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

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Large-scale biophysically detailed models are useful but challenging to implement

Detailed biophysical models provide interpretable, mechanistic predictions about neural data[1-3], however...

They're hard to use due to:
1) High computational cost
2) Difficult to fit parameters[4]

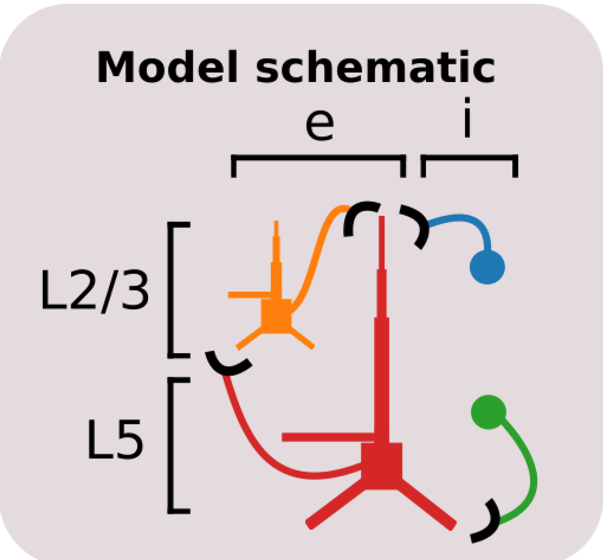
Solution: surrogate models
Deep neural networks trained to replicate activity of detailed neurons

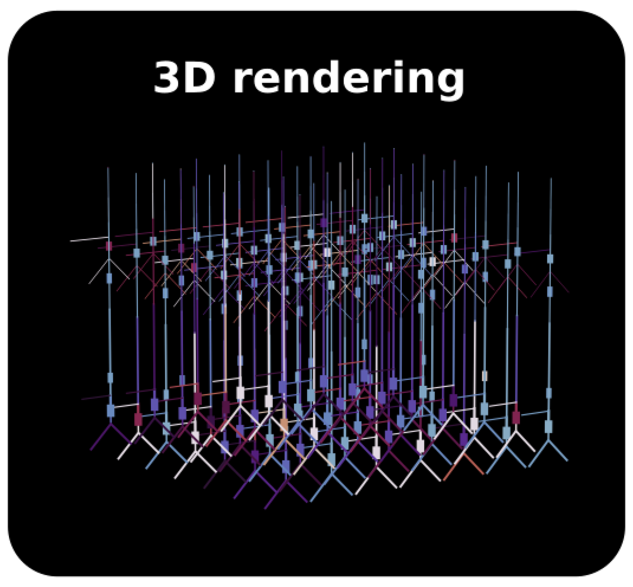
Surrogate models can help by:

1) Approximating simulators with faster deep neural networks[5,6]

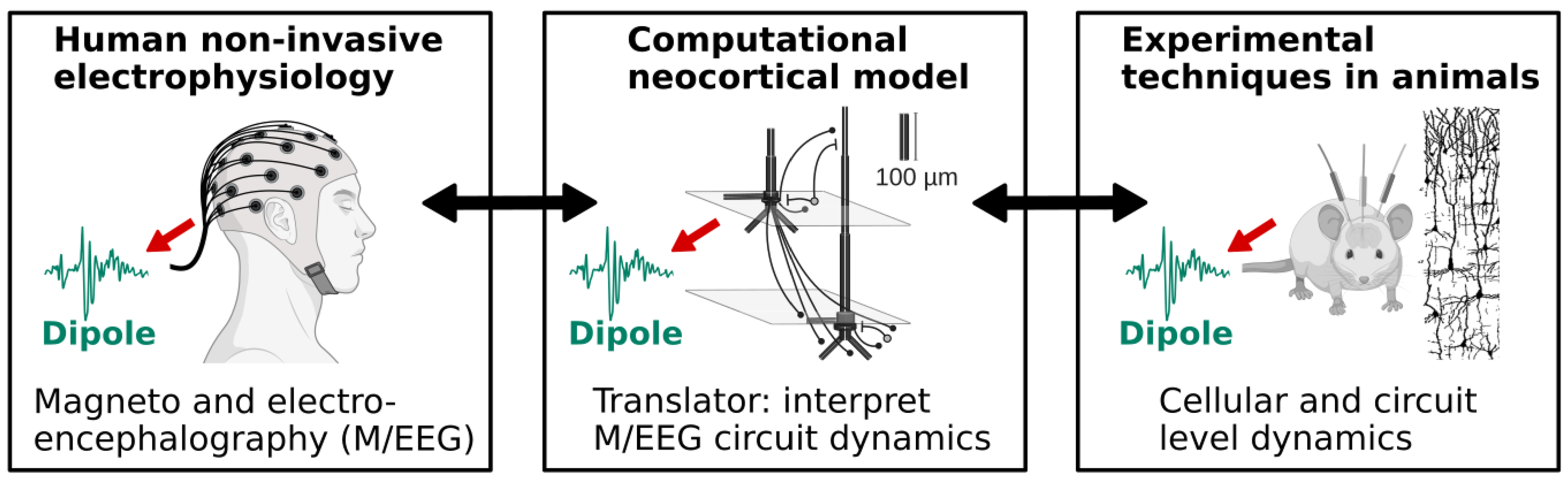
2) Optimizing parameters through gradient descent, a **novel approach**

