Elastic Properties of the Human Proximal Femur

This chapter examines the effects of femoral neck geometry and topological structure on elastic properties. A finite element code is used to calculate the full elastic tensor for thirteen human proximal femur specimens. We show that the micro-structure within the human femoral neck and head gives rise to approximate orthotropic elastic symmetry at the whole bone scale. The finite element code can also be used to calculate local stress and strain fields, which we demonstrate under a given loading environment.

5.1 Introduction

As the proportion of elderly people increase in many countries, the economic and social consequences of aging are also increasing. Osteoporosis is a disease which primarily affects the elderly and is rapidly becoming a significant public health burden [34]. As mentioned in the previous chapter osteoporosis is characterised by a deterioration of bone density and architecture. It is officially defined by the World Health Organisation as [258]:

A disease characterised by low bone mass and micro-architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk.

Although diminution of bone micro-architecture is mentioned explicitly in the definition, no clinical means of directly assessing this is currently available. The current diagnostic is to measure bone mineral density using a DEXA (see Figure 4.4). Bone mass and density alone have been unable to account for fracture incidence amongst an elderly population [157] [182]. Studies suggest that up to half of all cases of hip fracture do not meet the diagnostic criteria for osteoporosis [218]. Clearly, there are other fac-
tors which determine bone strength and fracture susceptibility. Bone fragility requires a comprehensive understanding of the bone mass as well as its spatial organisation. Some authors have lumped these factors together as 'bone quality' \[78, 256, 257\].

Quantification of trabecular bone structure was introduced as a way to characterise the ‘quality’ of bone. A range of new parameters were introduced specifically to address determinants of bone strength other than density. These parameters were initially derived from microscopy and 2D stereology, but also developed for 3D images from computed tomography. Parameters include: trabecular number, trabecular thickness, and topological measures, trabecular bone pattern factor (TBPf), structure model index (SMI), degree of anisotropy \[176, 79\]. Some of these parameters are completely independent of bone mineral density and some of the parameters have been shown to correlate to mechanical properties \[244\]. Other unrelated parameters have also been suggested as predictors of bone fragility: quantity of bone turnover sites, bone shape and size. One criticism is that these parameters are sometimes applied haphazardly with little concern for the underlying accuracy of the digital images and with little physical interpretation of the parameters.

5.1.1 Anatomy of the Femoral Neck

The femoral neck is classically thought of as a cantilever, with forces distributed over the acetabular surface and transferred via the internal trabecular network to the inferior femoral neck cortex (see Figure 5.1). Trabeculae run predominantly from the inferior femoral neck cortex (or calcar), through the center of the femoral head (FH) to the supero-medial surface of the femoral head. In the 19th century it was noted that the trabecular orientation in the proximal femur was remarkably similar to estimated trajectories of principal stresses when plotted in a 2D section of the proximal femur. This correspondence and the notion of an ideal mechanical form governed by mathematical rules became known as Wolff’s Law after Julius Wolff. Criticisms have been raised since Wolff’s initial observations \[38\], such as the assumption of the hip as a homogeneous, isotropic continuum. Gradually over time, and with advances in experimental techniques such as high precision mechanical testing and finite element methods, Wolff’s Law has been superseded by concepts of functional adaptation of bone \[206\]. Although the notation used by Singh \[228\] of primary and secondary compressive or tensile trabeculae are a misrepresentation of the biomechanics, the labels have persisted in the literature and we use them for identification purposes.
Figure 5.1: Coronal section through human proximal femur. The most conspicuous trabecular band connects the inferior cortex of the femoral neck to the supero-medial surface of the femoral head. Wolff’s law is often misrepresented to attach a particular function to bands of trabeculae. For example, the nomenclature of Singh [228] denotes primary, secondary tensile and compressive groups of the proximal femur.
### Elastic Properties of the Human Proximal Femur

<table>
<thead>
<tr>
<th>Authors</th>
<th>Bone type</th>
<th>Test method</th>
<th>Young’s modulus (GPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tissue scale (&lt; 1mm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Runkle [208]</td>
<td>Human distal femur</td>
<td>Buckling</td>
<td>8.7 (dry)</td>
</tr>
<tr>
<td>Townsend [239]</td>
<td>Human proximal femur</td>
<td>Buckling</td>
<td>14.1 (dry) 11.4 (wet)</td>
</tr>
<tr>
<td>Turner [241]</td>
<td>Human femur</td>
<td>Ultrasound Ultrasound Nanoindentation</td>
<td>17.5 (wet) 17.7 (wet) 18.1 (dry)</td>
</tr>
<tr>
<td>Zysset [265]</td>
<td>Human femur: trabecular</td>
<td>Nanoindentation</td>
<td>11.4 (wet) 19.1 (wet)</td>
</tr>
<tr>
<td>Rho [200]</td>
<td>Human vertebra: trabecular</td>
<td>Nanoindentation</td>
<td>13.5 (dry) 22.5-25.8 (dry)</td>
</tr>
<tr>
<td>Rho [198]</td>
<td>Human tibia: trabecular</td>
<td>Micro tensile</td>
<td>10.4 (dry) 18.6 (dry)</td>
</tr>
<tr>
<td>Rho [198]</td>
<td>Human tibia</td>
<td>Ultrasound</td>
<td>14.8 (wet) 20.7 (wet)</td>
</tr>
<tr>
<td><strong>Apparent scale (&gt;5mm, &lt;40mm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ashman [7]</td>
<td>Bovine femur</td>
<td>Ultrasonic</td>
<td>10.9 (wet) 13.0 (wet)</td>
</tr>
<tr>
<td>Brown [25]</td>
<td>Human femoral head</td>
<td>Compression</td>
<td>0.22-0.33</td>
</tr>
<tr>
<td>Choi [32]</td>
<td>Human tibia: trabecular</td>
<td>3-point bending</td>
<td>4.6 (wet) 5.4 (wet)</td>
</tr>
<tr>
<td>Kuhn [135]</td>
<td>Human ilium</td>
<td>3-point bending</td>
<td>3.7 (wet) 4.8 (wet)</td>
</tr>
<tr>
<td>Majumdar [154]</td>
<td>Human femur: trabecular</td>
<td>Compression</td>
<td>0.08</td>
</tr>
<tr>
<td>Mente [165]</td>
<td>Human femur</td>
<td>Cantilever + FEA</td>
<td>6.2 (wet)</td>
</tr>
<tr>
<td>Ryan [209]</td>
<td>Bovine femur</td>
<td>Tension</td>
<td>0.8 (drying)</td>
</tr>
<tr>
<td>Jensen [104]</td>
<td>Human vertebra</td>
<td>Structural analysis</td>
<td>3.8</td>
</tr>
<tr>
<td>Nazarian [173]</td>
<td>Human femur: trabecular</td>
<td>Compression</td>
<td>0.13-0.32</td>
</tr>
<tr>
<td>Rohlman [204]</td>
<td>Human femur: trabecular</td>
<td>Compression</td>
<td>0.4</td>
</tr>
<tr>
<td>van Krieterbergen [253]</td>
<td>Human tibia</td>
<td>3D FEA</td>
<td>6 (wet)</td>
</tr>
<tr>
<td>van Lenthe [247]</td>
<td>Bovine femur</td>
<td>FEA / ultrasound</td>
<td>4.5 (wet)</td>
</tr>
<tr>
<td>Reilly [197]</td>
<td>Cortical</td>
<td>Tensile</td>
<td>14-20 (wet)</td>
</tr>
<tr>
<td><strong>Whole bone scale (&gt;40mm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papini [183]</td>
<td>Human femur</td>
<td>Axial / bending</td>
<td>0.757kN/mm↑</td>
</tr>
<tr>
<td>Courtney [36]</td>
<td>Human femur</td>
<td>Fall loading</td>
<td>1.5-4.5kN/mm↑</td>
</tr>
</tbody>
</table>

Table 5.1: Table illustrating the range of Young’s modulus for a variety of trabecular bone specimens and testing methods. Based on information from Currey [45], Rice [202] and Rho [199]. ↑ value for whole bone are given as a rigidity in units of kN/mm.
5.1.2 Mechanics of Bone

The mechanical properties of bone are as variable as its structure. The variability in elastic properties for trabecular and cortical bone is demonstrated nicely by tabulated data in Currey [45] and Rice [202], which have been presented in modified form in Table 5.1. Young’s modulus for trabecular bone varies from approximately 0.1 to 25.0 GPa depending on scale, testing method, testing direction, anatomical site and individual. One can investigate elastic properties of bone at three distinct scales: the tissue level (< 1 mm), the apparent level (5 – 40 mm), and the whole bone level (>> 40 mm). Often studies imply that Young’s modulus is a surrogate for bone strength and fracture susceptibility. It is prudent to distinguish between the two terms: bone strength is defined as the stress at which bone yields or fails completely, Young’s modulus is the reversible elastic stiffness encountered with the application of small loads.

5.1.2.1 Experimental Data

At the tissue level (< 1 mm) bone has often been considered to be a homogeneous phase, or to paraphrase Carter: ‘all bone can be mechanically viewed as a single material’ [29] [28]. Recent nanoindentation experiments have both supported and contradicted this idea [241][201][200][265][87]. Results from these studies have shown moduli at this scale range between 6.9 GPa to 25 GPa and Zysset [265] argues that moduli varies for anatomical site, bone type, and individual, while Turner [241] present data that trabecular modulus is similar to that of cortical bone. Other methods such as buckling [208][239] and micro-tensile testing [6][198] have also been used to estimate Young’s modulus. A literature survey of experiments measuring elastic modulus at the tissue level are shown in the top section of Table 5.1.

At the apparent level (typically the continuum scale for trabecular bone is > 5mm [72] and up to 40 mm, depending on bone and species) Young’s modulus for trabecular bone has been estimated between 0.08 - 13 GPa. Previous studies have measured Young’s modulus using tensile tests (0.8 GPa, [209]), compression (0.08-0.4 GPa, [173][204][154][25]), 3-point bending (3.7-4.8 GPa, [32][135]), and sound wave propagation (10.9-13.0 GPa, [7]). Data for cortical bone modulus at this scale has also been measured and indicate a Young’s modulus of 4.8-5.4 GPa using 3-point bending. A study by Choi [32] also found a size dependency when measuring Young’s modulus in cortical bone. Tabulated data on the apparent level are shown in the middle part of Table 5.1.

Whole bone specimens have been tested mechanically using a variety of techniques: 3-point bending, 4-point bending, torsion and axial compression [183][36]. However, factors such as bone geometry have complicated analysis and calculation of
moduli. Results are typically reported in terms of rigidities rather than elastic moduli and comparisons with smaller scales is difficult. Values for whole bone moduli and rigidities are shown in the last section of Table 5.1.

Various difficulties arise when experimentally measuring elastic properties of bone. Measuring anisotropy requires re-using the specimens for repeated compression tests and the bone must not be plastically deformed. Additional difficulties include the edge effects of cutting across trabeculae which can fail under different modes (such as bending and sliding) than would otherwise be possible. The materials response to shear is difficult to test experimentally. Moreover, if one wants to find the elastic symmetry, then the subset must be cut in the same orientation as the symmetry axis.

5.1.2.2 Numerical FEM Data

The finite element method (FEM) allows one to measure the response of the material under arbitrarily complex loading conditions such as combined normal and shear strains without the above mentioned problems of physical testing. The caveat is that finite element requires a complete description of the material structure and its properties and boundary conditions, which is necessarily gained from experiment. Both FEM and experimental testing are complementary and drive each other. Finite element estimations of effective Young’s moduli are typically scaled by the modulus of the bulk material; for example, FEM estimation of effective trabecular bone moduli (approx. 1cm³ cubes with φ ≈ 0.7 – 0.9) reported values of between 5-20% of the bone tissue modulus. The modulus of the bone tissue is a parameter of the model and is assumed to be uniform and isotropic across the structure. Despite possible inhomogeneities and anisotropy at the tissue level, authors have shown comparisons of numerical models with experiment and shown that assuming isotropic and homogeneous bone tissue properties in a finite element simulation can accurately predict experimental measurement of trabecular bone elastic properties.

5.1.2.3 Empirical Relationships

Porosity, φ, or equivalently density, ρ, has been used widely as an explanatory variable of bone strength. The relationship between porosity and Young’s modulus has been studied extensively for trabecular bone (see Table 5.2). From this perspective, porosity gives a gross, and qualitative assessment of bone strength. Parameters of bone strength and structure are also customarily regressed against porosity. Various empirically derived regressions have been used to fit elastic properties to porosity (or
Table 5.2: Table of reported studies on relationship between Young’s modulus and porosity for bone and other porous media. We have converted those relationships given in terms of an apparent density, $\rho$, to a porosity using $\rho = 1800(1 - \phi)$ (kg·m$^{-3}$) (from [248]). We also standardise modulus in units of MPa. Finite element estimation of modulus-porosity relationships are reported in units of reduced moduli, $E/E_0$, which is the effective Young’s modulus divided by the tissue modulus parameter, $E_0$. $\dot{\varepsilon}$ is the strain rate.

$$E = A_0(1 - \phi)^{A_1}, \quad (5.1)$$

where $E$ is the modulus of the specimen, and $A_0$ and $A_1$ are experimentally derived constants. Carter and Hayes [29] found that a cubic relationship with a prefactor of $A_0 = 22103$ was the best fit for a set of human and bovine trabecular and cortical bone specimens, while subsequent work by Rice and others [202, 86, 7, 120] found an exponent of $A_1 \approx 2$ explained more of the variance in modulus when considering only trabecular bone specimens. When expressed in terms of porosity these studies reported different prefactors, $A_0$, ranging from 1429 to 35981. Other authors have reported an exponent of $A_1 \approx 1.4$ [151]. Finite element studies by Cowin and Kabel calculated reduced modulus (apparent modulus of medium divided by tissue modulus parameter) and reported exponents of 1.8 and 1.93 with prefactors of 1240 and 813 respectively. Figure 5.2 shows these and other modulus-porosity relationships published in the literature. Over the range of typical trabecular bone porosity, 0.7-0.9, the predicted modulus can vary over an order of magnitude depending on the model used. Gibson and Ashby [66] suggest the differences in the modulus-porosity relationship can be explained by the architecture and the predominant deformation mechanism of the system.

In this chapter we describe a 3D imaging and mechanical analysis study on thr-
teen proximal femurs. In order to quantitatively analyse the micro- and macro-structure and mechanics of proximal femur it is necessary to resolve structure across a range of length scales with sufficient resolution. The ANU micro-CT facility is capable of generating voxelated density maps of 60mm in dimension, with a resolution of approximately 25\(\mu\)m. We have developed a method to accurately phase separate bone from soft tissue and void space. From these images we predict elastic properties and determine statistics about the topology and structure of the system. This study has multiple objectives. First, to make qualitative and quantitative descriptions of 3D architecture of the proximal femur and the effect of bone aging. Second, to understand if correlations exist between structural factors and elastic properties and make inferences regarding the key structural components in bone strength. And third, we examine whether bone heterogeneity and sample size influence any relationship between structural parameters and elastic properties. We also illustrate the difference in the prediction of bone strength based on trabecular specimens versus whole hip specimens. The influence of resolution on the estimation of elastic properties is then examined in the discussion.

