High-resolution computational simulation of sound localization neurons in the barn owl

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PSTR170.01

Abstract

Sound localization in the barn owl (Tyto alba) relies on precisely tuned neurons in the inferior colliculus external nucleus (ICx) that integrate auditory spatial cues to form a map of auditory space [1-3]. Recent work by Sanculi et al. [4] revealed the presence of complex dendritic microstructures, termed ***toric spines***, in space-specific neurons, suggesting that fine-scale morphology may play a role in synaptic integration.

Here, we present a computational pipeline towards building morphologically-accurate, biophysically detailed models of ICx neurons incorporating toric spines, implemented in the Arbor simulation environment [5]. Using high-resolution 3D reconstructions, geometric skeletonization via mean-curvature flow, and custom SWC conversion tools, we generate compartmental models suitable for large-scale simulations of synaptic input. These models are used to investigate how spine morphology influences local integration of AMPA-mediated synaptic currents.

Integration is quantified for pairs of active synapses using a bilinear integration rule. We find that integration is generally sublinear, and this does not depend on the generally unique morphology of toric spines, but range and distribution of this nonlinearity measure varies significantly with morphology and input properties.

This work demonstrates a scalable approach to integrating detailed morphological data into functional circuit models, bridging microscopy and computation in auditory neuroscience.

Modeling Pipeline

1. Morphology from Imaging Data
We began with high-resolution 3D meshes of toric spines obtained from confocal reconstructions [4]. These meshes capture the full topology, including closed loops and fine processes. Spines and neuron shown in Section 1.

2. Mean-Curvature Flow Skeletons
Because SWC morphology format (used in Arbor, NEURON, etc.) prohibits loops, we applied a mean-curvature flow algorithm [CGAL] to compute a medial-axis skeleton from the surface mesh. This preserves local curvature and topological features while ensuring geometric consistency for later fitting. Figures 2.1-5 illustrate this process.

3. Morphology: SWC + Synapses + Sink
Using custom Python tools developed for this project, we fit an SWC tree structure to the skeleton and annotate cyclic regions, allowing loop closure restoration during Arbor simulation without violating SWC format constraints. To approximate the downstream cellular load, such as soma or dendrite, we append an idealized sink cylinder to the spine neck, enabling more realistic passive properties. Synaptic locations are mapped from imaging data onto the reconstructed surface and incorporated into the SWC structure.

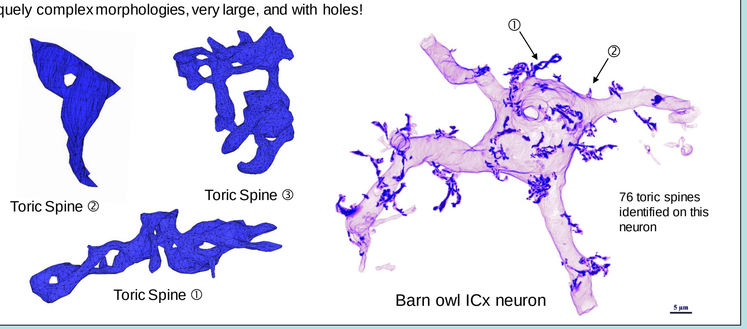
4. Biophysical Simulation in Arbor
We implemented AMPA-like synaptic models and ion channel mechanisms using Arbor's Python API. Presynaptic input streams were modeled as independent Poisson-distributed spike events to mimic convergent ICx input. Simulations computed the local membrane potential across compartments to assess temporal and spatial integration dynamics. Minimal voltage-gated ion channels are included, but a rigorous study of their effects on membrane excitability are part of future research plans. Simulation parameters derived from [4].

5. Simulating Simultaneous Stimuli
Simulation parameters are tuned using the results of patch-clamp experiments. For a combination of input streams, we measure the evolution of membrane potential in the sink to observe the integrated signal.

