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Towards a detailed mechanistic model of human cortical microcircuits that accurately predicts the cellular- and circuit-level effects of TMS

Transcranial magnetic stimulation (TMS) is a non-invasive neuromodulation technique that alters activity in a small brain region and can treat neurological conditions. TMS parameters, including location, intensity, and frequency, are typically chosen using a "one-size-fits-all" approach. Personalizing TMS can enhance target engagement and treatment efficacy but requires accurately predicting its effects on brain circuits, which remains unsolved. Mechanistic biophysical simulations offer a powerful approach to integrate experimental data and predict TMS effects at molecular, cellular, and circuit scales. They can simulate local field potentials (LFP), EEG, and TMS effects, informing optimal parameter selection.

We present preliminary results from simulating TMS in a detailed human cortical circuit model. Adapted from a rat somatosensory cortex model, our model includes 6,796 neurons of 55 cell types across 6 layers, with human-like morphology, physiology, and axons necessary for accurate TMS simulation. It incorporates distance-dependent connectivity, synaptic background activity, and short-term plasticity to reproduce in vivo-like firing. We implemented the model using NEURON and NetPyNE.

Simulating biphasic TMS pulses at 30 Hz (1 sec, 60 V/m) induced layer 5 pyramidal neuron spiking synchronized to stimulation pulses. At 80 V/m, neurons across all layers fired synchronously. Disconnected neurons did not spike, indicating that circuit connectivity and activity lower the TMS response threshold.

These results highlight the need to simulate circuit activity to characterize TMS effects. Next, we will validate against human TMS-EEG data, simulate disease-related electrophysiological biomarkers, and evaluate TMS parameters for restoring healthy dynamics.