Mechanics and Microstructurally Based Modeling of the Passive Right Ventricular Myocardium

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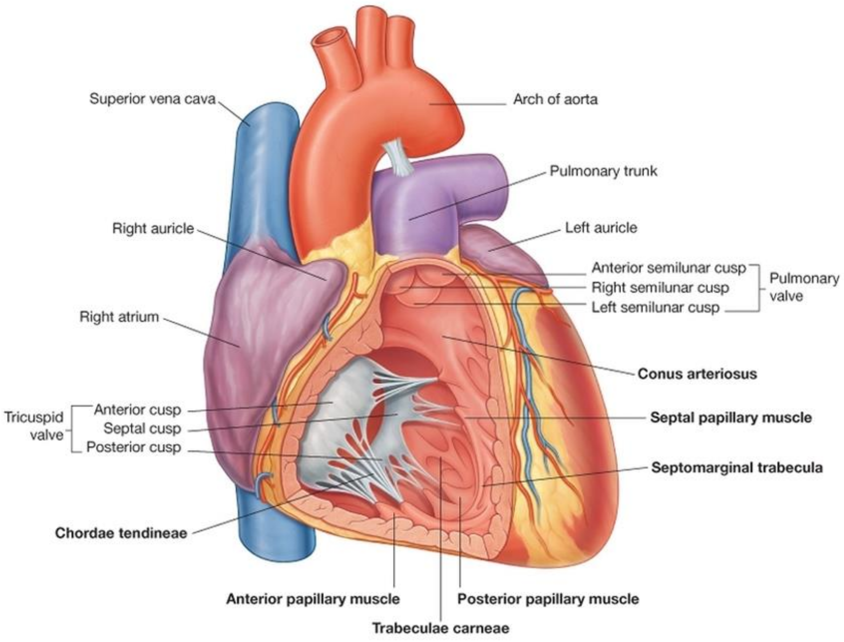
The right ventricle



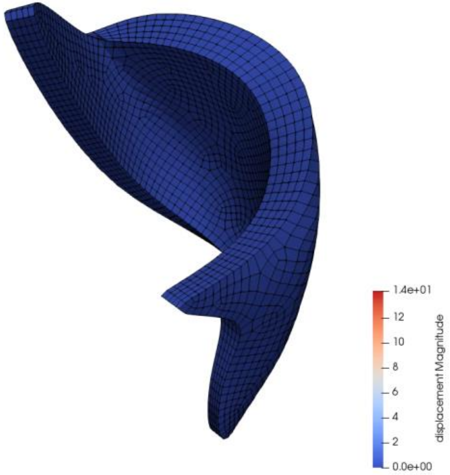
(Darke et al, 2009)

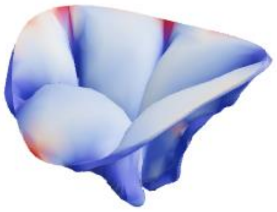
- Receives and pumps deoxygenated blood from the right atrium into the pulmonary circulation
- Historically understudied
- Pathological conditions and disease
  - Right ventricular dilation in Covid-19 infections
  - Tricuspid valve regurgitation
  - Pulmonary hypertension
  - Myocardial Infarction

Motivation

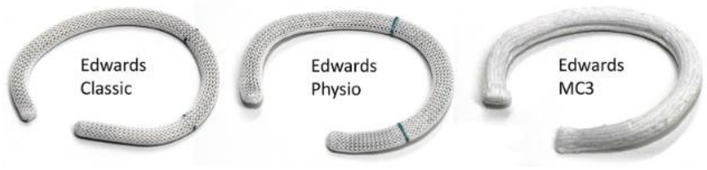
Mechanical properties | **Microstructure** | **Constitutive modeling**

- Mechanics of passive right ventricular myocardium
- Spatially-resolved description of microstructure
- Subject-specific computational models





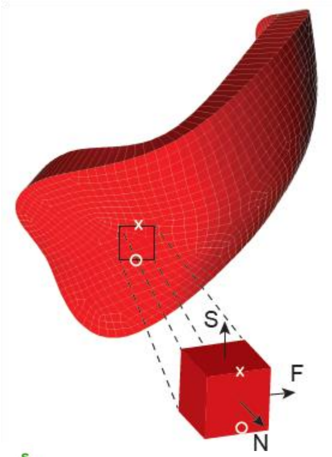
https://mrudangm.github.io

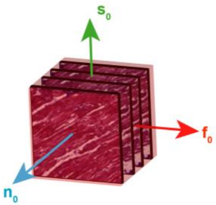


Mathur M, et al. *The Annals of Thoracic Surgery*, 2020.

Mechanical Testing

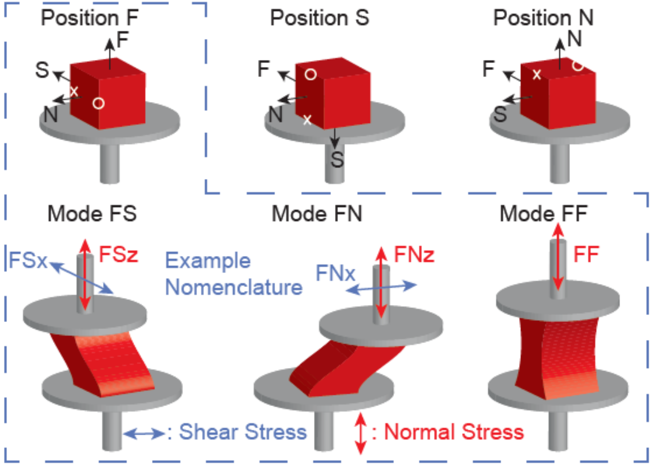
A. Specimen preparation (ovine animal model)



