

Fabric-Elasticity Property Relationships of the Human Cortical Femur

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ABSTRACT

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1. Introduction

Bone is a hierarchically structured natural material mainly composed of hydroxyapatite (HA), collagen type I, and water [5]. At the nanoscale, collagen molecules self-assemble to form fibrils staggered into their longitudinal direction with a gap of about 67 nm between adjacent molecules. In this gap, HA aggregate to form crystals leading to mineralisation of collagen fibrils. These mineralised collagen fibrils are arranged together into lamellae and this so-called lamellar bone is the building block of the two main bone structures observed at the macroscale: cortical and trabecular bone.

In cortical bone, lamellae are arranged concentrically around Haversian canals to form osteons. The Haversian canal contains nerves, blood, and lymphatic vessels and measure about 70 μm in diameter while the complete osteon is about 100–200 μm in diameter. At their external surface, osteons are bounded by a thin layer called the cement line, separating it from the older interstitial bone tissue. Altogether, they form the cortical bone tissue, being the outer shell of bones, with a porosity varying between 5 and 15%. Towards the inside and the epiphyses of bones, porosity of the bone tissue increases leading to trabecular bone structure. In trabecular bone, bone lamellae are concentrically arranged to form trabeculae and the porosity, ranging from 20 to 90%, is represented by the inter-trabecular space.

With ageing, a metabolic imbalance leads to a progressive loss of bone mass. This decrease of bone mass weakens the

skeleton, increasing fracture risk, and ultimately leading to osteoporosis. It is estimated that 1/5 men and 1/3 women over 65 years old will experience a fragility fracture induced by a load that shouldn't have caused a fracture in normal conditions. These fractures lead to pain, increased costs for the society, and an increased morbidity. The gold standard for the assessment of osteoporosis is dual-energy X-ray absorptiometry (DXA), typically performed at the lumbar spine or the femoral neck. DXA results in an areal bone mineral density (aBMD) value which is then compared to a reference population. However, DXA misses of specificity as an important part of fragility fractures happens to people above the osteoporosis threshold. Therefore, clinicians are looking for better surrogate to estimate bone strength.

High-resolution peripheral quantitative computed tomography (HR-pQCT) allows acquiring in vivo scans of the bone structure at peripheral sites such as the radius and tibia. These scans can serve as a basis for numerical analysis allowing to estimate bone strength. One way to perform these simulations is to convert every voxel to finite element and modelize a compression of the scanned section. This approach then leads to models containing millions of μm -sized finite elements which require heavy computational effort to solve. Another approach consists of using millimeter-sized elements, so-called homogenized finite elements (hFE) and corresponding constitutive models. This second approach, while being a less accurate representation of the bone geometry, lead to models considerably lighter to solve. Additionally, it was shown that such hFE models are able to provide accurate bone strength assessment. However, such models highly depend on the constitutive model used to describe the bone's tissue mechanical behavior.

Abbreviations: ROI, region of interest; μCT , micro-computed tomography;

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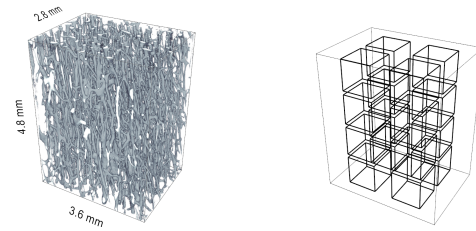
The mechanical properties of bone tissue are usually assessed using experimental approaches. **Cite studies showing experimental assessment of bone mechanical properties.** However, bone tissue properties can also be assessed via numerical approach. **Cite studies assessing bone properties using μ FE.** As mentioned previously, μ FE require expensive resources for large models. Therefore, hFE becomes an attractive alternative using adapted constitutive relations. Over the years, many constitutive models have been proposed to describe the mechanical behavior of bone. **Introduce the different models. Describe density and fabric. Introduce the Yang and Cowin model as well as the Zysset-Curnier model. Present investigations performed for trabecular bone** However, these relationships are not yet verified for cortical bone.

