Electrophysiological Models Derived from EM Reconstructions


Research Goals

Construct spatially realistic structural models of neuronal processes, organelles, and extracellular space. From stacks of serial EM images, we extract contours for all neuronal processes (dendrites, axons, glia) and internal organelles (mitochondria, endoplasmic reticulum, etc.). Contours are tagged, curated, and meshed into surfaces representing the cellular or extracellular boundaries in 3D. A conforming Delaunay method is used to construct volumetric meshes of the interiors as well as extracellular space.

Quantify structural properties of spatially realistic models and construct appropriately reduced domain models. Reconstruction and modeling tools are used to quantify the variation in surface area and volume of axons, dendrites, extracellular space, synapses, and core subcellular organelles (smooth endoplasmic reticulum, endosomal compartments, Golgi and spine apparatus, and mitochondria) that could impact electrical signaling in dendrites. We use a suite of tools to construct domain models from these spatially realistic quantifications suitable for incorporation into the NEURON simulation environment....

III: 3D Neuropil Reconstruction

Extracted contours are tiled using the ContourTiler algorithm [BCL’96, EB’10], incorporated into Volume Rover [CVC]. Single component reconstructions are guaranteed to be topologically correct and watertight. Post-reconstruction corrections guarantee that there are no intersections between components. The surface meshes produced by Contour Tiler in the 3D Reconstruction step are often unsuitable for BEMs. We use a suite of tools incorporated into the VolumeRover software package to smooth, decimate, and refine by fitting algebraic splines.

IV: Simulations

Ephaptic effects: an action potential is initiated at each of the three locations pointed to on spines 2 and 3. The resulting extracellular potential is plotted below as a function of time for indicated extracellular locations.

I: Hippocampal Image Stacks

Samples are acquired from the CA1 and CA3 hippocampal regions of a rat brain. Pyramidal cells in each strata appear in parallel configurations.

II: Curating Contour Stacks

On the left, 2D curation has detected and removed intersections at the indicated locations. On the right, a sample of how splines are used to resample the contours.

We use synapse data to identify connections between specific axons and dendrites. The resulting graph structure reveals complicated connectivity. Merging geometric measurements from the meshes with the graph data will yield a circuit diagram for the entire volume.

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References

Computational Visualization Center: VolRover Software
C. Rumsey, K. Harris, D. Johnston, C. Bajaj; Submitted (2010)