An Autocatalytic Model of STDP Timing from Slow Calcium Signals

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Abstract

Spike timing dependent plasticity (STDP) shows a sharp temporal transition between potentiation and depression despite a slow timecourse of calcium concentration. We show how autocatalytic amplification of initial concentration differences can enable a high degree of temporal selectivity despite having a longer time constant than the time difference measured, and produce the sharp STDP weight change curve. This simple model is robust to parameter changes, noise and details of the model. The model predicts the location of the maximum and minimum for STDP at ± 10 milliseconds from coincidence.

Key words: STDP, Autocatalysis, Calcium signal, Timing

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1 Introduction

Spike timing dependent synaptic plasticity (STDP) [1–3] shows LTP or LTD effects depending on the time relation between pre- and postsynaptic signals at a synapse. While the temporal window of STDP is on the order of $\approx$ 40 msec, the temporal precision of the LTP-LTD transition is on the order of 10 msec, short compared to the time constants involved in the Ca^{2+} dynamics [4] that regulate subsequent phosphorylation and plastic change.

The issue explored in this paper is how a sharp transition between LTD and LTP can occur when the temporal difference between the pre- and postsynaptic spike crosses zero, given the slow and stochastic nature of Ca^{2+} and other biochemical processes.

Our hypothesis is that a very small initial difference between the pre- and post-synaptic traces is amplified by autocatalysis in a competitive manner. The autocatalysis is gated by the combined pre- and postsynaptic signal, producing associative learning, while competition between two autocatalytic loops produces temporal selectivity. This process may take a long time compared to the spike timing, but will retain information about which trace arrived first. Thereby, it can amplify it beyond noise levels and can hence change synaptic weight in a temporally sensitive manner without assuming very fast chemical processes.

2 Model

The pre- and postsynaptic signals after an incoming EPSP and a back-propagating action potential leave the exponentially declining traces pre and $post$. $pre = \exp(-(t - t_{prespike})/\tau_T)$ (similarly for $post$), with $pre = 0$ if the presynaptic spike has not yet occurred.

Assume that the weight change Δw is the result of integrating two competing factors LTD and LTP: $\Delta w = \int (LTP - LTD)dt$. The factors are enhanced through autocatalysis at a rate dependent on the summed strength of the synaptic traces and decay at a constant rate.

$$\tau LTP' = k(pre + post - \theta)LTP + \mu(pre - post) \tag{1}$$

$$\tau LTD' = k(pre + post - \theta)LTD - \mu(pre - post) \tag{2}$$

With a bound limiting both to positive or zero values. We will also explore adding mutual inhibition terms $-LTD$ and $-LTP$ to equations 1 and 2.

The parameters of the model are: τ_T time constant of synaptic traces (set to 100 msec after [4]), τ time constant for LTP factor change, k strength of autocatalytic gain, θ threshold for enhancement, μ influence of trace difference on the factors.

3 Results

Before both spikes have arrived both LTP and LTD approach 0 due to the lack of autocatalysis. When both arrive $pre + post > \theta$ and the largest one

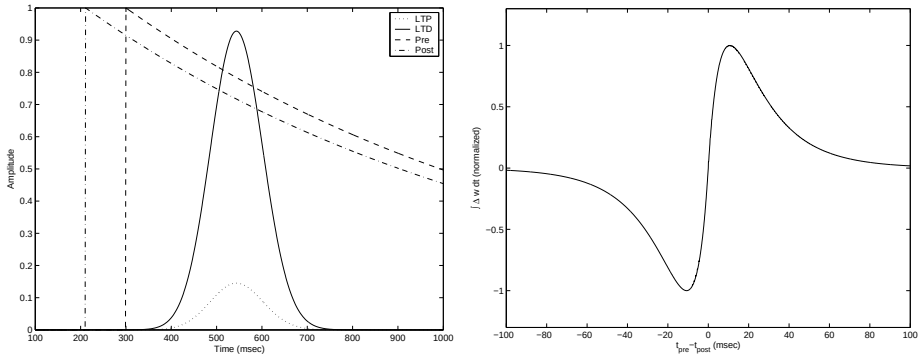

Fig. 1. Left: LTP, LTD, pre and $post$ dynamics. Right: Integral of Δw for different $t_{posttime} - t_{pretime}$. The scale has been normalized so the maximum = 1. Timestep 1 msec , $k = 20$, $\theta = 1.5$, $\mu = 0.1$, $\tau = 1$, $\tau_T = 100$ msec.

begins to grow exponentially until the traces have decayed below the threshold (figure 1 left). Note that the peak of the LTP curve occurs several hundred milliseconds after the initial spike, far from the temporal resolution of STDP. Despite this the integrated weight change $w = \int \Delta w dt$ forms the familiar STDP weight change curve (figure 1 right) with a temporal resolution similar to experimental STDP.

