Modeling Electrical Stimulation of Cortical Networks

Joseph Nelson[1,3], Bard Ermentrout[1,2], Jonathan Rubin[1,2]

1: Center For The Neural Basis of Cognition 2: Department of Mathematics, University of Pittsburgh 3: jon35@pitt.edu

Introduction

Experiments and computational models have provided evidence that Deep Brain Stimulation of the Subthalamic Nucleus can control the brain rhythms of populations of neurons in the motor cortex [1,2,3]. It has also been shown that stimulation of M1 Layer 5 projection neurons is more affective at improving akinesia in hemi-parkinsonian rats than excitation or inhibition of STN neurons [1].

Inspired by these papers, I used Hodgkin-Huxley conductance-based neural networks of excitatory and inhibitory neurons to model DBS-like stimulation of a small cortical network.

I found that high frequency DBS can disrupt beta rhythms in the network. However, all-to-all HH single compartment networks will too easily follow the frequency of the DBS stimulus without considering axonal heterogeneities.

Methods

The equations for all the Hodgkin-Huxley excitatory and inhibitory neurons which I use to model the cortical network are:

$$V_e' = I_e - I_{ionic}(V_e, n_e, m_e, h_e) - I_{Ca}V_e - I_{AHP}(V_e, [Ca]) - I_{ie} - I_{ee} + d_{sa}(V_{a0} - V_e)$$

$$V_i' = I_i - I_{ionic}(V_i, n_i, m_i, h_i) - I_{ei} - I_{ii}$$

The equation for the axon compartments is:

$$V_{a0}' = I - I_{ionic}(V_{a0}, n_{a0}, m_{a0}, h_{a0}) + d_{as}(V_e - V_{a0}) + input(t)$$

where:

$$I_{ionic}(V, n, m, h) = g_{Na}(V - E_{Na}) + g_K(V - E_K) + g_L(V - E_L)$$

is the sum of the transient sodium, rectifying potassium, and leak ionic channels.

$$I_{ee} = \frac{g_{ee}}{N}\sum_{j=1}^{N} S_e^j\,(V_e - E_{e,syn}),$$
$$I_{ei} = \frac{g_{ei}}{N}\sum_{j=1}^{N} S_e^j\,(V_e - E_{i,syn}),$$
$$I_{ie} = g_{ie}s_i(V_e - E_{i,syn}), \text{ and}$$
$$I_{ii} = g_{ii}s_i(V_i - E_{i,syn})$$

are the synaptic currents between neurons, where the first letter denotes the pre- and the second letter denotes the post-synaptic neuron (excitatory and inhibitory).

I_{Ca} is the calcium current.

I_{AHP} is the After Hyper-Potential current .

$input(t)$ is the DBS-like stimulus.

Results

Indirectly Disrupting Excitatory Cell Firing

Using a small network of excitatory and inhibitory cells as shown in Fig 1, I coupled a 10-compartment axon to the excitatory cell E1. I applied a 100 Hz square wave stimulus to the other end of the axon. With this, I managed to prevent excitatory cell E3 from firing Action Potentials.

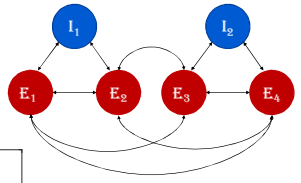
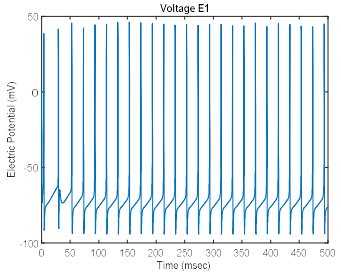
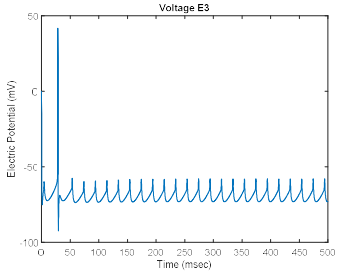


