What do we really mean by myocardial stiffness?

A modeler's perspective

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simula

Where can you find the slides?

bit.ly/norheart2021_myocardial_stiffness

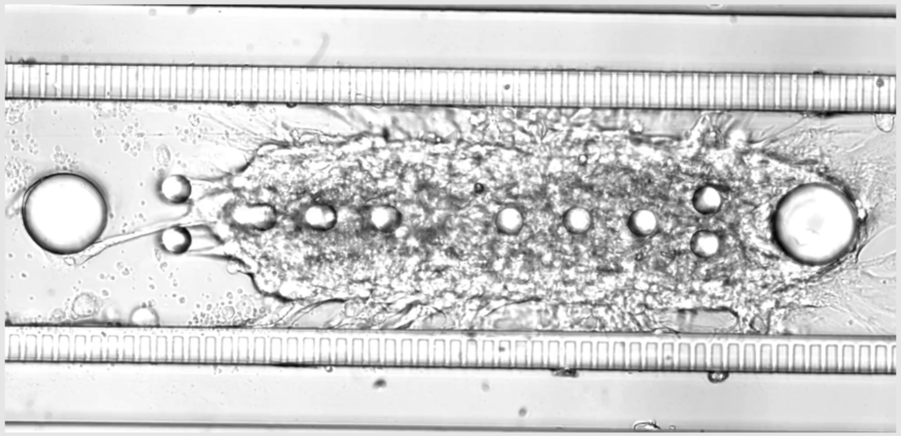
Disclaimer

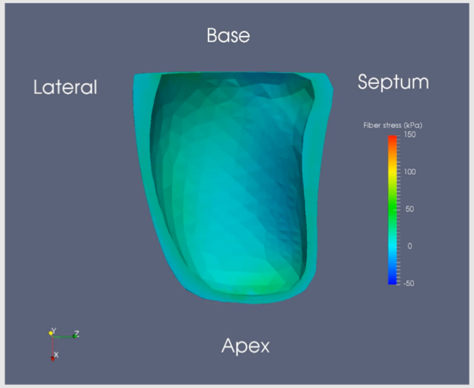
I am a mathematician, not a physician

Who am I?

- 2014 - Master of Science / Master in Applied and Engineering Mathematics (NTNU / DTU)
- 2017 - PhD Scientific Computing (Simula / UiO)
  Patient Specific Computational Modeling of Cardiac Mechancis
- Present – Senior Research Engineer
  Identifying drug effects in Heart-on-chip systems

Department of Computational Physiology





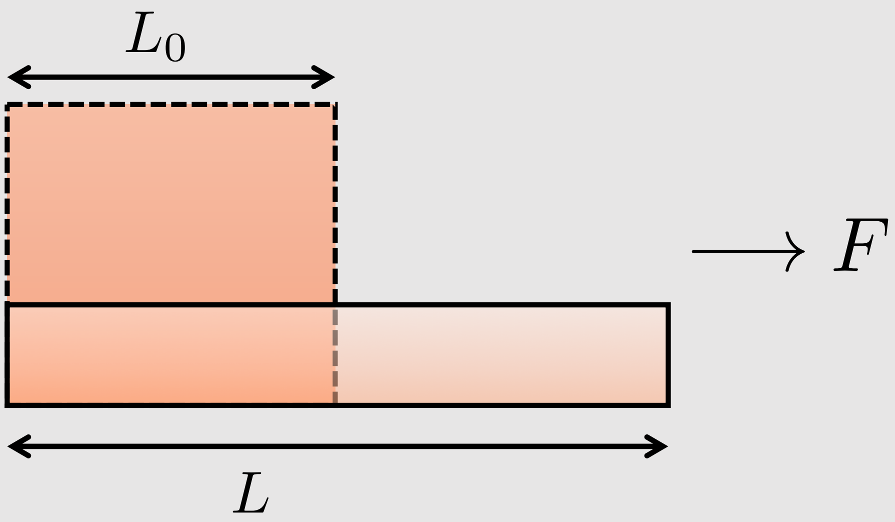
CENTER FOR CARDIOLOGICAL INNOVATION

Goal for the talk today

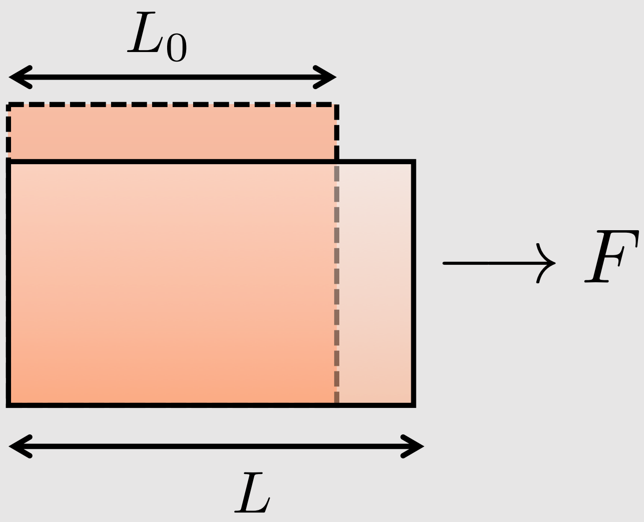
- What do we mean by stiffness?
- How can we model the passive myocardium?
- How can we use models to estimate passive properties of the myocardium?

