

## 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.**

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**TOTAL: 101pts**

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.

**Grading rubric: [20pts]**

- **Content**
  - (1) Why computation models of epilepsy are important [2pts]
  - (2) Three different published models [2pts each; 6pts total]
  - (3) Limitations [6pts]
- **Clarity [3pts]**
- **Grammar [3pts]**

### 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.

**ANSWER: [18pts]**

NOTE: OK to have no units throughout; as stated in Izhikevich 2003,  $v$ ,  $u$ ,  $a$ ,  $b$ ,  $c$ , and  $d$  are dimensionless.

- Equations & parameter values [0.5pts each; 8 pts total]

$$v(i+1) = v(i) + dt*(0.04(v(i))^2 + 5*v(i) + 140 - u(i) + I(i))$$

if ( $v(i+1) \geq 30$ )

$$v(i+1) = c$$

$$u(i+1) = u(i) + d$$

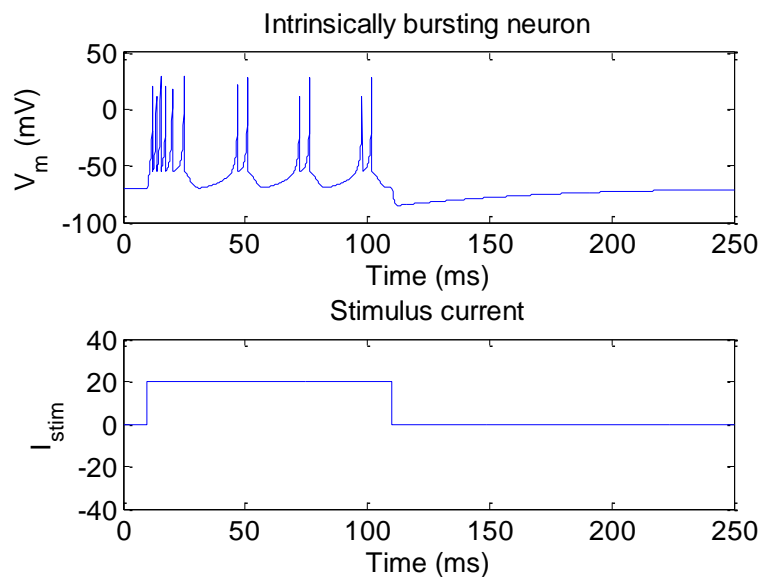
else

$$u(i+1) = u(i) + dt*(a*(b*v(i+1) - u(i)))$$

where  $a = 0.02$ ,  $b = 0.2$ ,  $c = -55$ ,  $d = 4$  for the intrinsically bursting neuron.

- $I$  is the stimulation current
- $v(t)$  is the transmembrane potential
- $u(t)$  is the membrane recovery variable
- $a$  is the time scale of the recovery variable  $u$
- $b$  is the sensitivity of the recovery variable to subthreshold fluctuations of  $v(t)$
- $c$  is the after-spike reset value of  $v$
- $d$  is the after-spike reset value of  $u$

- Axis labels [2pts]
- $I_{stim}(t)$  plot [2pts]
- $V_m(t)$  plot [6pts]



### Part 3 – Synapse

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

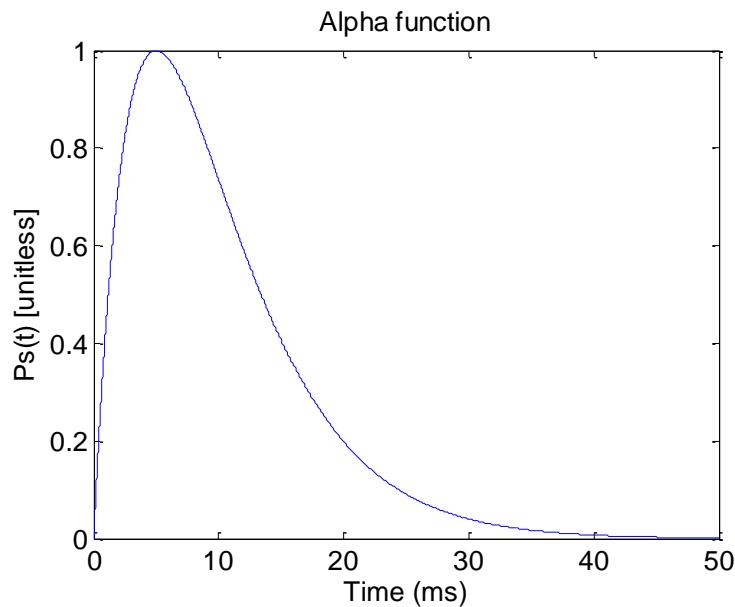
$$P_s(t) = P_{max} t * \frac{\exp\left(1 - \frac{t}{\tau_s}\right)}{\tau_s}$$