Figure 5.2: Illustration of different modulus-porosity relationships for bone published by various authors. The typical porosity range for trabecular bone is shown by vertical lines between porosity values of 0.7 and 0.9.
5.1.3 Elastic Anisotropy

The generalised form for Hooke’s Law in three dimensions is typically described as (see Appendix A)

\[ \tau_{ij} = C_{ijkl} \epsilon_{kl}, \]  

(5.2)

where \( \tau_{ij} \) is the stress tensor, \( \epsilon_{kl} \) is the strain tensor, and \( C_{ijkl} \) is the 4th rank stiffness tensor. The stiffness tensor observes the symmetry relations

\[ C_{ijkl} = C_{jikl} = C_{ijlk} = C_{klij}. \]  

(5.3)

Hooke’s Law can be written equivalently as

\[ \epsilon_{ij} = S_{ijkl} \tau_{kl}, \]  

(5.4)

where \( S_{ijkl} \) is called the compliance tensor. Both the \( C_{ijkl} \) and \( S_{ijkl} \) tensors are 4th rank 3 dimensional tensors, however because the stress and strain tensors are symmetric and the symmetry conditions mentioned above, the elasticity tensor can be represented with 21 independent components. Hooke’s Law can be written as a second rank tensor in 6 dimensions. This can be expressed in matrix notation using new indices as

\[ C_{\alpha\beta} = \begin{bmatrix} C_{11} & C_{12} & C_{13} & C_{14} & C_{15} & C_{16} \\ C_{21} & C_{22} & C_{23} & C_{24} & C_{25} & C_{26} \\ C_{31} & C_{32} & C_{33} & C_{34} & C_{35} & C_{36} \\ C_{41} & C_{42} & C_{43} & C_{44} & C_{45} & C_{46} \\ C_{51} & C_{52} & C_{53} & C_{54} & C_{55} & C_{56} \\ C_{61} & C_{62} & C_{63} & C_{64} & C_{65} & C_{66} \end{bmatrix}, \]  

(5.5)

where the symmetry condition \( C_{\alpha\beta} = C_{\beta\alpha} \) ensures that for an anisotropic medium the stiffness tensor will contain 21 independent components. Further symmetries within the medium can reduce the number of independent components.

5.1.3.1 Symmetry Groups

Elastic materials can exhibit different kinds of symmetry relating the strains to stresses. The symmetry arises from the micro-structural organisation or texture of the medium under consideration [41]. If a material exhibits a symmetry plane, the elastic properties are invariant for a coordinate reflection about that plane. It has been shown that in general a material can be classified into one of 8 symmetry groups [30]. A representation of the different symmetry groups are illustrated in Helbig [74]. Generally, when talking about materials with symmetries due to texture there are three common
symmetry groups: orthotropic (orthorhombic), transverse isotropic (tetragonal), and isotropic. Orthotropic materials have three mutually perpendicular planes of symmetry and can be characterised by 9 independent tensor components

$$C_{\alpha\beta} = \begin{bmatrix}
C_{11} & C_{12} & C_{13} & 0 & 0 & 0 \\
C_{12} & C_{22} & C_{23} & 0 & 0 & 0 \\
C_{13} & C_{23} & C_{33} & 0 & 0 & 0 \\
0 & 0 & 0 & C_{44} & 0 & 0 \\
0 & 0 & 0 & 0 & C_{55} & 0 \\
0 & 0 & 0 & 0 & 0 & C_{66}
\end{bmatrix}.$$  \hspace{1cm} (5.6)

The compliance tensor, $S_{\alpha\beta}$, can be found from the matrix inverse of the stiffness tensor \[39\]. The components of the compliance tensor are easily expressed in terms of directional elastic moduli

$$S_{\alpha\beta} = \begin{bmatrix}
\frac{1}{E_1} & \frac{-\nu_{12}}{E_2} & \frac{-\nu_{13}}{E_3} & 0 & 0 & 0 \\
\frac{-\nu_{12}}{E_1} & \frac{1}{E_2} & \frac{-\nu_{23}}{E_3} & 0 & 0 & 0 \\
\frac{-\nu_{13}}{E_1} & \frac{-\nu_{23}}{E_2} & \frac{1}{E_3} & 0 & 0 & 0 \\
0 & 0 & 0 & \frac{1}{G_{23}} & 0 & 0 \\
0 & 0 & 0 & 0 & \frac{1}{G_{31}} & 0 \\
0 & 0 & 0 & 0 & 0 & \frac{1}{G_{12}}
\end{bmatrix}.$$  \hspace{1cm} (5.7)

A closely related type of symmetry consists of 6 distinct elastic constants. This type of symmetry is referred to as transverse isotropy and sometimes as tetragonal in the crystallographic literature

$$C_{\alpha\beta} = \begin{bmatrix}
C_{11} & C_{12} & C_{13} & 0 & 0 & 0 \\
C_{12} & C_{11} & C_{13} & 0 & 0 & 0 \\
C_{13} & C_{13} & C_{33} & 0 & 0 & 0 \\
0 & 0 & 0 & C_{44} & 0 & 0 \\
0 & 0 & 0 & 0 & C_{44} & 0 \\
0 & 0 & 0 & 0 & 0 & C_{66}
\end{bmatrix}.$$  \hspace{1cm} (5.8)
Isotropic symmetry consists of symmetry planes around any axis, and reduces the number of independent elastic components to 2

\[
C_{\alpha\beta} = \begin{bmatrix}
C_{11} & C_{12} & C_{12} & 0 & 0 & 0 \\
C_{12} & C_{11} & C_{12} & 0 & 0 & 0 \\
C_{12} & C_{12} & C_{11} & 0 & 0 & 0 \\
0 & 0 & 0 & C_{44} & 0 & 0 \\
0 & 0 & 0 & 0 & C_{44} & 0 \\
0 & 0 & 0 & 0 & 0 & C_{44}
\end{bmatrix}.
\]

With the additional restrictions on the tensor components that \( C_{44} = \frac{1}{2}(C_{11} - C_{12}) \).

### 5.1.4 Finite Element Modelling of Femoral Neck

Continuum mechanics can be used to analyse the stress distributions within simplified geometric shapes. However, for objects of complex and irregular geometry, and complicated material properties the governing differential equations are difficult or impossible to solve analytically. It was found that a numerical solution could be estimated for mechanical problems involving complex geometry. One numerical method, the finite element method (FEM) has its roots in the early 1900’s. The solution approximates the exact solution over a set of discrete points (or a mesh) and with the use of interpolating functions the solution can be approximated in continuous space.

Throughout its history FEM has been viewed with some scepticism from those in biomedical research, primarily because the method was sometimes put forward as an absolute solution for complex biological problems. The practical capabilities of FEM were often over stated. Critics have argued that FEM can not adequately model the complex loading conditions and material properties of complex biological systems [94]. However, progress has been made in computer software and hardware and allowed for arbitrarily complex models and loading conditions that are only limited by the investigators knowledge of the system. Much of the early work on FEM is related to the demonstration and validation of the methodology rather than solving a specific problem pertaining to bone strength.

The advent of high resolution computed tomography and the associated advances in computational infrastructure allowed investigators to measure and visualise microstructural features of materials in three dimensions at micrometre scale [59]. Density and compositional distributions can be measured non-invasively without the need to section the specimen such as with conventional optical and scanning electron microscopy (SEM) and histomorphometric techniques [12].

Finite element methods have been used in biomechanics to quantitatively analyse
phenomena such as mechanics, fluid flow, and heat transfer within complex biological systems which would otherwise be intractable problems. Orthopaedic biomechanics has historically been one of most intense fields for applications of finite element analysis. For example, analysis of stress within bones and artificial prostheses were among the first applications of the FEM to biomechanics. Stochastic or idealised models of bone geometry could be used to generate the finite element model [190, 191, 11, 10, 227]. These models were proposed as a way of understanding the relationship of trabecular bone strength to its volume fraction and architecture. The basis of these earlier FEM models are repeated identical unit cells from which the behaviour of the entire system could be deduced from analysing one unit cell [66].

More recently, computed tomography image data has lent itself to micro-structure based numerical estimations of mechanical properties. However, low resolution models do not capture the complexity of the trabecular bone network [150, 122]. To compensate for a lack of structural information models have been proposed relating the apparent density to elastic moduli [123, 42] (such as those listed in Table 5.2). Only recently, high resolution micro-CT scans have been used to create finite element models, which incorporate structure resolved of the order of 20-100 µm [249, 211].

5.2 Methodology

Thirteen pairs of proximal hip specimens were obtained from Caucasian females cadavers aged 29-85 (mean 66.3). The specimens were cleaned and soft tissue and frozen at -20 °C. The right hand sided specimens (recall Table 4.1) are used in this chapter.

5.2.1 Image Acquisition and Reconstruction

Hip specimens were thawed overnight prior to imaging and mounted within an aluminium holder (see Figure 4.6). Image acquisition consisted of a series of radiographs captured at angular increments. Care was taken to ensure that for all specimens the femoral neck axis (running from the most medial point of the femoral head to the most lateral point of the greater trochanter) was aligned parallel to the imaging coordinate axis. Immediately after imaging the specimens were returned to -20 °C. All specimens were imaged using a protocol of 1440 projections of 1024×1024 pixels, resulting in a voxel size of 57.1 µm. One specimen, 180R, was imaged again at a higher resolution of 28.5 µm, which required 2880 projections of 2048×2048 pixels. We denote the higher resolution image as 180R,2K and the lower resolution image as 180R,1K. A 1mm aluminium filter was placed over the x-ray source aperture to minimise beam hardening artifacts. All specimens were then reconstructed using a modified Feldkamp algo-
5.2 Methodology

5.2.2 Segmentation

In Figure 5.3 [a] we illustrate a cross sectional slice of specimen 180R tomographic data. A continuous range of densities are present in the image; from pore space, through soft tissue and cartilage to low density and high density bone. In order to quantitatively characterise the hip structure and properties, it is necessary to phase separate the image into pore, soft tissue and bone phases. As mentioned in previous chapters this is not a trivial problem. The primary difficulty is the lack of contrast or the presence of a density overlap between different phases. For example, small trabecular features as shown in the lower right (inferior part of the femoral head) of Figure 5.3 [a] are indistinguishable in density from pockets of soft tissue. Features such as fenestrations and holes in the bone material may also have a density indistinguishable from trabecular bone in another part of the image. Figure 5.4 shows the distribution of attenuation coefficients within the filtered tomographic data. A simple approach to segmentation is to choose a cutoff threshold. Voxels with an attenuation above this threshold are assigned to the bone phase, and voxels below are assigned to a combined pore and soft tissue phase. An example of the segmented bone phase using a cutoff threshold is shown in Figure 5.3 [b]. In this image, (segmented at a relative X-ray attenuation of 24,000) one can see an over-estimation of bone phase in some regions such as the inferior FN cortex and central FH, where pores are assigned to the bone phase. However, in other regions there is an under-segmentation of bone, such as in the inferior femoral head, where there are fine, intermediate density trabeculae that are mistakenly assigned to the pore / soft tissue phase. One must choose a threshold which compromises between these two effects. This highlights the difficulty inherent in segmentation.

We apply a sophisticated three-phase active contours segmentation algorithm to separate the image into pore, soft tissue and bone phases. The segmentation procedure follows that of previous chapters. That is, a filtering step was performed to remove noise and sharpen edges on the original raw tomographic data. Subsequently, thresholds were chosen to create seed pore and bone regions. These regions were merged according to a speed function which depends on the gradient of the image. The segmentation procedure is based on active contours algorithm [222, 118]. We observe that pore, soft tissue and bone phases contain overlapping attenuation coefficients. Segmented slices of the intermediate density soft tissue and high density bone phases are shown in Figure 5.3[c,d] respectively. We compare the simple segmentation method and the three-phase method in Figure 5.5 and Figure 5.6.
Figure 5.3: Representative cross sections of a hip tomogram dataset. [a] Specimen 180R raw tomographic slice, [b] 180R segmented bone phase. Segmented using simple segmentation cutoff threshold, [c] 180R segmented intermediate density soft tissue with 3 phase segmentation algorithm, [d] 180R segmented bone phase with 3-phase segmentation algorithm, [e] fiducial mask for specimen 180R.
Figure 5.4: X-ray attenuation coefficient histograms with resultant distributions of pore, soft tissue and bone phases.

black, green, and red colours indicate voxels included in both segmentation methods, only simple segmentation, and only three-phase segmentation respectively. In subsets shown in Figure 5.5[b-d] we observe that simple segmentation method tends to oversegment in dense regions, such as filling in holes in the inferior cortex of the bone, and the centre of the femoral head. Figure 5.5[c] shows the red three-phase segmentation resolves trabecular connections which are poorly resolved and appear disconnected in the simple segmentation. The distribution of densities covered by these binary phases is shown as the resultant histogram - Figure 5.4. In Figure 5.6 we show the difference in connectivity between the simple segmentation and three-phase segmentation. In the central femoral head, there is little difference in connectivity (panel [a]), however a comparison in the inferior part of the femoral head (panel [b]) shows that the three phase segmentation (in red) captures more of thin trabeculae which are not detected using a simple segmentation method (in green). We believe that the three-phase segmentation gives a more accurate representation of the specimen data.
**Figure 5.5:** [a] Comparison of three-phase segmentation and simple cutoff threshold. Black represents bone included in both segmentations, while green represents the volume only in the simple segmentation, and red represents those voxels only contained in the three phase segmentation. Subsets reveal an over segmentation (porosity is filled with green) by the simple segmentation method in the dense femoral neck and central femoral head. The simple segmentation method also fails to capture thin trabecular regions, which are captured by the three phase method. [b] Subset near centre of femoral head, [c] subset near femoral neck, [d] subset near supero-medial femoral head.
5.2.3 Morphology

5.2.3.1 Estimation of Porosity

As mentioned previously porosity is customarily used as an explanatory variable for bone strength. A large body of work has studied relationships between porosity and bone modulus which is summarised in Table 5.2. Porosity of the proximal femur was determined by first creating a fiducial mask over the entire femoral head and neck. A morphological closing operation was performed on the solid bone phase with a sphere kernel of radius 200 voxels (11.5mm). The effect of this is to fill in the internal porosity of the bone. We show an example slice of the fiducial mask in Figure 5.3[e]. The bone volume fraction is then defined as the ratio of number of bone pore voxels to the total number of voxels in the fiducial volume

$$\phi_{\text{bone}} = \frac{N_{\text{bone}}}{N_{\text{fiducial}}}. \quad (5.10)$$

The porosity is one minus the bone volume fraction

$$\phi_{\text{pore}} = 1 - \phi_{\text{bone}}. \quad (5.11)$$

5.2.3.2 Network Representation

The topology of the trabecular bone network has been hypothesised to be a critical factor affecting bone mechanical properties [129] [125] [111] [244] [232] [188]. To investi-
gate this we describe a multistep procedure to define a network of trabecular junctions and rods from a segmented bone volume. We can use this network to derive quantitative statistics about the structure and its topology. First, the Euclidean distance map is calculated for each voxel on the solid phase, which is the linear distance to the nearest pore / solid boundary. A medial axis is then derived from the Euclidean distance using a distance-ordered thinning procedure \[189, 145\]. The medial axis is shown in Figure 5.7[a]. The junctions of the medial axis define centres of the individual trabecular elements composing the network. A junction and rod representation of the network can be derived by using a watershed transformation followed by a merging step similar to that described in Chapter 3. The resulting partition between trabecular junction elements is shown in Figure 5.7[a]. The colours represent different trabecular partitions. A topological network can be constructed by connecting the centre of adjacent trabecular elements together. This is illustrated by the red junction-rod model in Figure 5.7[b]. One can think of this as the junctions representing the connected elements in trabecular bone, while the rods represent the interconnections between the junctions. The network representation allows one to define a set of statistics for each bone junction element and each connecting rod. For example, we can define the bone coordination, the bone rod length, bone rod radius and the bone junction radius. The bone coordination number, \(Z\), is defined as the number of rods connecting to each bone junction element at the image resolution. The bone rod length is defined as the distance between two junctions and the bone rod radius is defined as the minimal Euclidean distance on the medial axis between the junctions. We define the bone junction radius as the largest maximum covering sphere contained within the bone junction element.