Stiffer material requires higher force / stress to stretch the material

Soft material



Stiff material



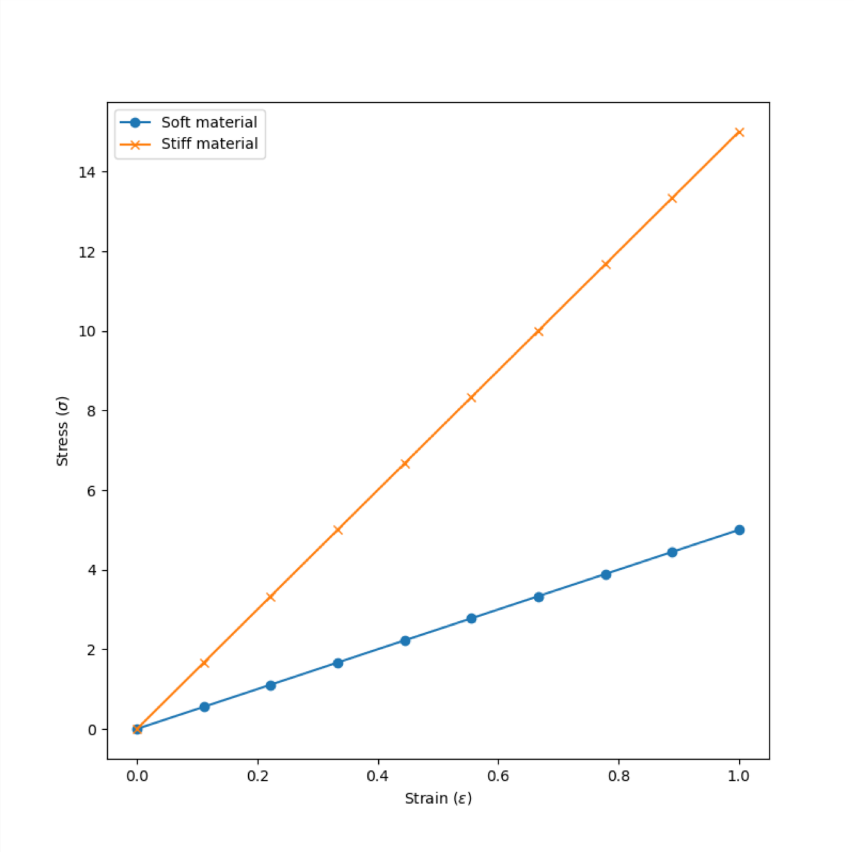
Stress is related to strain through a constitutive law

