Q. Rev. Biophys.* 30: 1-65.

¹⁷² Thomas, D. R., et al. (1999). Rotational symmetry of the C ring and a mechanism for the flagellar rotary motor. *Proc. Natl. Acad. Sci. U. S. A.* 96: 10134-10139.

¹⁷³ Magariyama, Y., et al. (1994). Very fast flagellar rotation. *Nature* 371: 752.

intracochlear pressure at threshold is 0.5 mPa, as before, this would produce a force on the sensory pore of 5×10^{-6} pN. In comparison, the force required for activation of a typical mechanosensitive ion channel¹⁷⁴ is 10–20 pN, so in these terms the oscillator system must operate with orders of magnitude greater sensitivity. Is this realistic? A legitimate doubt may be raised here, although we point out that there are possibilities for resonance – outer hair cells are graded in length from base to apex¹⁷⁵, suggesting something like a Helmholtz resonator – and there are also two positive feedback mechanisms that might be expected to improve sensitivity.

The first is mechanical, and relates to the observation that the Poisson ratio for the OHC is more than 0.5. This means that as the electromotility mechanism is engaged and the cell changes length, the volume will tend to change accordingly. For a hyperpolarisation (say) induced by initial increase in pressure on the sensory pore, the effect is towards increasing the volume – which will decrease the internal pressure and cause an increased pressure difference across the sensory pore; the result will be increased hyperpolarisation – a positive feedback effect. Depolarisation (induced by a transient decrease in intracochlear pressure) will lead to an opposite sequence, but producing positive feedback once again. The positive feedback loop acts so as to make the cell's contents appear more compressible than under static conditions. In effect, the cell contains not air but super-compressible or rarefied air, a conclusion with which the ancient Greeks would agree (see Chapter I1). The idea is revisited below (§D 8.5).

The second positive feedback loop is electrical. Electromotility causes OHCs to change length in accordance with imposed electrical fields¹⁷⁶; in the same way, the cochlear microphonic – the electrical potential generated by collective outer hair cell activity – might induce further length changes in those cells. The essential role of the cochlear microphonic in affecting the responses of hair cells (that is, it is not just an ineffectual by-product of cochlear action, an epiphenomenon) was first put forward

¹⁷⁴ Morris, C. E. (2001). Mechanosensitive ion channels in eukaryotic cells. In: *Cell Physiology Sourcebook: A Molecular Approach, Third Edition*, edited by N. Sperelakis (Academic Press: New York), 745-760. (p. 749).

¹⁷⁵ Pujol, R., et al. (1992). Correlation between the length of outer hair cells and the frequency coding of the cochlea. In: *Auditory Physiology and Perception (Advances in the Biosciences volume 83)*, edited by Y. Cazals et al. (Pergamon: Oxford), 45-51.

¹⁷⁶ Brownell, W. E. (2002). On the origins of the outer hair cell electromotility. In: *Hair Cell Micromechanics and Otoacoustic Emission*, edited by C. I. Berlin et al. (Delmar Learning (Singular Publishing): Clifton Park, NY), 25-47.

by Davis¹⁷⁷, and was taken up by Gold and a number of others since. Here, we can see that the electrical voltages generated by sensory transduction in the hair cell could feed back to it in a way that led to additional length changes and voltages, again a positive feedback loop. Sharks and other electrosensitive fish can detect voltage gradients¹⁷⁸ of less than $0.5 \mu\text{V}/\text{m}$, presumably by using this mechanism. These animals have specialised hair cells modified for electrical sensing; interestingly, these cells lack stereocilia, but retain a kinocilium¹⁷⁹.

Whether these refinements to the proposed scheme are sufficient to improve, to detectable levels, its sensitivity to direct pressure stimuli is a complex matter and beyond resolution here. Nevertheless, I take the position that there are a sufficiently wide range of indicators to suggest that the pressure-detection scheme may be physically possible; I hope I have set out the reasoning clearly enough for the reader to take seriously this somewhat unorthodox possibility. Further reinforcement of it is presented in the Appendix.

8.5 Towards a functional integration

We have described the outer hair cell as a pressure vessel, a proposition that provides a functional role for the cross-ply reinforcement of its cell wall as shown in Fig. 8.13. It also accommodates the finding that the cell wall supplies about 4 times greater tether force – is about 4 times stiffer – than neighbouring cells¹⁸⁰. Moreover, although the cell wall is stiff, and can resist internal (and external) pressure changes, its structure allows it – like a garden hose – to change length.

Another characteristic of outer hair cells is that their Poisson ratio appears to deviate from the 0.5 value expected if their contents were incompressible. This fact (in some measurements, the ratio appears to be between 1.85 and 2.3) was used to argue that the cell in fact contains an air bubble (§D 8.4/e). Extending the argument raised in §D 8.4/f, a Poisson ratio greater than 0.5 implies that the volume gets larger

¹⁷⁷ Davis et al. (1934).

¹⁷⁸ Zakon, H. H. (1988). The electroreceptors: diversity in structure and function. In: *Sensory Biology of Aquatic Animals*, edited by J. Atema et al. (Springer: New York), 813-850.

¹⁷⁹ Zakon (1988) // Kalmijn, A. J. (2000). Detection and processing of electromagnetic and near-field acoustic stimuli in elasmobranch fishes. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 355: 1135-1141.

¹⁸⁰ Zelenskaya, A., et al. (2005). Evidence for a highly elastic shell-core organization of cochlear outer hair cells by local membrane indentation. *Biophys. J.*

as the cell gets shorter, meaning that the air bubble appears as if it has *negative compressibility*¹⁸¹. As flagged in §D 8.4/e, the measurements may be suspect because they were done over extended periods with pipettes penetrating the cell, a situation which may not represent the actual dynamic situation.

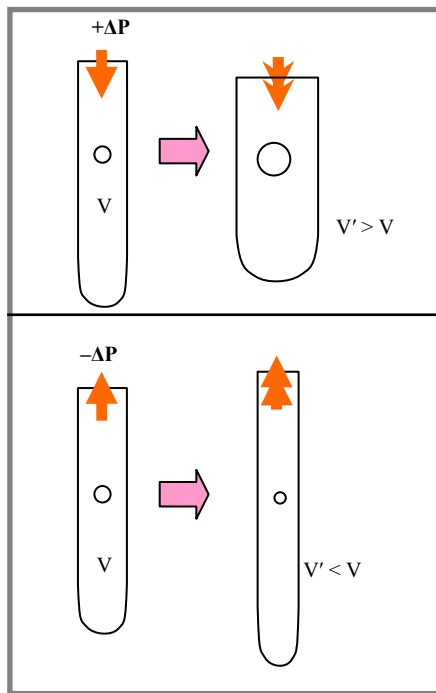


Fig. 8.17. Consequences of a Poisson ratio greater than 0.5. When positive pressure (top) is applied to the cell, inward flow occurs through the cuticular pore. This stimulus creates an electrical potential that leads, via electromotility, to contraction of the length and expansion of the radius – the volume expands. Because water in the cell is incompressible, the air bubble must expand, and the expansion will also tend to draw more flow through the pore (the pressure difference across the pore has increased), giving *positive feedback*. Conversely, when the outside pressure decreases (bottom), the flow is oppositely directed, and electromotility causes the cell to lengthen and its volume decrease, this time decreasing the size of the bubble but again *increasing the initial flow* through the pore. Overall, a pressure increase outside has led to an increase in internal volume, and a negative one to a decrease – therefore the cell displays a *negative compressibility*, and instead of absorbing energy it emits it. In response to oscillating intracochlear pressure, the cell oscillates in volume and radiates energy back into the ear canal.

Allen (2001) notes how the maximum physical value of Poisson's ratio is normally 0.5, but he gives an explanation of how complex cell properties could lead to larger values. If the dynamic value exceeds 0.5, it produces interesting

¹⁸¹ Mathematically, the situation can be described, due to N. H. Fletcher, as follows. For a material with Poisson ratio > 0.5 , its length necessarily decreases when external pressure is applied. Thus, for a cell of length L , it becomes $L(1-d)$. The Poisson ratio, s , is the increase in radius compared to decrease in length, so the radius R becomes $R(1+sd)$ and the cross-sectional area A becomes, neglecting second-order terms, $A(1+2sd)$. The volume V therefore becomes V' , where $V' = V(1-d)(1+sd)^2 = V(1-d)(1+2sd) = V[1+(2s-1)d]$. So if $s > 0.5$, $V' > V$ and the cell expands under external pressure.

implications. The diagram (Fig. 8.17) explains how a large Poisson ratio in an outer hair cell can lead to a *positive feedback system*.

A negative compressibility would show we are dealing with a thermodynamically unstable system. It was mentioned earlier that biological materials with negative compressibilities are known¹⁸², but little work has been done in this field. While we cannot exclude these exotic materials in outer hair cells, it is difficult to go past air as a simple and highly compressible substance. If the actual ratio exceeds 0.5, the compressibility will exceed that of air – something that in this case could perhaps be called rarefied air. In the next chapter further synthesis will be presented that sets out how this pressure detection could work electrophysiologically and how further physical principles could be used to further increase the sensitivity of the system.

¹⁸² See footnote 34. The reference cited is followed by a reply in which (its footnote 3) it is calculated that a negative compressibility requires a Poisson ratio exceeding unity.

Evidence and synthesis

9.1 Synthesis

- 9.1/a Outer hair cells as dual detectors
 - Pressure detection and transduction currents
 - The silent current
- 9.1/b Cancellation effects at 60–80 dB SPL
- 9.1/c Auditory nerve notches
- 9.1/d Tip drive and tail drive
- 9.1/e Psychophysical cancellation
- 9.1/f Dual components of the cochlear microphonic
- 9.1/g Two components in OHC receptor potentials?
- 9.1/h OHC mechanical responses differing by 180°
- 9.1/i Transduction confined not just to tip links
- 9.1/j Different membrane potentials between OHC rows
- 9.1/k Controlling the SAW resonator gain
- 9.1/l Two frequency maps and the half-octave shift

9.2 Pushing the limits of sensitivity

- 9.2/a Thermal and quantum limits
- 9.2/b Hair bundle or cell body as power source?
- 9.2/c Hopf oscillators

9.3 General evidence favouring the SAW model

- 9.3/a Anti-phase motion between rows
- 9.3/b Radial waves
- 9.3/c Fluid jet stimulation

9.4 Evidence against the SAW model

- 9.4/a Little leakage between ears
- 9.4/b Presence of the round window

9.5 Unanswered questions

The broad details of the SAW model were presented in chapter M4 of this thesis. The model explained how, by responding to the pressure wave, fast responses, far quicker than are possible on the traveling wave model, are possible. This was followed by three results chapters (R5–R7) that provided some analysis and evidence that the model was feasible. In this second discussion chapter we seek further integration and evidence from the literature that outer hair cells are dual detectors, able to sense pressure using their cuticular pore, where intricate molecular machinery is known to reside, and displacement via their stereocilia. A feasible electrophysiological model for this sensitivity is presented (§D 9.1/a), and it is speculated that the outer hair cells’ silent current is modulated by pressure. An integration with known cochlear mechanics, including cancellation effects, efferent effects, and multiple frequency maps, is presented. Then techniques are examined (§D 9.2) that could allow this pressure-activated current to be so sensitive that the cochlea approaches theoretical limits of detection. Finally, evidence for (§D 9.3) and against (§D 9.4) the picture are provided.

In brief, the picture presented here is that there is more to transduction than just stereocilia and gating by tip links.

9.1 Synthesis

9.1/a Outer hair cells as dual detectors

This section sets out how outer hair cells could be dual detectors, able to sense both displacement, via deflection of their stereocilia, and pressure, via movement at the cuticular pore. The former is well known, but the latter is a speculation that could account for the low-level detection of sound by the cochlea. The idea is that the outer hair cells are sensitive to the fast pressure wave, and that this process proceeds along resonance principles. It involves the well known “silent current” – which continually flows through the cell, even at rest. It is presumed that an appreciable fraction of this current flows through the cuticular pore and is modulated by pressure across it. Pressure may, through membrane stretch, directly

open these channels, but a more sophisticated and sensitive mechanism is proposed: a rotary electric motor operating in reverse. Such a motor has been identified at the basal body of motile bacteria, and the supposition is that the motor, minus flagellum, sits at the cuticular pore of outer hair cells and is activated by minute pressure fluctuations.

Although the account is not complete, it builds on the major structural features allowing the outer hair cell to detect pressure, as set out in Chapter D8, and adds details of the hypothetical sensor mechanism residing at the cuticular pore. The pressure-activated current is out of phase with the standard stereocilia-mediated current, leading to an explanation of known cancellation effects; furthermore, the current is voltage sensitive, so that it operates differently in OHC1 and 3 compared to OHC2, a situation maximising the efficiency by which the SAW resonator is excited. The material below begins by setting out how this sensor may be activated and its output converted into a receptor potential.

Pressure detection and transduction currents

It was mentioned earlier (§D 8.4/g) that a kinocilium can be either a sensor or an effector, and that in the case of the outer hair cell it is a sensor in which the cilium has dropped off at birth and left the sensory apparatus (the basal body or centriole) at the base. We do not therefore have to introduce anything basically new into what is known about cell biology and transduction in general (insects, for example, are well known to use kinocilia for sensing vibration); rather, the question is how *mammals* have adapted existing kinocilium machinery and turned it into a highly sensitive pressure detector.

The silent current

The simplest way of describing the electrical signaling process in the mammalian outer hair cell is to recognise that there are two transducer currents flowing into the cell through its apical end. One is the current associated with

deflection of its stereocilia, probably a K^+ current carried by the TRPA1 channel¹. The second is another well known, but largely unappreciated, K^+ current called the “silent current”, and the hypothesis put forward here is that a large fraction of the silent current flows through channels in the cuticular pore (rather than through stereocilia) and that this current is *modulated by sound-induced intracochlear pressure*. The major in-flowing currents of interest, entering the cell through its cuticular plate, are shown in Fig. 9.1.

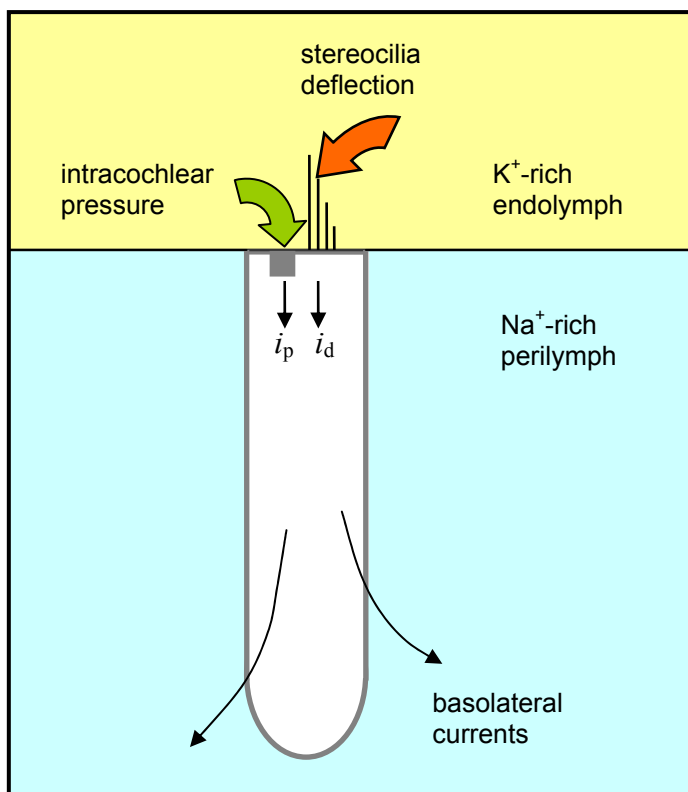


Fig. 9.1. Two transduction currents in an outer hair cell. One, i_d , is the current through the stereocilia caused by deflection. The other, i_p , is a standing current (the “silent current”) flowing through the cuticular pore and this is hypothesised to be modulated by intracochlear pressure; it is more sensitive than the other, but saturates at about 60 dB SPL. In response to a sound stimulus, the two currents have opposite phases.

Of course, there are numerous ionic currents – a “Babel-like confusion”² – carrying a balancing amount of current out of the cell through its basolateral membrane. These exiting currents preserve the homeostatic balance of the cell but

¹ Corey, D. P., et al. (2004). TRPA1 is a candidate for the mechanosensitive transduction channel of vertebrate hair cells. *Nature* 432: 723-730.

² Kros, C. J. (1996). Physiology of mammalian cochlear hair cells. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 318–385. [p. 376]

could also be involved in sensing. Overviews of these various currents are detailed in a number of reviews^{3,4,5}.

The silent current is the equivalent of the dark current in retinal cells. Just as an energetic standing current of sodium ions is sustained in rods in darkness, an equivalent standing current, appropriately termed the silent current by Brownell^{6,7}, flows through outer hair cells in silence. Brownell estimates the silent current to be as large as 500 pA per cell, whereas the transducer current in outer hair cells appears surprisingly small, about 10–110 pA⁸. The question is *why the cells should expend so much metabolic energy maintaining a current that doesn't appear to do anything*. One answer is that it improves system linearity, allowing for a stochastic opening and closing of ionic channels even at rest. That may be so, but it doesn't explain the striking disparity between the transduction current and the silent current. Another reason has been given by Ospeck and colleagues in terms of providing negative resistance (see §D 9.2/c), and it is in this context that I propose the refinement concerning the silent current: in brief, this large standing current, flowing through the cell's cuticular pore, is modulated by intracochlear pressure. Rather than a *silent* current, a more apt description may be that it is a *soft* (as in low sound intensity) current.

The result is two currents: a pressure-sensitive (soft or piano) current flowing through the cuticular pore and another (loud or forte) current flowing through the stereocilia. The latter is the well-studied transduction channel opened by tip links, and operates at moderate and high sound pressure levels, whereas the companion pressure-modulated signal is far more sensitive and operates below about 60 dB SPL. The first, stimulated by stereocilia deflection, can be considered a detector of the traveling wave; the second, triggered by intracochlear pressure variations, operates on resonance principles. The channels in the cuticular pore may be opened directly by pressure acting across the membrane (that is, by stretch), or they may be linked to

³ Kros (1996).

⁴ Ashmore, J. F. (1988). Ionic mechanisms in hair cells of the mammalian cochlea. *Prog. Brain Res.* 74: 3-9.

⁵ Ashmore, J. F. and F. Mammano (2001). Can you still see the cochlea for the molecules? *Curr. Opin. Neurobiol.* 11: 449-454.

⁶ Brownell, W. E. (1982). Cochlear transduction: an integrative model and review. *Hear. Res.* 6: 335-360.

⁷ Zidanic, M. and W. E. Brownell (1990). Fine structure of the intracochlear potential field. I. The silent current. *Biophys. J.* 57: 1253-1268.

⁸ Meyer, J., et al. (1998). Evidence for opening of hair-cell transducer channels after tip-link loss. *J. Neurosci.* 18: 6748-6756.

the turbine-shaped centriole, as depicted in Fig. 8.13, to give a mechanical advantage.

The two currents sum inside the cell, and produce a receptor potential, which, through electromotility, causes cellular length variations. These minute motions are the input to the SAW resonator mechanism and embody the cochlear amplifier. The two currents are out of phase with each other: inward motion of the stapes, causing an increase in intracochlear pressure, turns off the silent current and causes hyperpolarisation of the cell; at the same time, inward stapes motion causes deflection of the stereocilia away from the cochlear axis and causes depolarisation. The pressure-sensing mechanism is the more sensitive, and operates at low sound pressure levels (0–60 dB SPL), whereas stereocilia deflection operates at levels above that⁹. Clearly, at some intermediate level, the two currents will cancel, and observations consistent with this are seen (see following sections).

Again, Brownell's comparison with the dark current is apt, for increases in light intensity lead to a decrease in the current just like his observations that increases in low sound pressure levels lead to a decrease in the silent current. (Brownell, 1982, p. 340). The difference is that the dark current is carried by sodium ions, whereas the silent current is most probably carried by potassium ions. Brownell supposes that the purpose of the silent current is to provide a route for electrotonic interaction between OHCs and IHCs, but I envisage a fluid-mechanical interaction where the output of the OHC standing wave (the cochlear amplifier) is sent, via squirting waves, to the IHCs.

Brownell's paper also turns attention to Hensen bodies, subsurface cisterns, spaces of Nuel, the Wilson hair cell swelling model¹⁰, kinocilia, and the tectorial membrane; in highlighting many features important to the SAW model it offers a valuable array of references.

The following sections provide support for the piano-forte model and a consideration of what ion channel may be modulated directly by pressure is given in the Appendix.

⁹ That is, there is a threshold at about 60 dB SPL below which the whole partition effectively ceases to be displaced and stereocilia fail to bend; however, a pressure signal can still be reliably detected at the cuticular pore, although it saturates at about 60 dB SPL.

¹⁰ He calculates (p. 250) that a net change of 100 synaptic vesicles would result in an OHC volume change of 0.5%.

9.1/b Cancellation effects at 60–80 dB SPL

The clearest cancellation effect comes from direct observations of the basilar membrane at the base of the chinchilla cochlea¹¹. In that work, Rhode and Recio found that the response of the membrane to a tone exhibited sharp notches at particular frequencies and amplitudes (30–90 dB SPL). In their Fig. 11 they investigated a notch at 11.5 kHz and 80 dB SPL, and found that it appeared to be caused by interference between two sources, each with a different delay. Their figure is reproduced below (Fig. 9.2, left) and illustrates that when a 30-ms tone burst begins, one of the sources dominates and a large-amplitude (10 nm) motion of the basilar membrane is seen, but this is soon cancelled by a second source and the amplitude reduces to 1 or 2 nm. When the tone burst ends, another imbalance occurs and the amplitude momentarily builds again to more than 10 nm. Expansion of the time scale reveals (Fig. 9.2, right) that the delay between the two sources is about 9 cycles, and data not shown here reveals that they are 180° out of phase.

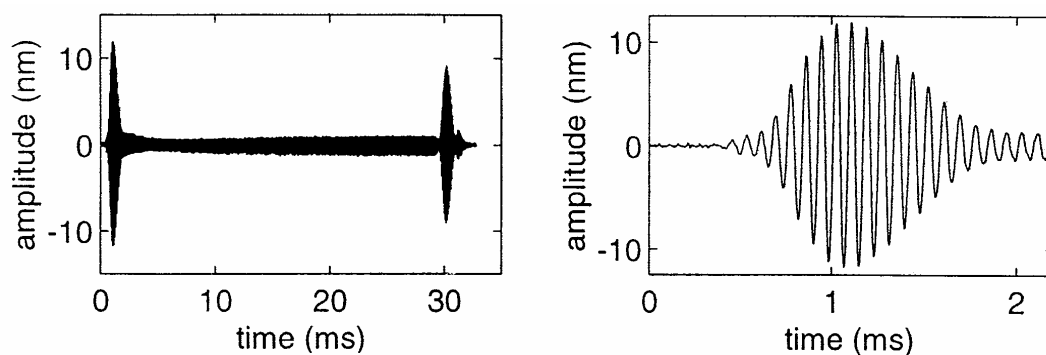


Fig. 9.2. Two sources in the cochlea, and their cancellation. When the levels and frequency are set correctly, deep interference notches are apparent in basilar membrane responses. This figure, adapted from Fig. 11 of Rhode and Recio (2000), shows the basilar membrane responses of a chinchilla when stimulated with an 11.5 kHz tone burst at 80 dB SPL, conditions producing a deep notch in the standing response. However, a tone burst 30-ms long shows that the beginning and end of the stimulus escape cancellation (left), and magnification of the time axis (right) reveals that there is about a 9-cycle delay between the two presumed sources. (Data not shown here confirms that the waveform at the 30 ms point is 180° out of phase with that at 0 ms.) [Reproduced with permission of the Acoustical Society of America]

¹¹ Rhode, W. S. and A. Recio (2000). Study of mechanical motions in the basal region of the chinchilla cochlea. *J. Acoust. Soc. Am.* 107: 3317-3332.

It is my contention that the first source is the immediate response to the fast pressure wave (henceforth the fast wave), and that the second source, occurring about 9 cycles later, is the delayed response to the traveling wave. This leads naturally to the position that there are two independent frequency maps in the cochlea, one contributed by the SAW mechanism, and another contributed by the traveling wave, a proposition that is examined in §D 9.1/m.

The Rhode and Recio paper actually makes mention of the interaction of fast waves and traveling waves, but no clear model is set forth. They say (p. 3326) that the notches they saw depended on a functional cochlear amplifier, and were not seen upon death of the animal. They searched for, but failed to see, any radial phase changes on the basilar membrane, but the use of reflective beads 25 μm in diameter would rule out the observation of short-wavelength squirting-wave interactions between rows of OHCs.

A defining paper¹² when considering any fast wave being involved in audition is that of Cooper and Rhode (1996). This work recognised that the fast wave could produce perceptible effects in the cochlea; however, it interpreted them as artefacts and secondary to the traveling wave. The fast wave was seen as producing motion at the fluid–air interface when a hole was drilled in the cochlea (to observe the basilar membrane), and in this way it interfered with observations. It was not considered that the fast wave could be *responsible* for the basilar membrane motion through its effect on outer hair cells. Following this same interpretation, later work from the Tübingen group^{13,14,15} separated the fast and slow components and *subtracted* the former from their recordings of basilar membrane motion because they believed the fast wave was an artifact of opening the cochlea and “contaminated” the vibration response (Hemmert et al. 2000a, p. 165). Interestingly, they report (Hemmert et al. 2000b, p. 2294) that “uncorrected frequency responses suggested a complicated 3D vibration pattern in which the relative motion between RL and TM appeared much more pronounced than for the slow component alone”.

¹² Cooper, N. P. and W. S. Rhode (1996). Fast travelling waves, slow travelling waves and their interactions in experimental studies of apical cochlear mechanics. *Auditory Neuroscience* 2: 289-299.

¹³ Hemmert, W., et al. (2000). Characteristics of the travelling wave in the low-frequency region of a temporal-bone preparation of the guinea-pig cochlea. *Hear. Res.* 142: 184-202.

¹⁴ Zinn, C., et al. (2000). Evidence for active, nonlinear, negative feedback in the vibration response of the apical region of the in-vivo guinea-pig cochlea. *Hear. Res.* 142: 159-183. [section 2.7]

¹⁵ Hemmert, W., et al. (2000). Three-dimensional motion of the organ of Corti. *Biophys. J.* 78: 2285-2297.

The Cooper and Rhode paper certainly provides firm evidence that the fast wave can give rise to artefacts. However, in not considering that the fast wave may actually be the *source* of the slow wave (through OHC stimulation), subtracting all trace of it may be an overreaction; the uncorrected situation may, in some measure, provide a view of how the outer hair cells are responding. In particular, the fast wave may dominate cochlear mechanics at low sound pressure levels, as some of the Cooper and Rhode data suggest¹⁶. The Tübingen group sometimes observed that the amplitude of the fast component exceeded that of the slow (Hemmert et al. 2000a, p. 191–2), and that subtraction did not always get rid of interference notches (p. 192).

Notches in the basilar membrane's mechanical response have also been observed in the apex of the chinchilla cochlea, and again it was accompanied by a rapid 180° phase change somewhat below the characteristic frequency at about 80 dB SPL. The waveform was similar to that seen by Rhode and Recio (2000), although in this case the notch was at 1.2 kHz and the delay between the two interacting stimuli was about 3 or 4 cycles¹⁷.

Notches are also observed in distortion product emissions in humans¹⁸ and cats¹⁹. On this basis, Mills (1998) suggested that there are two DPOAE sources: one due to an active mechanism at low sound pressure levels and another passive one dominating at high levels. The two are opposite in phase and lead to cancellation at about 65 dB SPL. Recently the two-source model has been subject to criticism²⁰, and although attractively simple, there are phenomena it cannot explain. Additional discussion of DPOAEs was presented in Chapter R7, where distortion was seen to arise from the interaction of a radial and oblique squirting wave. Since distortion is present at all sound pressure levels, it also seems possible that the distortion component could in fact cancel a traveling wave component, as Mills suggests.

¹⁶ Thus, extrapolation of the high level data in Fig. 5 (lower) shows a small excess of basilar membrane motion at 35 and 45 dB SPL, and the “unusual polarity” of the fast responses is described as “particularly problematical” (p. 297).

¹⁷ Fig. 8, p. 111.

¹⁸ Mills, D. M. (1998). Origin and implications of two “components” in distortion product otoacoustic emissions. In: *Otoacoustic Emissions: Basic Science and Clinical Applications*, edited by C. I. Berlin (Singular: San Diego), 85–104.

¹⁹ Fahey, P. F. and J. B. Allen (1997). Measurement of distortion product phase in the ear canal of the cat. *J. Acoust. Soc. Am.* 102: 2880–2891.

²⁰ Liberman, M. C., et al. (2004). Otoacoustic emissions without somatic motility: can stereocilia mechanics drive the mammalian cochlea? *J. Acoust. Soc. Am.* 116: 1649–1655. [p. 1653]

9.1/c Auditory nerve notches

Cancellation notches are well known in auditory fibre recordings, where they have become known as “Nelson’s notch” after the researcher (Nelson Kiang) who first recorded them. A good illustration of the notch²¹, and of how deep it can be, is found in Fig. 3 of Allen (1977). As Allen points out, it is noteworthy that the notch is accompanied by a phase shift of 180°, and he describes the situation in terms of a model where “pressure” and “displacement” terms cancel (although it is a *pressure difference* he is thinking of).

Many interference notches are also evident in auditory nerve transfer functions²². A more general effect is that the firings of nerve fibres jump in phase by 180° as intensity increases, leading to two populations in the rate–intensity function. This phenomenon, which has no clear micromechanical explanation, has become known as “peak splitting”^{23,24,25,26} and the split typically occurs at 70–90 dB SPL. One paper in which a synthesis is made²⁷ calls for two excitations: one sharply tuned and highly sensitive and a second broadly tuned and relatively insensitive. The first is associated with the tuning tip of a nerve fibre (its sensitive, narrowly tuned region), while the second derives from its tail (the fairly insensitive and broadly tuned lower frequency region).

²¹ Allen, J. B. (1977). Cochlear micromechanics: a mechanism for transforming mechanical to neural tuning within the cochlea. *J. Acoust. Soc. Am.* 62: 930-939.

²² Snyder, R. L. and C. E. Schreiner (1984). The auditory neurophonic: basic properties. *Hear. Res.* 15: 261-280.

²³ Ruggero, M. A. and N. C. Rich (1989). "Peak splitting": intensity effects in cochlear afferent responses to low frequency tones. In: *Cochlear Mechanisms: Structure, Function, and Models*, edited by J. P. Wilson and D. T. Kemp (Plenum: New York), 259-267.

²⁴ Zwislocki, J. J. (1985). Are nonlinearities observed in firing rates of auditory-nerve afferents reflections of a nonlinear coupling between the tectorial membrane and the organ of Corti? *Hear. Res.* 22: 217-221.

²⁵ Ruggero, M. A. (1995). What is the mechanical stimulus for the inner hair cell? Clues from auditory-nerve and basilar-membrane responses to low-frequency sounds. In: *Active Hearing*, edited by Å. Flock et al. (Pergamon: Oxford), 321-336.

²⁶ Cody, A. R. and D. C. Mountain (1989). Low-frequency responses of inner hair cells: evidence for a mechanical origin of peak splitting. *Hear. Res.* 41: 89-100.

²⁷ Kiang, N. Y. S., et al. (1986). Single unit clues to cochlear mechanisms. *Hear. Res.* 22: 171-182.

9.1/d *Tip drive and tail drive*

The concept of these dual stimuli to the nerve fibre have been consolidated in the concept of ‘tip drive’ for the sensitive component and ‘tail drive’ for the less sensitive one. This concept is incorporated by Mountain and Cody (1999) into a model for input to the inner hair cell²⁸. To accord with earlier findings, they stipulate that each of the two stimuli must be mechanical in nature – independent vibrational modes – and they suggest that one is due to basilar membrane displacement and the other OHC mechanical activity (p. 11). When acting antagonistically, a notch can result. The basilar membrane input to the inner hair cell is considered passive and, to accord with actual observations, has a gain of only 0.008, while the active OHC block is given a standard gain of 1 (p. 12). In explanation of the abnormally low gain, they say that the inner hair cell is relatively decoupled from the basilar membrane – hardly an efficient arrangement for a traveling wave model – whereas the OHCs are proposed to be well coupled to the inner hair cells so that length changes are communicated easily (an idea that is an essential part of the SAW model). In what I interpret as support for the SAW model, the Mountain and Cody model “raises the intriguing possibility that the OHCs may be driving the IHCs directly over a wide frequency range...” and “Since the RL is more compliant than the BM... it is likely that that influence of OHC motility on the RL side of the organ of Corti, and therefore on the IHCs, is significantly greater than on the BM side” (p. 13).

In two subsequent papers^{29,30}, Lin and Guinan provide additional evidence for multiple excitatory drives by examining the responses to clicks of auditory nerve fibres in cats and chinchillas. The first paper showed a range of anomalies and phase reversals that could be interpreted as the action of two out-of-phase stimuli, the tip drive and the tail drive, and perhaps even a third. At intermediate levels, they saw waxing and waning that appeared to be due to the beating of the tip drive and the tail drive, and suggest that there are multiple resonant modes in the cochlea. “An

²⁸ Mountain, D. C. and A. R. Cody (1999). Multiple modes of inner hair cell stimulation. *Hear. Res.* 132: 1-14.

²⁹ Lin, T. and J. J. Guinan (2000). Auditory-nerve-fibre responses to high-level clicks: interference patterns indicate that excitation is due to the combination of multiple drives. *J. Acoust. Soc. Am.* 107: 2615-2630.

³⁰ Lin, T. and J. J. Guinan (2004). Time–frequency analysis of auditory-nerve-fiber and basilar-membrane click responses reveal glide irregularities and non-characteristic-frequency skirts. *J. Acoust. Soc. Am.* 116: 405-416.

important implication of our working hypothesis is that standard cochlear models have serious shortcomings”, they conclude (p. 2628).

In their 2004 paper they examine other peculiar features of the click response, including frequency glides, which cannot be accounted for by a single, frequency-dispersive traveling wave. However, models containing two drives with different latencies and tunings appear to more successful in this regard, and the researchers consider the dual traveling wave model of Hubbard – in which one wave progresses down the basilar membrane and another, coupled to it, travels down the tectorial membrane³¹ – as having the most promise.

9.1/e *Psychophysical cancellation*

If the basilar membrane response cancels at 60–80 dB SPL, we might expect to be deaf to pure tones at this level, and yet experience tells us this does not appear to be the case. However, audiological examination of people with certain hearing anomalies reveals that they sometimes do indeed have such a “hole” in their hearing. Pure-tone audiometry on people suffering from monaural diplacusis (a not uncommon form of pitch anomaly where the person hears a pure tone as compound) sometimes shows bands of silence. These silent regions are bounded *at higher and lower intensities* by hearing sensations. An example³² is shown in Formby and Gjerdingen (1981) and interestingly the authors propose that “a nearly instantaneous cochlear-mechanical event” may play a role in the phenomenon and point to a second tone interacting with the stimulating tone (p. 223). The authors document other similar cases of “ein negatives Perceptionsfeld” in the literature, and these include studies by Wegel³³ and by Ward³⁴.

Why do not normal people not hear the “hole” at about 60 dB SPL? The answer could lie in the SAW model predicting multiple frequency maps in the cochlea (§R7), so that a single tone is detectable at multiple points along the

³¹ Hubbard, A. E. (1993). A traveling-wave amplifier model of the cochlea. *Science* 259: 68-71.

³² Formby, C. and D. B. Gjerdingen (1981). Some systematic observations on monaural diplacusis. *Audiology* 20: 219-233.

³³ Wegel, R. L. (1931). A study of tinnitus. *Arch. Otolaryngol.* 14: 158-165. [Chart 2 shows a silent area around 3.7 kHz at mid intensities]

³⁴ Ward, W. D. (1955). Tonal monaural diplacusis. *J. Acoust. Soc. Am.* 27: 365-372. Fig. 1B shows a “not heard” region around 3.3 kHz and 40 dB SPL.

cochlea³⁵. A second explanation is psychophysical, and suggests that the auditory system fills in interference holes in much the same way as the visual system fills in the blind spot.

Although these observed cancellations may be due to a dual OHC sensitivity, of course it cannot be ruled out that the interference effect may be occurring at the level of the IHC, where cancellation between the OHC squirting wave output and the traveling wave displacement could occur. However, the Rhode and Recio work suggests that cancellation is at the level of the basilar membrane. Like this more recent work, Formby and Gjerdingen (1981) noted that the region of silence could be maintained indefinitely for pure tones, but that pulsed tones always produced a hearing sensation, suggesting a small time delay between two antagonistic signals.