The distance between the maximum and minimum of the integrated weight change curve is small ($\approx$ 20 milliseconds) compared to the dynamic timescales of the variables (hundreds of milliseconds). This shows that slow dynamics can efficiently detect small timescale phenomena and amplify them.

3.1 Model and Parameter sensitivity

We explored several variations of the model and parameter set to test the robustness of the phenomenon.

Hebbian Autocatalysis Instead of an autocatalytic gating based on the sum $pre+post-\theta$ a multiplicative Hebbian term $pre*post-\theta$ can be used. For slightly shifted threshold values θ the response becomes practically identical to the non-Hebbian case: it is enough that the gate is activated by the presence of both spikes.

Mutual Inhibition Adding mutual inhibition between LTP and LTD did not change the behavior qualitatively since they already compete in the Δw integral. The exponential growth ensures that one is far larger than the other. However, it was found that mutual inhibition reduced the effects of noise on the system slightly.

Parameter sensitivity The transition between positive and negative weight change become sharper for increasing k. μ merely changes the scale. Faster τ can sharpen, while low values of τ_T gives a distorted curve showing LTP for the most positive values of $t_{prespike} - t_{postspike}$.

Noise Sensitivity Noise sensitivity was surprisingly good (figure 3) despite autocatalytic amplification. Adding noise to either the synaptic traces or the LTP/LTD values did not remove the overall properties of the curve. In particular, the transition between positive and negative synaptic change remained stable.

The Hebbian autocatalytic model was somewhat more stable to noise in the synaptic traces while the non-Hebbian model was more stable to noise in the LTP/LTD values. Interestingly, the noise appeared to sharpen the LTD-LTP transition.

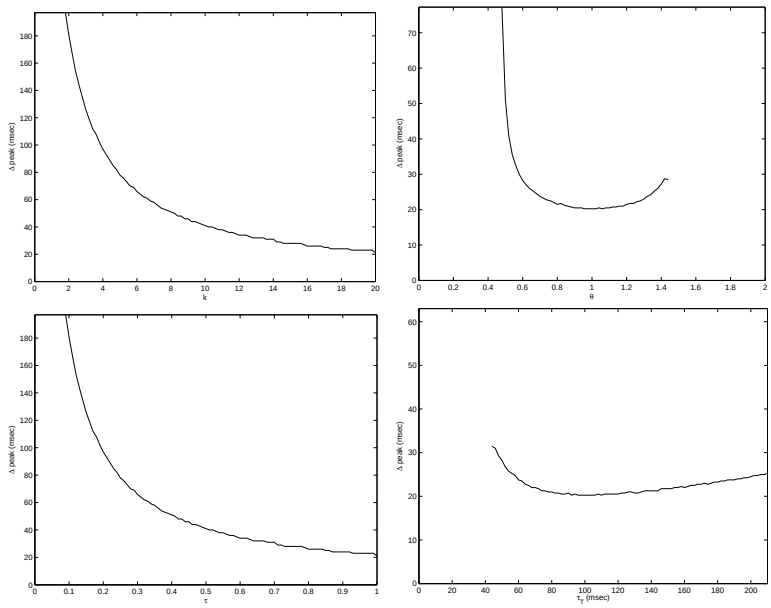

Fig. 2. Parameter effect on the distance between the maximum and minimum of $\int \Delta w dt$ for variations of k, θ, τ and τ_T.