Stress: $$\sigma = \frac{F}{A}$$

Strain: $$\varepsilon = \frac{L - L_0}{L_0}$$

Constitutive relation: $$\sigma = D\varepsilon$$

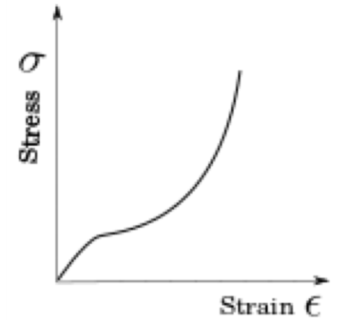
Stiffness / Youngs Modulus



Different materials have different constitutive laws

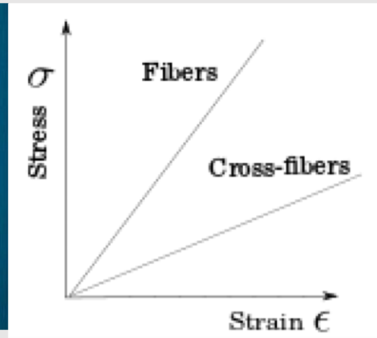
Rubber

Nonlinear isotropic



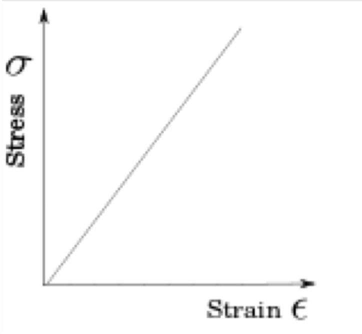
Fiber reinforced concrete

Linear anisotropic

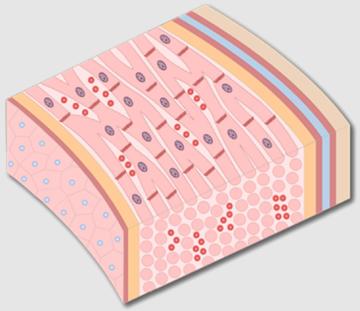


Steel

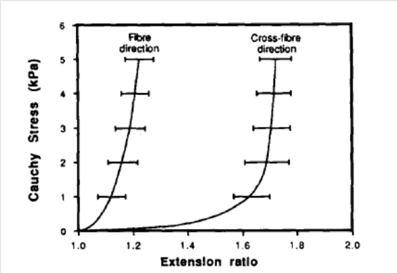
Linear isotropic



Myocardium

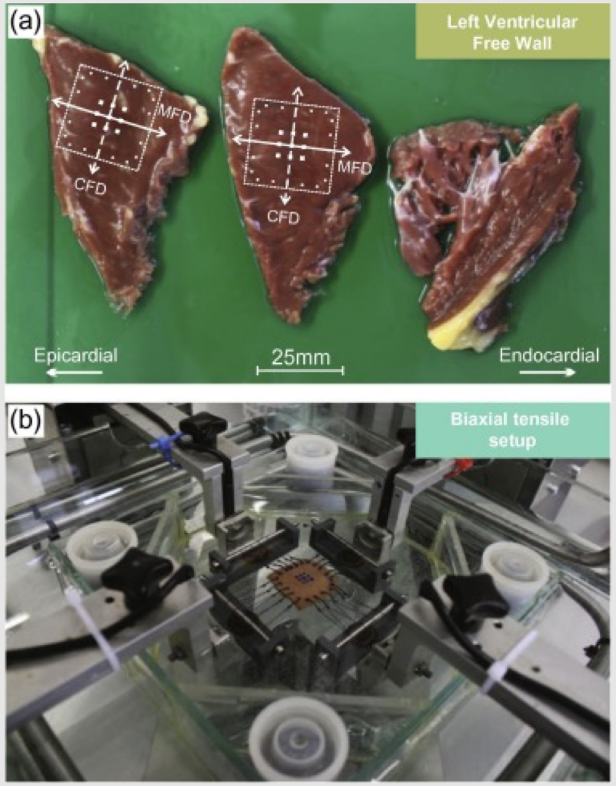


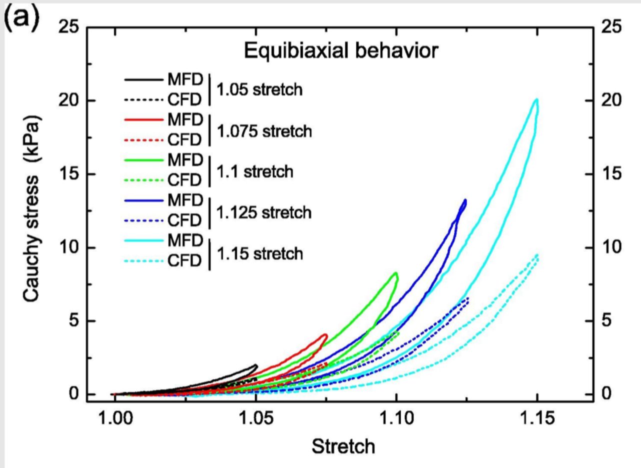
Nonlinear anisotropic

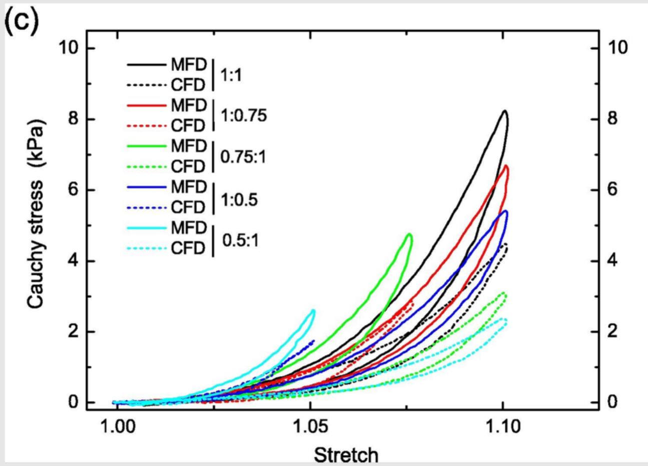


Hunter, P.J. and Smaill, B.H., 1988. The analysis of cardiac function: a continuum approach. Progress in biophysics and molecular biology, 52(2), pp.101-164.a

Material properties can be assessed through biaxial experiments

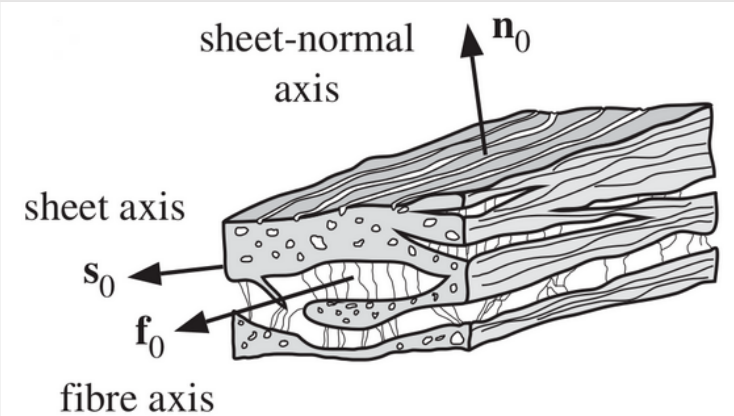




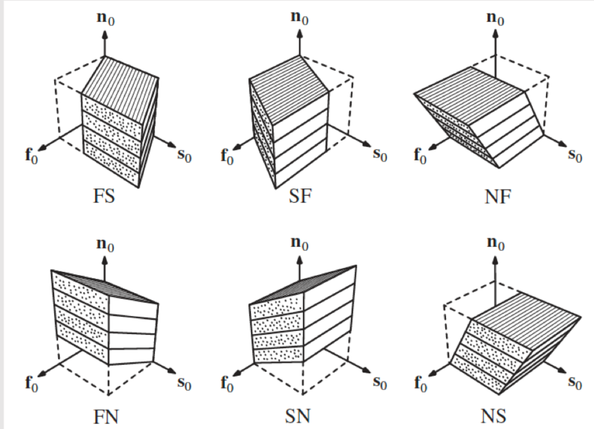


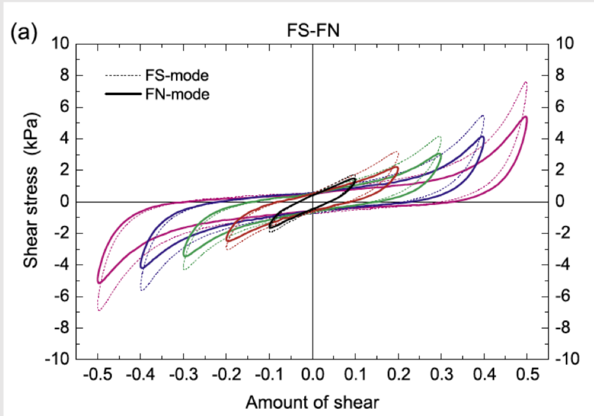
Sommer, G., Schriefl, A.J., Andrä, M., Sacherer, M., Viertler, C., Wolinski, H. and Holzapfel, G.A., 2015. Biomechanical properties and microstructure of human ventricular myocardium. Acta biomaterialia, 24, pp.172-192.