9.1/f Dual components of the cochlear microphonic

For some time it has been recognised that the cochlear microphonic potential recorded at the round window is the sum of two potentials of opposite polarity³⁶. Indeed, the earliest electrophysiological studies of the cochlea observed that, as sound levels became intense, the CM did not just saturate but in fact *decreased*, which could only happen if there were two sets of potential generators³⁷. The cochlear microphonic is now generally taken to be a record of the response of outer hair cells³⁸, so the implication is that there are either two (differentially active) populations of OHCs, or there are two currents within each cell. The SAW model actually embodies both of these options, although this chapter focuses more on the second possibility³⁹.

³⁵ That is, as well as the cochlea responding to a 1-kHz tone at the position with a CF (L_0) of 1 kHz, it might detect 1 kHz at the position where the first oblique L_1 has a 1 kHz resonance, where the second oblique has a 1 kHz resonance, and so on.

³⁶ Møller, A. R. (1986). Effect of click spectrum and polarity on round window N_1N_2 response in the rat. *Audiology* 25: 29-43.

³⁷ Karlán, M. S., et al. (1972). Dual origin of the cochlear microphonics: inner and outer hair cells. *Ann. Otol. Rhinol. Laryngol.* 81: 696-704.

³⁸ The CM decreases by 30–40 dB when the OHCs are disabled.

³⁹ Both aspects were placed in perspective in the modeling of Chapter R6.

Detailed studies of the cochlear microphonic^{40,41} have been performed by Pierson and Møller who found a cancellation notch at 65–85 dB SPL at a frequency 1/5 to 1/2 an octave above the characteristic frequency. Of interest, one component was labile, disappearing when the cochlea was exposed to loud sound, whereas the second component was not (pp. 137, 143). Subsequent work^{42,43} added the information that whereas the low-level CM becomes smaller under acoustic fatigue, associated action potentials actually became larger and had shorter latency (p. 61), suggesting a direct, but elusive, connection between the two phenomena (pp. 84, 97). Another interesting property of the CM is that it is sensitive to intracochlear pressure, so that pressing on the round window reduces the potential markedly or sometimes *reverses its polarity*⁴⁴.

9.1/g Two components in OHC receptor potentials?

If the hypothesis presented in this chapter is correct, it would suggest that the two components of the OHC receptor potential – the pressure-induced current through the cuticular pore and the displacement-induced current through the stereocilia – should be distinguishable electrophysiologically. However, studies of outer hair cells with voltage-clamp methods fail to show this, with the response phase of the cell being more or less constant – there seem to be no antiphasic components^{45,46}. Thus, in Fig. 9 of Dallos (1985), we see that the phase of an outer hair cell's a.c. response to sound stays constant from 85 dB to 45 dB SPL.

If OHCs are pressure sensors, impaling them with an electrode will compromise, if not destroy, their pressure-detection ability. Dallos describes the

⁴⁰ Pierson, M. and A. R. Møller (1980). Some dualistic properties of the cochlear microphonic. *Hear. Res.* 2: 135-149.

⁴¹ Pierson, M. and A. R. Møller (1980). Effect of modulation of basilar membrane position on the cochlear microphonic. *Hear. Res.* 2: 151-162.

⁴² Pierson, M. G. and A. R. Møller (1982). Corresponding effects of acoustic fatigue on the cochlear microphonic and the compound action potential. *Hear. Res.* 6: 61-82.

⁴³ Pierson, M. G. and A. R. Møller (1982). Corresponding effects of hypoxia on the cochlear microphonic and the compound action potential. *Hear. Res.* 6: 83-101.

⁴⁴ Wever, E. G. (1966). Electrical potentials of the cochlea. *Physiol. Rev.* 46: 102-127. [p. 106]

⁴⁵ Dallos, P. (1985). Response characteristics of mammalian cochlear hair cells. *J. Neurosci.* 5: 1591–1608.

⁴⁶ Although two components could underlie findings by Zwislocki, J. J. and R. L. Smith (1989). Phase reversal in OHC response at high sound intensities. In: *Cochlear Mechanisms: Structure, Function, and Models*, edited by J. P. Wilson and D. T. Kemp (Plenum: New York), 163-168.

“grave” difficulty of obtaining stable electrode recordings from outer hair cells⁴⁷, saying that “recording from OHCs is still an excruciatingly difficult task. Altogether we have recorded from a total of 33 third turn OHC [from] at least 400 experiments... It is not unusual to conduct two experiments per week for several months without a single success” (p. 1600). Holding times were short and “it is possible that all of our recordings are from suboptimally functioning OHCs”. He acknowledges that there are doubts about the recording conditions reflecting the in vivo situation so that “the majority of our recordings [may have been] collected from abnormal preparations – a conclusion that we like not to believe.” Nevertheless, I suspect it could be true. Reservations have commonly been expressed that patch-clamping interferes with the normal functioning of a cell, particularly because, by clamping the voltage at a fixed level, it compromises voltage-sensitive currents.

Therefore the reason that two components of the OHC receptor potential have not been clearly separated may be that one component is *the pressure signal deriving from a transient sodium or potassium current and this flows only when there is an uncompromised pressure signal at the cuticular pore and when the resting membrane potential of the OHC is correctly set (highly negative)*. Thus, patch-clamping is misleading in that (a) isolated outer hair cells do not then preserve the highly negative resting potential they have in vivo, and (b) impaling a pressure sensor with a pointed electrode destroys its pressure-sensing capability.

In regard to (a), isolated OHCs lose the normal separation between the K⁺-rich endolymph at their cuticular plate and the Na⁺-rich perilymph at their basal ends. The damaging effects of this mixing have been consistently commented on. Kros (1996) comments (p. 368) on the generally poor physiological state of isolated OHCs and says that, loaded with sodium ions, they are invariably depolarised compared to natural conditions. Evans et al. (1991) say that isolated cells are often depolarised compared to in vivo⁴⁸.

As for (b), again Kros (1996) points out that penetrating a cell is likely to introduce a large leak conductance (p. 360) and shunt out time-dependent and voltage-dependent conductances (p. 347). Isolating a cell is likely to damage it and the presence of a recording electrode could alter the mechanics of a penetrated OHC

⁴⁷ Dallos (1985).

⁴⁸ Evans, B. N., et al. (1991). Outer hair cell electromotility: the sensitivity and vulnerability of the DC component. *Hear. Res.* 52: 288–304. [p. 298]

(p. 352). In particular, he says it is “naïve” (p. 375) to expect to find the mechanisms of sharp tuning to survive intact. Again, Evans et al. (1991) note that patch clamping depressurises OHCs, which are naturally turgid and carry an internal pressure of about 1 kPa; reducing the internal pressure can diminish or even abolish the motile response⁴⁹. The considerations raised in Chapter D8 suggest that the outer hair cell may be detecting pressure-induced volume changes of the order of 10^{-24} m^3 , in which case puncturing it could easily compromise its sensitivity.

Finally, we note that clamp-patch recordings do show *d.c.* differences in cell response with intensity. Dallos notes that “the two-polarity nature of OHC receptor potentials represents a puzzling distinction” (p. 1602), and we see in his Fig. 9 that the *d.c.* component of the receptor potential goes from positive to negative as intensity falls below about 60 dB SPL; this changeover is a consistent feature of OHC recordings, and is seen more generally^{50,51}, although the transition intensity can vary. It parallels a change from cell elongation to contraction, and can be understood as reflecting a rectification of two *a.c.* currents of opposite polarity (one of which is not apparent under patch clamp), as discussed in the next section.

My conclusion is that the pressure-sensitive current has probably been compromised by the patch-clamping itself.

9.1/h OHC mechanical responses differing by 180°

Earlier (§D 8.3) we noted the work of Brundin, Flock, and co-workers where isolated OHCs were seen to be mechanically tuned. Importantly, these tonic (*d.c.*) responses resulted in *either lengthening or shortening*⁵², and it is assumed here that this is due to one or other of the transduction sensors (cell body pressure or

⁴⁹ Evans et al. (1991), p. 298.

⁵⁰ Evans, B. N., et al. (1989). Asymmetries in motile responses of outer hair cells in simulated in vivo conditions. In: *Cochlear Mechanisms*, edited by J. P. Wilson and D. T. Kemp (Plenum: New York).

⁵¹ Dallos, P., et al. (1982). Intracellular recordings from cochlear outer hair cells. *Science* 218: 582-584.

⁵² Brundin, L., et al. (1989). Tuned motile responses of isolated cochlear outer hair cells. *Acta Oto-Laryngologica, Supplement* 467: 229-234. The reason that more cells appear to shorten than lengthen is because the balance point is set by the resting membrane potential, and isolated OHCs are depolarised compared to in vivo.

stereocilia displacement) being involved at a phasic (a.c.) level⁵³. In particular, we note the observation⁵⁴ that *when a cell was stimulated at increasingly high levels, its phasic response suddenly changed phase by 180°*.

9.1/i **Transduction confined not just to tip links**

The currently accepted view is that transduction depends on stereocilia bending, which in turn stretches tip links and gates transducer currents in the stereocilia. However, for quite a few years previous there was debate about whether transduction currents entered a hair cell through the tips of its stereocilia or at their base^{55,56}. There was evidence for both positions and it would seem, as noted below, that perhaps both were right.

In many ways the argument about the site of transduction resembles the argument about whether outer hair cells are displacement transducers or pressure transducers. In the text books, the standard reference to work showing that a hair cell is a displacement transducer⁵⁷ is to Hudspeth and Corey (1977). Certainly these workers found that displacing the stereocilia from a bullfrog sacculus did cause transduction currents to flow. However, this does not rule out that transduction currents may also be gated by a pressure signal and, more aptly, that the additional mechanism may exist in mammalian outer hair cells in vivo. Similarly, Hudspeth and Jacobs (1979) tied down a kinocilium and saw little difference in the consequent behaviour of stereocilia, thereby downplaying the role of the kinocilium in transduction⁵⁸; however, this experiment does not rule out a synergistic role for the

⁵³ This accords with the suggestion made by Brundin and Russell (1993) that “The mechanically induced tonic length change is a non-linear rectification and amplification of the phasic mechanical response” (p. 187).

⁵⁴ Brundin, L. and I. J. Russell (1994). Tuned phasic and tonic motile responses of isolated outer hair cells to direct mechanical stimulation of the cell body. *Hear. Res.* 73: 35–45.

⁵⁵ Ohmori, H. (1988). Mechanical stimulation and Fura-2 fluorescence in the hair bundle of dissociated hair cells of the chick. *J. Physiol.* 399: 115–137. [p. 128]

⁵⁶ Hudspeth, A. J. (1982). Extracellular current flow and the site of transduction by vertebrate hair cells. *J. Neurosci.* 2: 1–10.

⁵⁷ Hudspeth, A. J. and D. P. Corey (1977). Sensitivity, polarity, and conductance change in the response of vertebrate hair cells to controlled mechanical stimuli. *Proc. Nat. Acad. Sci.* 74: 2407–2411.

⁵⁸ Hudspeth, A. J. and R. Jacobs (1979). Stereocilia mediate transduction in vertebrate hair cells. *Proc. Nat. Acad. Sci.* 76: 1506–1509.

kinocilium, nor that it might act over a different (lower) displacement range than the stereocilia.

More recently, evidence has been presented that there is transduction in the absence of tip links⁵⁹. Meyer et al. (2005) destroyed tip links pharmacologically (using BAPTA) and found, electrophysiologically, that the cell could respond to static displacements. Although the experiment is far from conclusive – because it used isolated OHCs, fluid jet stimulation⁶⁰, and invasive patch-clamping – it does suggest that there is more to transduction than tip links. “Evidence is mounting that [it] is not the case... that the tip link is the elastic element which gates the transduction channel” (p. 98) and “the existence of permanently opened channels, that are mechanically sensitive to static hair-bundle deflection in the inhibitory direction, is not consistent with the common assumption of *direct* gating of the MET channels only by the tip link” (p. 105). The experimenters only saw responses with long time constants, but this may have been because the conditions of the experiment were less than optimal. A micrograph of a cell under test⁶¹ shows it limp and lacking the turgor pressure of a healthy cell.

These latest findings support the idea that the standing current observed is the silent current and that this current can be modulated, efficiently so under in vivo conditions, when intracochlear pressure is the key stimulus.

A clear example of how a hair cell can display two currents, one through the stereocilia and another through the cuticular plate, is shown in Fig. 9.3.

⁵⁹ Meyer, J., et al. (2005). Tonic mechanosensitivity of outer hair cells after loss of tip links. *Hear. Res.* 202: 97-113.

⁶⁰ As mentioned in Chapter 8, fluid jet stimulation may provide a pressure stimulus to the cell, not just the intended stereociliar displacement. Meyer et al. (2005) measured cuticular plate motion as 30 dB below that of the hair bundle (p. 99), but the plate motion could be magnified enormously when the associated intracellular pressure change is transmitted to the cuticular pore.

⁶¹ Meyer et al. (1998), Fig. 7A. Obviously, fixation for the electron micrograph would have taken away even more of its live characteristics.

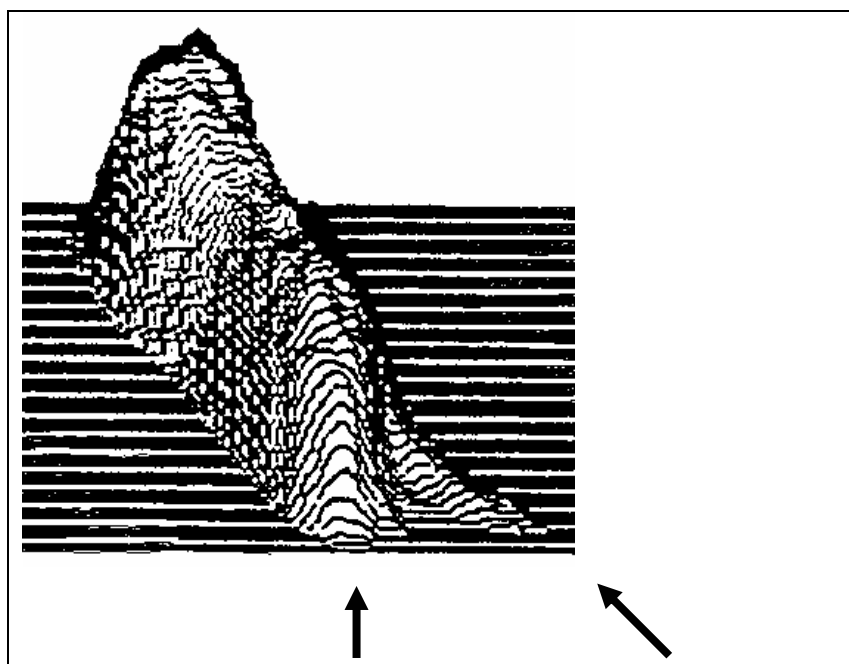


Fig. 9.3. A fluorescence image of a hair cell (from a chick) undergoing stimulation, showing current densities of Ca^{2+} , an ion mediating transduction. The apex of the cell is towards the front, and the peninsula to the lower right is the stereocilia. Note the current density of the companion peninsula associated with the cuticular plate. [From Fig. 7 of Ohmori (1988) and reproduced with permission of the Journal of Physiology]

The possibility that the cuticular pore is the locus of a large transducer current also raises interesting questions about its permeability to the vital fluorescent dye FM 1-43. This dye is a relatively large molecule, and yet a number of studies indicate it seems to enter the cell through transduction channels. This has generated some debate, some believing the dye enters a hair cell through endocytosis, while others argue it must enter through the stereocilia. If the dye can actually permeate through the cuticular pore, this might largely reconcile these apparently contradictory views. Thus, Meyer et al. (2001) observed that FM 1-43 entered guinea pig outer hair cells (*without kinocilia*) even when the tip links were disabled⁶², whereas Gale et al. (2001) found that entry of the dye – in mice *with kinocilia* – depended on transduction channels being open. Since the dye quickly penetrates cells during endocytosis, and the cuticular pore is a site of rapid endocytosis, the two view-points can be harmonised: in the first case the cuticular pore exists as a hole covered only by a thin plasma membrane, which the dye can readily penetrate, while in the case of mice with kinocilia, the pore is closed by the kinocilium and the dye can only enter

⁶² Meyer, J., et al. (2001). Pronounced infracuticular endocytosis in mammalian outer hair cells. *Hear. Res.* 161: 10–22.

through the stereocilia's transduction channels. Interestingly, this *lipophilic* dye labels Hensens body⁶³, an organelle closely linked to the cuticular pore and an entity that this thesis supposes may be the site of air bubble generation (see Chapter D8, where the key role of lipids in bubble generation is underscored).

9.1/j **Different membrane potentials between OHC rows**

Outer hair cells are distinguished by their high negative resting potential, measured in the range -50 to -90 mV or more in vivo^{64,65} (although considerably less in vitro). It is difficult to judge the undisturbed resting values because patch-clamping and electrode penetration is likely to impair the turgor pressure and polarization of these cells⁶⁶. The difficulties associated with patch-clamping and the way it might compromise outer hair cells electrophysiologically were described in §D 9.1/g. Interestingly, it is over just this in vivo range of membrane potentials that transient Na^+ (and presumably K^+) currents are seen to activate, and is the range in which the high negative slope in the current–voltage characteristic is found (Fig. A1).

Direct studies comparing the properties of outer hair cells between rows appear to be rare, and I have only been able to find two. One report⁶⁷ gives data on d.c. gradients across the sensory surface, and finds (Fig. 3) that 4 cells from OHC1 have a gradient of 100 – 120 mV compared to 20 – 90 mV for 10 cells from OHC2 and OHC3 (although the potentials were very unstable). Another report⁶⁸ looked, in explants, at the difference in growth factors between rows, and found some statistically significant differences. At the least, we can conclude from this fragmentary data that not all OHC rows behave identically.

⁶³ Meyer et al. (2001), Fig. 3.

⁶⁴ Dallos (1985). Response characteristics of mammalian cochlear hair cells. *J. Neurosci.* 5, 1591-1608.

⁶⁵ Cody, A. R. and I. J. Russell (1987). The responses of hair cells in the basal turn of the guinea-pig cochlea to tones. *J. Physiol.* 383: 551-569.

⁶⁶ Kros (1996), p. 369.

⁶⁷ Tanaka, Y., et al. (1980). Potentials of outer hair cells and their membrane properties in cationic environments. *Hear. Res.* 2: 431-438. Fig. 3.

⁶⁸ Malgrange, B., et al. (2002). Identification of factors that maintain mammalian outer hair cells in adult organ of Corti explants. *Hear. Res.* 170: 48-58.

9.1/k **Controlling the SAW resonator gain**

The concept of a difference in resting potential between the rows provides a way by which the gain of the SAW resonator can be readily altered. If all the rows have the same resting potential, there is no differential activity and no gain. On the other hand, if the resting potential of the rows is dynamically altered – by efferent neural control, perhaps – there is an opportunity for a small change in resting potential to effect a large change in SAW resonator gain.

As a pointer, Dallos (1985) found, even in single cells (although necessarily coupled mechanically, in vivo, to neighbouring cells), that “unexpected receptor potential variations may accompany the membrane potential changes...” and “... abnormal [DC] polarity reversals... may be seen during prolonged penetration” (p. 1595). Sometimes, low sound levels evoked hyperpolarising DC responses, whereas high levels tended to give the more prevalent depolarising response. Well defined responses were only seen above 50 dB SPL. The dual polarity response of OHC receptor potentials was found puzzling, and Dallos summarises by saying that “It appears that two rectifying mechanisms operate in the cochlear mechanics–OHC system in opposite directions, with one dominating at low levels and low frequencies, and the other dominating under all other conditions” (p. 1597). These ideas tend to conform with the proposition put here that there are two receptor currents in an outer hair cell, one of which is pressure sensitive. However, although the d.c. component of the receptor potentials fits this picture, the a.c. component does not, tending to exhibit a single, fixed phase irrespective of sound pressure level (Dallos 1985, Fig. 9). Possible reasons for this deviation are given in §D 9.1/g. On the other hand, *it is acknowledged that, prima facie, this evidence goes against the SAW model, and it would be on much stronger ground if direct evidence was forthcoming that the a.c. signal had two components of opposite phase*. Nevertheless, for now the evidence in sections 9.1/b to 9.1/h will have to suffice. The d.c./a.c. data of Dallos can perhaps be resolved in two ways: (1) the rectified signal may be effective in the SAW model; or, more simply, (2) in an *intact* OHC the a.c. phase reversal shows itself.

The second option gains some credibility from a companion paper⁶⁹ in which Dallos explores the way in which the gain of the a.c. response depends strongly on the resting membrane potential. For example, the stimulus-related response was seen to decrease 16 dB when the resting membrane potential changed by 50 mV (Dallos 1985b, Fig. 3b). He says that “it is reasonable to assume that the [membrane potential] variations are related to the presence of the foreign object [the electrode] within the cell” (p. 1612) and suggests it may be associated with a radical increase in apical resistance (p. 1615). In other words, gating at the cell apex, which could be mediated by stereocilia or, perhaps, pressure.

In terms of variable gain of an OHC triplet, there is no direct data because of the extreme difficulty of recording from more than one cell simultaneously. Nevertheless, two papers used patch-clamping of isolated pieces of the organ of Corti (outer hair cells and supporting Deiters cells) to show reciprocal coupling between OHC1 and OHC2. In the first⁷⁰, when one OHC was stimulated electrically, a voltage change of *opposite polarity* took place in the neighbouring cell. In the second, rather than impaling the OHCs, the supporting Deiters cells were monitored, and again in this case, stimulation of one cell produced a voltage change of opposite polarity in the other.

A general argument for cochlear gain control depending on resting membrane potential comes from the observation that cutting the nerve supply to the cochlea results almost immediately (within minutes) in loss of active cochlea properties (such as evoked emissions). This is unusual, in that, in vitro, outer hair cells normally continue to function for many minutes after isolation. The difference may be that the cochlear amplifier requires three or more coupled rows of cells, each row with a different membrane potential, in order to function, even though each separate component may still be active.

The unifying point is that the efferent system may act simply to change the resting membrane potential of one or more rows in such a way as to effectively control gain. This gives a simple explanation for how the efferent system functions.

⁶⁹ Dallos, P. (1985). Membrane potential and response changes in mammalian cochlear hair cells during intracellular recording. *J. Neurosci.* 5: 1609-1615.

⁷⁰ Zhao, H.-B. and J. Santos-Sacchi (1999). Auditory collusion and a coupled couple of outer hair cells. *Nature* 399: 359-362.

At the present time, a system-wide view of efferent system functioning is lacking^{71,72}.

9.1/I Two frequency maps and the half-octave shift

A multitude of findings in the literature point to there being more than just a single frequency map in the cochlea. In particular, the independent behaviour of the tip and tail of cochlear tuning curves⁷³, and the production of distortion components that interfere^{74,75,76}, give general evidence is that there may be at least two resonant elements in the cochlea. This has led to various models identifying two sources whose cancellation is the basis of notches seen at intermediate stimulus levels. The general proposition made at this point is that the two sources are the SAW resonance (pressure driven) and the partition resonance (involving the traveling wave).

At the level of the hair cell, one manifestation of the two stimuli is peak splitting, a phenomenon already noted in §D 9.1/c. At the level of the partition, these two stimuli can also lead to two response peaks, and here is where the curious half-octave shift comes into play. It may be worth briefly describing this phenomenon and how the SAW model can account for it.

The well-known, but mysterious, half-octave shift⁷⁷ imposes fundamental constraints on any theory of the cochlea, and here we sketch a resolution of the

⁷¹ Guinan, J. J. (1996). Physiology of olivocochlear efferents. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 435–502.

⁷² A clear conception that hearing is an interplay between afferent and efferent nerves was expressed as early as the 13th century by Bartholomaeus Anglicus in his encyclopedia: “Hearing comes about when two nerves issuing from the interior part of the brain carry the animal spirit to the *ossa petrosa*, to which the exterior air communicates the form of a sound. The animal spirit, altered according to the properties of the beaten air, returns to the chamber of the phantasy and presents its changed form to the mind” [paraphrased by Palisca, C. V. (2000). Moving the affections through music: pre-Cartesian psycho-physiological theories. In: *Number to Sound*, edited by P. Gozza (Kluwer: Dordrecht), 289–308] pp. 294–295.

⁷³ Patuzzi, R. B. (1987). A model of the generation of the cochlear microphonic with nonlinear hair cell transduction and nonlinear basilar membrane mechanics. *Hear. Res.* 30: 73–82.

⁷⁴ Brown, A. M. and D. M. Williams (1993). A second filter in the cochlea. In: *Biophysics of Hair Cell Sensory Systems*, edited by H. Duifhuis et al. (World Scientific: Singapore), 72–77.

⁷⁵ Lukashkin, A. N. and I. J. Russell (2003). A second, low-frequency mode of vibration in the intact mammalian cochlea. *J. Acoust. Soc. Am.* 113: 1544–1550.

⁷⁶ Allen, J. B. and P. F. Fahey (1993). A second cochlear-frequency map that correlates distortion product and neural tuning measurements. *J. Acoust. Soc. Am.* 94: 809–816.

⁷⁷ McFadden, D. (1986). The curious half-octave shift: evidence for a basalward migration of the traveling-wave envelope with increasing intensity. In: *Basic and Applied Aspects of Noise-induced Hearing Loss*, edited by R. J. Salvi et al. (Plenum: New York), 295–312.

problems it raises. It was suggested in §I 3.2/1 that this curious phenomenon, in which the sensitivity to a pure tone (of a given frequency) is virtually unaffected by temporary but immense overload, was one important reason for regarding the broadly tuned traveling wave mechanism as inadequate in being the sole cause of cochlear stimulation. In §D 8.3 a unifying hypothesis was made that there were in fact two input stimuli to the cochlea, a pressure stimulus operating below about 60–80 dB SPL and another displacement stimulus for levels above this. This range-splitting was suggested as the way by which the cochlea achieved its astonishing 120 dB dynamic range.

The evidence that the two components of the cochlear microphonic appear to be separated by half an octave apart (§D 9.1/m) also conforms with this idea. Although the question of the half-octave shift is large, a straight-forward unifying hypothesis can be framed, and it generally parallels the exposition given by McFadden (p. 297). Here he describes the Davis (1983) concept of the cochlear amplifier, and how this rides like a horn sitting on top and in front (half an octave ahead) of the body of the traveling wave as it runs along the basilar membrane. The account offered in this thesis differs only in detail: that the active, low-intensity tuning derives from the pressure-stimulated cochlear amplifier – the SAW resonance – which is tuned by the speed of the squirting wave and spacing between OHC rows. The second, high-intensity tuning could originate with mass and stiffness of the partition – the conventional traveling wave picture.

McFadden points out a limitation of such a model (p. 298): that it limits the shift to half an octave, whereas larger shifts seem to be sometimes observed. I accept the limitation, but given the lack of hard data on the shift, the explanation remains an attractive one.

Another explanation for the effect has invoked a separate resonance of the tectorial membrane^{78,79} half an octave below the best frequency; except for describing the particular form of the resonance, this is not unlike what is being proposed here. Zwislocki proposed that inner and outer hair cells were, at the same location, tuned half an octave apart⁸⁰, but this does not seem to be sustainable.

⁷⁸ Neely, S. T. and D. O. Kim (1986). A model for active elements in cochlear biomechanics. *J. Acoust. Soc. Am.* 79: 1472-1480.

⁷⁹ Gummer, A. W., et al. (1996). Resonant tectorial membrane motion in the inner ear: its crucial role in frequency tuning. *Proc. Nat. Acad. Sci.* 93: 8727-8732.

⁸⁰ Zwislocki, J. J. (1977). In: *Psychophysics and Physiology of Hearing*. (London: Academic), 125-135.

If the initial stimulus is a pressure wave that sets the outer hair cells into motion, there is then the possibility that a traveling wave may form just as readily in the tectorial membrane as in the basilar membrane. From this perspective, it is interesting to note that Békésy's observations were made from scala vestibuli and looked at motion of the Reissner's membrane⁸¹. In fact even observations of basilar membrane motion do not rule out that the motion may have been generated in the tectorial membrane. Nevertheless, we do have observations that show that, following outer hair cell stimulation, the plateau of Corti (reticular lamina) vibrates with an amplitude many times greater than that of the basilar membrane⁸². Generally, people are prepared to accept there may be multiple tunings in the cochlea, but it is difficult to make a convincing case for the identity of the separate elements. This aspect will require further investigation.

As set out elsewhere (§I 3.2/1), a pressure-sensitive mechanism can be made virtually overload-proof. Excessive pressure simply compresses the *bubble* inside the cell until it reaches a limit⁸³ or the cell wall deforms, the flow through the cuticular pore is viscously limited, and squirting waves between cells are limited in amplitude by the hair cell motor. On the other hand, stereocilia and their displacement sensitivity are prone to mechanical damage at high traveling wave amplitudes.

9.2 Pushing the limits of sensitivity

9.2/a Thermal and quantum limits

As described earlier (§I 1.1), the cochlea is so sensitive that its operation approaches theoretical limits, and, as suggested in earlier chapters, a consideration of this suggests that a resonance picture may be more realistic than a traveling wave

⁸¹ Greenwood, D. D. (1962). Approximate calculation of the dimensions of traveling-wave envelopes in four species. *J. Acoust. Soc. Am.* 34: 1364–1369. [p. 1367] Zwislocki's discussion (pp. 246-7) comparing vibration of Reissner's membrane with that of the basilar membrane does little to alleviate doubts that they are not identical.

⁸² Mammano, F. and J. F. Ashmore (1993). Reverse transduction measured in the isolated cochlea by laser Michelson interferometry. *Nature* 365: 838-841.

⁸³ The volume change varies simply as the reciprocal of the imposed pressure, which gives a natural "compression" of response towards a fixed limit.

one. By resonance, virtually all of the energy at the stapes can be communicated to the resonating elements. On the other hand, as Lighthill (1981) points out⁸⁴, in a traveling wave the pressure at the stapes is not perfectly in phase with volume flow, so that “this reduced the power of any given vibration of the stapes footplate to feed energy into the slow wave” (p. 193), an inefficiency which becomes increasingly pronounced at low frequencies⁸⁵.

By comparing the cochlea’s limits with considerations of thermal and quantum noise, Bialek and Schweitzer were the first to calculate that the ear must operate below thermal noise⁸⁶, and state that “there is *no* consistent classical theory of hearing” (p. 727, italics in original). The authors calculate that at hearing threshold, a stereocilium vibrates over a distance of about 10^{-11} m and detects an acoustic power of 10^{-18} W, figures which are below passive thermal noise limits (given stereocilia vibrating within a viscous fluid). But they did point out that $kT/\hbar\omega$, the ratio of thermal noise to quantum noise, is about 10^{10} , so we are still comfortably above quantum limits.

The suggested solution to overcoming thermal noise is to lower the effective temperature of the stereocilia by narrowing the effective bandwidth. Thermal noise in a mechanical system can be lowered by giving it a high mechanical Q and using active feedback. A passive mechanical resonance has no effect because all that happens then is that all of the available noise power gets pushed into the resonance peak⁸⁷. In the same way, Bialek and Wit suppose⁸⁸ that the cochlea might use feedback circuits – Gold is mentioned – to narrow its bandwidth and provide “cooling down by filtering” (p. 177). Properties of SOAEs are examined, and are shown to reflect those of an active oscillator, not passive, so that the effective kT is then only 0.3 eV, a figure consistent with observation^{89,90}. Bialek calculates that a

⁸⁴ Lighthill, J. (1981). Energy flow in the cochlea. *J. Fluid Mech.* 106: 149-213.

⁸⁵ The same conclusion is reached in Shera, C. A. and G. Zweig (1991). A symmetry suppresses the cochlear catastrophe. *J. Acoust. Soc. Am.* 89: 1276-1289. [footnote 1].

⁸⁶ Bialek, W. S. and A. Schweitzer (1985). Quantum noise and the threshold of hearing. *Physical Review Letters* 54: 725-728.

⁸⁷ Block, S. M. (1992). Biophysical principles of sensory transduction. In: *Sensory Transduction*, edited by D. P. Corey and S. D. Roper (Rockefeller University Press: New York), 1-17. p. 7.

⁸⁸ Bialek, W. S. and H. P. Wit (1984). Quantum limits to oscillator stability: theory and experiments on acoustic emissions from the human ear. *Physics Letters* 104A: 173-178.

⁸⁹ Wit, H. P. and R. J. Ritsma (1983). Sound emission from the ear triggered by single molecules? *Neurosci. Lett.* 40: 275-280.

filter bandwidth of 50 Hz or less would be adequate^{91,92}, and properties of SOAEs easily meet this criterion.

Incorporating an active feedback circuit into the ear therefore makes good physical sense. It increases sensitivity, reduces bandwidth, and reduces noise. Implementing it by coupling three outer hair cells together, as proposed in this thesis, gives a further advantage: instead of the system being limited by the thermal vibration of a single stereocilium, as considered by Bialek, the distributed system is much larger in extent (about $30 \times 10 \times 5 \mu\text{m}$). The thermal noise associated with such a parcel of fluid will depend on its viscous coupling to the subtektorial space and to its direct mechanical coupling to the outer hair cell machinery, and is not calculated here, but the increased size and mass is expected to reduce the effect of thermal noise considerably.

9.2/b Hair bundle or cell body as power source?

The focus I have put on positive feedback between OHC body and OHC stereocilia could reconcile the argument that has arisen about whether the cochlear amplifier is underlain by electromotility of the cell body or negative stiffness of the stereocilia. In this perspective, the answer is *it is both*.

Electromotility was the first motor property of OHCs to be discovered (by Brownell⁹³) and its fast properties must play a role in the cochlear amplifier. More recently, Hudspeth and his colleagues have measured the negative stiffness that stereocilia display upon probing, and they make the hypothesis that active hair bundle motility, driven by a fast Ca^{2+} current, is the engine of the system⁹⁴. The issue was discussed at the Titisee conference⁹⁵, and a number of researchers make the

⁹⁰ Wit, H. P. and R. J. Ritsma (1983). Two aspects of cochlear acoustic emissions: response latency and minimum stimulus energy. In: *Mechanics of Hearing*, edited by E. de Boer and M. A. Viergever (Delft University Press: Delft), 101-107.

⁹¹ Bialek, W. S. (1983). Thermal and quantum noise in the inner ear. In: *Mechanics of Hearing*, edited by E. de Boer and M. A. Viergever (Delft University Press: Delft), 185-192. p. 187.

⁹² Bialek, W. S. (1987). Physical limits to sensation and perception. *Ann. Rev. Biophys. Chem.* 16: 455-478. p. 465.

⁹³ Brownell, W. E., et al. (1985). Evoked mechanical responses of isolated cochlear outer hair cells. *Science* 227: 194-196.

⁹⁴ Chan, D. K. and A. J. Hudspeth (2005). Ca^{2+} current-driven nonlinear amplification by the mammalian cochlea *in vitro*. *Nat. Neurosci.* 8: 149-155.

⁹⁵ pp. 572-579 of *Biophysics of the Cochlea*, ed. A. W. Gummer, (World Scientific 2003).

point that both mechanisms might operate together. Although somewhat suggestive of hair bundle motion, Chan and Hudspeth (2005) used electrical stimulation of explanted gerbil cochleas, and did not directly observe outer hair cell bundle movement (only motion of the inner hair cell bundle); however, another recent experiment did directly measure forces exerted by rat outer hair cell bundles⁹⁶. It is likely, however, that hair-bundle motility may act predominantly in animals like frogs and turtles, whereas somatic motility may be the mammalian implementation. I think the apparent speed limitation of somatic motility can be overcome by the capacitance-compensation of fast transient K^+ currents, as proposed by Ospeck et al. (2003).

The presence of negative stiffness provides an interesting new ingredient in cochlear mechanics. Martin et al. (2000) describe the utility of this property⁹⁷: it is the mechanical equivalent to negative resistance, the electronic property that, embedded in tunnel diodes, for example, allows the construction of amplifiers and oscillators. In the cochlea, negative stiffness could be harnessed to amplify mechanical stimuli. Their study of the bullfrog hair cells with a fine probe revealed *negative stiffness* (negative slope in the force–displacement curve) and, when freed from their normal attachment to an overlying membrane, spontaneously oscillated. That is, when force was applied in one direction, displacement took place in the opposite, so that the bundle repeatedly hunted around a stable position. If a biasing element – an adaptation motor of some sort – could constantly work to hold the bundle in its unstable region, an oscillatory stimulus would be amplified.

