VolumeRoverN: Analysis-ready domain models of neuronal forests*

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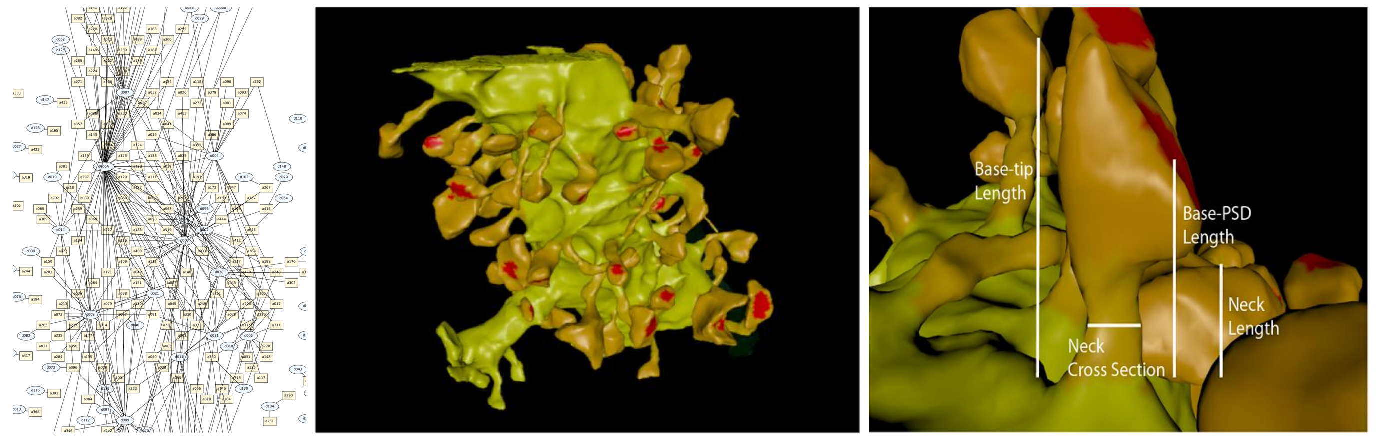
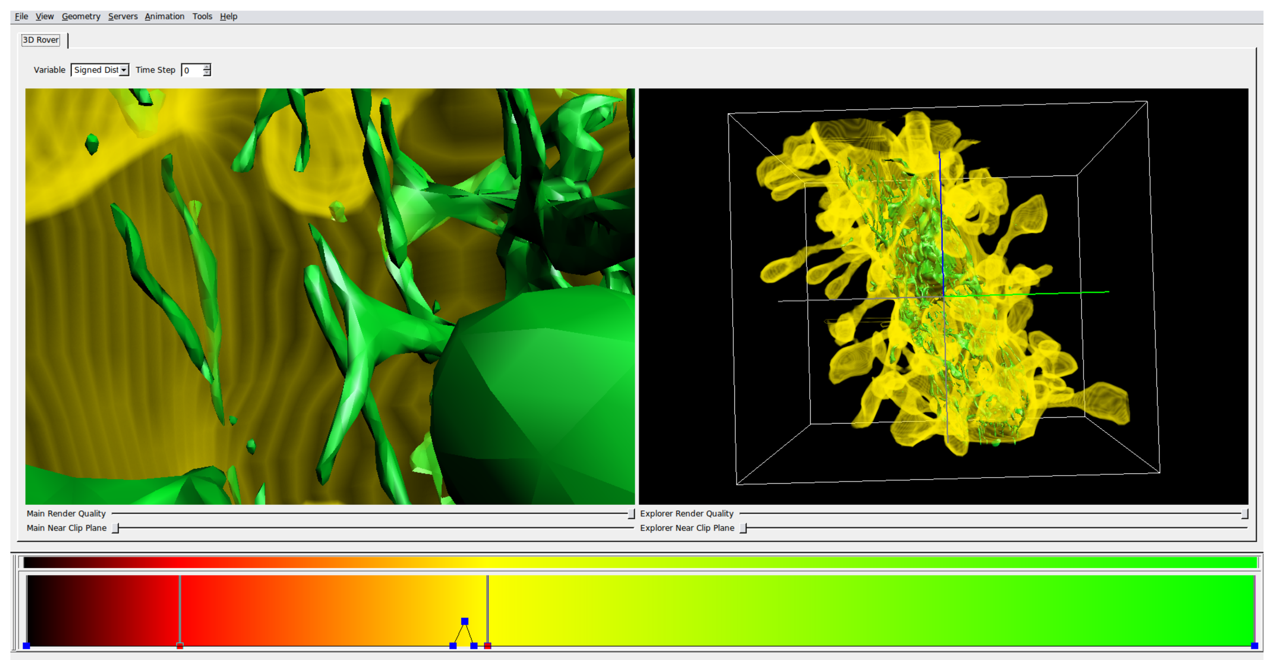
I. VolumeRoverN

