Multiscale data integration to generate atlas-based biophysical modeling of first- and higher-order mouse thalamic nuclei

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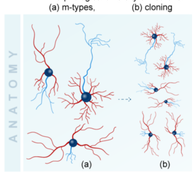
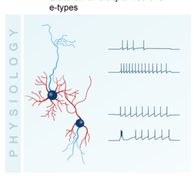
Digitally reconstructing and simulating the brain

PSTR576.03

Building an Atlas-based PO, RT, and VPL Circuit

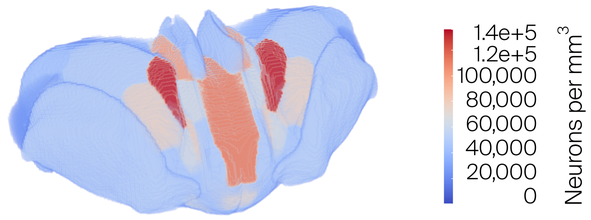
1. **Morphology:** First, we obtain reconstructions of individual neurons from experimental data. We then "clone" these cells, varying and swapping neurites for each cell-type. For the thalamus, we use 3 classes of **M-type**: **TC, IN,** and **RT**. (Iavarone et al., 2023)
2. **Electrophysiology:** Next, using ion channel parameters optimized against experimental data, we characterize different classes of neurons. These electrophysiological **E-types** are then fit to their relevant morphologies. For the thalamus, we use 5 E-type classes and organize our celltypes into **5 unique ME-type classes**. We have generated a combined **267,487 unique thalamus cells.**



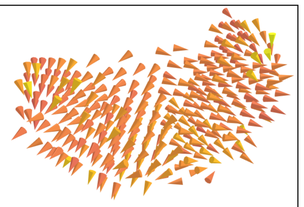


Interactive Studio for (Iavarone et al., 2023)

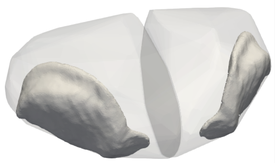
3. **Densities:** Using the spatial mapping of the Allen Mouse Brain Atlas (CCFv3) (Wang et al., 2020) and volumetric neuron densities from the Blue Brain Cell Atlas (Rodarie et al., 2022) and literature, we assign our cells to different thalamic regions in space.



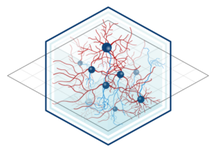
4. **Orientations:** Following anatomy, we compute the "principal axis" of cell directions in every voxel. We use a Gaussian blur applied to a scalar field, where non-RT thalamus is the source and RT is the target.



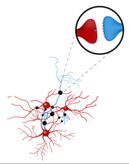
5. **Distances:** We generate meshes for different regions of the thalamus. We then use ray-tracing to compute the distances from voxels to the regions, which we use to establish boundaries for dendrites and axons.



6. **Placement:** Combining all prior steps, ME-type cells are placed in voxels according to their corresponding regional densities, orientations, and distances.



7. **Synapses:** Potential synapses are identified at relevant appositions ("touches") between celltypes. Synapses are then "pruned" to appropriate levels (Reimann et al., 2015).

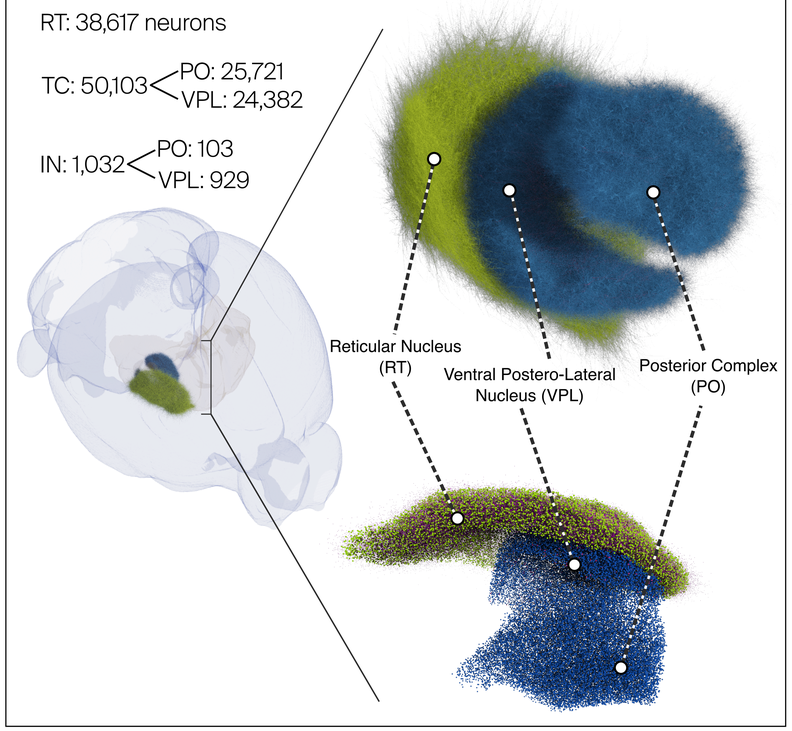


8. **Final Circuit:** The circuit ultimately comprises **89,752** total cells, **76,351,201** total synapses, and **3.576** mm^3 volume.

RT: 38,617 neurons

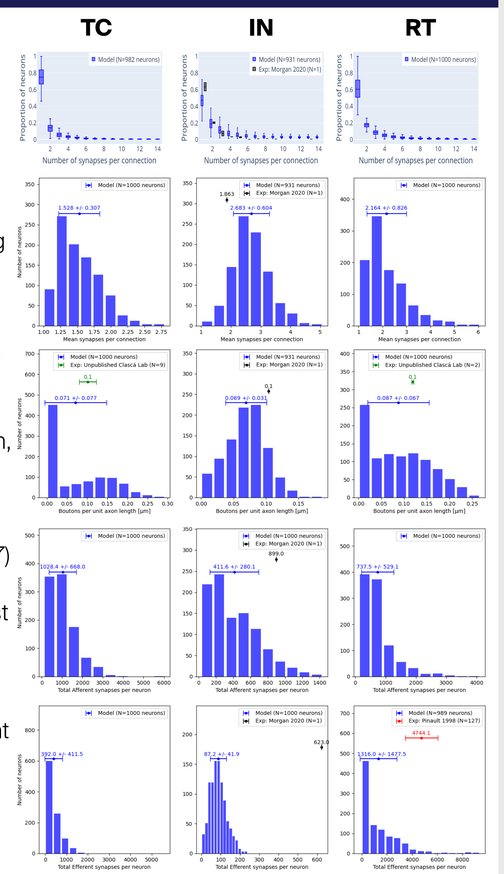
TC: 50,103 < PO: 25,721, VPL: 24,382

IN: 1,032 < PO: 103, VPL: 929



Connectivity Validations

- The precise scale of our modeling allows us to comprehensively analyze our connectivity from brain-region level to individual synapses and boutons. We are currently in the process of validating this model and a full thalamus model.
- Unfortunately, single-cell experimental data of synaptic ultrastructure is extremely difficult to obtain, limiting the existing data available for validation.
- Synaptic "pruning" (Step 7) of our modeling is an iterative process, and must be calibrated on a per-region basis.
- If you work with the rodent thalamus or rodent-based structural connectivity, please get in touch!



References and Acknowledgements

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Thank you to Elvis Boci and Cyrille Favreau for visualization help! This study was supported by funding to the Blue Brain Project, a research center of the École polytechnique fédérale de Lausanne (EPFL), from the Swiss government's ETH Board of the Swiss Federal Institutes of Technology.

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