The Human Neocortical Neurosolver (HNN): a large-scale modeling framework to study the origins of M/EEG



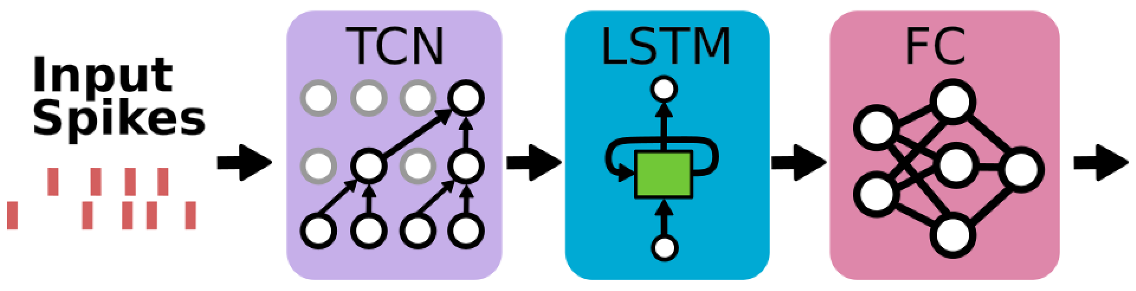


HNN (hnn.brown.edu) simulates a large-scale network of biophysically detailed cortical neurons, and is designed to bridge macroscale M/EEG to microscale cell and circuit level phenomena

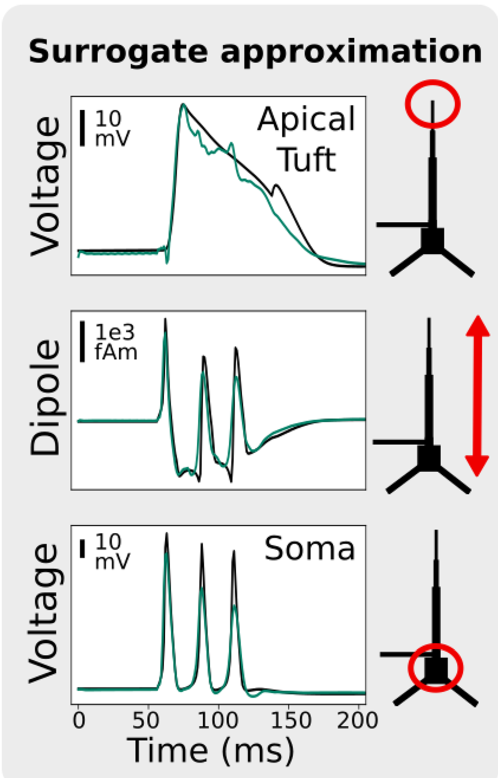


Deep neural networks can be used as surrogate models of biophysically detailed neurons

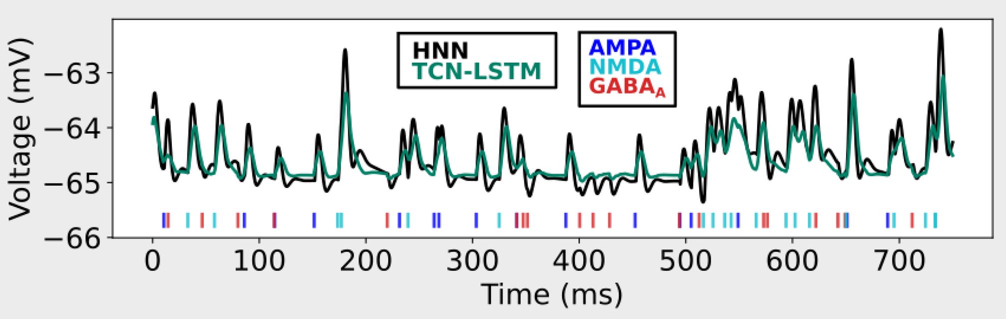
A **TCN-LSTM** architecture[6] was used to learn the voltage response of single neurons to input spikes (i.e. the **surrogate model**)