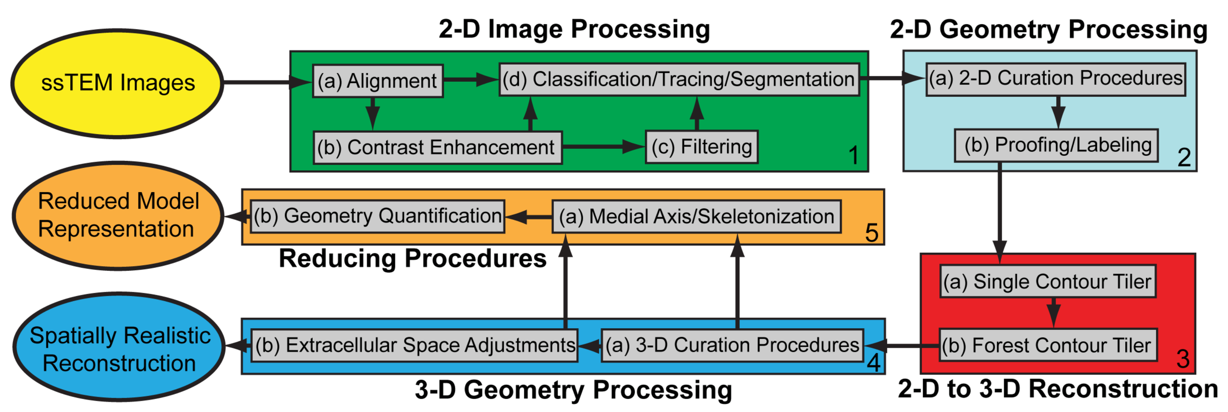
The morphology and distribution of dendritic spines are correlated with disease, substance abuse, and aging; but a quantitative understanding of this correlation has been elusive. A growing array of tools is available to study this through simulation, but this requires quality models. We produce, from stacks of electron microscopy (EM) images, quality surface meshes from which we generate derivative models suitable for various simulation environments. We also provide simple and powerful geometric quantification tools.



VolumeRoverN [3] is a sophisticated software package designed to assist neuroscientists in elucidating geometric and electrophysiological properties of neurons at very high resolutions. It contains algorithms for surface mesh reconstruction, mesh improvement, visualization, and export to NEURON [5] and MCell [4] analysis packages. The motivation is to take full advantage of high-resolution EM imagery in creating models that enable study of neuron morphology at the nanometer level.



