**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: Michael Henson, Erik Herzog and Yannis Kevrekidis**

**Institution(s): University of Massachusetts Amherst, Washington University and Johns Hopkins University**

**MSM U01 Grant Number: U01EB21956**

**Title of Grant:** Multiscale Modeling of the Mammalian Circadian Clock: The Role of GABA Signaling

**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*

3) Novel methods to fuse data-rich and data-poor scales to enable predictive modeling

The suprachiasmatic nucleus (SCN) is responsible for daily timekeeping in mammals. The SCN consists of approximately 20,000 neurons that coordinate their behavior to produce a coherent overall rhythm. The SCN network is highly heterogeneous with regards to the individual neurons and their connectivity. Neuron level understanding is relatively data rich with experimental methods available to interrogate the molecular mechanisms responsible for single neuron oscillations. By contrast, the network level is poorly understood due to limited data on intercellular communication and network topology. The goal of our modeling effort is to bridge these two disparate scales by combining detailed molecular models of single neurons with sophisticated network reduction techniques based on uncertainty quantification and diffusion maps. The developed methods based on machine learning (e.g. diffusion maps) allow heterogeneity at both the neuron and network levels and enable putative network topologies to be rapidly simulated and compared to our experiments aimed at eludicating the role of GABA signaling across SCN neuron populations. We envision that our work will provide new insights into SCN network organization and be transferable to other importart problems in computational neuroscience problems involving heterogeneous networks.

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

*You may insert images by copying and pasting below*

 We have used machine learning tools (in patricular, manifold learning/data mining tools like diffusion maps) to obtain compact and parsimonious descriptors of model networks. We just recently started using these tools on SCN models. We have not yet used data driven causal inference tools, but we expect this to occur within the duration of this grant.

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

*You may insert images by copying and pasting below*

 During the first 15 months of the project, we initiated our proposed research on experimental determination of functional GABA connectivity across suprachiasmatic nucleus (SCN) neuron populations, single cell modeling of SCN astroctyes and multicellular modeling of heterogeneous networks of coupled neural oscillators, and development of multiscale computational tools for efficiently coarse-graining and accelerating the simulation of large populations of networked heterogeneous cells. We completed and published the first analysis of the role of astrocytes in the SCN (Tso et al. 2017, Current Biology, 27: 1055-61).

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*

 We believe that MSM consortium would benefit by more focus on common computational techniques rather than the current focus on common application areas.

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

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

 *Circadian biology – Erik Herzog,* herzog@wustl.edu*; Neural modeling – Michael Henson,* mhenson@umass.edu*; Multiscale computation/machine learning – Yannis Kevrekidis,* *Ykevrek1@jhu.edu*

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