Multiscale modeling of the brain motor cortex circuits

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As part of our NIH U01 grant we developed a detailed multiscale computational model of mouse primary motor cortex (M1) microcircuits, based on novel data provided by experimentalist collaborators. The model simulates in full scale a cylindrical volume of diameter of 300 μm and cortical depth 1350 μm of M1, with over 10,000 neurons and 80 million synaptic connections. Neuron models were optimized to reproduce the electrophysiological properties of the main classes of excitatory and inhibitory cells, with a special emphasis layer 5 corticospinal and corticostriatal neurons. Their ionic channel distributions were constrained by literature and optimized to reproduce with high precision in vitro recordings (membrane voltages and firing rates). Detailed cell morphologies with 700+ compartments were derived from real neuron 3D microscopy reconstructions. Network connectivity was based on multiple optogenetic circuit mapping studies that found cell type- and sublayer-specific connectivity patterns. The synaptic input distribution across cell dendritic trees -- likely to subserve important neural coding functions-- was also mapped using optogenetic methods and incorporated into the model. The model was completed by adding the main long range inputs that drive and modulate M1 microcircuits, including thalamus and other sensorimotor cortical regions; employing published experimental data to determine the projection strength and the dendritic distribution of these long-range inputs as a function of the target cell type and cortical depth. This multiscale model enabled us to analyze neural dynamics and information flow in M1 microcircuits, to better understand how input activity from different regions is propagated and transformed across cortical layers. The model will help decipher the neural code underlying the brain circuits responsible for producing movement, help understand motor disorders, and evaluate novel pharmacological or neurostimulation treatments.

The model was developed using NEURON and NetPyNE, a new software tool our lab is developing. NEURON is a widely used neuronal simulator, with over 1600 published models. NetPyNE is a Python package to facilitate the development of biological neuronal networks in the NEURON simulator. NetPyNE emphasizes the incorporation of multiscale anatomical and physiological data at varying levels of detail. NetPyNE seamlessly converts a set of a simple, standardized high-level specifications in a declarative format into a NEURON model. NetPyNE also facilitates organizing and running parallel simulations by eliminating the burdensome task of manually distributing the workload and gathering data across computing nodes. It also provides a powerful set of analysis methods so the user can plot spike raster plots, LFP power spectra, information transfer measures, connectivity matrices, or intrinsic time-varying variables (eg. voltage) of any subset of cells. To facilitate data sharing, the package saves and loads the specifications, network, and simulation results using common file formats (Pickle, Matlab, JSON or HDF5), and can convert to and from NeuroML, a standard data format for exchanging models in computational neuroscience.