Center for Cardiovascular Simulation

The Institute for Computational Engineering & Sciences

Department of Biomedical Engineering

The University of Texas at Austin

The University of Texas at Austin
Biomedical Engineering
Cockrell School of Engineering

The University of Texas at Austin
201 E 24th St, Austin, TX 78712

Phone: 512-232-5784 **Fax:** 512-471-8694
www.ices.utexas.edu

Center for Cardiovascular Simulation

Mission

The overarching goal of the Center for Cardiovascular Simulation (CCS) is to provide cardiovascular scientists and clinicians with advanced simulations for the rational development of treatments for cardiovascular disease. Such simulations can ultimately lead to reduction in development time, lowering of morbidity and mortality, reduced re-operative rates, and lessened post-operative recovery time. Our specific research focus is the simulation of the biomechanical function of the cardiovascular system at the continuum-cellular, micro-fibrous tissue, and whole organ levels. To achieve this, we utilize integrated computational/experimental approaches that incorporate the latest bio-mechanical/biomedical data and mechanobiological information to develop an improved understanding of pathophysiology. Fundamental to our approach is the development and implementation of novel simulation technologies that exploit advances in computational methods to reduce the current trial-and-error approaches. Ultimately, we hope to develop simulation tools that will provide detailed dynamic information on disease progress and allow for "what-if" scenarios to physicians and biomedical engineers to devise new interventions. The development and use of these tools in the context of patient-specific models will ultimately also allow clinicians to craft cardiovascular therapies that are optimized for the cardiovascular system of individuals, with a resulting increase in success and decrease in risk of adverse side effects.

About Our Director

Dr. Michael Sacks is professor of biomedical engineering and holder of the W.A. "Tex" Moncrief Jr. Simulation-Based Engineering Science Chair I. He earned his B.S. and M.S. in engineering mechanics from Michigan State University, and his Ph.D. in biomedical engineering (biomechanics) from The University of Texas Southwestern Medical Center at Dallas. Dr. Sacks' fellowships include: Fellow of the American Heart Association, Royal Academy of Engineering Distinguished Visitor Fellowship, and Elected Fellow of the Biomedical Engineering Society. His awards include: Van C. Mow Medal in Bioengineering from ASME, one of the Scientific American Top 50 scientists, and the ICES Moncrief Grand Challenge Faculty Awardee.

Affiliated Faculty

Institute for Computational Engineering & Sciences

Dr. H. Kent Beasley	Cardiologist
Dr. Omar Ghattas	Professor
Dr. Thomas J.R. Hughes	Professor
Dr. Greg Rodin	Professor

Biomedical Engineering

Dr. Aaron Baker	Assistant Professor
Dr. James Tunnell	Associate Professor
Dr. Mia Markey	Professor

Aerospace Engineering

Dr. Nanshu Lu	Assistant Professor
Dr. Krishnaswamy Ravi-Chandar	Professor

Research Staff

Dr. Andrew Drach	Research Associate
Dr. João Soares	Research Associate
Dr. Reza Avazmohammadi Ruth L. Kirschstein Individual F32 Postdoctoral Fellow	Research Associate
Dr. Rana Zakerzadeh ICES Postdoctoral Fellow	Postdoctoral Fellow

Graduate Students

Salma Ayoub
Will Goth
Amir Khalighi
Alex Khang
David Li
Sam Potter
Bruno Rego
Will Zhang

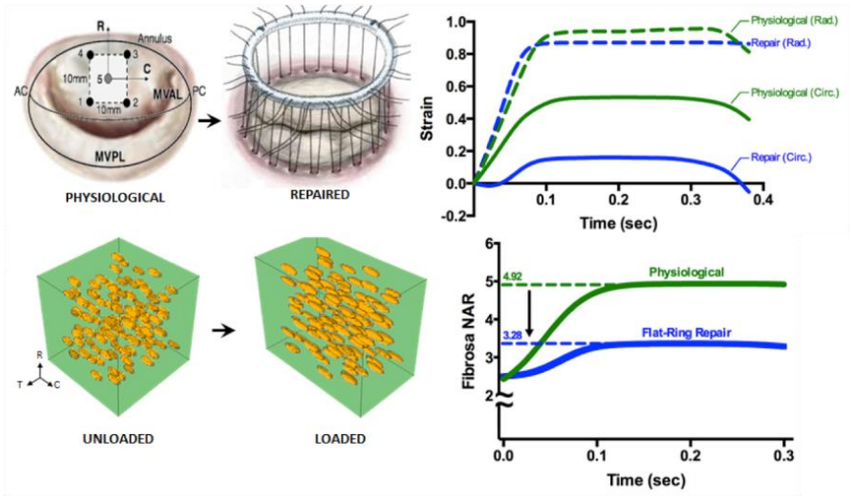
Regulation of Valve Interstitial Cell Homeostasis by Mechanical Deformation: Implications for Heart Valve Disease and Surgical Repair