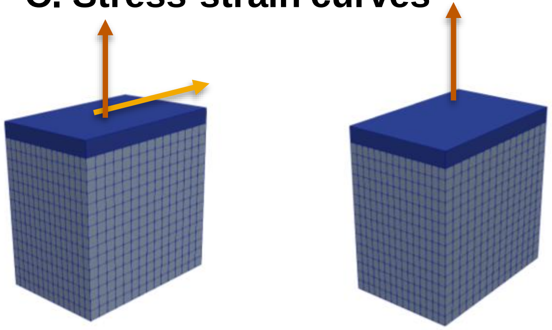


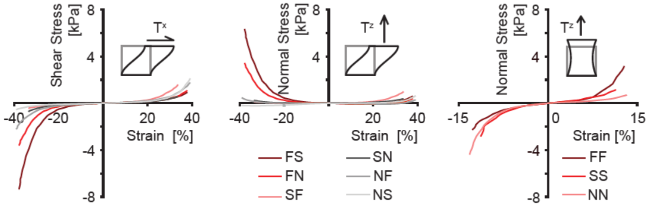
Anatomic Directions:
- **F**: Fiber
- **S**: Sheet
- **N**: Sheet-normal

B. Test in 9 different modes



C. Stress-strain curves



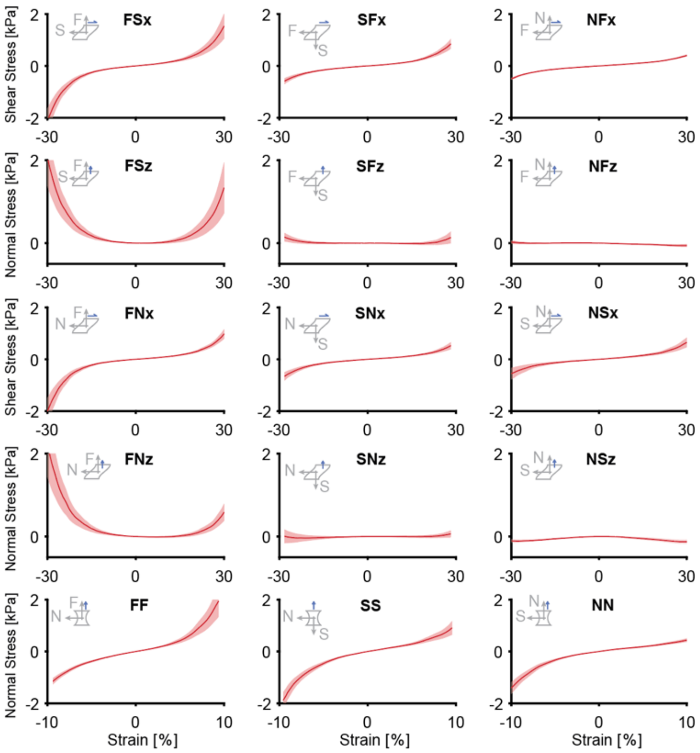


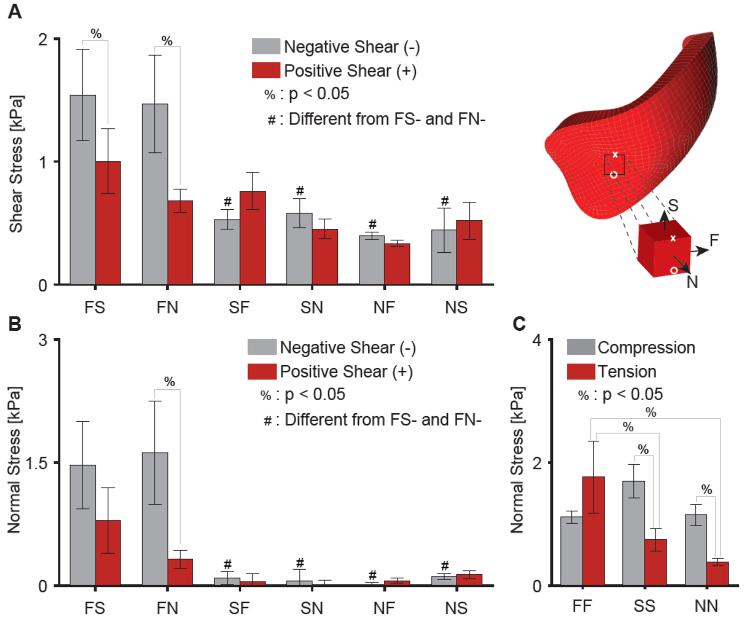
6 Simple shear modes

3 Uniaxial modes

15 Stress-strain curves per sample

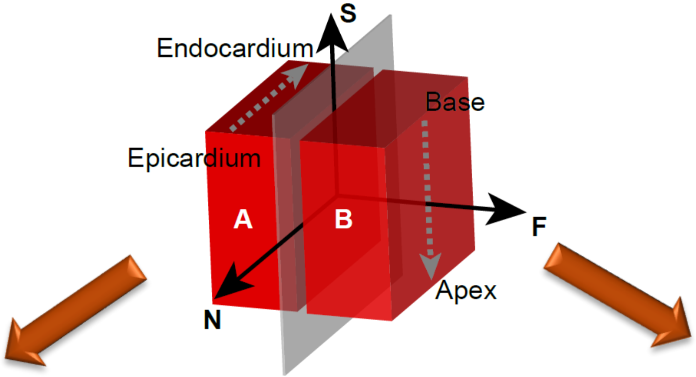
Stress-Strain Data



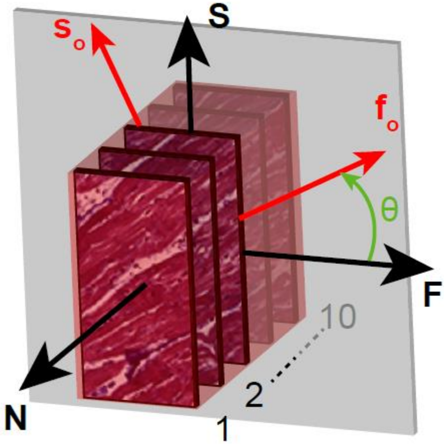


- Linear mixed model
- Anisotropy, tension-compression nonlinearity
- Negative Poynting effect