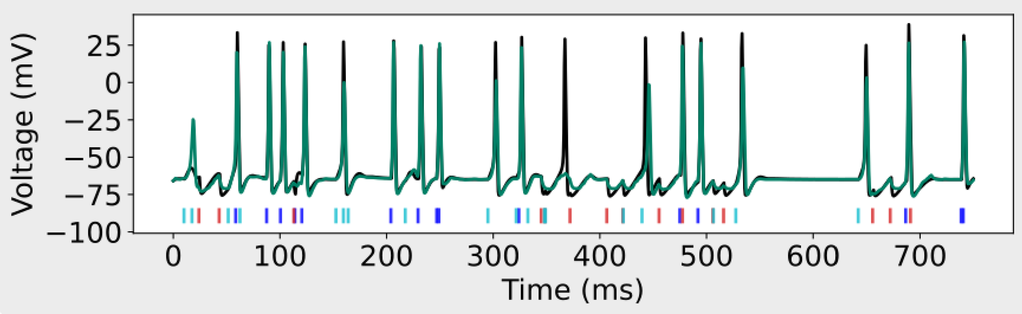
Training data was generated by simulating Poisson spike times that activated random sets of synapses spanning **sub- and suprathreshold** synaptic strengths



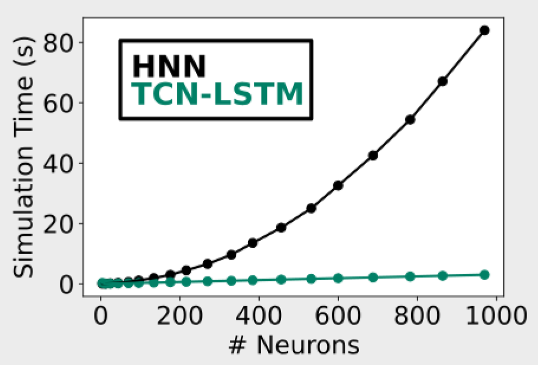
Surrogate model learns temporal summation of subthreshold inputs



Surrogate model learns firing threshold and shape of action potential



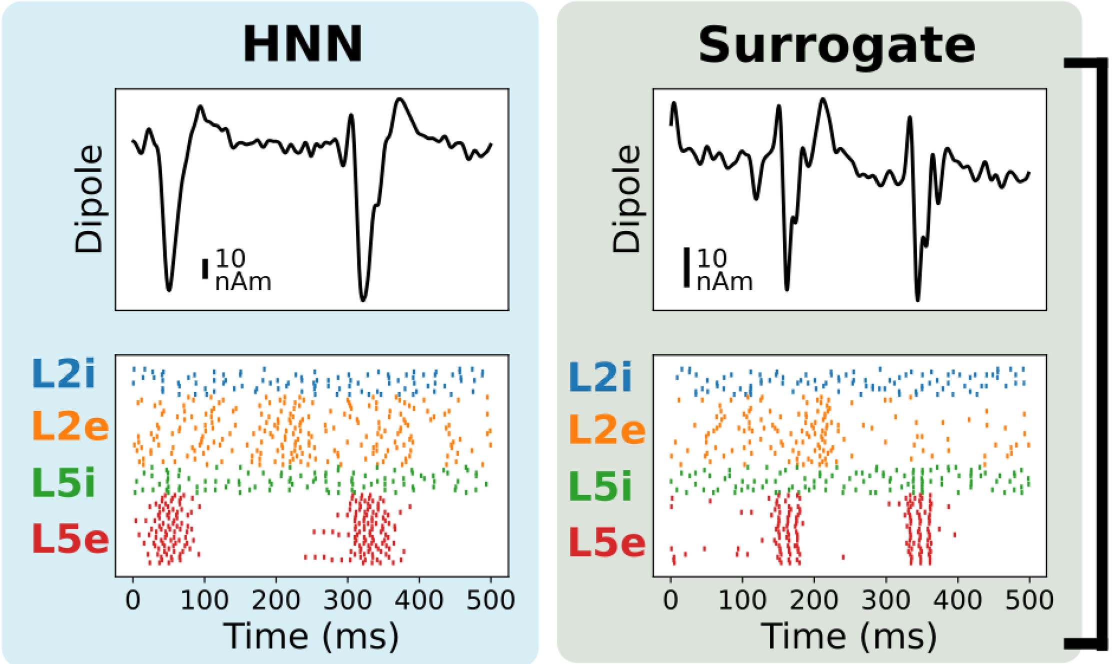
Simulation time



Savings in simulation time enable **massive scaling** of simulated **network size**