Chung-Hao Lee
Univ. of Oklahoma

Giovanni Ferrari
Univ. of Pennsylvania

Salma Ayoub
CCS

Mechanical stress is one of the main etiological factors of heart valve surgical repair failure. Stress-induced changes in valve interstitial cell (VIC) function affect long-term tissue structure and function. To link VIC strain-sensitive behavior to the organ-level *in vivo* state of the valve, we use an integrated experimental-computational approach. We employ a load-sensing tissue strip bioreactor to simulate valve tissue at different strain levels and a macro-micro finite element model to predict *in vivo* mitral VIC (MVIC) deformation. This integrated approach allows us to report an array of VIC deformations that capture both physiological behavior as well as deviations from homeostatic response induced by surgical repair. Taken together, our findings identify cellular deformation as a key player in cell-based remodeling and valve tissue homeostatic regulation after abnormal mechanical stimuli imposed by valvular disease and surgical repair.



Facilities

Computational Engineering Laboratory (CEL)

Institute for Computational Engineering & Sciences

Located in the Peter O'Donnell Building (POB), the CEL provides graduate students with state-of-the-art computers loaded with our own custom brew of open source and personally developed code. The building has a 196-seat auditorium providing wireless networking, video conferencing, and remote learning capabilities. There are 18 networked seminar rooms with high-resolution audiovisual systems.

Peter O'Donnell Building (POB)

Biomechanics Experimental Laboratory (BEL)

Department of Biomedical Engineering

Located in the Biomedical Engineering Building (BME), the BEL is a 1,294 ft^2 wet laboratory that houses specialized devices for mechanical and structural evaluation of biological tissues and biomaterials. The building has multiple seminar rooms for events such as research symposiums, presentations, receptions, meetings, etc.

Biomedical Engineering Building (BME)

