Relating STDP to BCM

Eugene M. Izhikevich and Niraj S. Desai
The Neurosciences Institute, 10640 John Jay Hopkins Drive, San Diego, CA, 92121

January 17, 2003

How STDP, a novel form of Hebbian plasticity that has attracted much attention recently, relates to classical long-term potentiation and depression in the form of the BCM synapse? It is commonly (though not universally) believed that these two forms of plasticity are incompatible, since the former is based on the exact timings of spikes, and the latter ignores it. We make a handful of biologically plausible assumptions, such as Poissonian spiking, and derive a simple equation that relates one form of plasticity to the other. We provide experimental data to support our findings.

Introduction

Over the past several years there has been an increasing interest in a novel form of Hebbian synaptic plasticity called spike-timing-dependent plasticity (STDP, Markram et al. 1997, Bi and Poo 1998, Debanne et al. 1998, Feldman 2000, Sjostrom et al. 2001, Froemke and Dan 2002), in which the temporal order of presynaptic and postsynaptic spikes determines whether a synapse is potentiated or depressed (Fig. 1A). While experiments to date have given us a fairly clear idea of how STDP affects synaptic weights when only isolated pairs of presynaptic and postsynaptic spikes are present, it is not clear how STDP should be applied to natural spike trains, which involve many spikes and many possible pairings of spikes (Froemke and Dan 2002). Specifically, what is not clear is how plasticity at a given synapse builds up over time. This problem is interesting for its own sake, but also because it promises to shed light on the relationship between STDP and the best-studied forms of Hebbian plasticity, long-term potentiation and depression (LTP and LTD), which explicitly make use of long spike trains (Bear and Malenka 1994). Presumably all of these forms of plasticity arise from the same underlying biophysical mechanisms, and it should be possible to consider them within a single framework. Here we examine different implementations of STDP, compare them with a standard LTP/LTD implementation called the BCM (Bienenstock-Cooper-Munro) synapse (Bienenstock et al. 1982), and *in so doing arrive at certain constraints on how STDP should be implemented when considering natural spike trains.*

In the BCM formulation, one considers instantaneous firing rates rather than individual spikes. Synaptic input that drives postsynaptic firing to high levels results in an increase in synaptic strength, whereas input that produces only low levels of postsynaptic firing results in a decrease (Fig. 1B). The threshold firing rate, the crossover point between potentiation and depression, is itself a slow function of postsynaptic activity, moving so as to make potentiation more likely when average activity is low and less likely when it is high. This sliding of the threshold serves to stabilize network activity and promote competition between synapses (Bienenstock et al. 1982). Considerable experimental evidence for this kind of plasticity has been obtained in neocortex and hippocampus at some of the same synapses at which evidence for STDP has also been obtained (Bi and Poo 1998, Froemke and Dan 2002, Kirkwood et al. 1993). Even so, it is not obvious how BCM plasticity and STDP are related or even if they are compatible. Consider, as an illustration, the extreme case in which all spikes of the postsynaptic neuron

occur right after those of the presynaptic one. *This will always result in potentiation by an STDP rule, but could result in either depression or potentiation by the BCM rule, depending on the exact value of the postsynaptic firing rate.* To clarify this issue we compare the two kinds of plasticity more closely, in a more biologically-realistic regime, that of uncorrelated or weakly correlated presynaptic and postsynaptic neurons that fire in a nearly Poisson manner, as do cortical neurons *in vivo*.

Classical Implementations of STDP

The form of the STDP curve, with its well-matched potentiation and depression portions, might cause one to guess that STDP applied to this kind of natural spike train should lead to a BCM-like curve similar to the one in Fig. 1C. On the one hand, the peak of the potentiation half of the curve is larger than the minimum of the depression half, which suggests that high firing rates (small interspike intervals) should result in a net potentiation. On the other hand, the tail of the depression half is longer than the tail of the potentiation one, which suggests that low firing rates (large interspike intervals) should result in a net depression. And at some intermediate firing rate a crossover should occur. But in fact, as we demonstrate in Fig. 1D, this is not necessarily true.