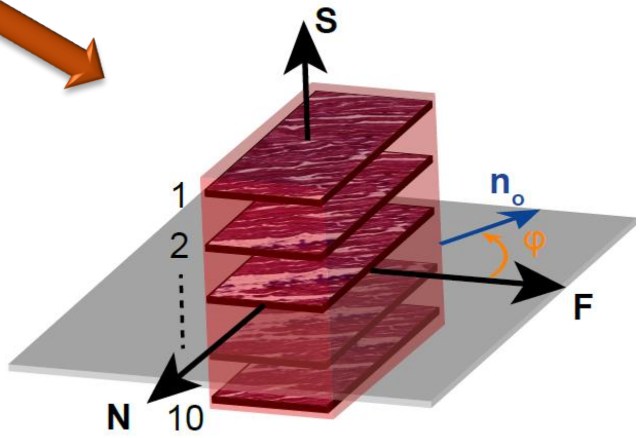
Histology



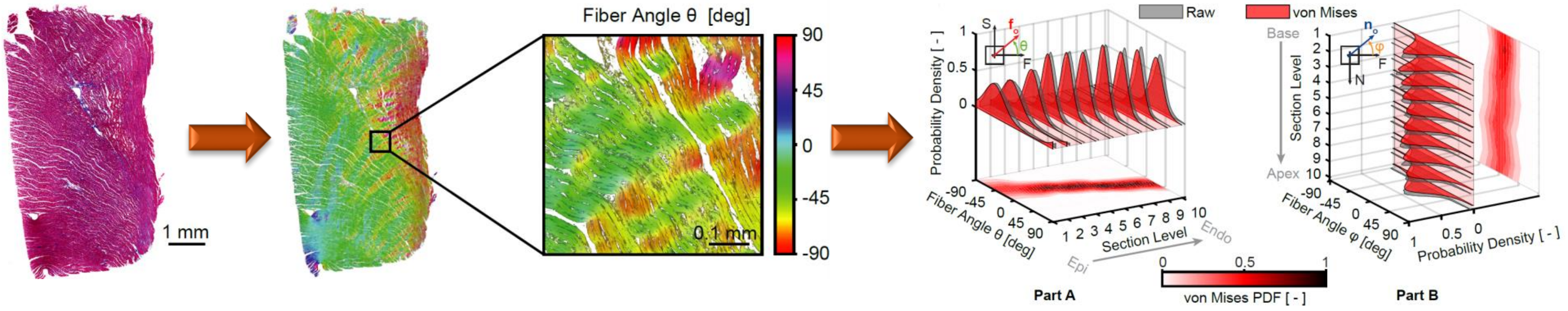
Epicardium to Endocardium Sections



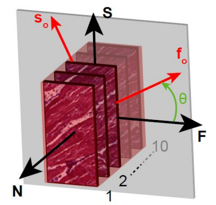
Base to Apex Sections

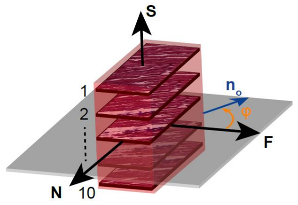


Fiber Orientation

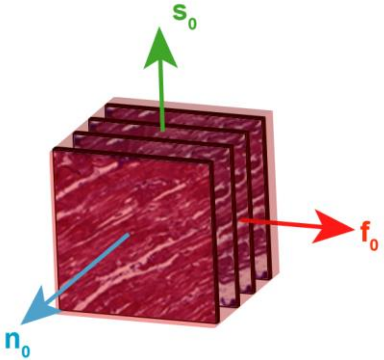


- High resolution images of histology slides
- Directional image analysis (ImageJ / OrientationJ)
- π-periodic von Mises distributions of fiber orientation angles at each section level





Holzapfel-Ogden Model



Right ventricular myocardium exhibited:

- Nonlinear response
- Anisotropic behavior
- Heterogeneous properties.

Structurally based constitutive model by Holzapfel & Ogden (2009):

$$W = \frac{a}{2b}\left(\exp[b(I_1 - 3)] - 1\right) + \frac{a_f}{2b_f}\left(\exp\left[b_f\left(I_{4f} - 1\right)^2\right] - 1\right) + \frac{a_s}{2b_s}\left(\exp[b_s(I_{4s} - 1)^2] - 1\right) + \frac{a_{fs}}{2b_{fs}}\left(\exp[b_{fs} I_{8fs}^2] - 1\right)$$

Isotropic term (amorphous matrix) | Fiber stiffness contribution | Sheet stiffness contribution | Shear coupling (fiber-sheet interaction)

Where the anisotropic **invariants** of the deformation tensor are given by:

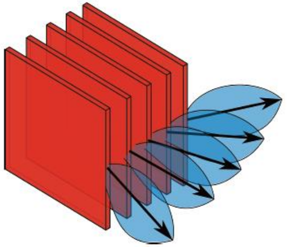
$$I_{4f} = \boldsymbol{f}_0 \cdot (\boldsymbol{C}\boldsymbol{f}_0) \qquad I_{4s} = \boldsymbol{s}_0 \cdot (\boldsymbol{C}\boldsymbol{s}_0) \qquad I_{8fs} = \boldsymbol{f}_0 \cdot (\boldsymbol{C}\boldsymbol{s}_0)$$

Include fiber dispersion

Modify strain energy to account for in-plane fiber dispersion:

$$W = \frac{a}{2b}(\exp[b(I_1-3)]-1) + \frac{a_f}{2b_f}\left(\exp\left[b_f(I_{4f}-1)^2\right]-1\right) + \frac{a_s}{2b_s}(\exp[b_s(I_{4s}-1)^2]-1) + \frac{a_{fs}}{2b_{fs}}\left(\exp\left[b_{fs}I_{8fs}^2\right]-1\right)$$

$$\int_0^{2\pi} H\left(I_{4f}-1\right)\left\{\frac{a_f}{2b_f}\left(\exp\left[b_f\left(I_{4f}-1\right)^2\right]-1\right)\right\} R(\theta)\, d\theta$$



where

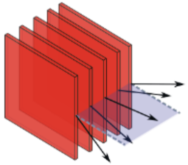
- $H\left(I_{4f}-1\right)$ the Heaviside step function to ensure fibers contribute **only under tension**
- $R(\theta)$ is π-periodic von Mises function with $R(\theta) = \frac{\exp(b\cos(2[\theta-\mu]))}{2\pi I_0(b)}$
- Angular integration approach

Hou C., Ateshian G.A. *Computer methods in biomechanics and biomedical engineering*, 2016.