Current Research Projects

In silico Heart Modeling

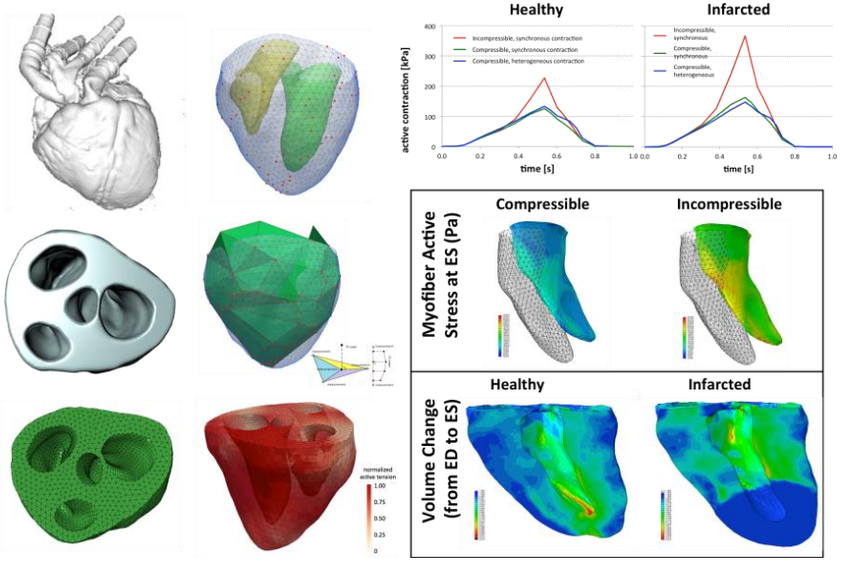
João Soares
CCS

David Li
CCS

Reza Avazmohammadi
CCS

Joshua Chen
Univ. of Texas at Austin

We are developing physiologically realistic 3D finite element models of the heart to study processes associated with cardiac function in health and disease. A computational platform is valuable to understand heart remodeling in myocardial infarction (MI) and its impact on organ-level function. We have developed an *in silico* model of MI based on extensive datasets from a single ovine heart and simulate the ovine model of MI. Magnetic resonance imaging (MRI) and diffusion tensor MRI (DT-MRI), Fung-based hyperelastic material models, and epicardial electrical activity are used to assemble the model geometry and drive its passive and active mechanics. Pressure-volume data measured through catheterization and sonomicrometry is used to fit the modulation of active contraction, and 2D echocardiography provides qualitative validation for the simulated deformations of the organ-level model.



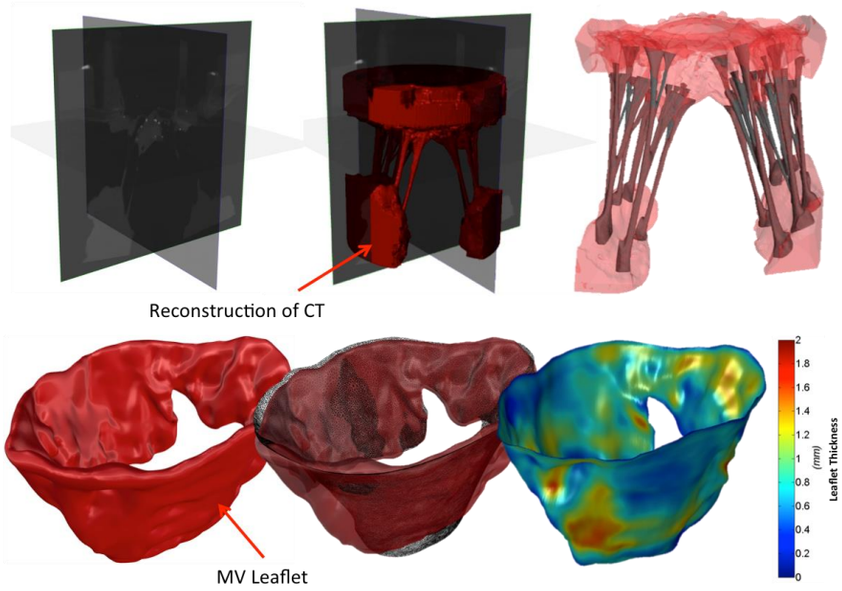
Geometrical Characterization of the Mitral Valve

Andrew Drach
CCS

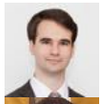
Bruno Rego
CCS

Amir Khalighi
CCS

We have developed a pipeline to quantitatively characterize the mitral valve (MV) leaflet geometry and build personalized models with an adjustable level of detail. While the MV leaflet geometry has been extensively studied, little quantitative geometric information exists on the MV chordae tendineae (CT), fibrous tendon-like structures projecting from the papillary muscles to the leaflets. We are performing a novel investigation of MV CT geometry to quantify their intricate anatomy. Our findings indicate that the chordal structure is sufficiently consistent to develop population-based computational models of the MV for improving the valve repair procedures and novel treatment strategies. The new approach allows us to build predictive biomechanical models of MV with an adjustable level of detail for geometric and attribute features.



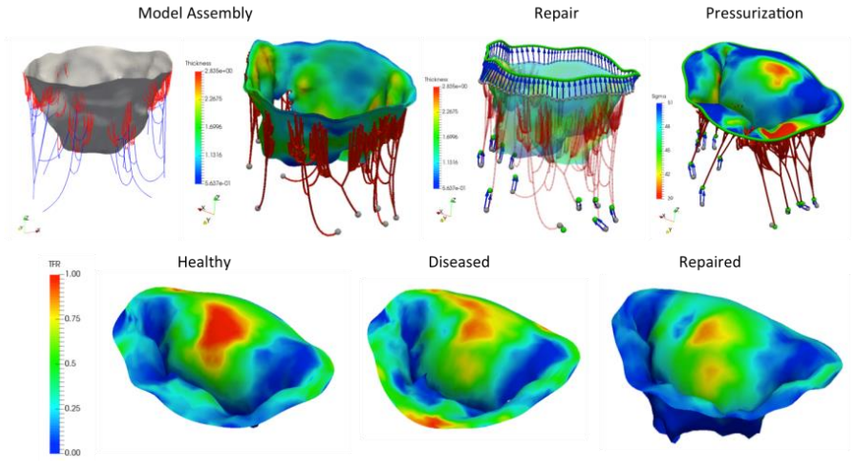
Biomechanical Simulation of the Mitral Valve