Figure 5.7: Illustration of pore partitioning procedure for trabecular bone on specimen 180R (age: 76, \(\phi = 0.717\)). Each partitioned element is labelled with a different colour. [a] A volume approximately 0.8mm \(\times\) 0.7mm \(\times\) 1mm showing a highly connected trabecular element (in blue). The image is skeletonised using a medial axis transform and followed by a pore partitioning procedure to find boundaries between trabecular elements. [b] Same volume with network overlay showing the coordination number of this element. [c] A larger volume representing the partitioning of many elements. This cube represents approximately (2.4mm)\(^3\).
5.2.4 Finite Element Model

In this section we describe the procedure used to model the elastic properties of the femoral neck and head. We use a finite element method similar to that described in Chapter 3 [3, 203], which has been modified for anisotropic media. We assume a linear Hookean behaviour for the material in our system. Briefly, the pixels form a convenient discretisation of the 3D space and are used as the finite element mesh. A variational principle is used where the sum of the energy in the medium is minimised according to nodal displacements given some boundary condition. The boundary condition can be specified as a constant stress or strain over a particular surface or subset of the finite element nodes and then all other nodes apart from the boundary are allowed to relax. Once the displacement field is found that minimises the energy, the stress and strain can be averaged over the entire system to find the effective elastic stiffness.

5.2.4.1 Choice of Elastic Properties

We assume at the individual voxel level that bone is a homogeneous and isotropic material and choose an isotropic modulus of $E_0 = 18.33$ GPa [241, 201, 85], and an isotropic Poisson’s ratio of $\nu_0 = 0.31$. We use these values as they represent tissue level moduli measured (using nanoindentation) at approximately the same scale as the voxel size (See Table 5.1). The resulting effective moduli are scaled by the input Young’s modulus and reported as reduced moduli, which allows comparisons with other studies.

We assume that bone is a linear elastic material; though bone is widely reported as a viscoelastic material, with its moduli depending on strain rate. This dependency on strain rate is weak with Young’s modulus being approximately proportional to strain rate raised to the power 0.06 [29]. As such, bone can be considered linear elastic to a good approximation, provided strain remains below the yield strain.

5.2.4.2 Boundary Conditions

Six planes were defined that contact the surface of the proximal femur in the anatomical directions: superior, inferior, anterior, posterior, medial and lateral (see Figures 5.8 [a-b]).

To estimate the full $C_{ijkl}$ elasticity tensor for an anisotropic medium, six independent strains were applied separately. We illustrate the six independent strains in Figure 5.9. For the three normal strain cases, $\epsilon_i^i, i = 1..3$, a strain is applied across the image on opposing faces in the x, y, z directions respectively. One face is held at con-
stant strain, while the opposing face has a zero strain boundary condition. For shear strain cases, $\epsilon^i, i = 4..6$ the boundary conditions are applied on four faces, whereby two faces are held at zero strain, and the opposing faces are given a constant shear strain.

Figure 5.8: [a] Coronal section of specimen 169R illustrating anatomical orientation and the planes used for boundary conditions. [b] Transverse section of 169R. $\epsilon^1$ is associated with normal strain along the anterior-posterior direction. $\epsilon^2$ is normal strain in the superior-inferior direction. $\epsilon^3$ is normal strain in the medial-lateral direction. $\epsilon^4$ is shear strain acting on the medial and inferior planes in the inferior and medial directions respectively. $\epsilon^5$ is shear strain on the posterior and medial planes in the medial and posterior directions respectively, $\epsilon^6$ is shear strain on inferior and posterior planes acting in the posterior and inferior.

\[
\epsilon^1 = \begin{bmatrix}
0.00001 \\
0 \\
0 \\
0 \\
0 \\
0 \\
0 \\
0
\end{bmatrix},
\epsilon^2 = \begin{bmatrix}
0 \\
0.00001 \\
0 \\
0 \\
0 \\
0 \\
0 \\
0
\end{bmatrix},
\epsilon^3 = \begin{bmatrix}
0 \\
0 \\
0.00001 \\
0 \\
0 \\
0 \\
0 \\
0
\end{bmatrix}.
\] (5.12)

\[
\epsilon^4 = \begin{bmatrix}
0 \\
0 \\
0 \\
0.00001 \\
0 \\
0 \\
0 \\
0
\end{bmatrix},
\epsilon^5 = \begin{bmatrix}
0 \\
0 \\
0 \\
0 \\
0.00001 \\
0 \\
0 \\
0
\end{bmatrix},
\epsilon^6 = \begin{bmatrix}
0 \\
0 \\
0 \\
0 \\
0 \\
0.00001 \\
0 \\
0
\end{bmatrix}.
\] (5.13)

Each column of $C_{ijkl}$ was found from the individual strain cases. The unit strains
provide a basis from which a linear combination of strains can be superimposed to
determine the local response to any imposed strain. The response of the system to
these independent strains, allowed construction of a tensor of elastic constants for an
equivalent homogeneous solid. By a linear combination of the six strain loading cases
we can simulate any loading case on the bone.

5.2.4.3 Computational Aspects

All simulations were run on an SGI Altix supercomputer at the Australian Partnership
for Advanced Computing (APAC) facility. The $1024^3$ (1 billion element) simulations
were run using 64 CPUs and with 100GB of memory. The $2048^3$ (8 billion element)
simulation required 512 CPUs with 600GB of memory. Typically, each hip dataset did
not occupy the entire field of view and we were able to subset the data to $900 \times 800 \times
800$ elements for the $1024^3$ images, or $1800 \times 1600 \times 1600$ for the $2048^3$ image. Local
displacement vectors and local stress and strain tensors were output for visualisation.
Each strain case for $1024^3$ size images took approximately 64 cpu hours to run, while
the $2048^3$ strain cases took approximately 200 CPU hours.

![Boundary conditions for each of the six independent strain cases.](image)

5.2.4.4 Convergence

The elastic simulations proceed using the energy minimisation routine until a suffi-
cient level of convergence is achieved. We illustrate the evolution of the elastic energy
in Figure 5.10 for a typical simulation. The derivative of the elastic energy is taken over nodal displacements, $u$. The norm squared of the derivative is shown in the solid line. The conjugate gradient routine is deemed to have found a stable solution and is ceased when the change in the relative change in effective stresses and strains are below a tolerance of $5 \times 10^{-3}$, while at the same time system energy, $E$, decreases monotonically. This criterion is consistent with works of Arns [4] and Garboczi [61].

Figure 5.10: Representative plot of convergence of elastic energy using conjugate gradient relaxation technique. The norm squared of the gradient is represented as the solid line. The simulation is stopped when the relative change in stress and strain is less than our tolerance ($< 5 \times 10^{-3}$) [4, 61]. The total elastic energy of the system is shown as the dotted line.

### 5.2.4.5 Compliance Tensors

A perfectly symmetric stiffness matrix will observe the matrix relation

$$C = C^T.$$  

(5.14)

However, the computed tensor approximates a symmetric tensor given some numerical error. We quantify the error by using the above relation that a symmetric elasticity matrix is equal to its transpose. We express the error by defining a distance function between the stiffness matrix and its transpose

$$\| C - C^T \| = \sqrt{\sum_{ij} (C_{ij} - C_{ji})^2}.$$  

(5.15)
The distance is normalised by the magnitude of the stiffness matrix, $\|C\|$, to give a percentage error

$$\text{Err} = \frac{\|C - C^T\|}{\|C\|} = \sqrt{\sum_{ij} (C_{ij} - C_{ji})^2} \sqrt{\sum_{ij} C_{ij}^2}.$$  

(5.16)

### 5.2.5 Estimation of Elastic Symmetry

Cowin and Mehrabadi [41, 40] decompose the 2nd rank 6 dimensional $C_{\alpha\beta}$ tensor into two second rank 3 dimensional tensors, denoted as A and B. If A and B share common eigenvectors, the eigenvectors will be indicative of the symmetry axis. However, in practise the eigenvectors and eigenvalues are never exactly equal and a numerical tolerance must be specified for the error between similar eigenvectors.

Spectral decomposition of the elasticity tensor has also been used to characterise symmetry groups [236, 260]. Yang and Cowin averaged the eigenbases for 141 cancellous bone specimens. The average eigenbases were found to approximate orthotropic symmetry at 95% confidence level. However, when using a matrix norm error function similar to those of Rietbergen and Dellinger [252, 46], the approximation appeared to be far less accurate - with an error up to 25%. In the next section we detail the methods we utilise to estimate the elastic symmetry.

#### 5.2.5.1 Identifying Elastic Symmetry

The stiffness tensor is calculated relative to the Cartesian coordinate system of the tomographic system. If the symmetry planes are not oriented along these Cartesian axes, then if symmetry exists, it may not be immediately apparent. The problem we face is this: given an arbitrary stiffness tensor, how can one determine the existence of any symmetry groups. And if symmetries exist, what are the orientations of the symmetry axes and how different is the arbitrary stiffness tensor from ideal symmetry groups.

We use the technique similar to Rietbergen [252] and Dellinger [46] to find the approximation to orthotropic and transverse isotropic symmetry by minimising an objective distance function. The measured $C_{ijkl}$ tensor was rotated into the new primed coordinate axis, $(X', Y', Z')$, for each specimen and the deviation away from orthotropic symmetry was measured. To find the best orthotropic estimation requires searching over 3 orientation parameters. The reported components of the stiffness tensor are those which best approximate orthotropic symmetry. The distance from symmetry can be expressed using the distance function normalised by the magnitude of the input using Equation 5.17.
Since orthotropic symmetry has 9 independent components, a permutation of $X'$, $Y'$, $Z'$ axes will not affect the overall symmetry classification. In other words, for orthotropic symmetry the order of the axes is not unique. However, this is not the case for transverse isotropy, where the elastic properties in the $Z'$ direction are distinctly different to the $X'$ and $Y'$ axes. We therefore introduce the convention that the axes for the orthotropic systems are ordered such that $Z'$ is closest to being a transverse isotropic axis of symmetry, followed by $Y'$ and $X'$ \[46\]. This is illustrated in the results section in Figure\[5.26\], where the elastic stiffnesses in the tomographic $X$, $Y$, $Z$ axes are transformed into symmetry axes $X'$, $Y'$, $Z'$. In the $Z'$ direction the stiffness is greater than the $X'$ and $Y'$ directions. Elastic stiffness constants in the $X'$ and $Y'$ directions (in the purple coloured plane) are approximately equal.

To measure the % deviance, $D$, from symmetry for any given general anisotropic tensor, $C_{\alpha\beta}$ we define an error function similar to Equation\[5.15\] above, but replacing $C^T$ with a reference tensor of the desired symmetry, $R_{\alpha\beta}$:

$$D = \frac{\|C - R\|}{\|C\|} = \frac{\sqrt{\sum_{ij}(C_{ij} - R_{ij})^2}}{\sqrt{\sum_{ij}C_{ij}^2}}.$$

(5.17)

5.3 Results

In this section we first present the results of the structural analysis including the porosity and structural statistics. We examine the variability between the structure within one specimen, and across multiple specimens. We then present the results of the elastic simulations and correlate the stiffness to structural measures.

5.3.1 Porosity

We observe a porosity range of between 0.596 (specimen 45R) to 0.821 (specimen 72R). This is qualitatively illustrated in Figure\[5.11\] where we show all specimens in ascending age. We show the two extrema in close up in Figure\[5.12\]. In Figure\[5.11\] [a-c] we show the youngest three specimens: 45R (age 29), 15R (age 37), and 169R (age 37), which are in general characterised by a high bone volume fraction. Specimen 45R [a] contrasts 169R [c] because it shows a less distinct orientation of primary compression trabeculae. The trabeculae appear more random in orientation; and trabeculae are distributed throughout the femoral neck and head. We also observe a thick acetabular cortex and clusters of dense packets of bone in the centre of the femoral head. Specimen 15R shows a band of primary compression trabecular bone, however the bone
Elastic Properties of the Human Proximal Femur

Figure 5.12: Illustration of extrema in porosity values: [a] specimen 45R, age: 29, $\phi_{\text{pore}} = 0.596$, and [b] specimen 72R, age: 72, $\phi = 0.821$.

Volume fraction is low in the inferior and superior femoral head regions. Specimen 169R has a distinct cross-hatched thick trabecular pattern characteristic of the primary compression and tensile trabeculae.

The older specimens are shown in ascending age in Figure 5.11[d-m]. In panels [e,f,j] we observe specimens 72R, 11R and A08R respectively, exhibiting an extremely low volume fraction of bone. The specimens all have a thin primary compression band and a lack of trabecular bone in the femoral neck. In contrast to younger specimens we observe a very narrow cortical shell on the acetabular surface. We also note there is a lack of trabecular connections in the primary tensile region in these cases. We observe a spread of densities and trabecular architectures amongst elderly individuals. In panels [h,l,m] we observe specimens 17R, 10R, and 177R respectively which contrast to the previously mentioned low density specimens. 17R, 10R, and 177R all display moderate bone volume fractions and relatively thick bands of primary compression trabeculae. There are also trabecular connections buttressing the superior femoral neck to the centre of the femoral head (primary tensile band).

