



Presentation Abstract

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Title: Reconstructing the neuropil from serial section transmission electron microscopy

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Abstract: Electron microscopy is used to reveal the structure of brain tissue at the micron and submicron scale. However, structural analysis of the spatial relationships between various cellular structures as well as the arrangement of organelles within cells is limited in two-dimensional electron microscopy images. Reconstruction from serial section transmission electron microscopy (ssTEM), however, offers the possibility of recreating the neuropil (including neuronal and glial processes and their organelles) in spatially realistic three-dimensional (3D) models. Primary structural features of neurons, such as dendrites and axons, are typically modeled as simple cylinders, but ssTEM reveals substantial deviation from these cylindrical approximations. Realistic dendrites are not cylindrical and have considerable variation in cross-sectional area, surface membrane, dendritic spine morphologies, and intracellular organelles, even along segments of dendrite as short as five microns. From a functional standpoint, it is an open question how this local variation in dendritic structure affects the local electrical signals in dendrites. Previous modeling of dendritic function has also lacked sufficient structural data to explore the effects of variation in the physical relationships between dendrites, axons, glia, and extracellular space in the local neuropil. A substantial amount of

ssTEM neuropil data has been collected previously, but the computational tools needed for transforming these 2D images into structurally realistic 3D models have been lacking. Here we apply new computational algorithms and geometry processing pipelines (incorporated in our NEUROMESH software tool) for generating and quantifying accurate reconstructions. Improved strategies for contour tiling and quality surface mesh generation and curation are used to construct realistic models suitable for computational simulations, for instance, using MCell. Our spatially realistic domain models are also used in multiscale electrodynamic simulations via a scalable, meshless 3D finite element method using weighted extended B-splines and implemented in our NEUROPHYS software tool. In addition, we employ skeletonization procedures in combination with quantifications of these reconstructions to generate reduced, 1D models of neural processes that can be incorporated into the NEURON or GENESIS simulation environments, allowing inclusion of more realistic features, such as small, dendritic diameter variations, accurate spine sizes and locations, and variable electrical parameters based on organelle distributions, into such simulations.

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