Hudspeth and colleagues have devoted considerable effort to study of this system^{98,99}, with the intention of showing how the low-frequency bullfrog sacculus system (its resonance is below 10 Hz) may be a model for high frequency auditory systems. The crucial factor is that a degree of cooperative interplay between the negative stiffness and the biasing element is needed, and various speculations about its structural basis are made involving the mechanics of gating channels. However, as

⁹⁶ Kennedy, H. J., et al. (2005). Force generation by mammalian hair bundles supports a role in cochlear amplification. *Nature* 433: 880-883. Note that this work was done under voltage clamp (p. 883), precluding involvement of prestin-mediated somatic motility.

⁹⁷ Martin, P., et al. (2000). Negative hair-bundle stiffness betrays a mechanism for mechanical amplification by the hair cell. *Proc. Nat. Acad. Sci.* 97: 12026-12031. p. 12029.

⁹⁸ Choe, Y., et al. (1998). A model for amplification of hair-bundle motion by cyclical binding of Ca^{2+} to mechanoelectrical-transduction channels. *Proc. Nat. Acad. Sci.* 95: 15321-15326.

⁹⁹ Hudspeth, A. J., et al. (2000). Putting ion channels to work: mechanoelectrical transduction, adaptation, and amplification by hair cells. *Proc. Nat. Acad. Sci.* 97: 11765-11772.

pointed out by Iwasa and Ehrenstein (2002), various forms of cooperative interaction are possible¹⁰⁰. It seems to me that one suitable adaptation process in outer hair cells is the tilting of the cuticular plate¹⁰¹, a process that could set outer hair cell bundles to their most sensitive operating point.

9.2/c Hopf oscillators

Analysis of oscillator dynamics leads in two directions. Firstly, it leads to positive feedback circuits and a simple topology is that of the regenerative receiver. As Eguíluz et al. (2000) point out, such an entity is simple, requiring only a minimal number of active elements and “because the tuner and the amplifier are one and the same, this mechanism is evolutionarily accessible”¹⁰². They note the contributions of Helmholtz and Gold and “Although the notion that the inner ear works like a musical instrument offers a beautiful esthetic symmetry, it has serious flaws” (p. 5232). They argue, perhaps prematurely¹⁰³, that the fluid in the cochlea “dampens any hope of simple mechanical tuning”.

Secondly, oscillators can act as tuned amplifiers, and Hopf oscillators are well-known examples of this kind in which an instability – a Hopf bifurcation – can amplify weak signals in a non-linear way^{104,105}. Eguíluz and colleagues interpret the cochlea as being essentially non-linear (p. 5232), and they build a mechanical model of the cochlea based on a Hopf oscillator. Since the SAW model fits nicely into this Hopf framework, it is worth setting out the properties of such an oscillator. Following Eguíluz et al, a Hopf bifurcation can be described by the equation

$$dz/dt = (\mu + i\omega_0) z - |z|^2 z \quad (9.1)$$

¹⁰⁰ Iwasa, K. H. and G. Ehrenstein (2002). Cooperative interaction as the physical basis of the negative stiffness in hair cell stereocilia. *J. Acoust. Soc. Am.* 111: 2208-2212.

¹⁰¹ Zenner, H. P., et al. (1988). Active movements of the cuticular plate induce sensory hair motion in mammalian outer hair cells. *Hear. Res.* 34: 233-240.

¹⁰² Eguíluz, V. M., et al. (2000). Essential nonlinearities in hearing. *Physical Review Letters* 84: 5232-5235. [p. 5235]

¹⁰³ In §R 5.7 a method of overcoming viscosity is proposed.

¹⁰⁴ Choe et al. (1998), p. 15326.

¹⁰⁵ Stoop, R., et al. (2004). Limit cycles, noise, and chaos in hearing. *Microsc. Res. Tech.* 63: 400-412.

where $z(t)$ is a complex variable of time, ω_0 is the natural frequency of oscillation, and μ is a control parameter (excitability) that, when positive, leads to stable oscillation around $z = 0$. If the system, with response R , is subject to a periodic forcing $F e^{i\omega t}$, entrainment is possible and the solution is

$$F^2 = R^6 - 2\mu R^4 + [\mu^2 + (\omega - \omega_0)^2] R^2, \quad (9.2)$$

which is a cubic in R^2 and solvable¹⁰⁶. At the critical bifurcation point, $\mu = 0$ (where the system is most sensitive to perturbation), and so

$$F^2 = R^6 + (\omega - \omega_0)^2 R^2, \quad (9.3)$$

from which, as the authors demonstrate, a number of interesting properties emerge.

First, at the centre of the resonance, when $\omega = \omega_0$, we see that $R \propto F^{1/3}$, which means that the response is non-linear, right down to the smallest forcing. Moreover, the amplification, R/F , becomes very large as F becomes small (because of the cube-root factor). The distinctive response of the system, following Equation 9.3, was calculated and is shown in Fig. 9.4. It shows that at resonance the response is cube-like, but away from resonance the response is approximately linear. The Q of the resonance is $\omega_0 / 2\mu$, so that at the bifurcation point it becomes infinite. This type of response broadly agrees with some basilar membrane measurements, and provides a simple model for their interpretation.

The parallels have been drawn closer by Duke and Jülicher (2003), where they model the cochlea in terms of a continuously graded set of Hopf oscillators arranged along the partition¹⁰⁷. The advantage of their model is that the characteristic frequency of a place on the partition is set not by its stiffness or inertia but by the frequencies of the Hopf oscillators at that location, meaning that the problem of inadequate range of the basilar membrane stiffness map (§I 3.2/b) can be bypassed.

¹⁰⁶ In terms of R , the solution given by Eguíluz et al. is $3R^2 = S^{1/3} + 2\mu - AS^{-1/3}$, where $S = \frac{1}{2}(D + (D^2 + 4B^3)^{1/2})$, $D = 27F^2 + 16\mu^3 - 18\mu A$, $A = \mu^2 + (\omega_0 - \omega)^2$, and $B = -\mu^2 + 3(\omega_0 - \omega)^2$.

¹⁰⁷ Duke, T. and F. Jülicher (2003). Active traveling wave in the cochlea. *Physical Review Letters* 90: 158101.

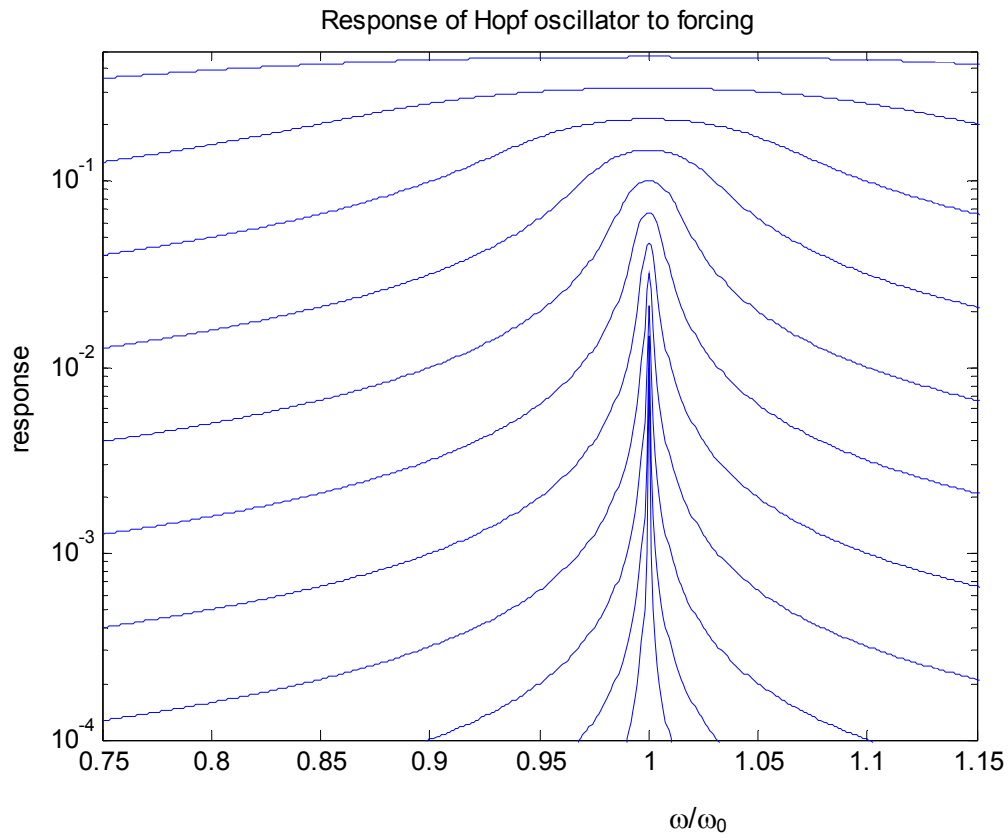


Fig. 9.4. Response, R , of a Hopf oscillator (set at its bifurcation point, $\mu = 0$) to periodic forcing, F , which decreases from 0.1 (top curve) to 10^{-6} (bottom). At resonance ($\omega = \omega_0$), the response depends on the one-third power of the forcing, making it responsive to weak signals at that frequency.

They consider the effect of a traveling wave on the partition, and the numerical solutions that emerge show the standard traveling wave profile, with the wavelength diminishing and the amplitude building as it progresses. However, one major drawback of their model is that the location of the peak shifts drastically – by octaves – as intensity increases. Thus, for a 4.6-kHz tone, the peak is 73% from the base at 40 dB SPL, but for 80 dB, the peak is only 39% from the base – a shift of one-third the length of the cochlea. They claim this shift is consistent with observations of Russell and Nilsen (1997), but those researchers did not see frequency shifts of that magnitude¹⁰⁸. Nevertheless, the work demonstrates that a bank of finely tuned oscillators will support a traveling wave, and the approach bears

¹⁰⁸ Russell, I. J. and K. E. Nilsen (1997). The location of the cochlear amplifier: spatial representation of single tone on the guinea pig basilar membrane. *Proc. Nat. Acad. Sci.* 94: 2660-2664. The shifts (e.g., Fig. 4) were a fraction of an octave.

closer investigation. In particular, simultaneous stimulation of the system with a pressure wave could be a promising avenue.

A similar approach in which Hopf oscillators are excited by a traveling wave has been investigated by Stoop and colleagues^{109,110,111}. In Stoop et al. (2004) they take an energy density at the base (p. 401) and consider how this might propagate along an array of Hopf oscillators poised on the basilar membrane, a standard traveling wave picture. The results deviate from typical observations, so they consider a *feed-forward scheme*, in which the Hopf oscillators are directly coupled, in order to overcome this limitation. The coupling takes the form of certain anatomical connections between outer hair cells¹¹², and this allows the traveling wave to proceed beyond the resonance point and resolve many of the discrepancies. The response is in fact made broader and the authors claim that “the final version of our model is able to faithfully reproduce experimentally measured BM response properties” (p. 403). Interestingly, the following section of their papers considers insect vibration detectors, which are “linear array of cells” without hydrodynamic coupling. They note that some insects use displacement detectors (exposed sensory hairs) for near-field hearing and *pressure detection* (air-filled cavities) for the far-field, and proceed to examine the role of stochastic resonance in improving the signal-to-noise ratio of such a detector. The neuronal dynamics of a single neuron on a fruit-fly antenna are considered in detail, but the far-field (pressure) detector is not mentioned again¹¹³.

In summary, Stoop and colleagues, and also Duke and Jülicher, have described all the necessary ingredients for building the SAW model. The essential difference lies in the mode by which the stimulus is considered to travel. Duke and Jülicher state in their 2003 paper that they do not wish to specify the physical basis of the oscillators, but the SAW resonator would clearly serve well as a candidate for the self-tuned oscillator. The two authors do list, as alternative candidates, the electromotile elements of OHC bodies or their active hair bundles. As for the feed-

¹⁰⁹ Kern, A. and R. Stoop (2003). Essential role of couplings between hearing nonlinearities. *Physical Review Letters* 91: 128101.

¹¹⁰ Stoop, R. and A. Kern (2004). Essential auditory contrast-sharpening is preneuronal. *Proc. Nat. Acad. Sci.* 101: 9179-9181.

¹¹¹ Stoop et al. (2004).

¹¹² Based on the ideas of Geisler [see Geisler, C. D. (1998). *From Sound to Synapse: Physiology of the Mammalian Ear*. (Oxford University Press: New York).]

¹¹³ Even though feed-forward schemes qualify as being non-causal in the same way as a fast pressure signal would.

forward scheme of Stoop and colleagues, we have already noted in §I 3.2/f that a feed-forward scheme is non-causal, and that from the point of view of a traveling wave, the fast pressure wave is also non-causal.

The advantage of the SAW model is that its tuning range can be made very wide (using squirting wave dispersion) and stable (based on the mechanical dimensions of the subtektorial space). An interesting possibility raised in Jülicher (2001) is that a Hopf instability may arise from interaction between the kinocilium and the stereocilia¹¹⁴, although of course this could not apply to the adult mammalian cochlea. In another interesting paper¹¹⁵, it is conjectured that the interaction of Hopf oscillators may be involved, psychophysically, in two-tone interference; a distinguishing feature of this paper is the fact that it was “Communicated by T. Gold, Cornell University” – probably the last contribution to hearing research by this pioneer at a time when the path had almost come full circle.

Electrophysiological observations of bullfrog hair cells oscillating spontaneously at 126 Hz showed they had properties consistent with Hopf oscillators¹¹⁶. Notably, an imposed electrical stimulus, at a suitable frequency, is able to entrain the natural resonance frequency. This lock-in can only happen within a restricted range of frequencies and amplitudes known as an Arnold tongue; outside this range, the stimulus will be unable to capture the resonance and a non-sinusoidal beat will be generated. This behaviour closely resembles that between an SOAE and an external tone¹¹⁷. Ospeck and colleagues build a hair cell model¹¹⁸ using three conductances – a K^+ transduction at the apex, a voltage-dependent Ca^{2+} channel in the basolateral wall, and a Ca^{2+} -gated K^+ channel (also through the wall) – and show how the currents can interact to give oscillation. This model could be employed in the SAW model as an amplifier of squirting wave feedback, in which case there would be two feedback paths poisoning the cell just below oscillation. Rather than a single stereocilia-gated K^+ current through the cell apex, however, the present SAW

¹¹⁴ Jülicher, F. (2001). Mechanical oscillations at the cellular scale. *C. R. Acad. Sci. Paris (Series IV)* 2: 849-860.

¹¹⁵ Jülicher, F., et al. (2001). Physical basis of two-tone interference in hearing. *Proc. Nat. Acad. Sci.* 98: 9080–9085.

¹¹⁶ Ospeck, M., et al. (2001). Evidence of a Hopf bifurcation in frog hair cells. *Biophys. J.* 80: 2597-2607.

¹¹⁷ Long, G. R., et al. (1991). Modeling synchronization and suppression of spontaneous otoacoustic emissions using Van der Pol oscillators: effects of aspirin administration. *J. Acoust. Soc. Am.* 89: 1201-1212.

¹¹⁸ Ospeck et al. (2001), Fig. 3, based on the work of Hudspeth and Lewis (1988).

model supposes that K^+ ions can also enter through high-conductance channels in the cuticular pore which are gated by pressure. The Ospeck model provides the explanation of the need for the silent current: the authors point out (p. 2602) that the cell must run a large (79 pA) quiescent current so that it can turn off a large fraction and obtain current gain (for example, in their model a 1 pA inward current blocks 19 pA from leaving).

9.3 General evidence favouring the SAW model

9.3/a *Anti-phase motion between rows*

If there were unequivocal observations that OHC2 moved in antiphase to OHC1 and OHC3, the model would rest on very strong ground. However, resolving sub-nanometre motion at a spatial scale below that of outer hair cell row spacing (typically 15 μm between rows) is difficult when the system is hidden deep inside the cochlea of a living animal. Non-invasive techniques offer an intact system that is less suspect scientifically and ethically preferred.

An additional hurdle comes from the SAW model's prediction that the combined activity of all the rows is a standing wave – that is, two waves moving in opposite directions, with the result that the phase across the system is *constant*. However, the model does suggest that there should be a progressive wave between OHC1 and the IHC.

The existing literature does in fact contain some evidence in accord with the SAW model, and this is set out below.

- The clearest indication is the work¹¹⁹ of Nilsen and Russell where they find that there are rapid spatial phase variations across the partition. This evidence was outlined in Chapter M4 and is collected together in the following section (§D 9.3/b).

¹¹⁹ Nilsen, K. E. and I. J. Russell (1999). Timing of cochlear feedback: spatial and temporal representation of a tone across the basilar membrane. *Nat. Neurosci.* 2: 642-648.

- A recent report¹²⁰ from Scherer and Gummer found that, even in a guinea pig explant, the IHC could be about 180° out of phase with the motion of OHC1/2 (Fig. 1). Moreover, about half of the observations of OHC3 showed, for the first turn, that they moved out of phase with OHC1/2 (Fig. 2). The explant is far removed from the conditions in the live cochlea, but even here antiphasic motion was produced.
- In another explant (of the gerbil), Karavitaki and Mountain found that, under electrical stimulation, the first and third rows of OHC nuclei moved out of phase¹²¹.
- Again with electrical stimulation of an explant, this time of an echolocating bat, Reuter and colleagues found that radial motion were sometimes evident and occasionally decoupled OHCs moved out of phase with the rest of the cells¹²².
- To place this work in a more general context, it is known in studies of the lateral line organ that paired cells of opposite phase commonly occur¹²³. When controlled stimulation is applied, units of each type fire alternately, in phase and 180° out of phase¹²⁴.

9.3/b Radial waves

The SAW model predicts closely spaced phase changes across the partition. As mentioned in Chapter M4, Nilsen and Russell observed the basilar membrane of a guinea pig with a scanning laser vibrometer and saw relative phase changes of up to 180° between locations only 10 μm apart radially¹²⁵. The Nilsen and Russell results

¹²⁰ Scherer, M. P. and A. W. Gummer (2004). Vibration pattern of the organ of Corti up to 50 kHz: evidence for resonant electromechanical force. *Proc. Nat. Acad. Sci.* 101: 17652-17657.

¹²¹ Karavitaki, K. and D. C. Mountain (2000). Comparing patterns of electrically-evoked vibrations from the apical and middle turns of the gerbil cochlea. Midwinter Meeting, Florida, Association for Research in Otolaryngology [Abstract #4751]

¹²² Reuter, G., et al. (1994). Electromotility of outer hair cells from the cochlea of the echolocating bat, *Carollia perspicillata*. *J. Comp. Physiol. A* 175: 449-455. [p. 452]

¹²³ Rouse, G. W. and J. O. Pickles (1991). Paired development of hair cells in neuroblasts of the teleost lateral line. *Proc. R. Soc. Lond. B* 246: 123-128.

¹²⁴ Sand, O., et al. (1975). Electrical and mechanical stimulation of hair cells in the mudpuppy. *J. Comp. Physiol. A* 102: 13-26. [Fig. 2C]

¹²⁵ Nilsen and Russell Timing of cochlear feedback: spatial and temporal representation of a tone across the basilar membrane. The key result is seen in Fig. 3d and 4d.

stand out because no one else before or since has seen such spatially rapid phase changes in the living animal, even though phase variations of 180° or more have now been seen in explants (§D 9.3/a above). The Nilsen and Russell findings contrast with the results of other workers^{126,127,128} who have only seen small or no phase gradients. Rapid phase variations strongly support the SAW model, and are otherwise difficult to explain.

9.3/c Fluid jet stimulation

The difficulty of using a fine probe to directly stimulate the stereocilia of an isolated outer hair cell has been repeatedly commented upon, and the accepted solution has been to employ a nearby fluid jet, which gives larger and more reliable responses^{129,130}. A possible explanation for the result may not be poor probe–stereocilia coupling, as usually thought, but that the fluid jet is actually supplying a pressure stimulus to the cell. This possibility was raised in Chapter D8, but, given the considerations raised in this thesis, bears reiterating. Clearly, a more considered experimental checking of this possibility is called for.

Two other general considerations that tend to favour the SAW model are given in the Appendix. One points to the effect of opening the cochlea as a loss of pressure in a pressure-sensitive system; the other looks at phase reversals in subjects without middle ears.

¹²⁶ Cooper, N. P. (2000). Radial variation in the vibrations of the cochlear partition. In: *Recent Developments in Auditory Mechanics*, edited by H. Wada et al. (World Scientific: Singapore), 109–115.

¹²⁷ Ren, T., et al. (2003). Measurements of basilar membrane vibration using a scanning laser interferometer. In: *Biophysics of the Cochlea*, edited by A. W. Gummer (World Scientific: Singapore), 211–219. [Fig. 2b]

¹²⁸ Rhode and Recio (2000), p. 3324.

¹²⁹ Preyer, S., et al. (1994). Frequency response of mature guinea-pig outer hair cells to stereociliary displacement. *Hear. Res.* 77: 116–124.

¹³⁰ Ashmore, J. F. (1988). What is the stimulus for outer hair cell motility? In: *Basic Issues in Hearing*, edited by H. Duifhuis et al. (Academic Press: London), 42–48.

9.4 Evidence against the SAW model

9.4/a Little leakage between ears

A long-standing case against a pressure wave being the adequate stimulus in the cochlea is due to Zwislocki. In 1953, he measured the acoustic isolation between the two ears¹³¹ and established figures of 40–90 dB, depending on frequency. Following the interpretation of Schubert¹³², this must rule out a compressional wave in the cochlea, because if it were effective in one cochlea then it would also travel through the cranial fluids and bone and stimulate the other cochlea. We would therefore see little isolation of the ears¹³³.

This argument rests on the assumption that there is only a small difference in acoustic impedance between the cochlear fluids and surrounding bone. However, as we have seen in §I 3.2/j, the otic capsule is exceptionally hard and dense, and this fact was put forward as evidence favouring a pressure stimulus. The impedance discontinuity between it and the cochlear fluids will prevent sound energy from leaking out of the cochlea. Zwislocki's argument has some force, but is not compelling.

Zwislocki's paper provides some further relevant data. Using a cancellation technique, he measured the phase of the sound in the opposite ear and obtained a phase–frequency plot (Fig. 11). Measuring its slope, he arrived at a time delay of 7.3 ms. Interestingly, even if the sound takes the longest route – 300 mm through the skull – this gives a wave speed of 41 m/s, less than the velocity of sound in bone or even air. Taking the shortest distance between the ears, some 80 mm, we arrive at a wave velocity of only 11 m/s. The importance of this result is that it seems to rule out sound leakage between the ears by common wave propagation modes.

¹³¹ Zwislocki, J. J. (1953). Acoustic attenuation between the ears. *J. Acoust. Soc. Am.* 25: 752-759.

¹³² Schubert, E. D. (1978). History of research on hearing. In: *Handbook of Perception, vol. IV, Hearing*, edited by E. C. Carterette and M. P. Friedman (Academic: New York), 41-80. [pp. 46-48]

¹³³ According to Schubert (p. 46): "If the adequate event in the fluid of the cochlea were a compressional wave, the stapes would have to be considered the source of such a wave, which would spread through the tissue, fluid, and bone relatively unimpeded since there is little change in density; and it is very difficult to envision such a pressure wave being attenuated to the extent indicated by measurements at the locus of the opposite cochlea. In fact, Hallpike and Scott as early as 1940, when discussing this same problem, pointed out that if one considers the stapes to be the source of a pressure wave in a homogeneous medium, the distance to the near cochlea would be about 2.8 mm and that to the far cochlea about 80 mm, making the maximum drop between ears about 30 dB."

Zwislocki hints at slow flexural modes (p. 759), although this is difficult to envisage. Perhaps the low speed is the result of neural energy transfer between the two ears, since action potentials travel at such speeds. There are ample neural connections between the ears, and sound projected into one ear affects otoacoustic emissions in the other¹³⁴. This question is one deserving closer investigation.

9.4/b Presence of the round window

In §I 3.2/h it was pointed out that people can still hear when the round window is blocked, a result not predicted from standard traveling wave theory. On the other hand, it is acknowledged that if pressure were the only stimulus then blocking the window might be expected to *increase* hearing sensitivity, and this obviously does not happen. This is a major drawback to the concept of pressure wave stimulation, and is clearly portrayed by Schubert. He goes further and says (p. 48) “it is pertinent to ask why fixation of both windows [should cause] any appreciable change in hearing level if the appropriate view is that acoustic energy – presumably in the form of a compressional wave – is being transferred [from bone to water]”.

Posed in this form, a key factor – that the radiation of acoustic energy depends on the vibrational amplitude of the radiator – comes into view, and this idea was put forward in §D 8.2, where the analogy was made to the cochlear windows acting like a reflex loudspeaker enclosure. The oval window is the driver, and the round window the port or, more aptly, drone cone. If the windows were fixed, the amplitude of stapes vibration would be much less and hence less acoustic energy would be radiated into the fluid. It therefore comes down to an impedance consideration of how well the vibration in the air is coupled to the outer and middle ear and ultimately to the inner ear fluids. At least some acoustic energy will be radiated by the stapes into the fluids and the outer hair cells might be able to detect it via their internal air bubbles. The question is how much energy is radiated, and how much energy is turned into fluid motion. The former could be a detectable by the hair cell body; the latter by deflection of the stereocilia.

¹³⁴ Pratt, H., et al. (1998). Contralaterally evoked transient otoacoustic emissions. *Hear. Res.* 115: 39-44.

This is a complex issue requiring detailed modelling and is not resolved here. It is again left as a question for further research, but pressure detection appears to be physically possible and is logically an essential component of any system wanting to detect acoustic power (since intensity requires both pressure and acoustic particle velocity).

9.5 Unanswered questions

Audition is a huge field, and there are many other questions that I leave unanswered. Nevertheless, I have attempted to sketch a model that synthesises most of the experimental data in a coherent way. In 1959, Licklider could say “There is no systematic, over-all theory of hearing. No one since Helmholtz [and he deliberately omitted Békésy] has tried to handle anything like all the known problems within a single framework.”¹³⁵ If true, this would be a severe lack, since coherence is a powerful integrating force in science. As Licklider goes on to say, “in hearing there is a tantalizing possibility of drawing up a model that will account for a truly wide variety of accumulated facts” (p. 43). The problem, as I perceive it, is that current auditory science does in fact try to fit all of its data within one framework – the traveling wave model – and the recurring anomalies (§13) may be hinting that some broader schema is needed. I offer the SAW model in this light, suggesting that the cochlea makes use of two complementary acoustic variables, pressure and displacement, in detecting auditory signals. I admit there are unanswered questions, and here I list, in no particular order, some of the more apparent.

1. Why does loudness appear to increase steadily when, for a pure tone at least, there is interference of two detection mechanisms and a null at 60–80 dB SPL?

¹³⁵ Licklider, J. C. R. (1959). Three auditory theories. In: *Psychology: A Study of a Science. Study 1. Conceptual and Systematic*, edited by S. Koch (McGraw-Hill: New York), 41–144. [p. 42] He adds that Helmholtz’s theory “was for years the main force in the field of hearing. The fact that both main parts of it were largely wrong did not lessen its influence” (p. 44). Now, he asserts, “The mechanical action of the cochlea is, most of us now believe, reasonably well understood” and “the initial phase of the process of hearing has been investigated almost to exhaustion” (p. 47).

2. What is the relationship between objective SOAEs and subjective tinnitus?¹³⁶

3. What is the origin of the cochlear tuning curve?

4. Is the function of the V shape of OHC stereocilia related to detection of frequency ratios (a different frequency in each arm)?

5. Following on from (3), are musical ratios detected in the cochlea?

6. How can the perception of the pitch of a tone appear constant, largely irrespective of loudness, when there are two frequency maps in the cochlea? The constancy of pitch – in the face of shifts in the peak (mechanical and neural) of the basilar membrane as intensity varies – is a long-standing problem¹³⁷ and the best suggestion may be that the SAW resonator peak is more stable than others.

7. What is the role of the cuticular pore of inner hair cells, when it seems the cells respond only to stereocilia deflection? Is displacement of the stereocilia converted, via tilting of the cuticular plate, into an internal pressure signal?

8. Extensive research has been done on the piezoelectric-like behaviour of outer hair cells, with often detailed analysis of stresses and strains within the cell wall. However, all of this effort has considered the cell contents to be incompressible, and it could be particularly illuminating to consider the effect an internal compressible element would have.

9. The precise mechanism of pressure detection at the cuticular pore remains unspecified. At one point (§D 8.4/f) it was suggested that sensing involved movement of fluid through the turbine-shaped centriole; later (§D 9.1/a) the sensing was attributed to some of the silent current flowing through voltage-sensitive channels in the membrane at the pore surface. These channels might be opened

¹³⁶ c.f. “Gradually I have ceased to verbalize my worry about the dichotomy of subjective and objective, of the experiential and the physical, that seemed so fundamental when as an undergraduate I encountered the mind–body problem.” [Licklider (1959), p. 47]

¹³⁷ Zwislocki (2002), p. 392-400.

directly by the pressure across the membrane (stretch), or the gating might be mechanically linked to rotation of the turbine.

All of these questions should be considered within the general perspective presented in the next concluding chapter.

Evaluation, predictions, and conclusions

10.1 Results and evaluation

10.1/a Reconsideration of the pressure-stimulus idea

10.1/b The traveling wave: phenomenon or epiphenomenon?

10.1/c Two stimuli or a second filter?

10.1/d Observation affects the thing observed

10.1/e Of fish and lizards

10.2 Predictions

10.3 Conclusions

The aim of this thesis has been to see whether an alternative account of cochlear mechanics can be constructed based on squirting wave resonance between outer hair cells. The picture that emerges can be made to accord with the standard traveling wave picture or the resonance picture depending on what the stimulus to the outer hair cells is. If the stimulus is deflection of stereocilia due to a traveling wave, then the squirting wave resonance mechanism provides a sharply tuned *second filter* sitting on top of a broadly tuned traveling wave. Alternatively, if the pressure wave is the effective stimulus to the body of the cell, then we arrive at a *pure resonance model* along the lines that Helmholtz advocated.

The plausibility of the latter pressure-detection model – in terms of the physical requirements on the one hand and the anatomical and audiological constraints on the other – has been explored in the previous two Discussion chapters.

In general, the literature does not rule out that outer hair cells could respond directly to a pressure stimulus; indeed, the idea appears to harmonise a number of persistent anomalies. If the pressure stimulus model is correct, outer hair cells might give rise to motion of the basilar membrane, and in this case an apparent traveling wave may appear as an epiphenomenon, a concept that differs from the causal, hydrodynamically coupled excitation that Békésy had in mind (even though the end result may be similar).

Given the major difference between the two cases, space has been devoted to describing a possible mechanism by which the fast pressure wave could excite outer hair cells. Several sections have explored the question by examining the literature for gaps and unexplained results that might suggest a direct mechanism; other sections have considered what physical properties outer hair cells would need to have to display such a sensitivity. The conclusion, based on comparative physiology of underwater sound detection, is that a compressible element – most likely an air bubble – inside the outer hair cell would provide the necessary ingredient, and several lines of evidence were set out pointing to fast responses only possible if a pressure wave were active. Hensen's body is suggested as the preferred candidate for the compressible pressure-sensitive element, and its presence induces motion at the cuticular pore that is registered by opening of ionic channels. The hope is that this thesis has outlined a coherent model, appropriate to low sound pressure levels (less than 60–80 dB SPL), that is worthy of further exploration.

But regardless of whether the resonance theory can be sustained, this thesis has arrived at a physically specified model for the cochlea's resonant elements, identifying the cochlear amplifier as a hydrodynamic standing wave.

10.1 Results and evaluation

This thesis can claim the following major results.

1. Squirting waves, with their slow speed and high dispersion, offer a way by which the subreticular space can be tuned over a range of 20 to 20 000 Hz.

At the lowest frequencies there is a gap between the calculated squirting wave velocity and that needed to provide a standing wave. However, more recent work by Elliott et al. (2005) provides support for the squirting wave model and offers a way of bridging this disparity¹. The equations they develop show that viscosity not only reduces the squirting wave amplitude but also its phase velocity. The velocity can be reduced by a factor of about 2, sufficient to bring the two curves of Fig. 5.2 into concordance.

2. Viscous damping in the subtectorial space is probably reduced by surface tension effects. Slip at the boundaries reduces the effective viscosity of the endolymph.

This factor relies on the repellency between water and oily surfaces, which has been demonstrated in many physical systems although the mechanism is still not fully understood. The equations developed by Elliott et al. (2005), applied in reverse, provide a way to put a figure on the effective viscosity in the subtectorial space.

3. Modeling of the feedback loop between the body of one outer hair cell and the stereocilia of its neighbours has shown that it can provide sharp tuning and high sensitivity.

Modeling of squirting wave interactions leaves it open as to whether the standing wave is a full-wave or half-wave mode, although it would seem that the former is more likely. The full-wave mode provides a satisfactory match between calculated squirting wave velocity and that expected for traversing the distance between OHC1 and OHC3 in a single period. Work by Elliott et al. (2005) corroborates the full wavelength mode.

4. Analysis of the OHC pattern shows that their spacing is consistent with squirting wave behaviour.

¹ Elliott, S. J., et al. (2005). Incorporation of an active feedback loop into the "squirting wave" model of the cochlear amplifier. Twelfth International Congress on Sound and Vibration, Lisbon, Portugal.

5. Tilt of the OHC unit cell produces two resonant cavities of slightly different length (and hence supporting two different frequencies) that could underlie DPOAE generation. These dimensions give an explanation of why the maximum DPOAE magnitude occurs at a ratio of the two primary frequencies of about 1.2.

Together, these findings provide a consistent basis for regarding the squirting wave model as possible, although no proof can presently be offered. Nevertheless, the explanatory power of the squirting wave model, particularly in regard to explaining the tuning range of the cochlea (§R 5) and the optimum frequency ratios of DPOAEs (§R 7), should encourage further investigation. Considerations put forward in §D 10.1/b provide further support.

The merit of the resonance hypothesis is its simplicity. It applies a near simultaneous, phase-coherent stimulus to the entire cochlea, allowing accurate timing comparisons to be made among all the frequency components of a sound stimulus. This allows the harmonic structure, or timbre, of a sound to be readily perceived, an advantage when compared to the complex dispersive relations associated with a traveling wave.

The hypothesis only applies in its pure resonance form at low sound pressure levels, and there is the expectation that the traveling wave comes to dominate cochlear mechanics at high sound pressure levels of 60–80 dB SPL and above.

10.1/a Two stimuli or a second filter?

Given the preferred picture of two separate stimuli in the cochlea, there remains an alternative: the traveling wave is the one causal mechanism at work and it drives both passive and active mechanics. Active mechanics does not then reflect the operation of a second stimulus; rather, the cochlear amplifier has the traveling wave as its input and it manages to amplify that minute, but broad, displacement by up to 60 dB (to give a stapes displacement at threshold of 0.001 nm). That is, the cochlear amplifier, via the positive feedback provided by the squirting wave mechanism, is the *second filter*.

Second filters have been in and out of consideration in cochlear mechanics since Evans and Wilson² raised the idea (see §I 2.3). It was originally introduced to explain the disparity between basilar membrane tuning and auditory nerve tuning, but once better experimental technique showed they were identical, the idea lost its distinct identity. Because modellers have continued to strike difficulty in accounting for the sharp peak in basilar membrane tuning, the second filter idea has come back as a way of describing the sharpening process. So the second filter, whatever it is, takes energy from the passive traveling wave and gives a sharp, amplified response.

I cannot rule out that a second filter process may happen in the cochlea. But an argument against it can be made in terms of energy efficiency. We have seen (§D 9.2) that the cochlea uses various strategies to push the limits of sensitivity right down to theoretical limits, and yet it is wasteful of energy to have a narrowly tuned resonator sitting on top of a broadly tuned one. Fletcher (1992) gives a general treatment (his Ch. 12.3) of simple passive second filters and shows why they are not energetically efficient³. When such resonant elements are cascaded – such as with one resonant spring–mass system sitting on top of another – the frequency selectivities of the first and second systems are not compounded as simply as one might expect. When the mass of the second system is very small compared to the first, as it may be in the cochlea, the resonances do in fact cascade (the individual Q s are multiplied), but *very little energy is transferred to the second resonator* (p. 218) and most is dissipated in losses in the primary one. If the relative mass of the second system is increased, the resonant peak broadens and eventually splits, and the response amplitude is *less* than that which would have been reached by either alone.

Active systems will behave somewhat differently but, as Gold put it to Békésy, a system cannot have unlimited discrimination against noise, so conserving energy is vital. In these terms, the advantage of a single pure resonance mechanism is that it can approach the utmost efficiency, the reason it must surely operate in the cochlea.

² Evans, E. F. and J. P. Wilson (1973). The frequency selectivity of the cochlea. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic: New York), 519-551.

³ Fletcher, N. H. (1992). *Acoustic Systems in Biology*. (Oxford University Press: New York).