A straightforward application of the STDP rule does not lead to potentiation in any case, when one uses independent Poisson spike trains with a mean postsynaptic firing rate x. In the standard additive implementation of STDP (Song et al. 2000), for each presynaptic spike one takes into account all preceding and all succeeding postsynaptic spikes, and then sums the contributions of the various pairings. If postsynaptic firing is a random process that is relatively independent of presynaptic firing, then the postsynaptic firing density is relatively flat, as in Fig. 1C (no peak). Consequently, all postsynaptic spikes that precede the presynaptic one essentially sample the depression curve, and all postsynaptic spikes that follow the presynaptic one sample the potentiation curve. The net effect is then the difference between the area under the positive portion of the STDP curve and the area under the negative portion, multiplied by the postsynaptic firing rate x. As a function of x, this is merely a straight line, in which potentiation never results no matter how high the firing rate (Izhikevich and Desai 2003).

One can relax the assumption of completely uncorrelated pre- and postsynaptic spike trains, and consider the case when postsynaptic firing density has a small peak right after the presynaptic firing (function $c(t)$ in Fig. 1C). The magnitude of the peak a may be constant or it may scale with the postsynaptic firing rate x. Both cases, considered in detail by Izhikevich and Desai (2003), result in a linear synaptic change similar to that produced by additive STDP without correlations. The case of constant a shifts the straight line up (Fig. 1D), while the case of a proportional to x changes the slope of the line. In any case, one does not see the transition from LTD to LTP, as is required by the BCM rule.

Also inadequate from this standpoint is a modification of the STDP rule recently proposed by Froemke and Dan (2002), in which the efficacy of each spike is suppressed by the preceding spikes of the same neuron, so that activity-induced synaptic modification depends not only on the relative spike timing between neurons, but also on the spiking pattern within each neuron. Specifically, these authors propose that associated with each presynaptic and postsynaptic neuron is an efficacy variable that drops to zero following a spike and that relaxes exponentially back to one (its maximal value) with a characteristic time τ^{pre} and τ^{post} on the order of tens of milliseconds. However, this proposal for treating multiple interactions cannot account for potentiation of synapses at high firing rates. As shown by Izhikevich and Desai (2003) and illustrated in Fig. 1D, this modification is basically equivalent to the standard STDP implementation, the only difference being that the presynaptic and postsynaptic spikes are now in chronic state of suppression. The precise numbers are changed but the qualitative picture is not.

In Izhikevich and Desai (2003) we explicitly consider eight implementations of STDP. In particular, we find that treating interactions between multiple pairs of spikes multiplicatively (van Rossum et al. 2000) rather than additively – that is, imagining that each pairing changes the conductance by a percentage of