Model Classes

Model Class 1

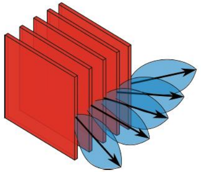
No dispersion



$$\frac{a_f}{2b_f}\left(\exp\left[b_f\left(I_{4f}-1\right)^2\right]-1\right)$$

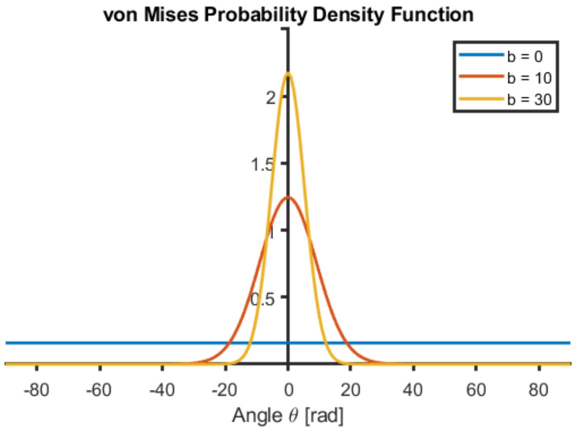
Model Class 2

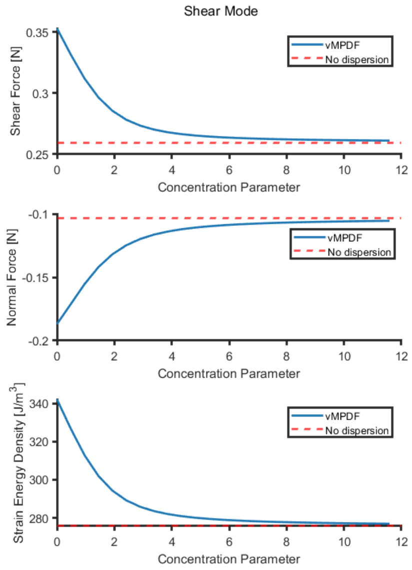
2D von Mises Distribution



$$\int_0^{2\pi} H\left(I_{4f}-1\right)\left\{\frac{a_f}{2b_f}\left(\exp\left[b_f\left(I_{4f}-1\right)^2\right]-1\right)\right\}R(\theta)\,d\theta$$

For highly concentrated fiber distributions (high concentration parameter b) the two classes are equivalent:





Incompressibility

- Decompose deformation gradient into volumetric and isochoric part:

$$\boldsymbol{F} = \left(J^{1/3}\boldsymbol{I}\right) \cdot \left(J^{-1/3}\boldsymbol{F}\right) = \boldsymbol{F_{vol}} \cdot \widetilde{\boldsymbol{F}}$$

where $\det(\boldsymbol{F_{vol}}) = J$ and $\det\left(\widetilde{\boldsymbol{F}}\right) = 1$.

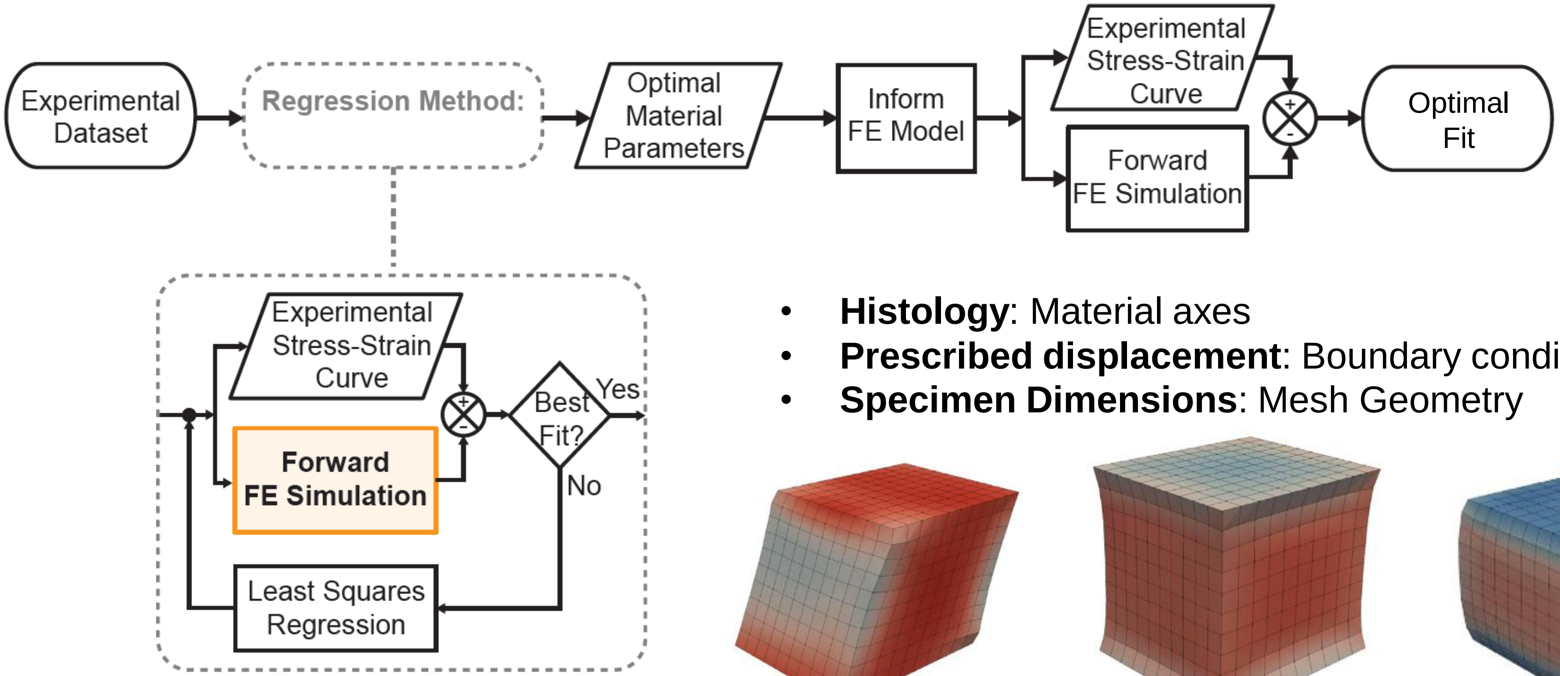
- Volumetric-Isochoric split of strain energy function

