Ultrafast connectivity optimization of large-scale biophysical network models with deep learning

Nicholas Tolley [1] **Stephanie R. Jones** [1]

Summary

Understanding the relationship between network connectivity and emergent neural dynamics is a fundamental and unsolved problem in neuroscience. Detailed biophysical models can simulate highly realistic neural circuits with biologically interpretable parameters, providing a powerful way to study neural dynamics. However, their use is challenged by an overwhelming number of model parameters, computationally expensive simulations, and complex mappings from model parameters to simulation outputs. Previous work has demonstrated that deep neural networks (surrogate models) can be trained to approximate compartmental neuron models, offering simulation speeds that are orders of magnitude faster. Here, we extend this work by implementing surrogate models of individual cells (Fig 1(B,C)) and using a spiking neural network (SNN) architecture to connect them into a biophysical network model. This construction permits efficient gradient-based optimization of cell-cell connectivity parameters (Fig 2(B,F)), and the ability to optimize to complex neural activity patterns. We demonstrate the effectiveness of this approach by using surrogate models to approximate a detailed model of the neocortex, the Human Neocortical Neurosolver (HNN) (Fig 1A). As a proof-of-concept, we infer the strength of connectivity among neurons that gives rise to 15-60 Hz oscillations from noisy background drive (Fig 2A-C), with corresponding predictions on cell spiking activity (Fig 2C-F).

These methods open detailed biophysical modeling to questions that have been previously restricted to more abstract mathematically-tractable models with limited biological interpretability. Important future applications include the study of multi-area network models and cortical traveling waves.

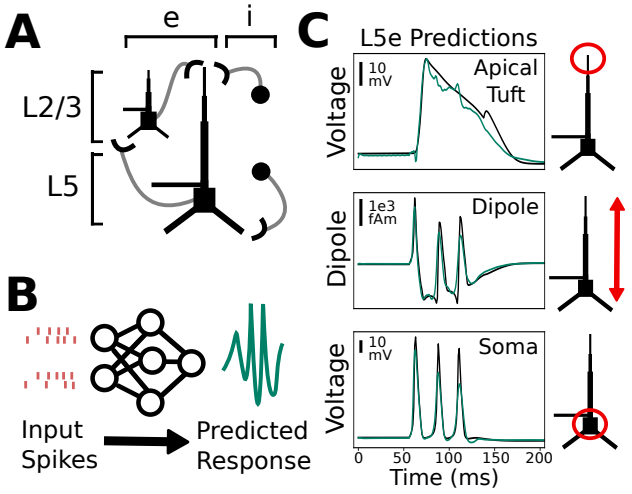

Figure 1. Surrogate model accurately predicts compartmental voltage responses and net current dipole of individual neurons in HNN. **A**: The HNN cortical column model is composed of 4 distinct cell types: L2/3 and L5 excitatory pyramidal (e) and inhibitory (i) neurons. **B**: The surrogate model is trained to take synapse activation times as input, and outputs compartmental voltages and current dipole signals. **C**: Predictions of the surrogate model (**teal**) compared to L5e neuron simulations (**black**).

Training deep neural networks to be surrogate models for biophysical neurons

We chose HNN (Neymotin et al., 2020) as the biophysical network model to be approximated by surrogate models (Fig 1A). HNN is a large-scale detailed model of a cortical column designed to simulate electrical currents (i.e., current dipoles) underlying M/EEG signals with interpretability at

[1]Department of Neuroscience, Brown University, Providence, RI, USA. Correspondence to: Nicholas Tolley <nicholas_tolley@brown.edu>.

the cell and circuit level. The 4 principle cell types in the model are L2/3 and L5 excitatory pyramidal (e) and inhibitory (i) neurons.

A CNN-LSTM implemented in PyTorch was trained to predict the response of individual neurons to a train of input spikes based on the methods of (Oláh et al., 2022) (Fig 1B). The training and validation sets were produced by activating all excitatory AMPA synapses with random spike trains of 10 Hz Poisson noise (independently across compartments). The final trained surrogate model accurately predicted compartmental voltages and current dipoles (Fig 1C). For L5e, the correlation between the HNN simulation and surrogate model predictions on a held-out validation set was 0.843 and 0.861 for the membrane potentials at the soma and apical tuft, and 0.772 for the current dipole.