Constitutive model are compared to mechanical experiments and numerical simulations. For cortical bone, nanoindentation experiment have shown that bone matrix is transverse isotropic. Combined with micro-computed tomography, it is possible to simulate the mechanical behavior of millimeter-size cortical bone samples. Experimentally, resonant ultrasound spectroscopy (RUS) measurements allows for estimation of elasticity tensor of cortical bone.

The aim of the present study is to investigate the influence of the bone matrix properties and microstructure on the mechanical properties of human bone. The relationships between density, fabric and mechanics are presented from the bone matrix (bone of full density) down to the low density of trabecular bone with a strong focus on the cortical bone. Additionally to relationships description, the objective is to provide material constants for bone properties estimation.

2. Material and Methods

The μ CT scans and corresponding mechanical data of cortical bone used in this study were provided by the Sorbonne Université, INSERM, CNRS, Laboratoire d'Imagerie Biomédicale (LIB), F-75006 Paris, France. The detailed process of the sample preparation, scanning and measurement is provided in the study of Cai et al.[2]. Briefly, rectangular parallelepiped samples of about 3x4x5 mm (radial, circumferential, and axial direction, respectively) were thawed from both lateral and medial part of the left femur from 29 human cadavers. The elasticity tensor of these samples was measured using resonant ultrasound spectroscopy (RUS) [1], assuming transverse isotropy. After mechanical measurement, the samples were scanned using synchrotron radiation micro-computed tomography (SR- μ CT) at the European Synchrotron Radiation Facility (ESRF, Grenoble, France). The original voxel size of these scans of 6.5 μ m was coarsened by a factor 2, allowing a good compromise between computational efficiency and structural accuracy. After coarsening, 16 cubic regions of interest (ROIs) of 1 mm side length were selected uniformly over the sample. A typical cortical sample with its porosities and the distribution of the selected ROIs are shown in Figure ??.



(a) Typical sample with its porosities (b) ROIs selected for analysis

The CT scans of trabecular bone samples were produced in a previous study [7] using high-resolution peripheral quantitative computed tomography (HR-pQCT). Briefly, HR-pQCT scans were performed on 120 healthy individuals' tibia with a voxel size of about 61 μ m. Then, 6 cubic ROIs of 5.2 mm side length were randomly selected within the proximal stack of the scan, leading to a total of 720 ROIs.

Both cortical and trabecular bone ROIs underwent numerical homogenisation. The homogenisation process was performed using medtool (Dr. Pahr Ingenieure e.U., Pfaffstätten, Austria) for pre- and postprocessing and ABAQUS (Dassault Systèmes Simulia Corp) for numerical simulation. The homogenisation scheme consist of simulating 6 loadcases (3 compression and 3 pure shearing) imposing an apparent strain of about 0.001 with kinematic uniform boundary conditions (KUBCs) and computing the resulting apparent stress. The bone geometry was generated by segmenting the ROIs using the mean Otsu threshold of each group. Then, every voxel segmented as bone tissue was converted to an hexahedral element. For trabecular ROIs, an isotropic material was assumed with a Young's modulus of 10 GPa and a Poisson's

Table 1

Nanoindentation - cortical bone matrix properties

Study	E1	E2	E3	Nu12	Nu13	Nu23	Mu12	M13	Mu23
Dall'Ara Fanzoso Present	14796.9	14796.9	21175.8	0.34	0.284214	0.284214	5521.23	6604.96	6604.96

ratio of 0.3. For cortical ROIs, the simulations were performed using 2 different material. First, an isotropic material with the same properties as for trabecular ROIs. Second, a transversely isotropic material with the plane of symmetry perpendicular to the scan 3rd axis. The properties of transversely isotropic material were determined from nanoindentation results of cortical bone presented in the work of Fanzoso and Zysset[4] and Dall'Ara et al.[3], see Table 1.