$$W(\boldsymbol{C}) = U(J) + W_{iso}\left(\widetilde{\boldsymbol{C}}\right)$$

where $U(J) = K/2\ln(J)^2$, $\widetilde{\boldsymbol{C}} = \widetilde{\boldsymbol{F}}^T\widetilde{\boldsymbol{F}}$ and W_{iso} as presented previously, by substituting the isochoric invariants

$$I_{4f} = \boldsymbol{f}_0 \cdot (\widetilde{\boldsymbol{C}}\boldsymbol{f}_0) \qquad I_{4s} = \boldsymbol{s}_0 \cdot (\widetilde{\boldsymbol{C}}\boldsymbol{s}_0) \qquad I_{8fs} = \boldsymbol{f}_0 \cdot (\widetilde{\boldsymbol{C}}\boldsymbol{s}_0)$$

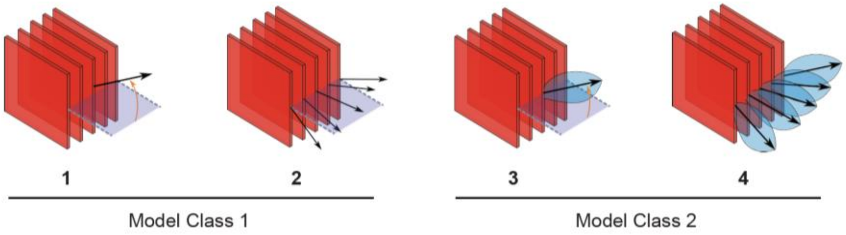
Material Parameter Estimation



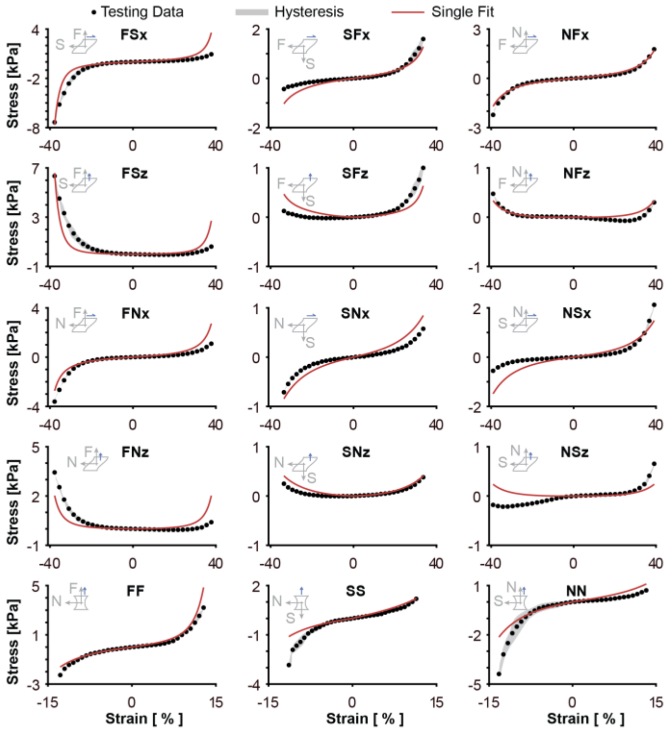
- **Histology**: Material axes
- **Prescribed displacement**: Boundary conditions
- **Specimen Dimensions**: Mesh Geometry

Material Parameter Estimation

Microstructure inclusion strategies:

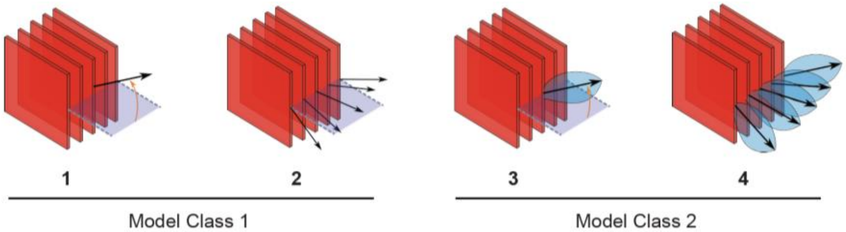


Sample	Strategy 1	2	3	4	NMSE min	max
1	1.0	3.2	10.0	9.3	0.913	0.932
2	1.0	10.0	8.4	5.8	0.852	0.901
3	6.1	4.6	10.0	1.0	0.858	0.868
4	10.0	9.9	1.0	3.0	0.636	0.734
5	10.0	9.6	9.1	1.0	0.713	0.761
6	1.0	1.2	10.0	1.3	0.750	0.765
7	1.0	9.3	4.9	10.0	0.692	0.781
8	7.1	10.0	1.0	4.7	0.642	0.683
9	1.0	4.1	3.5	10.0	0.569	0.582
10	1.0	6.0	8.7	10.0	0.799	0.893
11	10.0	9.8	1.5	1.0	0.813	0.835
Mean	4.5	7.1	6.2	5.2		
SE	1.3	1.0	1.2	1.2		