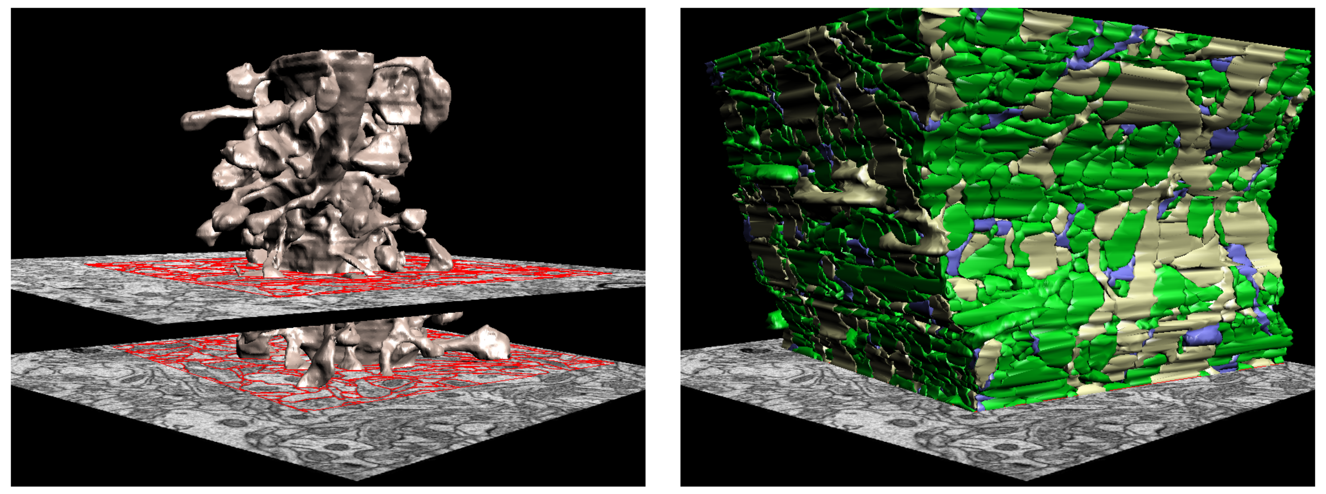
VolumeRoverN visualizes geometries and volumes. An apical dendrite is shown above with some transparency revealing reconstructions of endoplasmic reticulum (ER) inside. The dendrite is volume-rendered and the ER uses standard geometry rendering. We use the HDF5 hierarchical data format which enables volume-rendering at two scales simultaneously. It is also fully scalable, so as image data grows in size, VolumeRoverN is positioned to support it.



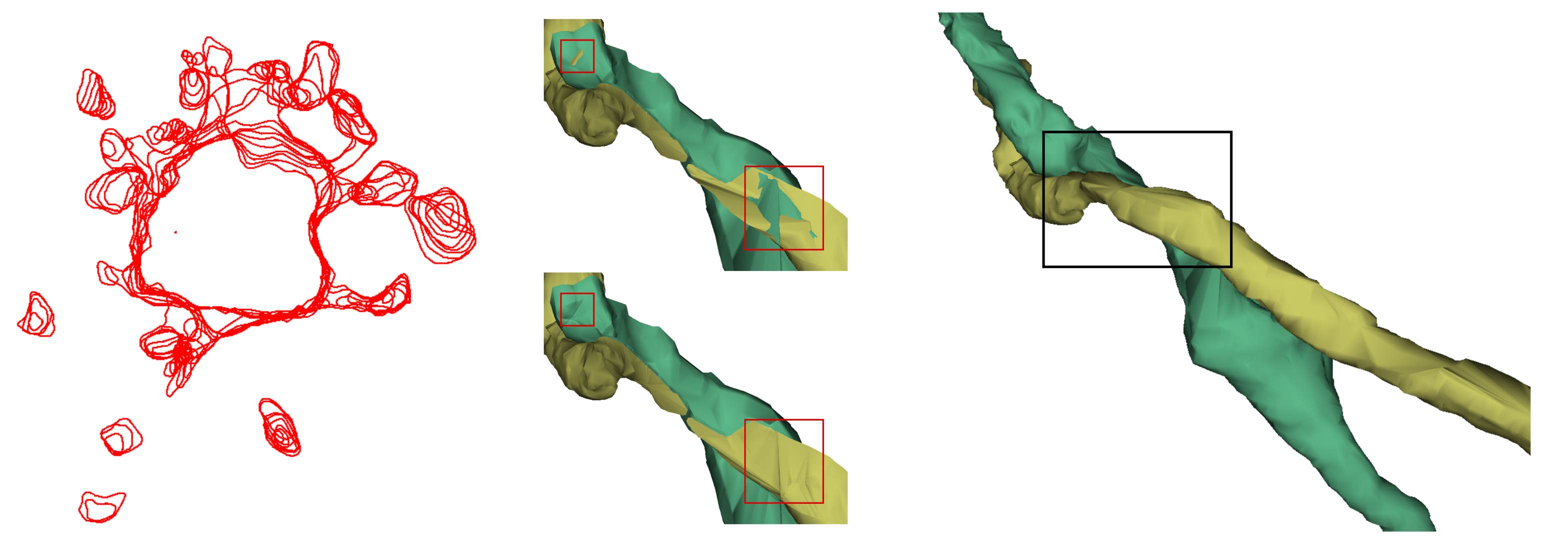
The input to our pipeline is a set of 2D contours obtained from tracing software such as RECONSTRUCT. VolumeRoverN then constructs 3D surface meshes that are correct, accurate, and of high-quality. The user can then perform geometric quantification studies or export models in different formats for analysis using other popular software packages.