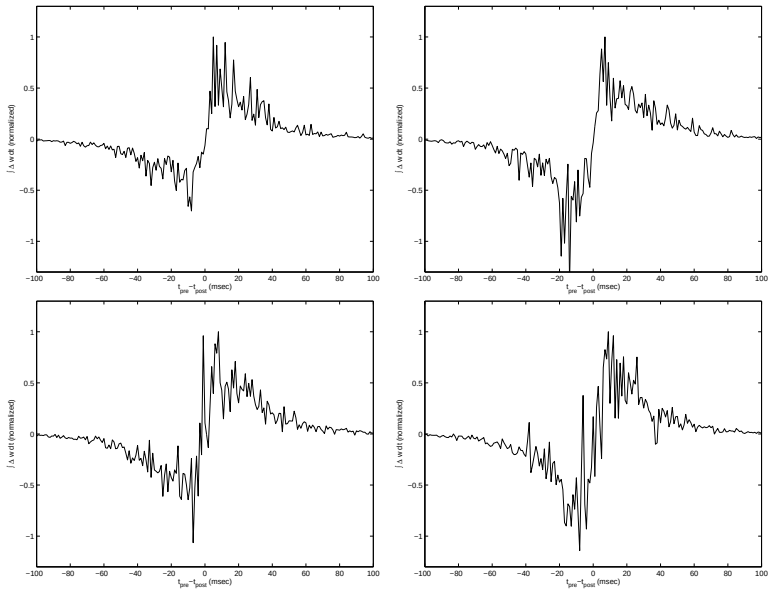

Fig. 3. Effect of adding $N(0, 0.1)$ noise to *pre* and *post* (first row) and to LTP' and LTD' (second row). Hebbian gating to the left and non-Hebbian gating to the right.

Trace shape Making the synaptic traces softer by replacing $\exp((t_{spike} - t)/\tau_T)$ with $\tanh(g(t - t_{spike}))\exp((t_{spike} - t)/\tau_T)$ did not change the qualitative behavior of the weight change. Increasing g sharpened the traces and made

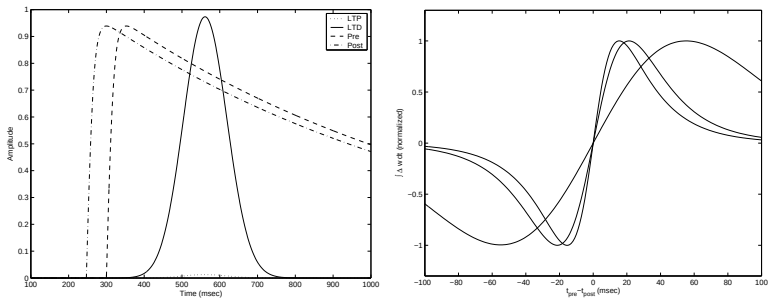

Fig. 4. (left) Softened synaptic traces, $g = 5$. (right) Effect of softer synaptic traces, for $g = 1$, 5 and 10 (the size of $\int \Delta w dt$ was normalized to $[-1, 1]$).

the LTD-LTP transition faster (figure 4).

4 Discussion

We have shown how a simple autocatalytic model can produce a high degree of temporal resolution despite having a slower internal timescale. In a simple synaptic model it produces a STDP-like weight change with a sharp transition from LTP to LTD. We specifically note that the model correctly produces the peaks at ± 10 milliseconds seen in experimental data when the Ca^{2+} decay τ_T is of the same size as observed in synaptic spines [4].

The assumption of separate *pre* and *post* traces is a strong assumption made mostly to clarify the essential points of the model. It is plausible that proteins localized in nanodomains [5] near the ion channels opened by synaptic action and backpropagating spikes, respectively, could act as detectors of different kinds of Ca^{2+} influx. However, different pathways could also be activated depending on the overall concentration, especially since EPSPs and APs sum sub- and supralinearly depending on order [4] and calmodulin modulates P/Q-type Ca^{2+} channels differentially depending on number of bound ions [6].

Autocatalysis has been suggested as a key component of learning and memory on many timescales [7,8]. While a single feedback loop enables bistability with a suitable dose-response curve, competing feedback loops enables multistability and sensitivity to timing. We make the following prediction: there should exist an autocatalytic loop leading to stronger LTD just as the enhancement of calcium influx due to CaMKII phosphorylation produces a candidate autocatalytic loop leading to stronger LTP.

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