Cross-frequency coupling and information flow in a multiscale model of M1 microcircuits

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We developed a model of primary motor cortex (M1) microcircuits [1] with over 10,000 biophysically detailed neurons [2] and 30 million synaptic connections. It simulates a cylindric cortical volume with a depth of 1350 μm and a diameter of 300 μm. Neuron densities, classes, morphology and biophysics, and connectivity at the long-range, local and dendritic scale were derived from experimental data published in over 30 studies. The model was developed using the NetPyNE tool [3], which facilitated the integration of this complex experimental data at multiple scales. Our model exhibited spontaneous neural activity patterns and oscillations consistent with M1 data. Neural activity depended on cell class, cortical layer and sublaminar location. Different output dynamics were seen when the network was driven by brief activation of particular long-range inputs, or in the setting of different neuromodulatory conditions. Results yielded insights into circuit information pathways, oscillatory coding mechanisms and the role of HCN in modulating corticospinal output.

LFP revealed physiological oscillations in delta (0.5-4 Hz) and high beta to low gamma (25-40 Hz) ranges across layers and populations. Oscillations occurred in the absence of rhythmic external inputs, emergent from neuronal biophysical properties and circuit connectivity. Filtering the LFP signal from the electrode located in upper L5B revealed phase-amplitude coupling of fast oscillations on delta wave phase. LFP spectrogram demonstrated that the fast oscillations occurred robustly during the time course of simulations. Strong LFP beta and gamma oscillations are characteristic of motor cortex activity, and have been found to enhance signal transmission in mouse neocortex. Phase-amplitude coupling may help integrate information across temporal scales and across networks.

Analysis of firing dynamics and information flow in our model confirmed and extended our understanding of information flow in cortical microcircuits. Consistent with existing models, sensory-related long-range inputs targeted superficial layers which in turn projected to deeper layers. Our simulations, however, provided further details: information flow was cell-class specific, going unidirectionally from IT to PT cells; sublaminar-specific, with superficial ITs targeting primarily the upper portion of L5B PT cells; and oscillation frequency-specific, with Granger causality peaks occurring at shifted beta/gamma range frequencies for different internal connections.

Our work provides insights into oscillatory mechanisms and information flow in M1 microcircuits. Our detailed computational model provides a useful tool for researchers in the field to evaluate novel hypothesis, understand motor disorders and develop novel pharmacological or neurostimulation treatments.

Acknowledgments

Research supported by NIH grant U01EB017695, DOH01-C32250GG-3450000, NIH R01EB022903.

References

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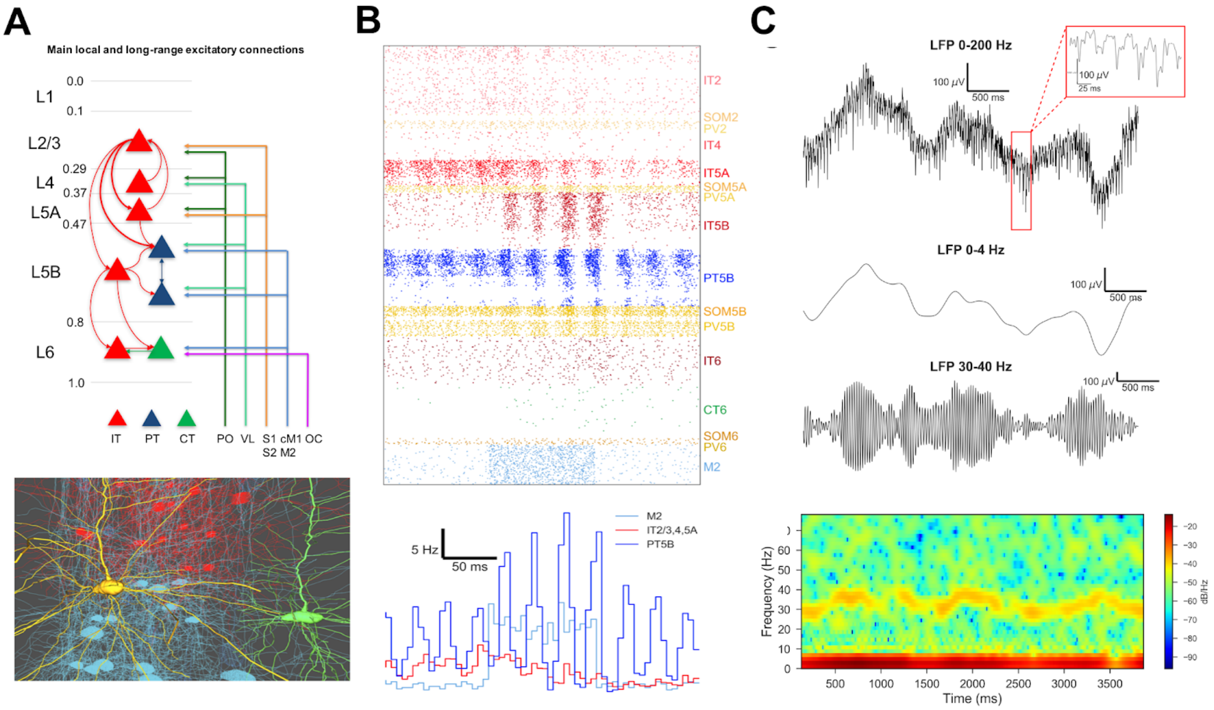

Figure 1: Multiscale model of M1 microcircuits. A) Major local and long-range excitatory connections (top) and 3D representation (bottom). B) Response M2 input pulse; raster plot (top) and spike histogram (bottom). C) LFP signal during spontaneous activity with phase-coupled delta (0-4Hz) and gamma (30-40Hz) oscillations (top and middle); and LFP spectrogram (bottom).