A large-scale 3D micromechanical computational myocardium model

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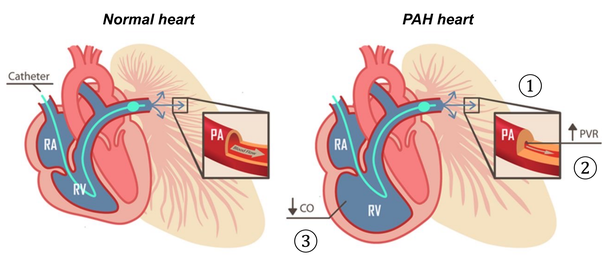
Pulmonary arterial hypertension (PAH)

PAH: Pressure overload in the right ventricle (RV) that causes maladaptive growth and remodeling of the RV free wall (RVFW) [1]

① Stenosis of pulmonary artery (PA)
② Increased pulmonary vascular resistance (PVR)

PAH negatively impacts cardiac function via ventricular dysfunction and reduction in cardiac output (CO) ③

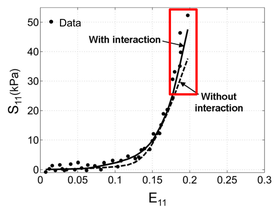


Modeling RVFW mechanical behavior

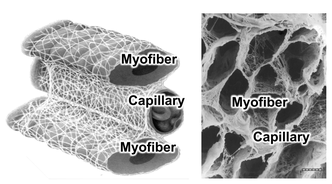
Computational modeling of RVFW mechanics: Allows for investigation of factors influencing onset, progression, and reversibility of post-PAH remodeling

Myofiber-collagen interaction: Modeling interaction is necessary to fully describe RVFW mechanical properties, hypothesized to arise from network of collagen fibers at the microanatomical scale

Modeling biaxial mechanical response [2]

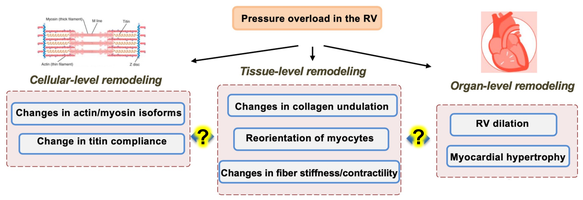


Myofiber-collagen microanatomy [3]



Challenge

Improved knowledge of myofiber-collagen interaction is required to link between multiscale adaptations in PAH



Objective

Develop a high-fidelity micromechanical myocardium model to elucidate the role of myofiber-collagen microanatomy

Finite element model of representative tissue element (RTE)

Finite element (FE) model generation: Semi-automatic segmentation approaches used to reconstruct myocytes, coronary vessels, fibroblasts, and extracellular space in confocal microscopy dataset of rabbit myocardium [4]

Tetrahedral mesh of 1.1x10^6 elements constructed from "myofiber" and combined "extracellular matrix" (ECM) phase

Compression-free mounting and imaging

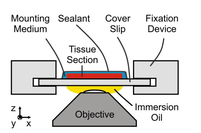
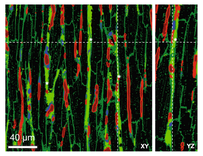
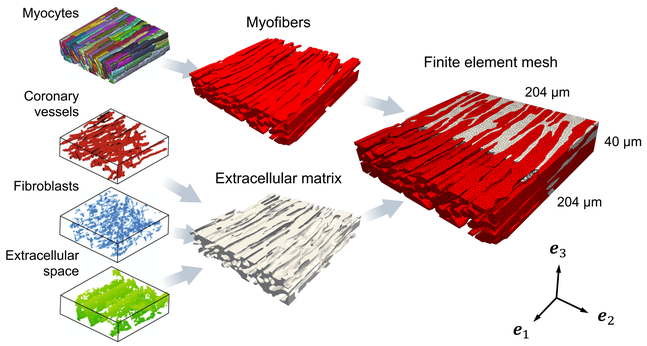


Image segmentation [4]

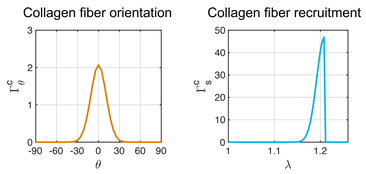


Two-phase RTE FE model



Constitutive modeling: Myofibers and ECM modeled with hyperelastic, anisotropic constitutive forms (ψ_{myo}, ψ_{ECM})

Collagen fibers in ECM distributed by Γ_θ^c and are recruited gradually via Γ_s^c when stretched beyond their slack stretch



Myofibers

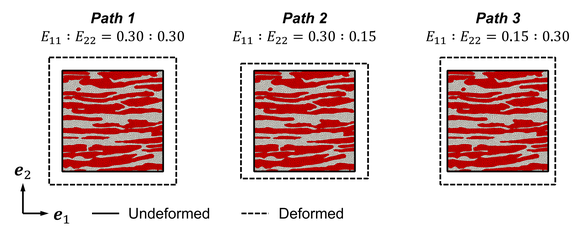
$$\psi_{\text{myo}} = \frac{a}{2b}\{\exp[b(I_1-3)]-1\} + \frac{a_f}{2b_f}\{\exp[b_f(I_{4f}-1)^2]-1\}$$

