Mitochondrial Size Gradients in Cortical Neurons Suggested by 3D Electron Microscopy

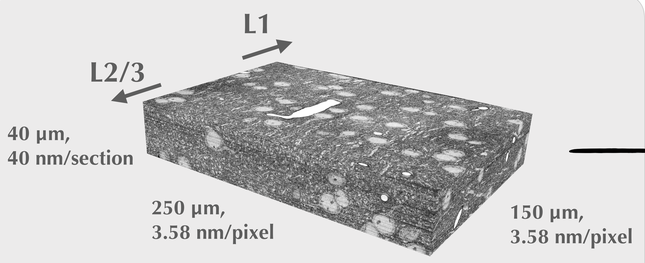
Nicholas L. Turner[1,2], Runzhe Yang[1,2], Agata Foryciarz[1,2], Kisuk Lee[2,3], William Silversmith[2], William Wong[2], Jingpeng Wu[2], Sven Dorkenwald[1,2], T. L. Lewis[4], Yusuke Hirabayashi[4], Franck Polleux[4], Nuno da Costa[5], R. Clay Reid[5], H. Sebastian Seung[1,2]

[1] Computer Science Dept., [2] Neuroscience Institute, Princeton University, Princeton, NJ; [3] Brain and Cognitive Sciences Dept., MIT, Cambridge, MA; [4] Zuckerman Mind Brain Behavior Institute, Columbia University, New York, NY; [5] Allen Institute for Brain Science, Seattle, WA

Highlights:

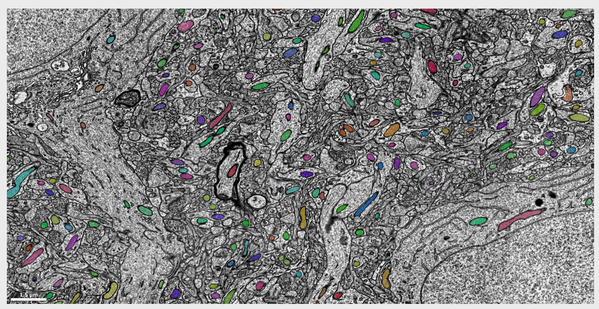
- **Mitochondria play a crucial role in the functioning of neurons** by synthesizing ATP and buffering intracellular Ca^{2+}, both necessary for synaptic function. The morphology and location of mitochondria can provide insights into specialized function they perform in different parts of the neuron.
- We **reconstruct 81,397 mitochondria within 180 pyramidal neurons** *segmented* and *skeletonized* within an electron microscopy volume of mouse V1.
- We **study their sizes and compartment locations distribution**, and **discover that somatic mitochondria are intermediate in size between (smaller) axonal and (larger) dendritic objects.**
- *Our data also suggest* ***a gradient of mitochondria size*** *at this scale, consistent with mitochondrial size filtering between compartments (Lewis et al., 2018).*

IARPA Mouse V1 Dataset



Serial Section TEM of Mouse V1 - Layer 2/3
(Allen Institute for Brain Science)

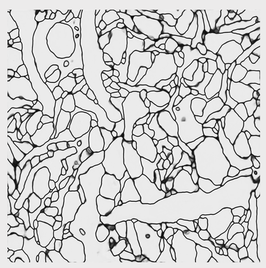
Automated Mito Reconstruction



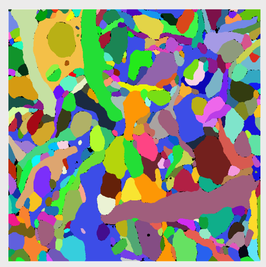
A **convolutional neural network** was trained to detect voxels which constitute mitochondria throughout the entire volume. Candidates were also *filtered by size* to remove noise components. Some merge and split errors each affect ~10% of the predicted objects.

The **volume** of each mitochondrion was estimated by *the number of voxels* that constitutes each predicted object. The **length** of each object was estimated by taking *the longest shortest path from one mesh node to another* along the skeleton.

