Computational Lab

In this assignment we will explore the synchronization of two Hodgkin-Huxley model neurons connected by reciprocal, inhibitory synapses. Use the the full HH model from homework 2.

1. **Uncoupled Neurons** [15 points].

Create two Hodgkin-Huxley model neurons and run the simulation of both uncoupled neurons for 500 ms, injecting a constant 10 $\mu$A/cm$^2$ current into one neuron and 20 $\mu$A/cm$^2$ into the other. Explain your results focusing on how, over time, their spiking drifts apart.

*Hint: It is convenient to vectorize variables so that $V(1)$, $m(1)$, ... are for neuron A and $V(2)$, $m(2)$, ... are for neuron B.*

2. **Inhibitory Synaptic Current** [15 points].

![Diagram of two neurons with inhibitory currents](image)

Add reciprocal, inhibitory (GABA$A$) synapses between the two neurons:

$$I_{syn} = g_{GABA_A} r (V_{post} - E_{Cl})$$

with receptor channel kinetics $r$ governing the synaptic dynamics:

$$\frac{dr}{dt} = \alpha_r [T] (1 - r) - \beta_r r$$

$$[T] = [T]_{max} / (1 + \exp(- (V_{pre} - V_p)/K_p))$$

with:

$$E_{Cl} = -80 \ mV$$

$$\alpha_r = 5 \ mM^{-1}ms^{-1}; \ \beta_r = 0.18 \ ms^{-1}$$

$$[T]_{max} = 1.5 \ mM$$

$$K_p = 5 \ mV; \ \ V_p = 7 \ mV$$

*In these equations, $V_{pre}$ and $V_{post}$ are the pre- and postsynaptic membrane voltage, which are $V(1)$ and $V(2)$ for the first synapse, and $V(2)$ and $V(1)$ for the second synapse, respectively.*
Run the simulation of the synaptically coupled neurons multiple times increasing the peak synaptic conductance $g_{GABA_A}$ from zero by steps of $0.1 \ mS/cm^2$ until the two neurons phase lock while injecting $10 \ \mu A/cm^2$ into one neuron and $20 \ \mu A/cm^2$ into the other. It can be helpful to plot $r_1$ and $r_2$ as well as $V_1$ and $V_2$.

Next, increase $g_{GABA_A}$ from 0.5 to 3.5 $mS/cm^2$ by steps of 0.5 $mS/cm^2$ and see how the behavior of the neurons changes. Why does this phenomenon happen?

Plot the spiking frequency of the two neurons as a function of $g_{GABA_A}$. In general, it is a good idea to have your program estimate the frequency (spike count over a time interval) after the neurons have had time to recover (e.g. after 250 ms). You can use the isi function to calculate the average and standard deviation of the interspike intervals.

3. **In-Phase Oscillations** [15 points].

When the current injected into the two neurons is more similar to each other, interesting phenomenon can be observed. Set the $I_{ext}$ currents to 10.0 and 10.1 $\mu A/cm^2$ respectively and hold $g_{GABA_A}$ at 1 $mS/cm^2$. Run multiple simulations decreasing the value of the backward rate constant, $\beta_r$, from 0.5 $ms^{-1}$ to 0.1 $ms^{-1}$ by steps of 0.1 $ms^{-1}$.

This increases the decay time of the current, and at some value of $\beta_r$, the neurons should settle into a nearly in-phase (as opposed to anti-phase) spiking pattern. Why do you think this happens?

Plot the phase of the two neurons as a function of $\beta_r$. You can use the spk.phase function from the course website to calculate the phase between spiking patterns.

**Homework Problems**

Expanding on the two state model, you will develop a model for the dynamics of an excitatory postsynaptic current and use it to investigate the dynamics of two 3-neuron network motifs.

4. **Excitatory Synapse Model** [20 points].

Create an excitatory synapse using the same form as the inhibitory synapse but with the parameters:

\[
\begin{align*}
E &= -38 \ mV \\
\alpha_r &= 2.4 \ mM^{-1}ms^{-1}; \quad \beta_r = 0.56 \ ms^{-1} \\
[T]_{max} &= 1.0 \ mM \\
g_{Glu} &= 0 \ to \ 0.5 \ mS/cm^2
\end{align*}
\]

Test the excitatory synapse by injecting current into A and recording spike(s) in B. Try many different values of $g_{Glu}$ and compare the spike rates in A and B. Tuning the strength of the connections will be important for the subsequent questions.
5. **Feedforward Inhibition** [20 points].

Feedforward inhibition occurs when a primary neuron has input current into an inhibitory neuron as well as the output neuron. How does this connectivity affect the dynamics of the input/output function? What is the relationship between the spike train in neuron A vs. C for various currents? You should play around with $g_{Glu}$ and $g_{GABA}$ to alter the connection strengths of the network.

6. **Feedback Inhibition** [10 points].

Feedback inhibition occurs through the connectivity shown above. How does the spike frequency of the output vary with the input?

7. **Function of Mini-Networks** [5 points].

Explore and describe the potential functions of these feedforward and feedback network motifs.

8. **Loop** [Bonus Problem: 20 points].

You can connect many cells in a loop with excitatory synapses to get continual firing from a small pulse applied to one cell ($10 \mu A/cm^2$ for 1 ms). The more cells you have, the easier it is to do. A 5-cell loop can be done with just changing $g_{Glu}$. A 4-cell loop needs a few more tweaks. A 3-cell loop should be possible. Once you get continual firing, what can you add to stop it?
Submission Guidelines

Solutions without work or explanations where applicable will receive no credit. Submit a single .zip file containing solutions, plots, and Matlab/Python code to both computational lab and homework problems by 3:00pm of due date via email to both TAs. The submission file should follow the naming scheme LastFirst_A12345678_HW4.zip. The email title should follow the naming scheme [BENG 260] Homework 4 - Last First. (Please use BENG 260 regardless of which section you registered for)