A Simulation of Heart Valve Interstitial Cell Contractile Behavior in 3D Gels

Xinzeng Feng[1], Alex Khang[1,2], Jake Sansom[3], Nicholas West[3], David Ilitzky[4], Nicholas Aufiero[5], Emma Lejeune[6], Michael Sacks[1,2]

[1]James T. Willerson Center for Cardiovascular Modeling & Simulation, The University of Texas at Austin, Austin, TX, USA

[2]The Department of Biomedical Engineering, The University of Texas at Austin, Austin, TX, USA

[3]The Department of Aerospace Engineering and Engineering Mechanics, The University of Texas at Austin, Austin, TX, USA

[4]The Department of Computational Chemistry and the Department of Applied Mathematics, The University of Texas at Austin, Austin, TX, USA

[5]The Department of Computational Engineering, The University of Texas at Austin, Austin, TX, USA

[6]The Department of Mechanical Engineering, Boston University, Boston, MA, USA

Introduction: Valvular interstitial cells (VICs) are responsible for maintaining heart valve tissues through their biosynthetic behaviors, which are closely related to their contractile properties. To understand the contractile behavior of VICs, our group has previously developed a computational biomechanical VIC model based on the solid-mixture theory [1]. To extend the work, in this study we aim to 1) simulate VIC contractile behavior based on real cell geometry, and 2) investigate the effects of the spatial distribution of stress fibers and contraction strength on gel deformation, both informed by the single-cell 3D traction force microscopy (TFM) measurements.

Materials and Methods: In the TFM experiment, porcine aortic VICs were encapsulated in a 3D PEG hydrogel and imaged by a confocal microscope. As VIC contraction was modulated by the addition of chemical agents, the gel deformation was quantified *via* densely seeded fluorescent markers (0.5μm in diameter, density = 3×10^9 beads/ml). Using *FM-track* [2], an open-source tracking software, and a customized image analysis pipeline, we obtained the marker displacements in a 150μm×150μm×140μm volume surrounding each VIC as well as the associated cellular geometries. In the computational model, a VIC was modeled as an elastic body that actively contracts through the stress fibers. Key cellular components modeled included the (basal) cytoskeleton, cell nucleus, considered as homogeneous hyper-elastic materials, and stress fibers, which can either deform as passive elastic or actively contracting structures. The PEG gel was modeled as a neo-Hookean functionally graded material with spatially varying material properties. Given the measured marker displacements, we first estimated the distribution of PEG material properties assuming a nodal mapping between the cell surfaces at different contraction states. With the PEG material properties, the contraction strength of stress fibers was then optimized considering full VIC-PEG interaction wherein the distribution of stress fibers at the non-contractile state was constructed according to VIC shapes.

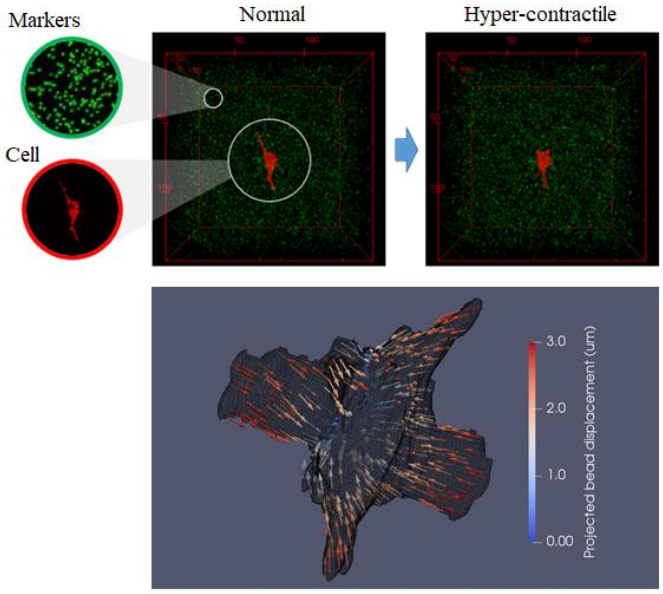

Figure 1 Top: Marker and cell positions at the normal and hyper-contractile states. Bottom: projected marker displacements on the surface of the VIC suggesting cell contraction between the states.

Results and Discussion: Our results indicated that the VIC-PEG model can effectively explain the TFM data. Additionally, higher VIC contraction strength was observed compared to previously reported experiments such as micropipette aspiration and atomic force microscopy in which the VICs were not in a fully 3D gel environment.

Conclusions: This study extended our previous work by calibrating the VIC model in real cell geometry against 3D TFM data, allowing us to better understand VIC contractile behavior in 3D.

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References:

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