Andrew Drach
CCS


Amir Khalighi
CCS


Bruno Rego
CCS

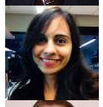
Simulations of the biomechanical behavior of the Mitral Valve (MV) have proven to effectively predict the valvular biomechanical behavior and design of valvular prosthesis. However, due to the complexity of MV structure, computational models are still struggling to account for all the underlying factors that impact the MV response to repair. Most standard biomechanical models of the MV have relied on suboptimally reconstructed geometric models. In the current study, we have developed a pipeline based on the robust methodology to convert imaging data into the attribute-rich finite element models in order to quantitatively characterize the MV leaflet geometry, build personalized models with an adjustable level of detail, and incorporate structural attributes within the geometric models. Anatomical variations are studied in the context of the multi-scale morphable geometric model, which allows for building the representative (population-averaged) models. Repair strategies are simulated using the patient-specific and population-averaged models.



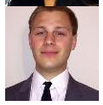
Coupled Fluid-Structure Interaction and Fatigue Damage Modeling of Bioprosthetic Heart Valves


Keefe Manning
Pennsylvania State Univ.

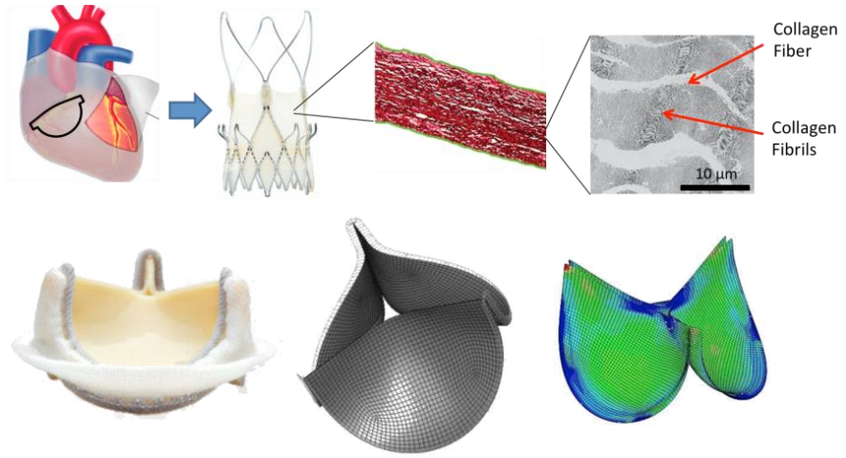

Ming-Chen Hsu
Iowa State Univ.


Rana Zakerzadeh
CCS


Will Zhang
CCS


Sam Potter
CCS

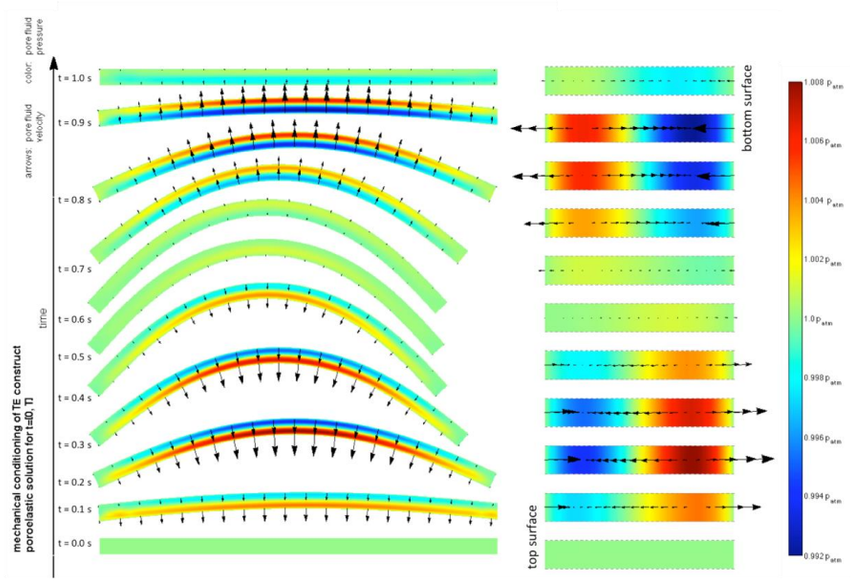
Replacement heart valves fabricated from biologically derived materials, referred to as bioprosthetic heart valves (BHVs), have provided great benefits for many patients. However, leaflet structural deterioration mediated by fatigue and/or tissue mineralization continues to drive device failure. We are developing a computational framework suitable for integrating the fluid-structure interaction (FSI) analysis of novel BHV fatigue damage models (FDM) to predict BHV performance. This coupled FSI-FDM framework allows us to handle the coupling of complex fluid flows, large structural deformations, contact problems, and geometric variability for many millions of cycles. We simulate the BHV fatigue process in the accelerated wear test environment and quantitatively compare the results with matched experimental validation studies.