We investigated the relationship between porosity within the FN/FH region with age (see Figure 5.13) and tabulated results in Table 5.3. We observe a trend of increasing porosity of the femoral neck and head region with age. A linear regression was fitted to the data: $\phi = 0.54693 + 0.0028282x$, where $x$ is age in years. This linear regression has a coefficient of determination, $r^2 = 0.59$. This corresponds to an increase in porosity of approximately 0.028 per decade ($p < 0.01$). This data is consistent with results for femoral neck bone volume fraction (BV/TV) measured by Stauber and Muller [231]. They noted a decrease of BV/TV at approximately 70 years of age.
Due to a lack of data at ages < 70 we can not test their observation.

\[
\phi = 0.54693 + 0.0028282 \times x, \quad r^2 = 0.587, \quad (p < 0.01)
\]

Confidence intervals at the 95% level for the linear regression are shown in red.

### 5.3.2 Structural Visualisation

In Figures 5.14, 5.15, and 5.16 we present three dimensional renderings and qualitatively illustrate the gross structural differences between femora from young and old individuals.

In Figure 5.14 panel [a] we show 15R which is from a 37 year old individual and of porosity 0.673. A thick band of trabeculae run from the inferior femoral neck cortex (on the left of the image) towards the centre of the femoral head. The femoral head is packed with progressively finer trabecular struts up to the acetabular surface. There are some high density clusters within the femoral head near the acetabular surface. This is in contrast to a specimen from an older individual (72R, porosity: 0.821) shown in panel Figure 5.14 [b] which shows distinctly more void space within the proximal femur. We observe a similar band of trabeculae oriented from the inferior femoral neck cortex to the medial acetabular surface. The trabeculae are markedly thinner and have a more prominent orientation than the younger specimen. Moreover, the femoral head is of lower density compared to the younger specimen.

In Figure 5.15 panel [a] specimen 169R is shown, which is a specimen from a younger individual (age: 37, porosity: 0.648). This specimen has a thick inferior FN
Figure 5.14: Three dimensional visualisations from: [a] younger (specimen 15R, age 37) and [b] older (specimen 72R, age 72) individuals. The inferior FN cortex is on the left for both specimens.
Figure 5.15: Three dimensional visualisations from: [a] younger (specimen 169R, age 37) and [b] older (specimen 177R, age 85) individuals. The inferior FN cortex is on the left for both specimens.
Figure 5.16: Three dimensional visualisations from: [a] younger (specimen 45R, age 29) and [b] older (specimen 180R, age 76) individuals. The inferior FN cortex is on the left for both specimens.
Table 5.3: Summary of hip specimens by label and age. Data include the fiducial volume, bone volume, and overall porosity of the specimen.

<table>
<thead>
<tr>
<th>Label</th>
<th>Fiducial volume [mm$^3$]</th>
<th>Bone volume [mm$^3$]</th>
<th>Porosity</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>45R</td>
<td>46300</td>
<td>18700</td>
<td>0.596</td>
<td>29</td>
</tr>
<tr>
<td>15R</td>
<td>51600</td>
<td>16800</td>
<td>0.673</td>
<td>37</td>
</tr>
<tr>
<td>169R</td>
<td>44600</td>
<td>15700</td>
<td>0.648</td>
<td>37</td>
</tr>
<tr>
<td>A3R</td>
<td>56200</td>
<td>14400</td>
<td>0.744</td>
<td>67</td>
</tr>
<tr>
<td>72R</td>
<td>36300</td>
<td>6500</td>
<td>0.821</td>
<td>72</td>
</tr>
<tr>
<td>11R</td>
<td>39800</td>
<td>7300</td>
<td>0.817</td>
<td>74</td>
</tr>
<tr>
<td>19R</td>
<td>35800</td>
<td>7700</td>
<td>0.784</td>
<td>74</td>
</tr>
<tr>
<td>17R</td>
<td>50500</td>
<td>15800</td>
<td>0.686</td>
<td>75</td>
</tr>
<tr>
<td>180R</td>
<td>45800</td>
<td>13100</td>
<td>0.714</td>
<td>76</td>
</tr>
<tr>
<td>A08R</td>
<td>38300</td>
<td>7600</td>
<td>0.802</td>
<td>78</td>
</tr>
<tr>
<td>9R</td>
<td>50300</td>
<td>10600</td>
<td>0.790</td>
<td>79</td>
</tr>
<tr>
<td>10R</td>
<td>52900</td>
<td>14200</td>
<td>0.731</td>
<td>79</td>
</tr>
<tr>
<td>177R</td>
<td>47600</td>
<td>12300</td>
<td>0.742</td>
<td>85</td>
</tr>
</tbody>
</table>

cortex and thick bands of trabeculae running to the centre of the femoral head. The femoral head has a high density of trabeculae, with an exception for the inferior region of the femoral head (left of image). A specimen from an older individual is contrasted in panel [b]. Here we show specimen 177R (age: 85, porosity: 0.742) which appears to have a lower density of trabecular bone throughout the femoral head and neck. We observe relatively thin bands of trabeculae radiating from the inferior cortex through the centre of the femoral head to the acetabular surface.

In Figure 5.16[a] we illustrate specimen 45R (age: 29, porosity: 0.596). This specimen has the highest bone volume fraction of all specimens analysed in this chapter. We observe trabecular bone distributed throughout the entire femoral head and neck, with large dense bone clusters appearing within the femoral head. The primary compression trabeculae are not as prominent as within some specimens and the specimen appears to have a more homogeneous distribution of trabeculae. A second band of trabeculae, believed to be the epiphyseal growth line, is observed running orthogonal to the primary compression trabeculae. Specimen 180R (age: 76, porosity:0.714) is shown in Figure 5.16[b] and illustrates the variation across older individuals; while some older individuals have a low bone volume fraction within the femoral head, specimen 180R has relatively high bone volume fraction. There are prominent and thick trabeculae running from the inferior cortex running through the centre of the femoral head, and a secondary epiphyseal growth band running orthogonal to the primary compression trabeculae.


5.3.3 Structural Characterisation

In this section we describe the quantitative characterisation of the hip micro-structure in terms of network parameters. First, we describe differences within individual specimens and then show differences between younger and older individuals. We then show the mean values for all specimens, and we present results for the variance of the network parameters and how these change with age.

5.3.3.1 Variability Within a Specimen

Variability across the set of 13 specimens is clear from Figures 5.14, 5.15, 5.16 and Table 5.3; one also notes from the image data a strong variability within the individual femoral head regions. To investigate the variability within one particular specimen, we extracted 4 subsets from different regions of the proximal femur of specimen 180R: the junction of the primary compressive trabeculae with the inferior cortex (1), the center of the femoral head (2), the supero-medial surface of the femoral head (3), and the inferior part of the femoral head near the foveal insertion (4). These regions are illustrated in Figure 5.17.

We observe a great difference in local heterogeneity across the specimen. In Figure 5.18 we illustrate the local heterogeneity in the pore partitioning and networks for different sites in specimen 180R. In Figure 5.18[a] we show the pore partitioning at site 1 which illustrates the highly anisotropic, thick trabecular plates near the FN cortex. The network representation for the same region in Figure 5.18[b] demonstrates that this region has relatively low coordination and few, but thick interconnections. In Figure 5.18[c] the pore partitioning for the centre of the femoral head is shown. This site has a more isotropic orientation of trabecular struts. Figure 5.18[d] shows the network for the equivalent volume; we observe a high average coordination and a high density of interconnections and junctions.

Figure 5.18[e] illustrates the morphology at the femoral head acetabular surface (site 3). The trabecular struts are narrower than in regions 1 and 2, and are highly aligned. The equivalent network representation is shown in Figure 5.18[f], which shows the relatively high coordination and narrow interconnections in this region. In Figure 5.18[g] we illustrate the micro-structure at site 4: the inferior femoral head. On visual inspection, this region has a relatively more isotropic orientation of trabeculae and a lower density of trabeculae. Connectivity and trabecular thickness decrease nearer the inferior plane. The network is shown in Figure 5.18[h] and is composed of the narrowest interconnections of all regions.

In Figure 5.19 and Table 5.4 we summarise the intra-specimen variation in network parameters over four different sites for specimen 180R. We observe that site 2 (the
§5.3 Results

Figure 5.17: [a] The four sites which are compared for purposes of highlighting the heterogeneity within specimens. [b] Site 1 is at the junction of the trabecular band with the inferior cortex. [c] Site 2 is the centre of the femoral head. [d] Site 3 is the acetabular surface of the femoral head. [d] Site 4 is the inferior part of the femoral head.

<table>
<thead>
<tr>
<th>Site</th>
<th>Mean coordination</th>
<th>Mean rod length [µm]</th>
<th>Mean rod radius [µm]</th>
<th>Mean junction radius [µm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.14±2.67</td>
<td>1054±399</td>
<td>119±35</td>
<td>199±55</td>
</tr>
<tr>
<td>2</td>
<td>8.70±3.77</td>
<td>833±261</td>
<td>103±34</td>
<td>176±37</td>
</tr>
<tr>
<td>3</td>
<td>6.96±2.60</td>
<td>747±209</td>
<td>82±23</td>
<td>135±29</td>
</tr>
<tr>
<td>4</td>
<td>5.96±2.46</td>
<td>670±194</td>
<td>73±18</td>
<td>119±19</td>
</tr>
</tbody>
</table>

Table 5.4: Summary of intra-specimen hip network parameters: coordination number at 57.1 µm voxel size, mean rod length, mean rod radius and mean junction radius. The standard deviations are included about the mean. The statistics are measured over 200 voxel cubed regions.
Figure 5.18: Illustration of the variability in pore partitioning within one specimen: 180R. [a,b] Site 1 at the junction of the femoral neck inferior cortex and the primary compression trabeculae. [c,d] Site 2 at the centre of the femoral head. [e,f] Site 3 at the supero-medial surface of the femoral head. [g,h] Site 4 at the inferior part of the femoral head. Each picture represents $100 \times 100 \times 50$ voxels.
central femoral head) has the highest mean coordination, \( < Z > = 8.70 \), followed by site 1 at the junction of the inferior femoral neck cortex and primary compression trabeculae. Sites 3 and 4 have a lower mean coordination number at 6.96 and 5.96, respectively. The rod radius distributions are shown in Figure 5.19[b]; there is a clear distinction between sites 1, 2 and 3, 4. Sites 1 and 2 are characterised by relatively high mean rod radii: 119\( \mu m \) and 103\( \mu m \) respectively, while sites 3 and 4 have lower mean radii at 82\( \mu m \) and 73\( \mu m \) respectively. Site 1 displays the highest mean rod length of 1054\( \mu m \), followed by sites 2, 3 and 4. The junction radius distributions are shown in Figure 5.19[d]. We observe that sites 1 and 2 have relatively broader distributions and higher mean radii compared to sites 3 and 4.

![Figure 5.19: Illustration of intra-specimen difference in network parameters for 180R: [a] coordination number, [b] rod radius, [c] rod length, [d] junction radius.](image)

### 5.3.3.2 Variability Across Specimens

We observe distinct differences in morphology and network properties across specimens. We illustrate this with four subsets taken from the same region (central femoral head) from younger individuals (169R, 45R) and older individuals (11R, A08R). Figures 5.20[b and c] illustrate the pore partitioning and network respectively for specimen 169R. A dense and highly connected web of trabecular bone is observed in the centre of the femoral head. This is paralleled by specimen 45R in Figure 5.20[e and
<table>
<thead>
<tr>
<th>Specimen</th>
<th>Age [years]</th>
<th>Mean coordination</th>
<th>Mean rod length [µm]</th>
<th>Mean rod radius [µm]</th>
<th>Mean junction radius [µm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>45R</td>
<td>29</td>
<td>8.93±3.86</td>
<td>1237±393</td>
<td>131±36</td>
<td>226±50</td>
</tr>
<tr>
<td>169R</td>
<td>37</td>
<td>8.90±3.70</td>
<td>1205±387</td>
<td>130±40</td>
<td>229±48</td>
</tr>
<tr>
<td>11R</td>
<td>74</td>
<td>5.99±2.70</td>
<td>1349±472</td>
<td>112±33</td>
<td>190±44</td>
</tr>
<tr>
<td>A08R</td>
<td>78</td>
<td>6.64±2.90</td>
<td>1209±384</td>
<td>104±29</td>
<td>181±39</td>
</tr>
</tbody>
</table>

Table 5.5: Summary of inter-specimen hip network parameters: coordination number, mean rod length, mean rod radius and mean junction radius. The standard deviations are included about the mean. The statistics are measured over 200 voxel cubed regions.

Both of the specimens show a predominant trabecular orientation, but also display significant connections between trabeculae in the predominant band. In Figure 5.20 [g-i] we illustrate the pore partitioning of specimen 11R. The trabeculae have a markedly lower density and lower coordination number. The trabeculae are exclusively oriented from the FN cortex to FH surface. This contrasts to the other older specimen: A08R, shown in Figure 5.20 [j-l], which is of higher density and has secondary trabeculae bracing the predominate trabecular orientation.

In Figure 5.21 we show the distributions of network parameters for four subsets taken from the centre of the femoral head from specimens 11R, 45R, 169R, and A08R and present tabulated mean values for the network parameter distributions in Table 5.5. We observe that the coordination number distribution is shifted to lower values for the specimens from older individuals with $Z > 8.5$ for younger individuals and $Z \approx 6 – 6.7$ for older individuals. We also note that the mean rod radius and the trabecular junction radius distributions are shifted towards lower radii for the older specimens. Illustrations of the bone junction and rod network for young versus old specimens are shown in Figure 5.22.

