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On the anisotropy of the myocardium

M. Genet[1,2], N. Tueni[1,2], and J.-M. Allain[1,2]

[1] *Laboratoire de Mécanique des Solides, École Polytechnique/Institut Polytechnique de Paris/CNRS, {martin.genet, nicole.tueni, jean-marc.allain}@polytechnique.edu*

[2] *INRIA, France*

Résumé — The myocardium is a highly anisotropic material. However, the link between the microstructure and the macroscopic mechanical properties is still not fully understood. In order to shed light on this question, we analyzed the macroscopic mechanical behavior of cardiac tissue homogenized from different mesostructures. The anisotropic material behavior induced by these microstructures was compared to available experimental data. This study confirms the importance of collagen in assuring the tissue's anisotropic response observed experimentally.
Mots clefs — Cardiac Mechanics; Anisotropy; Micromechanics; Homogenization; Optimization.

1. Introduction

Over the years, the myocardium has been modeled at the tissue scale as an isotropic (Demiray, 1976), transversely isotropic (Humphrey & Yin, 1987) or orthotropic (Costa et al., 2001) continuum. One breakthrough experiment is the one from (Dokos et al., 2002), who subjected 3×3×3 mm^3 samples of porcine left ventricles to shear tests in six directions, revealing the somewhat light but still clear anisotropy of the myocardium at the tissue scale. An important question arises, of the microstructural origin of this anisotropy. Indeed, a better understanding of the structure-properties relationships in the myocardium could lead to more robust model-based biomedical engineering computational tools for the diagnosis and treatment of cardiac diseases (Lee et al., 2014). At the cellular level, the cardiomyocytes, which account for *ca*. 80% of the myocardial volume, are shaped as elongated cylinders and surrounded by a thin layer of collagen (the endomysium), suggesting a transversely isotropic symmetry. At least two microstructural features could explain the macroscopic anisotropy: *(i)* the local orientation of the cardiomyocytes varies rapidly throughout the myocardium, with an helix angle varying by *ca*. 120º between endocardium and epicardium; *(ii)* at an intermediate (meso) scale, the arrangement of cardiomyocytes into bundles forming branching laminae and surrounded by thicker collagen layers (the perimysium) (Costa et al., 2001; Tueni et al., 2020). In order to investigate these various hypotheses, we designed a multi-scale model of the myocardium, bridging the cell, sheetlet and tissue scales. The model is associated to an optimization procedure, allowing to find the microscopic parameters that best match the macroscopic data. Thus, the model and optimization procedure, presented now, permit the quantitative selection of hypothesis regarding structure-properties relationships.

2. Methods

2.1. Data

In this work, we use the data from (Dokos et al., 2002). We verified that the anisotropy, *i.e.*, the ratio between the different shear components, did not vary significantly with the applied deformation. Thus, we selected the shear values at 5% deformation, and fit them with a linear elastic model where each constituent obeys the Hooke law.

2.2. Model

2.2.1. Cellular scale

Based on standard assumptions (Humphrey & Yin, 1987), we considered the myocardium to be transversely isotropic at the cellular scale. We considered both compressible and quasi-incompressible laws.

2.2.2. Sheetlet scale

We considered two different arrangements on the sheetlet scale. The first model (H) is homogeneous, that is to say that no mesostructure is considered. The second model (S) is stratified, with a thin layer (5% total volume) of perimysial collagen in between layers of transversely isotropic myocardium. To reduce the number of microscopic parameters, we considered an isotropic law for the collagen. Again, both compressible and quasi-incompressible laws have been studied. The stratified mesostructure (S) was homogenized through periodic homogenization.

2.2.3. Tissue scale.

On the tissue scale, we reproduced the experimental configuration, with cubic samples subjected to simple shear tests. Variations of fibers and sheetlets orientation were taken into account within the cubes. All finite element computations were performed using the FEniCS library (Logg et al., 2012).

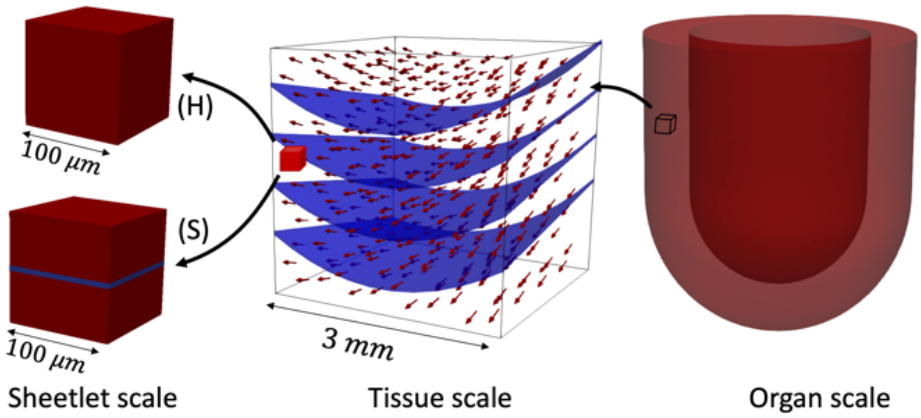


Figure 1 — Schematic of the hierarchy of scales.