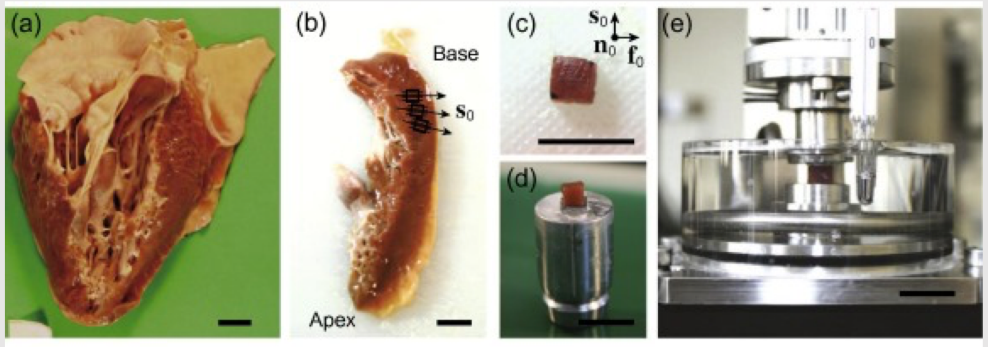
Today experimental data suggests that the myocardium is orthotropic



Holzapfel, G.A. and Ogden, R.W., 2009. Constitutive modelling of passive myocardium: a structurally based framework for material characterization. Philosophical Transactions of the Royal Society of London A: Mathematical, Physical and Engineering Sciences, 367(1902), pp.3445-3475.







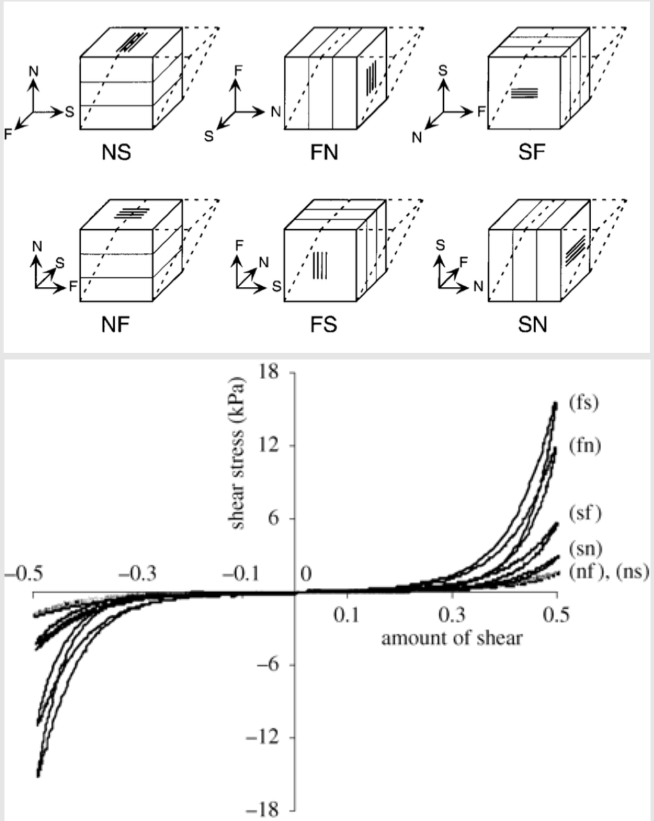
Sommer, G. et. al, 2015. Biomechanical properties and microstructure of human ventricular myocardium. Acta biomaterialia, 24, pp.172-192.

To capture anisotropy of the myocardium, more complex models has to be employed

$\Psi =$

	Contribution from	Extracellular matrix
$+$	Contribution from	Fibers
$+$	Contribution from	Sheets
$+$	Contribution from	Angle between fibers and sheets

$$\sigma = J^{-1} \frac{\partial \Psi}{\partial \mathbf{F}} \mathbf{F}^T$$

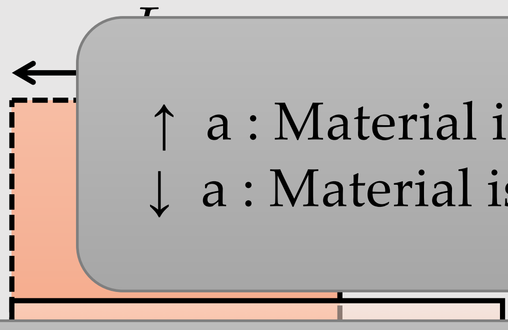


Dokos, S. et. al, 2002. Shear properties of passive ventricular myocardium. American Journal of Physiology-Heart and Circulatory Physiology, 283(6), pp.H2650-H2659.

How to interpret the parameters?

