**THE QUESTION OR PROBLEM**

We aim to integrate artificial and biological neural network computation starting in the simple animal C. elegans. To do this, we will design a closed-loop system where an artificial network can receive input from an animal while sending outputs to its nervous system. Artificial networks can receive information about the animal through a camera. They can send signals to its nervous system with optogenetics, in which animals are genetically modified so their neurons can be activated with light. We will use this setup to see whether neural subcircuits and their functions can be replaced or augmented by a learning computer algorithm (**Figure 1**).

In building integrated artificial-biological neural networks, we will learn about how the components interact with and adapt to each other. We also want to compare the solutions that both kinds of learning algorithms find when solving biologically relevant problems. This project will build on the Ramanathan Lab’s previous work in identifying key control neurons in C. elegans nervous systems, combining it with modern tools in bioengineering and machine learning.

**THE APPROACH TO BE TAKEN**

We will use a tractable biological system, the soil-dwelling nematode C. elegans. C. elegans is highly amenable to genetic modification and optical manipulation. The 300 neurons and 6000 synapses are compact, yet can execute sophisticated search programs to locate bacteria or mates, do associative learning to avoid or pursue biochemical targets, and trigger stress-resistant long-lived states in dire conditions.

We will first identify neurons that underlie some specific behavior. The goal is to replace or augment the functionality of those neurons. For replacement, we can give a computational agent control over the key neurons and have it learn to reproduce the behavior. The agent effectively replaces the role of inputs to the key neurons. For augmentation, we can design our own target behavior and thus expand the repertoire of animal behaviors.

The agent will use reinforcement learning in both approaches. Reinforcement learning is a field of machine learning that attempts to maximize rewards collected over time by exploration and interaction with an environment. We hope to achieve our goals through careful design of the reward function, as well as the computer-animal interface.

Our preliminary work provides a proof-of-concept for our idea. We linked a simple computational agent to a key interneuron that can control C. elegans’ movement. After heavily preprocessing the agent’s input (images of the nematode) and a few minutes of real-time computer learning, our agent can direct the nematode solely through an optogenetic link (**Figure 2**). We would next like to expand to more complex inputs, agents, and behaviors.

**POTENTIAL IMPACTS**

Practical impacts of the work include taking steps toward replacing lost neural function. We can also imagine the possibility of augmenting neural function, in the form of learning tasks more quickly or acting based on memories stored in an external agent. We note that substantial work on human and vertebrate brain-machine interfaces has been done in this direction.

Consequently, our emphasis will be on studying computations within the entire biological-artificial system on a single-neuron level to promote basic understanding of these interactions. The proposed theoretical impact would be in seeing how artificial and biological networks might interact and learn together. Studying the solutions found by artificial vs. biological learning will show us where they differ algorithmically. We hope this will contribute to our current understanding of learning in both animals and machines.