10.1/b Reconsideration of the pressure-stimulus idea

Since Pohlman raised the possibility in 1933 that hair cells may respond to a pressure stimulus⁴, the idea has been largely out of favour. Recently, however, the idea has undergone a degree of reconsideration, and Ruggero (2004) treats it as a real possibility and provides five references discussing it in some form⁵. Two of these are journal papers already discussed^{6,7}; the other three are conference contributions^{8,9,10}. To summarise Ren's position: "These results contradict the current [traveling wave] theory and show that the ear emits sounds through the cochlear fluids as compression waves rather than along the basilar membrane as backward-travelling waves" (p. 333).

In the coherent reflection filtering model of Shera and Zweig (discussed in §I 3.1/d), it was pointed out that the round trip delay tended to be less than twice the expected traveling wave delay. Instead of a factor of 2, average values from three different studies were 1.6¹¹, 1.7¹², and 1.86¹³. Ruggero reconsiders the issue, and examines four possible ways that DPOAEs can be carried from the cochlea, including fast pressure waves and traveling waves (via combinations of the latter's phase and group velocities). He graphs round trip travel times measured by different observers and compares them with theory. On this basis he rules out the two-way traveling wave theory, leaving two options: the stimulus either travels as a pressure-wave or at a phase velocity in excess of the group velocity.

⁴ Pohlman, A. G. (1933). A reconsideration of the mechanics of the auditory apparatus. *J. Laryngol. Otol.* 48: 156-195.

⁵ Ruggero, M. A. (2004). Comparison of group delays of $2f_1$ - f_2 distortion product otoacoustic emissions and cochlear travel times. *ARLO* 5: 143-147.

⁶ Ren, T. (2004). Reverse propagation of sound in the gerbil cochlea. *Nat. Neurosci.* 7: 333-334. Discussed in §I 3.2/n.

⁷ Avan, P., Magnan, P., Smurzynski, J., Probst, R., and Dancer, A. (1998). Direct evidence of cubic difference tone propagation by intracochlear acoustic pressure measurements in the guinea-pig. *Eur. J. Neurosci.* 10: 1764-1770. Discussed in §I 2.2/f.

⁸ Ruggero's own comments as reported on pp. 584-585 of *Biophysics of the Cochlea* (ed. A. W. Gummer). An omission from the listing is the contribution by Bell (2003) to this question in the same volume (pp. 429-431).

⁹ Cooper, N. P. and C. A. Shera (2004). Backward-traveling waves in the cochlea? *Association for Research in Otolaryngology, Midwinter Meeting, Abstract 342*.

¹⁰ Narayan, S. S., Recio, A., and Ruggero, M. A. (1998). Cubic distortion products at the basilar membrane and in the ear canal of chinchillas. ARO Abstract [not seen; title only viewable on Web site]

¹¹ Shera, C. A. and J. J. Guinan (2003). Stimulus-frequency-emission group delay: a test of coherent reflection filtering and a window on cochlear tuning. *J. Acoust. Soc. Am.* 113: 2762-2772.

¹² Shera and Guinan (2003), p. 2765.

¹³ Cooper and Shera (2004).

The issue has been raised again by Shera and colleagues in a recent publication¹⁴ where they demonstrate that use of a two-dimensional model (rather than the one-dimensional one on which the theory was initially propounded) improves the situation and weakens the argument I raise here of a potential inconsistency. The two-dimensional analysis yields slightly longer group delays and “improves the accuracy of the first-order approximation $\tau \cong 2\hat{\tau}_{BM}$ ” (p. 302). Nevertheless, it is of interest that this latest paper does briefly discuss compressional wave activity in the cochlea. They explicitly note that their analysis neglects the possibility that “the accelerations of structures within the organ of Corti (e.g., the outer hair cells) also produce significant acoustic compressional waves that propagate through the cochlear fluids at the speed of sound uninfluenced by the basilar membrane (or other tuned mechanical structures, in the case of nonmammalian tetrapods such as frogs and lizards)” (p. 305). It is encouraging to read that the (one-way) compressional wave mechanism appears to be gaining ground: “In principle, back propagation via compressional waves provides an additional mechanism for energy to escape from the inner ear, and *mounting albeit not unequivocal evidence suggests that the mechanism operates in the mammalian ear*” (p. 305, italics added). A conference abstract by the authors¹⁵ indicates that modeling effort is currently being directed at seeing how compressional waves can be incorporated, as an add-on, into cochlear models and what effect they may produce.

Ruggero also draws attention to the presence of DPOAEs in frogs and lizards, creatures who lack a basilar membrane and do not have a traveling wave. This is discussed in a following section (§D 10.1/e). He circumspectly suggests that “Hypothesis III” (the pressure wave hypothesis) “may also apply to mammals” (p. 146).

Ruggero’s reference for the origin of Hypothesis III is Wilson (1980). Although it is good to see Wilson’s seminal idea back under consideration, the hypothesis is the *one-way* version in which a traveling wave takes the stimulus from the stapes to the hair cells, and it is only the return trip that is carried by the fast

¹⁴ Shera, C. A., et al. (2005). Coherent reflection in a two-dimensional cochlea: short-wave versus long-wave scattering in the generation of reflection-source otoacoustic emissions. *J. Acoust. Soc. Am.* 118: 287-313.

¹⁵ Shera, C. A., et al. (2005). Coherent-reflection models of reflection-source OAEs with and without slow transverse retrograde waves. *Assoc. Res. Otolaryngol. Abs.* 413.

pressure wave. This seems inelegant and lacking in symmetry. If the pressure hypothesis is valid, I regard its *two-way* formulation as the form that makes the most sense and which should be under scrutiny.

Ruggero omits mention of several other attempts that have been made to reintroduce the pressure wave idea. There is the paper of Rybalchenko and Santos-Sacchi (2003) which suggests, somewhat obliquely, that the OHC soma may use chloride currents as a detector complementary to the stereocilia. Additionally, there is the paper of Nobili et al. (2003) and his instantaneous connection between middle ear and basilar membrane. Other references could have been to the conference contribution of Bell (2004) and the 1997 review by Ulfendahl¹⁶.

Emerging research indicates that Ruggero's list could now be extended, with publication of a paper by Dong and Olson on direct intracochlear pressure measurements¹⁷. These workers studied distortion product generation in the gerbil cochlea, and found that when a pressure probe was slowly retracted from the basilar membrane, it sometimes sensed large phase variations (up to 180°) with distance and with intensity (above and below 60 dB SPL). This behaviour could be the result of squirting wave interactions (see Fig. 6.28 where the separate output of each row is plotted) or, more likely, might be an effect due to interference between a dominant active resonance source below 60 dB SPL and a dominant passive basilar membrane source above (see §D 9.1/b). The paper draws attention to the findings of Ren (2004) and his pressure-stimulation idea, and concludes that the unusual phase behaviour “confirms the feasibility that [distortion products] could drive the stapes by a direct fluid route, as proposed by Ren” (p. 2999). There are also a number of other studies by Olson that indicate unusual cochlear behaviour^{18,19}, and these may be able to be interpreted in terms of the SAW model.

¹⁶ Ulfendahl, M. (1997). Mechanical responses of the mammalian cochlea. *Prog. Neurobiol.* 53: 331–380. He discusses sound-induced motile responses of outer hair cells (pp. 348, 371–375), work in which he was involved, and relates that “The mechanical responses [of OHCs] to sound stimulation exhibit tuning properties comparable to those measured intracellularly or from nerve fibres” (p. 331). Yet, “despite its obvious relation to the naturally occurring stimulation of the hearing organ” this behaviour has been largely ignored (p. 374). This work also discusses the view that “outer hair cells produce the mechanical vibrations seen at the basilar membrane” (p. 357). It also gives perspectives on fast waves (p. 345), radial waves (p. 357 and elsewhere), and cautions about the validity of invasive measurements. However, the review offers no alternative model.

¹⁷ Dong, W. and E. S. Olson (2005). Two-tone distortion in intracochlear pressure. *J. Acoust. Soc. Am.* 117: 2999–3015.

¹⁸ Olson, E. S. (2004). Harmonic distortion in intracochlear pressure and its analysis to explore the cochlear amplifier. *J. Acoust. Soc. Am.* 115: 1230–1241.

A recent paper by Konrad-Martin and O’Keefe on latencies of SFOAEs (§I 3.2/k) also supports the fast wave²⁰. Consideration of fast responses suggests that, when gathering click-evoked responses, much more valuable data lies in the early 0–5 ms window, data that is now normally discarded because it is believed to contain only middle-ear generated artefacts.

Finally, the forthcoming Mechanics of Hearing Conference this month (Portland, OR, July 2005) shows that the pressure stimulus idea is steadily gaining ground, so far as can be judged by the issued preprints. In particular, a paper by Guinan et al. (2005)²¹ highlights “the need for a new conceptual paradigm for cochlear mechanics, a paradigm in which the classic BM traveling wave is not the only motion that excites AN fibres.” They suggest that the fast pressure wave may excite the outer hair cells and produce a vibrational mode that could involve a “peristaltic-like” wave. Another paper by Gummer et al.²² proposes “pulsating fluid motion” similar to the squirting wave put forward in Bell and Fletcher (2004). Other key papers also discuss direct pressure wave excitation^{23,24}.

Currently there are at least a handful of researchers examining the idea of a dynamic interaction between pressure and outer hair cells. The number has grown since Guild’s first formulation of the concept and Naftalin’s vigorous reworking of it.

Historically, the biggest stumbling block to considering hair cells as pressure sensors appears to be the fact that they possess hairs. The natural, but perhaps misleading, inference is that the cells therefore only detect displacement. The key to moving beyond this limited perspective is to consider an evolutionary adaptation in which cilia machinery operates in reverse, so that they become motors as well as sensors. There is in fact an intricate feedback loop between the two, and it will

¹⁹ Olson, E. S. (2001). Intracochlear pressure measurements related to cochlear tuning. *J. Acoust. Soc. Am.* 110: 349-367.

²⁰ Konrad-Martin, D. and D. H. Keefe (2005). Transient-evoked stimulus-frequency and distortion-product otoacoustic emissions in normal and impaired ears. *J. Acoust. Soc. Am.* 117: 3799-3815. The data at low and moderate levels “mainly” support the theory of coherent reflection filtering, but “the presence of short-latency SFOAEs in some ears support the existence of an additional cochlear source of SFOAE generation” (p. 3813).

²¹ Guinan, J. J., et al. (2005). Insights into cochlear mechanics from the effects of medial olivocochlear efferents. Proceedings, Auditory Mechanisms: Processes and Models, Portland, OR.

²² Gummer, A. W., et al. (2005). Pulsating fluid motion and deflection of the stereocilia of the inner hair cells due to the electromechanics of the outer hair cells. Proceedings, Auditory Mechanisms: Processes and Models, Portland, OR.

²³ Kemp, D. T. and P. F. Tooman (2005). DPOAE micro- and macrostructure: their origin and significance. Proceedings, Auditory Mechanisms: Processes and Models, Portland, OR (in press)

²⁴ Siegel, J. H. (2005). The biophysical origin of otoacoustic emissions. Proceedings, Auditory Mechanisms: Processes and Models, Portland, OR (in press).

require considerable research to understand the different ways each type of animal has implemented this idea. The universe is reflexive, and so are our sensors.

10.1/c The traveling wave: phenomenon or epiphenomenon?

This thesis has raised the question of whether the traveling wave on the basilar membrane is a prime cause or a side-effect. In the first case, it is a causal mechanism right down to the threshold of hearing; in the second, it is only a secondary manifestation of another effective stimulus whose presence is hard to see directly.

The hypothesis put forward here is that the traveling wave is an epiphenomenon at low sound pressure levels, where the motion of the partition is caused by stimulation of the outer hair cells by the fast pressure wave. At levels above 60–80 dB SPL, however, sufficient differential pressure does exist to directly give rise to differential motion of the partition – the motion that Békésy first observed and which has continued to be regarded as the sole cause of cochlear stimulation. Of course, simplicity and Occam’s razor would favour a single mechanism, but with anomalies growing in cochlear mechanics, it seems that more is happening in the live cochlea than can be accounted for in terms of a single stimulus.

Observing the complexity, Zwislocki takes the position that “the cochlea [is] simplified by death”²⁵ and chooses to base his modeling on passive mechanics. Something crucial may have been discarded in making this simplification. To validate his choice, Zwislocki cites (p. 246) experiments²⁶ where complete removal of the organ of Corti had an almost imperceptible effect on the amplitude and phase of basilar membrane vibration. I take this work as evidence that such experiments are almost certainly missing important aspects of the active, living process (see §D 10.1/d). Pressure-detection could be a facility that owes its existence to living

²⁵ Zwislocki, J. J. (2002). *Auditory Sound Transmission: An Autobiographical Perspective*. (Erlbaum: Mahwah, NJ). Chapter 4.

²⁶ Cooper, N. P. and W. S. Rhode (1995). Nonlinear mechanics at the apex of the guinea-pig cochlea. *Hear. Res.* 82: 225-243.

outer hair cells, and disappears on death. In this case, the compressible air bubble – the “implanted air” – disappears²⁷.

If true, then the active process, relying on pressure-stimulation of outer hair cells, creates an effect in a bank of resonating elements that looks like a traveling wave: hence, the traveling wave then becomes an epiphenomenal effect. Conjointly, at higher intensities a passive traveling wave could dominate. There are thus two tuning maps in the cochlea, and the surprise is that our pitch perception remains constant irrespective of stimulation level.

In a few words, the idea is that the traveling wave is an epiphenomenon at low levels and a phenomenon at high levels. However, the very narrow length of basilar membrane over which hair cells suffer damage to overload (Fig. 3.5) suggests that the SAW mechanism plays an important role at high levels also.

10.1/d Observation affects the thing observed

It is a fundamental principle in physics that making an observation disturbs the thing observed. The same applies to the cochlea, and drilling a hole in a sensitive pressure transducer in order to observe its function invites misleading results²⁸. Making a hole is a recipe for destroying hydrostatic pressure and for exaggerating differential pressure. Békésy is reputed to have said²⁹ that “Dehydrated cats and the application of Fourier analysis to hearing problems become more of a handicap for research in hearing”, and there is a sense in which he is right. How many wrong paths have been followed through observations of the basilar membrane of experimental animals? For many years the tuning of the basilar membrane was thought to be broad because coarse experiments said so³⁰. Now we know that the

²⁷ Note that the case for a bubble derives from analogy with some marine animals, and direct confirmation that air is the compressible element is lacking.

²⁸ Ulfendahl (1997), p. 339.

²⁹ Lyon, R. F. and C. Mead (1988). An analog electronic cochlea. *IEEE Transactions on Acoustics, Speech, and Signal Processing* 36: 1119-1134. [p. 1120]

³⁰ Holes have been drilled, fluids have been drained, and oval and round windows removed. Thus, Fletcher (1952) wanted to know the pressures in the fluid just behind the oval window and the round window: “In order to make these measurements, it was necessary to remove both the round window and the oval window” [p. 129, Fletcher, H. (1952). The dynamics of the middle ear and its relation to the acuity of hearing. *J. Acoust. Soc. Am.* 24: 129–131].

membrane is as sharply tuned as the cochlear nerve³¹, but spatial resolution is still inadequate, and researchers still often place reflector beads on the membrane as large as, or larger than, the SAW resonators. Only one set of experimenters – Nilsen and Russell³² – have observed behaviour approaching what I consider is an approximation to the true state of affairs, and even then their results were from compromised cochleas. Membranes have been perforated, allowing perilymph and endolymph to mix³³, and vibrations have been measured transversely when radial vibrations are probably more important³⁴.

For the cochlea to behave normally, non-invasive experiments are required, a consideration which adds weight to ethical arguments against animal experimentation³⁵.

10.1/e Of fish and lizards

The evolutionary fact is that our hearing evolved in the seas, and this thesis has found that a consideration of underwater acoustics adds considerably to understanding how outer hair cells may detect pressure. One suggestion made (§D 8.4/b) is that outer hair cells detect pressure in a way similar to how sharks hear long-distance sounds. Understanding how certain fish can detect ultrasound to over 150 kHz leads us once again to take an underwater perspective. Fay and Popper take an “ichthyocentric” perspective in a review of hearing in vertebrates³⁶, but the pressure component of acoustic signals is not considered.

A curious feature of reptile and amphibian ears is that they hear without a traveling wave, and yet their hearing organ is tonotopically organised in a similar

³¹ Narayan, S. S., et al. (1998). Frequency tuning of basilar membrane and auditory nerve fibers in the same cochlea. *Science* 282: 1882-1884.

³² Nilsen, K. E. and I. J. Russell (2000). The spatial and temporal representation of a tone on the guinea pig basilar membrane. *Proc. Nat. Acad. Sci.* 97: 11751-11758.

³³ Robles, L. and M. A. Ruggero (2001). Mechanics of the mammalian cochlea. *Physiol. Rev.* 81: 1305–1352. [p. 1315]

³⁴ Robles and Ruggero (2001), in trying to explain anomalies in measurements of *transverse* basilar membrane vibration at the apex, raise the possibility (p. 1332) that “even the most sensitive responses so far measured at the apex have underestimated, by as much as 25 dB, the magnitude of vibrations in normal cochleae.”

³⁵ The issue was first raised on p. vi and my position is set out more fully at <http://eprints.anu.edu.au/archive/00001532/01/LAPEA.txt>

³⁶ Fay, R. R. and A. N. Popper (2000). Evolution of hearing in vertebrates: the inner ears and processing. *Hear. Res.* 149: 1–10. [p. 1]

way to ours, and gives rise to “traveling wave-like” behaviour^{37,38,39}. There is an extensive literature on reptile hearing that we do not have space to discuss, but the very presence of tonotopically tuned hearing organs in these animals is a clear demonstration that the traveling wave may not be essential for stimulating mammalian cochleas either⁴⁰. In lizards, we often find a blob of tectorial membrane – a sallet or culmen – sitting on top of two or three hair cell bundles⁴¹, and this structural arrangement for an active oscillator has strong parallels with the standing wave produced by squirting waves. More generally, in birds and reptiles, multiple rows of cells are found sitting in mirror symmetry along a clear dividing line, and this looks like an arrangement for setting up standing waves in the tectorial membrane^{42,43}. The frequent presence of a “foamy” tectorial membrane^{44,45,46} suggests that in these creatures the tectorial membrane, not Hensens body, is the compressible, sound-detecting element. Fig. 10.1 gives an illustration of how such an arrangement is strongly suggested by the appearance of the hearing organ of a frog.

³⁷ Lewis, E. R., et al. (1985). *The Vertebrate Inner Ear*. (CRC Press: Boca Raton, FL).

³⁸ Lewis, E. R., et al. (1982). The tonotopic organization of the bullfrog amphibian papilla, an auditory organ lacking a basilar membrane. *J. Comp. Physiol. A* 145: 437–445.

³⁹ Klinke, R. and M. Pause (1980). Discharge properties of primary auditory fibres in Caiman crocodilus: comparisons and contrasts to the mammalian auditory nerve. *Exp. Brain Res.* 38: 137-150. [p. 147]

⁴⁰ Manley, G. A. (2000). Cochlear mechanisms from a phylogenetic viewpoint. *Proc. Nat. Acad. Sci.* 97: 11736-11743.

⁴¹ Morales, J. and V. Garcia-Martinez (1990). Differentiation of hair cells in the reptile basilar papilla. In: *Inner Ear Pathobiology*, edited by M. Ciges and A. Campos (Karger: Basel), 111-118. [Fig. 6]

⁴² In birds, “hair cells producing sensitive responses are not found on the free basilar membrane... and presumably receive their main stimulation via the tectorial membrane” (p. 225, Manley, G. A. (1995). The avian hearing organ: a status report. In: *Advances in Hearing Research*, edited by G. A. Manley et al. (World Scientific: Singapore), 219-229.)

⁴³ Manley, G. A., et al. (2001). In vivo evidence for a cochlear amplifier in the hair-cell bundle of lizards. *Proc. Nat. Acad. Sci.* 98: 2826-2831.

⁴⁴ Köppl, C. (1988). Morphology of the basilar papilla of the bobtail lizard *Tiliqua rugosa*. *Hear. Res.* 35: 209-228. [Fig. 9b]

⁴⁵ Wever, E. G. (1978). *The Reptile Ear*. (Princeton University Press: Princeton). [e.g., Fig. 19-7, which shows “a cap... of light, sponge-like construction with numerous vacuities both large and small” (p. 664).] This book’s richly detailed illustrations show that reptiles have remarkably intricate hearing organs. Hair cells are clearly interacting via the tectorial membrane to produce resonant mechanical amplification. The network of delay lines connecting kinocilia (apparent in Figs 4-10, 4-20, and 4-21) are particularly striking. Slow wave propagation, mode unknown, is taking place.

⁴⁶ In frogs, similarly, “the tectorial tissue is [mostly] a spongy mass containing numerous interconnected canals with thin membranous walls” p. 976, Wever (1978). Moreover, in a later book [Wever, E. G. (1985). *The Amphibian Ear*. (Princeton University Press: Princeton)] we read (p. 85) that the honeycomb of “thin-walled canals and vesicles that make up the main mass of the tectorial body, and always constitute its lowermost part, clearly have the function of taking up the vibratory motions of the surrounding fluid as produced by the action of sounds”, although he considers them fluid-filled, not air filled, as I suspect. Functionally, an air-filled centre in the tectorial body shown in his Fig. 6-9 [Fig. 10.1 here] makes sense in terms of this vibrating point source being detected by the encircling rows of regularly arranged hair cells.

Here a (presumably compressible) bubble at the centre of its tectorial membrane seems ideally located to create a vibration source that is then detected by a regular array of surrounding hair cells.

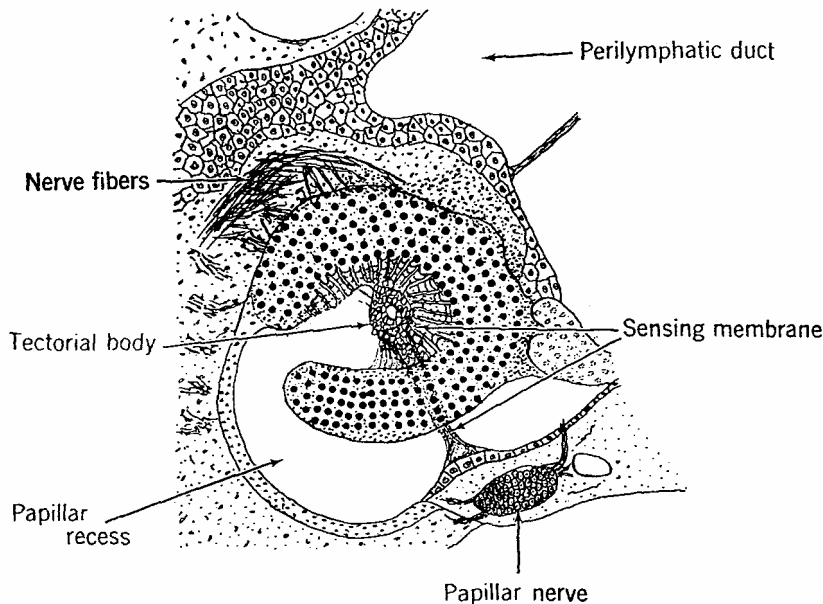


Fig. 10.1. A frog's hearing organ shows what appears to be a bubble in its tectorial membrane encircled by an array of sensing cells. This seems to be a sound-sensing arrangement in which sound pressure causes oscillation in the volume of the bubble, the vibration of which is detected by the cooperatively tuned array of cells surrounding it. Note that the cell rows are spaced more closely at one end than the other. [From Fig. 6-9 of *The Amphibian Ear* by Wever and used with permission of Princeton University Press]

For some time Manley and his group have been attempting to show the similarity between mammalian cochleas and the hearing organs of reptiles and birds⁴⁷, but apparently without denting general reliance on the mammalian traveling wave. The reason probably relates to the general way science works: anomalies are only recognised as such, argue Lightman and Gingerich, after they are given a compelling explanation within a new conceptual framework⁴⁸. A new model is needed before the old can be abandoned.

The standard Békésy traveling wave has met with immense success, and has supplanted Helmholtz's simple and direct idea of one frequency, one resonator. This thesis has highlighted some of the problems surrounding traveling wave theory and suggested that the Helmholtz picture of independent resonators on the partition may

⁴⁷ Manley et al. (2001).

⁴⁸ Lightman, A. and O. Gingerich (1991). When do anomalies begin? *Science* 255: 690-695.

provide a way around them, at least at low sound pressure levels. The resonance alternative is not immune from difficulty, of course, and the major question – how the long build-up and decay is overcome – is still not definitely answered, but an avenue has been provided (§D 9.1/k). In this sense, the thesis provides something of a foot-hold, perhaps allowing Helmholtz’s theory, interpreted in terms of squirting wave resonators, to gain access to firmer ground.

There are many types of wave able to propagate within the structural intricacies of the cochlea⁴⁹. Taking heed of history, squirting waves may not be the final answer, but it provides a plausible candidate for the cochlea’s resonant elements.

10.2 Predictions

How could the Helmholtz view attract renewed favour? Along the way, some or all of the following will need to be demonstrated.

1. That OHCs are directly sensitive to pressure.
2. That OHCs contain a compressible element, probably Hensen’s body.
3. That there are radial standing waves – most likely due to squirting waves – on the basilar membrane.
4. That each row of outer hair cells has different anatomical and functional properties. A row responds either in-phase or in anti-phase to a sound stimulus, creating a succession of antinodes of alternating polarity so that, like a plucked string

⁴⁹ Fig. 17 of Békésy (1961/1999) shows a compression wave, shear wave, *dilatation wave*, Rayleigh wave, and bending wave (also Fig. 12-12 of *EiH*). The question Békésy posed to himself was (p. 735) “which of these waves are present in the inner ear, and which one contributes to the stimulation of the auditory end organs?” He finally became convinced (p. 736) that “at least over the lower frequency range, the ordinary bending of the basilar membrane furnished an adequate description of the vibrations that stimulate the nerve endings.” Békésy, G. v. (1961, 1999). Concerning the pleasures of observing, and the mechanics of the inner ear. In: *Nobel Lectures in Physiology or Medicine 1942–1962*. (World Scientific: Singapore). <http://www.nobel.se/medicine/laureates/1961/bekesy-lecture.pdf>

or laser cavity, standing waves are excited. Gain (and Q) of the system may depend on efferent effects on inter-row potentials.

5. That the tilt of the unit cell in which outer hair cells lie will be found to be an important feature in distinguishing the hearing abilities of different species, sexes, and individuals. Human cochleas, which show the largest otoacoustic emissions, are expected to show the largest amount of tilt (about 7°) and of variability in this parameter. Perhaps people with ‘musical ears’ have a more precise arrangement of outer hair cells.

6. To humans, music means a 12-tone scale. To other animals, a different scale may be important in resolving harmonic structure. The geometry of the unit lattice may dictate the fundamental properties of an animal’s auditory perception.

7. That fish, reptiles, amphibians, and many marine creatures have more in common with mammalian hearing than so far suspected. Their ears probably contain a compressible bubble, too, and again there is an intricate feedback loop between sensory and motile elements.

8. That there is no reverse traveling wave on the basilar membrane, and the oval window and the round window move in phase at low sound levels. There are fast pressure waves in and out of the cochlea, and in between is a long filter delay due to high Q of the resonators. Acoustically, the cochlea might best be described as resembling a reflex loudspeaker enclosure within which the sensing cells of the organ of Corti are suspended.

9. That static pressure could be an efficient way of regulating the gain of the cochlear amplifier. It may be worthwhile revisiting the intralabyrinthine pressure theory of middle ear muscle action.

10. That in addition to confirmation of fast DPOAE and SFOAE responses, fast EOAE responses of cochlear origin will be found in the 0–5 ms time window.

11. That the phalangeal process of the Deiters cell is important in functionally connecting rows of outer hair cells in oblique directions, and that this connection allows the interaction of two frequencies at one cochlear location, thereby generating distortion products at a frequency ratio close to 1.2.

12. Finally, that the coherent reflection filtering model may need to be reinterpreted in terms of *radial* standing waves instead of the current *longitudinal* picture.

10.3 Conclusions

This thesis claims to have identified a prime candidate for resonating elements in the cochlea – a positive feedback loop of squirting waves between rows of outer hair cells. Calculations show that the physical properties of the subtektorial space are about right to support waves of the correct speed, allowing the partition to be tuned over the full range of human hearing. Modeling the cochlea in this way mirrors the operation of a surface acoustic wave resonator and supports the idea that feedback interaction between outer hair cells can generate the high gain and sharp tuning characteristic of the cochlear amplifier. In this way⁵⁰, many properties of the active cochlea can be explained, including an account of how distortion product emissions reach a maximum at a ratio of the primary frequencies of about 1.2. The SAW model is put forward as a simple hypothesis with wide-ranging explanatory power and providing many testable predictions.

The principal question is what stimulates the cochlea's resonant elements? After a century or two of speculation and research, we still cannot be certain what the adequate stimulus for the hair cells is. If it is a causal traveling wave, then we have a hybrid of resonance and traveling wave mechanisms, where the traveling wave is the primary filter and the squirting wave interaction is the second filter. Perhaps, as

⁵⁰ Robles and Ruggero (2001) say that “cochlear amplification in the mammalian cochlea could conceivably involve both the stereociliar mechanism and somatic electromotility” (p. 1341).

Johnstone and colleagues⁵¹ suggested, “the future will see reconciliation of the theories of the two giants of auditory physiology”. But if the adequate stimulus is the fast pressure wave, we have a pure resonance system, at least at sound pressure levels in the range of active mechanics (below about 60–80 dB SPL), and this possibility offers a return to a Helmholtzian approach to cochlear mechanics. A way by which outer hair cell might detect this fast pressure wave is set out, and, while the calculated motion within the cuticular pore of 0.1 nm at threshold is comparable to, or larger than, calculated stereocilia deflections, the associated force (of the order, perhaps, of 10^{-6} pN) is much smaller than the forces (some piconewtons) normally associated with opening ionic channels. Either the calculation is erroneous, the model is wrong, or some way of magnifying the mechanical advantage is involved. If the scheme turns out to be workable then Helmholtz and Gold may have been right all along⁵².

The SAW model, in its pure resonance form, calls for a small, but highly compressible, volume within outer hair cells. This would change the assumptions underlying much current cochlear modeling, and would require delicate work to verify. Nevertheless, I find the simplicity and elegance of the resonance picture philosophically satisfying, and it has been a prime motivation behind this thesis. The new model, in both its pure resonance and second filter forms, is presented as a stimulus to further work, and the wide scope of this thesis is intended to place further experiments within the broadest possible context, including the ethical.

~ ≈ ~

⁵¹ Johnstone, B. M., Patuzzi, R. B., and Yates, G. K. (1986). Basilar membrane measurements and the travelling wave. *Hear. Res.* 22: 147–153. [p. 152]

⁵² “We were happy at Keele to make some retrospective amends to Thomas Gold by displaying an impressive body of evidence to the effect that he had been right all along.” [p. 12, Lighthill, J. (1991). Biomechanics of hearing sensitivity. *Journal of Vibration and Acoustics* 113: 1-13.]

REFERENCES

- Abnet, C. C. and D. M. Freeman (2000). Deformations of the isolated mouse tectorial membrane produced by oscillatory forces. *Hear. Res.* 144: 29-46.
- Afzelius, B. A. (1983). Basal bodies in the immotile-cilia syndrome. *J. Submicrosc. Cytol.* 15: 111-114.
- Aibara, R., et al. (2001). Human middle-ear sound transfer function and cochlear input impedance. *Hear. Res.* 152: 100-109.
- Albrecht-Buehler, G. (1992). Function and formation of centrioles and basal bodies. In: *The Centrosome*, edited by V. I. Kalnins (Academic: San Diego), 69-102.
- Alkon, D. L. (1983). Sensory function of cilia. *J. Submicrosc. Cytol.* 15: 173-176.
- Alkon, D. L. (1983). The role of statocyst sensory cilia in mechanotransduction. *J. Submicrosc. Cytol.* 15: 145-150.
- Allen, J. B. (1977). Cochlear micromechanics: a mechanism for transforming mechanical to neural tuning within the cochlea. *J. Acoust. Soc. Am.* 62: 930-939.
- Allen, J. B. (1980). A cochlear micromechanic model of transduction. In: *Psychophysical, Physiological and Behavioural Studies in Hearing*, edited by G. van den Brink and F. A. Bilsen (Delft University Press: Delft), 85-95.
- Allen, J. B. (2001). Nonlinear cochlear signal processing. In: *Physiology of the Ear (2nd ed.)*, edited by A. F. Jahn and J. Santos-Sacchi (Singular Thomson Learning: San Diego, CA), 393-442.
- Allen, J. B. and M. M. Sondhi (1979). Cochlear mechanics: time-domain solutions. *J. Acoust. Soc. Am.* 66: 123-132.
- Allen, J. B. and P. F. Fahey (1993). A second cochlear-frequency map that correlates distortion product and neural tuning measurements. *J. Acoust. Soc. Am.* 94: 809-816.
- Allen, J. B. and S. T. Neely (1992). Micromechanical models of the cochlea. *Physics Today* 45(7): 40-47.
- Ashmore, J. F. (1988). Ionic mechanisms in hair cells of the mammalian cochlea. *Prog. Brain Res.* 74: 3-9.
- Ashmore, J. F. (1988). What is the stimulus for outer hair cell motility? In: *Basic Issues in Hearing*, edited by H. Duifhuis et al. (Academic Press: London), 42-48.
- Ashmore, J. F. (2002). Biophysics of the cochlea: biomechanics and ion channelopathies. *Br. Med. Bull.* 63: 59-72.
- Ashmore, J. F. and F. Mammano (2001). Can you still see the cochlea for the molecules? *Curr. Opin. Neurobiol.* 11: 449-454.
- Avan, P., et al. (2003). Physiopathological significance of distortion-product otoacoustic emissions at $2f_1-f_2$ produced by high- versus low-level stimuli. *J. Acoust. Soc. Am.* 113: 430-441.
- Avan, P., Magnan, P., Smurzynski, J., Probst, R., and Dancer, A. (1998). Direct evidence of cubic difference tone propagation by intracochlear acoustic pressure measurements in the guinea-pig. *Eur. J. Neurosci.* 10: 1764-1770.
- Baker, G. J. (2000). *Pressure-feedforward and piezoelectric amplification models for the cochlea*. (PhD thesis, Department of Mechanical Engineering, Stanford University).
- Ballantine, D. S., et al. (1997). *Acoustic Wave Sensors: Theory, Design, and Physico-Chemical Applications*. (Academic: San Diego).

REF [2]

- Bannister, L. H., et al. (1988). The cortical lattice: a highly ordered system of subsurface filaments in guinea pig cochlear outer hair cells. *Prog. Brain Res.* 74: 213-219.
- Bausch, A. R., et al. (1999). Measurement of local viscoelasticity and forces in living cells by magnetic tweezers. *Biophys. J.* 76: 573-579.
- Beare, J. I. (1906). *Greek Theories of Elementary Cognition*. (Clarendon Press: Oxford).
- Békésy, G. v. (1955). Paradoxical direction of wave travel along the cochlear partition. *J. Acoust. Soc. Am.* 27: 137-145.
- Békésy, G. v. (1956). Current status of theories of hearing. *Science* 123: 779-783.
- Békésy, G. v. (1960). *Experiments in Hearing*. (McGraw-Hill: New York).
- Békésy, G. v. (1961, 1999). Concerning the pleasures of observing, and the mechanics of the inner ear. In: *Nobel Lectures in Physiology or Medicine 1942-1962*. (World Scientific: Singapore). <http://www.nobel.se/medicine/laureates/1961/bekesy-lecture.pdf>
- Békésy, G. v. (1967). Some similarities in sensory perception of fish and man. In: *Lateral Line Detectors*, edited by P. H. Cahn (Indiana University Press: Bloomington), 417-435.
- Békésy, G. v. (1969). Resonance in the cochlea? *Sound* 3: 86-91.
- Békésy, G. v. (1970). Travelling waves as frequency analysers in the cochlea. *Nature* 225: 1207-1209.
- Békésy, G. v. and W. A. Rosenblith (1948). The early history of hearing – observations and theories. *J. Acoust. Soc. Am.* 20: 727-748.
- Békésy, G. v. and W. A. Rosenblith (1951). The mechanical properties of the ear. In: *Experimental Psychology*, edited by S. S. Stevens (Wiley: New York), 1075-1115.
- Bell, A. (1992). Circadian and menstrual rhythms of spontaneous otoacoustic emissions from human ears. *Hear. Res.* 58: 91-100.
- Bell, A. (1998). A study of frequency variations of spontaneous otoacoustic emissions from human ears. MSc thesis, Australian National University, Canberra.
- Bell, A. (2002). Musical ratios in geometrical spacing of outer hair cells in the cochlea: strings of an underwater piano? 7th Intl Conference on Music Perception and Cognition, Sydney, Causal Productions, Adelaide
- Bell, A. (2003). Are outer hair cells pressure sensors? Basis of a SAW model of the cochlear amplifier. In: *Biophysics of the Cochlea: From Molecules to Models*, edited by A. W. Gummer (World Scientific: Singapore), 429-431.
- Bell, A. (2004). Hearing: travelling wave or resonance? *PLoS Biology* 2: e337.
- Bell, A. (2004). Resonance theories of hearing: a history and a fresh approach. *Acoustics Australia* 32: 108-113.
- Bell, A. and N. H. Fletcher (2004). The cochlear amplifier as a standing wave: "squirting" waves between rows of outer hair cells? *J. Acoust. Soc. Am.* 116: 1016-1024.
- Bell, D. T. and R. C. Li (1976). Surface-acoustic-wave resonators. *Proc. IEEE* 64: 711-721.
- Bialek, W. S. (1983). Thermal and quantum noise in the inner ear. In: *Mechanics of Hearing*, edited by E. de Boer and M. A. Viergever (Delft University Press: Delft), 185-192.
- Bialek, W. S. (1987). Physical limits to sensation and perception. *Ann. Rev. Biophys. Chem.* 16: 455-478.
- Bialek, W. S. and A. Schweitzer (1985). Quantum noise and the threshold of hearing. *Physical Review Letters* 54: 725-728.
- Bialek, W. S. and H. P. Wit (1984). Quantum limits to oscillator stability: theory and experiments on acoustic emissions from the human ear. *Physics Letters* 104A: 173-178.
- Block, S. M. (1992). Biophysical principles of sensory transduction. In: *Sensory Transduction*, edited by D. P. Corey and S. D. Roper (Rockefeller University Press: New York), 1-17.
- Bohren, C. F. (1983). How can a particle absorb more than the light incident on it? *Am. J. Phys.* 51: 323-327.

