Lab 1

January 12, 2007

Modeling Synaptic Currents

In this lab we will explore the behavior of a silicon synapse. Our goals are to understand the behavior and limits of the synapse and become familiar with hardware and software that we will use throughout future labs.

We focus on the two components of the silicon synapse:

- The cleft models the release and uptake of neurotransmitter into the intercellular space between presynaptic and postsynaptic neurons.
- The receptor models conductance change in response to a pulse of neurotransmitter released into the cleft.

1.1 Reading

Synaptic models range from complex to simple. Most models are simplified to reduce the cost of implementation in software or hardware. The following paper, located on the class website, provides an example synapse model similar to the silicon one used in this lab:

- A. Destexhe, Z. Mainen, and T. Sejnowski. An efficient method for computing synaptic conductances based on a kinetic model of receptor binding. *Neural Computation*, 6(1):14-8, 1994.

1.2 Prelab

This prelab is meant to familiarize you with analyzing cleft and receptor behavior. There is an intuitive aspect to understanding these systems, as well as a mathematical formalism. The prelab attempts to develop both types of analysis.

1. Synaptic Cleft

   (a) The input to the synapse (Figure 1.1) is a spike's brief depolarization, which results in a rapid release of neurotransmitter into the cleft. We model the cleft's neurotransmitter concentration, $[T]$, in response to a spike (at time zero) as an instantaneous increase, Q, followed by a linear decrease at rate I_{LEAK} due to neurotransmitter uptake. If $[T]$ is zero before a spike, solve for $[T](t)$ immediately after it and the following waveform. Sketch the waveform.

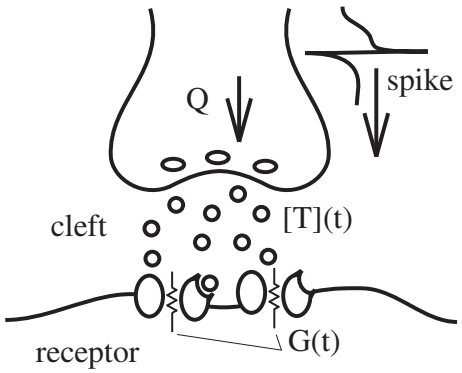

Figure 1.1: The silicon synapse consists of the cleft, which models neurotransmitter concentration, $[T](t)$, and the receptor, which models conductance, $G(t)$. When a spike arrives it causes an increase in $[T](t)$, which bind to receptors increasing $G(t)$.

(b) We model the effect of $[T](t)$ on the receptor as all-or-none. When $[T](t)$ is above (or below) a threshold, $\mathrm{K_D}$, all (or none) of the receptors are activated. That is the fraction of channels that are open is given by:

$$P(t) = \begin{cases} 1, & [T](t) \geq \mathrm{K_D} \\ 0, & [T](t) < \mathrm{K_D} \end{cases} \tag{1.1}$$

What is $P(t)$'s width, t_p, assuming $Q > \mathrm{K_D}$? What is t_p if n spikes arrive simultaneously?

2. Synaptic Receptor

(a) As channels open, the conductance, $G(t)$, increases towards its maximum, $\mathrm{G_{max}}$; as they close, it decreases towards zero. Both processes are described by:

$$\tau_\mathrm{G}\,\dot{G} + G(t) = \mathrm{G_{max}}\,P(t) \tag{1.2}$$

where τ_G is the synaptic decay-constant, and $\dot{G} = dG/dt$. We present the receptor with inputs $P_1(t)$ and $P_2(t)$ at different times. Show that the sum of the individual responses we obtain is the same as the response produced by the input $P_1(t) + P_2(t)$. A differential equation that passes this test is referred to as being linear.

(b) $G(t)$ approaches zero or $\mathrm{G_{max}}$ with exponential dynamics when $P(t)$ is zero or one, respectively. Verify that the rising and falling phases are given by:

$$G(t) = \begin{cases} G(0)\,e^{-t/\tau_\mathrm{G}}, & P(t) = 0 \\ \mathrm{G_{max}} + (G(0) - \mathrm{G_{max}})\,e^{-t/\tau_\mathrm{G}}, & P(t) = 1 \end{cases} \tag{1.3}$$

where $P(t)$ is constant for $t > 0$. The duration of the rising phase is called the rise-time.

(c) Using this solution, sketch $G(t)$ for two rise-times: $t_\mathrm{p} = \tau_\mathrm{G}/2$ and $t_\mathrm{p} = 3\tau_\mathrm{G}$ (assume $G(0) = 0$). For each waveform, indicate when $G(t)$ reaches its peak and when $G(t)$ has decayed to $1/e$ times its peak.

1.3 Setup

All labs use the same setup, consisting of a silicon neuron and synapse array embedded in a PC board that uses USB to send and receive information from a PC. All parameters of the

neuron-array system are controlled by software; therefore, you should refrain from tinkering with the hardware. If a problem arises, contact the TA to fix it. The details of the hardware are outside of the scope of these labs; however, if you are interested the TA can explain the system functionality and refer you to resources describing it in depth. Those inclined to do so are encouraged to experiment, exploring the synapse beyond the prescribed experiments.

Synapse and Neuron Array

The lab chip has 1024 excitatory neurons and 256 inhibitory neurons. Each excitatory neuron has one excitatory synapse, which we will be using in this lab. The excitatory synapse consists of a cleft and a receptor as described in the Prelab.