Predictive ability

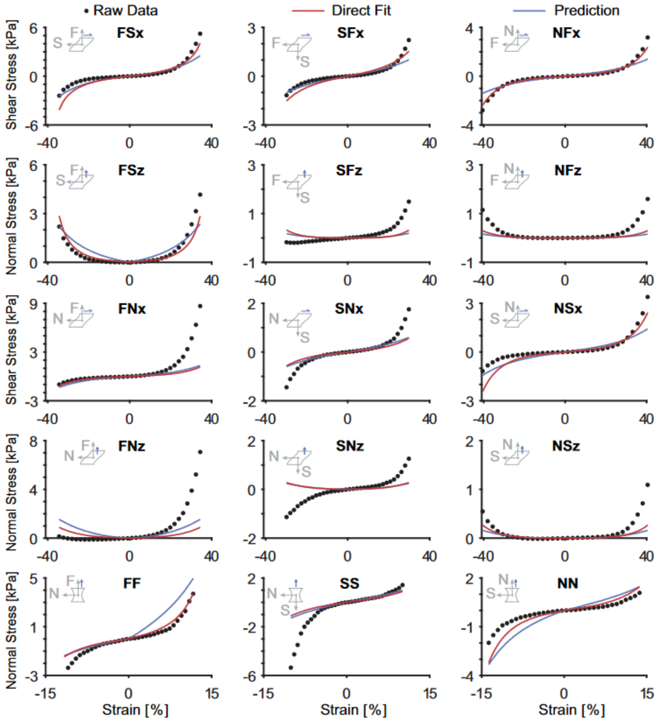
Microstructure inclusion strategies:



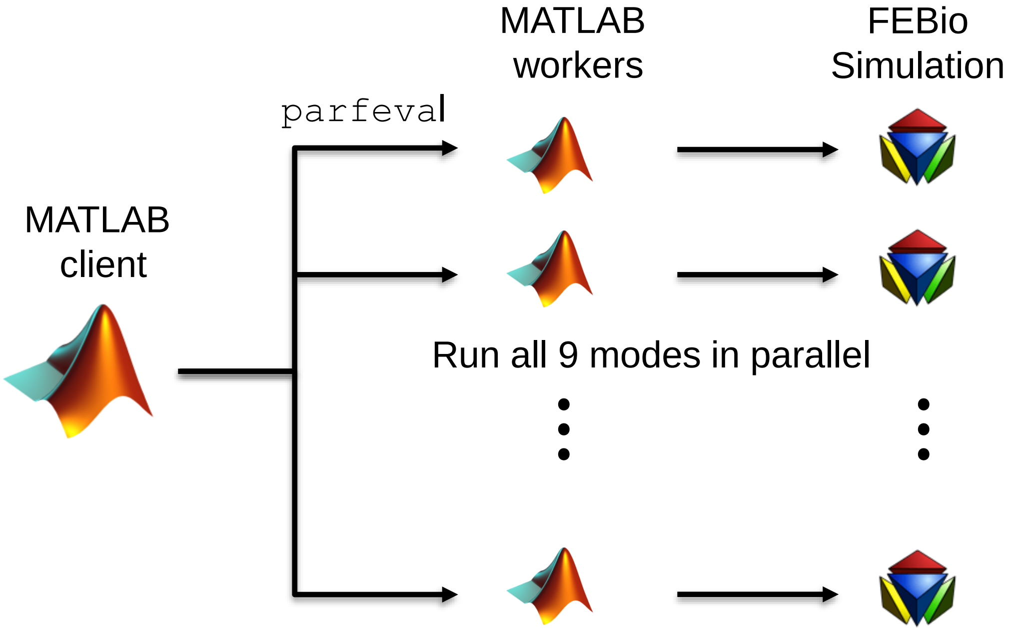
		Strategy			
		1	2	3	4
a	(Pa)	2088.75	2163.74	2176.85	2113.71
b	(–)	4.427	4.239	4.200	4.319
a_f	(Pa)	4254.81	3847.00	5402.66	6595.44
b_f	(–)	5.027	10.794	7.174	4.340
a_s	(Pa)	966.50	634.37	78.53	0.82
b_s	(–)	0.0	0.002	0.110	0.004
a_{fs}	(Pa)	1152.72	1119.13	0.0	393.86
b_{fs}	(–)	9.149	1.263	0.0	1.154
Direct Fit NMSE		0.569	0.573	0.572	0.582
Prediction NMSE		0.500	0.510	0.512	0.515

Predictive power

Microstructure inclusion complexity



Practical Aspects



	Element Type	Run Time 9 modes [sec]	Run Time 9 modes [min]	Run time for 15 iterations [h]
Class 1	Linear	23.2	0.4	**0.9**
	Quad	167.8	2.8	**6.3**
Class 2	Linear	70.3	1.2	**2.6**
	Quad	184.7	3.1	**7.0**

