Project Proposal: A "Focused Research Organization" to Measure Complete Neuronal Input-Output Functions

Measuring how neurons integrate their inputs and respond to them is key to understanding the impressive and complex behavior of humans and animals. However, a complete measurement of neuronal Input-Output Functions (IOFs) has not been achieved in any animal. Undertaking the complete measurement of IOFs in the model system C. elegans could refine critical methods and discover principles that will generalize across neuroscience.

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Problem Statement

Systems neuroscience aims to understand the complex interplay of neurons in the brain, which enables the impressive behaviors of animals. A critical component of this understanding is the Input-Output Function (IOF) of neurons, which characterizes how a neuron integrates its inputs and responds to them. However, despite its importance, a complete measurement of IOFs in any animal has not been achieved, creating a significant blind spot in our understanding of brain function. While parts of IOFs have been measured through various experiments, these efforts only control a narrow subset of the inputs to any given neuron, providing only a small slice of the true IOF. Furthermore, the output of neurons is a complex nonlinear function of their inputs, adding to the complexity of the problem. To truly understand the computation and function of the brain, we need a detailed functioning of the IOFs, which requires controlling all of the inputs and observing the factors that shape IOFs. Pursuing this in a single animal model would uncover new methods, tools, and scientific principles that could catalyze large-scale innovation across neuroscience.

Project Concept

The project aims to unlock a deeper understanding of how neurons in the brain process information through the complete mapping of neuronal IOFs using the model organism C. elegans. This comprehensive mapping is a vital step in understanding how the brain's neurons receive, integrate, and respond to signals. The project will use a combination of advanced techniques including optogenetics, modern microscopy, and microfluidics to control and observe the nervous system of the worms, and will develop models to predict how neurons respond based on their inputs. The team will also explore how different factors, such as chemicals, drugs, and non-neural cells influence these responses. To ensure maximal benefit to the field and the scientific community, all data and findings will be shared openly and resources will be allocated to promoting collaboration with outside experts on experimental design, technology development, and computational and theoretical analysis.

What is a Focused Research Organization?

Focused Research Organizations (FROs) are time-limited mission-focused research teams organized like a startup to tackle a specific mid-scale science or technology challenge. FRO projects seek to produce transformative new tools, technologies, processes, or datasets that serve as public goods, creating new capabilities for the research community with the goal of accelerating scientific and technological progress more broadly. Crucially, FRO projects are those that often fall between the cracks left by existing research funding sources due to conflicting incentives, processes, mission, or culture. There are likely a large range of project concepts for which agencies could leverage FRO-style entities to achieve their mission and advance scientific progress.

This project is suited for a FRO-style approach because it requires a level of coordinated development and engineering that is too big for a single academic lab, too complex for a loose multi-lab collaboration, and not directly profitable enough for a venture-backed startup or industrial R&D project. The project also aims to create a suite of public goods through its commitment to open science, with plans to share data and code as they are developed. More broadly, the work lends itself well to the development of a new set of tools and methodologies rather than the products or papers incentivized by traditional research models.

How This Project Will Benefit Scientific Progress

This project aims to revolutionize neuroscience by providing the first complete measurement of neuronal Input-Output Functions (IOFs) in the model organism C. elegans. Identifying causal interactions between neurons will provide unprecedented insight into brain function, and the methods developed in the process pave the way for understanding more complex nervous systems.

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