- Boring, E. G. (1942). *Sensation and Perception in the History of Experimental Psychology*. (Appleton-Century-Crofts: New York).
- Bornens, M. (1979). The centriole as a gyroscopic oscillator. Implications for cell organization and some other consequences. *Biol. Cellulaire* 35: 115-132.
- Braun, M. (1994). Tuned hair cells for hearing, but tuned basilar membrane for overload protection: evidence from dolphins, bats, and desert rodents. *Hear. Res.* 78: 98-114.
- Bredberg, G. (1968). Cellular pattern and nerve supply of the human organ of Corti. *Acta Otolaryngol. Suppl.* 236: 1-135.
- Brinkley, B. R. and E. Stubblefield (1970). Ultrastructure and interaction of the kinetochore and centriole in mitosis and meiosis. *Adv. Cell Biol.* 1: 119-185.
- Brown, A. M. and D. M. Williams (1993). A second filter in the cochlea. In: *Biophysics of Hair Cell Sensory Systems*, edited by H. Duifhuis et al. (World Scientific: Singapore), 72-77.
- Brown, A. M. and D. T. Kemp (1985). Intermodulation distortion in the cochlea: could basal vibration be the major cause of round window CM distortion? *Hear. Res.* 19: 191-198.
- Brown, D. K., et al. (2000). The effects of maturation and stimulus parameters on the optimal f_2/f_1 ratio of the $2f_1-f_2$ distortion product otoacoustic emission in neonates. *Hear. Res.* 145: 17-24.
- Brownell, W. E. (1982). Cochlear transduction: an integrative model and review. *Hear. Res.* 6: 335-360.
- Brownell, W. E. (1986). Outer hair cell motility and cochlear frequency selectivity. In: *Auditory Frequency Selectivity*, edited by B. C. J. Moore and R. D. Patterson (Plenum: New York).
- Brownell, W. E. (1990). Outer hair cell electromotility and otoacoustic emissions. *Ear Hear.* 11: 82-92.
- Brownell, W. E. (1998). How the ear works: Nature's solutions for listening. *Volta Review* 99: 9-28.
- Brownell, W. E. (2002). On the origins of the outer hair cell electromotility. In: *Hair Cell Micromechanics and Otoacoustic Emission*, edited by C. I. Berlin et al. (Delmar Learning (Singular Publishing): Clifton Park, NY), 25-47.
- Brownell, W. E. and A. S. Popel (1998). Electrical and mechanical anatomy of the outer hair cell. In: *Psychophysical and Physiological Advances in Hearing*, edited by A. R. Palmer et al. (Whurr: London), 89-96.
- Brownell, W. E. and W. E. Shehata (1990). The effect of cytoplasmic turgor pressure on the static and dynamic mechanical properties of outer hair cells. In: *Mechanics and Biophysics of Hearing*, edited by P. Dallos et al. (Springer: Berlin), 52-59.
- Brownell, W. E., et al. (1985). Evoked mechanical responses of isolated cochlear outer hair cells. *Science* 227: 194-196.
- Brundin, L. and I. J. Russell (1993). Sound-induced movements and frequency tuning in outer hair cells isolated from the guinea pig cochlea. In: *Biophysics of Hair Cell Sensory Systems*, edited by H. Duifhuis et al. (World Scientific: Singapore), 182-191.
- Brundin, L. and I. J. Russell (1994). Tuned phasic and tonic motile responses of isolated outer hair cells to direct mechanical stimulation of the cell body. *Hear. Res.* 73: 35-45.
- Brundin, L., et al. (1989). Tuned motile responses of isolated cochlear outer hair cells. *Acta Otolaryngologica, Supplement* 467: 229-234.
- Brundin, L., et al. (1992). Sound induced displacement response of the guinea pig hearing organ and its relation to the cochlear potentials. *Hear. Res.* 58: 175-184.
- Brundin, L., Flock, Å., and Canlon, B. (1989). Sound-induced motility of isolated cochlear outer hair cells is frequency-specific. *Nature* 342: 814-816.
- Burns, E. M., et al. (1998). Energy reflectance in the ear canal can exceed unity near spontaneous otoacoustic emission frequencies. *J. Acoust. Soc. Am.* 103: 462-474.
- Burns, E. M., et al. (1998). Energy reflectance in the ear canal can exceed unity near spontaneous otoacoustic emission frequencies. *J. Acoust. Soc. Am.* 103: 462-474.

REF [4]

- Cai, H. and R. S. Chadwick (2003). Radial structure of traveling waves in the inner ear. *SIAM J. Appl. Math.* 63: 1105-1120.
- Cai, H., et al. (2004). Evidence of tectorial membrane radial motion in a propagating mode of a complex cochlear model. *Proc. Nat. Acad. Sci.* 101: 6243-6248.
- Camalet, S., et al. (2000). Auditory sensitivity provided by self-tuned critical oscillations of hair cells. *Proc. Nat. Acad. Sci.* 97: 3183-3188.
- Campbell, C. K. (1998). *Surface Acoustic Wave Devices for Mobile and Wireless Communications*. (Academic Press: San Diego).
- Canlon, B. and L. Brundin (1991). Mechanically induced length changes of isolated outer hair cells are metabolically dependent. *Hear. Res.* 53: 7-16.
- Canlon, B., et al. (1988). Acoustic stimulation causes tonotopic alterations in the length of isolated outer hair cells from guinea pig hearing organ. *Proc. Nat. Acad. Sci.* 85: 7033-7035.
- Chadwick, R. S. (1997). What should be the goals of cochlear modeling? *J. Acoust. Soc. Am.* 102: 3054.
- Chadwick, R. S., et al. (1996). Active control of waves in a cochlear model with subpartitions. *Proc. Natl. Acad. Sci. U. S. A.* 93: 2564-2569.
- Chan, D. K. and A. J. Hudspeth (2005). Ca^{2+} current-driven nonlinear amplification by the mammalian cochlea *in vitro*. *Nat. Neurosci.* 8: 149-155.
- Chan, E. and M. Ulfendahl (1999). Mechanically evoked shortening of outer hair cells isolated from the guinea pig organ of Corti. *Hear. Res.* 128: 166-174.
- Choe, Y., et al. (1998). A model for amplification of hair-bundle motion by cyclical binding of Ca^{2+} to mechanoelectrical-transduction channels. *Proc. Nat. Acad. Sci.* 95: 15321-15326.
- Christiansen, J. A. (1964). On hyaluronate molecules in the labyrinth as mechano-electrical transducers, and as molecular motors acting as resonators. *Acta Otolaryngol.* 57: 33-49.
- Claiborne, L. T., et al. (1976). Scanning the issue. *Proc. IEEE* 64: 579-580.
- Cody, A. R. (1992). Acoustic lesions in the mammalian cochlea: implications for the spatial distribution of the 'active process'. *Hear. Res.* 62: 166-172.
- Cody, A. R. and D. C. Mountain (1989). Low-frequency responses of inner hair cells: evidence for a mechanical origin of peak splitting. *Hear. Res.* 41: 89-100.
- Cody, A. R. and I. J. Russell (1987). The responses of hair cells in the basal turn of the guinea-pig cochlea to tones. *J. Physiol.* 383: 551-569.
- Cooper, N. P. (2000). Radial variation in the vibrations of the cochlear partition. In: *Recent Developments in Auditory Mechanics*, edited by H. Wada et al. (World Scientific: Singapore), 109-115.
- Cooper, N. P. (2004). Compression in the peripheral auditory system. In: *Compression: From Cochlea to Cochlear Implants*, edited by S. P. Bacon et al. (Springer: New York), 18-61.
- Cooper, N. P. and C. A. Shera (2004). Backward-traveling waves in the cochlea? *Association for Research in Otolaryngology, Midwinter Meeting, Abstract 342*.
- Cooper, N. P. and W. S. Rhode (1995). Nonlinear mechanics at the apex of the guinea-pig cochlea. *Hear. Res.* 82: 225-243.
- Cooper, N. P. and W. S. Rhode (1996). Fast travelling waves, slow travelling waves and their interactions in experimental studies of apical cochlear mechanics. *Auditory Neuroscience* 2: 289-299.
- Corey, D. P. (2000). Sound amplification in the inner ear: it takes TM to tango. *Neuron* 28: 7-9.
- Corey, D. P. and A. J. Hudspeth (1979). Ionic basis of the receptor potential in a vertebrate hair cell. *Nature* 281: 675-677.
- Corey, D. P., et al. (2004). TRPA1 is a candidate for the mechanosensitive transduction channel of vertebrate hair cells. *Nature* 432: 723-730.

- Corwin, J. T. (1977). Morphology of the macula neglecta in sharks of the genus *Carcharhinus*. *J. Morphol.* 152: 341-361.
- Corwin, J. T. (1981). Audition in elasmobranchs. In: *Hearing and Sound Communication in Fishes*, edited by W. N. Tavolga et al. (Springer: New York), 81-105.
- Corwin, J. T. (1981). Peripheral auditory physiology in the lemon shark: evidence of parallel otolithic and non-otolithic sound detection. *J. Comp. Physiol.* 142: 379-390.
- Cottin-Bizonne, C., et al. (2003). Low-friction flows of liquid at nanopattern interfaces. *Nature Materials* 2: 237-240.
- Coulouvrat, F., et al. (1998). Lamb-type waves in a symmetric solid-fluid-solid trilayer. *Acustica* 84: 12-20.
- Counter, S. A. (1993). Electromagnetic stimulation of the auditory system: effects and side-effects. *Scand. Audiol. Suppl.* 37: 1-32.
- Craig, V. S. J., et al. (2001). Shear-dependent boundary slip in an aqueous Newtonian liquid. *Physical Review Letters* 87: 054504.
- Dallos, P. (1985). Membrane potential and response changes in mammalian cochlear hair cells during intracellular recording. *J. Neurosci.* 5: 1609-1615.
- Dallos, P. (1985). Response characteristics of mammalian cochlear hair cells. *J. Neurosci.* 5: 1591-1608.
- Dallos, P. (1996). Overview: cochlear neurobiology. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 1-43.
- Dallos, P., et al. (1982). Intracellular recordings from cochlear outer hair cells. *Science* 218: 582-584.
- Dancer, A. (1992). Experimental look at cochlear mechanics. *Audiology* 31: 301-312.
- Dancer, A. L. and R. B. Franke (1989). Mechanics in a "passive" cochlea: travelling wave or resonance? *Il Valsalva* 54 (Suppl. 1): 1-5.
- Davis, H. (1960). Mechanism of excitation of auditory nerve impulses. In: *Neural Mechanisms of the Auditory and Vestibular Systems*, edited by G. L. Rasmussen and W. F. Windle (Thomas: Springfield, IL), 21-39.
- Davis, H. (1973). Introduction: v. Békésy. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic Press: New York), 1-7.
- Davis, H. (1973). The cocktail hour before the serious banquet. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic: New York), 259-271.
- Davis, H. (1981). The second filter is real, but how does it work? *Am. J. Otolaryngol.* 2: 153-158.
- Davis, H. (1983). An active process in cochlear mechanics. *Hear. Res.* 9: 79-90.
- Davis, H., et al. (1934). The electric response of the cochlea. *Am. J. Physiol.* 107: 311-332.
- Davis, H., et al. (1949). Aural microphonics in the cochlea of the guinea pig. *J. Acoust. Soc. Am.* 21: 502-510.
- de Boer, E. (1980). Auditory physics. Physical principles in hearing theory. I. *Physics Reports* 62: 87-174.
- de Boer, E. (1980). Nonlinear interactions and the 'Kemp echo'. *Hear. Res.* 2: 519-526.
- de Boer, E. (1984). Auditory physics. Physical principles in hearing theory. II. *Physics Reports* 105: 141-226.
- de Boer, E. (1991). Auditory physics. Physical principles in hearing theory. III. *Physics Reports* 203: 125-231.
- de Boer, E. (1996). Mechanics of the cochlea: modeling efforts. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 258-317.
- de Boer, E. (1999). Abstract exercises in cochlear modeling: reply. *J. Acoust. Soc. Am.* 105: 2984.

REF [6]

- de Boer, E. and A. L. Nuttall (2003). Properties of amplifying elements in the cochlea. In: *Biophysics of the Cochlea: From Molecules to Models*, edited by A. W. Gummer (World Scientific: Singapore), 331-342.
- Dieler, R., et al. (1991). Concomitant salicylate-induced alterations of outer hair cell subsurface cisternae and electromotility. *J. Neurocytol.* 20: 637-653.
- Dimitriadis, E. K. and R. S. Chadwick (1994). Local wave dispersion in the cochlea [abstract]. *J. Acoust. Soc. Am.* 95: 2840.
- Ding, J. P., et al. (1991). Stretch-activated ion channels in guinea pig outer hair cells. *Hear. Res.* 56: 19-28.
- Donaldson, G. S. and R. A. Ruth (1993). Derived band auditory brain-stem response estimates of traveling wave velocity in humans. I: Normal-hearing subjects. *J. Acoust. Soc. Am.* 93: 940-951.
- Dong, W. and E. S. Olson (2005). Two-tone distortion in intracochlear pressure. *J. Acoust. Soc. Am.* 117: 2999-3015.
- Dong, X., et al. (2002). Piezoelectric reciprocal relationship of the membrane motor in the cochlear outer hair cell. *Biophys. J.* 82: 1254-1259.
- Dorn, E. (1961). Über den Feinbau der Schwimmblase von *Anguilla vulgaris* L. *Zeitschrift für Zellforschung* 55: 849-912.
- Drexler, M., et al. (2004). Isoflurane increases amplitude and incidence of evoked and spontaneous otoacoustic emissions. *Hear. Res.* 194: 135-142.
- Duke, T. (2003). Hair bundles: nano-mechosensors in the inner ear. *Journal of Physics: Condensed Matter* 15: S1747-S1757.
- Duke, T. and F. Jülicher (2003). Active traveling wave in the cochlea. *Physical Review Letters* 90: 158101.
- Echteler, S. M., et al. (1994). Structure of the mammalian cochlea. In: *Comparative Hearing: Mammals*, edited by R. R. Fay and A. N. Popper (Springer: New York), 134-171.
- Edge, R. M., et al. (1998). Morphology of the unfixed cochlea. *Hear. Res.* 124: 1-16.
- Eguíluz, V. M., et al. (2000). Essential nonlinearities in hearing. *Physical Review Letters* 84: 5232-5235.
- Elliott, S. J., et al. (2005). Incorporation of an active feedback loop into the "squirting wave" model of the cochlear amplifier. Twelfth International Congress on Sound and Vibration, Lisbon, Portugal.
- Engström, H. and H. W. Ades (1973). The ultrastructure of the organ of Corti. In: *The Ultrastructure of Sensory Organs*, edited by I. Friedman (North-Holland: Amsterdam), 83-151.
- Engström, H. and J. Wersäll (1958). Structure and innervation of the inner ear: sensory epithelia. *Int. Rev. Cytol.* 7: 535-583.
- Engström, H. and J. Wersäll (1958). The ultrastructural organization of the organ of Corti and of the vestibular sensory epithelia. *Exp. Cell Res. Suppl.* 5: 460-492.
- Engström, H., et al. (1962). Structure and functions of the sensory hairs of the inner ear. *J. Acoust. Soc. Am.* 34: 1356-1363.
- Evans, B. N. and P. Dallos (1993). Stereocilia displacement induced somatic motility of cochlear outer hair cells. *Proc. Nat. Acad. Sci.* 90: 8347-8351.
- Evans, B. N., et al. (1989). Asymmetries in motile responses of outer hair cells in simulated in vivo conditions. In: *Cochlear Mechanisms*, edited by J. P. Wilson and D. T. Kemp (Plenum: New York).
- Evans, B. N., et al. (1991). Outer hair cell electromotility: the sensitivity and vulnerability of the DC component. *Hear. Res.* 52: 288-304.
- Evans, E. F. and J. P. Wilson (1973). The frequency selectivity of the cochlea. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic: New York), 519-551.

- Ewing, A. W. (1989). *Arthropod Bioacoustics: Neurobiology and Behaviour*. (Edinburgh University Press: Edinburgh).
- Fahey, P. F. and J. B. Allen (1997). Measurement of distortion product phase in the ear canal of the cat. *J. Acoust. Soc. Am.* 102: 2880-2891.
- Fänge, R. (1953). The mechanisms of gas transport in the euphysoclist swimbladder. *Acta Physiologica Scandinavica Suppl.* 110: 1-133.
- Fänge, R. (1966). Physiology of the swimbladder. *Physiol. Rev.* 46: 299-322.
- Fay, R. R. (1992). Ernest Glen Wever: a brief biography and bibliography. In: *The Evolutionary Biology of Hearing*, edited by D. B. Webster et al. (Springer: New York), xliii-li.
- Fay, R. R. and A. N. Popper (2000). Evolution of hearing in vertebrates: the inner ears and processing. *Hear. Res.* 149: 1-10.
- Feng, L., et al. (2002). Super-hydrophobic surfaces: from natural to artificial. *Advanced Materials* 14: 1857-1860.
- Fex, J. (1974). Neural excitatory processes of the inner ear. In: *Handbook of Sensory Physiology*, vol 5.1, edited by W. D. Keidel and W. D. Neff (Springer: Berlin), 585-646.
- Fletcher, H. (1929). *Speech and Hearing*. (Van Nostrand: New York). <http://auditorymodels.org>
- Fletcher, H. (1951). Acoustics. *Physics Today* 4(12): 12-18.
- Fletcher, H. (1952). The dynamics of the middle ear and its relation to the acuity of hearing. *J. Acoust. Soc. Am.* 24: 129-131.
- Fletcher, N. H. (1992). *Acoustic Systems in Biology*. (Oxford University Press: New York).
- Flock, Å. (1967). Ultrastructure and function in the lateral line organs. In: *Lateral Line Detectors*, edited by P. H. Cahn (Indiana University Press: Bloomington), 163-197.
- Flock, Å. (1971). Sensory transduction in hair cells. In: *Handbook of Sensory Physiology*, edited by W. R. Loewenstein (Springer: Berlin), vol. 5.1, 396-441.
- Flock, Å., et al. (1962). Morphological basis of directional sensitivity of the outer hair cells in the organ of Corti. *J. Acoust. Soc. Am.* 34: 1351-1355.
- Flock, Å., et al. (1977). Studies on the sensory hairs of receptor cells in the inner ear. *Acta Otolaryngol.* 83: 85-91.
- Flock, Å., et al. (1998). Vital staining of the hearing organ: visualization of cellular structure with confocal microscopy. *Neuroscience* 83: 215-228.
- Forge, A., et al. (1993). Structural variability of the sub-surface cisternae in intact, isolated outer hair cells shown by fluorescent labelling of intracellular membranes and freeze-fracture. *Hear. Res.* 64: 175-183.
- Formby, C. and D. B. Gjerdingen (1981). Some systematic observations on monaural diplacusis. *Audiology* 20: 219-233.
- Frank, G., et al. (1999). Limiting dynamics of high-frequency electromechanical transduction of outer hair cells. *Proc. Nat. Acad. Sci.* 96: 4420-4425.
- Freeman, D. M., et al. (2003). Dynamic material properties of the tectorial membrane: a summary. *Hear. Res.* 180: 1-10.
- Freeman, S., et al. (2000). Bone conduction experiments in animals: evidence for a non-osseous mechanism. *Hear. Res.* 146: 72-80.
- Frommer, G. H. and C. R. Steele (1979). Permeability of fluid flow through hair cell cilia. *J. Acoust. Soc. Am.* 65: 759-764.
- Fukazawa, T. (2002). How can the cochlear amplifier be realized by the outer hair cells which have nothing to push against? *Hear. Res.* 172: 53-61.
- Fuller, R. B. (1975). *Synergetics: Explorations in the Geometry of Thinking*. (Macmillan: New York).
- Furgason, E. S. and V. L. Newhouse (1973). Convolution and correlation using nonlinear interactions of Lamb waves. *IEEE Transactions on Sonics and Ultrasonics* SU-20: 360-364.

REF [8]

- Furst, M., et al. (1988). Ear canal acoustic distortion at $2f_1$ – f_2 from human ears: relation to other emissions and perceived combination tones. *J. Acoust. Soc. Am.* 84: 215-221.
- Gale, J. E. and J. F. Ashmore (1994). Charge displacement induced by rapid stretch in the basolateral membrane of the guinea-pig outer hair cell. *Proc. Roy. Soc. Lond. B* 255: 243–249.
- Gale, J. E., et al. (2001). FM1-43 dye behaves as a permeant blocker of the hair-cell mechanotransducer channel. *J. Neurosci.* 21: 7013-7025.
- Gaskill, S. A. and A. M. Brown (1990). The behavior of the acoustic distortion product, $2f_1$ – f_2 , from the human ear and its relation to auditory sensitivity. *J. Acoust. Soc. Am.* 88: 821-839.
- Geisler, C. D. (1976). Mathematical models of the mechanics of the inner ear. In: *Handbook of Sensory Physiology*, edited by W. D. Keidel and W. D. Neff (Springer: Berlin), vol. 5.3, 391-415.
- Geisler, C. D. (1998). *From Sound to Synapse: Physiology of the Mammalian Ear*. (Oxford University Press: New York).
- Geisler, C. D. and A. E. Hubbard (1972). New boundary conditions and results for the Peterson–Bogert model of the cochlea. *J. Acoust. Soc. Am.* 52: 1629-1634.
- Givelberg, E. and J. Bunn (2003). A comprehensive three-dimensional model of the cochlea. *J. Comp. Phys.* 191: 377-391.
- Gold, T. (1948). Hearing. II. The physical basis of the action of the cochlea. *Proc. Roy. Soc. Lond. B* 135: 492-498.
- Gold, T. (1953). Hearing. *IEEE Transactions on Information Theory* 1: 125-127.
- Gold, T. (1987). The theory of hearing. In: *Highlights in Science*, edited by H. Messel (Pergamon: Sydney), 149-157.
- Gold, T. (1989). Historical background to the proposal, 40 years ago, of an active model for cochlear frequency analysis. In: *Cochlear Mechanisms: Structure, Function, and Models*, edited by J. P. Wilson and D. T. Kemp (Plenum: New York), 299-305.
- Gold, T. (1989). New ideas in science. *Journal of Scientific Exploration* 3: 103-112.
- Gold, T. and R. J. Pumphrey (1948). Hearing. I. The cochlea as a frequency analyzer. *Proc. Roy. Soc. Lond. B* 135: 462-491.
- Goldstein, S. (1965). Note on the conditions at the surface of contact of a fluid with a solid body. In: *Modern Developments in Fluid Dynamics [reprint of 1938 edition]*, edited by S. Goldstein (Dover: New York), 676-680.
- Goode, R. L., et al. (1993). Measurement of umbo vibration in human subjects: method and possible clinical applications. *Am. J. Otol.* 14: 247-251.
- Goodman, S. S., et al. (2003). The origin of SFOAE microstructure in the guinea pig. *Hear. Res.* 183: 7-17.
- Goycoolea, M. V. (1992). The round window membrane under normal and pathological conditions. *Acta Otolaryngol.* 493: 43-55.
- Granick, S., et al. (2003). Slippery questions about complex fluids flowing past solids. *Nature Materials* 2: 221-227.
- Gray, E. G. and R. J. Pumphrey (1958). Ultra-structure of the insect ear. *Nature* 181: 618.
- Gray, J. D. (1964). Comment: The transmission of acoustic energy from air to the receptor organ in the cochlea. *J. Laryngol. Otol.* 78: 877-878.
- Green, D. M. and C. C. Wier (1975). Gold and Pumphrey revisited, again. *J. Acoust. Soc. Am.* 57: 935-938.
- Greenwood, D. D. (1962). Approximate calculation of the dimensions of traveling-wave envelopes in four species. *J. Acoust. Soc. Am.* 34: 1364–1369.
- Griesinger, C. B., et al. (2002). FM1-43 reveals membrane recycling in adult inner hair cells of the mammalian cochlea. *J. Neurosci.* 22: 3939-3952.

- Guelke, R. (1951). A theory of the action of the cochlear resonators. *J. Acoust. Soc. Am.* 23: 717-719.
- Guelke, R. W. and A. E. Bunn (1984). Resonance in theories of hearing. *J. Laryngol. Otol.* 98: 1177-1183.
- Guild, S. R. (1937). Comments on the physiology of hearing and the anatomy of the inner ear. *Laryngoscope* 47: 365-372.
- Guinan, J. J. (1996). Physiology of olivocochlear efferents. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 435-502.
- Guinan, J. J., et al. (2005). Insights into cochlear mechanics from the effects of medial olivocochlear efferents. Proceedings, Auditory Mechanisms: Processes and Models, Portland, OR
- Gulick, W. L., et al. (1989). *Hearing: Physiological Acoustics, Neural Coding, and Psychophysics*. (Oxford University Press: Oxford).
- Gummer, A. W., et al. (1996). Resonant tectorial membrane motion in the inner ear: its crucial role in frequency tuning. *Proc. Nat. Acad. Sci.* 93: 8727-8732.
- Gummer, A. W., et al. (2005). Pulsating fluid motion and deflection of the stereocilia of the inner hair cells due to the electromechanics of the outer hair cells. Proceedings, Auditory Mechanisms: Processes and Models, Portland, OR
- Hallpike, C. S. and P. Scott (1940). Observations on the function of the round window. *J. Physiol.* 99: 76-82.
- Hallpike, C. S., Hartridge, H., and Rawdon-Smith, A. F. (1937). On the electrical responses of the cochlea and the auditory tract of the cat to a phase reversal produced in a continuous musical tone. *Proc. Roy. Soc. Lond. B* 122: 175-185.
- Harada, Y., et al. (1990). Three-dimensional ultrastructure of cochlea: a review. In: *Inner Ear Pathobiology (Adv. Otorhinolaryngol. v. 45)*, edited by M. Ciges and A. Campos (Karger: Basel), 49-68.
- Hardesty, I. (1908). On the nature of the tectorial membrane and its probable role in the anatomy of hearing. *Am. J. Anat.* 8: 109-179 (+ plates).
- Hardesty, I. (1915). On the proportions, development and attachment of the tectorial membrane. *Am. J. Anat.* 18: 1-73.
- Hartmann, W. M. (1998). *Signals, Sound, and Sensation*. (Springer: New York).
- Hartridge, H. (1921). A vindication of the resonance hypothesis of audition. *Br. J. Psychol.* 11: 277-288.
- Hartridge, H. (1921). A vindication of the resonance hypothesis of audition. II. *Br. J. Psychol.* 12: 142-146.
- Hassan, W. and P. B. Nagy (1997). On the low-frequency oscillation of a fluid layer between two elastic plates. *J. Acoust. Soc. Am.* 102: 3343-3348.
- Hawkins, J. E. (1965). Cytoarchitectural basis of the cochlear transducer. *Symposia on Quantitative Biology* 30: 147-157.
- Hawkins, J. E. (1976). Drug ototoxicity. In: *Handbook of Sensory Physiology*, vol. 5.3, edited by W. D. Keidel and W. D. Neff (Springer: Berlin), 707-748.
- Hawkins, J. E. (2004). Sketches of otohistory. Part 1: otohistory, how it all began. *Audiol. Neurotol.* 9: 66-71.
- Helmholtz, H. L. F. v. (1874). *The Mechanism of the Ossicles and the Membrana Tympani [translated by J. Hinton]*. (New Sydenham Society: London).
- Helmholtz, H. L. F. v. (1875). *On the Sensations of Tone as a Physiological Basis for the Theory of Music*. (Longmans, Green: London).
- Hemmert, W., et al. (2000). Characteristics of the travelling wave in the low-frequency region of a temporal-bone preparation of the guinea-pig cochlea. *Hear. Res.* 142: 184-202.

REF [10]

- Hemmert, W., et al. (2000). Mechanical impedance of the tectorial membrane. Midwinter Meeting, Florida, Association for Research on Otolaryngology
<http://www.aro.org/archives/2000/4838.html>.
- Hemmert, W., et al. (2000). Three-dimensional motion of the organ of Corti. *Biophys. J.* 78: 2285-2297.
- Hiesey, R. W. and E. D. Schubert (1972). Cochlear resonance and phase-reversed signals. *J. Acoust. Soc. Am.* 51: 518-519.
- Higgs, D. M. (2004). Neuroethology and sensory ecology of teleost ultrasound detection. In: *The Senses of Fish*, edited by G. von der Emde et al. (Kluwer: Boston, MA), 173-188.
- Hild, W., et al. (2003). The effect of wetting on the microhydrodynamics of surfaces lubricated with water and oil. *Wear* 254: 871-875.
- Hillman, D. E. (1969). New ultrastructural findings regarding a vestibular ciliary apparatus and its possible functional significance. *Brain Res.* 13: 407-412.
- Hillman, D. E. and E. R. Lewis (1971). Morphological basis for a mechanical linkage in otolithic receptor transduction in the frog. *Science* 174: 416-419.
- Horrobin, D. F. (1990). The philosophical basis of peer review and the suppression of innovation. *Journal of the American Medical Association* 263: 1438-1441.
- Howard, J. (1997). Molecular motors: structural adaptations to cellular functions. *Nature* 389: 561-567.
- Hubbard, A. E. (1993). A traveling-wave amplifier model of the cochlea. *Science* 259: 68-71.
- Hubbard, A. E. and D. C. Mountain (1996). Analysis and synthesis of cochlear mechanical function using models. In: *Auditory Computation*, edited by H. L. Hawkins et al. (Springer: New York), 62-120.
- Hudspeth, A. J. (1982). Extracellular current flow and the site of transduction by vertebrate hair cells. *J. Neurosci.* 2: 1-10.
- Hudspeth, A. J. (1997). Mechanical amplification of stimuli by hair cells. *Curr. Opin. Neurobiol.* 7: 480-486.
- Hudspeth, A. J. and D. P. Corey (1977). Sensitivity, polarity, and conductance change in the response of vertebrate hair cells to controlled mechanical stimuli. *Proc. Nat. Acad. Sci.* 74: 2407-2411.
- Hudspeth, A. J. and R. Jacobs (1979). Stereocilia mediate transduction in vertebrate hair cells. *Proc. Nat. Acad. Sci.* 76: 1506-1509.
- Hudspeth, A. J., et al. (2000). Putting ion channels to work: mechanoelectrical transduction, adaptation, and amplification by hair cells. *Proc. Nat. Acad. Sci.* 97: 11765-11772.
- Hunt, F. V. (1978). *Origins in Acoustics*. (Yale U. P.: New Haven, CT).
- Huxley, A. F. (1969). Is resonance possible in the cochlea after all? *Nature* 221: 935-940.
- Ikeda, K. and T. Takasaka (1993). Confocal laser microscopical images of calcium distribution and intracellular organelles in the outer hair cell isolated from the guinea pig cochlea. *Hear. Res.* 66: 169-176.
- ITER [International Team for Ear Research] (1989). Cellular vibration and motility in the organ of Corti. *Acta Oto-Laryngologica, Supplement* 467: 1-279.
- Iwasa, K. H. and G. Ehrenstein (2002). Cooperative interaction as the physical basis of the negative stiffness in hair cell stereocilia. *J. Acoust. Soc. Am.* 111: 2208-2212.
- Iwasa, K. H. and R. S. Chadwick (1992). Elasticity and active force generation of cochlear outer hair cells. *J. Acoust. Soc. Am.* 92: 3169-3173.
- Iwasa, K. H., et al. (1991). Stretch sensitivity of the lateral wall of the auditory outer hair cell from the guinea pig. *Neurosci. Lett.* 133: 171-174.
- Jahn, A. F. (1988). Bone physiology of the temporal bone, otic capsule, and ossicles. In: *Physiology of the Ear*, edited by A. F. Jahn and J. Santos-Sacchi (Raven: New York), 143-158.

- Johnstone, B. M., Patuzzi, R. B., and Yates, G. K. (1986). Basilar membrane measurements and the travelling wave. *Hear. Res.* 22: 147–153.
- Jordan, E. J. (1970). The design and use of moving-coil loudspeaker units. *Wireless World* Nov: 533-537.
- Jordan, E. J. (1971). Loudspeaker enclosures. Types of baffle and the acoustical laws governing their application. *Wireless World* Jan: 2-6.
- Jülicher, F. (2001). Mechanical oscillations at the cellular scale. *C. R. Acad. Sci. Paris (Series IV)* 2: 849-860.
- Jülicher, F., et al. (2001). Physical basis of two-tone interference in hearing. *Proc. Nat. Acad. Sci.* 98: 9080–9085.
- Junger, M. C. and D. Feit (1993). *Sound, Structures, and Their Interaction*. (Acoust. Soc. Am.: New York).
- Kalmijn, A. J. (1988). Hydrodynamic and acoustic field detection. In: *Sensory Biology of Aquatic Animals*, edited by J. Atema et al. (Springer: New York), 83-130.
- Kalmijn, A. J. (2000). Detection and processing of electromagnetic and near-field acoustic stimuli in elasmobranch fishes. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 355: 1135-1141.
- Karavitaki, K. and D. C. Mountain (2000). Comparing patterns of electrically-evoked vibrations from the apical and middle turns of the gerbil cochlea. Midwinter Meeting, Florida, Association for Research in Otolaryngology
- Karavitaki, K. D. and D. C. Mountain (2003). Is the cochlear amplifier a fluid pump? In: *Biophysics of the Cochlea: From Molecules to Models*, edited by A. W. Gummer (World Scientific: Singapore), 310-311.
- Karlan, M. S., et al. (1972). Dual origin of the cochlear microphonics: inner and outer hair cells. *Ann. Otol. Rhinol. Laryngol.* 81: 696-704.
- Kemp, D. T. (1978). Stimulated acoustic emissions from within the human auditory system. *J. Acoust. Soc. Am.* 64: 1386-1391.
- Kemp, D. T. (1979). Evidence of mechanical nonlinearity and frequency selective wave amplification in the cochlea. *Arch. Otorhinolaryngol.* 224: 37-45.
- Kemp, D. T. (2002). Exploring cochlear status with otoacoustic emissions: the potential for new clinical applications. In: *Otoacoustic Emissions: clinical applications*, edited by M. S. Robinette and T. J. Glatke (Thieme: New York), 1-47.
- Kemp, D. T. (2003). Twenty five years of OAEs. *ENT News* 12(5): 47-52.
- Kemp, D. T. and P. F. Tooman (2005). DPOAE micro- and macrostructure: their origin and significance. Proceedings, Auditory Mechanisms: Processes and Models, Portland, OR
- Kennedy, H. J., et al. (2005). Force generation by mammalian hair bundles supports a role in cochlear amplification. *Nature* 433: 880-883.
- Kern, A. and R. Stoop (2003). Essential role of couplings between hearing nonlinearities. *Physical Review Letters* 91: 128101.
- Khanna, S. M. and D. G. B. Leonard (1982). Basilar membrane tuning in the cat cochlea. *Science* 215: 305-306.
- Kharakoz, D. P. (2000). Protein compressibility, dynamics, and pressure. *Biophys. J.* 79: 511-525.
- Kiang, N. Y. S., et al. (1986). Single unit clues to cochlear mechanisms. *Hear. Res.* 22: 171-182.
- Kim, J. and C.-J. Kim (2002). Nanostructured surfaces for dramatic reduction of flow resistance in droplet-based microfluidics. Proc. 2002 IEEE Conf. MEMS, Las Vegas, 479-482
- Kimura, R. S. (1975). The ultrastructure of the organ of Corti. *Int. Rev. Cytol.* 42: 173–222.
- Kino, G. S. (1976). Acoustoelectric interactions in acoustic-surface-wave devices. *Proc. IEEE* 64: 724-748.