II. Analysis-ready meshes

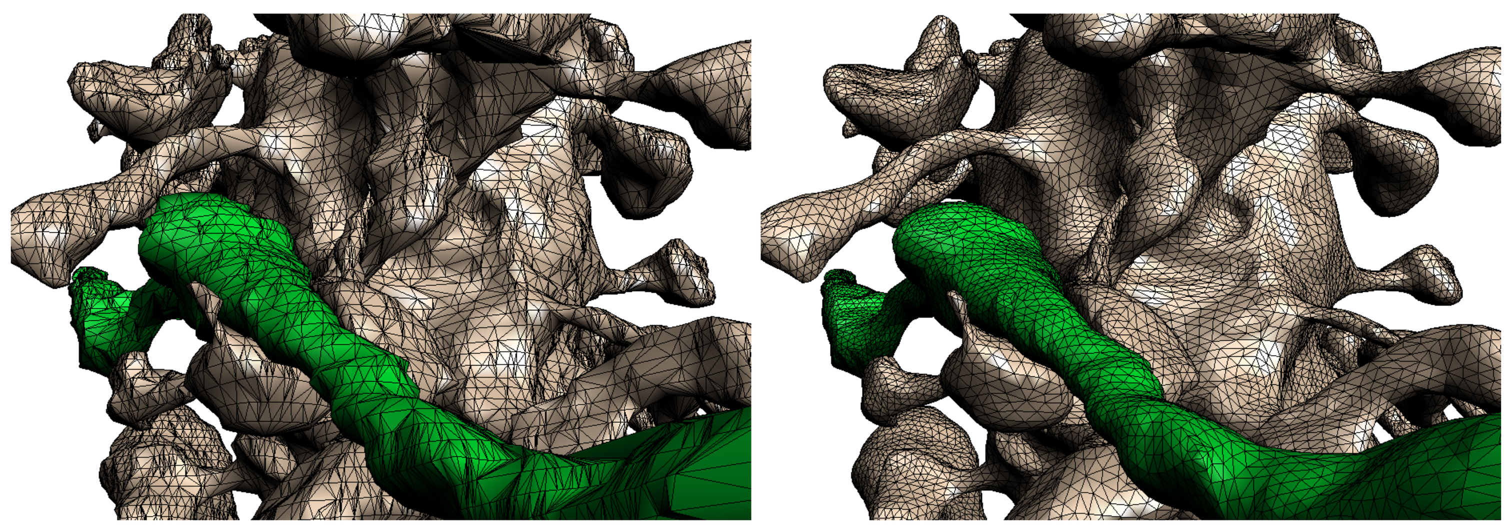
Our pipeline of algorithms converts EM images to spatially realistic models of neuronal processes. There are four main phases. The first two deal with 2D processing. The third bridges the gap from 2D to 3D. The last two process the 3D data to render simulation quality surface meshes as well as reduced models.



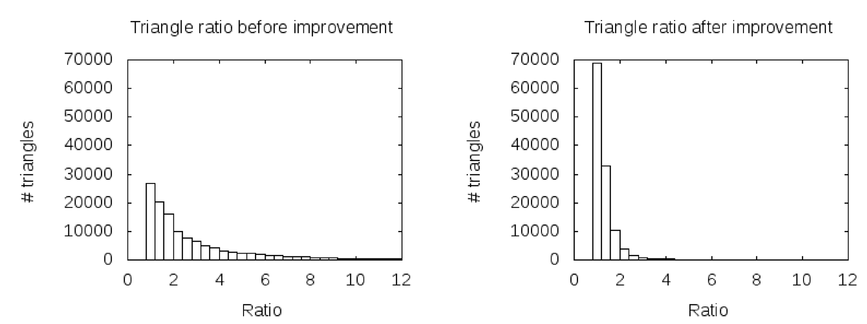
Our reconstruction pipeline is as follows. Components are singly reconstructed from the contours [1]. Contours are shown in red on the image slices. Components are added to the full reconstruction forming a tightly packed block of geometries.



Because of tight packing and high tortuosity, interpolation between slices frequently yields inter-component intersections that must be curated in 3D [2]. Ours is the only topologically accurate algorithm that guarantees that there will be no inter-component intersections.