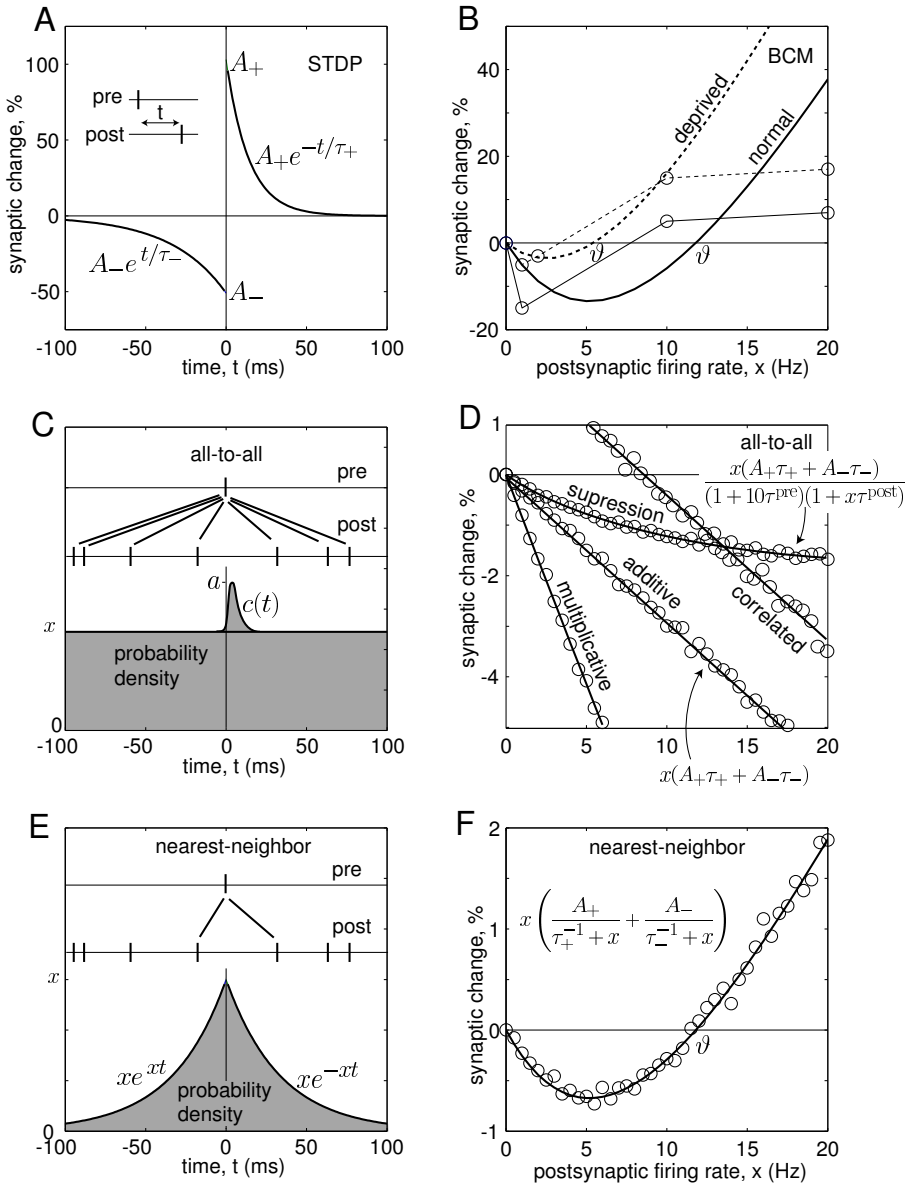

Figure 1: A. The STDP curve. The parameters $A_+ = 103\%$, $\tau_+ = 0.014$ sec, $A_- = -51\%$, $\tau_- = 0.034$ sec are taken from Froemke and Dan (2002). B. Function controlling synaptic plasticity at the Cooper synapse receiving 20 Hz pre-synaptic stimulation; Data points (circles) are from visual cortex experiments by Kirkwood et al. (1996); Blue corresponds to normal activity, green corresponds to reduced activity due to light deprivation. Parameters from Fig. 1A in eq. (1) result in the blue curve; Increasing τ_+ by 10% results in the green curve. C. All-to-all implementation of STDP: the net synaptic change is a combination of small changes induced by all possible pre/post synaptic pairs. D. The result of application of STDP rule to Poisson spike trains; Presynaptic: 10 Hz and 100,000 spikes. Postsynaptic: x Hz and matching number of spikes. The analytical curves are derived by Izhikevich and Desai (2003). E. The nearest-neighbor implementation of STDP: for each presynaptic spike only one preceding and one succeeding postsynaptic spike are considered. F. The resulting BCM function; parameters as in Fig. 1A.

its existing value rather than by a fixed amount – makes no real difference. Additive and multiplicative models are in some cases equivalent because the latter often reduces to the former when one considers the logarithms of weights, rather than the weights themselves.

Nearest-Neighbor Implementation of STDP

What does make a difference – what does make STDP compatible with BCM (and with classical LTP/LTD more generally) – is restricting which pairings contribute to plasticity (Sjostrom et al. 2001, van Rossum et al. 2000). Rather than considering all presynaptic and postsynaptic pairings equally, there are good reasons to consider only nearest-neighbor pairs. One is that postsynaptic spikes back-propagate into the dendritic tree and reset the membrane voltage in dendritic spines. Consequently the most recent postsynaptic spike overrides the effect of all the earlier spikes, so that the membrane voltage is really only a function of time since the latest postsynaptic spike. Similarly, the first succeeding postsynaptic spike may override the effect of subsequent spikes due to calcium saturation or glutamate receptor desensitization. Making this assumption, one finds that, when the postsynaptic spike train is a Poisson process with firing rate x, the postsynaptic probability density (the probability of observing a spike with a certain delay t) becomes exponential in time, xe^{-xt}, as in Fig. 1E (here we consider uncorrelated trains again). High (low) firing rates x result in predominantly small (large) intervals and hence in potentiation (depression). The expected magnitude of synaptic modification per one presynaptic spike has the form