5.3.3.3 Overall Network Statistics

Statistics from the network analysis for all specimens at 57.1 µm voxel size are tabulated in Table 5.6. The mean coordination number ranges from 5.95 (specimen 19R) to 7.71 (specimen 45R). The distribution of coordination numbers for each specimen is shown in Figure 5.23 [a]. All specimens show a similarly shaped distribution, with specimens 169R, 45R, 17R shifted towards a higher coordination number. The mean rod radius gives an indication of the size of the trabecular bone ‘rods’ joining the junction elements of the network. The rod radius distributions are shown in Figure 5.23 [b]. The mean rod radii vary between 97±33µm (specimen 9R) and 135±56µm (specimen 45R). When compared to the voxel size, the mean rod radii are approximately between 1.7–2.4 times the voxel size. This has implications on the quality of the elas-
Figure 5.20: Variation of micro-architecture between specimens. In this figure we illustrate specimens from younger individuals, [a] specimen 169R (age: 37, \(\phi = 0.648\)) subset, [b] 169R pore partitioning, [c] 169R pore partitioning with network overlay indicating the connectivity of this specimen, [d] specimen 45R (age: 29, \(\phi = 0.596\)) subset, [e] 45R pore partitioning, [f] 45R network, [g] specimen 11R (age: 74, \(\phi = 0.817\)) subset, [h] 11R pore partitioning, [i] 11R network, [j] specimen A08R (age: 78, \(\phi = 0.802\)) subset, [k] A08R pore partitioning, [l] A08R network. Each volume represents \(100 \times 100 \times 50\) voxels or approximately \(5.7 \text{mm} \times 5.7 \text{mm} \times 2.8 \text{mm}\).
Figure 5.21: Illustration of intra-specimen difference in network parameters for 180R: [a] coordination number, [b] rod radius, [c] rod length, [d] junction radius.

tic simulation which will be addressed in the discussion. The rod lengths provide some indication of the separation of the trabecular bone junctions. All specimens show a broad distribution with means around 1200 µm. Junction radius distributions are shown in Figure 5.23 [d], for which the specimens show a broad range of junction radii with means between 161 ± 47 µm (9R) and 233 ± 85 µm (45R). This gives an indication of the local bone thickness in the trabecular junction regions.

5.3.3.4 Relationship of Age and Network Parameters

We observe in Figure 5.24 the network parameters plotted as a function of age. In panel [a] we show the mean coordination as a function of age. There is a general downward trend with age. A linear fit yielded the line \( y = 8.1479 - 0.022833x \), with \( r^2 = 0.55 \). This corresponds to a decrease in mean coordination of approximately 0.22 per decade (\( p < 0.01 \)). In Figure 5.24 [b] a linear fit of \( y = 1366 \mu m - 1.0431x \) is found with \( r^2 = 0.05 \), however no significant relationship is established between mean rod length and age. The mean rod radius as a function of age is shown in panel [c]. We observe a linear fit of \( y = 139.08 \mu m - 0.36957x, r^2 = 0.43 \) and with a decrease of 3.6 µm (\( p < 0.05 \)) in rod radius per decade. The mean junction radius is shown in [d]; we observe a linear fit of \( y = 233.81 \mu m - 0.64446x, r^2 = 0.37 \) and with a decrease
Figure 5.22: Network representation of the two specimens with differing porosity. The network representations retain the topology of the bone phase and illustrate the anisotropy within the femoral neck. [a,b] Transverse and coronal view of specimen 72R with a porosity 0.821, [c,d] Transverse and coronal view of specimen 15R with porosity 0.673.
Table 5.6: Summary of hip network parameters: coordination number, mean rod length, mean rod radius and mean junction radius. The standard deviations are included about the mean.
of 6.44 µm ($p < 0.05$) in pore radius per decade.

![Figure 5.24](image)

**Figure 5.24:** Mean network parameters as a function of age. We fitted a linear model to each dataset (blue line) and show 95% confidence intervals for linear regressions in red lines. [a] Mean coordination number, $< Z >$, with linear regression $y = 8.1479 - 0.022833x$, $r^2 = 0.55$ ($p < 0.01$), [b] mean rod length, with linear regression $y = 1366\mu m - 1.0431x$, $r^2 = 0.05$ (n.s.), [c] mean rod radius, with linear regression $y = 139.08\mu m - 0.36957x$, $r^2 = 0.43$ ($p < 0.05$), [d] mean junction radius, with linear regression $y = 233.81\mu m - 0.64446x$, $r^2 = 0.37$ ($p < 0.05$).

In Figure 5.25 we illustrate the standard deviation, $\sigma$, of network properties with age. We observe that with increasing age the standard deviation shows a decreasing trend for all parameters. The strongest trend is for coordination number with $r^2 = 0.56$ and a linear regression model of a decrease of 0.15$\sigma$ per decade ($p < 0.05$). The trabecular junction and rod radii have similarly modest trends with $r^2 = 0.49$, and $r^2 = 0.50$ and a decreases of 4.4$\sigma$ ($p < 0.01$) and 2.7$\sigma$ ($p < 0.01$) per decade respectively. There is no significant trend established for the standard deviation of rod length with age, giving an $r^2 = 0.20$ when fitted with a linear model and a decrease of 14.2$\sigma$ per decade.

### 5.3.4 Elasticity

An example of one of the calculated stiffness tensors $C_{\alpha\beta}$ relative to the Cartesian tomographic coordinate axes is shown below for specimen 180R. A full list of elasticity
Figure 5.25: Illustration of standard deviation, $\sigma$, of network parameters as a function of age. [a] Coordination number, $\sigma_Z$, with linear regression: $y = 4.5346 - 0.01537x$, $r^2 = 0.56$ ($p < 0.05$). [b] Rod radius, $\sigma_{Rr}$, $y = 61.122\mu m - 0.2669x$, $r^2 = 0.50$ ($p < 0.01$). [c] Rod length, $\sigma_{Lr}$, with linear regression $y = 711.71\mu m - 1.4193x$, $r^2 = 0.20$ (n.s.). [d] Junction radius, $\sigma_{Rj}$, with linear regression $y = 90.418\mu m - 0.43867x$, $r^2 = 0.49$ ($p < 0.01$). 95% confidence intervals for linear regression models are indicated by red lines.
tensors and orthotropic, transverse isotropic approximations for all 13 specimens is given in Appendix B.

\[
C_{\alpha\beta} =
\begin{bmatrix}
0.795 & 0.229 & 0.251 & -0.002 & -0.024 & -0.009 \\
0.237 & 0.828 & 0.288 & -0.004 & -0.105 & -0.020 \\
0.255 & 0.283 & 1.065 & -0.005 & -0.122 & -0.001 \\
-0.003 & -0.003 & -0.007 & 0.244 & -0.000 & -0.033 \\
-0.014 & -0.090 & -0.124 & -0.001 & 0.307 & -0.003 \\
-0.003 & -0.011 & 0.004 & -0.033 & -0.002 & 0.205
\end{bmatrix}.
\]

(5.18)

On first inspection we note that the stiffness tensor in Equation 5.18 has non-zero components in \(C_{25}, C_{35}\) and \(C_{52}, C_{53}\) that are also above the range of the numerical error (estimated from Equation 5.16 at a maximum of 6.6%). These components do not match any of the previously mentioned symmetry groups in this Cartesian axes. We use the optimisation procedure to find the coordinate system which transforms the tensor into best fitting orthotropic and transverse isotropic approximations. The rotated tensor is similar for both symmetry approximations. The rotated tensor that best fits an orthotropic approximation is given by:

\[
C_{\alpha\beta}^{ORT} =
\begin{bmatrix}
0.829 & 0.172 & 0.341 & -0.041 & 0.004 & -0.009 \\
0.172 & 0.768 & 0.217 & -0.014 & -0.001 & -0.008 \\
0.341 & 0.217 & 1.161 & 0.020 & -0.001 & 0.004 \\
-0.041 & -0.014 & 0.020 & 0.272 & -0.000 & 0.002 \\
0.004 & -0.001 & -0.001 & -0.000 & 0.261 & -0.008 \\
-0.009 & -0.008 & 0.004 & 0.002 & -0.008 & 0.187
\end{bmatrix}.
\]

(5.19)

where the orthotropic approximation, \(R_{\alpha\beta}^{ORT}\), is given by:

\[
R_{\alpha\beta}^{ORT} =
\begin{bmatrix}
0.829 & 0.172 & 0.341 & 0 & 0 & 0 \\
0.172 & 0.768 & 0.217 & 0 & 0 & 0 \\
0.341 & 0.217 & 1.161 & 0 & 0 & 0 \\
0 & 0 & 0 & 0.272 & 0 & 0 \\
0 & 0 & 0 & 0 & 0.261 & 0 \\
0 & 0 & 0 & 0 & 0 & 0.187
\end{bmatrix}.
\]

(5.20)
For the transverse isotropic symmetry, the rotated tensor that best fits is given by:

\[
C_{\alpha\beta}^{\text{TI}} =
\begin{bmatrix}
0.828 & 0.174 & 0.339 & 0.046 & 0.003 & 0.008 \\
0.174 & 0.770 & 0.215 & 0.014 & -0.002 & 0.008 \\
0.339 & 0.215 & 1.163 & -0.010 & -0.006 & -0.004 \\
0.046 & 0.014 & -0.010 & 0.270 & 0.001 & 0.000 \\
0.003 & -0.002 & -0.006 & 0.001 & 0.261 & 0.010 \\
0.008 & 0.008 & -0.004 & 0.000 & 0.010 & 0.188 \\
\end{bmatrix}.
\] (5.21)

And in this case the transverse isotropic approximation, \( R_{\alpha\beta}^{\text{TI}} \), is given by:

\[
R_{\alpha\beta}^{\text{TI}} =
\begin{bmatrix}
0.737 & 0.237 & 0.277 & 0 & 0 & 0 \\
0.237 & 0.737 & 0.277 & 0 & 0 & 0 \\
0.277 & 0.277 & 1.16 & 0 & 0 & 0 \\
0 & 0 & 0 & 0.266 & 0 & 0 \\
0 & 0 & 0 & 0 & 0.266 & 0 \\
0 & 0 & 0 & 0 & 0 & 0.250 \\
\end{bmatrix}.
\] (5.22)

By comparing \( C_{\alpha\beta}^{\text{ORT}} \) with \( C_{\alpha\beta}^{\text{TI}} \) we observe that the orthotropic and transverse isotropic symmetry axes are closely aligned. For this particular specimen the symmetry axis is given by the vector \( Z' = (-0.3756, -0.0049, 0.9268) \), which is relative to our original \( x, y, z \) cartesian coordinates. We show in Figure 5.26 a plane normal to the symmetry axis and therefore that the symmetry axis is aligned with the prominent trabecular struts traversing from the inferior cortex to the supero-medial acetabular surface. This is consistent with the work of Odgaard and Cowin, which showed a correlation between fabric and elasticity tensors [177]. The reduced compliance tensor \( S_{\alpha\beta} \) is found by taking the inverse of the rotated tensor (which best fits orthotropy) and scaling by the tissue modulus.

\[
S_{\alpha\beta}^{\text{ORT}} = (C_{\alpha\beta}^{\text{ORT}})^{-1} =
\begin{bmatrix}
26.01 & -3.75 & -7.02 & 4.28 & -0.36 & 1.16 \\
-3.75 & 25.79 & -3.73 & 1.01 & 0.19 & 1.05 \\
-7.02 & -3.73 & 18.60 & -2.64 & 0.13 & -0.89 \\
4.28 & 1.01 & -2.64 & 68.29 & -0.03 & -0.27 \\
-0.36 & 0.19 & 0.13 & -0.03 & 70.25 & 2.98 \\
1.16 & 1.05 & -0.89 & -0.27 & 2.98 & 98.22 \\
\end{bmatrix}.
\] (5.23)

The values of directional moduli and Poisson’s ratio are calculated equating components from the reduced compliance tensor with the matrix in Equation 5.7.

A summary of all elastic tensors is given in the Appendix [8].
Figure 5.26: Illustration of symmetry axes $X'$, $Y'$, $Z'$ in femoral neck specimen 180R. The tomo
graphic Cartesian $X$, $Y$, $Z$ axes are shown to illustrate the coordinate transformation. Axes
$X'$ and $Y'$ define a plane in which the elastic stiffnesses are similar (i.e. transverse isotropic
symmetry). The symmetry axis $Z'$ is normal to the plane and the elasticity tensor shows a
higher stiffness along this axis.
Elastic Properties of the Human Proximal Femur

<table>
<thead>
<tr>
<th>Label</th>
<th>% deviation from orthotropic symmetry, (D)</th>
<th>% deviation from transverse isotropic symmetry, (D)</th>
<th>% deviation of $C_{\alpha\beta}$ from transpose symmetry, (Err)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45R</td>
<td>8.6</td>
<td>13.2</td>
<td>5.7</td>
</tr>
<tr>
<td>15R</td>
<td>4.9</td>
<td>11.5</td>
<td>4.7</td>
</tr>
<tr>
<td>169R</td>
<td>5.8</td>
<td>10.5</td>
<td>6.6</td>
</tr>
<tr>
<td>A3R</td>
<td>5.9</td>
<td>12.8</td>
<td>1.9</td>
</tr>
<tr>
<td>72R</td>
<td>7.1</td>
<td>12.8</td>
<td>4.5</td>
</tr>
<tr>
<td>11R</td>
<td>6.4</td>
<td>12.5</td>
<td>2.6</td>
</tr>
<tr>
<td>19R</td>
<td>6.5</td>
<td>13.2</td>
<td>2.6</td>
</tr>
<tr>
<td>17R</td>
<td>5.3</td>
<td>9.9</td>
<td>1.9</td>
</tr>
<tr>
<td>180R</td>
<td>5.3</td>
<td>12.6</td>
<td>1.9</td>
</tr>
<tr>
<td>A08R</td>
<td>6.7</td>
<td>14.2</td>
<td>2.7</td>
</tr>
<tr>
<td>9R</td>
<td>6.1</td>
<td>10.6</td>
<td>2.2</td>
</tr>
<tr>
<td>10R</td>
<td>7.6</td>
<td>15.6</td>
<td>2.1</td>
</tr>
<tr>
<td>177R</td>
<td>6.6</td>
<td>13.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Artibone (256)</td>
<td>0.358</td>
<td>2.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Table 5.7: Summary of normalised distances away from orthotropic, transverse isotropic, and symmetrical tensor.

5.3.4.1 Orthotropy and Transverse Isotropy Estimation

A model dataset was created to validate our FEM methodology. We created a model hip of a solid elliptic cylinder with a solid spherical cap. This model was used for comparison of the actual hip elasticity tensor. Slices of the model hip dataset are shown in Figure 5.27[a-c].

![Figure 5.27](image)

**Figure 5.27:** [a] Model hip dataset X cross section, [b] Y cross section, [c] Z cross section. The different colours in the model dataset represent a different phase with different moduli. For the femoral neck we used input moduli: $K = 1.0$ and $G = 0.7$, and for the femoral head we used: $K = 0.5$ and $G = 0.3$.

We observe (Table 5.7) that the elastic stiffness tensor for the model hip dataset displays a higher symmetry than the real hip data. For example the model hip (denoted
as artibone (256)) has \( \approx 0.3\% \) deviation from orthotropic symmetry, and 2.1% deviation from transverse isotropic symmetry. The next closest hip dataset is Hip180R.2K with 3.8% and 8.4% deviations respectively. The maximum deviation from orthotropic symmetry occurs in specimen 45R at 8.6%, and maximum deviation from transverse isotropic occurs in specimen 10R at 15.6%.