REF [12]

- Klinke, R. and M. Pause (1980). Discharge properties of primary auditory fibres in Caiman crocodilus: comparisons and contrasts to the mammalian auditory nerve. *Exp. Brain Res.* 38: 137-150.
- Kohllöffel, L. U. E. (1983). Problems in aural sound conduction. In: *Mechanisms of Hearing*, edited by E. de Boer and M. A. Viergever (Delft University Press: Delft), 211-217.
- Kohllöffel, L. U. E. (1984). Notes on the comparative mechanics of hearing. II. On cochlear shunts in birds. *Hear. Res.* 13: 77-81.
- Kondrachuk, A. V. (2002). Models of otolithic membrane–hair cell bundle interaction. *Hear. Res.* 166: 96-112.
- Kondrachuk, A. V., et al. (1991). Mathematical simulation of the gravity receptor. *The Physiologist* 34: S212-S213.
- Konrad-Martin, D. and D. H. Keefe (2005). Transient-evoked stimulus-frequency and distortion-product otoacoustic emissions in normal and impaired ears. *J. Acoust. Soc. Am.* 117: 3799-3815.
- Konrad-Martin, D., et al. (2001). Sources of distortion product otoacoustic emissions revealed by suppression experiments and inverse fast Fourier transforms in normal ears. *J. Acoust. Soc. Am.* 109: 2862-2879.
- Köppl, C. (1988). Morphology of the basilar papilla of the bobtail lizard *Tiliqua rugosa*. *Hear. Res.* 35: 209-228.
- Kornblatt, J. A. (1998). Materials with negative compressibilities. *Science* 281: 143a.
- Kössl, M. and M. Vater (1985). The cochlear frequency map of the mustache bat, *Pteronotus parnelli*. *J. Comp. Physiol. A* 157: 687–697.
- Kosteljik, P. J. (1950). *Theories of Hearing*. (Universitaire Pers Leiden: Leiden).
- Kringlebotn, M. (1995). The equality of volume displacements in the inner ear windows. *J. Acoust. Soc. Am.* 98: 192-196.
- Kros, C. J. (1996). Physiology of mammalian cochlear hair cells. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 318-385.
- Krstic, R. V. (1979). *Ultrastructure of the mammalian cell: an atlas*. (Springer: Berlin).
- Lafuma, A. and D. Quéré (2003). Superhydrophobic states. *Nature Materials* 2: 457-460.
- Lamb, H. (1925). *The Dynamical Theory of Sound*. (Edward Arnold: London).
- Lavigne-Rebillard, M. and R. Pujol (1986). Development of the auditory hair cell surface in human fetuses. *Anat. Embryol.* 174: 369–377.
- Legan, P. K., et al. (2000). A targeted deletion in a-tectorin reveals that the tectorial membrane is required for the gain and timing of cochlear feedback. *Neuron* 28: 273-285.
- Leighton, T. G. (2004). From seas to surgeries, from babbling brooks to baby scans: the acoustics of gas bubbles in liquids. *Int. J. Modern Phys. B* 18: 3267-3314.
- Leonova, E. V. and Y. Raphael (1998). Alteration of membranous structures in ototoxically damaged outer hair cells of the organ of Corti. Midwinter Meeting, Florida, Association for Research in Otolaryngology
- LePage, E. L. (2003). The mammalian cochlear map is optimally warped. *J. Acoust. Soc. Am.* 114: 896-906.
- Lesser, M. B. and D. A. Berkley (1972). Fluid mechanics of the cochlea. Part 1. *Journal of Fluid Mechanics* 51: 497-512.
- Lewis, E. R., et al. (1982). The tonotopic organization of the bullfrog amphibian papilla, an auditory organ lacking a basilar membrane. *J. Comp. Physiol. A* 145: 437–445.
- Lewis, E. R., et al. (1985). *The Vertebrate Inner Ear*. (CRC Press: Boca Raton, FL).
- Liberman, M. C., et al. (2004). Otoacoustic emissions without somatic motility: can stereocilia mechanics drive the mammalian cochlea? *J. Acoust. Soc. Am.* 116: 1649-1655.

- Licklider, J. C. R. (1953). Hearing. *Annu. Rev. Psychol.* 4: 89–110.
- Licklider, J. C. R. (1959). Three auditory theories. In: *Psychology: A Study of a Science. Study 1. Conceptual and Systematic*, edited by S. Koch (McGraw-Hill: New York), 41-144.
- Lighthill, J. (1978). *Waves in Fluids*. (Cambridge University Press: Cambridge).
- Lighthill, J. (1981). Energy flow in the cochlea. *J. Fluid Mech.* 106: 149-213.
- Lighthill, J. (1991). Biomechanics of hearing sensitivity. *Journal of Vibration and Acoustics* 113: 1-13.
- Lighthill, J. (1992). Acoustic streaming in the ear itself. *J. Fluid Mech.* 239: 551-606.
- Lightman, A. and O. Gingerich (1991). When do anomalies begin? *Science* 255: 690-695.
- Lim, D. J. (1986). Functional structure of the organ of Corti: a review. *Hear. Res.* 22: 117-146.
- Lin, T. and J. J. Guinan (2000). Auditory-nerve-fibre responses to high-level clicks: interference patterns indicate that excitation is due to the combination of multiple drives. *J. Acoust. Soc. Am.* 107: 2615-2630.
- Lin, T. and J. J. Guinan (2004). Time–frequency analysis of auditory-nerve-fiber and basilar-membrane click responses reveal glide irregularities and non-characteristic-frequency skirts. *J. Acoust. Soc. Am.* 116: 405-416.
- Linder, T. E., et al. (2003). Round window atresia and its effect on sound transmission. *Otology and Neurotology* 24: 259-263.
- Lindgren, A. G. and W. Li (2003). Analysis and simulation of a classic model of cochlea mechanics via a state-space realization. *unpublished manuscript*: <http://www.ele.uri.edu/SASGroup/cochlea.html>.
- Lloyd, P. and M. Redwood (1965). Wave propagation in a layered plate composed of two solids with perfect contact, slip, or a fluid layer at their interface. *Acustica* 16: 224-232.
- Londero, A., et al. (2002). Magnitudes and phases of human distortion-product otoacoustic emissions at $2f_1-f_2$ against f_2/f_1 : effects of an audiometric notch. *Hear. Res.* 167: 46-56.
- Long, G. R., et al. (1991). Modeling synchronization and suppression of spontaneous otoacoustic emissions using Van der Pol oscillators: effects of aspirin administration. *J. Acoust. Soc. Am.* 89: 1201-1212.
- Lonsbury-Martin, B. L. and G. K. Martin (1987). Repeated TTS exposures in monkeys: alterations in hearing, cochlear structure, and single-unit thresholds. *J. Acoust. Soc. Am.* 81: 1507-1518.
- Lonsbury-Martin, B. L., et al. (1988). Spontaneous otoacoustic emissions in a nonhuman primate. II. Cochlear anatomy. *Hear. Res.* 33: 69-94.
- Lonsbury-Martin, B. L., et al. (1990). Distortion product emissions in humans I. Basic properties in normally hearing subjects. *Ann. Otol. Rhinol. Laryngol.* 99: 3-29.
- Lonsbury-Martin, B. L., et al. (1997). Distortion product otoacoustic emissions. In: *Otoacoustic Emissions: Clinical Applications*, edited by M. S. Robinette and T. J. Glatke (Thieme: New York), 83-109.
- Lowenstein, O. and J. Wersäll (1959). A functional interpretation of the electron-microscopic structure of the sensory hairs in the cristæ of the elasmobranch *Raja clavata* in terms of directional sensitivity. *Nature* 184: 1807–1808.
- Lukashkin, A. N. and I. J. Russell (2003). A second, low-frequency mode of vibration in the intact mammalian cochlea. *J. Acoust. Soc. Am.* 113: 1544-1550.
- Lukashkin, A. N. and I. J. Russell (2005). Dependence of the DPOAE amplitude pattern on acoustical biasing of the cochlear partition. *Hear. Res.* 203: 45-53.
- Lukashkin, A. N., et al. (2002). One source for distortion product otoacoustic emissions generated by low- and high-level primaries. *J. Acoust. Soc. Am.* 111: 2740-2748.
- Lynch, T. J., et al. (1982). Input impedance of the cochlea in cat. *J. Acoust. Soc. Am.* 72: 108-130.

REF [14]

- Lyon, R. F. and C. Mead (1988). An analog electronic cochlea. *IEEE Transactions on Acoustics, Speech, and Signal Processing* 36: 1119-1134.
- Macdonald, A. G. and P. J. Fraser (1999). The transduction of very small hydrostatic pressures. *Comp. Biochem. Physiol.* 122A: 13-36.
- Magariyama, Y., et al. (1994). Very fast flagellar rotation. *Nature* 371: 752.
- Maines, J. D. and E. G. S. Paige (1976). Surface-acoustic-wave devices for signal processing applications. *Proc. IEEE* 64: 639-652.
- Malgrange, B., et al. (2002). Identification of factors that maintain mammalian outer hair cells in adult organ of Corti explants. *Hear. Res.* 170: 48-58.
- Mammano, F. and J. F. Ashmore (1993). Reverse transduction measured in the isolated cochlea by laser Michelson interferometry. *Nature* 365: 838-841.
- Mammano, F., et al. (1999). ATP-induced Ca^{2+} release in cochlear outer hair cells: localization of an isositol triphosphate-gated Ca^{2+} store to the base of the sensory hair bundle. *J. Neurosci.* 19: 6918-6929.
- Manley, G. A. (1995). The avian hearing organ: a status report. In: *Advances in Hearing Research*, edited by G. A. Manley et al. (World Scientific: Singapore), 219-229.
- Manley, G. A. (2000). Cochlear mechanisms from a phylogenetic viewpoint. *Proc. Nat. Acad. Sci.* 97: 11736-11743.
- Manley, G. A., et al. (2001). In vivo evidence for a cochlear amplifier in the hair-cell bundle of lizards. *Proc. Nat. Acad. Sci.* 98: 2826-2831.
- Manoussaki, D. and R. S. Chadwick (2000). Effects of geometry on fluid loading in a coiled cochlea. *SIAM J. Appl. Math.* 61: 369-386.
- Martin, C., et al. (2002). Isolated congenital round window absence. *Ann. Otol. Rhinol. Laryngol.* 111: 799-801.
- Martin, G. K., et al. (1988). Spontaneous otoacoustic emissions in a nonhuman primate. I. Basic features and relations to other emissions. *Hear. Res.* 33: 49-68.
- Martin, P., et al. (2000). Negative hair-bundle stiffness betrays a mechanism for mechanical amplification by the hair cell. *Proc. Nat. Acad. Sci.* 97: 12026-12031.
- Martin, P., et al. (2001). Comparison of a hair bundle's spontaneous oscillations with its response to mechanical stimulation reveals the underlying active process. *Proc. Nat. Acad. Sci.* 98: 14380-14385.
- Martin, P., et al. (2003). Spontaneous oscillation by hair bundles of the bullfrog's sacculus. *J. Neurosci.* 23: 4533-4548.
- Mauermann, M. and B. Kollmeier (2004). Distortion product otoacoustic emission (DPOAE) input/output functions and the influence of the second DPOAE source. *J. Acoust. Soc. Am.* 116: 2199-2212.
- McFadden, D. (1986). The curious half-octave shift: evidence for a basalward migration of the traveling-wave envelope with increasing intensity. In: *Basic and Applied Aspects of Noise-induced Hearing Loss*, edited by R. J. Salvi et al. (Plenum: New York), 295-312.
- McFadden, D. (1993). A speculation about the parallel ear asymmetries and sex differences in hearing sensitivity and otoacoustic emissions. *Hear. Res.* 68: 143-151.
- McFadden, D. and E. G. Pasanen (1999). Spontaneous otoacoustic emissions in heterosexuals, homosexuals, and bisexuals. *J. Acoust. Soc. Am.* 105: 2403-2413.
- McFadden, D. and H. S. Plattsmier (1984). Aspirin abolishes spontaneous oto-acoustic emissions. *J. Acoust. Soc. Am.* 76: 443-448.
- Merchan, M. A., et al. (1980). Morphology of Hensen's cells. *J. Anat.* 131: 519-523.
- Meyer, J., et al. (1998). Evidence for opening of hair-cell transducer channels after tip-link loss. *J. Neurosci.* 18: 6748-6756.

- Meyer, J., et al. (2001). Pronounced infracuticular endocytosis in mammalian outer hair cells. *Hear. Res.* 161: 10–22.
- Meyer, J., et al. (2005). Tonic mechanosensitivity of outer hair cells after loss of tip links. *Hear. Res.* 202: 97–113.
- Meyers, J. R., et al. (2003). Lighting up the senses: FM1-43 loading of sensory cells through nonselective ion channels. *J. Neurosci.* 23: 4054–4065.
- Mills, D. M. (1998). Origin and implications of two "components" in distortion product otoacoustic emissions. In: *Otoacoustic Emissions: Basic Science and Clinical Applications*, edited by C. I. Berlin (Singular: San Diego), 85–104.
- Mills, D. M. and E. W. Rubel (1994). Variation of distortion product otoacoustic emissions with furosemide injection. *Hear. Res.* 77: 183–199.
- Møller, A. R. (1986). Effect of click spectrum and polarity on round window N₁N₂ response in the rat. *Audiology* 25: 29–43.
- Moore, B. C. J. (1977). *Introduction to the Psychology of Hearing*. (Macmillan: London).
- Morales, J. and V. Garcia-Martinez (1990). Differentiation of hair cells in the reptile basilar papilla. In: *Inner Ear Pathobiology*, edited by M. Ciges and A. Campos (Karger: Basel), 111–118.
- Morris, C. E. (2001). Mechanosensitive ion channels in eukaryotic cells. In: *Cell Physiology Sourcebook: A Molecular Approach, Third Edition*, edited by N. Sperelakis (Academic Press: New York), 745–760.
- Morse, P. M. (1991). *Vibration and Sound*. (Acoustical Society of America: New York).
- Moulin, A. (2000). Influence of primary frequencies ratio on distortion product otoacoustic emissions amplitude. II. Interrelations between multicomponent DPOAEs, tone-burst-evoked OAEs, and spontaneous OAEs. *J. Acoust. Soc. Am.* 107: 1471–1486.
- Moulin, A. and D. T. Kemp (1996). Multicomponent acoustic distortion product otoacoustic emission phase in humans. II. Implications for distortion product otoacoustic emissions generation. *J. Acoust. Soc. Am.* 100: 1640–1662.
- Mountain, D. C. and A. R. Cody (1999). Multiple modes of inner hair cell stimulation. *Hear. Res.* 132: 1–14.
- Murphy, W. J., et al. (1995). Relaxation dynamics of spontaneous otoacoustic emissions perturbed by external tones. II. Suppression of interacting emissions. *J. Acoust. Soc. Am.* 97: 3711–3720.
- Myrberg, A. A. (2001). The acoustical biology of elasmobranchs. *Environmental Biology of Fishes* 60: 31–45.
- Naftalin, L. (1963). The transmission of acoustic energy from air to the receptor organ in the cochlea. *Life Sci.* 2: 101–106.
- Naftalin, L. (1964). Comment: Reply to criticisms by Mr. A. Tumarkin and Mr. J. D. Gray. *J. Laryngol. Otol.* 78: 969–971.
- Naftalin, L. (1965). Some new proposals regarding acoustic transmission and transduction. *Symposia on Quantitative Biology* 30: 169–180.
- Naftalin, L. (1970). Biochemistry and biophysics of the tectorial membrane. In: *Biochemical Mechanisms in Hearing and Deafness*, edited by M. M. Paparella (Thomas: Springfield, ILL), 205–210; 290–293.
- Naftalin, L. (1976). The peripheral hearing mechanism: a biochemical and biological approach. *Ann. Otol. Rhinol. Laryngol.* 85: 38–42.
- Naftalin, L. (1977). The peripheral hearing mechanism: new biophysical concepts for transduction of the acoustic signal to an electrochemical event. *Physiol. Chem. Phys.* 9: 337–382.
- Naftalin, L. (1981). Energy transduction in the cochlea. *Hear. Res.* 5: 307–315.
- Naidu, R. C. (2001). Mechanical properties of the organ of corti and their significance in cochlear mechanics, PhD thesis, Boston University.

REF [16]

- Naidu, R. C. and D. C. Mountain (1998). Measurements of the stiffness map challenge a basic tenet of cochlear theories. *Hear. Res.* 124: 124–131.
- Namba, K. and F. Vonderviszt (1997). Molecular architecture of bacterial flagellum. *Q. Rev. Biophys.* 30: 1-65.
- Narayan, S. S., et al. (1998). Frequency tuning of basilar membrane and auditory nerve fibers in the same cochlea. *Science* 282: 1882-1884.
- Nedzeltnitsky, V. (1980). Sound pressures in the basal turn of the cat cochlea. *J. Acoust. Soc. Am.* 68: 1676-1689.
- Neely, S. T. and D. O. Kim (1986). A model for active elements in cochlear biomechanics. *J. Acoust. Soc. Am.* 79: 1472-1480.
- Neubert, K. (1950). Die Basilarmembran des Menschen und ihr Verankerungssystem: ein morphologischer Beitrag zur Theorie des Hörens. *Zeitschrift für Anatomie und Entwicklungsgeschichte* 114: 539-588.
- Nevenzel, J. C., et al. (1966). Lipids of the living coelacanth, *Latimeria chalumnae*. *Science* 152: 1753-1755.
- Nevenzel, J. C., et al. (1969). The lipids of some lantern fishes (family Myctophidae). *Comp. Biochem. Physiol.* 31: 25-36.
- Nielsen, J. G. and O. Munk (1964). A hadal fish (*Bassogigas profundissimus*) with a functional swimbladder. *Nature* 204: 594-595.
- Nilsen, K. E. and I. J. Russell (1999). Timing of cochlear feedback: spatial and temporal representation of a tone across the basilar membrane. *Nat. Neurosci.* 2: 642-648.
- Nilsen, K. E. and I. J. Russell (2000). The spatial and temporal representation of a tone on the guinea pig basilar membrane. *Proc. Nat. Acad. Sci.* 97: 11751-11758.
- Nobili, R., et al. (2003). Otoacoustic emissions from residual oscillations of the cochlear basilar membrane in a human ear model. *J. Assoc. Res. Otolaryngol.* 4: 478-494.
- Offutt, G. (1970). A proposed mechanism for the perception of acoustic stimuli near threshold. *J. Aud. Res.* 10: 226-228.
- Offutt, G. (1974). Structures for the detection of acoustic stimuli in the Atlantic codfish, *Gadus morhua*. *J. Acoust. Soc. Am.* 56: 665-671.
- Offutt, G. (1984). *The Electromodel of the Auditory System*. (GoLo Press: Shepherdstown, WV).
- Offutt, G. (1986). Wever and Lawrence revisited: effects of nulling basilar membrane movement on concomitant whole-nerve action potential. *J. Aud. Res.* 26: 43-54.
- Ohinata, Y., et al. (2000). Intense noise induces formation of vasoactive lipid peroxidation products in the cochlea. *Brain Res.* 878: 163-173.
- Ohmori, H. (1988). Mechanical stimulation and Fura-2 fluorescence in the hair bundle of dissociated hair cells of the chick. *J. Physiol.* 399: 115–137.
- Olson, E. S. (2001). Intracochlear pressure measurements related to cochlear tuning. *J. Acoust. Soc. Am.* 110: 349-367.
- Olson, E. S. (2004). Harmonic distortion in intracochlear pressure and its analysis to explore the cochlear amplifier. *J. Acoust. Soc. Am.* 115: 1230-1241.
- Olson, E. S. and D. C. Mountain (1990). In vivo measurement of basilar membrane stiffness. In: *Mechanics and Biophysics of Hearing*, edited by P. Dallos et al. (Springer: Berlin), 296-303.
- Ospeck, M. C., et al. (2002). RC time constant paradox of outer hair cells [abstract]. *Biophys. J.* 82: 251a.
- Ospeck, M., et al. (2001). Evidence of a Hopf bifurcation in frog hair cells. *Biophys. J.* 80: 2597-2607.
- Ospeck, M., et al. (2003). Limiting frequency of the cochlear amplifier based on electromotility of outer hair cells. *Biophys. J.* 84: 739-749.

- Palisca, C. V. (2000). Moving the affections through music: pre-Cartesian psycho-physiological theories. In: *Number to Sound*, edited by P. Gozza (Kluwer: Dordrecht), 289-308.
- Patuzzi, R. B. (1987). A model of the generation of the cochlear microphonic with nonlinear hair cell transduction and nonlinear basilar membrane mechanics. *Hear. Res.* 30: 73-82.
- Patuzzi, R. B. (1996). Cochlear micromechanics and macromechanics. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 186-257.
- Patuzzi, R. B. and D. Robertson (1988). Tuning in the mammalian cochlea. *Physiol. Rev.* 68: 1009–1082.
- Paul, H. and R. Fischer (1983). Light absorption by a dipole. *Sov. Phys. Usp.* 26: 923-926.
- Pelling, A. E., et al. (2004). Local nanomechanical motion of the cell wall of *Saccharomyces cerevisiae*. *Science* 305: 1147-1150.
- Pelster, B. (1995). Metabolism of the swimbladder tissue. In: *Biochemistry and Molecular Biology of Fishes*, vol. 4, edited by P. W. Hochachka and T. P. Mommsen (Elsevier: Amsterdam), 101-118.
- Pesic, P. (2000). *Labyrinth: A search for the hidden meaning of science*. (MIT Press: Cambridge, MA).
- Peterson, L. C. and B. P. Bogert (1950). A dynamical theory of the cochlea. *J. Acoust. Soc. Am.* 22: 369-381.
- Phleger, C. F. (1991). Biochemical aspects of buoyancy in fishes. In: *Biochemistry and Molecular Biology of Fishes*, Vol. 1, edited by P. W. Hochachka and T. P. Mommsen (Elsevier: Amsterdam), 209-247.
- Pickles, J. O. (1988). *An Introduction to the Physiology of Hearing*, Second edition. (Academic Press: London).
- Pierson, M. and A. R. Møller (1980). Effect of modulation of basilar membrane position on the cochlear microphonic. *Hear. Res.* 2: 151-162.
- Pierson, M. and A. R. Møller (1980). Some dualistic properties of the cochlear microphonic. *Hear. Res.* 2: 135-149.
- Pierson, M. G. and A. R. Møller (1982). Corresponding effects of acoustic fatigue on the cochlear microphonic and the compound action potential. *Hear. Res.* 6: 61-82.
- Pierson, M. G. and A. R. Møller (1982). Corresponding effects of hypoxia on the cochlear microphonic and the compound action potential. *Hear. Res.* 6: 83-101.
- Pohlman, A. G. (1933). A reconsideration of the mechanics of the auditory apparatus. *J. Laryngol. Otol.* 48: 156-195.
- Pollice, P. A. and W. E. Brownell (1993). Characterization of the outer hair cell's lateral wall membrane. *Hear. Res.* 70: 187-196.
- Polvogt, L. M. and S. J. Crowe (1937). Anomalies of the cochlea in patients with normal hearing. *Ann. Otol. Rhinol. Laryngol.* 46: 579-591.
- Pratt, H., et al. (1998). Contralaterally evoked transient otoacoustic emissions. *Hear. Res.* 115: 39-44.
- Prentiss, C. W. (1913). On the development of the membrana tectoria with reference to its structure and attachments. *Am. J. Anat.* 14: 425–457.
- Preyer, S., et al. (1994). Frequency response of mature guinea-pig outer hair cells to stereociliary displacement. *Hear. Res.* 77: 116–124.
- Preyer, S., et al. (1995). Abolition of the receptor potential response of isolated mammalian outer hair cells by hair-bundle treatment with elastase: a test of the tip-link hypothesis. *Hear. Res.* 89: 187–193.
- Pujol, R., et al. (1992). Correlation between the length of outer hair cells and the frequency coding of the cochlea. In: *Auditory Physiology and Perception (Advances in the Biosciences volume 83)*, edited by Y. Cazals et al. (Pergamon: Oxford), 45-51.
- Pumphrey, R. J. (1950). Hearing. *Symp. Soc. Exp. Biol.* 4: 3-18.

REF [18]

- Pumphrey, R. J. and T. Gold (1947). Transient reception and the degree of resonance of the human ear. *Nature* 160: 124-125.
- Pumphrey, R. J. and T. Gold (1948). Phase memory of the ear: a proof of the resonance hypothesis. *Nature* 161: 640.
- Puria, S., et al. (1997). Sound-pressure measurements in the cochlear vestibule of human-cadaver ears. *J. Acoust. Soc. Am.* 101: 2754-2770.
- Quate, C. F. and R. B. Thompson (1970). Convolution and correlation in real time with nonlinear acoustics. *Appl. Phys. Lett.* 16: 494-496.
- Rabinowitz, W. M. and G. P. Widin (1984). Interaction of spontaneous oto-acoustic emissions and external sounds. *J. Acoust. Soc. Am.* 76: 1713-1720.
- Raftenberg, M. N. (1990). Flow of endolymph in the inner spiral sulcus and the subtektorial space. *J. Acoust. Soc. Am.* 87: 2606-2620.
- Ratnanather, J. T., et al. (1993). Mechanical properties of the outer hair cell. In: *Biophysics of Hair Cell Sensory Systems*, edited by H. Duifhuis et al. (World Scientific: Singapore), 199–206.
- Ravicz, M. E., et al. (1996). An upper bound on the compressibility of the human cochlea. Midwinter Meeting, Association for Research in Otolaryngology
- Ravicz, M. E., et al. (2004). Mechanisms of hearing loss resulting from middle-ear fluid. *Hear. Res.* 195: 103-130.
- Recio, A., Rich, N. C., Narayan, S. S., and Ruggero, M. A. (1998). Basilar-membrane responses to clicks at the base of the chinchilla cochlea. *J. Acoust. Soc. Am.* 103: 1972-1989.
- Ren, T. (2002). Longitudinal pattern of basilar membrane vibration in the sensitive cochlea. *Proc. Nat. Acad. Sci.* 99: 17101-17106.
- Ren, T. (2004). Reverse propagation of sound in the gerbil cochlea. *Nat. Neurosci.* 7: 333-334.
- Ren, T., et al. (2003). Measurements of basilar membrane vibration using a scanning laser interferometer. In: *Biophysics of the Cochlea*, edited by A. W. Gummer (World Scientific: Singapore), 211-219.
- Reuter, G., et al. (1994). Electromotility of outer hair cells from the cochlea of the echolocating bat, *Carollia perspicillata*. *J. Comp. Physiol. A* 175: 449-455.
- Reysenbach de Haan, F. W. (1956). Hearing in whales. *Acta Oto-Laryngologica Suppl.* 134: 1-114.
- Rhode, W. S. and A. Recio (2000). Study of mechanical motions in the basal region of the chinchilla cochlea. *J. Acoust. Soc. Am.* 107: 3317-3332.
- Ricci, A. J., et al. (2000). Active hair bundle motion linked to fast transducer adaptation in auditory hair cells. *J. Neurosci.* 20: 7131-7142.
- Robinette, M. S. and T. J. Glatke (2002). *Otoacoustic Emissions: Clinical Applications*. (Thieme: New York).
- Robles, L. and M. A. Ruggero (2001). Mechanics of the mammalian cochlea. *Physiol. Rev.* 81: 1305–1352.
- Rogers, P. H. and M. Cox (1988). Underwater sound as a biological stimulus. In: *Sensory Biology of Aquatic Animals*, edited by J. Atema et al. (Springer: New York), 131-149.
- Rossing, T. D. and N. H. Fletcher (1995). *Principles of Vibration and Sound*. (Springer: New York).
- Rouse, G. W. and J. O. Pickles (1991). Paired development of hair cells in neuroblasts of the teleost lateral line. *Proc. R. Soc. Lond. B* 246: 123-128.
- Ruggero, M. A. (1994). Cochlear delays and traveling waves: comments on 'Experimental look at cochlear mechanics'. *Audiology* 33: 131-142.
- Ruggero, M. A. (1995). What is the mechanical stimulus for the inner hair cell? Clues from auditory-nerve and basilar-membrane responses to low-frequency sounds. In: *Active Hearing*, edited by Å. Flock et al. (Pergamon: Oxford), 321-336.

- Ruggero, M. A. (2004). Comparison of group delays of $2f_1-f_2$ distortion product otoacoustic emissions and cochlear travel times. *ARLO* 5: 143-147.
- Ruggero, M. A. and A. N. Temchin (2003). Middle-ear transmission in humans: wide-band, not frequency-tuned? *Acoustics Research Letters Online* 4: 53-58.
- Ruggero, M. A. and N. C. Rich (1989). "Peak splitting": intensity effects in cochlear afferent responses to low frequency tones. In: *Cochlear Mechanisms: Structure, Function, and Models*, edited by J. P. Wilson and D. T. Kemp (Plenum: New York), 259-267.
- Russell, I. J. and K. E. Nilsen (1997). The location of the cochlear amplifier: spatial representation of single tone on the guinea pig basilar membrane. *Proc. Nat. Acad. Sci.* 94: 2660-2664.
- Rybalchenko, V. and J. Santos-Sacchi (2003). Cl^- flux through a non-selective, stretch-sensitive conductance influences the outer hair cell motor of the guinea-pig. *J. Physiol.* 547: 873-891.
- Saito, K. (1983). Fine structure of the sensory epithelium of guinea-pig organ of Corti: subsurface cisternae and lamellar bodies in the outer hair cells. *Cell Tissue Res.* 229: 467-481.
- Sand, O., et al. (1975). Electrical and mechanical stimulation of hair cells in the mudpuppy. *J. Comp. Physiol. A* 102: 13-26.
- Santi, P. A. (1988). Cochlear microanatomy and ultrastructure. In: *Physiology of the Ear*, edited by A. F. Jahn and J. Santos-Sacchi (Raven Press: New York), 173-199.
- Santi, P. A., et al. (1986). A computer-assisted morphometric analysis of the organ of Corti. *Hear. Res.* 24: 189-201.
- Santos-Sacchi, J. (1991). Isolated supporting cells from the organ of Corti: some whole cell electrical characteristics and estimates of gap junctional conductance. *Hear. Res.* 52: 89-98.
- Schacht, J. and H. P. Zenner (1987). Evidence that phosphoinositides mediate motility in cochlear outer hair cells. *Hear. Res.* 31: 155-160.
- Schacht, J., et al. (1995). Slow motility of outer hair cells. In: *Active Hearing*, edited by Å. Flock et al. (Pergamon: Oxford), 209-220.
- Scherer, M. P. and A. W. Gummer (2004). Vibration pattern of the organ of Corti up to 50 kHz: evidence for resonant electromechanical force. *Proc. Nat. Acad. Sci.* 101: 17652-17657.
- Schiff, M. and H. Christiansen-Lou (1967). The nature of lipid globules in Hensen's cells. *Ann. Otol. Rhinol. Laryngol.* 76: 624-637.
- Schliwa, M. (1992). Cell polarity and centrosomes. In: *The Centrosome*, edited by V. I. Kalnins (Academic: San Diego), 331-351.
- Schubert, E. D. (1978). History of research on hearing. In: *Handbook of Perception, vol. IV, Hearing*, edited by E. C. Carterette and M. P. Friedman (Academic: New York), 41-80.
- Schweitzer, L., et al. (1996). Anatomical correlates of the passive properties underlying the developmental shift in the frequency map of the mammalian cochlea. *Hear. Res.* 97: 84-94.
- Sens, P., et al. (1993). Hydrodynamic modes of viscoelastic soap films. *Langmuir* 9: 3212-3218.
- Shambaugh, G. E. (1907). A restudy of the minute anatomy of structures in the cochlea with conclusions bearing on the solution of the problem of tone perception. *Am. J. Anat.* 7: 245-257 (+ plates).
- Shera, C. A. (2001). Intensity-invariance of fine-structure in basilar-membrane click responses: implications for cochlear mechanics. *J. Acoust. Soc. Am.* 110: 332-348.
- Shera, C. A. (2003). Mammalian spontaneous otoacoustic emissions are amplitude-stabilized cochlear standing waves. *J. Acoust. Soc. Am.* 114: 244-262.
- Shera, C. A. (2004). Mechanisms of mammalian otoacoustic emission and their implications for the clinical utility of otoacoustic emissions. *Ear Hear.* 25: 86-97.
- Shera, C. A. and G. Zweig (1991). A symmetry suppresses the cochlear catastrophe. *J. Acoust. Soc. Am.* 89: 1276-1289.
- Shera, C. A. and G. Zweig (1992). An empirical bound on the compressibility of the cochlea. *J. Acoust. Soc. Am.* 92: 1382-1388.

REF [20]

- Shera, C. A. and G. Zweig (1992). Middle-ear phenomenology: the view from the three windows. *J. Acoust. Soc. Am.* 92: 1356-1370.
- Shera, C. A. and J. J. Guinan (1999). Evoked otoacoustic emissions arise by two fundamentally different mechanisms: a taxonomy for mammalian OAEs. *J. Acoust. Soc. Am.* 105: 782-798.
- Shera, C. A. and J. J. Guinan (2003). Stimulus-frequency-emission group delay: a test of coherent reflection filtering and a window on cochlear tuning. *J. Acoust. Soc. Am.* 113: 2762-2772.
- Shera, C. A., et al. (2002). Revised estimates of human cochlear tuning from otoacoustic and behavioural measurements. *Proc. Nat. Acad. Sci.* 99: 3318-3323.
- Shera, C. A., et al. (2004). Do forward- and backward-traveling waves occur within the cochlea? Countering the critique of Nobili et al. *J. Assoc. Res. Otolaryngol.* 5: 349-359.
- Shera, C. A., et al. (2005). Coherent reflection in a two-dimensional cochlea: short-wave versus long-wave scattering in the generation of reflection-source otoacoustic emissions. *J. Acoust. Soc. Am.* 118: 287-313.
- Shera, C. A., et al. (2005). Coherent-reflection models of reflection-source OAEs with and without slow transverse retrograde waves. *Assoc. Res. Otolaryngol. Abs.* 413.
- Shoelson, B., et al. (2003). Theoretical and experimental considerations for the study of anisotropic elastic moduli of the mammalian tectorial membrane. Mid-Winter Meeting, Florida, Association for Research in Otolaryngology
- Shoelson, B., et al. (2004). Evidence and implications of inhomogeneity in tectorial membrane elasticity. *Biophys. J.* 87: 2768-2777.
- Siegel, J. H. (2005). The biophysical origin of otoacoustic emissions. Proceedings, Auditory Mechanisms: Processes and Models, Portland, OR
- Sigworth, F. J. (2003). Life's transistors. *Nature* 423: 21-22.
- Sinn, C. (2000). Acoustic spectroscopy of aerogel precursors. *Progr. Colloid Polym. Sci* 115: 325-328.
- Sinn, C. (2004). When jelly gets the blues: audible sound generation with gels and its origins. *Journal of Non-Crystalline Solids* 347: 11-17.
- Slepecky, N. B. (1995). Sensory and supporting cells in the organ of Corti: cytoskeletal organization related to cellular function. In: *Active Hearing*, edited by Å. Flock et al. (Pergamon: Oxford), 87-101.
- Slepecky, N. B. (1996). Structure of the mammalian cochlea. In: *The Cochlea*, edited by P. Dallos et al. (Springer: New York), 44-129.
- Slepecky, N. B. and S. C. Chamberlain (1982). Distribution and polarity of actin in the sensory hair cells of the chinchilla cochlea. *Cell Tissue Res.* 224: 15-24.
- Smith, W. R. (1981). Circuit-model analysis and design of interdigital transducers for surface acoustic wave devices. In: *Physical Acoustics*, edited by W. P. Mason and R. N. Thurston (Academic: New York), 15, 99-189.
- Snyder, R. L. and C. E. Schreiner (1984). The auditory neurophonic: basic properties. *Hear. Res.* 15: 261-280.
- Sobkowicz, H. M., et al. (1995). The kinocilium of auditory hair cells and evidence for its morphogenetic role during the regeneration of stereocilia and cuticular plates. *J. Neurocytol.* 24: 633-653.
- Sohmer, H. and S. Freeman (2004). Further evidence for a fluid pathway during bone conduction auditory stimulation. *Hear. Res.* 193: 105-110.
- Sohmer, H., et al. (2000). Bone conduction experiments in humans: a fluid pathway from bone to ear. *Hear. Res.* 146: 81-88.
- Sohmer, H., et al. (2004). Semicircular canal fenestration: improvement of bone- but no air-conducted auditory thresholds. *Hear. Res.* 187: 105-110.