$$\begin{aligned} C(x) &= \overbrace{\int_0^\infty A_+ \, e^{-t/\tau_+} \, xe^{-xt} \, dt}^{\text{average potentiation}} + \overbrace{\int_{-\infty}^0 A_- \, e^{t/\tau_-} \, xe^{xt} \, dt}^{\text{average depression}} \\ &= x\left(\frac{A_+}{\tau_+^{-1}+x} + \frac{A_-}{\tau_-^{-1}+x}\right) \end{aligned} \tag{1}$$

depicted in Fig.1F. It coincides with the BCM synapse in the sense that low activity results in depression and large activity results in potentiation.

Having an analytic expression for STDP's effects at a given firing rate x (Eq. 1) allows us to attempt to relate data obtained using STDP and LTP/LTD experimental protocols more quantitatively. In particular, Eq. 1 indicates that the threshold between potentiation and depression (the zero crossing of $C(x)$),

$$\vartheta = -\frac{A_+/\tau_- + A_-/\tau_+}{A_+ + A_-} \tag{2}$$

has positive values when

$$\begin{aligned} A_+ > |A_-| \quad & \text{(potentiation dominates depression for short intervals)} \\ |A_-|\tau_- > A_+\tau_+ \quad & \text{(depression area is greater than potentiation area).} \end{aligned}$$

Using the STDP parameters obtained in layer 2/3 rat visual cortex (Froemke and Dan 2002), we calculate a threshold value of around 12 Hz, which is near the value of 9 Hz found using LTP/LTD protocols in the same brain area (Kirkwood et al. 1996). One key feature of the BCM learning rule is that the threshold does not have a fixed value, but slides between higher and lower values as a slow function of postsynaptic activity (Bienenstock et al. 1982). Eq. 1 can be used to relate the sliding of the threshold to the biophysical processes underlying plasticity. In particular, the potentiation time constant τ_+ most likely depends on the kinetics of NMDA receptors, which in turn depend on their subunit composition. It has been shown (Philpot et al. 2001) that low levels of postsynaptic activity due to light deprivation

increase the ratio of NR2B subunits to NR2A subunits in NMDA receptors. This in turn increases the time constant of NMDA receptors by up to 10-20%. As one can see from Eq. 2 and in Fig. 1B, increasing τ_+ by as little as 10% results in sliding the calculated threshold by a factor of two, which is in agreement with the experimental data (Kirkwood et al. 1996).

Discussion

The question of how interactions between multiple spike pairs should be treated given an STDP rule has been considered previously (Sjostrom et al. 2001, Froemke and Dan 2002, Song et al. 2000, van Rossum et al. 2000). In theoretical papers the choice between applying the rule to all spike pairings or only to nearest-neighbor pairings has been made on a somewhat ad hoc basis, without a real empirical or biological justification. In experimental papers in which the question has been considered, the answers given have been limited in scope – specifically they have been limited to explaining data generated by applying STDP experimental protocols. What they have neglected is that a proper approach should take into account both STDP and classical LTP/LTD. Here we have attempted to do so, and our study suggests that the most widely-used STDP implementations may not be adequate: the pairings should be restricted to only proximal spike pairs. And we see that a handful of reasonable assumptions generate a simple equation that can link the parameters of STDP to the BCM formulation of LTP/LTD, resulting in a more intuitive picture of how these forms of plasticity are related.

The reader should realize that we have been considering two phenomenological models of plasticity, STDP and BCM, and important questions remain about how these models relate to the actual biophysical processes underlying synaptic plasticity. Although considerable data have been gathered about STDP applied to a single pair of spikes, many other aspects of this rule have yet to be worked out experimentally. For example, the issue of multiple spike pairs that we address in this theoretical paper, as well as whether changes in synaptic efficacy depend upon the size of the synapse, etc. While the BCM formulation of LTP/LTD has been influential, quite how well it describes the empirical data is open to question. Tests of the BCM idea have been largely indirect and have not convincingly validated certain aspects of the theory, in particular the idea that only postsynaptic activity determines the sign of plasticity.