Modeling Growth, Development, and Interaction of Scaffold-*de novo* Engineered Tissue

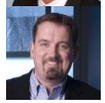
João Soares
CCS

Mechanical conditioning enhances engineered tissue growth and development, and optimal levels of dynamic conditioning can be exploited to augment mechanical behavior in smooth muscle cell-seeded elastomeric scaffolds. We develop novel models to describe the improvement of dense connective tissue formation in triphasic mixtures composed of nutrient, cells, and extracellular matrix (ECM). Strain-energy structural modeling approaches allow the separation of the fibrous structure and its intrinsic mechanical properties for better interpretation and insight of the underlying characteristics of the *de novo* ECM collagenous network. Our models are able to differentiate the ECM growth observed in smooth muscle cell-seeded scaffolds under static and flexure training regimes, and subsequently, allow the *in silico* exploration of the impact of different training regimes.



Integrated Numerical-experimental Framework for Investigating Tissue-scale 3D Mechanical Properties of Myocardium

Robert Gorman
Univ. of Pennsylvania



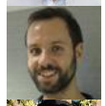
Jason Burdick
Univ. of Pennsylvania

Reza Avazmohammadi
CCS

David Li
CCS

Joseph Gorman
Univ. of Pennsylvania

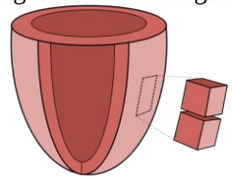
Edward Hsu
Univ. of Utah

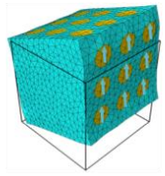


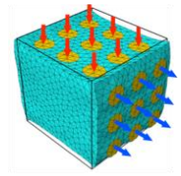
João Soares
CCS

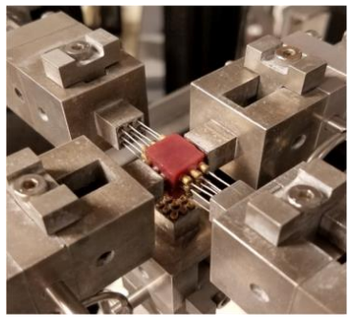
Joshua Chen
Univ. of Texas at Austin

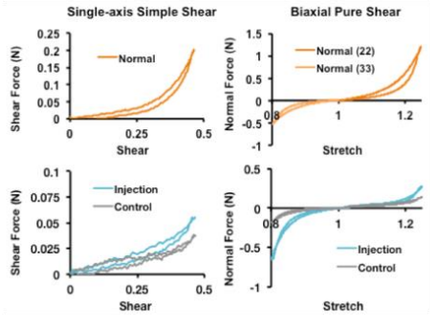
Characterizing the structural and mechanical properties of cardiac tissue is critical toward understanding heart function, improving virtual surgery technologies, and guiding medical device development. Myocardium anisotropy and nonlinearity require the use of a comprehensive three-dimensional stress-strain formulation in order for its mechanical properties to be fully captured. We have developed an innovative integrated numerical-experimental methodology to investigate the mechanical behavior of ovine myocardium, which serves as a basis for more robust mechanical models of myocardium to aid in effectively evaluating treatment strategies for cardiac disease.









