

Lab 4

January 28, 2009

Neuron Phase Response

In this lab, we study the effect of one neuron's spikes on another's, combined synapse and neuron behavior. In Lab 2, we characterized a neuron's response to a constant input current. Here, we augment the neuron's constant input with synaptic stimulation.

We explore how much spikes from one neuron advance (or delay) the spikes of another, focusing on:

- How the input spike's phase (i.e., when in the neuron's cycle it is applied) influences its efficacy
- How the neuron's phase-response enables it to phase-lock to the input (i.e., spike at a fixed delay)

4.1 Reading

The following book chapter, located on the class website, discusses the response of model neurons similar to the one in this class to synaptic input, defining the concept of phase and introducing the phase response (Section 10.1). It also provides specific examples (Section 10.4.2).

- E. M. Izhikevich. *Dynamical systems in neuroscience: The geometry of excitability and bursting*. MIT Press, 2007, Section 10.1, pp. 444-57, and Section 10.4.2, pp. 477-9.

4.2 Prelab

This prelab is meant to familiarize you with analyzing the phase response of simple neurons, providing intuition into why an input spike's phase matters.

1. Phase Response

- (a) We examine how an input's phase influences its effect on a neuron's subsequent spike times, the neuron's phase-response curve (PRC). Consider the positive-feedback neuron, which we excite with a very brief current pulse that moves the membrane up by A_E . If the pulse arrives when the neuron's membrane is changing quickly (high membrane slope), it only advances the neuron's phase a small amount, ΔT ; however, if the pulse arrives when the neuron's membrane

is changing slowly (low membrane slope), ΔT is large. Why does exciting the neuron while the membrane slope is low, skipping that portion of its period, advance phase more effectively than while the membrane slope is high?

- (b) The neuron's phase response is inversely proportional to its membrane slope. For weak pulses that move the membrane little, we can approximate the advance in the neuron's phase as:

$$\Delta T = \frac{A_E}{\dot{x}} \quad (4.1)$$

where we define \dot{x} as in Lab 2:

$$\dot{x} = \frac{1}{\tau_m} \left(r - x + \frac{x^3}{3} \right) \quad (4.2)$$

When does ΔT equal its maximum, ΔT_A ? What is its value at this point? For r slightly greater than $2/3$ (and $A_E \ll 1$), we can approximate the PRC as:

$$\Delta T(\theta) \approx \frac{\Delta T_A}{2} \left(1 - \cos \left(\frac{2\pi\theta}{T} \right) \right), 0 < \theta < T \quad (4.3)$$

where a spike arrives at phase θ (in units of time) and T is the neuron's period in the absence of the spike. For $A_E = 0.1$, $r = 1$, and $\tau_m = 10\text{ms}$, calculate ΔT_A and sketch the PRC.

2. Entrainment

- (a) Knowing a neuron's PRC enables us to predict how it will respond to a periodic stimulus.

$$\theta_{n+1} = (\theta_n + \Delta T(\theta_n) + T_S) \bmod T \quad (4.4)$$

where T_S is the stimulus period and θ_n is the phase at which the stimulus' n th spike occurs. The neuron phase-locks to the stimulus if a stable fixed point exists (similar to a stable equilibrium). At a fixed point, $\theta_{n+1} = \theta_n$, which we replace with θ_{lock} . Show that:

$$\Delta T(\theta_{\text{lock}}) = T - T_S \quad (4.5)$$

Using the value you calculated for ΔT_A , solve for the smallest value of T_S that will entrain the neuron.

- (b) If T_S is larger than the minimum value, there are two fixed points. Show this using your PRC sketch and determine the stability of each fixed point. That is, reason about what happens when an input spike occurs near a fixed point. Will the next input spike move closer or farther? If it moves closer, the fixed point is stable; if it moves farther, it is unstable.

4.3 Setup

As in previous labs, there will be a folder on the Desktop; this one is named **Phase Response Lab**. This folder contains the instrument control program to acquire and view the neuron membrane potential and phase response in real-time. The TA will instruct you on the use of the software.