5.3.4.2 Trends in Compliance Tensor Components

We plot the elastic tensor components for all 57.1\( \mu m \) voxel size tomograms together to observe qualitative trends in elastic properties. In Figure 5.28[a-c] we show the trend in Young’s modulus, shear modulus and Poisson’s ratio, respectively, as a function of porosity. The Young’s modulus values show a distinct decrease with increasing porosity. We observe an ordering of the Young’s modulus values such that \( E_3 > E_2 \approx E_1 \). In other words, we observe an anisotropy where the stiffness in the \( Z' \) symmetry axis, \( (E_3) \), is greater than the other two directions \( (X' \leftrightarrow E_1, Y' \leftrightarrow E_2) \) which are approximately equal. We show fitted power law equations using the form

\[
\frac{E}{E_0} = A_0(1 - \phi)^{A_1} \quad \text{and} \quad \frac{E}{E_0} = (1 - \phi)^{A_1}.
\]

Equations including a pre factor were observed to give a significantly better fit to the data. We observe that the exponent, \( A_1 \), for bone fraction varies between 1.122–1.351 with a prefactor much smaller than 1; i.e. \( A_0 \approx 0.2 \) for Young’s modulus and \( A_0 \approx 0.05 \) for shear modulus. Regressions with \( A_0 = 1 \) yielded an exponent, \( A_1 = 2.4 - -2.7 \) and a relatively poor fit; this is in contrast to many foam and porous media modulus-porosity regressions which have good fits with \( A_0 = 1 \)[66] (recall Figure 5.16[b]). We have chosen to compare porosity-modulus relationships with the data from Yang [260], because Yang gives comprehensive regressions for orthotropic elastic constants. Although the study of Yang is from much smaller trabecular bone specimens (8mm\( \times \)8mm\( \times \)8mm cubes) and is averaged over different anatomic sites including vertebra, calcaneus, tibia, distal and proximal femur, and humerus. The coordinate axes of Yang are ordered such that \( E_1 > E_2 > E_3 \) which differs from our convention. Yang’s regressions are shown for comparison by dashed lines; the agreement is poor.

We observe that the shear modulus components reflect a similar decreasing trend with porosity (see Figure 5.28[b]). The shear moduli values also display anisotropy with \( G_{23} \approx G_{31} > G_{12} \). Again, we observe that power law equations with a pre factor provide a better explanatory power compared to equations without a pre factor. We measure an exponent of between 1.077–1.230 with a pre factor and 3.74–4.11 without. Directional shear moduli estimations from Yang [260] (with an exponent of approximately 2) are plotted in dashed lines for comparison.

The directional Poisson’s ratios are shown in Figure 5.28[c]. We observe no rela-
tionship of the Poisson’s ratio with porosity, however we do note an ordering of the components such that \( \nu_{31} > \nu_{32} > \nu_{21} \). Fitted power law equations are shown along with comparisons from Yang [260].

The reduced compliance tensor components as a function of age are shown in Figure 5.29[a-c]. The results mirror the relationship with porosity; linear regression models were fitted to the data and we observe a trend of decreasing Young’s modulus and shear modulus with age, and little, if any, relationship between Poisson’s ratio and age.

We plot the Young’s modulus, shear modulus and Poisson’s ratio as a function of the mean bone network coordination, \( < Z > \), in Figure 5.30[a-c]. Young’s modulus and coordination show a positive correlation, which indicates a relationship between stiffness and topology. Shear moduli also display a positive correlation with coordination number, while no association is noted between Poisson’s ratio and coordination number. These data are in contradiction to those found by Kabel [111], where a possible increase in connectivity density was associated with a decrease in stiffness. Kabel’s study was slightly different in that specimens from a range of anatomical sites, and presumably a range of architectures, were used. The study also measured connectivity density, which is related, but not the same as mean coordination number.

In Table 5.8 we show tabulated values of the compliance tensor components. The Young’s modulus and shear modulus components are normalised by the tissue Young’s modulus, \( E_0 \). We observe that the largest component of the reduced Young’s modulus is \( E_3 \) for all specimens ranging from 0.034 in specimens 72R and A08R to 0.083 in 169R. This implies a stiffer structure in the \( Z’ \) direction in comparison to \( X’ \) and \( Y’ \) directions (See Figure 5.31). We observe that the compliance components relating the normal \( X’ \), \( Y’ \) stresses and strains, \( E_1 \) and \( E_2 \), vary from 0.021 (minimum \( E_1 \)) in 11R and 0.019 (minimum \( E_2 \)) in A08R to 0.057 (maximum \( E_1 \)) in 45R and 0.055 (maximum \( E_2 \)) in 45R. The anisotropy ratio shows little, if any, trend with age (See Figure 5.31). It is also remarkable that \( E_1 = E_2 \) across all specimens; the discrepancy between \( E_1 \) and \( E_2 \) being less than 0.004, or approximately 10%, for all specimens. The anisotropy varies between specimen and ratios of Young’s moduli are shown in Table 5.8. The ratio of \( E_3 \) to \( E_2 \) and \( E_3 \) to \( E_1 \) are 1.77 in 72R to 1.87 in 11R compared to \( E_3/E_2 = 1.35 \) and \( E_3/E_1 = 1.30 \) for specimen 15R.

We can compare these values with those shown in Brown et al. [25], which summarise experiments measuring apparent moduli in small cubes (5mm edge length) excised from the femoral head of a 19 year old man. Brown found moduli of 48,458psi (0.334 GPa) in the superior-inferior direction (equivalent to our \( Z’ \) direction), 32,430psi (0.224 GPa) in the anterior-posterior direction (equivalent to our \( X’ \) direction), and 36,367psi (0.251 GPa) in the medial-lateral direction (equivalent to our \( Y’ \) direction).
5.3 Results

Figure 5.28: Components of $S_{ijkl}$ compliance tensor as a function of porosity. Components are represented as [a] directional Young’s modulus, [b] shear modulus, and [c] Poisson’s ratio. The Young’s and shear moduli are normalised by the tissue modulus giving a reduced modulus. Comparisons are made with values from Yang [260].
Figure 5.29: Components of reduced $S_{ijkl}$ compliance tensor as a function of age. [a] Directional reduced Young’s modulus; $E_1 = 0.069217 - 0.00051415x$, $r^2 = 0.57$, $p < 0.01$. $E_2 = 0.064974 - 0.00044194x$, $r^2 = 0.44$, $p < 0.05$. $E_3 = 0.095977 - 0.00064602x$, $r^2 = 0.53$, $p < 0.01$, [b] reduced shear modulus; $G_{23} = 0.021457 - 0.00013108x$, $r^2 = 0.29$, $p < 0.1$. $G_{31} = 0.022886 - 0.0001411x$, $r^2 = 0.40$, $p < 0.05$. $G_{12} = 0.016203 - 0.00010614x$, $r^2 = 0.40$, $p < 0.05$, and [c] Poisson’s ratio; $\nu_{21} = 0.22255 - 0.000908x$, $r^2 = 0.22$, n.s. $\nu_{32} = 0.24983 + 0.00038166x$, $r^2 = 0.02$, n.s. The Young’s and shear moduli are normalised by the tissue modulus giving a reduced modulus.
Figure 5.30: Components of reduced $S_{ijkl}$ compliance tensor as a function of mean coordination, $<Z>$. Components are represented as directional [a] reduced Young’s modulus. $E_1 = -0.103803 + 0.020942x$, $r^2 = 0.90$, $p < 0.001$. $E_2 = -0.098112 + 0.020167x$, $r^2 = 0.87$, $p < 0.001$. $E_3 = -0.125354 + 0.026907x$, $r^2 = 0.87$, $p < 0.001$, [b] reduced shear modulus; $G_{23} = -0.031042 + 0.006604x$, $r^2 = 0.71$, $p < 0.001$. $G_{31} = -0.028965 + 0.006376x$, $r^2 = 0.75$, $p < 0.001$. $G_{12} = -0.0250939 + 0.0051643x$, $r^2 = 0.89$, $p < 0.001$ and [c] Poisson’s ratio; $\nu_{21} = 0.01727 + 0.02187x$, $r^2 = 0.15$, n.s. $\nu_{31} = 0.64699 - 0.04180x$, $r^2 = 0.10$, n.s. $\nu_{32} = 0.14447 + 0.01207x$, $r^2 = 0.02$, n.s. The Young’s and shear moduli are normalised by the tissue Young’s modulus giving reduced moduli.
Figure 5.31: Relationship between ratios of elastic moduli and age. Black circles indicate the ratio of $E_3/E_1$, while red squares indicate the ratio $E_3/E_2$. There is no evidence of any significant trend in anisotropy with age.

When our reduced modulus values are multiplied by the tissue modulus, they tend to be much higher than Brown’s data, i.e. $E_1 = 0.62\text{GPa}$ to $E_3 = 1.54\text{GPa}$ versus Brown data $0.224\text{GPa}$ to $0.334\text{GPa}$. Discrepancies between the studies may be explained by the assumption of a homogeneous tissue modulus in FEM or potential underestimation of Young’s modulus associated with experimental compressive testing of trabecular bone [178][121].

5.4 Discussion

In this section we outline some of the limitations and errors associated with our study.

5.4.1 Cross Sectional Studies

A limitation of our study is that the specimens contained in this paper are a cross sectional sample of the population. We can not exclude the possibility that porosity-age, elasticity-age, and topology-age relationships are influenced by temporal trends in the population [43]. For example factors such as nutrition, smoking and exercise habits may vary with time and have some effect on the results, particularly with a low sample size. Longitudinal studies have shown decreases in bone mineral density with age [108], though longitudinal studies in micro-architectue, elasticity and topology
Table 5.8: Components of reduced $S_{ijkl}$ compliance tensor represented as directional Young’s moduli, ratio of Young’s moduli, shear moduli, and Poisson’s ratio. Moduli are normalised by the tissue modulus, $E_0$. 

<table>
<thead>
<tr>
<th>Label</th>
<th>$\phi$</th>
<th>$E_1$</th>
<th>$E_2$</th>
<th>$E_3$</th>
<th>$E_3/E_1$</th>
<th>$E_2/E_1$</th>
<th>$\nu_{21}$</th>
<th>$\nu_{31}$</th>
<th>$\nu_{32}$</th>
<th>$G_{23}$</th>
<th>$G_{31}$</th>
<th>$G_{12}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>45R</td>
<td>0.596</td>
<td>0.0574</td>
<td>0.0548</td>
<td>0.0768</td>
<td>1.34</td>
<td>1.40</td>
<td>0.200</td>
<td>0.291</td>
<td>0.210</td>
<td>0.0162</td>
<td>0.0176</td>
<td>0.0139</td>
</tr>
<tr>
<td>15R</td>
<td>0.673</td>
<td>0.0486</td>
<td>0.0465</td>
<td>0.0632</td>
<td>1.30</td>
<td>1.36</td>
<td>0.196</td>
<td>0.279</td>
<td>0.209</td>
<td>0.0159</td>
<td>0.0171</td>
<td>0.0112</td>
</tr>
<tr>
<td>169R</td>
<td>0.648</td>
<td>0.0518</td>
<td>0.0510</td>
<td>0.0840</td>
<td>1.62</td>
<td>1.65</td>
<td>0.170</td>
<td>0.363</td>
<td>0.289</td>
<td>0.0203</td>
<td>0.0204</td>
<td>0.0133</td>
</tr>
<tr>
<td>A3R</td>
<td>0.744</td>
<td>0.0325</td>
<td>0.0347</td>
<td>0.0547</td>
<td>1.69</td>
<td>1.58</td>
<td>0.140</td>
<td>0.438</td>
<td>0.194</td>
<td>0.0131</td>
<td>0.0139</td>
<td>0.0092</td>
</tr>
<tr>
<td>72R</td>
<td>0.821</td>
<td>0.0220</td>
<td>0.0193</td>
<td>0.0342</td>
<td>1.55</td>
<td>1.77</td>
<td>0.181</td>
<td>0.199</td>
<td>0.371</td>
<td>0.0053</td>
<td>0.0075</td>
<td>0.0050</td>
</tr>
<tr>
<td>11R</td>
<td>0.817</td>
<td>0.0209</td>
<td>0.0221</td>
<td>0.0393</td>
<td>1.87</td>
<td>1.77</td>
<td>0.187</td>
<td>0.402</td>
<td>0.201</td>
<td>0.0085</td>
<td>0.0086</td>
<td>0.0052</td>
</tr>
<tr>
<td>19R</td>
<td>0.784</td>
<td>0.0226</td>
<td>0.0238</td>
<td>0.0391</td>
<td>1.73</td>
<td>1.64</td>
<td>0.149</td>
<td>0.426</td>
<td>0.179</td>
<td>0.0090</td>
<td>0.0095</td>
<td>0.0061</td>
</tr>
<tr>
<td>17R</td>
<td>0.686</td>
<td>0.0475</td>
<td>0.0515</td>
<td>0.0720</td>
<td>1.52</td>
<td>1.40</td>
<td>0.203</td>
<td>0.358</td>
<td>0.229</td>
<td>0.0186</td>
<td>0.0171</td>
<td>0.0134</td>
</tr>
<tr>
<td>180R</td>
<td>0.714</td>
<td>0.0384</td>
<td>0.0388</td>
<td>0.0538</td>
<td>1.40</td>
<td>1.39</td>
<td>0.145</td>
<td>0.377</td>
<td>0.201</td>
<td>0.0146</td>
<td>0.0142</td>
<td>0.0102</td>
</tr>
<tr>
<td>108R</td>
<td>0.802</td>
<td>0.0223</td>
<td>0.0220</td>
<td>0.0341</td>
<td>1.53</td>
<td>1.55</td>
<td>0.146</td>
<td>0.425</td>
<td>0.177</td>
<td>0.0079</td>
<td>0.0085</td>
<td>0.0062</td>
</tr>
<tr>
<td>9R</td>
<td>0.790</td>
<td>0.0235</td>
<td>0.0253</td>
<td>0.0381</td>
<td>1.62</td>
<td>1.51</td>
<td>0.175</td>
<td>0.366</td>
<td>0.234</td>
<td>0.0091</td>
<td>0.0096</td>
<td>0.0067</td>
</tr>
<tr>
<td>10R</td>
<td>0.731</td>
<td>0.0355</td>
<td>0.0398</td>
<td>0.0546</td>
<td>1.54</td>
<td>1.37</td>
<td>0.092</td>
<td>0.489</td>
<td>0.216</td>
<td>0.0148</td>
<td>0.0166</td>
<td>0.0096</td>
</tr>
<tr>
<td>177R</td>
<td>0.742</td>
<td>0.0336</td>
<td>0.0341</td>
<td>0.0471</td>
<td>1.40</td>
<td>1.38</td>
<td>0.126</td>
<td>0.393</td>
<td>0.208</td>
<td>0.0127</td>
<td>0.0126</td>
<td>0.0092</td>
</tr>
<tr>
<td>art256</td>
<td>n/a</td>
<td>0.0361</td>
<td>0.0379</td>
<td>0.0375</td>
<td>1.04</td>
<td>0.99</td>
<td>0.137</td>
<td>0.134</td>
<td>0.130</td>
<td>0.0147</td>
<td>0.0144</td>
<td>0.0155</td>
</tr>
</tbody>
</table>
are relatively few in humans. For human femoral bone such a longitudinal study is prohibitive due to radiation dose or resolution inadequacies of in vivo imaging.