Strain

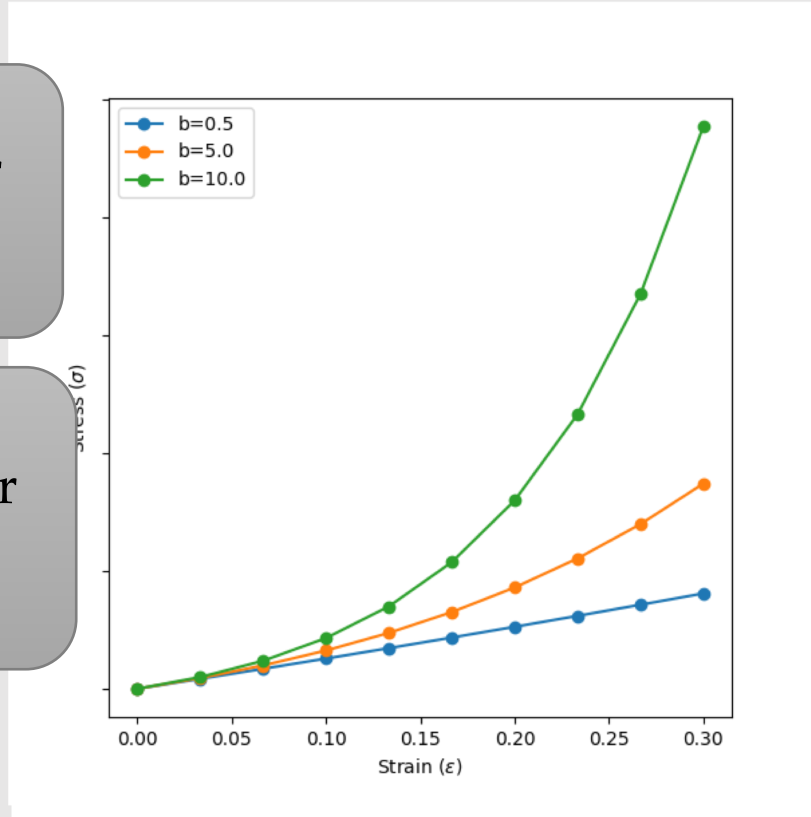
$$\Psi = \frac{a}{2b}\left(e^{b(I_1-3)} - 1\right)$$



↑ a : Material is stiffer
↓ a : Material is softer

↑ b : Material is more non-linear
↓ b : Material is more linear

A



Strain: $$\varepsilon = \frac{L - L_0}{L_0}$$

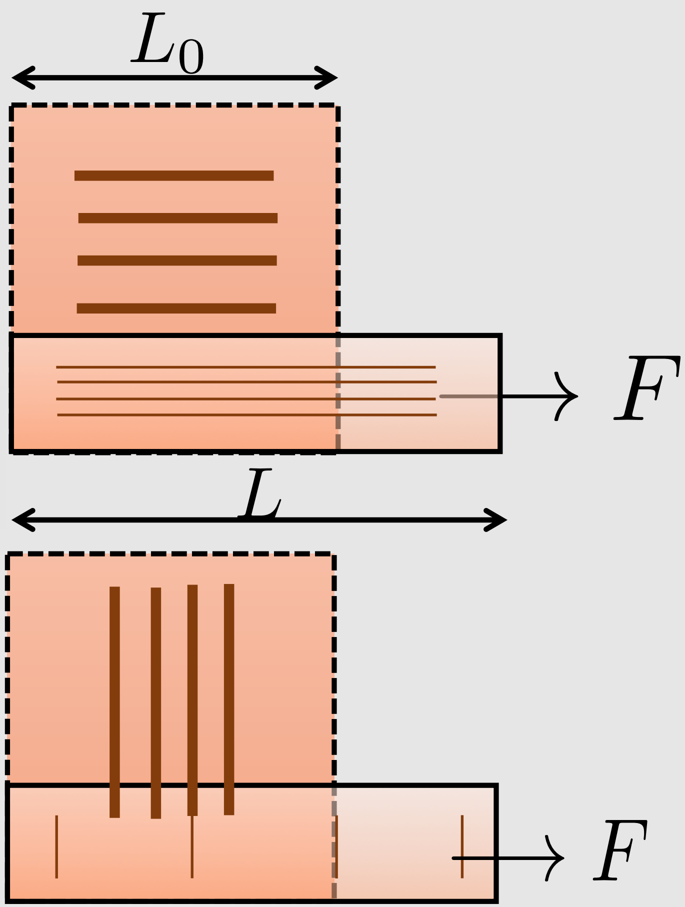
What about the microstructure?

