

## Lab 7

February 19, 2009

# Spike Timing-Dependent Plasticity

In previous labs, we explored synapses and neurons that were incapable of long-term changes. In this lab, we study the criteria necessary for a synapse to undergo long-term potentiation (LTP) or depression (LTD), focusing on spike timing-dependent plasticity (STDP). In addition, we explore plasticity's ability to alter a neuron's spike timing relative to its inputs.

## 7.1 Prelab

In this prelab, we analyze the behavior of an STDP synapse model in response to a presynaptic spike paired with a postsynaptic one at regular intervals. In addition, we explore STDP's ability to modulate the phase of spikes relative to inputs.

### 1. STDP

We model STDP as potentiating a synapse when a potentiation integrator reaches a threshold. The integrator increments when a presynaptic spike precedes a postsynaptic spike within a brief time window. The increment increases linearly as the spikes' spacing decreases:

$$S(t_{\text{pair}}) = 1 - \frac{t_{\text{pair}}}{t_p} \quad (7.1)$$

where  $t_p$  is the time window size.

We model depression in the same manner except the its integrator is incremented by post-before-pre pairings.

We drive a STDP synapse with pre-before-post pairs  $t_{\text{pair}}$  apart, generated at stimulus period  $T_S$ . After  $n$  pairings the potentiation integrator's output is:

$$P = nS(t_{\text{pair}}) - (n - 1)L(T_S) \quad (7.2)$$

where  $L(T_S) = T_S/\tau_p$  is the integrator's leakage in  $T_S$  seconds. After  $n_{\text{th}}$  pairings,  $P$  reaches the integrator threshold,  $P_{\text{TH}}$ . Solve for the efficacy of each pairing  $1/n_{\text{th}}$  in terms of  $T_S$ ,  $\tau_p$ ,  $t_p$ , and  $P_{\text{TH}}$ . Rearrange your expression to find the maximum value of  $t_{\text{pair}}$  that can potentiate the synapse ( $1/n_{\text{th}} > 0$ ).

### 2. Plasticity Enhanced Timing Precision

We drive a neuron with a suprathreshold input that causes it to spike  $T_I$  seconds after the input starts. At the same time, the neuron receives input from 21 STDP synapses (initially depressed), one activated every  $\Delta T_S$  seconds. After several repetitions, some synapses will potentiate, causing the neuron to spike earlier  $T_F$  seconds after the input start. Since only synapses active before  $T_F$  are potentiated (in steady state), the number of potentiated synapses  $n_P$  must be the largest integer less than  $1 + T_F/\Delta T_S$ .

The effect of each potentiated synapse is to advance the neuron's spike  $\Delta T_P$  seconds earlier, yielding:

$$T_F = T_I - n_P \Delta T_P + T_\alpha \quad (7.3)$$

where  $T_\alpha$  is a constant that accounts for less effective synapses (active immediately before the neuron spikes; see Lab 4). Approximate  $n_P = T_F / \Delta T_S$  and solve for  $T_F$ .

Now imagine we drive a population of neurons whose variability in excitability yields a distribution in  $T_I$  values. We characterize this variation with *timing precision*, defined as twice the standard deviation in spike times ( $\sigma_I$ ). Use your result above to determine the timing precision after STDP in terms of  $\sigma_I$ ,  $\Delta T_P$ , and  $\Delta T_S$ ? How could you alter  $\Delta T_P$  and  $\Delta T_S$  to improve timing precision?

## 7.2 Setup

As in previous labs, there will be a folder on the Desktop; this one is named **STDP Lab**. This folder contains the instrument control program to acquire and view the neuron spikes and excitatory postsynaptic currents (EPSC) 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 for Experiment 1 are:

- Pairing frequency in Hz ( $\frac{1}{T_S}$ )
- Neuron  $x$  address
- Neuron  $y$  address
- Synapse number

The parameters of interest for Experiment 2 are:

- Inhibitory interneuron input current ( $I_{INT}$ )
- Excitatory neuron input current ( $I_{EXC}$ )
- Excitatory synapse strength ( $A_E$ )
- Inhibitory synapse strength ( $A_I$ )

As you increase the inhibitory interneuron input current and the excitatory neuron input current biases,  $I_{INT}$  and  $I_{EXC}$  increase exponentially. As you decrease the excitatory synapse strength and inhibitory synapse strength biases,  $A_E$  and  $A_I$  increase exponentially. Note that  $t_p$ ,  $\tau_p$ , and  $P_{TH}$  are set to reasonable values for both potentiation and depression.

## 7.3 Experiments

In the first experiment, we will acquire a plastic synapse's STDP curve. In the second experiment, we will use STDP to improve a neuronal population's timing precision.

## Experiment 1: STDP Curve

In this experiment, we will

- Study how timing differences between pre- and postsynaptic spikes influences plasticity

Choose a synapse, selecting  $x$  and  $y$  addresses and synapse number with any criteria you want—set  $x$  and  $y$  between 0 and 31 and the synapse number between 0 and 20. Set the pairing frequency to 20Hz ( $T_S = 50$  ms).