- Spicer, S. S., et al. (1998). Cytologic evidence for mechanisms of K^+ transport and genesis of Hensen bodies and subsurface cisternae in outer hair cells. *Anat. Rec.* 251: 97-113.
- Steel, K. P. (1983). The tectorial membrane of mammals. *Hear. Res.* 9: 327-359.
- Steele, C. R. (1973). A possibility for sub-tectorial membrane fluid motion. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic: New York), 69-93.
- Steele, C. R. (1990). Elastic behaviour of the outer hair cell wall. In: *Mechanics and Biophysics of Hearing*, edited by P. Dallos et al. (Springer: Berlin), 76-83.
- Steele, C. R. (1999). Toward three-dimensional analysis of cochlear structure. *ORL – Journal for Oto-Rhino-Laryngology and Its Related Specialities* 61: 238-251.
- Steele, C. R. and J. G. Zais (1983). Basilar membrane properties and cochlear response. In: *Mechanics of Hearing*, edited by E. de Boer and M. A. Viergever (Delft University Press: Boston, MA), 29-36.
- Steele, C. R. and J. G. Zais (1985). Effect of coiling in a cochlear model. *J. Acoust. Soc. Am.* 77: 1849-1852.
- Steele, C. R. and J. G. Zais (1985). Effect of opening and draining the cochlea. *J. Acoust. Soc. Am.* 78: 84-89.
- Steele, C. R. and K.-M. Lim (1999). Cochlear model with three-dimensional fluid, inner sulcus and feed-forward mechanism. *Audiol. Neurotol.* 4: 197-203.
- Stenfelt, S., et al. (2003). Basilar membrane and osseous spiral lamina motion in human cadavers with air and bone conduction stimuli. *Hear. Res.* 181: 131-143.
- Stenfelt, S., et al. (2004). Fluid volume displacement at the oval and round windows with air and bone conduction stimulation. *J. Acoust. Soc. Am.* 115: 797-812.
- Stenfelt, S., et al. (2004). Round window membrane motion with air conduction and bone conduction stimulation. *Hear. Res.* 198: 10-24.
- Stewart, M. J. (2003). Contrast echocardiography. *Heart* 89: 342-348.
- Steyger, P. S., et al. (1989). Tubulin and microtubules in cochlear hair cells: comparative immunocytochemistry and ultrastructure. *Hear. Res.* 42: 1-16.
- Stoop, R. and A. Kern (2004). Essential auditory contrast-sharpening is preneuronal. *Proc. Nat. Acad. Sci.* 101: 9179-9181.
- Stoop, R., et al. (2004). Limit cycles, noise, and chaos in hearing. *Microsc. Res. Tech.* 63: 400-412.
- Stylis, S. C. (1973). The duplex theory of hearing. A new concept. *J. Laryngol. Otol.* 87: 727-738.
- Sukharev, S. and D. P. Corey (2004). Mechanosensitive channels: multiplicity of families and gating paradigms. *Sci. SKTE 2004*: re4.
- Talmadge, C. L., et al. (1999). Experimental confirmation of the two-source interference model for the fine structure of distortion product otoacoustic emissions. *J. Acoust. Soc. Am.* 105: 275-292.
- Tanaka, Y., et al. (1980). Potentials of outer hair cells and their membrane properties in cationic environments. *Hear. Res.* 2: 431-438.
- Tardent, P. and V. Schmid (1972). Ultrastructure of mechanoreceptors of the polyp *Coryne pintneri* (Hydrozoa, Athecata). *Exp. Cell Res.* 72: 265-275.
- Tavolga, W. N. (1981). Retrospect and prospect: listening through a wet filter. In: *Hearing and Sound Communication in Fishes*, edited by W. N. Tavolga et al. (Springer: New York), 573-587.
- Thiele, A. N. (2004). The Thiele–Small parameters for measuring, specifying and designing loudspeakers. *Address to Singapore Engineering Society, July 2004*: www.aes-singapore.org/LSPRMTRS604.doc.
- Thomas, D. R., et al. (1999). Rotational symmetry of the C ring and a mechanism for the flagellar rotary motor. *Proc. Natl. Acad. Sci. U. S. A.* 96: 10134-10139.
- Thurm, U., et al. (1983). Cilia specialized for mechanoreception. *J. Submicrosc. Cytol.* 15: 151-155.

REF [22]

- Tiedemann, H. (1970). A new approach to theory of hearing. *Acta Oto-Laryngologica Suppl.* 277: 1-50.
- Tonndorf, J. (1959). The transfer of energy across the cochlea. *Acta Otolaryngol.* 50: 171-184.
- Tonndorf, J. (1962). Time/frequency analysis along the partition of cochlear models: a modified place concept. *J. Acoust. Soc. Am.* 34: 1337-1350.
- Tsang, P. T. S. K. (1997). *Laser interferometric flow measurements in the lateral line organ*. PhD thesis. (Rijksuniversiteit: Groningen). www.ub.rug.nl/eldoc/dis/science/p.t.s.k.tsang/
- Tumarkin, A. (1964). Comment: Criticisms of Dr. Naftalin's theories. *J. Laryngol. Otol.* 78: 874-876.
- Tumarkin, A. (1980). The controversial cupula and the enigmatic kinocilium. *J. Laryngol. Otol.* 94: 917-927.
- Tumarkin, A. (1984). Multi modal hearing, the fundamental importance of the kinociliary servo system and the folly of psychoacoustics. Part I. The struggle for power and the anthropocentric obsession. *J. Laryngol. Otol.* 98: 557-566.
- Tumarkin, A. (1984). Multi modal hearing: the fundamental importance of the kinociliary servo mechanism and the folly of psychoacoustics. Part II. The garrulous fish and the unemployed kinocilium. *J. Laryngol. Otol.* 98: 659-670.
- Tumarkin, A. (1984). Multi modal hearing: the fundamental importance of the kinociliary servo mechanism and the folly of psychoacoustics. Part III. Psychologists try to capture the unknowable in a net of mathematical equations. *J. Laryngol. Otol.* 98: 747-757.
- Tumarkin, A. (1986). Stereocilia versus kinocilia part III: the efferent innervation. *J. Laryngol. Otol.* 100: 1219-1224.
- Tumarkin, A. (1986). Stereocilia versus kinocilia. Part I: in the acoustic sensors. *J. Laryngol. Otol.* 100: 1009-1018.
- Tumarkin, A. (1986). Stereocilia versus kinocilia. Part II: The vestibular sensors. *J. Laryngol. Otol.* 100: 1107-1114.
- Ulfendahl, M. (1997). Mechanical responses of the mammalian cochlea. *Prog. Neurobiol.* 53: 331-380.
- Ulfendahl, M., et al. (1991). Effects of opening and resealing the cochlea on the mechanical response in the isolated temporal bone preparation. *Hear. Res.* 57: 31-37.
- van Bergeijk, W. A. (1964). Directional and nondirectional hearing in fish. In: *Marine Bio-Acoustics*, edited by W. N. Tavolga (Pergamon: Oxford), 1, 281-299.
- van den Berg, A. V. and A. Schuijf (1983). Discrimination of sounds based on the phase difference between particle motion and acoustic pressure in the shark *Chiloscyllium griseum*. *Proc. Roy. Soc. Lond. B* 218: 127-134.
- Vater, M. (1988). Cochlear physiology and anatomy in bats. In: *Animal Sonar: Processes and Performance*, edited by P. E. Nachtigall and P. W. B. Moore (Plenum: New York), 225-241.
- Vento, B. A., et al. (2004). Development of f_2/f_1 ratio in humans. *J. Acoust. Soc. Am.* 115: 2138-2147.
- Viergever, M. A. (1978). Basilar membrane motion in a spiral-shaped cochlea. *J. Acoust. Soc. Am.* 64: 1048-1053.
- Vinnikov, Y. A. and L. K. Titova (1964). *The Organ of Corti*. (Consultants Bureau: New York).
- Vogel, S. (2003). *Comparative Biomechanics*. (Princeton University Press: Princeton).
- von Eggeling, H., et al. (1927). *Haut und Sinnesorgane*. (Springer: Berlin).
- Voss, S. E., et al. (1996). Is the pressure difference between the oval and round windows the effective acoustic stimulus for the cochlea? *J. Acoust. Soc. Am.* 100: 1602-1616.
- Wada, H., et al. (1998). Measurement of guinea pig basilar membrane using computer-aided three-dimensional reconstruction system. *Hear. Res.* 120: 1-6.
- Ward, W. D. (1955). Tonal monaural diplacusis. *J. Acoust. Soc. Am.* 27: 365-372.

- Wartzok, D. and D. R. Ketten (1999). Marine mammal sensory systems. In: *Biology of Marine Mammals*, edited by J. E. Reynolds and S. A. Rommel (Smithsonian: Washington), 117-175.
- Wegel, R. L. (1931). A study of tinnitus. *Arch. Otolaryngol.* 14: 158-165.
- Wenzel, S. W. and R. M. White (1988). A multisensor employing an ultrasonic Lamb-wave oscillator. *IEEE Transactions on Electron Devices* 35: 735-743.
- Wersäll, J. and P.-G. Lundquist (1966). Morphological polarization of the mechanoreceptors of the vestibular and acoustic systems. Second Symposium on the Role of the Vestibular Organs in Space Exploration, Washington, DC, NASA, SP-115, 57-72
- Wersäll, J., et al. (1965). Structural basis for directional sensitivity in cochlear and vestibular sensory receptors. *Symposia on Quantitative Biology* 30: 115-132.
- Wever, E. G. (1949). *Theory of Hearing*. (Dover: New York).
- Wever, E. G. (1962). Development of traveling-wave theories. *J. Acoust. Soc. Am.* 34: 1319-1324.
- Wever, E. G. (1966). Electrical potentials of the cochlea. *Physiol. Rev.* 46: 102-127.
- Wever, E. G. (1978). *The Reptile Ear*. (Princeton University Press: Princeton).
- Wever, E. G. (1985). *The Amphibian Ear*. (Princeton University Press: Princeton).
- Wever, E. G. and M. Lawrence (1950). The acoustic pathways to the cochlea. *J. Acoust. Soc. Am.* 22: 460-467.
- Wever, E. G., Lawrence, M., and Békésy, G. v. (1954). A note on recent developments in auditory theory. *Proc. Nat. Acad. Sci.* 40: 508-512.
- Wheatley, D. N. (1982). *The Centriole: a central enigma of cell biology*. (Elsevier: Amsterdam).
- White, R. M. (1970). Surface elastic waves. *Proc. IEEE* 58: 1238-1277.
- Wiederhold, M. L. (1976). Mechanosensory transduction in "sensory" and "motile" cilia. *Annu. Rev. Biophys. Bioeng.* 5: 39-62.
- Wilkinson, G. (1927). Is the question of analysis of sound by resonance in the cochlea or by 'central analysis' in the brain still an open one? *Am. J. Psychol.* 38: 257-265.
- Wilkinson, G. and A. A. Gray (1924). *The Mechanism of the Cochlea: A Restatement of the Resonance Theory of Hearing*. (Macmillan: London).
- Wilson, J. P. (1980). Model for cochlear echoes and tinnitus based on an observed electrical correlate. *Hear. Res.* 2: 527-532.
- Wilson, J. P. (1992). Cochlear mechanics. *Adv. Biosci.* 83: 71-84.
- Wilson, J. P. and G. J. Sutton (1981). Acoustic correlates of tonal tinnitus. In: *Tinnitus*, edited by D. Evered and G. Lawrenson (Pitman: London), 82-107.
- Wit, H. P. and R. J. Ritsma (1980). Evoked acoustical responses from the human ear: some experimental results. *Hear. Res.* 2: 253-261.
- Wit, H. P. and R. J. Ritsma (1983). Sound emission from the ear triggered by single molecules? *Neurosci. Lett.* 40: 275-280.
- Wit, H. P. and R. J. Ritsma (1983). Two aspects of cochlear acoustic emissions: response latency and minimum stimulus energy. In: *Mechanics of Hearing*, edited by E. de Boer and M. A. Viergever (Delft University Press: Delft), 101-107.
- Witt, C. M., et al. (1994). Physiologically silent sodium channels in mammalian outer hair cells. *J. Neurophysiol.* 72: 1037-1040.
- Wittenberg, J. B. (1958). The secretion of inert gas into the swim-bladder of fish. *J. Gen. Physiol.* 41: 783-804.
- Wright, A. (1984). Dimensions of the cochlear stereocilia in man and the guinea pig. *Hear. Res.* 13: 89-98.
- Wysocki, J. (2005). Topographical anatomy of the guinea pig temporal bone. *Hear. Res.* 199: 103-110.

REF [24]

- Zakon, H. H. (1988). The electroreceptors: diversity in structure and function. In: *Sensory Biology of Aquatic Animals*, edited by J. Atema et al. (Springer: New York), 813-850.
- Zalin, A. (1967). On the function of the kinocilia and stereocilia with special reference to the phenomenon of directional preponderance. *J. Laryngol. Otol.* 81: 119-135.
- Zelenskaya, A., et al. (2005). Evidence for a highly elastic shell-core organization of cochlear outer hair cells by local membrane indentation. *Biophys. J.*
- Zenner, H. P., et al. (1988). Active movements of the cuticular plate induce sensory hair motion in mammalian outer hair cells. *Hear. Res.* 34: 233-240.
- Zhang, L., et al. (1996). Shape and stiffness changes of the organ of Corti from base to apex cannot predict characteristic frequency changes: are multiple modes the answer? In: *Diversity in Auditory Mechanics*, edited by E. R. Lewis et al. (World Scientific: Singapore), 472-478.
- Zhao, H.-B. and J. Santos-Sacchi (1999). Auditory collusion and a coupled couple of outer hair cells. *Nature* 399: 359-362.
- Zheng, J., et al. (2000). Prestin is the motor protein of cochlear outer hair cells. *Nature* 405: 149-155.
- Zhu, Y. and S. Granick (2001). Rate-dependent slip of Newtonian liquid at smooth surfaces. *Physical Review Letters* 87: 096105.
- Zidanic, M. and W. E. Brownell (1990). Fine structure of the intracochlear potential field. I. The silent current. *Biophys. J.* 57: 1253-1268.
- Zinn, C., et al. (2000). Evidence for active, nonlinear, negative feedback in the vibration response of the apical region of the in-vivo guinea-pig cochlea. *Hear. Res.* 142: 159-183.
- Zweig, G. and C. A. Shera (1995). The origin of periodicity in the spectrum of evoked otoacoustic emissions. *J. Acoust. Soc. Am.* 98: 2018-2047.
- Zwislocki, J. J. (1953). Acoustic attenuation between the ears. *J. Acoust. Soc. Am.* 25: 752-759.
- Zwislocki, J. J. (1957). Some measurements of the impedance at the eardrum. *J. Acoust. Soc. Am.* 29: 349-356.
- Zwislocki, J. J. (1965). Analysis of some auditory characteristics. In: *Handbook of Mathematical Psychology*, edited by R. D. Luce et al. (Wiley: New York), 3, 1-97.
- Zwislocki, J. J. (1973). Concluding remarks. In: *Basic Mechanisms in Hearing*, edited by A. R. Møller (Academic Press: New York), 119-121.
- Zwislocki, J. J. (1980). Five decades of research on cochlear mechanics. *J. Acoust. Soc. Am.* 67: 1679-1685.
- Zwislocki, J. J. (1980). Theory of cochlear mechanics. *Hear. Res.* 2: 171-182.
- Zwislocki, J. J. (1985). Are nonlinearities observed in firing rates of auditory-nerve afferents reflections of a nonlinear coupling between the tectorial membrane and the organ of Corti? *Hear. Res.* 22: 217-221.
- Zwislocki, J. J. (2002). *Auditory Sound Transmission: An Autobiographical Perspective*. (Erlbaum: Mahwah, NJ).
- Zwislocki, J. J. and E. J. Kletschy (1979). Tectorial membrane: a possible effect on frequency analysis in the cochlea. *Science* 204: 639-641.
- Zwislocki, J. J. and E. J. Kletschy (1982). What basilar-membrane tuning says about cochlear micromechanics. *Am. J. Otolaryngol.* 3: 48-52.
- Zwislocki, J. J. and L. K. Cefaratti (1989). Tectorial membrane II: stiffness measurements in vivo. *Hear. Res.* 42: 211-228.
- Zwislocki, J. J. and R. L. Smith (1989). Phase reversal in OHC response at high sound intensities. In: *Cochlear Mechanisms: Structure, Function, and Models*, edited by J. P. Wilson and D. T. Kemp (Plenum: New York), 163-168.

APPENDIX

1. What carries the pressure-modulated current?
 - A TRPA1 channel?
 - A fast voltage-gated potassium channel?
 - Stretch-activated channels in the basolateral wall?
2. Kinocilia, source of a positive feedback loop
3. The cochlea as an aerial for acoustic radiation
 - 3.1 Negative resistance antennas
 - 3.2 A dipole aerial and the role of the third window
4. Spontaneous oscillation of yeast cells
5. Effect of opening the cochlea
6. Phase reversals in “middleless” ears
7. Resistance to overload

The following sections present material which is germane to the thesis but not crucial in terms of the arguments they carry. The sections outline perspectives from which additional research may bear fruit.

1. What carries the pressure-modulated current?

This may be an ambitious question to answer, since even the identity of the stereocilia's transduction channel still eludes us. “Despite two decades of physiological research that have defined the selectivity, pharmacology, speed, and

Appendix [2]

molecular mechanics of this [hair cell] channel, its molecular identity is not known.”¹ Nevertheless, we can make some educated guesses. Since the endolymph carries a high concentration of potassium ions, it is natural to assume that K^+ is the ion carrying the receptor current through the stereocilia and, potentially, also through the cuticular pore. Indeed, experimental findings point in this direction², although the channel itself is non-selective, and other ions, like Ca^{2+} , or even molecules, like ATP, could also play a role. The silent current is a standing current, whereas the pressure-sensitive current may be a transient one; nevertheless, a transient current relies on turning off a standing current to permit potential variations to be fully expressed (see §D 9.2/c). The standing current is probably carried by K^+ , but the transient channel’s carrier and identity is examined below.

A TRPA1 channel?

As mentioned previously, the latest findings point to a TRP (transient receptor potential) ion channel called TRPA1 as being the mechanosensitive channel in vertebrate hair cells, each cell having several hundred such channels³. Although the authors of that paper consider the channel to lie in the stereocilia, anti-body labeling actually showed that the channels were distributed among the stereocilia, *kinocilia*⁴, and area surrounding the cuticular plate. Given the close association between the kinocilium and the cuticular pore, the channel may therefore also occur in this space, especially given the apparent facility with which FM 1-43 penetrates through (a) TRPA1 (p. 723 and Fig. 3) *and* (b) the cuticular pore (set out in §D 9.1/i). The cuticular pore is about 100 nm in diameter, and the diameter of the TRPA1 channel⁵ is less than 1 nm, suggesting that the pore could easily accommodate a multitude of TRPA1 channels.

¹ Sukharev, S. and D. P. Corey (2004). Mechanosensitive channels: multiplicity of families and gating paradigms. *Sci. SKTE* 2004: re4.

² Corey, D. P. and A. J. Hudspeth (1979). Ionic basis of the receptor potential in a vertebrate hair cell. *Nature* 281: 675-677.

³ Corey et al. (2004).

⁴ The diagrams in Fig. 2 are in error in showing the kinocilium emerging from the cuticular plate; in fact, it always emerges from a portion of the cell apex devoid of cuticle.

⁵ Given that the channel is just able to pass FM 1-43 molecules, which have a molecular weight of 741 and a diameter of 0.8 nm [Gale, J. E., et al. (2001). FM1-43 dye behaves as a permeant blocker of the hair-cell mechanotransducer channel. *J. Neurosci.* 21: 7013-7025. p. 7023]

Sukharev and Corey estimate (p. 4) that at human auditory threshold, stereocilia are deflected by a few tenths of a nanometer and that tip links are stretched by a tenth of that distance, say 0.01 nm (again, this dimension should be compared with the displacement of 0.1 nm calculated in §D 8.4/f for fluid flow through the cuticular pore at threshold). At the same time, the channels must open by a nanometre or two to let ions through; this apparent paradox is explained by noting that channel gating is probabilistic, and there is a continuous grading in opening probability as gating forces increase⁶.

TRPA1 channels are non-selective, and I propose that in the cochlea they would admit K^+ ions in response to acoustic pressure across them in the same way as tip link tension lets K^+ ions enter via the stereocilia.

A fast voltage-gated potassium channel?

A key property of certain K^+ channels, notably one called KCNQ4, is that they are voltage sensitive⁷, so that their conductance strongly depends on the resting membrane potential of the cell. In this way, like transient Na^+ channels, a steep negative slope of the current–voltage curve gives increased sensitivity to small currents. This transconductance action resembles that of a transistor⁸, and it offers an attractive way for the outer hair cell to increase its sensitivity in a regenerative-like way. Thus if, like the Na^+ current, the membrane potential is in the range of the steep negative slope, sensitivities of 200 pA/mV can be achieved, as illustrated in Fig. A1 for a fast voltage-activated sodium current.

⁶ Sukharev and Corey, p. 3.

⁷ Ashmore, J. F. (2002). Biophysics of the cochlea: biomechanics and ion channelopathies. *Br. Med. Bull.* 63: 59-72.

⁸ Sigworth, F. J. (2003). Life's transistors. *Nature* 423: 21-22.

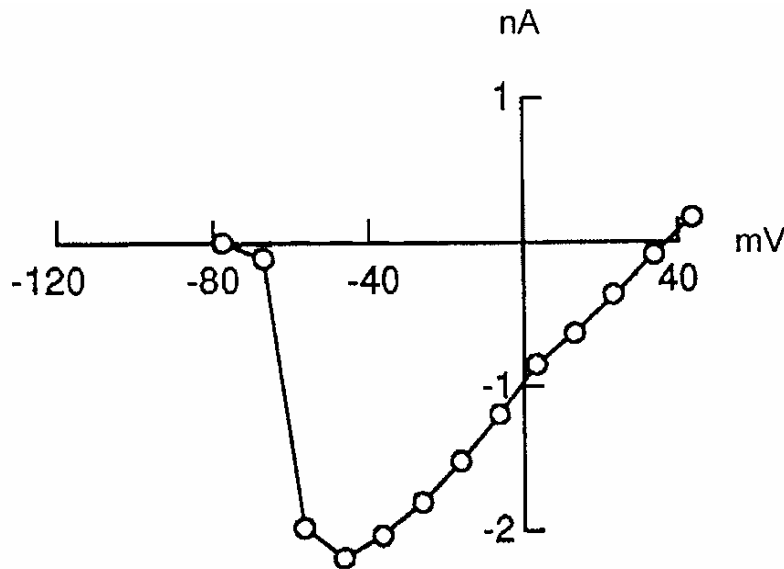


Fig. A1. The cochlea's transistor? The electrical characteristics of a voltage-activated inward sodium current as observed by Witt et al. (1994) in a voltage-clamped outer hair cell of a mature guinea pig⁹. The steep negative slope at -70 mV, near the resting membrane potential of the cell, has a transconductance of -200 pA/mV, a property that might also arise in related fast K^+ currents. [Used with permission of the American Physiological Society and Springer-Verlag]

Fast voltage-activated potassium currents have now been observed in the outer hair cells¹⁰. They have conductances of greater than 100 nS and activate in much less than 1 ms at 22°C ¹¹. These authors outline how such a current can counteract capacitive currents, thereby extending the cell's frequency response. Ricci et al. (2000) observed a "very fast" motion in hair bundle movements¹² (of opposite polarity), but later thought it unrelated to transducer gating. This current could be pressure-related.

In terms of the SAW model, the crucial property of fast-acting Na^+ and K^+ currents is that they depend critically on membrane potential. So looking at the

⁹ Witt, C. M., et al. (1994). Physiologically silent sodium channels in mammalian outer hair cells. *J. Neurophysiol.* 72: 1037-1040. Interestingly, the authors call the current "physiologically silent" because they thought it was not activated at normal OHC resting potentials and could identify no useful role for it. They were concerned (p. 1037) that "The presence of a regenerative voltage-dependent sodium current in the OHC could initiate an inappropriate electromotile event that would disrupt cochlear mechanics."

¹⁰ Ospeck, M. C., et al. (2002). RC time constant paradox of outer hair cells [abstract]. *Biophys. J.* 82: 251a.

¹¹ Ospeck, M., et al. (2003). Limiting frequency of the cochlear amplifier based on electromotility of outer hair cells. *Biophys. J.* 84: 739-749.

¹² Ricci, A. J., et al. (2000). Active hair bundle motion linked to fast transducer adaptation in auditory hair cells. *J. Neurosci.* 20: 7131-7142. Fig. 10 shows that, over the physiological range of membrane potential, the slope (nm/mV) of the fast current is about the same as, but negative to, that of the slow current.

characteristics of Fig. A1, we see that the current will have a high conductance at -70 mV but will be turned off at membrane potentials more negative than -80 mV. So if OHC2 has a membrane potential of -70 mV and OHC1 and OHC3 have a more negative (or less negative) potential, sound will activate potassium currents only in the centre of the triplet of OHCs, stimulating the SAW's resonant element like a string plucked at its middle. In this case, the transient nature of the current does not matter: the differential action of the current is sufficient to energise the SAW resonator. The fact that TRPA1 is a member of a family of transient currents lends support to the idea that fast potassium currents are involved in hair cell transduction, and the conjunction of fast pressure waves and cuticular pores would be an elegant way to harness their speed and sensitivity.

In this case we find an arrangement in which the cochlear amplifier is effectively transistor-powered. As noted by Hudspeth and Corey (1977), an endogenous action potential-like mechanism based on a regenerative sodium current could serve as an amplifier of receptor potentials¹³. They also relate how cochlear hair cells, lacking kinocilia, may operate in a different manner from most other hair cells.

Stretch-activated channels in the basolateral wall?

For completeness, a further possibility is mentioned. Although it does not seem as elegant a solution as the fast K^+ channel mentioned above, there are also a multiplicity of stretch-activated channels along the cell wall^{14,15,16} and it is possible that one of these is involved in sensing sound pressure, similar to the way bacteria

¹³ Hudspeth and Corey (1977), p. 2411. A mechanism like this and involving voltage-activated potassium ions has been observed in the lateral line of the skate electroreceptor [Clusin, W. T. and M. V. L. Bennett (1979). The ionic basis of oscillatory responses of skate electroreceptors. *J. Gen. Physiol.* 73: 703-723.]; however, in this case it operates in the basolateral membrane over a voltage range near zero resting potential and has a negative conductance of -5 nA/mV.

¹⁴ Ding, J. P., et al. (1991). Stretch-activated ion channels in guinea pig outer hair cells. *Hear. Res.* 56: 19-28.

¹⁵ Iwasa, K. H., et al. (1991). Stretch sensitivity of the lateral wall of the auditory outer hair cell from the guinea pig. *Neurosci. Lett.* 133: 171-174.

¹⁶ Gale, J. E. and J. F. Ashmore (1994). Charge displacement induced by rapid stretch in the basolateral membrane of the guinea-pig outer hair cell. *Proc. Roy. Soc. Lond. B* 255: 243-249.

Appendix [6]

use them to sense membrane stretch¹⁷. In this case, we might expect fast sodium channels to underlie the sensing (because of the sodium-rich perilymph adjoining the body of the cells). Another possibility, put forward by Rybalchenko and Santos-Sacchi¹⁸, is that the channel is carried by Cl^- ions, since Cl^- has an effect on prestin, the motor protein in the OHC wall. These authors belong to the small group directly canvassing outer hair cell pressure sensitivity, stating “we hypothesise that the OHC soma has adopted a mechanism similar to that which stereocilia may use to provide cochlear amplification in lower vertebrates” (p. 889).

While the soma may carry many candidate currents, on general design grounds – that the pressure-vessel-like construction of OHCs seems intended to focus the pressure stimulus to that one point – it seems to me that the cuticular pore provides the best candidate for this complementary sensor.

2. Kinocilia, source of a positive feedback loop

In §8.4/f, an account was given of the sensory pore, but it also invited the question, what is the purpose of the kinocilium in the first place? Why does nature go to such trouble in designing a sensory system that includes not only stereocilia, sensitive to bending, but an auxiliary system that includes a kinocilium, presumed sensitive to pressure. The auxiliary system is essentially different, sitting not on the cuticular plate but on a compliant spot nearby, and using a motile cilia structure, not just a microvillar one. And yet the two systems are intimately related, physically close and often directly touching each other. Understanding the function of the kinocilium is useful for seeing how a whole range of hair cells work, and also gives an insight into why a hair cell should choose to discard its kinocilium at birth.

The unifying idea I want to present is that the kinocilium provides direct positive feedback to the stereocilia, increasing sensitivity. In animals with kinocilia, deflection of the stereocilia provides an initial electrical signal (receptor potential) that I suggest drives the kinocilium from the basal body, causing the tip of the

¹⁷ Sukharev and Corey (2004).

¹⁸ Rybalchenko, V. and J. Santos-Sacchi (2003). Cl^- flux through a non-selective, stretch-sensitive conductance influences the outer hair cell motor of the guinea-pig. *J. Physiol.* 547: 873-891.

kinocilium to extend (see Fig. A2). Since the tip is in direct contact with the stereocilia bundle, this provides positive feedback path. This is invaluable to the cell; why would it ever want to lose a kinocilium?

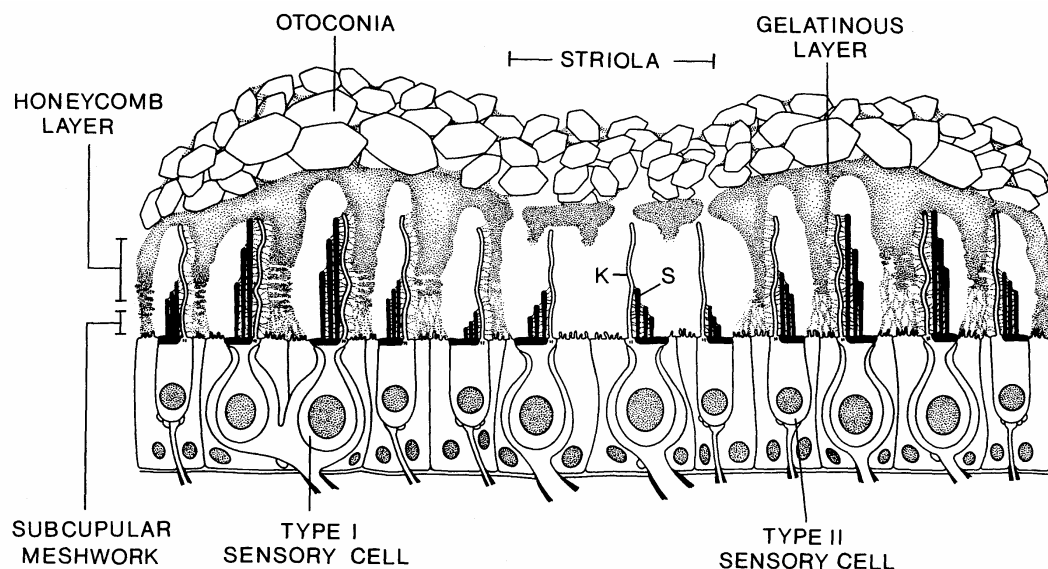


Fig. A2. Cooperative function of kinocilia (K) and stereocilia (S). This diagram shows the intimate relationship between the two types of cilia in the gravity receptor (sacculus) of a mouse. Note in particular how the stereocilia sit on top of the cuticular plate at the top of the hair cell, whereas the kinocilia emerge from the basal body in a cuticle-free gap, a near-universal arrangement. In the mammalian cochlea, of course, the kinocilia have disappeared, but the basal bodies remain. In the mouse saccule, the kinocilia could, motor-like, provide feedback motion to the stereocilia; in the cochlea, the basal bodies could act in reverse, as pressure sensors. Notice also here that the cells are arranged in mirror symmetry across the striola, so that a shuttle-like motion could be set up; if so, high frequency shuttling might occur close to the midline where path lengths are short, but at lower frequencies further away. Correspondingly, we see that stereocilia are largely graded in length as distance from the midline increases. [From Fig. 10.6 of Friedmann and Ballantyne (1984) and used with the permission of Butterworths]

The answer lies in seeing that when a kinocilium becomes sensory – when it operates in reverse and generates a potential in response to motion at its tip – then motion at its base is just as effective. If the stimulus to be detected is sound pressure, then sensing the pressure directly (at the basal body) has clear advantages over detecting it indirectly (via traveling wave induced deflection). Speed of action is one mentioned earlier, and the cleaner the signal (higher signal-to-noise ratio), the more the gain can be pushed. (As calculated elsewhere, in terms of volume displacements it appears possible for the pressure signal to be at least as readily detectable as the traveling wave displacement.) Furthermore, when operating in reverse, positive

Appendix [8]

feedback remains a useful stratagem (provided it remains below the oscillatory threshold) and the process that mammalian cochleas have discovered is electromotility. This produces three opportunities for increasing gain: the mechanical one involving Poisson's ratio, the electrical one involving the cochlear microphonic, and the SAW mechanism. And it can all be done without a kinocilium – just a basal body.

A prediction, therefore, is that the time when the human kinocilium falls off is the time when electromotility is established. The positive feedback path now changes: instead of the kinocilium feeding back motion to the stereocilia (an evolutionarily early invention), the basal body now works in reverse (it becomes a pressure sensor) and electromotility – a late discovery in evolution – becomes the way by which its signal can be fed back to the whole system.

To reach this perspective, it is useful to go back and see how ideas about the kinocilium have developed.

Our knowledge of the structure, function, and motile properties of kinocilia has been derived almost exclusively from studies on unicellular animals or multicellular ones with fairly simple sensory systems¹⁹. The role of the enigmatic structure in vertebrate hearing has been largely passed over, mostly because the displacements involved in sound transduction are too small for easy experimental study. Despite the name *kinocilium*, no motion of the structure has been seen in mammalian hearing²⁰.

There are two major reasons why kinocilia function has been discounted in hearing. The first, already mentioned, is that mammalian kinocilia degenerate at birth, and yet we still manage to hear perfectly well, if not better. The second is the influential paper by Hudspeth and Jacobs²¹ reporting experiments on hair bundles in the bullfrog sacculus. They found no sign of a receptor potential when a loosened kinocilium's tip was deflected with a probe; furthermore, disabling the kinocilium (holding it down flat against the surface) made no difference to receptor potentials generated when the whole bundle was deflected with a fine probe (Fig. A3).

¹⁹ Wiederhold (1976).

²⁰ The closest to it may be observed kinocilium movement in a frog [Martin et al., 2003]]. A slow, continuous, whip-like beating was also seen in the isolated crista ampullaris of the frog [Flock, Å., et al. (1977). Studies on the sensory hairs of receptor cells in the inner ear. *Acta Otolaryngol.* 83: 85-91. p. 89].

²¹ Hudspeth, A. J. and R. Jacobs (1979). Stereocilia mediate transduction in vertebrate hair cells. *Proc. Nat. Acad. Sci.* 76: 1506-1509.

