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 Ca²⁺, 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,
kinocilia⁴, 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.

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
Appendix [3]

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 increase.

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 sensitive, 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 transistor, 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.

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6 Sukharev and Corey, p. 3.
Fast voltage-activated potassium currents have now been observed in the outer hair cells\(^9\). 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 movements\(^12\) (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

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\(^9\) 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.”


\(^12\) 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 potentials\(^{13}\). 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 electrorreceptor [Clusin, W. T. and M. V. L. Bennett (1979). The ionic basis of oscillatory responses of skate electrorreceptrors. 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.


Appendix [6]

use them to sense membrane stretch\textsuperscript{17}. 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-Sacchi\textsuperscript{18}, is that the channel is carried by Cl\textsuperscript{−} ions, since Cl\textsuperscript{−} 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

\textsuperscript{17} Sukharev and Corey (2004).
\textsuperscript{18} Rybalchenko, V. and J. Santos-Sacchi (2003). Cl\textsuperscript{−} 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?

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 systems. 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 hearing.

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 Jacobs 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].
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 elsewhere, these hair cells seem

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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 Flock\textsuperscript{23} 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 proposal\textsuperscript{24} 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 papers\textsuperscript{25} 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,


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 paper\textsuperscript{26} by Camalet and colleagues (Duke, Jülicher, and Prost), and a later one by Duke\textsuperscript{27}, 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 experiments\textsuperscript{28}, again in the bullfrog, showed that hair cells in the saccus 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


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 (§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 subtectorial 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 antenna$^{29}$. At the same

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 frequencies\(^{30}\), 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 inductance\(^{31}\).

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.

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.

![Diagram of a resonant antenna](image)

*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 Fischer\(^\text{32}\) (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 area\(^\text{33}\). 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.


Appendix [15]

For an isolated acoustical resonator distanced from a sound source, Lamb\textsuperscript{34} shows that the resonator’s effective cross-section is $\frac{\lambda^2}{\pi}$, 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 cm$^2$, considerably greater than the area of our external ear; at 500 Hz, the equivalent area exceeds 1300 cm$^2$. 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\textsuperscript{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 model\textsuperscript{37} 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 model\textsuperscript{38} and illustrates how the same cochlear behaviour can be seen either from a resonance perspective or as a traveling wave (epi)phenomenon.

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Appendix [16]

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 form. 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.](image)

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

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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 pressure ⁴⁰). 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 route ⁴¹. 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 phase ⁴⁷, 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-

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 book.\cite{48}

Fig. A7. The cochlear dipole in birds and marsupials.

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.

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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.
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”.

When an atomic force microscope touches the cell wall of a yeast cell\textsuperscript{54}, 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 proteins\textsuperscript{55}, 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 sensitivity\textsuperscript{56}. 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 sensitivity\textsuperscript{57}, Ulfendahl et al. (1991) found differences of up to 20 dB between the intact and open conditions\textsuperscript{58}, 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.


\textsuperscript{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. \textit{Nature} 389: 561-567.]

\textsuperscript{56} An early study is that of Davis, H., et al. (1949). Aural microphonics in the cochlea of the guinea pig. \textit{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.


Appendix [22]

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 $180^\circ$ 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 Hz. 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 sounds. 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 (§1 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.

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60 McFadden (1986).
Appendix [24]

by high *pressures*. Of course, the second, less-sensitive stereociliar system is still susceptible to damage by excessive *displacements*. 