Math 572A: Mathematical and Computational Neuroscience Final Project Outline

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I. Biological Background

A. Hodgkin-Huxley Model [A]

i. The HH model has long been used to model neurons

ii. Considered the most biologically accurate model

iii. Authors of [A] proposed a novel, scalable, adaptable, modular model for use in analyzing and simulating three different types of neurons found in the human brain

a. Fast spiking (FS) neurons - Fast regular rate

b. Regular spiking with adaptation (RSA) neurons - High frequency spikes are followed by lower constant frequency spikes

c. Intrinsically bursting (IB) neurons - Fast spiking train followed by period of quiescence

B. Importance of Inhibition

i. Inhibition plays just as important of a role in neuronal networks as excitation

a. Allows for feedback and blocking of specific signals

ii. Irregular inhibition is linked to many neurological disorders

a. Schizophrenia - Impaired inhibition and gamma frequencies [B]

b. Epilepsy - Ratio of excitatory to inhibitory neurons [C]

II. Previous Mathematical Models [A]

A. Base HH model neurons:

$$\begin{cases} \dot{V}(t) = & 1/C_M(I_{inj}(t) - \bar{g}_K n^4(t)\,(V(t) - V_K) \\ & -\bar{g}_M p(t)\,(V(t) - V_K) - \bar{g}_{Ca} q^2(t) s(t)\,(V(t) - V_{Ca}) \\ & -\bar{g}_{Na} m^3(t) h(t)\,(V(t) - V_{Na}) - \bar{g}_L\,(V(t) - V_L)), \\ \dot{x}(t) = & \alpha_x(t)(1 - x(t)) - \beta_x(t) x(t), \;\; x \in \{n, m, h, s, q\}, \\ \dot{p}(t) = & \frac{p_\infty(t) - p(t)}{\tau_p(t)}. \end{cases} \tag{1}$$

i. FS neurons use sodium, potassium, and leak currents

ii. RSA neurons use sodium, potassium, slow non-inactivating potassium, and leak currents

iii. IB neurons use sodium, potassium, slow non-inactivating potassium, calcium and leak currents.

B. Additional component for electrical synapses:

$$V_{el} = \sum_{j=1}^{N} \epsilon_{ij}^{el}(V_j(t) - V_i(t)). \tag{2}$$

i. This equation is used to represent pre-synaptic excitatory RSA and IB neurons

C. Additional component for chemical synapses:

$$\begin{cases} V_{ch} = \sum_{j=1}^{N} \epsilon_{ij}^{ch} r_j(t)(V_{syn}^{i} - V_j(t)), \\ \dot{r}_j(t) = \left(\frac{1}{\tau_r} - \frac{1}{\tau_d}\right) \frac{(1 - r_j(t))}{1 + e^{-V_j(t)+V_0}} - \frac{1}{\tau_d} r_j(t). \end{cases} \tag{3}$$

i. This equation is used to represent pre-synaptic excitatory RSA and IB neurons and inhibitory FS neurons

III. Contributions

A. The contributions made will be primarily exploratory in nature

B. Changing the strength of inhibition and how that affects various neuronal networks

i. Two Neuron Networks

a. One excitatory, one inhibitory neuron

b. How does changing the level of inhibition affect the frequency and behavior of spiking of both neurons?

c. If time, could compare the results to simpler network models, such as theta networks, to see if there are major differences between a phenomenological approach and a more biologically accurate approach

ii. Larger Networks

a. Recreate networks from original model [A] such as feedback inhibition, feedforward inhibition, lateral inhibition, and disinhibition

b. Vary level of inhibition and examine how it affects the larger network dynamics

C. Update the model to allow for RSA and IB neurons to be inhibitory

i. Two Neuron Networks

a. One excitatory, one inhibitory neuron

b. Do different types of inhibitory neurons affect the frequency and behavior of the network?

c. If time, compare to theta network to see how results compare between phenomenological approach and a more biologically accurate approach

IV. Expected Conclusions

A. Strength of Inhibition

i. Two Neuron Networks

a. As the strength of inhibition increases, the network frequency should decrease
b. However, there is likely to be a minimum, non-zero frequency as the inhibitory neuron cannot permanently disable the excitatory neuron
c. It is expected that this model will yield similar long-term dynamics when compared to the theta network model from varying the synaptic strength in both. However, local dynamics might differ as the theta network model cannot account for the different types of neurons

ii. Larger Networks
a. Feedback Inhibition - Increasing inhibition will lead to a decrease in the frequency of the network as whole
b. Feedforward Inhibition - Increasing inhibition will lead to a decrease in the firing of the final neuron in the network, or potentially complete silencing
c. Lateral Inhibition - Increasing inhibition should lead to similar results as feedforward inhibition as this network is effectively two parallel feedforward networks
d. Disinhibition - Increased inhibition can either increase activity of the final neuron or decrease it. This is because inhibitory neurons are connected to one another in the network

B. Allowing RSA and IB neurons to be inhibitory

i. Two Neuron Networks
a. As each neuron has different spiking behavior, there should be differences between each network if the strength of inhibition is kept constant
b. More analysis into the behavior of each neuronal type is needed to determine how allowing them to be inhibitory will affect the dynamics of the system
c. Again, in comparison to the theta network model, results should be similar, but the theta network will have trouble accounting for differences in each neuronal type

V. References

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