Field of Interest and the Role of Computational Science

1. In terms a general audience would understand, describe an important, outstanding scientific or engineering challenge in your field of interest where computational science can play an important role.
2. Describe the particular science or engineering problem that you would like to pursue in your research. What would be the impact on the field and/or on science, engineering and/or society in general if this challenge could be successfully addressed?

(Max characters is 2250)

Higher-order functions such as learning, reasoning, and memory are enabled by the cortex, the outermost layer of the mammalian brain. The cortex is composed of excitatory and inhibitory neurons, which follow a regular pattern of connectivity based on their type, forming the cortical microcircuit. The microcircuit is thought to be essential for intelligent thought and behavior (*1*–*3*). Much remains unknown about how the microcircuit's components contribute to function, and how it is tuned during learning, or disrupted in disease (*4*–*6*).

To understand the dynamics arising from microcircuit architectures and how these lead to flexible computational function, I will build biologically realistic, tunable models of microcircuits. I hypothesize that stereotyped microcircuits facilitate different modes of computation and mode-switching, such that simple modulatory changes can drive the circuit from integrating sensory and predictive information, important for learning, to modulating between bottom-up and top-down information, important for attention. This work will create better machine learning (ML) algorithms, enabling rapid adaptation, contextual processing, and learning. It will also illuminate how disruptions to microcircuits - such as imbalances of excitation and inhibition, a factor in diseases such as autism or depression (*7*) - affect systems-level function. I will also explore synaptic learning rules for updating the weights between neurons, to study how brains learn rich function more robustly and with much less training data than current ML models, without the biologically implausible backpropagation algorithms used in ML. Modeling will allow me to manipulate specific neurons and connections in an exponentially more precise and high-throughput way than is possible experimentally.

To validate the microcircuit models, I will fit them to real neural data. Phenomena emerging from the architecture and tuning of the microcircuits, such as oscillations at specific frequencies, are directly observable in neural recordings. Understanding microcircuits will shed light on the basis of intelligence, provide architectural motifs for more brain-like ML, and illuminate the cause of diseases affecting microcircuit function.

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Use of Computational Science in your research

1. What is the most complex calculation you have run on a high-performance machine as part of your research experience? Or if you haven't run a high-performance computing system, tell us about the most complex computational problem you have tackled.
2. Imagine if you were given access to resources 100 times more powerful than what you have access to. What would that enable you to do, and what do you perceive the mathematical and computer science challenges to be?

(Max characters is 2250)

My past research has focused on modeling the activity of single neurons on a high-performance computing (HPC) system. My goal was to understand the computational properties afforded to neurons by the structure of their dendrites, the thin branches extending from the cell body. Studying dendrites *in vivo* is difficult due to their small size and complexity. To explore how signals propagate through dendrites, I used detailed compartmental models consisting of dynamical systems of hundreds of equations describing the flow of current within a neuron. Simulation of inputs to different dendrites and the ability to model activity in various parts of the neuron provided insights that were not experimentally accessible (*8*). My work demonstrated a potential mechanism for inputs from neighboring neurons onto the central dendrites to modulate a neuron’s response to sensory and predictive information.

While studying single neurons is requisite to fully understand the brain’s operation, to understand higher-order function we must study how the properties of individual neurons influence network-level dynamics. Modeling networks of neurons has relied upon abstracting away such properties to simplify simulations, since studying networks with sub-neuronal detail would require orders of magnitude more computational power. With access to exponentially more powerful HPC, I could study phenomena across scales from the individual neuron to the network, answering questions such as how the composition of ion channel types or branching of dendrites affects the dynamics of microcircuits.

A challenge in this area is a lack of neural analysis tools optimized for HPC (*9*). As neuroscientists record activity from increasingly large areas of the brain, conventional computers are now unable to process the data at the rate at which it is being collected. In turn, simulating such data also requires extensive computational power. I will use my program of study and practical research experience to adapt existing tools and create new tools to run simulations and analyze recordings efficiently on HPC systems. I hope that my work with the DOE CSGF will pave the way for more widespread adoption of the capabilities of HPC in neuroscience and beyond.

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Program of Study

Describe how the courses listed in your planned program of study would help prepare you to address the challenges you have described in questions 1 and 2. Discuss your rationale for choosing these courses.

(Max characters is 2250)

Neural Circuits for Cognition (BCS 9.490) (taken) introduced me to the modeling of neural circuits as dynamical systems. It explored computational motifs in neural circuits and the assessment of stability and noise in neural circuits, which will be directly relevant to my analysis of computations performed by the cortical microcircuit.

Emergent Computations Within Distributed Neural Circuits (BCS 9.530) will help me to understand the computational properties that can arise from extensive parallel processing present in the cortex. I will also learn about biologically plausible learning rules that could be employed by cortical microcircuits.

Network Science and Models (EECS 6.7260), on the dynamics of large networks, will be relevant to analyzing the models of neuronal networks that I will create. It will help me to evaluate the dynamics that emerge in scaled-up versions of microcircuit networks.

Parallel Computing (EECS 6.5920) will teach me how high-performance computers work, and I will do a semester project to hone my skills in using these systems. This knowledge will help me to engage in my modeling and neural recording analysis work at a large scale and allow me to make the best use of the high-performance computing resources available at MIT and the DOE.

Discrete-Time Signal Processing (EECS 6.7000) will help me to perform advanced analyses of the neural oscillations that I want to study by teaching me how to analyze signals from noisy data and how to perform spectral analysis.

Mathematical Statistics: a Non-Asymptotic Approach (Math 18.656) will teach me statistical methods particularly relevant to my field. Despite the increasingly large amounts of data available to neuroscientists, the standard statistical assumptions of large sample sizes often do not apply, so this course will be relevant to my analysis of neural data for validation of my models.

Nonlinear Dynamics and Chaos (Math 18.385) will help me to expand upon my knowledge of dynamical systems, by teaching me how to analyze the properties of nonlinear dynamical systems that represent many real neural circuits, including the ones I will be modeling.