**2018 IMAG Futures Meeting – Moving Forward with the MSM Consortium (March 21-22, 2018)**

*Pre-Meeting Abstract Submission Form*

*\*Please submit to the NIBIB IMAG mailbox (*NIBIBimag@mail.nih.gov*) by* ***January 8th, 2018***

*\*Save your abstract as “MSM PI Last Name \_ 2018 IMAG Futures Pre-Meeting Abstract”*

**PI(s) of MSM U01: Jay D. Humphrey and George Em Karniadakis**

**Institution(s): Yale University and Brown University**

**MSM U01 Grant Number: U01 HL116323**

**Title of Grant:** Multiscale Multiphysics Model of Thrombus Biomechanics in Aortic Dissection

**Abstract**

Which MSM challenges are you addressing from the IMAG 2009 Report and how?

<https://www.imagwiki.nibib.nih.gov/content/2009-imag-futures-report-challenges>

(indicate which challenge (#) you’re addressing)

*You may insert images by copying and pasting below*

First, and foremost (challenges #6 and #9), this project has developed a strong experimental-computational coupling. Our experimental data have driven computational model development; our models have motivated the development of new experimental methods. A key example is our melding of in vivo ultrasound, in vitro optical coherence tomography, and co-registered histology to build improved computational domains for models of blood flow within murine aortic dissections in order to predict thrombus formation using both continuum and particle-based methods. We had not envisioned this multimodal experimental approach until the computational model demanded higher precision in defining the computational domain. We have similarly melded a novel panoramic digitial image correlation method to measure surface strains, an optical coherence tomography system to measure volumetric strains, and co-registered histology to build models of the aortic wall, again both standard continuum and particle based, to model the dissection process. It was the inverse characterization model that demanded the addition of the optical coherence tomographic data.

Second (challenge # 8), we have developed a multi-resolution continuum model for thrombus formation and deposition within either the lumen of the aorta or false lumen of an aortic dissection. This modeling required integration of standard Eulerian-based Navier-Stokes solutions and Lagrangian-based particle tracking, which together enabled calculation of two novel metrics of thrombus formation and deposition that have predicted well our available data. It is emphasized further that this approach required us to exploit high performance computing, with one result (paper) requiring 100 years of computing time that was rendered possible with parallel computing on hundreds of nodes.

Finally (challenge #5), we have recently shown that our growth and remodeling models, developed to understand vascular disease progression, can also be used in the traditionally biomechanically data-poor field of vascular tissue engineering. Indeed, we expect that our models will soon be able to be used both to design improved polymeric scaffolds for implantation and improved therapeutic procedures (to control the foreign body response).

Are you using machine learning and or causal inference methods and how?

*You may insert images by copying and pasting below*

 We are not currently using machine learning, but we feel that our worked has now evolved to a point that machine learning is appropriate. Hence, machine learning plays a prominent role in our “renewal” application that is pending.

Please briefly describe significant MSM achievements made (or expected).

*You may insert images by copying and pasting below*

 The focus of this project has been to understand better the formation of intramural thrombus in aortic dissection, with data-driven modeling aided by studies in a well accepted mouse model. Toward this end, we have progressively realized that prior methods of data collection were not sufficient for yielding the requisite data (to drive the modeling). Hence, this project has focused both on the development of new multi-modality experimental methods (noted above) and new multi-scale computational methods. The latter includes new dissipative particle dynamics (DPD) models of the aortic wall and new smoothed particle models of the wall as well as DPD models and force couple methods of platelet activation and aggregation. We are currently working to synthesize the multiphysics / multiscale models (solids, fluids, particles) and show congruency across scales.

Please suggest any new MSM challenges that should be addressed by the MSM Consortium moving forward.

*You may insert images by copying and pasting below*

 Much of classical biomechanics focuses on computation of outcomes at the current (biological) time given information on geometry, material properties, and boundary conditions. For example, how is the hemodynamic field altered in the presence of a dissection, aneurysm, or stenosis? A key future challenge of modeling in biomechanics will be to predict how the dissection, aneurysm, or stenosis actually evolves and how the hemodynamics and wall mechanics evolve in concert. Hence, there is a need to predict future outcomes, in particular how a cell, tissue, organ, or organism will respond to changes in the bio-chemo-mechanical environment over long periods. As another example, we need to be able to model how cell phenotype or extracelluar matrix organization will change during disease progression, healing in response to an injury, or even a clinical treatment. Such modeling will require knowledge of biomechanics and mechanobiology and necessarily require multiscale and multiphysics simulations; it will benefit from a fusion of physics-based and systems biology based approaches.

What expertise are on your team (e.g. engineering, math, statistics, computer science, clinical, industry) and who?

*Please list as “Expertise – Name, email”*

 *Experimental and Computational Vascular Mechanics – Jay Humphrey jay.humphrey@yale.edu, Vascular Biology and Clinical Expertise – George Tellides George.tellides@yale.edu, Applied Mathematics – George Karniadakis George\_karniadakis@brown.edu:*

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