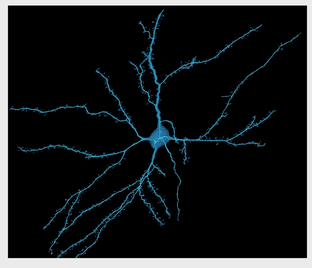
Neuron Segmentation & Skeletonization



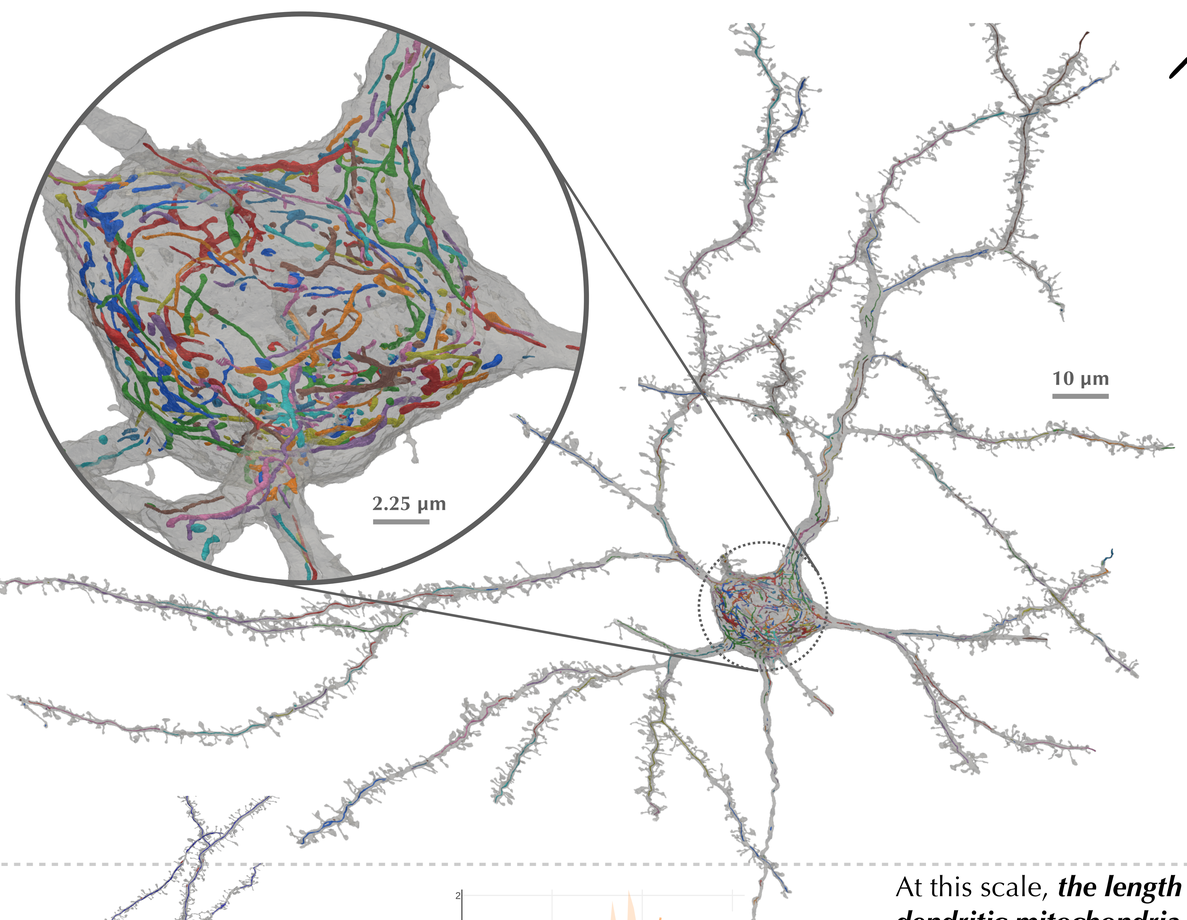
(a) **Cell boundaries detection** with aligned 3D images using a *convolutional neural network.*



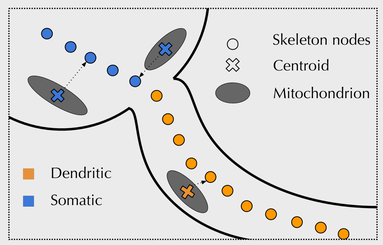
Over-segmented by a *modified watershed algorithm* (Zlateski & Seung, 2015), and **agglomerated** by *mean affinity agglomeration.*



The **skeletons** of pyramidal cells were obtained by a *modified version of the TEASAR algorithm* (Sato et al., 2000).