After homogenisation, the analyses were performed as follow:

1. Averaging the 16 cortical ROIs stiffness tensor per sample with transverse isotropic material, projection onto transverse isotropy, and comparison to RUS measurements.
2. Project cortical ROIs stiffness (with transverse material) onto orthotropy and fit to Zysset-Curnier model
3. Project cortical ROIs stiffness (with transverse material) onto transverse isotropy and fit to Zysset-Curnier model
4. Project cortical ROIs stiffness (with transverse material) onto transverse isotropy and fit to Yang and Cowin model
5. Project cortical and trabecular ROIs stiffness (with isotropic material) onto transverse isotropy and fit to Yang and Cowin model

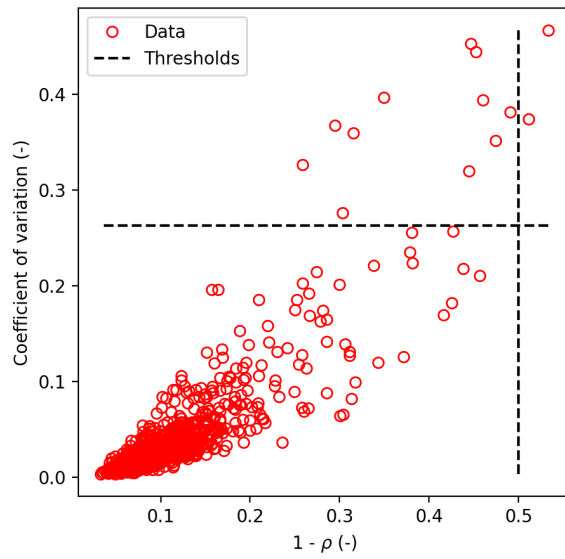


Figure 2: Coefficient of variation as function of porosity

3. Results

3.1. Cortical Bone Morphology

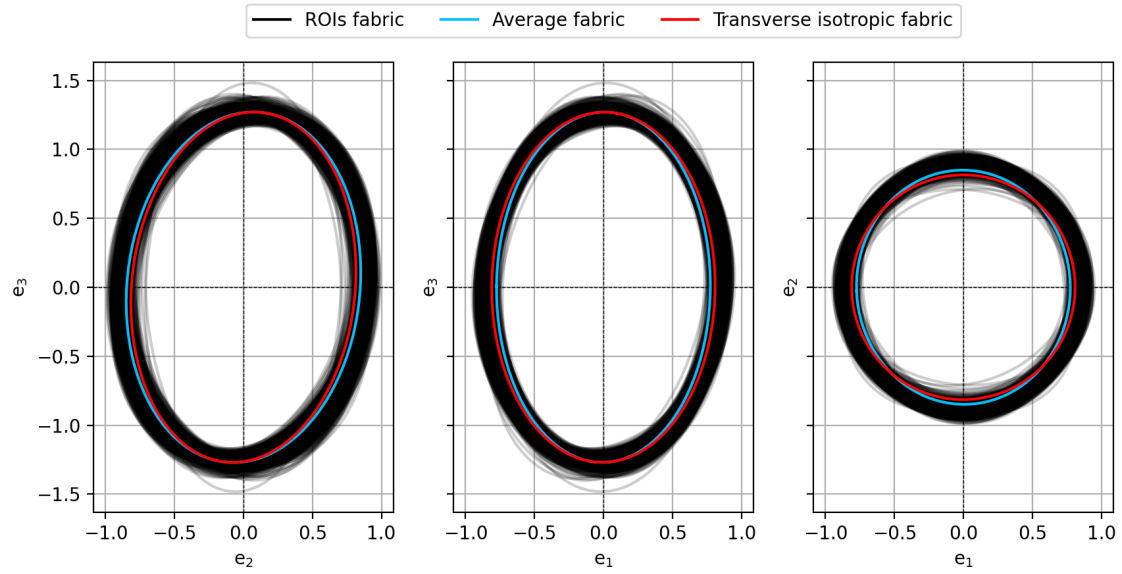


Figure 3: ROIs fabric projected on principal planes

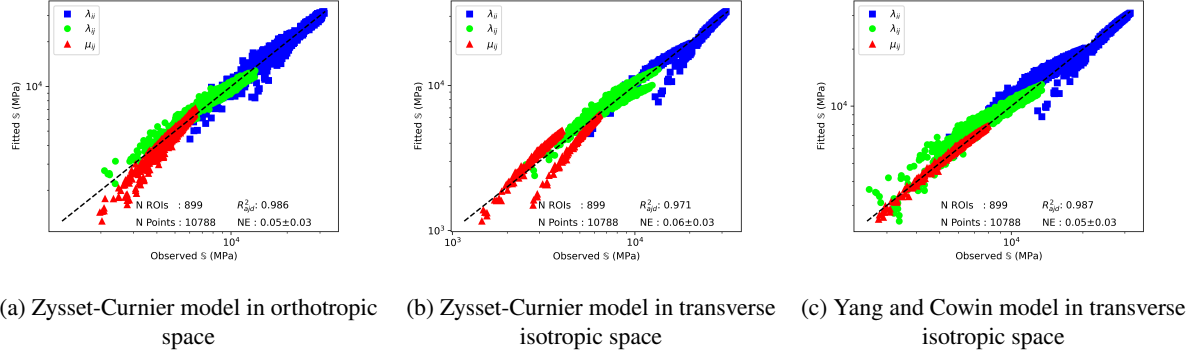


Figure 4: Models fitting results

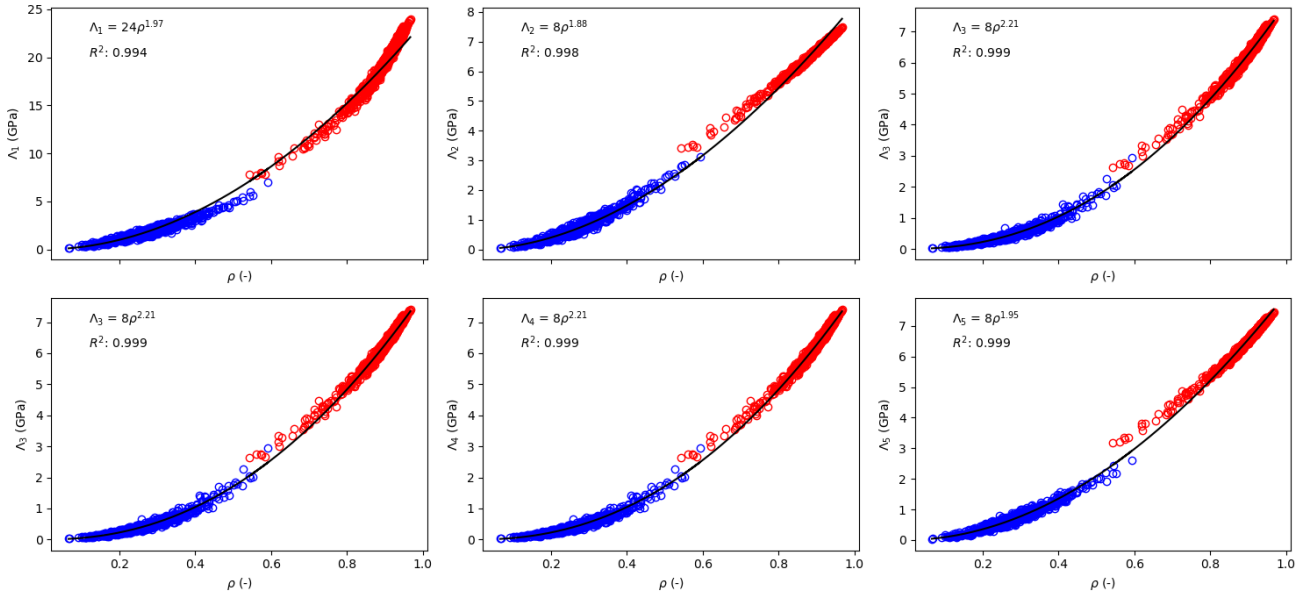


Figure 5: Eigenvalues of the stiffness tensor as function of porosity

Table 2

Parameters and fit quality coefficient obtained with the standard Zysset-Curnier model in orthotropic and transverse isotropic space.

