BENG/BGGN 260 Neurodynamics Fall 2015

Week 4 Exercise

1 Computational Lab

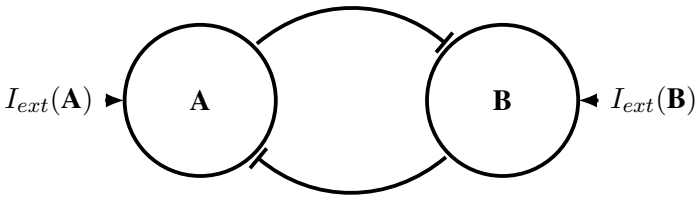
In this lab we will explore the synchronization of two Hodgkin-Huxley model neurons connected by recip-rocal, inhibitory synapses. For both neurons reuse the full HH model from last week.

1.1 Two uncoupled neurons

Create two Hodgkin-Huxley model neurons. 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** (in Python this is $V[0]$, $m[0]$, ... and $V[1]$, $m[1]$, ...).

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. Over time their spiking drifts apart.

1.2 Adding an inhibitory synaptic current



Now add reciprocal, inhibitory ($GABA_A$) synapses between the two neurons:

$$I_{syn} = g_{GABA_A}\, r\, (V_{post} - E_{Cl}) \tag{1}$$

with receptor channel kinetics r governing the synaptic dynamics:

$$\frac{dr}{dt} = \alpha_r [T]\,(1-r) - \beta_r\, r \tag{2}$$

$$[T] = [T]_{max}/(1+\exp(-(V_{pre}-V_p)/K_p)) \tag{3}$$

with:

$$\begin{aligned} E_{Cl} &= -80\ mV \\ \alpha_r &= 5\ mM^{-1}ms^{-1}; \quad \beta_r = 0.18\ ms^{-1} \\ [T]_{max} &= 1.5\ mM \\ K_p &= 5\ mV; \qquad\qquad V_p = 7\ mV \end{aligned} \tag{4}$$

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.

Again injecting $10\ \mu A/cm^2$ into one neuron and $20\ \mu A/cm^2$ into the other run the simulation of the synaptically coupled neurons a number of 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. It can be helpful to plot r_1 and r_2 as well as V_1 and V_2. Then 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 "settle," e.g. after $250\ ms$ or so. You can use the `isi` function to calculate the average and standard deviation of the interspike intervals. Which can be downloaded from the course website for MATLAB (isi.m) and Python (part of ndtools imported like `from ndtools.spikes import *`

1.3 In-phase oscillations

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 $1\ mS/cm^2$. Now run a number of simulations, decreasing the value of the backward rate constant, β_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. At some value of β_r, the neurons should settle into a nearly in-phase, rather than 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 from the course website to calculate the phase between spiking patterns.

1.4 [*Optional*]

If you want to explore some more, there are many other things you can try. For example, you could see the effect of including only a single synapse or you can also synchronize the neurons with an electrical synapse.

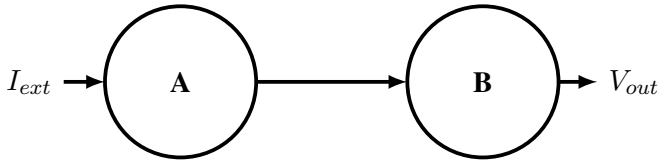
2 **Homework** (Optional)

For the homework you are going to expand beyond this simple two neuron model. This will involve developing a model for the dynamics of an excitatory postsynaptic current and using it to investigate the dynamics of two 3-neuron network motifs. Make sure to also submit your work and answers for the lab portion.

2.1 Excitatory synapse model

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

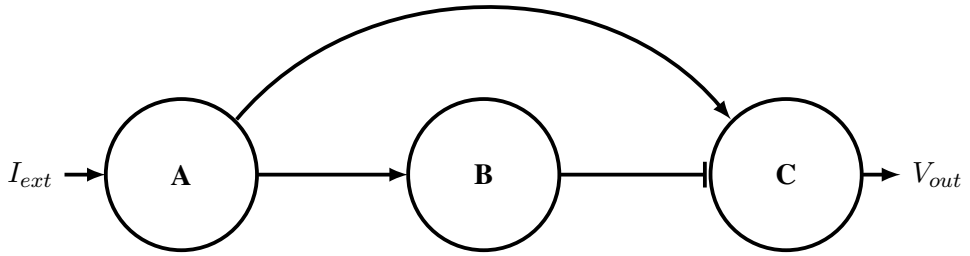
$$\begin{aligned} E &= -38\ mV \\ \alpha_r &= 2.4\ mM^{-1}ms^{-1};\quad \beta_r = 0.56\ ms^{-1} \\ [T]_{max} &= 1.0\ mM \\ g_{Glu} &= 0 \text{ to } 0.5\ mS/cm^2 \end{aligned} \tag{5}$$



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 other parts.

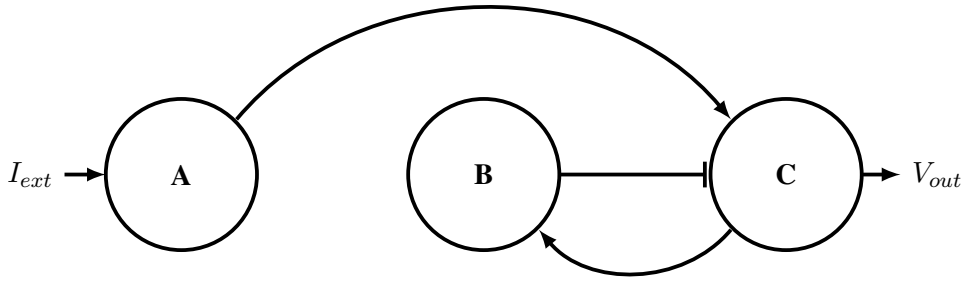
2.2 Feedforward inhibition

Feedforward inhibition is when a primary neuron has input current into an inhibitory neuron as well as your 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_A} to alter the connection strengths of the network.



2.3 Feedback inhibition

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



2.4 Function of mini-networks

What could the functions of these feedforward and feedback network motifs be?

2.5 [*Bonus*] Loop

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?