With intersections removed we can now run our mesh improvement algorithm, which includes both decimation and smoothing. Our smoothing algorithm yields triangles that are near-equilateral.

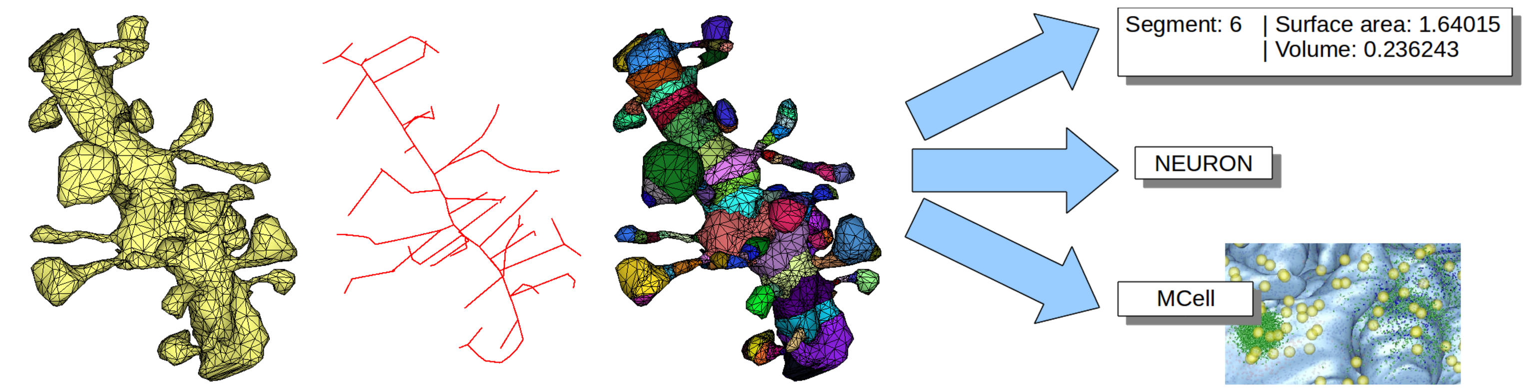


Triangle quality histograms before and after mesh improvement. The ratio of an equilateral triangle is 1.

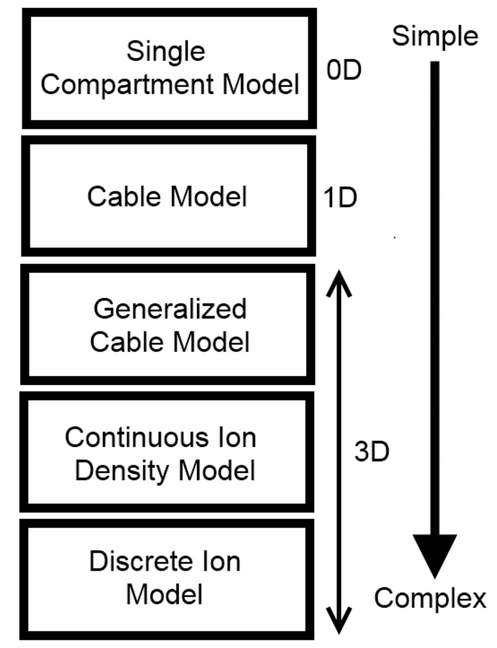
dataset	slices	reconstruction time (s)	num triangles
CA1 (axons)	116-117	78.6	50308
CA1 (axon a001)	61-160	12.2	7199
CA3 (2 dendrites)	149-150	99.1	7607

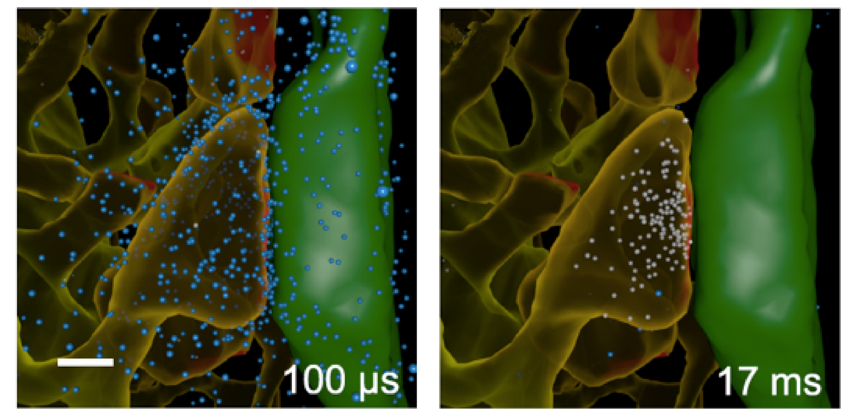
Table of tiling timing and triangle statistics.