Before each test, edit the contents of *parameters.txt*. In this lab, the parameters of interest are:

- Input current (I_{IN})

- Leak conductance (G_{lk})
- Excitatory current amplitude (A_E)
- Inhibitory conductance amplitude (A_I)
- Stimulus period in ms (T_S)

As you increase the input current and the leak conductance biases, I_{IN} and G_{lk} increase exponentially. As you decrease the excitatory conductance amplitude and inhibitory current amplitude biases, A_E and A_I increase exponentially. The excitatory (τ_E) and inhibitory (τ_I) decay-constants are set to reasonable values such that both are fast. Use the *F1* key to display a list of available key commands.

4.4 Experiments

Experiment 1: Phase Response Curves

We study the interaction between the synapse and the neuron. Specifically, we will measure the effects of

- a single excitatory spike on a postsynaptic neuron
- a single inhibitory spike on a postsynaptic neuron

We will inject a constant current into the neuron by stimulating an excitatory synapse at a high rate (see Lab 1). Adjust this background current (I_{IN}) until the neuron spikes at 30Hz for both experiments.

We will stimulate a separate excitatory synapse set to deliver a brief current pulse to the neuron at a low rate (once every 250ms); therefore, set $T_S = 250$. This synapse will excite the neuron at a random phase, advancing spiking. We will record this time advance, ΔT , induced by excitation and build up a plot of ΔT versus input phase; this is the PRC. Measure A_E directly from the increase in membrane potential, using an event that occurred near the center of the neuron's cycle. Normalize this measurement by a visual estimate of the inflection point. Be sure to remove any ADC offset from your estimate.

Repeat this experiment several (5-10) times, with a different synaptic strength selected each time, such that the measured A_E ranges between about 0.1 and 0.3 (normalized). Be sure to run the experiment long enough to sketch out the full PRC (try 40-50s). If your data is very noisy you may need to use a longer run time and average the data. A good starting point for the A_E bias is about 1.35V; the inhibition bias should be set to 2.4V to remove any inhibition. On a single graph, plot all of the PRCs aligned to the end of the period. On a separate figure, plot the maximum (absolute) value of ΔT versus A_E . What is the trend? Fit the data accordingly and show your equation.

Repeat the preceding procedure for the inhibitory synapse, changing A_I . A good starting point to try is about 1.65V. Be sure to set the A_E bias to 2.4V to turn off excitation. Note the similarities and differences between the excitatory and inhibitory synapses. Why are they different?

Experiment 2: Entrainment

In this experiment, we will phase-lock the neuron's spike to the input spike train. In particular, we will determine the

- criteria for synaptic excitation or inhibition to entrain a neuron.

This experiment is similar to the last, except we will stimulate the neuron at higher rates. Apply three rates of stimulation to the neuron: 25Hz, 32Hz, and 40Hz. At each rate, choose two values for A_E , a small and large value that increase x by approximately 0.1 and 0.3, respectively; refer to your measurements from Experiment 1. Plot the phase that the spikes arrive versus the spike number for all six cases on a single plot; label each case. At which frequencies does the neuron phase lock? At which does it fail to phase lock? How does the large value of A_E influence the phase locking?

Repeat the preceding procedure for the inhibitory synapse at rates: 20Hz, 28Hz, and 35Hz. Note the similarities and differences between the excitatory and inhibitory synapses. Why are they different?

4.5 Postlab

Reyes and Fetz (1993) stimulated a cat layer V sensorimotor cortical neuron with a constant background current and additional excitatory current pulses (Figure 4.1 *top*). When a pulse arrived late, the period decreased up to 15 % (relative to its unstimulated value). When a pulse arrived early, the period did not change. The adapting positive-feedback neuron we studied in Lab3 behaves similarly (Figure 4.1 *bottom*).

Notice that both of these neurons' membrane voltages exhibit a nearly constant slope; yet, their PRCs are similar to the ones you recorded. This is not what you would expect based on this lab. However, there is an important difference between these neurons and the one we studied in this lab: in the latter r is always greater than r_{th} whereas in the former r is less than r_{th} for most of the period due to the action of the potassium conductance. Unlike the situation in Lab 3, the potassium conductance activates strongly after a spike (large Δg_k) and decays quickly (small τ_k). Explain how this potent potassium could account for the observed PRC, including the large zero-region. Hint: Think about and sketch the neuron's phase plot (\dot{x} versus x), focusing on how it changes as the potassium conductance increases after a spike and decreases thereafter.