ECM

$$\psi_{\text{ECM}} = \frac{\mu_{\text{col}}}{2}(I_1-3) + \frac{\eta_{\text{col}}}{2}\int_\theta \Gamma_\theta^c(\theta)\int_1^{\lambda_\theta}\Gamma_s^c(\lambda_s)\left(\frac{\lambda_\theta}{\lambda_s}-1\right)^2 \mathrm{d}\lambda_s \mathrm{d}\theta$$

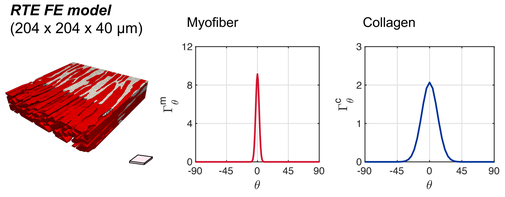
Planar biaxial simulations: Equibiaxial (1) and non-equibiaxial (2,3) deformations, assuming perfect bonding

Simulations performed on Stampede2 supercomputer at the Texas Advanced Computing Center



Connecting RTE-level and tissue-level mechanics

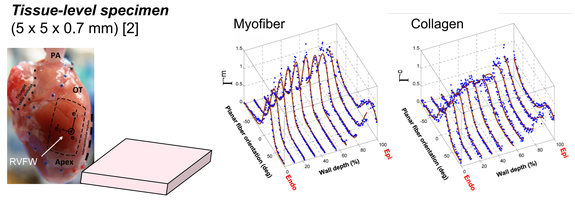
RTE FE model (204 x 204 x 40 μm)



Top-down

Bottom-up

Tissue-level specimen (5 x 5 x 0.7 mm) [2]



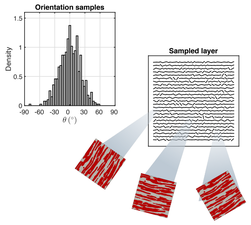
Top-down model: Derived from previous tissue-level model (Avazmohammadi et al. [2]), specialized for highly aligned (~3° splay) RTE fiber orientation distributions (Γ_θ^m, Γ_θ^c)

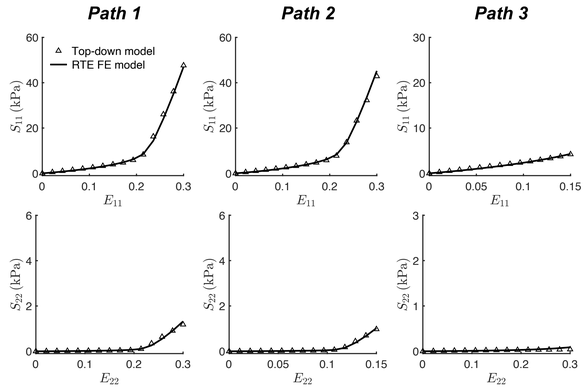
RTE FE model successfully fitted stress-strain predictions of top-down model under biaxial loading

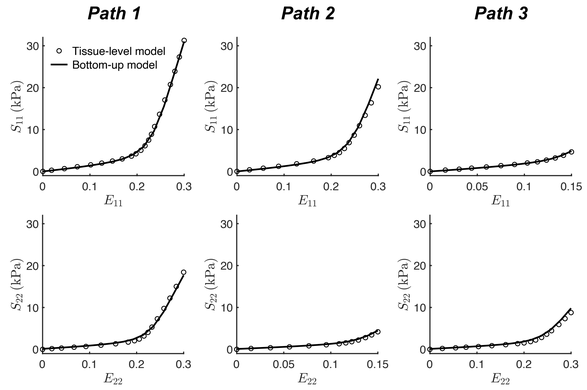
a (kPa)	b	a_f (kPa)	b_f	μ_{col} (kPa)	η_{col} (MPa)	σ^c (deg)	λ_{ub}	σ_s
0.0565	1.59	8.94	1.59	0.01	4.11	13.2	1.209	0.017

Bottom-up model: Represented bulk tissue behavior as effective response of ~10^4 rotated RTE model stress-strain responses

Reproduced previously predicted tissue-level model (~20° splay) in all biaxial responses [2]







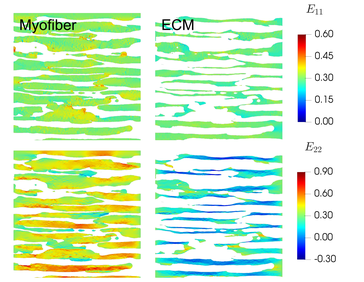
Summary & Ongoing Work

Key findings

Micromechanical myocardium model recapitulates RVFW mechanics top-down and bottom-up to link the tissue and sub-tissue scales

Cardiac microanatomy drives myofiber-collagen interactions essential in myocardial behavior

Ongoing Work: Compute stress-strain profiles at the sub-tissue scale to quantify the myocardium micro-environment in normal and diseased conditions



Acknowledgments & References

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[3] Macchiarelli, G et al., Histol Histopathol, 17(3):699-706, 2002.
[4] Seidel, T et al., Ann Biomed Eng, 44(5):1436-1448, 2016.