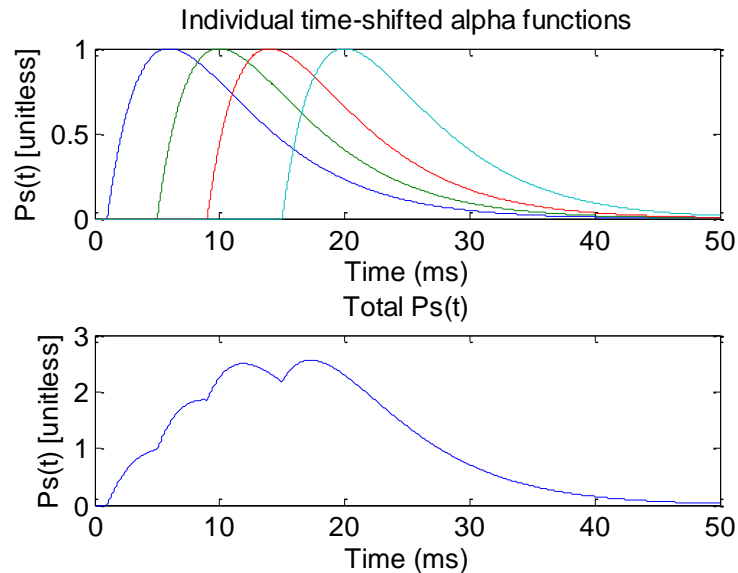
where  $P_{max}$  is the peak value. This function starts rising at  $t=0$ , reaches its peak at  $t=\tau_s$ , then decays with time constant  $t=\tau_s$ .  $P_s(t)$  is the probability that a postsynaptic channel opens, given that the presynaptic terminal released neurotransmitter. For now, use  $P_{max}=1$  and  $\tau_s=5\text{ms}$ . 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  $t=\{1,5,9,15\}\text{ms}$ . 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  $P_s(t)$ .

ANSWER: [10pts]

- Axis labels [2pts]
- Simple  $P_s(t)$  plot [2pts]
- Four time-shifted  $P_s(t)$  plots [4pts]
- Total  $P_s(t)$  plot [2pts]





#### 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  $I - P_s$ .  $P_s$  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  $I + P_s$ .  $P_s$  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:  $P_{\max}$ ,  $\tau_s$ , and applied current (amplitude, start time, end time).

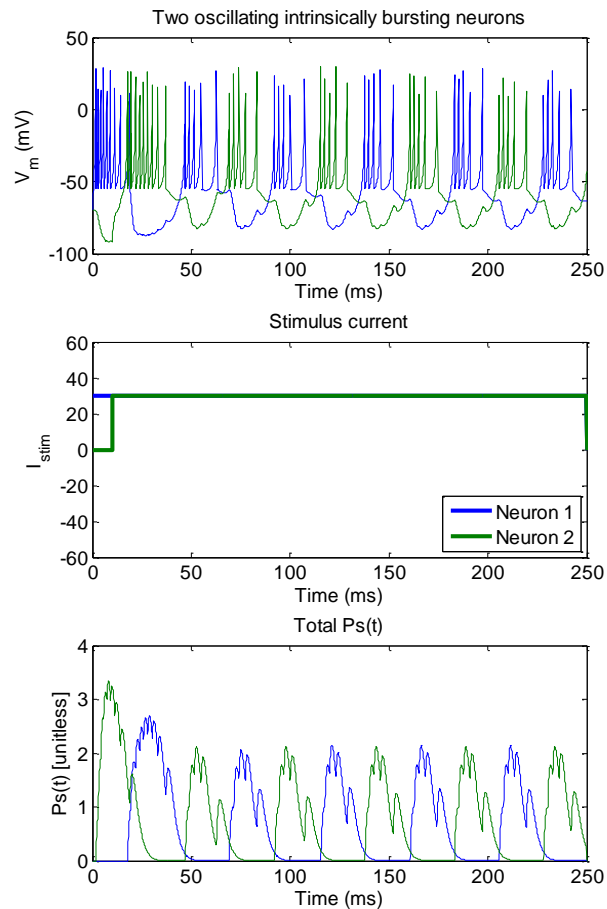
Provide a plot with three subplots. Each subplot should have two curves, one curve per neuron. The subplots should show  $v(t)$ ,  $I(t)$ , and  $P_s(t)$ . Make sure that your  $P_s(t)$  plots make sense by looking at the  $v(t)$  time courses.

ANSWER: [20pts]

- Axis labels [2pts]
- Explanation of design [5pts]
- Table of parameters [0.5pts per parameter; 5pts total]
- 3 subplots [3pts]
- Achieving oscillation [5pts]

I connected my neurons to have mutual inhibition. The imbalance in my network was incorporated by starting the applied current to neuron 1 at  $t=0$ , but at  $t=10\text{ms}$  for neuron 2.

	Neuron 1	Neuron 2
$P_{\max}$	1	1
$\tau_s$	2ms	2ms
Current amplitude	30	30
Current start time	0ms	10ms
Current end time	Infinity	Infinity



### 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.

ANSWER: [10pts]

- $t > ?$  for SS [1pt]
- Phase offset equation and explanation [3pts]

- Period of oscillation [2pts]
- Number of spikes [2pts]
- Phase offset [2pts]

$$\phi = \frac{\Delta t}{T} * 360^\circ$$

### Part 6 – Perturbation of the system

What happens if we try to disturb the oscillation? Perturb the system in two 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.

ANSWER: [22pts]

- Axis labels [2pts]
- 2x 3 subplots [6pts]
- 2x {Period of oscillation, number of spikes for each neuron, phase offset} [0.5pts each; 4pts total]
- Explanations of perturbations [2.5pts each; 5pts total]
- Discussion of findings [2.5pts each; 5pts total]

Ex.: Could perturb with a pulse of current or with a sinusoid of current to one neuron.

The goal is to see two different cool effects of perturbing the system. Maybe the oscillation dies entirely. Maybe its period changes. Maybe it goes back to the way it was before the perturbation.