Modeling stimulation-enhanced synchrony among distributed brain areas

Proposed project for UCLA Research in Industrial Projects for Students (RIPS) 2015

Industrial sponsor: HRL Laboratories, LLC

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Problem description

There has been a recent surge in applications that involve applying weak current stimulation to the brain either invasively or non-invasively for enhancing and/or restoring various brain functions. These interventions range from augmenting performance in behavioral tasks, including attention, memory, and motor function, to treating neurological conditions such as anxiety, depression, and Parkinson's disease. While there are numerous demonstrations of positive behavioral and clinical effects with brain stimulation in both animal and human subjects, the underlying neural mechanisms are poorly understood. This lack of understanding coincides with highly variable results across subjects and behavioral tasks for the same stimulation protocol. In this regard, HRL Laboratories is currently leading a DARPA program (Restoring Active Memory) to rigorously investigate the effects of invasive and non-invasive stimulation in modulating neural activity and synchrony across multiple brain areas and enhancing memory function in healthy non-human primates (NHPs). Another equally important goal is to develop a mathematical model that provides a systems-level neural explanation of stimulation-induced memory enhancement.

For the RIPS project, we would like the team to investigate a key hypothesis that the application of alternating current stimulation (ACS) to task-relevant brain areas can enhance performance by improving the temporal synchrony in their dynamic neural responses. We believe that the communication between two regions can be controlled externally using ACS based on the modulation of their local field potentials (LFPs) in the extracellular media. A computational study of this hypothesis requires modeling interactions among excitatory and inhibitory neurons in multiple inter-connected brain areas and analyzing the effects of various stimulation patterns on temporal synchrony. Such a framework would be extremely valuable to rationally optimize spatiotemporal stimulation patterns to enhance and/or restore a given behavioral function, and could have a direct impact on society in the near future. This project provides a great opportunity to also explore fundamental concepts in computational neuroscience such as firing rate vs. temporal coding in the brain, and oscillatory modulation of neural signaling within and between brain areas.

Detailed task list

The suggested task list for this project follows, along with identification of which members of the team [theory, software implementation, simulation analysis] could serve as primary contributors. This proposed work will complement what we are doing in our DARPA program.

- Gain familiarity with basic principles of spiking neural networks including neural firing, mean field approximation for local field potential (LFP), and neural synchrony [entire team].
- Simulate a generic spiking model comprising $n > 3$ populations of excitatory and inhibitory neurons for different network motifs, responding to static and dynamic stimuli [software implementation].
- Analyze the rate and temporal code of neuronal responses, spectral content of LFPs, and synchrony between various populations in different frequency bands [simulation analysis].
- Investigate neural synchrony effects for different current stimulation parameters from literature; e.g., pulse train, AC, DC, space-variant pattern, spatially uniform, focal, distributed – vary amplitude, frequency, and duration of applied currents [simulation analysis].
- Define and characterize rate of information transmission between various cell populations, and determine which aspects of current stimulation have the most effect [theory; simulation analysis].
- Identify extensions to the developed neural synchrony model for addressing well-known behavioral correlates such as top-down attention and suppression [entire team].

Desired qualifications

This project involves simulating and analyzing spiking neural networks as scalable systems of coupled nonlinear differential equations. Students are expected to have some experience in signal processing and statistics. At least two students should have strong software development skills (MATLAB/C/C++). An interest in brain mechanisms and modeling will be a big plus.

Recommended reading

[1] Wallisch, P., Lusignan, M. E., Benayoun, M. D., Baker, T. I., Dickey, A. S., & Hatsopoulos, N. G. (2014). *MATLAB for neuroscientists: an introduction to scientific computing in MATLAB*. Academic Press.

[2] Buzsaki, G. Rhythms of the Brain. Oxford University Press. 2006.

[3] Uhlhaas, P., Pipa, G., Lima, B., Melloni, L., Neuenschwander, S., Nikolić, D., & Singer, W. (2009). Neural synchrony in cortical networks: history, concept and current status. *Frontiers in Integrative Neuroscience*, *3*, 17.

[4] Fries, P. (2009). Neuronal gamma-band synchronization as a fundamental process in cortical computation. *Annual Review of Neuroscience*, *32*, 209-224.

[5] Srinivasa, N., & Cho, Y. (2014). Unsupervised discrimination of patterns in spiking neural networks with excitatory and inhibitory synaptic plasticity. *Frontiers in Computational Neuroscience*, *8*.

[6] Reato, D., Rahman, A., Bikson, M., & Parra, L. C. (2010). Low-intensity electrical stimulation affects network dynamics by modulating population rate and spike timing. *The Journal of Neuroscience*, *30*(45), 15067-15079.

[7] Reato, D., Rahman, A., Bikson, M., & Parra, L. C. (2013). Effects of weak transcranial alternating current stimulation on brain activity—a review of known mechanisms from animal studies. *Frontiers in Human Neuroscience*, *7*.

[8] Fröhlich, F., & Schmidt, S. L. (2013). Rational design of transcranial current stimulation (TCS) through mechanistic insights into cortical network dynamics. *Frontiers in Human Neuroscience*, *7*.

[9] Suthana, N., & Fried, I. (2014). Deep brain stimulation for enhancement of learning and memory. *Neuroimage*, *85*, 996-1002.