CDI-Type I: Semi-Automated Tracing and Validation of Mouse Brain Microstructures Using Eye Tracking

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- **Primary Theme**: From Data to Knowledge
- **Secondary Theme**: Understanding Complexity in Natural, Built, and Social Systems

Background: Acquisition of unprecedented amounts of cellular level data has been made possible by innovative, high-throughput, high-resolution three-dimensional imaging instruments. The *Knife-Edge Scanning Microscope* (KESM), developed and hosted by the PI's research laboratory, is one of the first such instruments currently producing massive three-dimensional data sets including vascular and neuronal data from whole mouse brains. Data like these are extremely valuable in understanding the computational function of the brain which can lead to a paradigm shift in computational thinking. However, analyzing the raw data to extract structured geometrical knowledge poses a serious challenge, because automated reconstruction algorithms do not have high enough accuracy and it is hard to validate the results.

Approach: Recent years have seen increased interest in the potential of the human perceptual and cognitive system and utilizing them as part of a computing framework (known as human computing or distributed human computing). However, human computing has yet to harvest the rich capability of the human motor system. The human computing framework can be extended to include more dynamic interaction involving the human motor/perceptuo-motor system, not just the perceptual system, e.g., through the use of the rapidly evolving eye tracking technology and novel analysis techniques associated with the technology. The main idea of this project is to integrate eye tracking and automated tracing algorithms to trace and validate structures embedded in 3D mouse brain data while humans are interacting with the data volume in realtime.

Research Goals: The research goal of this project is to develop a seamlessly integrated computational framework of eye tracking and automated tracing algorithms, for tracing and validation of mouse brain microstructure. Specific objectives are as follows:

- Acquire vascular and neuronal morphology data from whole mouse brains, using the KESM.
- Develop automated vector-based tracing algorithms for rapid and accurate tracing of fiber-like structures.
- Develop a framework for the use of eye-tracking technology in interactive tracing.
- Develop a confidence-based rapid validation method using eye-tracking.
- Conduct large-scale statistical analysis of morphological variability in neuronal and vascular networks in the mouse brain.

Education Goals: The project team will train graduate (through this grant) and undergraduate students (through the REU mechanism) in an interdisciplinary curriculum, and organize annual high school contests, by modifying the research platform into an interactive tracing game.

Innovations in Computational Thinking: The most fundamental computation is the computation by the human brain. This project will take a two-pronged approach for the further understanding of computation in the brain: (1) the use of human perceptuomotor system as a component in the tracing and validation, and (2) statistical analysis of the neural circuit underlying such computation. These two approaches are expected to lead to novel innovations in computational thinking.

Intellectual Merit: The new tracing algorithms, coupled with the use of the human perceptuomotor system (eye tracking) in a unique human-machine system will help advance our understanding of computations in the brain, and lead to robust engineered systems.

Broader Impact: The neuronal and vascular data and extracted structural information will serve as an invaluable resource for neuroscience and computer science research (data will be publicly released). Graduate, undergraduate, and high school students will be involved in this unique interdisciplinary project.