Figure 5.32: Illustration of coarse graining procedure for specimen 180R: [a] voxel size of 28.39 $\mu$m, [b] voxel size of 56.78 $\mu$m, [c] voxel size of 113.57 $\mu$m, [d] voxel size of 227.14 $\mu$m

5.4.2 Resolution Scaling Relationships

To investigate the scaling effect of discretisation on elastic properties, we compared the components of the elasticity tensor versus the voxel size for one specimen, 180R, using a coarse-graininging procedure. The coarse graining procedure interpolates a segmented bone phase by averaging a (factor)$^3$ region of voxels. The average is rounded to a binary number, 0 or 1, and if the average is exactly 0.5, the interpolated point is assigned randomly to 0 or 1. We repeat the coarse graining on a 28.5 $\mu$m voxel size image (denoted 180R_2K) with coarse graining factors 2, 4, and 8 to
generate a range of degraded discretisations. The resulting datasets and their voxels sizes are respectively: 180R_2K (28.5 \( \mu \)m), 180R_2K_222 (57.1 \( \mu \)m), 180R_2K_444 (114.2 \( \mu \)m), 180R_2K_888 (228.4 \( \mu \)m). A representative slice from each dataset is shown in Figure 5.32.

We also investigate the disparity in network properties between the original 28.5 \( \mu \)m voxel size image and the coarse grained 57.1 \( \mu \)m voxel size image. This gives insight into the change in topology with discretisation.

5.4.2.1 Resolution Effects on Topology

There are different types of scaling relationships in a 3D imaging and finite element study, each of which introduces error into our analysis. First, errors associated with the experimental acquisition and reconstruction may result in noise or reduced contrast between phases and effectively reduce the resolution of the imaging system and the accuracy of the segmentation. These are systematic errors that affect all experiments and are difficult to quantify. Although these errors will affect the quantification of absolute elasticity values, trends noted over the entire dataset should be valid because of the systematic nature of the error.

Second, spatial discretisation of the image features also influence the numerical result [169, 185, 133, 35]. If one changes the voxel size so that the image features are below the resolution, then one could expect to alter the properties of the image. Even at voxel sizes below the image feature size, there is some influence on physical properties. Garboczi and Meille [161] found a linear relationship between Young’s modulus and voxel size for a random fiber dataset. The linear fit regression can be extrapolated back to infinite resolution (voxel size approaches limit of 0) to determine the scaling relation due to resolution.

To test the effects of discretisation on topology we derived artificially degraded images from a master image (Hip180R_2K with 28.5\( \mu \)m voxel size) assuming that the master image contains a fully resolved representation of the structure under investigation. The coarsened images are shown in Figure 5.32. The network parameters for the 28.5\( \mu \)m and 57.1\( \mu \)m voxel size images are shown in Figure 5.33. The mean coordination number for the 57.1\( \mu \)m voxel size image has a peak at coordination number of 4, while the lower voxel size has a corresponding shift in peak coordination to 6. This indicates that some 4-connected trabeculae may be shifted to 6-connected system with increased resolution. We can not differentiate whether this apparent shift to higher connected trabeculae results from resolving more fenestrations in the trabeculae, or from resolving more trabecular struts as these are topologically equivalent [126].

In Figure 5.33 [c] we show the change in rod radius with increased voxel size.
Mean rod radius increases from 79 µm to 87 µm with increasing voxel size. An explanation is the possible disconnection of rod with radii below 57.1 µm for the higher voxel size image. Mean rod length (Figure 5.33[b]) increases with voxel size from 828 µm to 959 µm, indicating that at higher resolutions more connections are resolved, and with more connections, there is an associated reduction in the mean distance between junctions. Little change in junction radius is noted with voxel size (Figure 5.33[d]).

One must consider an important caveat: analysis on network statistics assume that the structural features are greater than the voxel size and that one can measure the parameters with accuracy. Referring to Table 5.6 we note that the mean rod radius for 57.1 µm voxel size specimens is between 97.6 µm and 132.6 µm. If one considers half the voxel size as the maximum error in any individual radius measurement, then the relative error can be almost 25% for a radius size of 100 µm, or around 12.5% for features of 200 µm radius. These errors are for individual measurements on junctions and rods, not their mean values. The network rod sizes are critical to an accurate portrayal of the structure because of their role as the minimal feature size required to resolve connections. Generally, it is accepted that the rod dimension to voxel size ratio must be greater than 4–5 [70, 175].

Figure 5.33: Comparison of network parameters for coarsening process: [a] coordination number distribution, [b] rod length distribution, [c] rod radius distribution, [d] junction radius distribution.
5.4.2.2 Resolution Effects on Elastic Properties

Keaveny and Hollister [70, 175] have shown that a trabecular size four to five times the voxel size is the minimum requirement for quantitative elastic property measurements. To investigate this, we measured trends in elastic modulus with discretisation from data generated from a coarsening procedure. Our results show a reduction in Young’s and shear moduli with increasing voxel size (See Figure 5.34). The shape of the scaling relationships are similar for both Young’s and shear moduli: an initial sharp decrease between 28.5 $\mu$m and 114 $\mu$m and then flattening out to 228 $\mu$m. The relative values of $E_i/E_0$ and $G_i/E_0$ are consistent across different voxel sizes. We note that the scaling relationship does not follow a linear profile as reported in Meille [161]. We suspect that the structural origins of this increasing stiffness are increases in coordination and are independent of porosity since porosity remains relatively unchanged by coarsening. The shift of some nodes from 6-connected to 4-connected with an increase of voxel size from 28.5 to 57.1 $\mu$m cause a degradation in elastic stiffness. This parallels the work of Kinney [126], who showed that an overall loss in connectivity with an erosion / dilation procedure is associated with a decrease in stiffness. Kinney uses a topological measure of connectivity based on the Euler characteristic which is directly related to the mean coordination number [54].

Observations of resolution effects on elastic properties by Ulrich [243] parallel our data. Ulrich investigated the effects on elastic stiffness by coarsening a 28 $\mu$m voxel size trabecular bone specimen. A reduction in effective Young’s modulus was observed with increasing voxel size. It was suggested, though not definitively shown, that the coarsening procedure caused a loss of connectivity on the trabecular network and thus reduced stiffness. The reduction in stiffness from 28 $\mu$m-168 $\mu$m voxel size was reported as high as 86% for some specimens. This parallels the trend observed in our data. For example in specimen 180R we see a comparable reduction in the elasticity tensor components. Directional moduli components $E_1$, $E_2$, $E_3$ are shown in Figure 5.34[a] as increasing from 0.017, 0.02 and 0.03 at 228 $\mu$m resolution to 0.067, 0.067, 0.081 at 28 $\mu$m resolution. The same trend is repeated for the shear components (Figure 5.34[b]), though not for directional Poisson’s ratio (Figure 5.34[c]). Ulrich shows a scaling relationship that plateaus at voxel sizes less than 56 $\mu$m. It is not clear whether the scaling relationship in our data would plateau with a smaller voxel size. We infer that the elastic properties are dependent on the image resolution even up to 28 microns, and therefore to gain quantitative values of modulus one may require resolutions better than 28 microns. To resolve FN specimens up to 60mm in size at resolutions better than 28 $\mu$m would conceivably require $3000^3$ and $4000^3$ voxel images, which in turn would require increases in computing capacity. For this work, we can
<table>
<thead>
<tr>
<th>Label</th>
<th>$\phi$</th>
<th>$E_1$</th>
<th>$E_2$</th>
<th>$E_3$</th>
<th>$\nu_{21}$</th>
<th>$\nu_{31}$</th>
<th>$\nu_{32}$</th>
<th>$G_{23}$</th>
<th>$G_{31}$</th>
<th>$G_{12}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>180R_2K</td>
<td>0.717</td>
<td>0.0670</td>
<td>0.0672</td>
<td>0.0812</td>
<td>0.178</td>
<td>0.367</td>
<td>0.2532</td>
<td>0.0250</td>
<td>0.0262</td>
<td>0.0208</td>
</tr>
<tr>
<td>180R_2K_222</td>
<td>0.701</td>
<td>0.0472</td>
<td>0.0495</td>
<td>0.0675</td>
<td>0.171</td>
<td>0.419</td>
<td>0.1988</td>
<td>0.0191</td>
<td>0.0207</td>
<td>0.0153</td>
</tr>
<tr>
<td>180R_2K_444</td>
<td>0.719</td>
<td>0.0257</td>
<td>0.0272</td>
<td>0.0505</td>
<td>0.161</td>
<td>0.464</td>
<td>0.1323</td>
<td>0.0122</td>
<td>0.0138</td>
<td>0.0097</td>
</tr>
<tr>
<td>180R_2K_888</td>
<td>0.729</td>
<td>0.0174</td>
<td>0.0200</td>
<td>0.0305</td>
<td>0.134</td>
<td>0.399</td>
<td>0.0252</td>
<td>0.0088</td>
<td>0.0105</td>
<td>0.0075</td>
</tr>
</tbody>
</table>

Table 5.9: Components of $S_{ijkl}$ compliance tensor for specimens coarsened from 180R_2K dataset. Components are directional Young’s modulus, shear modulus, and Poisson’s ratio and are normalised by the tissue modulus.
Figure 5.34: Components of $S_{ijkl}$ compliance tensor as a function of voxel size. Components are represented as directional Young’s moduli, shear moduli, and Poisson’s ratios. The Young’s and shear moduli are normalised by the tissue modulus giving a reduced modulus. All data are derived from the same coarsened specimen - 180R.2K.
make relative comparisons between specimens at the same voxel size and acquisition parameters, but we make the qualification that estimations of elastic moduli may not be quantitative representations of real physical values. Indications of trends in elastic moduli suggest that reported values may be a lower bound.

We examined the effect of scaling on elastic properties for another system - a 22\(\mu\)m voxel size image of trabecular bone from an equine vertebra. The coarsened images are shown in Figure 5.35[a-c]. In comparison to our human hip data, we observe that the elastic properties are influenced very little by the voxel size (See Figure 5.36). From this data, we can infer that the resolution of 22\(\mu\)m is sufficient for the equine bone system, but this may not the case for the 28\(\mu\)m voxel size image of the human proximal femur. One must have an appreciation for the critical sized features of the system and with knowledge of the limitations of the imaging system, acquisition and image processing, make a decision about appropriate voxel size.

![Figure 5.35: Illustration of equine trabecular bone specimen coarsening procedure. [a] 22\(\mu\)m voxel size image, [b] 44\(\mu\)m voxel size image, [c] 88\(\mu\)m voxel size image.](image)

### 5.4.3 Elastic Property Assumption

The finite element method in this study assumes a single tissue modulus and Poisson’s ratio. However, bone is known to have variation in mineral density and stiffness both inter and intra-specimen [22]. Data from nanoindentation studies have begun to elucidate the spatial distribution of inhomogeneities in elastic modulus at the tissue level. Nanoindentation allows one to measure modulus upon exposed surfaces, and relationships of modulus to the local density can be established [56]. However, this technique suffers from problems of anisotropy and alignment of the bone lamellae and underlying collagen phase. Typically, finite element studies assume a homogeneous and isotropic modulus at the tissue level. Though this assumption has the limitation of making absolute quantitative estimates of elastic constants very difficult [248], it allows measurement of elastic properties that are independent of tissue level properties and are due purely to the micro-structure. Jaasma [103] investigated the effects of
Figure 5.36: Components of $S_{ijkl}$ compliance tensor as a function of voxel size for equine trabecular bone specimen. Components are represented as directional Young’s moduli, shear moduli, and Poisson’s ratios. The Young’s and shear moduli are normalised by the tissue modulus giving a reduced modulus. All data are derived from the same coarsened specimen.
intra-specimen variation of elastic modulus on apparent level properties. It was concluded that if the intra-specimen variations are large, then finite element estimations of linear elastic properties may differ significantly from those assuming homogeneous tissue modulus. This is consistent with a study by Kabel [112] that demonstrated the assumption of isotropic and homogeneous tissue properties in a numerical model can generate reliable estimates of apparent level properties.

5.5 Concluding Remarks

In this section we summarise conclusions from this chapter. First, we mention the estimations of bone symmetry and anisotropy, the relationship of age and porosity to elastic modulus, and the relationship of topology to elastic modulus. Last, we discuss measurements of local stress and strain fields for a given loading pattern.

5.5.1 Estimations of Bone Symmetry

It has previously been reported that trabecular bone systems closely approximate orthotropic symmetry to within an error variously reported as between 1-5% [260, 252] (measured as percentage deviance from symmetry using an objective function). These results were reported for (10mm)$^3$ volumes of bone [252]. However, this approximation has never been tested at the whole hip scale (> 50mm). In this study we found real hip data also exhibits approximate orthotropic symmetry. It deviates by a maximum of 8.6% from orthotropic and 15.6% from transverse isotropic. Note that the % deviation measure in this study is not the same as used by Rietbergen [252] - however use of the % deviation measure allows for an appreciation of the symmetry. This compares to the model hip data which shows markedly higher symmetry and indicates a greater heterogeneity in the real data. We conclude that the anisotropy and symmetry of the elastic tensor for real hip data arises because of the strong alignment and orientation of the internal trabeculae.

5.5.2 Elastic Anisotropy

In Figure 5.31 we show the anisotropy in directional Young’s modulus. The ratio of $Z'$ direction to $X'$ direction stiffness ($E_3/E_1$) and ratio of $Z'$ direction to $Y'$ direction stiffness ($E_3/E_2$) range from approximately 1.3 to 1.8. The trends in the anisotropy ratios tend to correlate with visual differences in structure; of the three younger specimens, 169R exhibits a large ratio and visually the clearest anisotropy (see Figure 5.11). The anisotropies observed within our data are consistent with the lower range of anisotropies reported from FEM studies on small trabecular subsets by Rietbergen [248].
where the ratio of Young’s moduli ranged from 1.3–8. Our data are less than those reported by Ladd [137] and Ashman [8], where the ratio of Young’s moduli ranged from between 2–5.

5.5.3 The Relationship of Porosity to Elastic Properties

Many authors have published models relating the elastic moduli of trabecular bone to its porosity (or inverse, bone phase fraction). We summarise some of these relationships underpinning different models in Table 5.2. Generally, power law models of the form $E = A_0(1 - \phi)^{A_1}$ are reported [44].

