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# EN.580.694: Statistical Connectomics

## Final Project Proposal

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### Images to Graph Inference: Analysis of Errors.

A fundamental challenge in the emerging field of high-resolution connectomics is transforming large three-dimensional images of brain tissue into a neuronal connectivity map (i.e., a connectome). Recent advances in technology have enabled imaging volumes at nanometer resolution; in serial section electron microscopy, it is possible to identify individual neurons (i.e., graph vertices) and their connecting synapses (i.e., graph edges). From these data, a putative “brain graph” can be estimated. Inference on these connectomes is expected to lead to the identification of neural motifs [6], which can be used to understand true neural networks and make rapid advances in biofidelic machine learning algorithms. It is believed that brain pathologies (e.g., schizophrenia and autism) result from the miswiring of neural circuits; understanding these connectopathies may lead to exciting new treatments.

**Previous Work** Existing efforts to generate connectomes [1; 10; 11] have pursued manual or semi-automated approaches. Unfortunately, relying on humans to trace individual neurons and find synapses is unrealistic as volumes scale. A recent study estimated that manual annotation of 1  $mm^3$  would require hundreds of thousands of person-years [4]. Computer vision efforts [5; 7; 9] have focused on important subproblems, but these algorithms have been developed and evaluated without considering the larger problems of graph estimation and inference.

**Pipeline Engineering** We recently developed the first automated images-to-graphs computer vision pipeline to estimate and assess brain graphs [3], using the Open Connectome Project infrastructure [2]. This provides an initial proof-of-concept result and research platform for the community. However, the automated results produced to date are of insufficient quality for inference and neuroscience discovery.

**Computer Vision Frontiers** In order to prove the viability of a fully-automated connectomics approach, we propose to characterize and reduce the existing errors toward answering graph inference challenges. We plan to take a holistic, systems approach; this will enable the processing of much larger volumes and exciting neuroscience discoveries. Understanding the wiring of the brain is expected to lead to both new algorithmic insights and understanding of disease pathologies.

**Impact** Assembling the nanoscale wiring diagram of the brain addresses a major knowledge gap in modern neuroscience. While alternative methodologies provide information at a single neuron resolution (e.g., two-photon microscopy) and at the macroscale (e.g., Magnetic Resonance Imaging, Electroencephalography), the mesoscale circuits are largely unexplored. In the next few years, image volumes of brain tissue are soon expected to reach the size required to test the cortical column hypothesis proposed by Vernon Mountcastle at JHU sixty years ago [8].

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