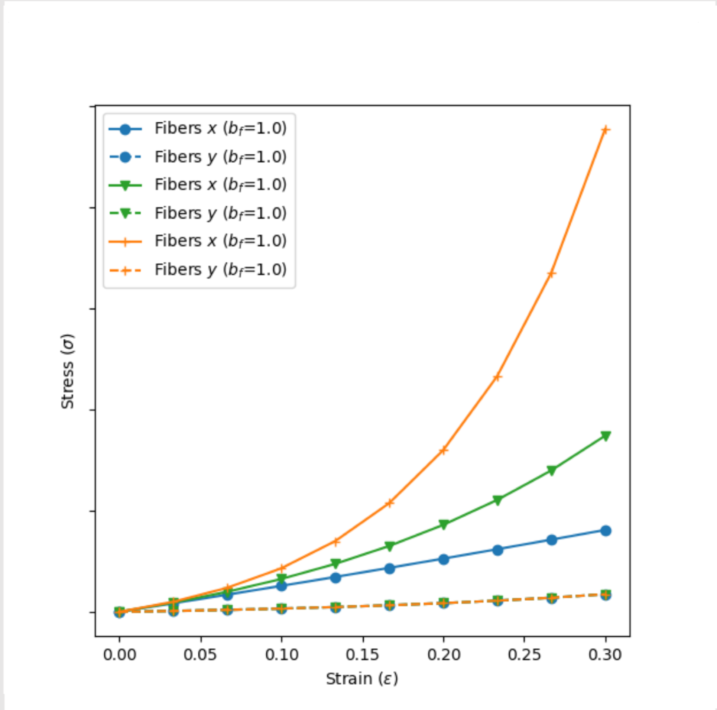
Myofiber

Strain

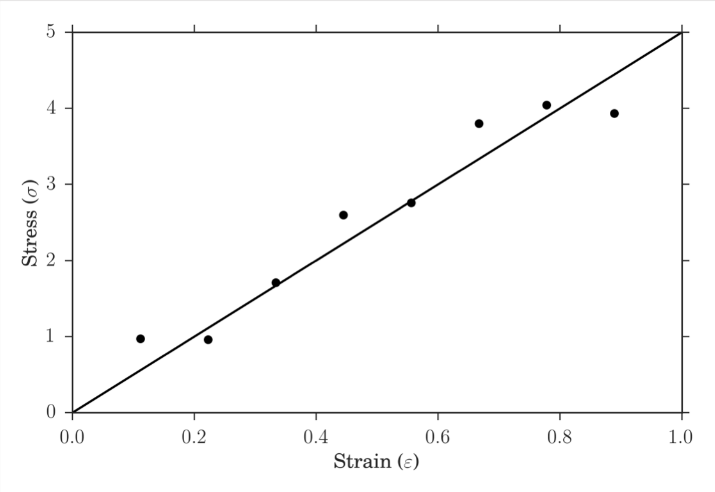
$$\Psi = \frac{a}{2b}\left(e^{b(I_1-3)} - 1\right)$$

Strain in the direction normal to the fibers





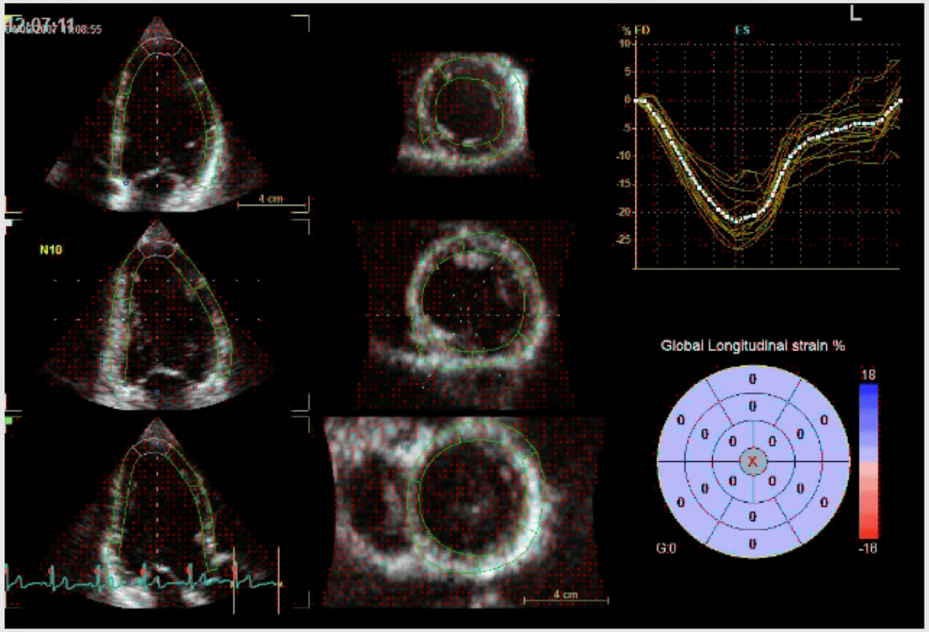
In order to estimate the stiffness of the material we need to cut out a piece of tissue and perform stress-strain experiments

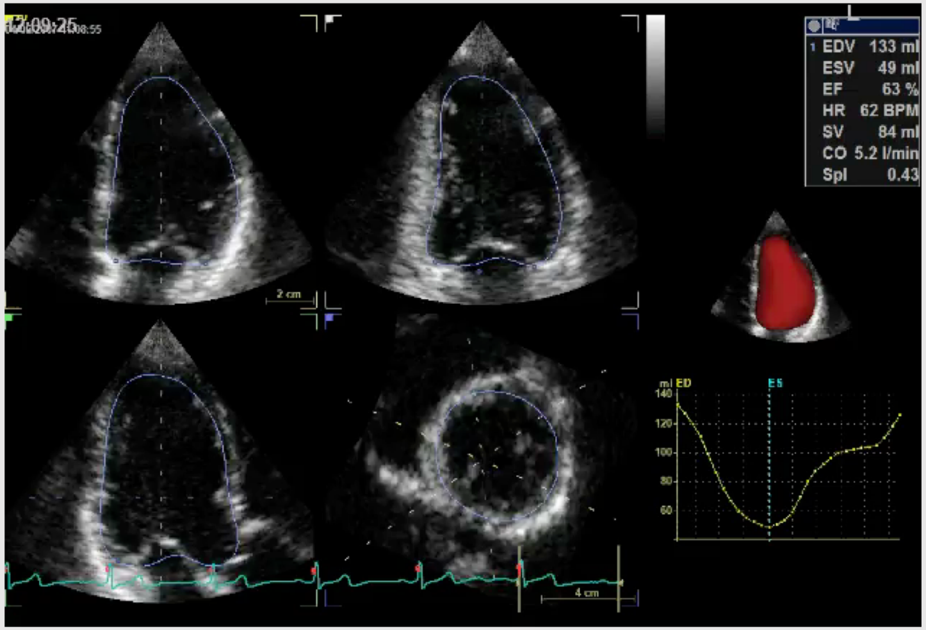


Or is there another way?