6. Quantifying Sublinear Integration
We describe integration from pairs of inputs with a scale-free per-mV scalar coefficient. For a number of random variations in inputs, we aggregate membrane potential traces during the stimulus and fit to the results.

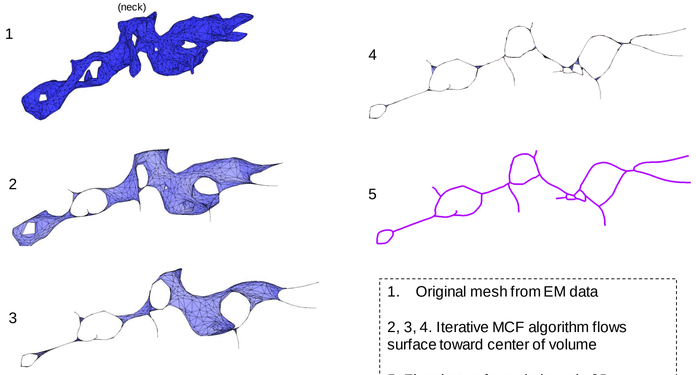
1. Morphology from Imaging Data

Meshes of toric spines (left) collected from EM imaging data of a barn owl ICx neuron (right). Uniquely complex morphologies, very large, and with holes!



2. Mean-Curvature Flow (MCF) Skeletons

Each spine skeletonized individually using topology-preserving MCF algorithm [CGAL]. Similar operations in large imaging software were not generally reliable for such complex topology. MCF is robust.



1. Original mesh from EM data

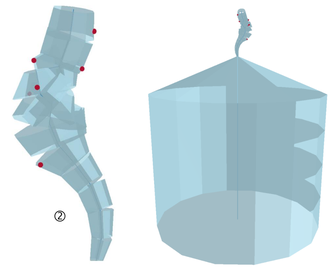
2, 3, 4. Iterative MCF algorithm flows surface toward center of volume

5. Fit points to form skeleton in 3D

3. Morphology: SWC + Synapses + Sink

Using our MCF results, fitting a SWC-format (x, y, z, radius) directed graph model is straightforward. Cycles are identified and annotated in SWC files for continuity implementation at simulation stage.

Imaging data is labelled with active zones (red). A spine can have up to 49 active zones from 11 presynaptic axons, though the small example shown here has 6.



We attach an idealized sink structure to the spine neck representing a downstream soma or dendrite compartment to model realistic diffusion of membrane potentials.

4. Biophysical Simulation in *Arbor*

We use ***Arbor*** [6], a fast and modern multi-compartmental neuron simulation software, to model electrical dynamics. Synapses are modeled using event-based conductance mechanisms, and integration of signals is analyzed in the sink.

$$\left\{ C_j \dot{V}_j = \sum_k \frac{V_k - V_j}{r_{jk}} + I_j^{\mathrm{dyn}} \right\}_{j \to k}$$

$$I_{\mathrm{syn}}(t) = g(t)(V - E) : \dot{g} = -g/\tau + \bar{g}\omega(t)$$

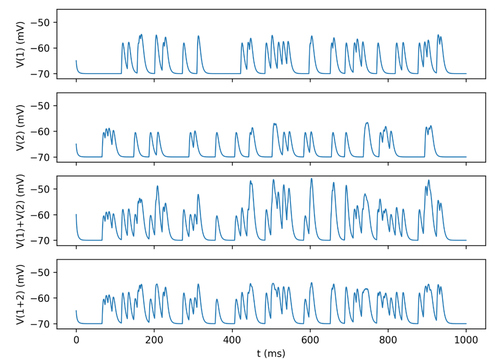
Membrane potential of adjacent compartments i, j depend on electrical diffusion and dynamical current terms, including phenomenological passive leak current. (Voltage-gated ion channels can be included but will be explored more fully in future work.)

AMPA synapses are modeled using a typical exponential curve and triggered by an impulse event stream $\omega(t)$.