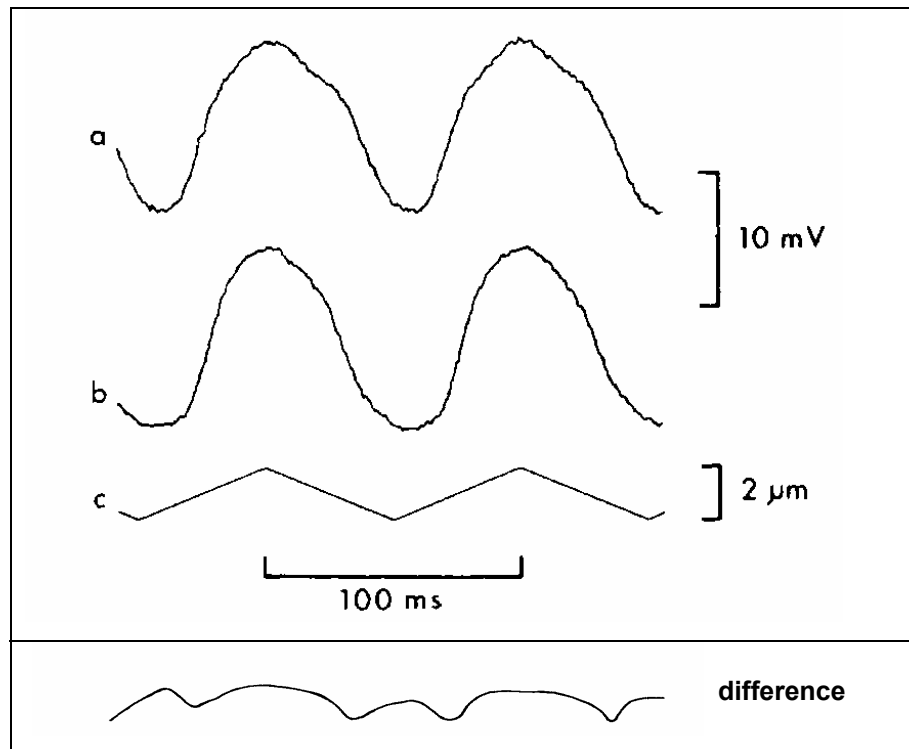


Fig. A3. Top two traces show the receptor potentials obtained by Hudspeth and Jacobs (1979) (their Fig. 2) when a hair bundle was deflected by a fine probe (in the way shown in the third trace), first with the kinocilium in place and second with it held flat. Noting that the top two traces are not identical, pointwise subtraction produces the trace shown to the same scale at bottom, showing the second-harmonic contribution made by the kinocilium. [Top portion of figure reproduced from PNAS with permission of the National Academy of Sciences, USA]

I find these conclusions unsatisfying: surely the kinocilium must be doing something. I have two reservations. One concerns the observation that the two traces shown in Fig. 2 of their paper are not identical, despite the authors' claim they are indistinguishable. Algebraically subtracting them gives the trace shown in the bottom of Fig. A3, and it shows the difference waveform due to the kinocilium. The kinocilium might be producing a signal proportional to the displacement of the probe away from the mean level. Perhaps, therefore, it is a directionally invariant sensor, responding to the rocking of the cuticular plate in the way described by Engström, or to displacement at its base in the way of Hillman's plunger. In any event, contrary to first appearances, it does seem to be exhibiting some response. Another reservation concerns the use of microelectrodes; as noted elsewhere²², these hair cells seem

²² Hudspeth and Corey (1977), p. 2410.

Appendix [10]

sensitive to electrode penetration. If the cells were sensitive to pressure, impaling them with a sharp point is likely to compromise their responses.

Given the lack of anything substantial to hang a theory on, it is not surprising that theories of the role of the kinocilium in the hearing process are sparse. I do not claim the following is comprehensive, but I will present four illuminating approaches.

A. The review by Flock²³ is useful because he mentions the parallel with motile cilia and the idea that by working in reverse they may work as sensors. He alludes to centrioles but has to conclude that the functional significance of the kinocilium is obscure. However, he does suggest that this structure, or the basal body, may influence transduction, perhaps by regulating ionic conductances.

B. Zalin's proposal²⁴ is interesting because he emphasises the “singular and extraordinary fact” that the cochlea, after birth, lacks kinocilia. He assumes that kinocilia are only useful for dc biasing, as needed in balance organs, so that the cochlea, as a detector of ac signals, does not need them.

C. Tumarkin, obviously intrigued by the kinocilium, presented a series of seven provocatively titled papers²⁵ that attempted to make sense of it all, with some degree of success (and a few nice turns of phrase). He makes the worthwhile suggestion that, by acting as motile flagella, kinocilia could increase the stereocilia's output. Accordingly, in the first of his 1986 papers, he draws a figure (his Fig. 2) showing linkages between a cell's motile kinocilium and its stereocilia. The text is rather unclear, but the diagram shows a “leak” in the semi-permeable membrane surrounding the base of the kinocilium and this leak varies from closed to open as the basal body moves the membrane up and down, alternately relaxing and stretching it,

²³ Flock, Å. (1967). Ultrastructure and function in the lateral line organs. In: *Lateral Line Detectors*, edited by P. H. Cahn (Indiana University Press: Bloomington), 163-197. [pp. 184-185]

²⁴ Zalin, A. (1967). On the function of the kinocilia and stereocilia with special reference to the phenomenon of directional preponderance. *J. Laryngol. Otol.* 81: 119-135.

²⁵ Tumarkin, A. (1980). The controversial cupula and the enigmatic kinocilium. *J. Laryngol. Otol.* 94: 917-927. // Tumarkin, A. (1984). Multi modal hearing, the fundamental importance of the kinociliary servo system and the folly of psychoacoustics. Part I. The struggle for power and the anthropocentric obsession. *J. Laryngol. Otol.* 98: 557-566. // Tumarkin, A. (1984). Multi modal hearing: the fundamental importance of the kinociliary servo mechanism and the folly of psychoacoustics. Part II. The garrulous fish and the unemployed kinocilium. *J. Laryngol. Otol.* 98: 659-670. // Tumarkin, A. (1984). Multi modal hearing: the fundamental importance of the kinociliary servo mechanism and the folly of psychoacoustics. Part III. Psychologists try to capture the unknowable in a net of mathematical equations. *J. Laryngol. Otol.* 98: 747-757. // Tumarkin, A. (1986). Stereocilia versus kinocilia. Part I: in the acoustic sensors. *J. Laryngol. Otol.* 100: 1009-1018. // Tumarkin, A. (1986). Stereocilia versus kinocilia. Part II: The vestibular sensors. *J. Laryngol. Otol.* 100: 1107-1114. // Tumarkin, A. (1986). Stereocilia versus kinocilia part III: the efferent innervation. *J. Laryngol. Otol.* 100: 1219-1224.

and in this way providing positive feedback to cell stimulation. This idea comes close to the one I favour, that the kinocilium normally provides a direct feedback path to the stereocilia. However, it fails to appreciate that pressure at the sensory pore may, in the human cochlea at least, be the prime stimulus – not deflection of the stereocilia. From the lack of kinocilia in the human cochlea – a major enigma, in his view – he concludes that the amplification function they give to the stereocilia has been dispensed with.

D. There are two modern treatments that take the kinocilium seriously. A paper²⁶ by Camalet and colleagues (Duke, Jülicher, and Prost), and a later one by Duke²⁷, propose a model of the cochlea based on self-tuned critical oscillators in which a dynamic system is set at the threshold of oscillation (a dynamic instability known as a Hopf bifurcation), in this way providing tuning and amplification. (This arrangement was also referred to in Chapter R5, where the instability it calls for could be filled by the radial standing waves identified in this thesis.) In their papers, the researchers assume that the instability derives from positive feedback of kinocilium motors to a stereocilia, or from myosin motors inside the stereocilia channels themselves. A drawback is that the kinocilium pathway cannot act in human cochleas – because we lack kinocilia. Nevertheless, as well as providing a direct opening for squirting waves, their model returns kinocilia to consideration. Additionally, Duke makes the point (ibid., p. S1757) that the Hopf scheme allows the detection of forces considerably weaker than those exerted by a single molecular motor.

My preferred model of the kinocilium reflects the idea common to all these authors: a motile cilium supplying positive feedback to the stereocilia. The model provides a harmonious synthesis of a diverse literature and supplies an essential role to the kinocilium; whether it is correct is still very much open. Recent experiments²⁸, again in the bullfrog, showed that hair cells in the sacculus continued their low-level oscillation even after the kinocilium had been removed, indicating that, at least in this animal, stereocilia too appear to have some capacity for movement. If one

²⁶ Camalet, S., et al. (2000). Auditory sensitivity provided by self-tuned critical oscillations of hair cells. *Proc. Nat. Acad. Sci.* 97: 3183-3188.

²⁷ Duke, T. (2003). Hair bundles: nano-mechosensors in the inner ear. *Journal of Physics: Condensed Matter* 15: S1747-S1757.

²⁸ Martin, P., et al. (2003). Spontaneous oscillation by hair bundles of the bullfrog's sacculus. *J. Neurosci.* 23: 4533-4548.

Appendix [12]

accepts that the bullfrog's haircell reflects its function in mammals we are again left wondering what the kinocilium is for.

3. The cochlea as an aerial for acoustic radiation

The argument was developed in Chapter 9 that the cochlea was pushing the limits of sensitivity to the utmost. Here I outline one way by which the cochlea, considered as a receiving aerial for acoustic radiation, could improve its sensitivity. The analogy integrates the concepts that the cochlea emits acoustic energy and that it exhibits negative acoustic impedance. The aerial model provides a useful theoretical basis on which to pursue further investigation and gives an understanding of the cochlea's comparative anatomy across many species. The perspective is not crucial for the main drive of the thesis, but provides a broad, albeit speculative, integration.

3.1 *Negative resistance antennas*

Gold's key idea was that positive feedback could overcome damping and produce a sensitive narrow-band detector, an acoustic version of a regenerative receiver (§I 1.4). This thesis has described prime candidates for the positive feedback network underlying such a device: squirting waves reverberating between triplets of outer hair cells (§R 5). In this way, viscous damping in the subreticular space can be cancelled, improving the sensitivity and Q of the system.

However, the regenerative receiver parallel can be pursued further, for if a triplet of cells is in fact resonantly oscillating (in phase with incoming sound), then a pressure wave is also being sent to the ear canal and being broadcast into the space surrounding the listener. An acoustic field is thereby generated around the head – in the same way as a regenerative receiver fills the surrounding ether with electromagnetic energy when it breaks into oscillation. The implications of this activity are worth noting, for a negative resistance antenna – or “black hole” aerial – provides a powerful way of increasing the effective size of the antenna²⁹. At the same

²⁹ Beaty, W. [n.d.] “Energy-sucking” radio antennas: N. Tesla's power receiver.
<http://www.amasci.com/tesla/tesceive.html>. Viewed 2005/04/06.

time it is recognised that the acoustic resistance of the ear canals of people with strong SOAEs can be *negative*, indicating a power gain at these frequencies³⁰, the suggestion being that the cochlea does suck acoustic energy from the space surrounding the listener.

The simplest antenna is the dipole, which resonates when each of its two arms are a quarter-wavelength of the incoming radiation. Electrically, the dipole can be considered as a circuit in which a resistor, capacitor, and inductor resonate. The resonance frequency is that at which the reactance of the inductance and capacitance cancel, leaving only the resistance to determine the Q of the resonance. The idea behind negative resistance antennas is to reduce this residual resistance to zero (or less) so that the Q increases without bounds. This can be done using active electronics, so that the inductance of the coil can be countered by a matched negative inductance³¹.

Tesla first came up with the idea of a regenerative receiver in 1899 during his efforts to transmit useful amounts of electrical power over long distances without wires. He conceived of receiver circuits in which radio-frequency currents were fed back from the secondary side of a resonant transformer to a “coherer” located on the primary side. Tesla described this “self-exciting process” as a way by which effects “too feeble to be recorded in other ways may be rendered sufficiently strong to cause the operation of any suitable device.” (Peterson, op.cit., p. 1).

Although Tesla may have been the first, Rudenberg described the general principles in 1908 and Armstrong designed a practical regenerative detector in 1912 (Peterson, op.cit.). Armstrong’s idea was widely used in the early days of radio, but problems associated with oscillating front ends filling up the neighbourhood led to the general phasing out of regenerative receivers. The idea was resurrected in 1992 by Sutton and Spaniol who used modern solid state electronics to produce negative inductance in the search coil of a metal detector; they called it a “black hole antenna” because the search coil acted as if it were as large as a quarter-wavelength of ultra-

³⁰ Burns, E. M., et al. (1998). Energy reflectance in the ear canal can exceed unity near spontaneous otoacoustic emission frequencies. *J. Acoust. Soc. Am.* 103: 462-474. This work demonstrates that at low sound pressure levels the acoustic resistance could be -50 cgs acoustic ohms or less, giving rise to power gain. In one subject the power gain was 8, indicating that an order of magnitude more power was reflected back from the ear canal than was received.

³¹ Peterson, G. L. Regeneration revisited. The Tesla connection. *Feed-Line* nr 5 [n.d.] (Twenty First Century Books). <http://www.tfcbooks.com/articles/tws5.htm>. Viewed 2005/04/05.

Appendix [14]

low frequency electromagnetic waves, which have wavelengths measured in kilometres.

A negative resistance antenna acts like a funnel, bending the field lines so that they pass through the antenna, thereby sucking in energy over a large area, as shown in Fig. A4.

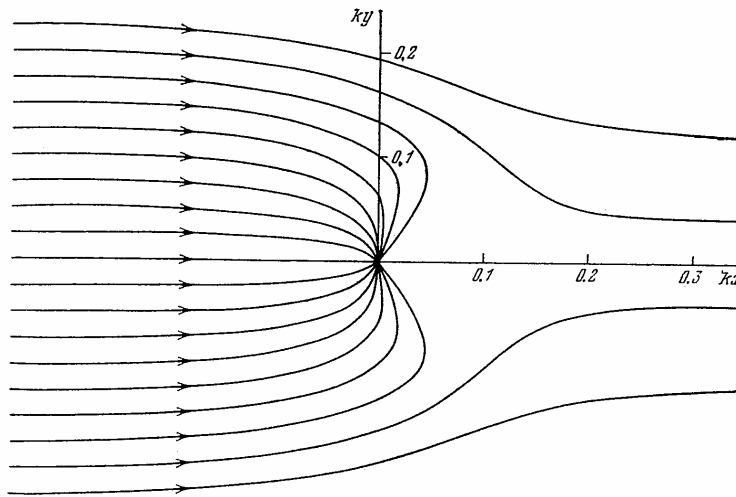


Fig. A4. A resonant antenna swallows much more energy from a passing field than one expects from its geometrical cross-section. This is because field lines bend in toward the antenna due to interference between the passing and resonant fields. Given appropriate resonant conditions, a similar situation could hold at low sound pressure levels when spontaneous emissions interfere with the acoustic field surrounding the head, increasing sensitivity to sound. [From Fig. 1 of Paul and Fischer³² (1983), and reproduced with permission of the American Institute of Physics]

The phenomenon is readily explained in terms of resonant absorption, and is the basis by which individual atoms, considered as minuscule dipoles, can absorb weak radiation impinging on them over a wide area³³. Beaty goes on to draw our attention to Gold and his regenerative receiver in the ear; he makes the astute observation that when the ear emits sound, it might be acting as a resonant antenna for acoustical radiation at that frequency. Here, then, at a basic level, is an explanation of why the ear, as a resonant detector, gives out sound.

³² Paul, H. and R. Fischer (1983). Light absorption by a dipole. *Sov. Phys. Usp.* 26: 923-926.

³³ See Beaty; also Bohren, C. F. (1983). How can a particle absorb more than the light incident on it? *Am. J. Phys.* 51: 323-327.

For an isolated acoustical resonator distanced from a sound source, Lamb³⁴ shows that the resonator's effective cross-section is λ^2/π , and this will increase if it resides on a baffle (as in the case of ears located on the side of the head). Therefore, at 1 kHz, the effective cross-section is at least 300 cm², considerably greater than the area of our external ear; at 500 Hz, the equivalent area exceeds 1300 cm². Of course, the effect only works for the frequency of generation, but given that acoustic emissions can be “pulled” by external nearby frequencies and lock onto them^{35,36}, the scheme provides an acoustic detector of great sensitivity. All we need is a tuned bank of regenerative receivers, and this is just what the ear employs.

By actively emitting acoustic energy – by straining to hear – we can indeed achieve an increase in hearing sensitivity.

This resonant model sees a direct and nearly instantaneous connection between the sound field at the head and activity of the outer hair cells, not disjoint and delayed as the traveling wave picture has it. The two-way connection is mediated by fast sound waves, and in this it is like the cochlear model³⁷ put forward by Nobili et al. (2003), who proposed instantaneous fluid coupling between the stapes and an active basilar membrane. Their model does not require a causal traveling wave; instead it relies on feedback gain between a multi-component middle ear and a simply specified basilar membrane to produce sharply tuned emissions and other cochlear amplifier effects. The traveling wave is only apparent, they say, and time delays are just associated with filter delays in a highly tuned system. While such an outlook mirrors my perspective, on a number of grounds I do not think Nobili's model realistic. Nevertheless, it has the virtue of challenging the coherent reflection filtering model³⁸ and illustrates how the same cochlear behaviour can be seen either from a resonance perspective or as a traveling wave (epi)phenomenon.

³⁴ Lamb, H. (1925). *The Dynamical Theory of Sound*. (Edward Arnold: London). §88.

³⁵ Wilson, J. P. and G. J. Sutton (1981). Acoustic correlates of tonal tinnitus. In: *Tinnitus*, edited by D. Evered and G. Lawrenson (Pitman: London), 82-107.

³⁶ Rabinowitz, W. M. and G. P. Widin (1984). Interaction of spontaneous oto-acoustic emissions and external sounds. *J. Acoust. Soc. Am.* 76: 1713-1720.

³⁷ Nobili, R., et al. (2003). Otoacoustic emissions from residual oscillations of the cochlear basilar membrane in a human ear model. *J. Assoc. Res. Otolaryngol.* 4: 478-494.

³⁸ A rebuttal has since appeared: Shera, C. A., et al. (2004). Do forward- and backward-traveling waves occur within the cochlea? Countering the critique of Nobili et al. *J. Assoc. Res. Otolaryngol.* 5: 349-359.

3.2 A dipole aerial and the role of the third window

Considering the ear as an antenna provides potentially useful insights into bone conduction and the role of the cochlear aqueduct.

First, we recognise that any aerial must be a dipole of some form³⁹. A dipole has two arms between which is a detector, as shown below (Fig. A5).

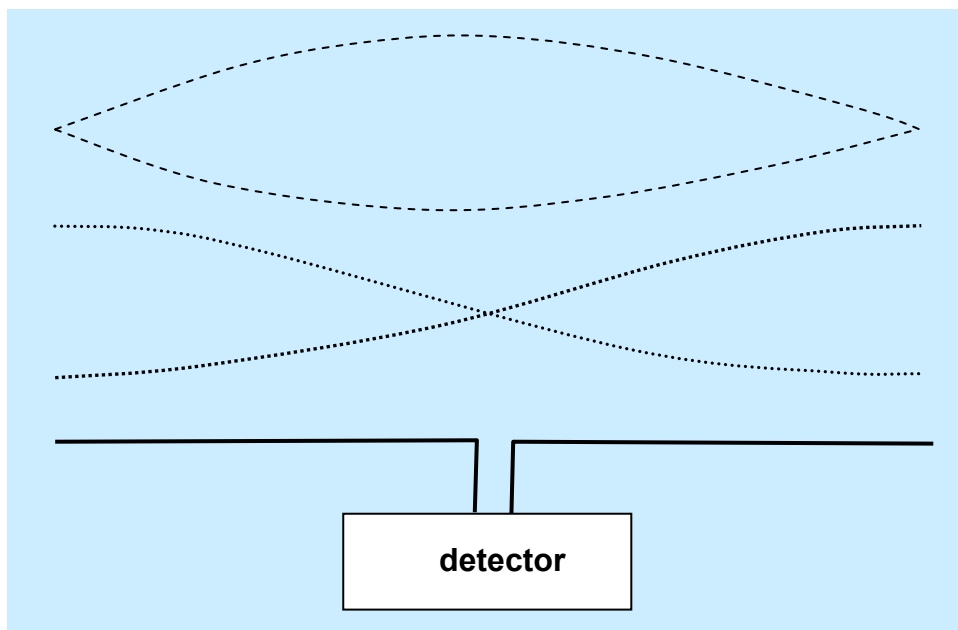


Fig. A5. A dipole with a detector sited between its arms. The dipole is half a wavelength long, and the lines above it illustrate the voltage (dashed) and current (dotted) distribution.

The key feature is that the dipole is a balanced arrangement, and the current (or voltage) it detects surges back and forth symmetrically between the arms, and this is what the detector senses. In the case of our ears, when the external ear gathers an acoustical signal and delivers it to the cochlea (the detector), how is the system balanced? In the case of humans, the signal is balanced largely by the round window, as shown in Fig. A6, so that the oval and round windows move out of phase. Given the elasticity inherent in the middle ear suspension and in the round window membrane, acoustic energy can surge back and forth through the cochlea.

However, this picture leaves out the role of the cochlear aqueduct. This channel connects the perilymph of the cochlea with the cerebrospinal fluid of the

³⁹ Monopoles are, in an electrostatic sense, a fiction in that every charge must have a complementary charge of opposite sign. Applied to aerials, a 'monopole' is in fact a dipole in which the projecting arm acts (capacitively) with a companion one – the chassis or other effective ground plane.

skull, and is sometimes called ‘the third window’. In humans, the channel is narrow and filled with fibrous tissue, so that it is of high impedance hydraulically and acoustically. Nevertheless, the channel is the source of the cochlea’s perilymph, and because of the channel intracochlear pressure accurately follows cerebrospinal fluid pressure (so that the frequency of spontaneous emissions varies in step with CSF pressure⁴⁰). The channel must therefore be capable of carrying some acoustic signal.

One implication I want to emphasise here is that the cochlear aqueduct appears to be a natural conduit for bone-conducted hearing. Bone conduction is a major contributor to sound reception, although its contribution to hearing appears to have been somewhat overlooked in modern times in favour of the obvious air conducted route⁴¹. However, recent experiments by Sohmer and colleagues have shown the importance of bone conduction^{42–45} and thrown light on the mechanism behind it. Noteworthy here is their conclusion that “This fluid pathway [between skull and cochlea via interconnecting fluid channels] would induce audio-frequency pressures uniformly within the cochlear fluids (without bulk flow), exciting the outer hair cells (OHCs) directly, without necessitating the formation of a classical traveling wave on the basilar membrane. It is likely that such is the case (direct activation of the OHCs) not only during BC stimulation, but also during AC where the stapes footplate induces audio-frequency pressures in the cochlear fluids.”⁴⁶ Importantly, air conducted sound can be precisely cancelled with bone conducted sound of the right amplitude and phase⁴⁷, indicating that they are independent routes that feed into the one detector. The dipole circuit of Fig. A6 provides a straightforward understanding of this behaviour. In other words, the cochlea sits at the middle of a dipole antenna, one arm of which forms the standard air-borne route and the other the bone-

⁴⁰ Bell, A. (1992). Circadian and menstrual rhythms of spontaneous otoacoustic emissions from human ears. *Hear. Res.* 58: 91-100.

⁴¹ Stenfelt, S., et al. (2004). Fluid volume displacement at the oval and round windows with air and bone conduction stimulation. *J. Acoust. Soc. Am.* 115: 797-812.

⁴² Freeman, S., et al. (2000). Bone conduction experiments in animals: evidence for a non-osseous mechanism. *Hear. Res.* 146: 72-80.

⁴³ Sohmer, H., et al. (2000). Bone conduction experiments in humans: a fluid pathway from bone to ear. *Hear. Res.* 146: 81-88.

⁴⁴ Sohmer, H., et al. (2004). Semicircular canal fenestration: improvement of bone- but no air-conducted auditory thresholds. *Hear. Res.* 187: 105-110.

⁴⁵ Sohmer, H. and S. Freeman (2004). Further evidence for a fluid pathway during bone conduction auditory stimulation. *Hear. Res.* 193: 105-110.

⁴⁶ Sohmer et al. (2004), p. 109. BC = bone conduction; AC = air conduction.

⁴⁷ *EiH*, p. 128-129. Interestingly, although Békésy says that “direct stimulation of the sensory cells by compressional waves is unlikely” (p. 128), he reports that the cancellation is especially susceptible to heartbeat (p. 129), an observation that suggests a pressure effect, in the same way that modulation of SOAEs by heartbeat does (Bell, 1998).

Appendix [18]

conducted one. This means that the round window is not necessary for hearing, as acoustic signals can be exchanged between the external ear (one arm of the antenna) and the skull (the second arm) via the cochlear aqueduct. This scheme explains why blocking of the round window, and also loss of the middle ear, does not automatically lead to deafness, as detection of bone-conducted sound is still possible. It also gives an explanation of the phase reversed hearing in ears of people lacking middle ears (*EiH*, p. 107), a curious phenomenon that is otherwise not easy to explain.

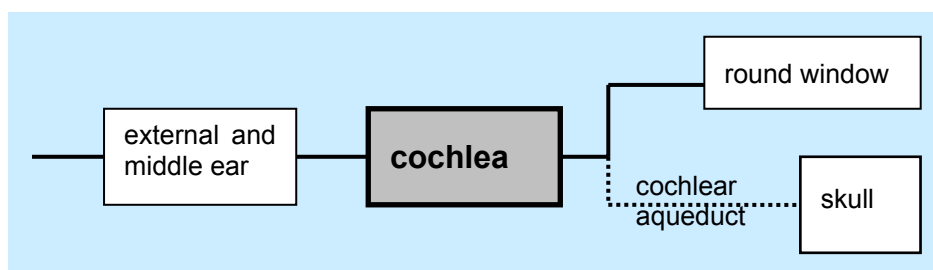


Fig. A6. The cochlea as a dipole, human case. Acoustical circuit with two arms, one for the external and middle ear, and another for the round window (low impedance route) and the skull (high impedance route).

In other creatures, however, the cochlear aqueduct can become wide (in birds, for example) and the round window become stiff or non-existent (in bats and whales). In this case (Fig. A7), the impedance of the round window is high and that of the cochlear aqueduct is low, the reverse of the human case. Indeed, comparative anatomy indicates a continuous transition between the two forms, and this is well described in Wilkinson and Gray's classic book⁴⁸.

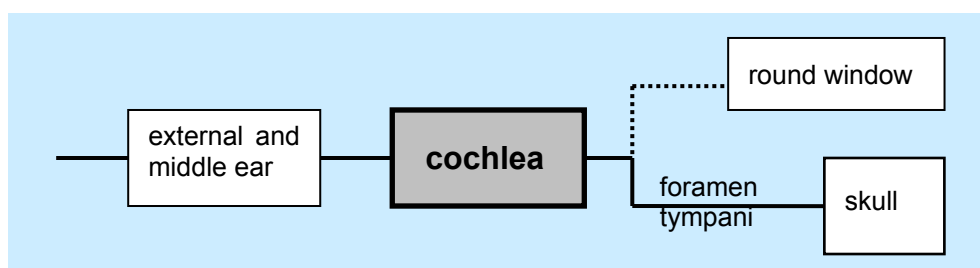


Fig. A7. The cochlear dipole in birds and marsupials.

⁴⁸ Wilkinson, G. and A. A. Gray (1924). *The Mechanism of the Cochlea: A Restatement of the Resonance Theory of Hearing*. (Macmillan: London). Chapter 2.

These authors point out that the round window of mammals is morphologically equivalent to a hole in the wall of the lower gallery in birds and reptiles called the foramen scalae tympani (f.s.t.). The foramen, located at the basal end of the cochlea, leads into the skull of the animal. The foramen is of wide calibre, sometimes occupying a third of the length of the cochlea, a situation that contrasts with the fine bore of the human cochlear aqueduct. In fact, the human case is unusual, in that the aqueduct in most mammals comprises a wide tube. Although the presence of this third window presents no unusual problem to the traveling wave theory, for the resonance picture presented here, where direct detection of vibrational energy is proposed, we need to give an account of how the additional window does not cause loss of acoustic energy, and the balanced dipole arrangement provides a basic sketch of how this might be possible.

The basic idea, as set out in Chapter D8, is that motion of the stapes launches vibrations into the liquid of the cochlea, and these are resonantly detected by the high- Q outer hair cell triplets. The sharp tuning filters the ambient thermal noise, explaining how the ear is able to detect sounds below what is expected from thermal noise considerations and begins to approach quantum noise limitations⁴⁹. As we will see below, the “cooling down by filtering” has been developed to the stage where the effective temperature of the cochlear oscillators differs from thermodynamic equilibrium by a factor of 100 or more⁵⁰.

Of course, this picture still leaves open the question of whether the detector – the cochlea – senses the voltage (pressure) or current (velocity) component of the wave, and this question is left open.

The model of resonant detection of propagating liquid-borne waves helps us see why birds, with small heads, rely on bone conduction to detect sound⁵¹. A small head provides little scope for satisfactory binaural hearing (which is based on timing differences between the ears), so they employ the skull as a bigger and more efficient antenna than its tiny ears. Water birds, in particular, are willing to forego the external ear route⁵² and we find ample fluid connections between their ears⁵³.

⁴⁹ Bialek and Wit (1984).

⁵⁰ Martin, P., et al. (2001). Comparison of a hair bundle's spontaneous oscillations with its response to mechanical stimulation reveals the underlying active process. *Proc. Nat. Acad. Sci.* 98: 14380-14385.

⁵¹ Watching a magpie unerringly home in on a worm that has clearly been sensed through its feet leaves no doubt about its sensitivity to body-borne sound.

⁵² Since, when underwater, binaural hearing is almost useless.

Appendix [20]

The homology between the round window and the f.s.t. is apparent in Fig. 13 of Wilkinson and Gray who give an evolutionary account of how the reptiles, with a single round window, developed an aqueduct that evolved into a wide form in birds and a narrow one in mammals. Along the way were the marsupials – kangaroo, echidna, platypus – who, exceptionally, have *two* effective round windows: one that opens into the tympanic cavity (to air) and another that joins the cranial cavity (fluid throughout). The fluid-borne sound hypothesis makes sense of all these intricate (one could almost say labyrinthine) hydraulic channels.

Wilkinson and Gray nicely summarise the situation. “We cannot assume that there is any essential difference between the case of ‘bone conduction’ and that of transmission of the impulse via the stapes... We cannot assert that any such single impulse causes a movement of the stapes; all we know is that it must communicate a corresponding pressure change to the fluid of the cochlea, which will be propagated as a longitudinal wave of compression to every point on the surface of the fluid, just as in the case of impulses conveyed through the bone” (ibid., p. 88–89).

4. Spontaneous oscillation of yeast cells

Spontaneous oscillations in the cochlea are intriguing, but it may well be that vibration is a general characteristic of all living cells. We pointed out earlier that a bacterium uses an electrically powered rotary motor at its centriole to rotate the attached flagellum at 1700 Hz, an ability that casts new light on the ability of outer hair cells and their centrioles to respond to auditory stimuli. This thesis suggests that the locus of sound detection could be the outer hair cell’s cuticular pore, the place where a centriole resides and where, during development, a kinocilium once resided. In the context of oscillators, it is also worth drawing attention to the behaviour of yeast cells, which also precisely vibrate in the auditory range, a phenomenon called “sonocytology”.

⁵³ Kohlöffel, L. U. E. (1983). Problems in aural sound conduction. In: *Mechanisms of Hearing*, edited by E. de Boer and M. A. Viergever (Delft University Press: Delft), 211-217.

When an atomic force microscope touches the cell wall of a yeast cell⁵⁴, it vibrates at precise frequencies between 0.8 and 1.6 kHz and with amplitudes of about 3 nm. The forces involved are about 10 nN, far greater than those exerted by single motor proteins⁵⁵, suggesting cooperative nanomechanical activity. The paper makes reference to some Hopf oscillator work, and the spectra displayed could easily be mistaken for those of spontaneous otoacoustic emissions.

5. Effect of opening the cochlea

Almost invariably, when holes are drilled in the cochlea to gain access for experimental observations, the organ suffers an appreciable loss in sensitivity⁵⁶. The explanation given is usually in terms of surgical trauma, but it follows that if the cochlea is designed to detect intracochlear pressure, then drilling holes in it will automatically reduce the pressure signal and compromise sensitivity. As an example, Narayan et al. (1998) observed threshold elevations of 6–8 dB when the cochlea was opened (their footnote 12). Although Steele and Zais (1985) could find no theoretical basis for a hole in the cochlea affecting sensitivity⁵⁷, Ulfendahl et al. (1991) found differences of up to 20 dB between the intact and open conditions⁵⁸, particularly at low frequencies, and attributed it to shunting of the partition's impedance. Resealing the cochlea restored the responses. Nilsen and Russell (1999) found losses of 0–5 dB after opening the cochlea.

⁵⁴ Pelling, A. E., et al. (2004). Local nonomechanical motion of the cell wall of *Saccharomyces cerevisiae*. *Science* 305: 1147-1150.

⁵⁵ A single molecule of kinesin can move hundreds of nanometres along a microtubule, for example, overcoming opposing forces of up to 5 pN [Howard, J. (1997). Molecular motors: structural adaptations to cellular functions. *Nature* 389: 561-567.]

⁵⁶ An early study is that of Davis, H., et al. (1949). Aural microphonics in the cochlea of the guinea pig. *J. Acoust. Soc. Am.* 21: 502-510. Significantly, the loss is frequency-dependent (but nearly always worse at low frequencies) and varies with the size and number of holes. It is often associated with leakage of fluid.

⁵⁷ Steele, C. R. and J. G. Zais (1985). Effect of opening and draining the cochlea. *J. Acoust. Soc. Am.* 78: 84-89.

⁵⁸ Ulfendahl, M., et al. (1991). Effects of opening and resealing the cochlea on the mechanical response in the isolated temporal bone preparation. *Hear. Res.* 57: 31-37.

6. Phase reversals in “middleless” ears

Békésy observed a most peculiar phenomenon in people who lacked middle ears. As set out in §I 3.2/g, it is remarkable that these subjects can still hear, for the sound should impinge directly and equally on the oval and round windows and no traveling wave should result. The earlier chapter said that escape clauses may be found to rescue the standard interpretation, and that ground will not be gone over again. However, a fairly compelling reason for raising it afresh is Békésy's observation that the afflicted ear heard sound 180° out of phase to the normal ear (*EiH*, p. 107). Seeking an answer in terms of middle ear mechanics is only of limited help, and attention is drawn to the model set out in Fig. 9.1: that *the pressure signal and the displacement signal are in opposite phase*.

The proffered explanation, then, is that OHCs in the middleless ear are responding only to pressure, whereas in the normal ear, with intensities above 60 dB SPL, they are responding predominantly to displacement (stereocilia deflection). The implication is that we hear differently at low sound pressure levels than at high, and psychophysical testing may be able to pick this up. However, this may not be as straightforward as it sounds: not only does each ear operate synergistically, but cooperative effects between the two ears may also confound the picture. Another possible explanation may lie in the contribution of a bone conduction signal to the middle-less situation, which would again be of opposite phase (see Appendix 3.2) to the normal configuration.

7. Resistance to overload

An impressive aspect of the cochlea is that it is capable of operating over a dynamic range of some 120 dB which, in power terms, is a million million times. At the same time, the cochlea's resilience to temporary overload is so astounding that it calls into question that a traveling wave mechanism provides the key stimulus at both ends of the dynamic range. Consider that when an intense tone (say 1000 Hz at 120 dB SPL for 1 minute) is impressed on the cochlea, it has *little effect* on its

sensitivity to 1000 Hz⁵⁹. The cochlea will still be able to detect that frequency at close to 0 dB; what will have suffered is sensitivity to frequencies about half an octave higher, near 1400 Hz. This loss in sensitivity, called temporary threshold shift (TTS), will gradually recover, usually over minutes but as long as days.

Clearly, the cochlea has suffered from the insult, but the surprise is that the mechanism responsible for the utmost sensitivity has not been damaged. Given that the traveling wave is supposed to be broad, particularly at high intensities, it is difficult to imagine how the sensing mechanism at 1000 Hz remains immune to the effect of a 1000-Hz traveling wave passing through the system at a level a million million times larger than threshold. The paradox has become known as the “curious half-octave shift”, a term used by McFadden to describe the TTS produced by loud sounds⁶⁰. McFadden describes it as “among the oldest, best known, and most widely cited facts of psychoacoustics, yet it stands without a generally accepted explanation” (p. 295). Moreover, “the effect the term denotes is truly curious, and it is surprising that the half-octave shift has received so little experimental and theoretical attention during the 50 years it has been known” (p. 296). Attempted explanations have generally invoked a basalward shift of the traveling wave peak as intensity increases, for example, by a stiffening reaction of the partition. But it is hard to see how this shift can be accomplished and, even more, how the shift can provide such effective protection to cells only 2 mm away (the distance corresponding to half an octave). In this context we need to remember Shera’s constraint (§I 3.2/f) about zero-crossing invariance, under which outer hair cells cannot be called on to affect partition stiffness.

Note that if the resonant elements are squirting waves, involving an interaction between fluid parcels and outer hair cells, then the system is self-limiting: when the output of the outer hair cells reaches saturation, no further vibration amplitude is possible. No matter how hard the system is driven in terms of common-mode pressure, there is no more output (and fluid parcels are inherently destruction-proof). By limiting the size of the enclosed air bubble, and having a low buckling strength for the outer hair cell wall, no damage can be done to the sensitive system

⁵⁹ McFadden, D. (1986). The curious half-octave shift: evidence for a basalward migration of the traveling-wave envelope with increasing intensity. In: *Basic and Applied Aspects of Noise-induced Hearing Loss*, edited by R. J. Salvi et al. (Plenum: New York), 295-312.

⁶⁰ McFadden (1986).

Appendix [24]

by high *pressures*. Of course, the second, less-sensitive stereociliar system is still susceptible to damage by excessive *displacements*.