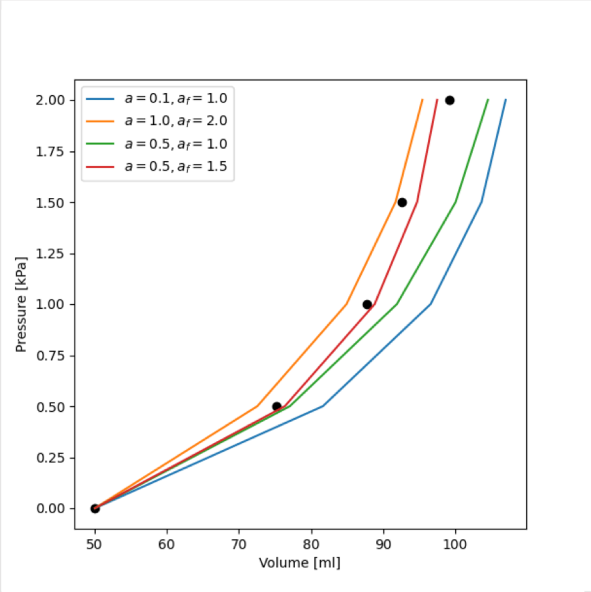
$$\sigma = D\varepsilon$$

How can we use these models when we don’t have access to the data that we need?





Data assimilation is a technique for estimating parameters based on clinical observations



Assume this relation

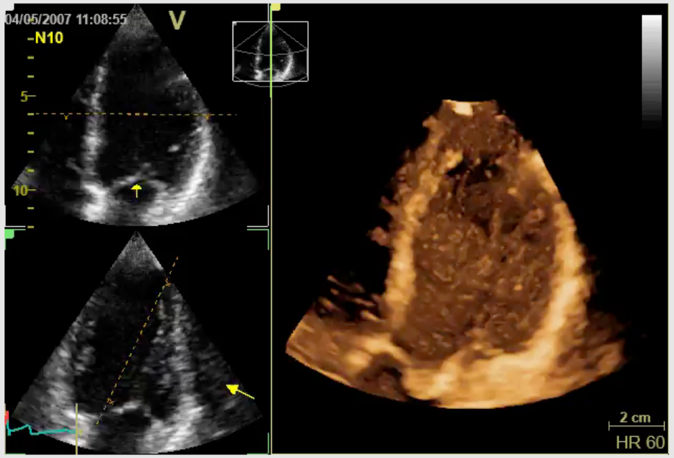
$$\Psi = \frac{a}{2b}\left(e^{b(I_1-3)} - 1\right) + \frac{a_f}{2b_f}\left(e^{b_f(I_{4f}-1)^2} - 1\right)$$

$$\text{minimize : (observations} - \text{simulations)}^2$$

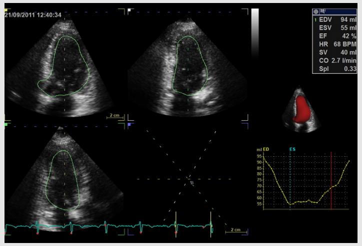
$$\text{subject to : Newton's laws should hold} \qquad \nabla \cdot \sigma = 0 \qquad \sigma = J^{-1}\frac{\partial \Psi}{\partial \mathbf{F}}\mathbf{F}^T$$

Applications

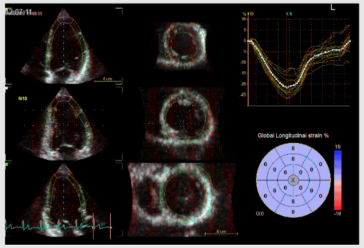
Model creation from medical images

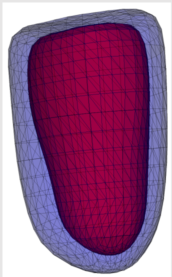


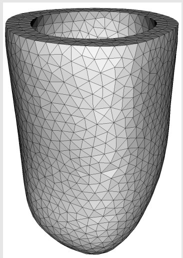
Volume

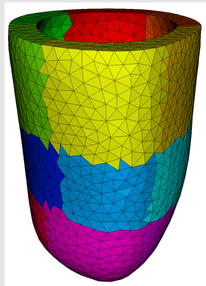


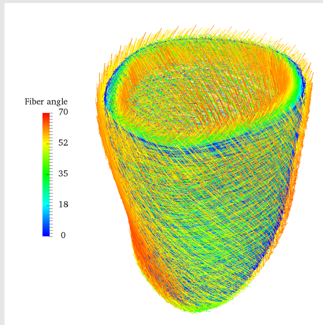
Regional strain



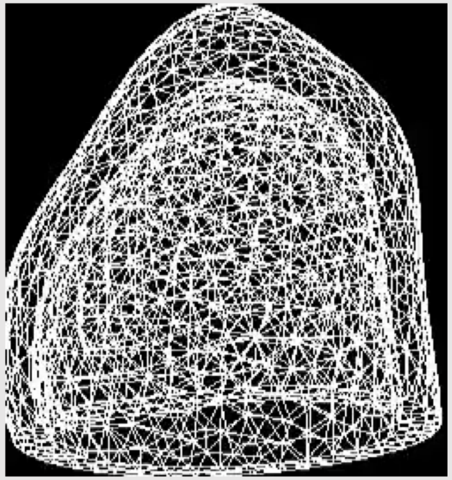




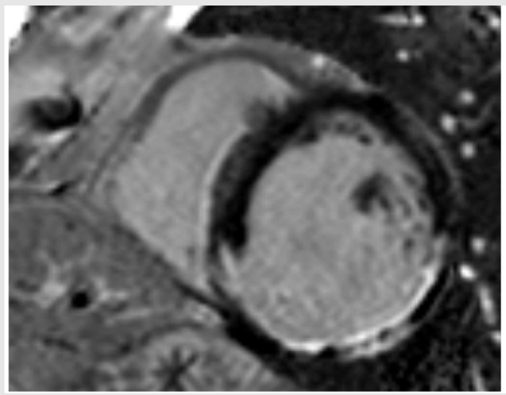




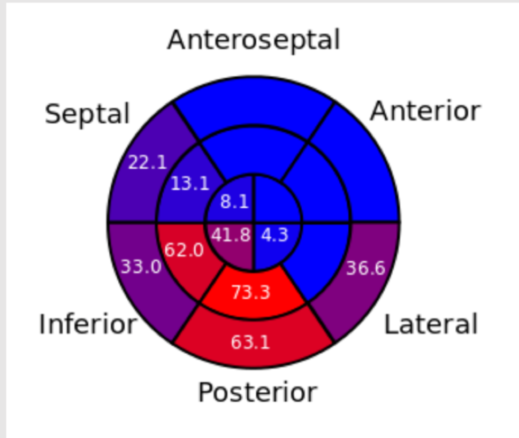
Rule-based fibers
(or DT-MRI)