III. Quantification for multi-scale analysis

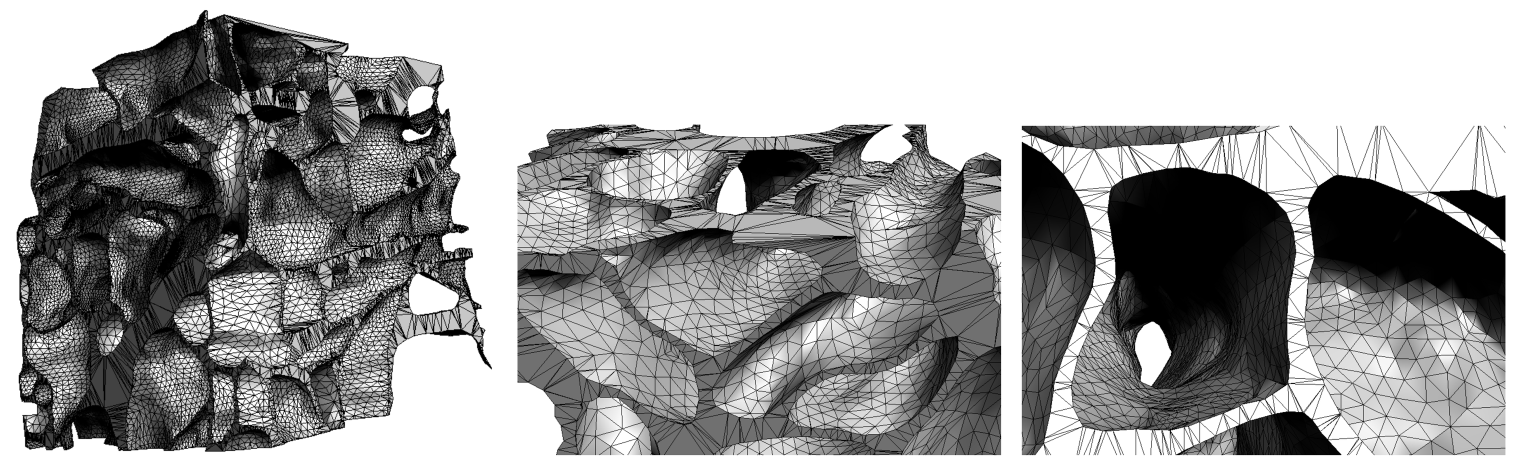


VolumeRoverN has the capability of skeletonizing and segmenting a neuronal surface mesh. Regions can then be marked for merging, thereby isolating regions such as spines and spine heads. Our surface area and volume tools, together with our measure tool can assist in quantifying morphological properties of neurons, such as spine head volume, total spine surface area and axonal bouton diameter. Cylinder primitives can be fitted to the regions and exported to NEURON.





Once regions are labeled, the mesh and labels can be exported to MCell for use in local discrete ion diffusion simulation. The importance of quality meshes is especially acute at this stage, as the quality of the simulation is directly affected by the quality of the triangles.



Our extra-cellular space (ECS) tool produces dual meshes that can be used in reaction-diffusion simulations.

References

[1] C.L. Bajaj, E.J. Coyle, and K. Lin. Arbitrary topology shape reconstruction from planar cross sections. *Graphical Models and Image Processing*, 58(6):524–543, 1996.

[2] J. Edwards and C Bajaj. Topologically correct reconstruction of tortuous contour forests. *Computer-Aided Design*, 43(10):1296 – 1306, 2011.

[3] J. Edwards, E. Daniel, J. Kinney, T. Sejnowski, T. Bartol, D. Johnston, K. Harris, and C. Bajaj. Analysis-ready domain models of neuronal forests. *Manuscript submitted for publication*, 2012.

[4] MCell: A Monte Carlo Simulator. `http://www.mcell.cnl.salk.edu`.

[5] Neuron simulator. `http://www.neuron.yale.edu/neuron`.

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