Model	λ_0	λ'_0	μ_0	k	l	R^2_{adj}	NE
Orthotropic	19831	12618	3527	2.48	0.57	0.99	0.05
Transverse	17505	13117	4016	2.49	0.39	0.94	0.11

3.2. Fit to model

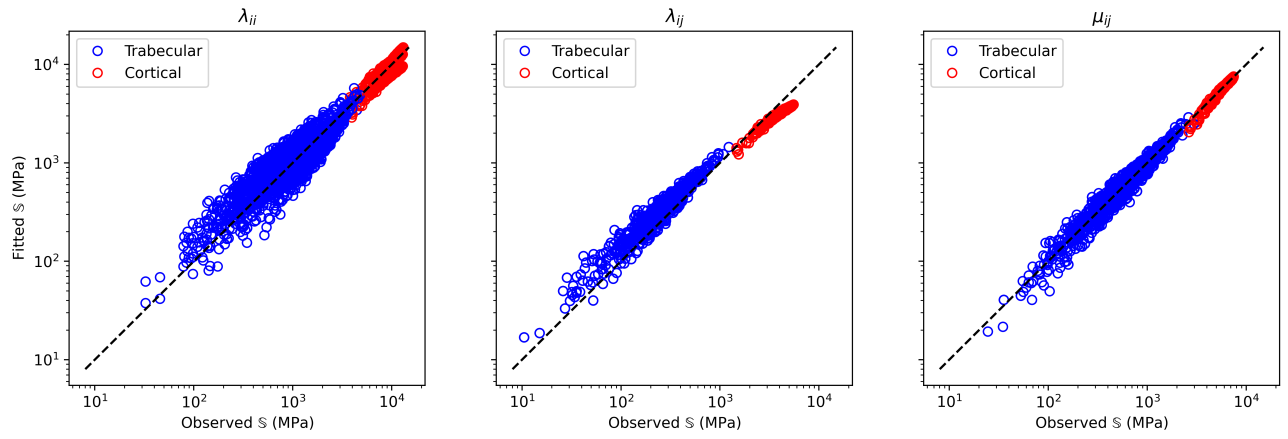


Figure 6: Result of fitting to Yang and Cowin model

3.3. Comparison to RUS

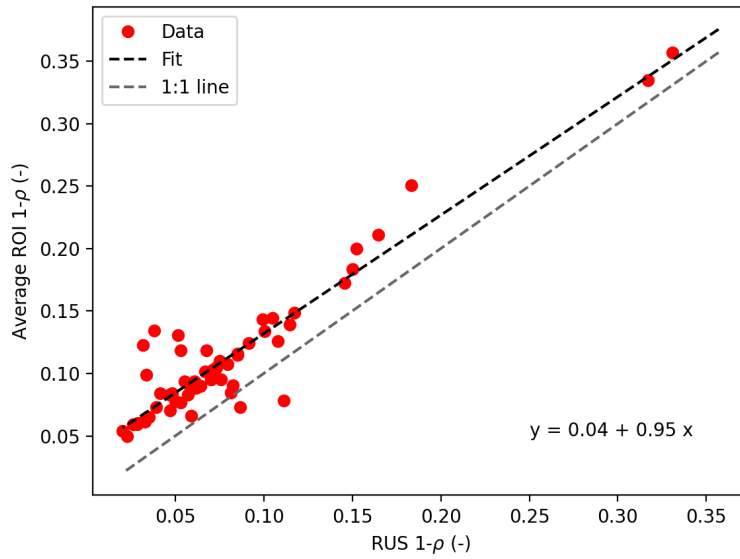


Figure 7: Average ROI porosity vs porosity from Cai et al.