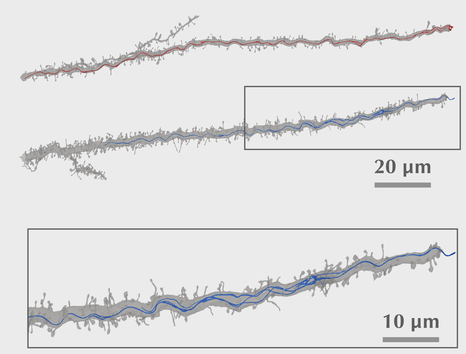


Compartment Association

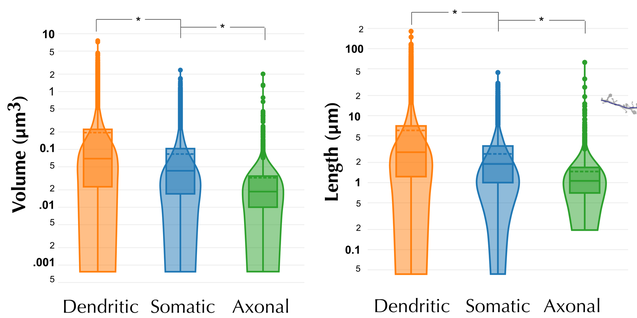


- We use **random forest classifier** predicted if a region belongs to *axon, dendrite, or soma*. Features were extracted within an 8 µm window along the skeleton based on synapses, contacts, and cell volume.
- The final prediction was improved by a **majority voting** on cell parts branching proximal to the soma.
- Mitochondria were associated to the semantic class of **the skeleton node closest to its centroid coordinate.**

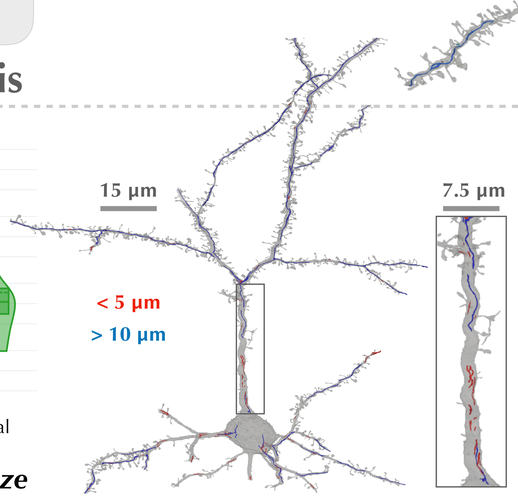
Very long mitochondria in apical dendrites.

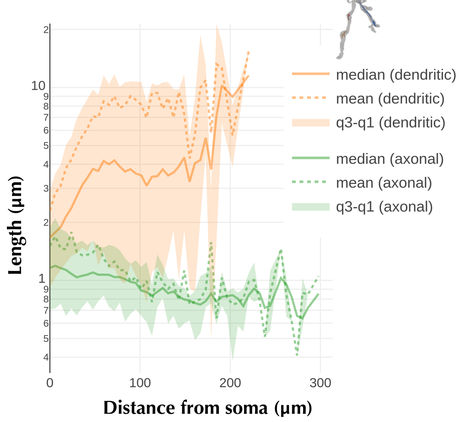


Morphology and Location Analysis



Somatic mitochondria are intermediate in size between dendritic and axonal mitochondria.





At this scale, ***the length of dendritic mitochondria increases as distance from the soma increases, while axonal length decreases.*** This is consistent with mitochondrial size filtering (Lewis et al., 2018). Extending our method to larger volumes may provide stronger evidence to this hypothesis.

References

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[2]Zlateski, Aleksandar, and H. Sebastian Seung. "Image segmentation by size-dependent single linkage clustering of a watershed basin graph." *arXiv preprint arXiv:1505.00249*(2015).
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Acknowledgments

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