Homework Assignment 1

*** Due **Tuesday 9/16/14 by noon** on Sakai under HW1. Upload your submission as a **Word document**. ***

Please reaffirm the Duke Community Standard at the top of your assignment:
"I have adhered to the Duke Community Standard in completing this assignment." [Electronic Student Signature]

Please explain your methods, show all work, explain your results, include units, and label your axes. Upload your .m files with clear filenames.

Rhythmic oscillations in a population of neurons are common in the central nervous system. For example, central pattern generators in the spinal cord can produce the periodic signals required for walking (or other gaits) without the brain having to intervene. Populations of neuron in the brain can rhythmically fire at a given frequency to convey information. However, sometimes these oscillations become excessive, causing an epileptic seizure.

We will model a simple neural oscillator.

Part 1 – Why model epilepsy?

Citing peer-reviewed literature, write one page (single-spaced, 12pt font, 1" margins) discussing: (1) why computational models of epilepsy are important, (2) three different published computational models of epilepsy, and (3) the primary limitations of each model. The essay will be graded on content, clarity, and grammar.

Part 2 – Intrinsically bursting Izhikevich neuron

In MATLAB, implement an Izhikevich (2003) intrinsically bursting neuron. Note that this is a single compartment model; there is no propagation of action potentials. Use Euler's forward method to numerically solve the differential equation in a time loop. Provide your set of discretized equations (in the form implemented in MATLAB); define/describe each variable and give values to the parameters.

Create a plot in which the top subplot shows v(t) and the bottom subplot shows $I_{stim}(t)$. Make $I_{stim}=0$ initially to show that the neuron is not active without an applied current. $I_{stim}(t)$ should be a positive pulse of current that starts at t>0 with an amplitude that generates an initial rapid burst of action potentials, followed by slower spiking. After I_{stim} turns off, the neuron's potential should return to rest.

Part 3 – Synapse

In MATLAB, code the alpha synapse function (Dayan and Abbott, "Theoretical Neuroscience", 2001, p. 178-189):

$$P_s(t) = P_{max} t * \frac{\exp\left(1 - \frac{t}{\tau_s}\right)}{\tau_s}$$

where P_{max} is the peak value. This function starts rising at t=0, reaches its peak at $t=\tau_s$, then decays with time constant $t=\tau_s$. $P_s(t)$ is the probability that a postsynaptic channel opens, given that the presynaptic terminal released neurotransmitter. For now, use $P_{max}=1$ and $\tau_s=5$ms. Plot $P_s(t)$, showing the full decay back to zero.

In reality, spikes do not only arrive at the synaptic terminal at t=0 and there are multiple spikes. Expand your code to respond to a series of spikes arriving at the terminal at t={1,5,9,15}ms. Create a second plot with two subplots. The top subplot should have four curves overlaid, one showing $P_s(t)$ for each spike. The bottom subplot should show the total $P_s(t)$.

Part 4 – Two-neuron oscillating network

Let's put Parts 2 and 3 together! We're going to connect two Izhikevich intrinsically bursting neurons such that they take turns bursting.

- Expand the Part 2 code for two neurons. You should store your applied current parameters (amplitude, delay, duration) in vectors so that you can have different values for each neuron. Also add another dimension to your output arrays (e.g. v(t)) to keep track of the results for each neuron.
- Implement vectors that keep track of the spike times for each cell. Check the contents of these vectors to make sure they're right!
- Compute the total $P_s(t)$ for each neuron as in Part 3. Note that $P_s(t)$ for neuron 1 uses the spike times for neuron 2, and vice versa.

Ok, now we're ready to connect the neurons. There are at least a couple of ways in which this can be done:

- Mutual inhibition
  - Constant applied current to both cells.
  - In the dv/dt equation, change I to I-Ps. Ps is subtracted, meaning it's having an inhibitory effect.
- Mutual excitation
  - Only use an initial pulse of applied current.
  - In the dv/dt equation, change I to I+Ps. Ps is added, meaning it's having an excitatory effect.

With either choice, you'll have to do some parameter tweaking to achieve a sustained oscillation where the neurons burst out of phase with each other. You'll need to impose some imbalance in your model such that they get out of phase with each other.

Clearly and concisely explain how you connected your neurons and how you designed the system to produce oscillatory behavior, i.e. alternating bursts of activity between neurons 1 and 2. Provide a table with your chosen parameter values for each neuron: P_{max}, τ_s, and applied current (amplitude, start time, end time).

Provide a plot with three subplots. Each subplot should have two curves, one curve per neuron. The subplots should show v(t), I(t), and P_s(t). Make sure that your P_s(t) plots make sense by looking at the v(t) time courses.

Part 5 – Quantification of the oscillation

Let's quantify the network's oscillation. Look at your plots of both v(t) and Ps(t) from Part 4 to make sure that your system is in steady-state for these measurements. State what block of time you're using for your measurements. Determine the following quantities:

- Period of oscillation of the system.
- Number of spikes per neuron per period.
- Phase offset between the neurons. Provide an equation showing how you calculated this. Explain why your equation is suitable.

For each quantity, average a few measurements. Present your data in a table, including individual measurements and your averaged value for each quantity.

Part 6 – Perturbation of the system

What happens if we try to disturb the oscillation? Perturb the system in <u>two</u> different ways of your choice. Consider at which phase you're applying your perturbation (but don't just apply the same perturbation at two different phases). For each perturbation, provide the same three subplots as Part 4 (v(t), I(t), Ps(t)) and the same measurements as Part 5 (period of oscillation, numbers of spikes, phase offset). Clearly explain your chosen perturbations (with plots/diagrams as needed) and discuss your findings.