Surrogate network models approximate features of network activity even with changed connectivity

Surrogate models of each cell type in HNN were connected in a large-scale neocortical circuit

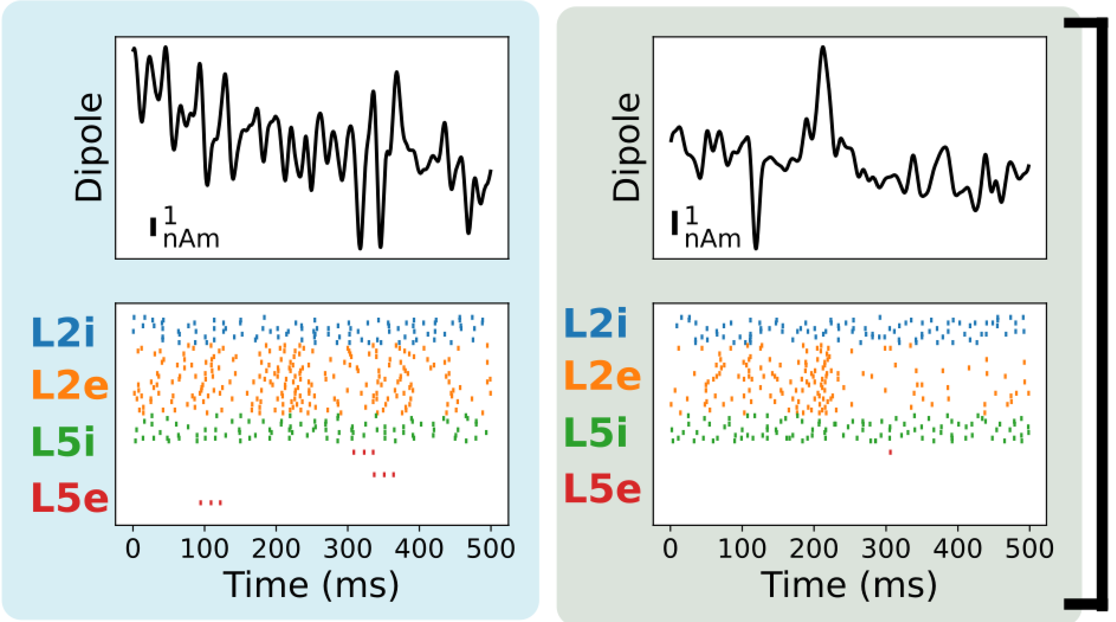


Default connectivity

Network level simulations produce spontaneous oscillations given noisy drive to proximal synapses

Close agreement between surrogate model and HNN

Dipole signal is largely created by synchronous spiking of L5e neurons



Increased L5i → L5e

L5e spiking is disrupted due to inhibition by L5i

Surrogate model accurately captures changes in network activity due to connectivity

This allows us to efficiently **optimize connectivity without retraining**

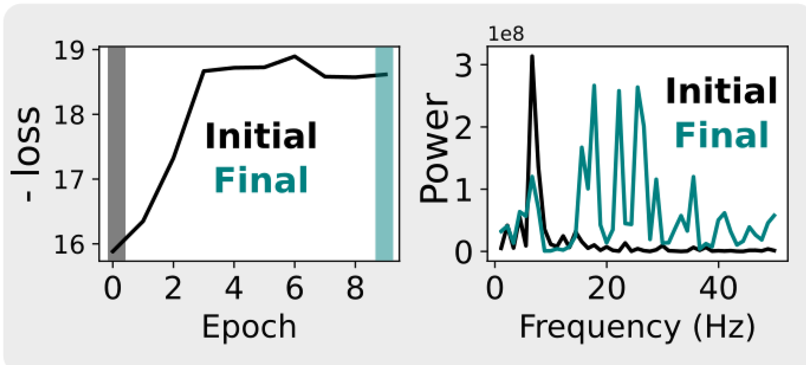
Connectivity can be efficiently optimized with gradient descent in surrogate network models