USB board

In all labs you will be using a custom-designed USB board. The TA will describe the functionality of the board, but a brief overview follows.

The USB board allows you to record one variable at a time, either a synapse current or neuron potential, from the silicon neuron array. The board also asynchronously stimulates synapses and records spikes from the neuron array. It is entirely software-controlled, and you need only to understand what it does—not how it does it.

A text file, *parameters.txt*, instructs the interface program which neuron or synapse to observe and determines the parameters of the synapses and neurons on the chip. The parameters of interest are:

- Cleft pulse-width (I_{LEAK})
- Saturation-amplitude ($\mathrm{G}_{\mathrm{max}}$)
- Receptor decay-constant (τ_{G})
- Stimulation frequency
- Number of spikes
- Synapse x address
- Synapse y address

The cleft pulse-width, saturation-amplitude, and receptor decay-constant (and all other parameters) are determined by bias voltages applied to the chip. For instance, as you increase the cleft pulse-width bias voltage the pulse-width decreases exponentially. The same applies to the receptor decay-constant and saturation-amplitude. There are other parameters that increase exponentially as their bias voltage increases. The reason is that the bias voltages modulate currents in transistors that express an exponential current-voltage relation, and transistors come in two types (p- and n-type), with opposite sign.

The computer directly controls the frequency (Hz) and number of spike sent to the synapse in an experiment. Synapse x and y addresses determine which synapse is activated and observed.

1.3.1 Software Control

There will be a folder on the Desktop named **Synapse Lab**. This folder contains the instrument control program to acquire and view the synaptic waveform in real-time. The TA will instruct you on the use of the software.

1.4 Experiments

In the first experiment, we will characterize the synapse's cleft and receptor components, focusing on the synaptic rise and decay. In the second experiment, we will evaluate the linearity of the synapse.

Experiment 1: Cleft and Receptor

In this experiment, we will

- Become familiar with USB data acquisition and associated software.
- Study the spike response of the synapse while varying the cleft's pulse width and the receptor's decay constant.

We will use the USB link to repetitively excite one synapse at a time. Open *parameters.txt*. Choose a synapse, selecting x and y addresses with any criteria you want as long as both are between 0 and 31. Set the frequency (Hz) to 10. Set the number of spikes to 0, which will cause to the program to run until you press **Esc**. Vary the biases and observe their effects on the synaptic waveform.

Experiment 1.1: Rise-time

The purpose of this experiment is to explore how the cleft pulse-width bias affects the rise-time of the synapse. We will vary the cleft pulse-width bias about 250mV and observe the effects. For both high and low values of the pulse-width bias, play with the saturation-amplitude and receptor decay-constant biases until the synaptic waveform is not cutoff (flat on top) and has a modest exponential tail (50ms is reasonable). Once you have found a good regime, set the number of spikes to 1.

Vary the cleft pulse-width (5-10 values), recording the membrane trajectory at each bias voltage. Each time you change the bias, rename the output file so it is not overwritten. Include several waveforms (obtained for different bias voltages) in a single plot. Extract each waveform's decay-constant and plot the values on a log scale, versus the decay-constant bias. Fit this data appropriately. From your fit determine how much must you change the cleft pulse-width bias to double the rise-time?

Experiment 1.2: Decay Constant

The purpose of this experiment is to explore how the receptor decay-constant bias affects the decay constant of the synapse. Similar to the rise-time experiment, we will vary the

receptor decay-constant bias about 400mV and observe the effects. For both high and low values of the decay-constant bias, play with the saturation-amplitude and pulse-width biases until the synaptic waveform is not cutoff (flat on top) and has a modest rise-time (10ms is reasonable).

Vary the decay-constant bias (5-10 values), recording the spike-response waveform at each bias voltage. Remember to rename the output file each time you change the bias, so it is not overwritten. Include several waveforms (obtained for different bias voltages) in a single plot. Extract each waveform's decay-constant and plot the values on a log scale, versus the decay-constant bias. Fit this data appropriately. From your fit determine how much must you change the receptor decay-constant bias to double the decay-constant? How close is this value to that needed to double the rise-time?

Experiment 2: Synapse Linearity

In this experiment, we will

- Characterize synapse linearity for inputs at various frequencies

We will compare the synapse's response to a train of spikes to the arithmetic sum of copies of its single-spike response, each shifted in time appropriately. Set the rise-time and decay constant to about 10ms and 50ms, respectively (refer to your data from Experiments 1.1 and 1.2). And set the saturation amplitude well below cutoff; cutoff occurs when the computer attempt to measure a current outside its operating range.

Drive the synapse with a single spike and save the response. Now drive the synapse with five spikes at a frequency of 20Hz. Compare this response with the linear prediction: Five instances of the single-spike response, shifted to arrive at 20Hz, and summed together. How good is the prediction? What if anything is different? Repeat the experiment at 50Hz and 100Hz. What effect does frequency have on linearity? Explain how the nonlinearity described in the prelab could result in the observed frequency dependence.

To estimate linearity, we use percent linearity, P_{L}. We calculate P_{L} as the ratio between the measured response and the arithmetic sum of the single-spike response, times one hundred. Calculate P_{L} for the peak after each spike. On a single graph, plot P_{L} as a function of spike number for all three frequencies.

1.5 Postlab

In Experiment 2, we observed that the silicon synapse is linear at low frequency (20Hz) but is supralinear at high frequency (100Hz). Explain why this is the case. Will the highest linear frequency increase or decrease if you decrease the rise-time?