9 modes * 9 param var. = **81 FEBio runs / iteration**

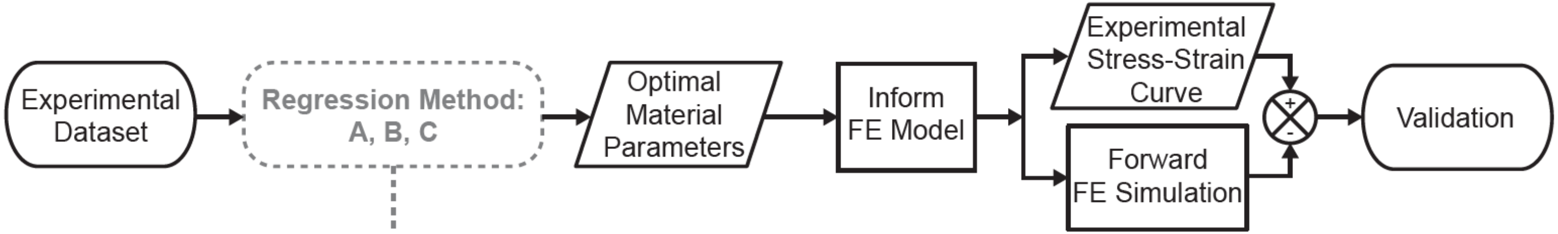
15 iter. * 81 = **1,215 FEBio runs for converged parameters**

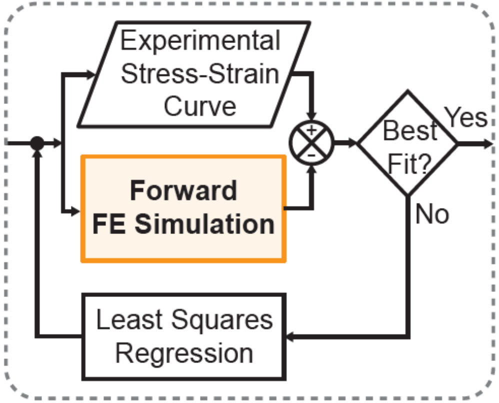
Expensive!