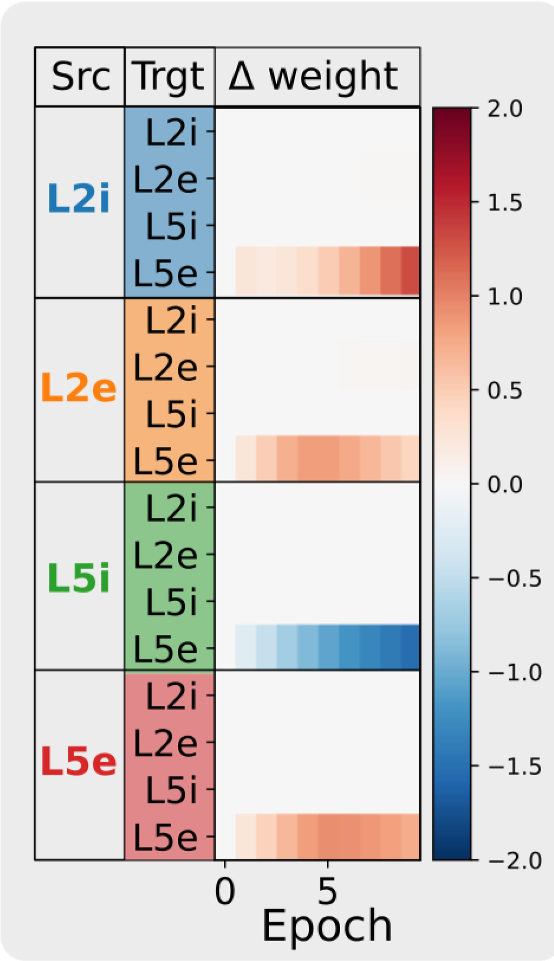
Given a network that **generates alpha (10 Hz) oscillations** with noisy inputs, can I find a **connectivity configuration** that produces **high frequency (15-60 Hz) oscillations?**

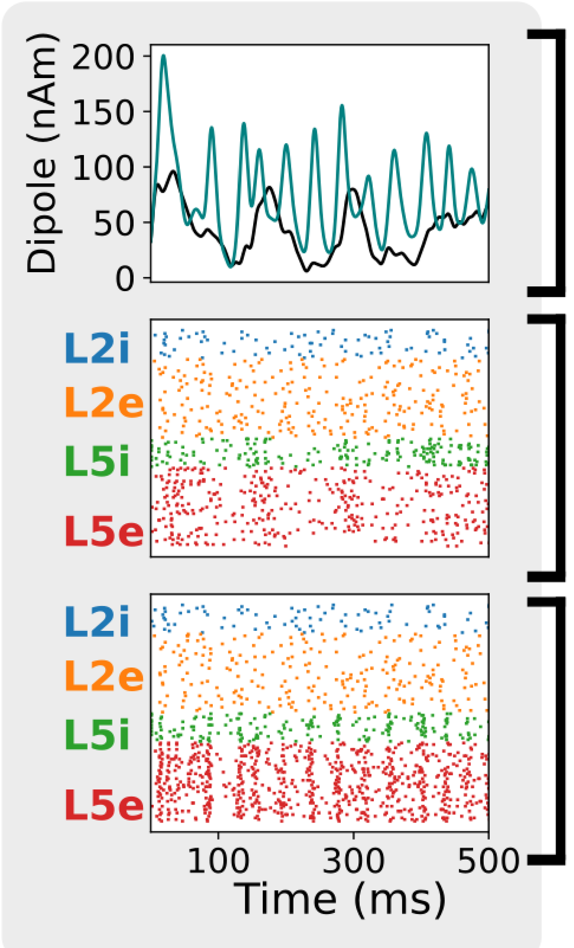
We treated a single TCN-LSTM (neuron) as a node in a spiking neural network (SNN), this approach allows:

1) **Fitting connectivity parameters** with off-the-shelf deep learning optimizers (e.g. Adam)

2) **Complex optimization objectives** (e.g. maximize band power)







Gradient descent was used to find the optimal connections for spontaneous high frequency oscillations

Initial connectivity produced alpha frequency (10 Hz) oscillations

Final connectivity produced higher frequency beta (13-30 Hz) oscillations

Conclusions and future directions

1) Deep neural network-based surrogate models decrease simulation time, and enable rapid connectivity optimization

2) Surrogate modeling can permit large scale biophysically detailed simulations previously restricted to abstract, mathematically tractable models (e.g. examination of cortical traveling waves)

3) Future work is necessary to improve training efficiency of surrogate models, and better understand when gradient descent may fail to optimize parameters

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[1] Jones et al., J. Neurophysiol. (2009) [2] Neymotin et al., eLife (2020) [3] Sherman et al., Proc. Natl. Acad. Sci. (2016) [4] Tolley et al., PLoS Comput. Biol. (2024) [5] Oláh et al., eLife (2022) [6] Verhellen et al., bioRxiv (2023)

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HNN conceptual figure created with BioRender.com