5. Simulating Simultaneous Stimuli

❖ For a pair of synapses $(i, j) = (1,2)$ on the spine, we compute the membrane potential in the sink for isolated inputs $V(1)$ and $V(2)$, then compute the same with both inputs, $V(1 + 2)$. This plot shows these three time series, as well as the pure sum $V(1) + V(2)$. Note that $V(1 + 2) < V(1) + V(2)$ especially when inputs coincide. This is evidence of sublinear integration in the system.

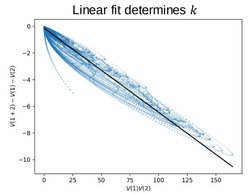
❖ Input event streams are generated by independent Poisson point processes. In reality they are correlated, but our integration results should not depend on input correlations.



6. Quantifying Sublinear Integration

We use a bilinear integration rule to quantify nonlinearity: the coefficient k_{ij} describes scale-free per-mV nonlinearity for a pair of synapses i, j on the spine. Sublinearity means $k < 0$, but k varies with input rate and synapse attributes. (Voltages in this equation are measured relative to resting potential, not membrane potential.)

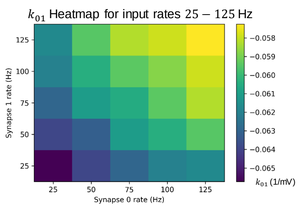
Linear fit determines k

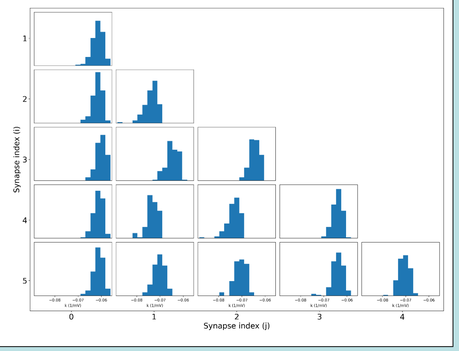


$$V(i + j) - V(i) - V(j) = k_{ij} V(i) V(j)$$

Below shows a grid of histograms of k_{ij} for each pair of synapses (i, j) on toric spine ② for a range of input rates $10 - 130$ Hz. We see that the range and distribution of k varies depending on the pair of active synapses.

k_{01} Heatmap for input rates $25 - 125$ Hz





Conclusions

MORPHOLOGY PROCESSING
The lack of robust algorithmic processing of complex morphologies into simulator-usable format has been a significant road block in the past. This project solves this by providing a clean pipeline that preserves high-resolution topology.

Our Python tools for morphologies are open source and we welcome collaboration!
https://github.com/jmrfox/swctools
https://gitlab.com/penalab/mcf2swc

BIOPHYSICAL SIMULATION
With this pipeline we can construct high-resolution morphologically accurate biophysical simulations of individual toric spines and study their dynamical properties with realistic synapse and ion channel models. Arbor provides a fast and flexible framework for multi-compartmental neuron simulation.

INTEGRATION STUDIES
We observe general sublinear integration in all cases. While the observed sublinearity itself is not due to the unique morphological structure of the toric spines, the characteristics of the sublinearity change with spine morphology, synapse attributes and locations, and input rates.

FUTURE RESEARCH PLANS
- ☞ Biophysical parameters derived from [4] have large uncertainty bands. Perform a systematic uncertainty quantification to measure variability of system behavior and integration results on parameter values (e.g., membrane capacitance).
- ☞ Explore the effects of voltage-gated ion channels on membrane excitability in toric spines and subthreshold integration.
- ☞ Develop a model for the whole ICx space-specific neuron in Arbor with inputs generated from a realistic auditory stimulus-driven spiking neural network.

References

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Acknowledgements

This research is supported by NIH NINDS Grant #1RF1**NS132812**-01: *Integrative Analysis of Adaptive Information Processing and Learning-Dependent Circuit Reorganization in the Auditory System*. Special thanks to Roland Ferger for his expertise and passion for neuroscience.