Connectomics: The dense reconstruction of neuronal circuits

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The mapping of neuronal connectivity is one of the main challenges in neuroscience. Only with the knowledge of wiring diagrams is it possible to understand the computational capacities of neuronal networks, both in the sensory periphery, and especially in the mammalian cerebral cortex. Our methods for dense circuit mapping are based on 3-dimensional electron microscopy (EM) imaging of brain tissue, which allows imaging at nanometer-scale resolution across substantial volumes (typically hundreds of micrometers per spatial dimension) using Serial Block-Face Scanning Electron Microscopy (SBEM). The most time-consuming aspect of circuit mapping, however, is image analysis; analysis time far exceeds the time needed to acquire the data. Therefore, we developed methods to make circuit reconstruction feasible by increasing analysis speed and accuracy, using a combination of crowd sourcing and machine learning. We have applied these methods to circuits in the mouse retina, mapping the complete connectivity graph between almost a thousand neurons, and we are currently improving these methods for the application to much larger neuronal circuits in the cerebral cortex. Using these methods, we want to measure the similarity between neuronal networks in the cortex of different individuals and different species in search for the algorithms of sensory perception, search for engrams of sensory experience in the cerebral cortex, and ultimately understand the alterations in neuronal network structure in psychiatric disease.