2.3. Optimization procedure

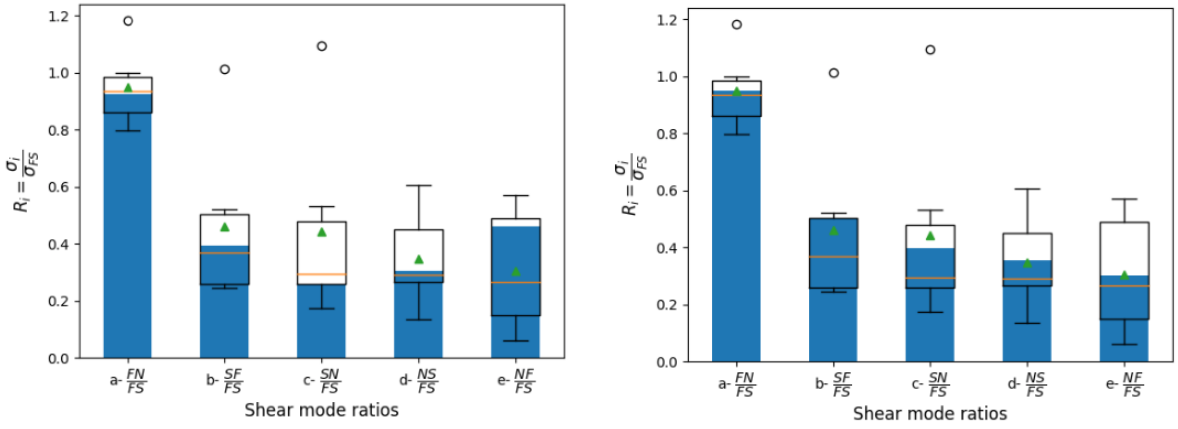
The proposed model being linear, the stress depends linearly on the stiffness, so we only fitted five macroscopic shear ratios (taking the largest of the six shear values as reference), and fixed one microscopic Young modulus to reduce the number of parameters. Our cost function is

$$J := \sum_{i=1}^{5} \frac{1}{2} \frac{(R_i - \mu_i)^2}{\sigma_i^2},$$

where R_i are the computed shear ratios, and μ_i & σ_i are the experimental means and standard deviations of the shear ratios. The compressible transversely isotropic model had 5 free parameters, while the stratified model had 8. Optimization was performed using CMA-ES (Auger & Hansen, 2005), a derivative-free optimization tool.

3. Results and discussion

Results for the optimal models based on homogeneous and stratified mesostructures, and compressible material laws, are shown in Figure 2.



(a) Homogeneous mesostructure (H). (b) Stratified mesostructure (S).

Figure 2 — Comparison of experimental (box plot: lower to upper quartile; whiskers: lowest datum above Q1 – 3*(Q3-Q1)/2, and highest datum below Q3 + 3*(Q3-Q1)/2, where Q1 and Q3 are the first and third quartiles; green triangle: mean; orange line: median; hollow circles: data points outside the whiskers) and theoretical (blue bar plot) shear stresses (normalized with respect to largest value).

It is clear that only the model based on the stratified meso-structure, hence taking into account the sheetlet arrangement, can reproduce the order of the various shear components. Moreover, we saw that quasi-incompressible material laws did not allow to properly fit the experimental data.

4. Conclusions

Our main conclusion is that it is not possible to fit the Dokos shear experiments data with a transversely isotropic model. In other words, solely taking into account the transversely isotropic nature of the myocardium at the cellular scale, plus the variation of myofiber orientation through the myocardium, but no intermediate structure such as collagen planes, does not allow to describe the measured anisotropy at the macroscopic scale. Conversely, by taking into account the microstructural organization at the sheetlet scale, and the variation of the sheetlet orientation through the ventricle, it is possible to reproduce the macroscopic data. An additional finding is that some level of compressibility is required to fit the data. These findings call for a more thorough analysis of the mesostructural arrangement of the myocardium, and its role on the ventricular mechanics.

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