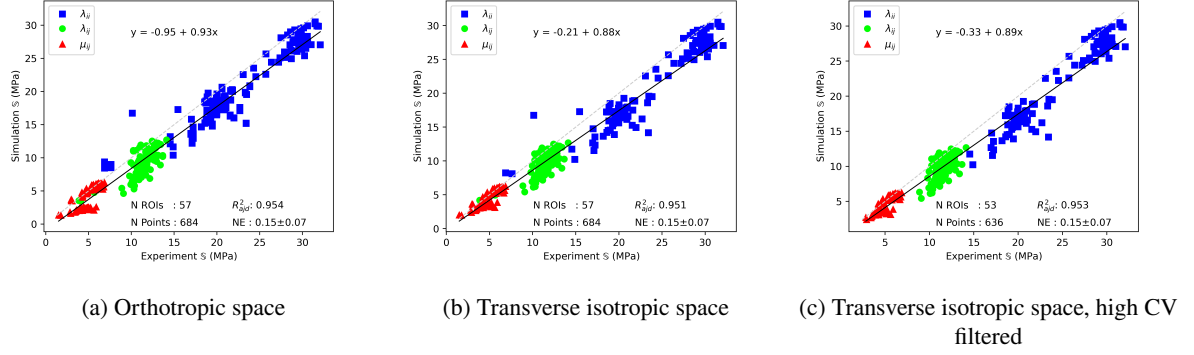


Figure 8: Simulation vs experimental stiffness tensor components

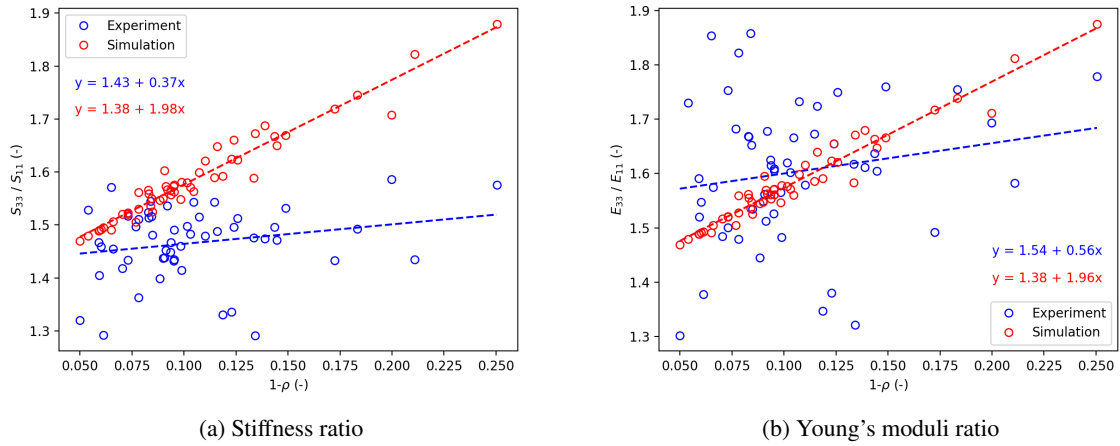


Figure 9: Degree of anisotropy

4. Discussion and Conclusion

Declaration of competing interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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Data availability statement

The data that support the findings of this study are available on request. The data are not publicly available due to privacy/ethical restrictions. The scripts used for the analyses performed in the present study are available on Github: <https://github.com/artorg-unibe-ch/FABTIB>

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

CRedit author statement

Mathieu Simon: Data Curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing - original draft. **Philippe Zysset:** Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision, Validation, Writing - review and editing.

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