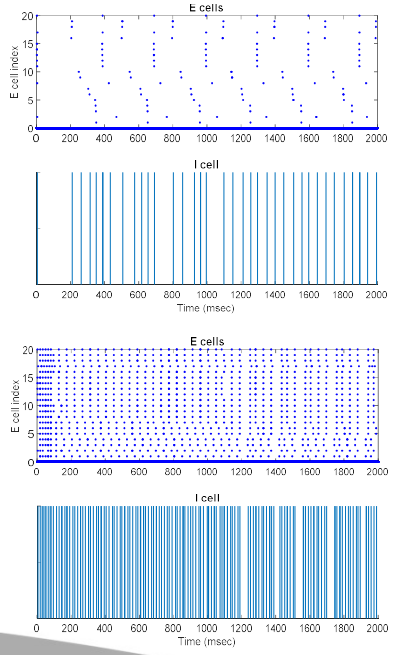
Fig. 1



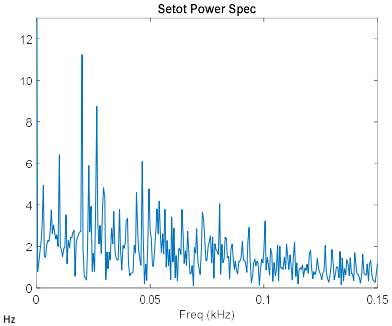


Increasing the Power of High Frequencies in Local Field Potential

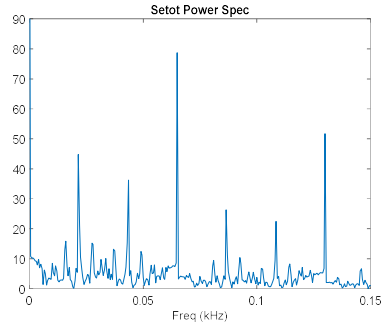
In a network with 20 excitatory cells and 1 inhibitory cell, I applied a 130 Hz stimulus to the end of each excitatory cell's axon. The Local Field Potential of the network showed a max in the Power Spectrum around 65 Hz, in the Gamma Range.



Raster and LFP Power Spec Without Stimulus



Raster and LFP Power Spec With 130 Hz Stimulus



Discussion

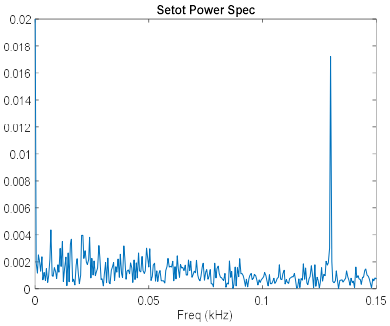
The work shown in the Results section is from simulations where the stimulus was guaranteed to propagate into the excitatory cell (the probability of success = 100%).

I also simulated the network when there was a probability of failure. This addition was inspired by the observation [2] that antidromic spikes traveling from the STN to the motor cortex have a probability of canceling with an orthodromic spike.

It was hypothesized [1] that this stochastic stimulation of the motor cortex was disrupting the beta rhythm. For our simple model, I computed the average power in the beta range (12-30 Hz) and found a decrease in the average beta power as the probability of successful stimulus propagation decreased (from an average power of $1.0 * 10^{-3}$ when the probability of success = 100% to $6.73 * 10^{-4}$ when the probability of success = 25%).

To verify this result, however, I would need to use a much larger, multicompartment model network.

An issue we had with our simulation was that the power spectrum of the Local Field Potential of our network followed the stimulus frequency as the stimulus amplitude increased.



Currently, I am adding randomly distributed stimulus signal delays to model axonal heterogeneities with the hope of significantly decreasing the power of the DBS stimulus frequency in the LFP.

Future Work

In future work, I would use small networks to model the STN-Gpe-Gpi network and connect it to my current cortical network to verify the effects of STN DBS on the Motor Cortex [2].

References

1. Gradinaru, V. et al. (2009). Optical Deconstruction of Parkinsonian Neural Circuitry. Science.

2. Li, Qian. Et all. (2012). Therapeutic Deep Brain Stimulation in Parkinsonian Rats Directly Influence Motor Cortex. Cell Press.

3. Kang, Gulyeom, Lowery, Madeleine M. (2014). Effects of antidromic and orthodromic activation of STN afferent axons during DBS in Parkinson's disease: a simulation study. Frontiers in Computational Neuroscience.