Neurodynamics - Fall 2019

BENG 260 / BGGN 260 / PHYS 279

Homework 4: Due November 4

1 Computational Lab

In this assignment we will explore the synchronization of two Hodgkin-Huxley model neurons connected by reciprocal, inhibitory synapses. For both neurons use the full HH model.

The equations describing the HH dynamics are replicated here for convenience **(Note: Parameters and equations are slightly changed for a baseline voltage of -70 mV, it is recommended you use these parameters)**:

$$
\begin{aligned}
\frac{dV}{dt} &= \frac{1}{C}\left(-I_{Na} - I_K - I_L + I_{ext}\right) && (1)\\
I_{Na} &= g_{Na}\, m^3 h\, (V - E_{Na}) && (2)\\
I_K &= g_K\, n^4\, (V - E_K) && (3)\\
I_L &= g_L\, (V - E_L) && (4)
\end{aligned}
$$

with parameters:

$$
\begin{array}{rclrcl}
C &=& 1\,\mu F/cm^2 & & & \\
E_{Na} &=& 45\,mV; & g_{Na} &=& 120\,mS/cm^2 \\
E_K &=& -82\,mV; & g_K &=& 36\,mS/cm^2 \\
E_L &=& -59.387\,mV; & g_L &=& 0.3\,mS/cm^2
\end{array} \qquad (5)
$$

where the dynamics of gating variables:

$$
\begin{aligned}
\frac{dm}{dt} &= \alpha_m(V)\,(1-m) - \beta_m(V)\,m && (6)\\
\frac{dh}{dt} &= \alpha_h(V)\,(1-h) - \beta_h(V)\,h && (7)\\
\frac{dn}{dt} &= \alpha_n(V)\,(1-n) - \beta_n(V)\,n && (8)
\end{aligned}
$$

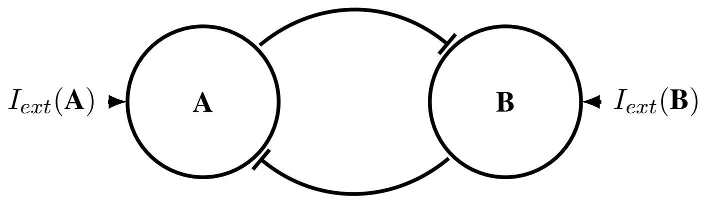
is determined by rate functions (note: these equations are different from Homework 2):

$$
\begin{aligned}
\alpha_m(V) &= 0.1(V+45)/(1-\exp(-(V+45)/10)) && (9)\\
\beta_m(V) &= 4\ \exp(-(V+70)/18) && (10)\\
\alpha_h(V) &= 0.07\ \exp(-(V+70)/20) && (11)\\
\beta_h(V) &= 1/(1+\exp((-(V+40))/10)) && (12)\\
\alpha_n(V) &= 0.01(V+60)/(1-(\exp((-(V+60)/10)-1)) && (13)\\
\beta_n(V) &= 0.125\ \exp(-(V+70)/80) && (14)
\end{aligned}
$$

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. Plot the last 100ms of the simulations and explain your results focusing on how their spiking frequencies and phases.

   *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].



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

$$I_{syn} = g_{GABA_A}\, r\, (V_{post} - E_{Cl}) \tag{15}$$

   with receptor channel kinetics r governing the synaptic dynamics:

$$\frac{dr}{dt} = \alpha_r[T]\,(1-r) - \beta_r\, r \tag{16}$$

$$[T] = [T]_{max}/(1+\exp(-(V_{pre}-V_p)/K_p)) \tag{17}$$

   with:

$$\begin{aligned} E_{Cl} &= -80\, mV \\ \alpha_r &= 5\, mM^{-1}ms^{-1}; \quad \beta_r = 0.18\, ms^{-1} \\ [T]_{max} &= 1.5\, mM \\ K_p &= 5\, mV; \quad V_p = 7\, mV \end{aligned} \tag{18}$$

   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 a number of times, increasing the peak synaptic conductance g_{GABA_A} from zero to 0.5 mS/cm^2 by steps of 0.1 mS/cm^2 while injecting 10 $\mu A/cm^2$ into one neuron and 20 $\mu A/cm^2$ into the other. Plot the last 100ms of each simulation and describe how the spiking frequency and phase change with changing g_{GABA_A}. 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 mS/cm^2 to 3.5 mS/cm^2 by steps of 0.5 mS/cm^2. Plot the last 100ms of each simulation and describe the changing behavior. Why does this phenomena 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, another 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 1.0 mS/cm^2. Run multiple simulations, decreasing the value of the backward rate constant, β_r, from 0.2 ms^{-1} to 0.1 ms^{-1} by steps of 0.01 ms^{-1}, plot the last 100ms of each simulation.

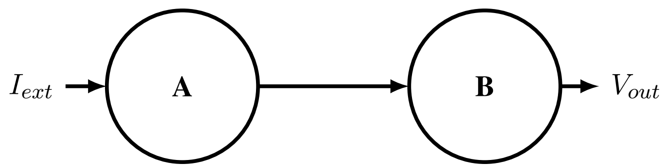
This increases the decay time of the current, and at some value of β_r, the neurons should settle into a nearly in-phase (as opposed to anti-phase) spiking pattern. Why do you think this happens?