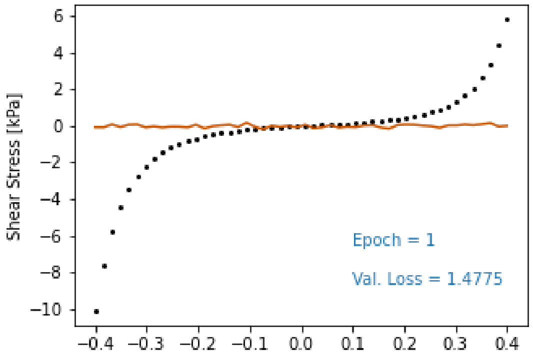
Machine Learning Approach

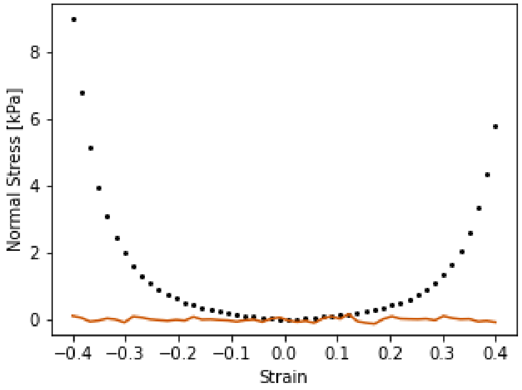
Parameter Identification

Validation





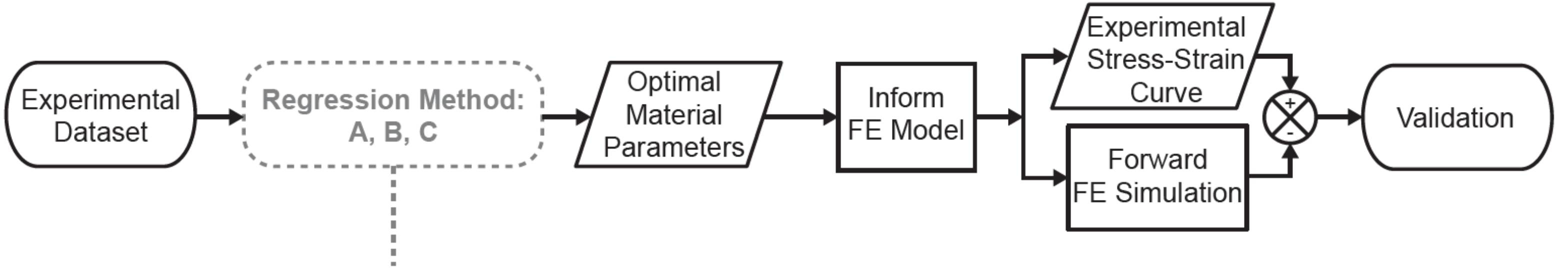


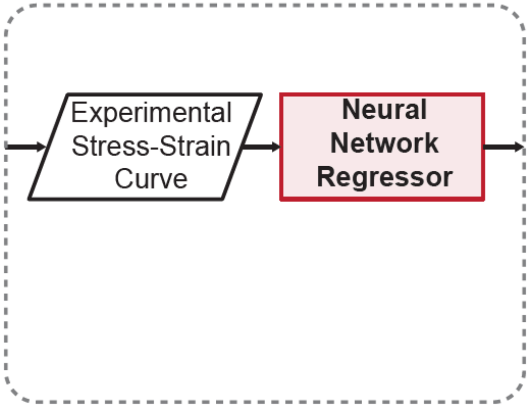


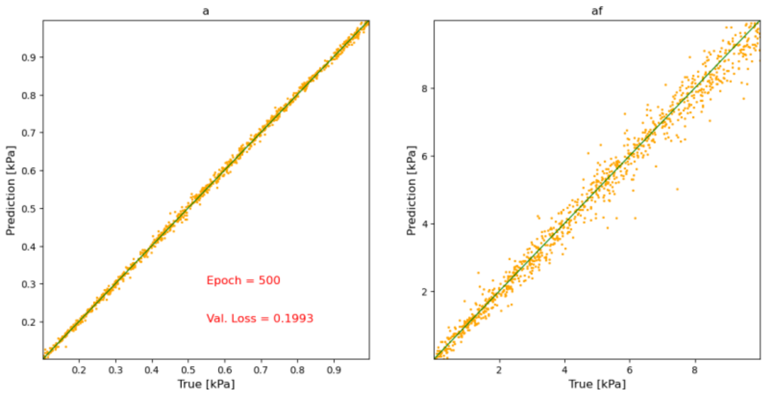
Machine Learning Approach

Parameter Identification

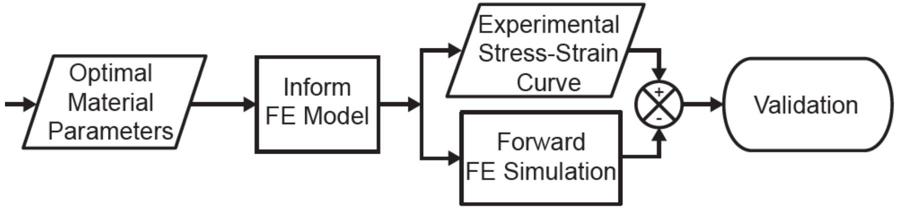
Validation



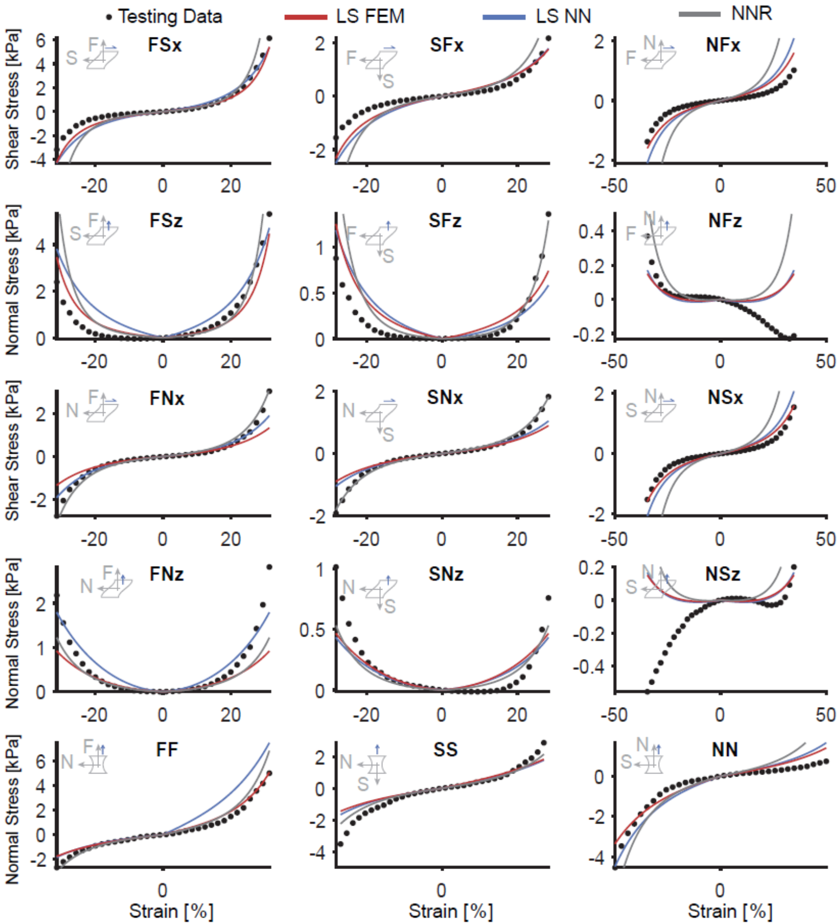




Validation



Method	a (Pa)	b (-)	af (Pa)	bf (-)	as (Pa)	bs (-)	afs (Pa)	bfs (-)	NMSE (-)	Accuracy Loss (%)
A: LS FEM	1928.4	9.29	3925.4	19.42	1592.0	0.00	1587.8	0.00	0.878	0.0
B: LS NN	2065.4	11.04	11580.1	8.72	780.1	0.03	0.1	18.59	0.758	13.7
C: NNR	2319.3	18.88	3215.9	27.24	410.0	24.20	162.8	29.96	0.275	68.7



Conclusions

- Right ventricular myocardium fibers are dispersed in the longitudinal-circumferential plane and the radial-circumferential plane, in consistency with the anisotropic, nonlinear passive response.

- The Holzapfel constitutive model can represent well the right ventricular myocardial mechanics.

- Detailed inclusion of microstructural information improves the predictive ability of the constitutive model.

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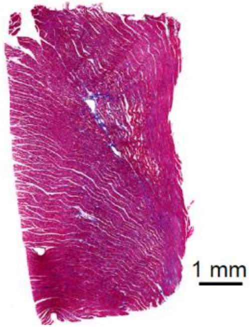
Open Data

High Resolution Histology Images



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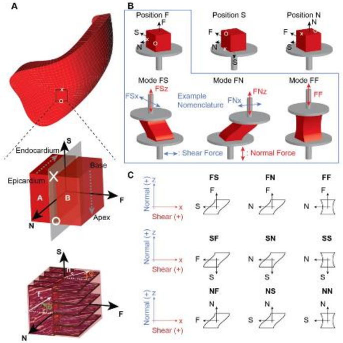
Mechanical Testing Data



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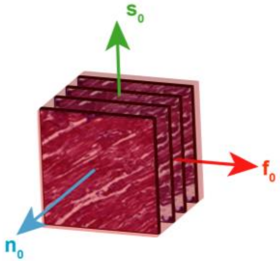
Holzapfel-Ogden FEBio material plugin



www.febio.org/plugins

Reference:

Kakaletsis, S., Meador, W.D., Mathur, M., Sugerman, G.P., Jazwiec, T., Malinowski, M., Lejeune, E., Timek, T.A. and Rausch, M.K., 2020. Right Ventricular Myocardial Mechanics: Multi-Modal Deformation, Microstructure, Modeling, and Comparison to the Left Ventricle. *Acta Biomaterialia*.

Thank you! Questions?

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Dr. Tomasz Jazwiec

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