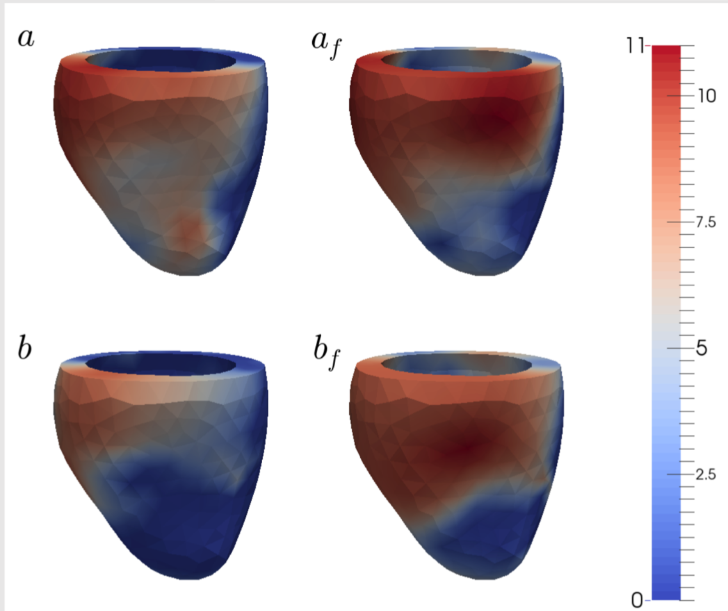


Estimation of tissue stiffness



Myocardial Scar





$$\Psi =$$

$$\frac{a}{2b}\left(e^{b(I_1-3)}-1\right)$$ Extracellular matrix

$$+\frac{a_f}{2b_f}\left(e^{b_f(I_{4f}-1)^2}-1\right)$$ Fibers

Balaban, G., Finsberg, H., Funke, S., Håland, T. F., Hopp, E., Sundnes, J., ... & Rognes, M. E. (2018). In vivo estimation of elastic heterogeneity in an infarcted human heart. Biomechanics and modeling in mechanobiology, 17(5), 1317-1329.

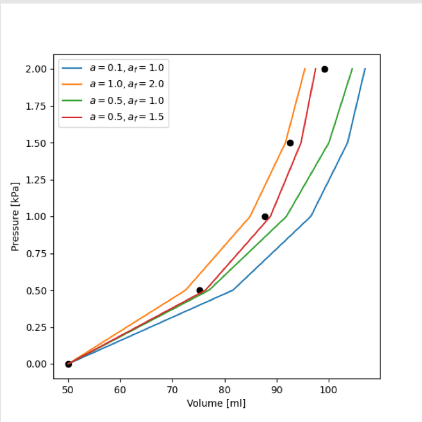
Summary

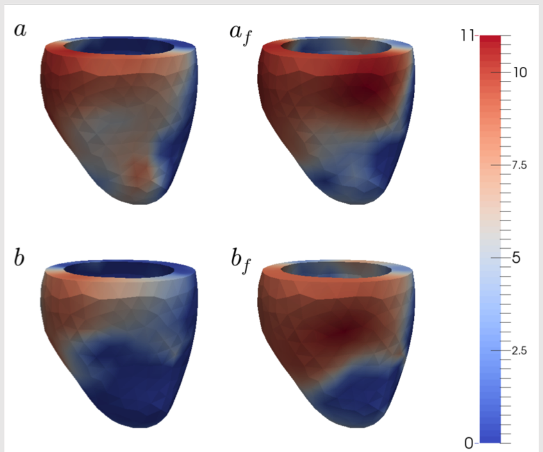
Stiffness of the extracellular matrix

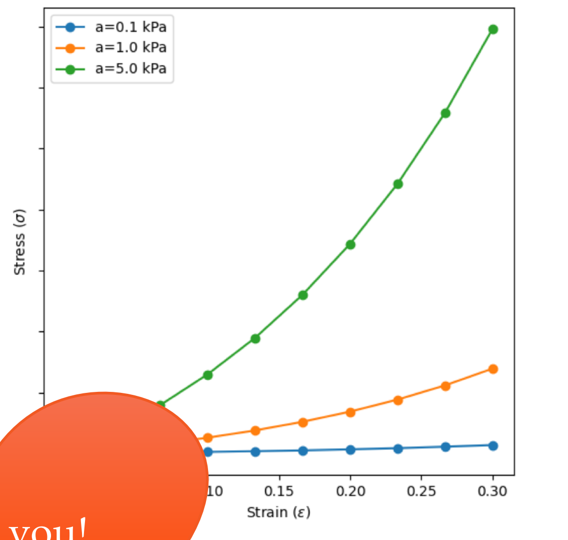
$$\Psi = \frac{a}{2b}\left(e^{b(I_1-3)} - 1\right)$$

ness
in the myofibers

- What do we mean by stiffness?
- How can we model the passive myocardium?
- How can we use models to estimate passive properties of the myocardium?







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