Plot the phase of the two neurons as a function of β_r. You can use the `spk_phase` function to calculate the phase between spiking patterns.

2 Homework

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

4. *Excitatory synapse model* [20 points].

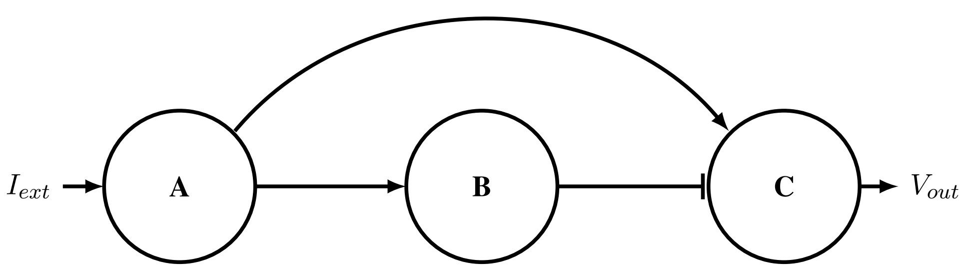


Create an excitatory synapse using the same form as the inhibitory synapse but with the parameters:

$$\begin{aligned} E &= -38\,mV \\ \alpha_r &= 2.4\,mM^{-1}ms^{-1}; \quad \beta_r = 0.56\,ms^{-1} \\ [T]_{max} &= 1.0\,mM \\ g_{Glu} &= 0 \text{ to } 0.5\,mS/cm^2 \end{aligned} \tag{19}$$

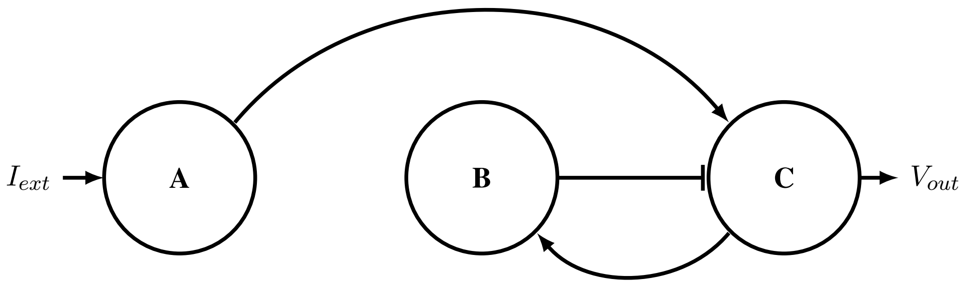
Test the excitatory synapse by injecting current into **A** and recording spike(s) in **B**. First simulate with $I_{ext} = 10\mu A/cm^2$ and $g_{Glu_{AB}} = 0.3$. Plot the results and compare the spike rates in **A** and **B**. Try different values of $g_{Glu_{AB}}$ and compare the spike rates in **A** and **B**. Tuning the strength of the connections will be important for the subsequent parts.

5. *Feedforward inhibition* [20 points].



Feedforward inhibition is when a primary neuron has input current into an inhibitory neuron as well as your output neuron. First simulate with $I_{ext} = 10\mu A/cm^2$ and $g_{GABA_{BC}} = 1$, $g_{Glu_{AB}} = g_{Glu_{AC}} = 0.4$. Plot the results and comment on how this connectivity affects 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_A} to alter the connection strengths of the network.

6. *Feedback inhibition* [10 points]

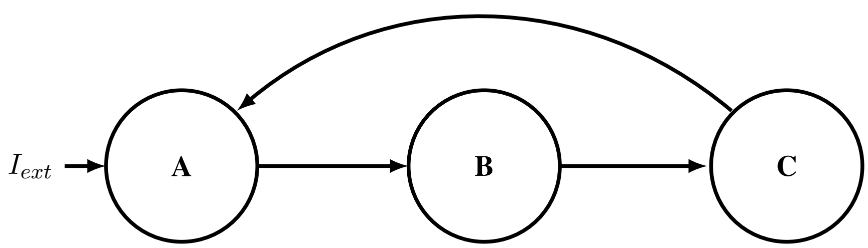


Feedback inhibition occurs through the connectivity shown below. First simulate with $I_{ext} = 10\mu A/cm^2$ and $g_{GABA_{BC}} = 1$, $g_{Glu_{AC}} = g_{Glu_{CB}} = 0.5$. Plot the results. Try other connectivity weights and comment on how the spike frequency of the output varies with the input?

7. *Function of mini-networks* [5 points]

   Explore and describe the potential uses of these feedforward and feedback network motifs in neuroscience and other fields.

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



You can connect many cells in a loop with excitatory synapses to get continual firing from just a small pulse 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 a single PDF with all your solutions, plots, and any handwritten code as well as your Matlab/Python code to both computational lab and homework problems by 3:00pm of due date on Canvas.

The submission file should follow the naming scheme `LastFirst_A12345678_HW2.zip`