When you run the program,  $t_{\text{pair}}$  will vary automatically, selecting ten points linearly distributed between 0.2ms and half of  $T_S$ . For each  $t_{\text{pair}}$  value, the program will drive the STDP synapse with 50 pre-before-post pairings, repeated at  $T_S$ , then followed by the same number of post-before-pre pairings.

Observe the resulting EPSCs. After you run the program, you will be provided with the peak value of each EPSC for each pre-before-post pairing at each  $t_{\text{pair}}$  value. Determine the number of pairings ( $n_{\text{th}}$ ) required to potentiate or depress the synapse, where we define an EPSC as potentiated if the stimulus results in a peak that is greater than half of the maximum value. The inverse of the number of pairings tells us how effective each pairing was in potentiating or depressing the synapse. Plot  $1/n_{\text{th}}$  versus  $t_{\text{pair}}$  (the STDP curve). Decrease  $T_S$  by 33% and 100% (67ms and 100ms) and collect two more STDP curves, plotting them on the same graph as the first one. Fit all curves with the expression from Prelab Question 1. How does STDP change as a function of  $T_S$ ?

## Experiment 2: Plasticity Enhanced Timing Precision

In this experiment, we will

- Study the role of STDP in enhancing timing precision

We will drive 100 excitatory neurons and 100 inhibitory interneurons with a 20Hz suprathreshold background current, set by  $I_{\text{EXC}}$  and  $I_{\text{INH}}$ , respectively, for 50 cycles. At the same time, we will activate each excitatory neuron's 21 plastic synapses in sequence, one every  $\Delta T_S = 0.6$ ms. All synapses are initialized to be depressed (potentiated amplitude set by  $A_E$ ). We will observe the excitatory neuron population's timing precision before and after STDP.

Set  $A_E$  to a low value (bias to about 1.50V). Compute the timing precision in the first cycle, before STDP has had the chance to occur, and in the last cycle, after STDP is complete (include all spikes). Plot  $T_F$  versus  $T_I$  with each point corresponding to a neuron's phase in the first and last cycles (ignore subsequent spikes). Fit your plot using the expression derived in Prelab Question 2, and report your values for  $\Delta T_P$  and  $T_\alpha$ .

Repeat the experiment two more times for  $A_E$  set to medium (about 1.40V) and high (about 1.30V) values. What limits the timing precision as  $A_E$  becomes larger?

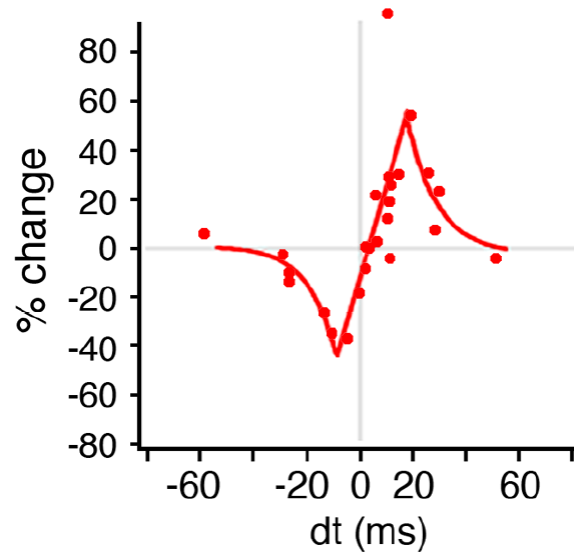


Figure 7.1: STDP in Locusts: Kenyon cell afferents onto beta-lobe neurons potentiate when presynaptic precede postsynaptic spikes by more than 5ms and depress otherwise.[Laurent 2007].

## 7.4 Postlab

In Experiment 2, we observed that STDP potentiates synapses onto lethargic neurons, providing them with additional input. The additional input advances the lethargic neurons' spikes, bringing them closer to the excitable neurons, thereby improving timing precision.

In our model, STDP results in depression and potentiation for spike timing differences ( $t_{\text{pre}} - t_{\text{post}}$ ) less and greater than zero, respectively. Efficacy is greatest near this transition (at zero). In neurobiology, different forms of STDP have been found where the transition from depression to potentiation occurs at spike timing differences several milliseconds past zero, with efficacy weak near this transition (Figure 7.1).

A possible reason for the transition to occur at positive spike timing differences is that it prevents ineffective synapses from potentiating. Synaptic spikes that arrive immediately before a neuron spikes do not contribute to the spike because the synapse takes time to rise and spike generation takes time as well. In our model, are some potentiated synapses ineffective since the neuron has already decided to spike when they arrive? Can you use your computed  $T_\alpha$  to estimate how many potentiated synapses don't contribute? Notice that when  $A_E$  is strong, some neurons spike multiple times in one cycle; how could a STDP curve similar to the locust's alleviate this problem?