**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](mailto: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:** Silvia Salinas Blemker and Shayn Peirce-Cottler

**Institution(s):** University of Virginia

**MSM U01 Grant Number:** 1U01AR069393

**Title of Grant:** Multi-scale Modeling for Treatment Discovery in Duchenne Muscular Dystrophy

**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*

We are addressing the following challenges:

1. Next-generation multiscale models that integrate between different scientific fields and predict integrated functions.

*We are addressing this by coupling biomechanical models and agent-based models to predict the integrated, regenerative response of muscle to injury and disease.*

1. Novel methods to fuse biological and/or behavioral processes and mechanisms to model outcomes as a result of various interventions.

*We are developing new modeling approaches, along with experimental models of muscle injury and associated tools for automated image analysis of muscle histology, to study muscle degeneration and regeneration as a result of different pharmacological interventions.*

1. Reproducible and reusable multiscale models that will be integrated and adopted into model-poor fields (e.g.  tissue engineering, regenerative medicine, drug and gene delivery, preventive interventions)

*Our multiscale modeling efforts are directly focused on regenerative medicine in the context of skeletal muscle regeneration in the face of muscular dystrophy.*

1. Implementing virtual clinical trials with multiscale models to predict outcomes.

*We are using our multiscale models to simulate different interventions on diseased muscle at different ages and stages of disease.*

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

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Click or tap here to enter text.

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

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The overall goal of our U01 project is to develop and validate multi-scale models that link biomechanical models of human movement, muscle contraction, & muscle micromechanics with agent-based models of muscle inflammation and regeneration in order to predict disease progression in Duchenne muscular dystrophy.

We have made significant strides towards developing the computational framework and establishing protocols for novel experiments to test the models. To date, we have developed a novel agent-based model of muscle degeneration and regeneration, in both healthy and diseased (dystrophic) muscle. We used the model predictions to develop hypotheses and design experiments to tests the effects of an intervention on muscle regeneration following injury. We have also created macro-scale models of both human and mouse locomotion to investigate how relative muscle loads differ between mice and humans and how this difference could give rise to the observation that mouse models of DMD do not have the same phenotype as the human condition. Finally, we have developed simulation interface platforms: the first integrates Opensim simulations of movement (both human and mouse) with finite-element simulations in FEBio, and the second integrates FEBio simulations of muscle contraction with REPast agent-based simulations of muscle regeneration. We are now working to validate these new platforms and integrate into one seamless pipeline.

Further, experimentally, we have developed an entirely new protocol for testing the injury susceptibility of mouse muscles in a way that mimics muscle loading during gait. Further, we have established novel microscopy and image-processing techniques to precisely quantify the extent to which muscles are injured during a contraction – unique data that will empower the computational models.

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*

In general, it would be very helpful to our community if we could take a leadership role in how best to serve as peer reviewers for multi-scale modeling papers, in particular those that involve agent-based models.

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

*Biomedical Engineering (biomechanics, skeletal muscle, finite-element modeling, imaging) – Silvia Blemker,* [*ssblemker@virginia.edu*](mailto:ssblemker@virginia.edu)

*Biomedical Engineering (microcirculation, muscle, agent-based modeling, in vivo experiments) – Shayn Peirce-Cottler,* [*shayn@virginia.edu*](mailto:shayn@virginia.edu)

*Biomedical Engineering (medical imaging) – Fred Epstein,* [*fhe6b@virginia.edu*](mailto:fhe6b@virginia.edu)

*Muscle Physiology – Rob Grange,* [*rgrange@vt.edu*](mailto:rgrange@vt.edu)

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