- A. D. Reyes and E. E. Fetz. Two modes of interspike interval shortening by brief transient depolarizations in cat neocortical neurons. *Journal of Neurophysiology*, 69:1661-72, 1993.

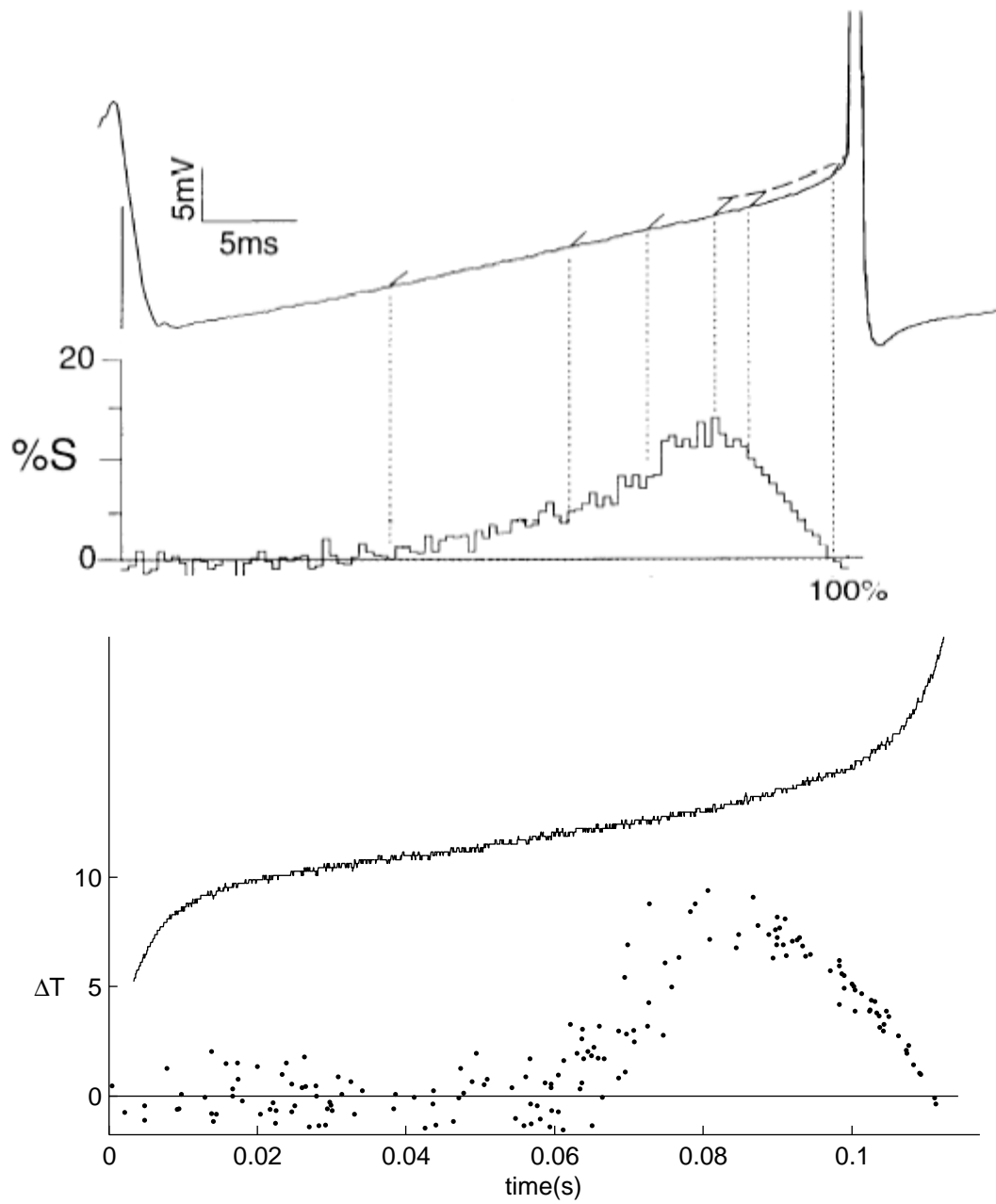


Figure 4.1: Current pulses decrease the period of a cat layer V sensorimotor cortical neuron up to 15 % (*top*) [Modified from Reyes and Fetz (1993)]. The adaptive positive-feedback neuron expresses a similar response (*bottom*).