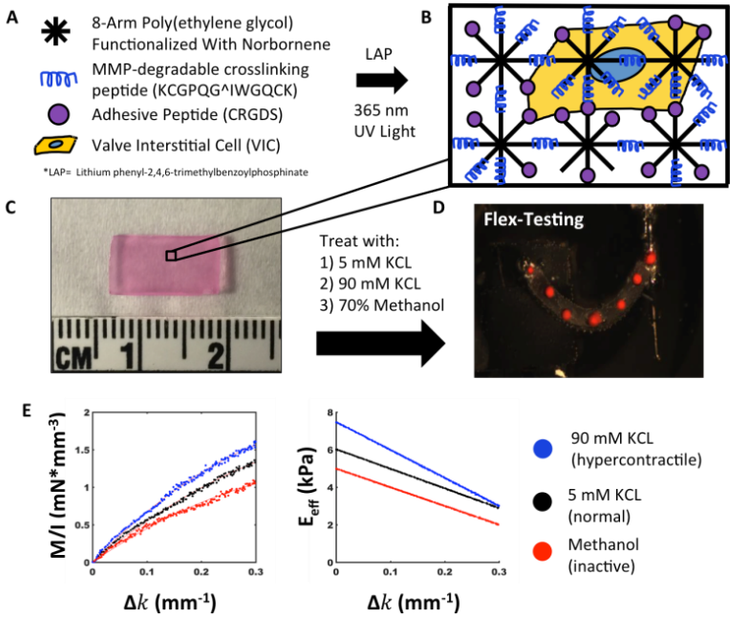


Mechanobiology of Valve Interstitial Cells Within a Poly(ethylene glycol) Hydrogel Environment

Kristi Anseth
Univ. of Colorado at Boulder

Alex Khang
CCS

The aortic valve is comprised of three distinct layers (fibrosa, ventricularis, spongiosa), which contain valve interstitial cells (VICs) that maintain the extracellular matrix (ECM). VICs are dynamic with respect to phenotype and have fibroblast-like characteristics when healthy (quiescent). In diseased or injured valves, VICs switch to a myofibroblast-like phenotype (activated) and become contractile. 3D hydrogel encapsulation is an increasingly popular technique for studying VICs. A need still exists for the investigation of VIC mechanics within 3D hydrogels. We employ poly(ethylene glycol) (PEG) gels for VIC encapsulation to study their mechanical response to the surrounding hydrogel stiffness and to varying levels of adhesion. Cell contraction is elicited through chemical treatments and the resulting mechanical properties of the constructs are measured by end-loading flexural deformation testing.



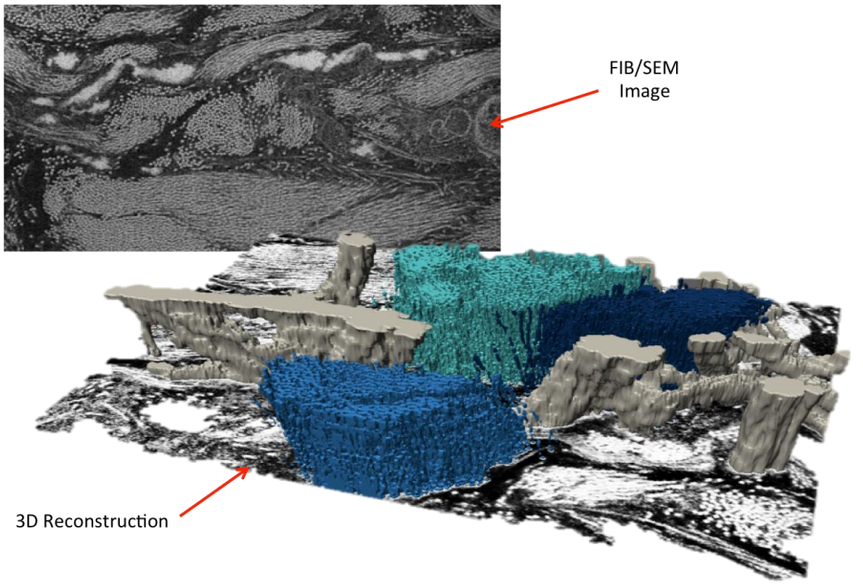
Three-Dimensional Microenvironment of Valve Interstitial Cells