5.5.3.1 Whole Hip Versus Femoral Head Subset

To date most modulus-porosity relationships reported for the femoral head have been based on the measurement of a subset of the trabeculae from within the femoral head. Some of these correlations are summarised in Table 5.2 and Figure 5.2. In this chapter we have analysed the modulus-porosity relationship for the whole hip; comparison of this modulus-porosity data to one set of reported data on trabecular subsets (Yang [260]) are shown in Figure 5.28[a,b]. The data found for the full hip analysis gives a lower modulus than the conventional empirical data.

To test for differences in the modulus-porosity relationship based on the whole bone versus a large subset of trabeculae we extracted a $200^3$ voxel (approximately $11\text{mm} \times 11\text{mm} \times 11\text{mm}$) subset taken from the centre of the femoral head of each specimen. The porosity of each subset was generally similar to the whole hip counterpart. The prediction of elastic moduli for the 13 subsets versus the whole hip data is shown in Figure 5.37. The moduli of each subset is approximately 2-3 times larger compared to moduli of the whole hip counterpart. Larger variations are evident at lower porosities. In Figure 5.38 we compare these two sets of data to the conventional empirical fits of Yang [260]; we observe that the elastic constants from these smaller subsets give a good match to the regression models to Yang. There are distinctly different modulus-porosity relationships for whole hip compared to smaller trabecular subsets.

In conclusion, we can differentiate between whole hip and trabecular subsets when considering modulus-porosity relationships and emphasise the need to consider scale, and heterogeneity when comparing such relationships. This has implications for the relevance of small trabecular measurements on estimations of whole hip strength.
Figure 5.37: Components of $S_{ijkl}$ reduced compliance tensor as a function of porosity for whole hip (empty symbols) and trabecular subsets (filled symbols). Moduli are represented as directional Young’s moduli [a], and shear moduli [b]. We can observe distinct modulus-porosity relationships between the whole hip scale and femoral head trabecular subsets.
§5.5 Concluding Remarks

Figure 5.38: Components of $S_{ijkl}$ reduced compliance tensor as a function of porosity for whole hip (empty symbols) and trabecular subsets (filled symbols). Moduli are represented as directional Young’s moduli [a], and shear moduli [b]. We illustrate non linear regressions of the form $y = A_0(1 - \phi)^{A_1}$ and the resulting $r^2$ coefficients for whole hip and the trabecular subset data. We can observe distinct modulus-porosity relationships between the whole hip scale and femoral head trabecular subsets; the smaller, less heterogeneous subsets better fit models from Yang [250].
5.5.3.2 Comparison with Empirical Models

The modulus-porosity relationship of the entire hip does not match empirical relationships derived from small trabecular subsets and standard cellular media. These empirical models are characterised by the standard form \( E/E_0 = (1 - \phi)^A \); \( A \approx 2 \). Fits derived for the femoral head trabecular subsets, shown in Figure 5.38, do fit the standard cellular solids theory of \( E/E_0 = (1 - \phi)^A \). We find a better fit for the whole hip scale data by using the more general equation of \( E/E_0 = A_0(1 - \phi)^A \).

5.5.4 Porosity-Age Relationship

The porosity-age relationship derived in this work (see Figure 5.13) are consistent with the works of Ding [48], McCalden [160] and Muller [231]. Ding shows a decrease in bone volume fraction with age. We observe the analogous increase in porosity with age. McCalden reported a linear regression relating the apparent density to age. By assuming the apparent density of bone, \( \rho = 1800 \text{kg.m}^{-3}\phi_{\text{bone}} \) (from [248]) into McCalden’s linear model we obtain \( \phi_{\text{bone}} = 0.32 - 0.0016x \) with \( r^2 = 0.51 \), i.e. a linear decrease in bone volume fraction of 0.016 per decade. Our data (Figure 5.13) indicates a analogous linear increase in porosity of 0.028 per decade. Stauber and Muller [231] show a decrease in bone volume fraction at age around age 70 for the femoral head. This difference in bone volume fraction between young and old is consistent with our linear decrease, however we can not compare the exact profile of this decrease due to a lack of data between 40 and 70 years.

5.5.5 The Relationship of Topology to Elastic Properties

Various studies have suggested a link between osteoporosis and perforations of trabecular bone leading to reduced bone quality and fracture likelihood [184, 167]. A study by Bell [14] demonstrated that strength decreased disproportionately with bone mass and hypothesised that this could explain by the loss of connections between trabeculae. It was reasoned that bone resorption can perforate trabecular struts, and lead to a loss of connectivity. We observe a trend of increasing elastic Young’s and shear moduli with mean connectivity (Figure 5.30). However observations by Kinney and Kabel [125, 111] have questioned the utility of connectivity in assessing bone elastic properties. We also note, like Kabel [111], that mean connectivity correlates to porosity (Figure 5.39, \( r^2 = 0.87 \), \( p < 0.001 \)). However, our coarse grained data corroborates the hypothesis that coordination (or connectivity) is associated with stiffness independent of bone volume fraction.
5.5.6 Local Fields as Predictors of Local Fragility

The notion of Wolff’s Law and that optimally adapted bone will equally distribute stress and strain over the entire structure equally was tested by Rietbergen and van der Linden [251, 246]. By estimating the local stress distributions Rietbergen showed that bone is well adapted for a range of loading conditions, rather than a single loading direction. One commonly held belief of the mechanism of FN fracture is that under normal standing conditions the inferior FN is in compression, while the superior FN is under tension (or relatively reduced compression), akin to a cantilever [152]. A fracture may occur if, during a fall, the superior FN becomes loaded in compression and the inferior neck is under tension. With information on realistic fall trajectories and loading directions, one can test the plausibility of the classical idea of hip fracture. Here we demonstrate the use of local strain fields as a tool to help understand these questions.

In Figure 5.40[a] we show the superposition of normal strains in superior-inferior and medial-lateral directions (y and z directions). We observe that most regions are in compression (red) with higher strains focused on the trabecular band running from the acetabular surface to the inferior cortex. In panel [b] we show the superposition of normal strains in the same directions, however this time the medial-lateral strain is set to negative (-y and z directions), and we observe tensile and compressive regions in the FH and FN. The regions of tension appear to be oriented in the y direction, while compressive regions are aligned in the z direction.

Resolving the 3D architecture of the trabecular and cortical bone systems allows one to study the relationship between apparent level loading and the local stresses and strains. Muller estimated that local trabecular strains can be up to a multiple...
5-8 times greater than the apparent level [168]. Keyak [123] used a local von Mises stress criteria to predict fracture load in finite element models of the proximal femur. In a recent paper Eswaran et al [52] suggested that regions of high local strain can give insight to regions of local fragility, although this has yet to be correlated with experimental studies at the scale of individual trabeculae.

Figure 5.40: Cross sections of local strain fields. We calculate the trace of the strain tensor (change in volume) at each point within the bone phase for 3 loading cases ($\epsilon_1, \epsilon_2, \epsilon_3$). The colour illustrates whether the local region is in compression or tension and the colour intensity reflects the magnitude of the strain. Red represents bone under compression, with brighter regions of higher magnitude. Regions of tensile strain are shown in blue, and regions of close to zero strain are shown in black. [a] Loading in positive y and z directions; $\epsilon = 0.5\epsilon_2 + 0.5\epsilon_3$, [b] loading in negative y and positive z directions; $\epsilon = -0.5\epsilon_2 + 0.5\epsilon_3$. 
Conclusion and Outlook

In this thesis we have demonstrated the concept of a virtual material laboratory to advance the understanding of problems related to porous biomaterials. At the crux of these problems are correlations between structure - shape and topology - and physical properties such as transport and mechanics.

6.1 Part I: Scaffold Architecture and Properties

In Part I we studied the relationship between orthopaedic tissue engineering scaffolds, their pore structure, topology, elastic and transport properties and correlations with bone ingrowth. We demonstrated a 3-phase segmentation algorithm to enable quantitative phase separation of pore, bone and scaffold regions. This overcame unwanted artifacts associated with more rudimentary segmentation routines.

In the first chapter of Part I - Scaffold Morphology - we described a method to accurately phase separate pore, scaffold and bone phases to allow quantitative measurements directly on the images. We derived local and non-local measures of pore size and illustrated how these correlate with bone ingrowth at the voxel scale. We also qualitatively described differences in pore interconnectivity between scaffolds and the effect on bone ingrowth. We noted a stronger correlation with bone ingrowth using accessible pore radius over local pore radius. This is because the accessible pore radius captures details of the local pore size and pore interconnectivity.

In the second chapter of Part I - Simulation of Scaffold Physical Properties - we performed a comprehensive study of the pore scale features of a range of different scaffold architectures. We derived a pore partitioning scheme to measure pore scale statistics of pore size and interconnectivity and found a strong quantitative and visual correlation between accessible pore size and bone ingrowth. We found that mechanical and transport properties of the different architectures were consistent with the standard cellular solids theory: \((E/E_0 = (\rho/\rho_s)^n)\). The addition of the bone phase increased the effective stiffness by between 2-30%. Hydraulic conductance and diffu-
sive properties were calculated; results were consistent with the concept of a threshold conductance for bone ingrowth. Simple simulations of local flow velocity and local shear stress showed no correlation to \textit{in vivo} bone ingrowth patterns. These results demonstrate the ability for 3D imaging and analysis to assist in the design of tissue engineered implants.

A comprehensive and well controlled study is needed to identify the particular 3D scaffold architectures that enhance bone ingrowth. We suggest that extension of this work can be focused towards building a database of scaffold types and comparative performance evaluations. The work described in Chapters 2 and 3 has been limited to a set of seven specimens of two different architectural types. The hardware and software exist to extend this study to significantly more specimens; a broader range of architectures and time points. Extensions of this work may also consider combining information from multiple imaging techniques; for example, combining histological sections with micro-CT data using image registration. We also acknowledge the potential of an \textit{in vivo} time series experiment to provide longitudinal data on the progression of bone ingrowth and scaffold resorption.

Another area where this research can be extended is towards more complex diffusive and reactive flow transport modelling. The means by which nutrients are delivered to the centre of the biomaterial are highly complex and \textit{in vivo} processes difficult to model. One may be able to test a mixed diffusion / flow model with experimental observations of tissue growth in a bioreactor to correlate local transport properties with areas of tissue growth. One could also modify the basic transport equations to develop a reactive flow where species are dissolved or deposited within the system. In the context of tissue engineering scaffolds, as bone ingrowth occurs, the scaffold material will ideally follow a concomitant resorption process. One may wish to develop a reactive flow scheme to predict the dissolution of the scaffold. Changes in structure, transport, and mechanical properties could be investigated as a function of the predicted dissolution. As with the diffusion / flow equations, one may choose to compare the model against a carefully controlled dissolution experiment.

6.2 Part II: Femoral Neck Architecture and Properties

In Part II we examined the structure and properties of the human proximal femur. In the first chapter of Part II we focused on the cross sectional properties of the femoral neck and estimations of strength based on those properties. We have demonstrated that the cross sectional shape of the femoral neck varies with the size of the bone. Assumptions made by standard Hip Structural Analysis assumptions can have a maximum error of 30% when estimating vBMD using circle or square cross sections, and
that the error changes with bone size. This has implications for current bone fragility estimation. We demonstrate an improvement in cross sectional parameters of strength using ellipse models of the femoral neck cross section.

In the latter chapter - Elastic Properties of the Human Proximal Femur - a method to extract the topology of the trabecular bone network, quantify statistics of this network and correlate to age and elastic properties was developed. We qualitatively observed significant variation in trabecular bone structure and porosity both within, and between specimens. Quantitative trends were observed relating the mean coordination and trabecular junction radius to age.

The full elastic stiffness tensor of the whole human femoral head and femoral neck was estimated using a finite element method. The results were consistent with previously described elastic symmetry classes of trabecular bone systems. Power law correlations of moduli-porosity were in general consistent with trends noted by other authors, however differences in modulus-porosity relationships from the trabecular scale to the whole hip were noted. Moduli predictions for the whole hip were 2-3 times smaller than for the femoral head trabecular subsets. Empirical relationships for trabecular bone of the type \( E/E_0 = (\rho/\rho_s)^{A_1} \) are consistent with data for trabecular subsets within the femoral head, however we note that these empirical relationships do not match data at the whole hip scale; a more general relationship of the type \( E/E_0 = A_0(\rho/\rho_s)^{A_1} \) was required. We noted significant decreases in Young’s and shear moduli with age and increases in moduli with mean coordination.

We studied the scaling effect of elastic constants with voxel size and noted the need for voxel sizes below 28 \( \mu \)m for quantitative estimation of elastic properties. However, this is not a universal rule and the required resolution may vary depending on the bone under investigation and the imaging system. While other studies have presented scaling relationships for elastic and morphological measures, and suggested voxel sizes below 100 microns for accurate results, our results suggest even higher resolutions are needed. We have developed and applied a comprehensive 3D image analysis toolkit to study the strength of the human proximal femur. These results demonstrate the importance of considering length scale, image quality and resolution and 3D bone micro-architecture in studies of femoral neck strength.

Two areas are suggested in which this work could be extended. First, suggestions that bone is homogeneous [29, 28] are contradicted by studies showing the great heterogeneity in bone tissue [241, 201, 200, 265, 87]. Bone properties vary with species, site, and orientation. One way to incorporate this into our model is to use x-ray attenuation to define a differential elasticity depending on density. The relationship between bone modulus and its porosity has been shown to vary depending on anatomical site and type. Further investigation of modulus-porosity relationships for differ-
ent bone types and other porous media may elucidate the structural basis for different modulus-porosity relationships. Another possibility is the use of an anisotropic stiffness tensor at the voxel scale based on some a priori knowledge of the collagen orientation in bone.

The second area in which this work could be extended is to understand the anisotropy of the elastic tensor in the context of fall directions. We have demonstrated a technique to completely characterise the macroscopic and microscopic response (Figure 6.1) of thirteen human femurs to varied loading conditions using superposition of strains. Falls and fall direction are significant factors affecting fracture risk [73, 186]. Using anisotropic stiffness tensors, one may be able to identify directions of weakness for the whole hip. For example, in Chapter 5 we show that $E_1$ and $E_2$ are of approximately equal value and smaller than $E_3$. The inference is that the whole hip may be more susceptible to fracture from a fall impact in the anterior-posterior ($E_2$) direction (see Figure 5.26) or the superolateral-inferomedial directions ($E_1$). FEM may also be useful in developing patient specific prediction of directions of weakness and associated regions of local fragility [261].
Figure 6.1: Stress tensor field visualisation for specimen 180R. Glyphs represent the principal components of stress under a given loading condition. The orientation of the principal stress components are represented by the orientation of the glyph. Each axis of the glyph is scaled by the magnitude of the principal stress component in that direction. Tensor field visualisation can give insight into the direction and magnitude of the stress in local regions.