Connecting single-cell surrogate models with a deep learning-based SNN architecture

The single-cell surrogate models were then connected in a cortical microcircuit based on the cell-cell connectivity structure defined by HNN, with 50 excitatory and 16 inhibitory cells in each layer. A potential benefit of surrogate modeling is the ability to use gradient-based optimizers to tune the connectivity structure (Adam implemented in PyTorch used below). A naive implementation of a surrogate network model cannot be optimized because thresholding functions used to determine spiking are not differentiable. Therefore, we adopted techniques from SNN methods and equipped our spike threshold function with an approximate gradient (the fast sigmoid function) which is critical for performing backpropogation through the surrogate network model. The major benefit of this approach is the ability to define complex neural activity patterns as the optimization objective, enabling rapid identification of connectivity parameters that produce desired outputs.

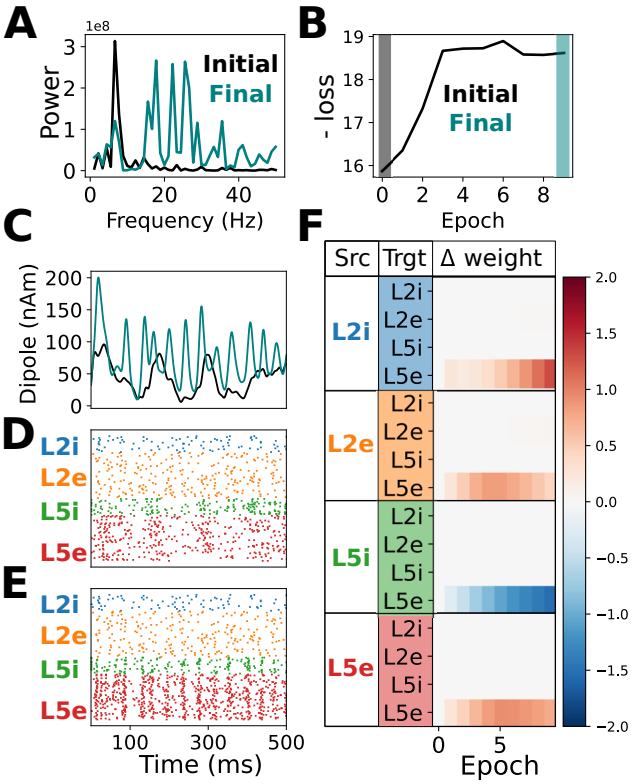

Figure 2. **A**: Power spectral density of dipole produced by initial (**black**) and final (**teal**) connectivity parameters. **B**: The optimizer efficiently maximized high frequency band power. **C**: Simulated dipole shows high frequency oscillations (**teal**) with final connectivity parameters. **D**: Spike raster of initial parameters. **E**: Spike raster of final parameters. **F**: Optimization of cell-cell connection weights on each epoch.

Inferring excitatory-inhibitory connectivity that produces neural oscillations

We tested the network's ability to optimize connectivity parameters by tasking it to maximize spontaneous high frequency oscillations (15-60 Hz) in a network driven by 10 Hz Poisson noise (Fig 2A). The loss function was defined as $L = -\log(\int_{15}^{60} S_X(\omega)\,\mathrm{d}\omega)$ and effectively maximizes 15-60 Hz power in the dipole signal $X(t)$. The optimizer rapidly increased high frequency power from an initial connectivity configuration that produced low frequency activity in the alpha (8-12 Hz) range to a final configuration that produced substantially more activity in the beta (15-30 Hz) range after 10 epochs (Fig 2A-C). Spike rasters of the initial (Fig 2D) and fi-

nal (Fig 2E) configurations show that both oscillations are due to synchronous firing of L5e cells. Inspection of connectivity modifications (Fig 2F) reveals changes were made exclusively to L5e targeting projections, reflecting L5 pyramidal cells as the main contributor to M/EEG dipoles. L2i→L5e connections were strengthened, whereas L5i→L5e connections were weakened, suggesting that L2 and L5 inhibitory neurons play opposing roles in determining oscillation frequency in this proof-of-concept example.

References

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