Salma Ayoub
CCS

Amir Khalighi
CCS

Karen Tsai
Los Alamos Natl. Laboratory

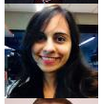
Valve interstitial cells (VICs) are important in valve tissue homeostasis and pathophysiology: they maintain the structural integrity of the leaflet via protein synthesis and enzymatic degradation of extracellular matrix (ECM) components. While cell phenotype and ECM regulation under physiological stress have been previously studied, little attention has been paid to the VIC microenvironment. Our goal is to fully characterize the 3D microenvironment of VICs and identify major changes that occur in the cell microenvironment under physiological loads using a biaxial bioreactor and focused ion beam scanning electron microscopy (FIB/SEM). This study highlights the previously unrecognized complexity of the interconnection between VICs and ECM fiber networks and enables us to develop more structurally accurate computational models that incorporate the heterogeneities of the VIC microenvironment.



Simulating the Response of Bioprosthetic Heart Valves to Long Term Cyclic Loading

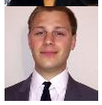
Keefe Manning
Pennsylvania State Univ.

Ming-Chen Hsu
Iowa State Univ.



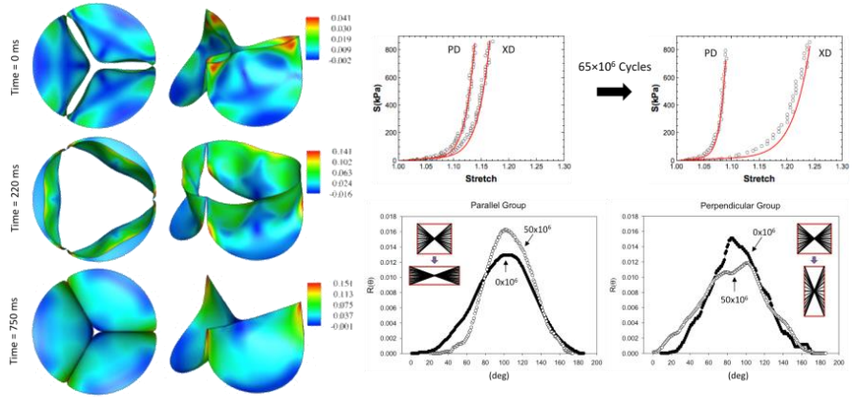
Rana Zakerzadeh
CCS

Will Zhang
CCS



Sam Potter
CCS

Understanding the underlying mechanisms associated with failure of bioprosthetic heart valves (BHVs) is a crucial part of being able to predict the durability of different BHV design. BHVs undergo the greatest change in geometry in the first 2-3 years (50-70 million heart cycles) after implantation, due to a phenomenon known as permanent set (PS). PS is a result of the scission healing of the glutaraldehyde crosslinker, which allows for recrosslinking of the extracellular matrix in the BHV leaflets. We are developing constitutive models for the exogenously crosslinked tissue and the PS process using a mixture approach based on the reference state evolution of the material subcomponents. This approach splits the material into many different parts, where the reference state of each part is changed over time systematically based on the strain history applied to the tissue. We seek to construct computational simulations using real BHV geometries to predict the effect of PS on BHVs and evaluate different geometrical and material designs, paving the path to simulating BHV damage and failure in the future.



Computational Modeling of Adaptive Remodeling of the Right Ventricle

Richard Dixon
Texas Heart Institute

Reza Avazmohammadi
CCS

Right ventricular (RV) failure is a major cause of mortality for patients suffering from pulmonary arterial hypertension (PAH). PAH imposes a pressure overload on the right ventricular free wall (RVFW) leading to elevated transmural wall stress, which ultimately results in mechanical failure of the right heart. Relatively little is known about the structural and mechanical alterations of the RVFW during PAH and its relation to the changes in RV function. Our objective is to improve our understanding of how the RV adapts to PAH disease at fiber, tissue and organ levels, and to develop a computational model that predicts these adaptations. We use a simple biventricular model of the heart, together with a structurally based constitutive model for RVFW, to estimate *in vivo* values of the RV wall stress components and investigate how the wall stress regulates the structural changes during PAH. We then implement novel microstructure-based hypertrophy and remodeling laws into a 3D image-based biventricular model of rat to build a complete animal-specific computational model. The outcome of this study will help to identify of key remodeling mechanisms through which pulmonary hypertension leads to adverse clinical outcomes, and thus help to alleviate therapeutic complications.