Conclusion

This paper addresses an important theoretical issue: how STDP, a novel form of Hebbian plasticity that has attracted much attention recently, relates to classical long-term potentiation and depression, in the form of the Cooper (or BCM) synapse. It is commonly (though not universally) believed that these two forms of plasticity arise from the same underlying biophysical process. The relationship between the two has been explored e.g., by van Rossum et al. (2000), Senn et al. (2001), Kempter et al. (1999, 2001), Castellani et al. (2001), though no attempts have been to contrast different implementations of STDP with respect to BCM.

Here we have determined conditions under which one is equivalent to the other, and by making a handful of biologically plausible assumptions, such as Poissonian spiking, we have derived a simple equation that relates one form of plasticity to the other (Eq. 1 or Fig. 1F). We believe that this is an important step in reconciling STDP and classical LTP/LTD, and will be of use to a broad range of researchers, ranging from electrophysiologists studying synaptic plasticity to computational neuroscientists interested in understanding dynamics of networks.

References

- Bear, M.F., Cooper, L.N. and Ebner, F.F., (1987). A physiological basis for a theory of synapse modification. Science 237, 42-48.
- Bear, M.F. and Malenka, R.C. (1994). Synaptic plasticity: LTP and LTD. Curr. Opn. Neurobiol. 4, 389-399.
- Bi, G.Q., and Poo, M.M. (1998). Synaptic modifications in cultured hippocampal neurons: dependence on spike timing, synaptic strength, and postsynaptic cell type. J. Neurosci. 18, 10464-10472.
- Bienenstock, E.L., Cooper, L.N. and Munro, P.W. (1982). Theory for the development of neuron selectivity: orientation specificity and binocular interaction in visual cortex. J. Neurosci. 2, 32-48.
- Castellani G. C., Quinlan E.M. , Cooper L.N., and Shouval H.Z. (2001). A biophysical model of bidirectional synaptic plasticity: Dependence on AMPA and NMDA receptors, PNAS, 98, 12772-12777.
- Cooper, L.N., Liberman, F. and Oja, E. (1979). A theory for the acquisition and loss of neuron specificity in visual cortex. Biol. Cybernet. 33, 9-28.
- Debanne, D., Gahwiler, B.H. Thomson, S.M. (1998). Long-term synaptic plasticity between pairs of individual CA3 pyramidal cells in rat hippocampal slice cultures. J. Physiol. (London) 507, 237-247.
- Feldman, D.E. (2000). Timing-Based LTP and LTD at Vertical Inputs to Layer II/III Pyramidal Cells in Rat Barrel Cortex. Neuron 27, 45-56.
- Froemke, R.C. & Dan, Y. (2002). Spike-timing-dependent synaptic modification induced by natural spike trains. Nature, 416, 433-438.
- Izhikevich E.M. and Desai N.S. (2003) Relating STDP to BCM. Neural Computation, *in press*.
- Kempter, R. , Gerstner, W., van Hemmen, J. L. (1999). Hebbian learning and spiking neurons. Phys. Rev. E, 59, 4498-4514.
- Kempter, R., Gerstner, W., van Hemmen, J. L. (2001). Intrinsic Stabilization of Output Rates by Spike-Based Hebbian Learning. Neural Comput, 13, 2709-2741
- Kirkwood, A., Dudek, S.M., Gold, J.T., Aizenman, C.D. and Bear, M.F. (1993). Common forms of synaptic plasticity in the hippocampus and neocortex in vitro. Science, 260, 1518-1521.
- Kirkwood, A., Rioult, M.G. and Bear, M.F. (1996). Experience-dependent modification of synaptic plasticity in visual cortex. Nature, 381, 526-528.
- Markram, H., Lubke, J., Frotscher, M. and Sakmann, B. (1997). Regulation of synaptic efficacy by coincidence of postsynaptic APs and EPSPs. Science, 275, 213-215.
- Philpot, B.D., Sekhar, A.K., Shouval, H.Z. and Bear, M.F. (2001). Visual experience and deprivation bidirectionally modify the composition and function of NMDA receptors in visual cortex. Neuron, 29, 157-169.
- van Rossum, M.C., Bi, G.Q. and Turrigiano, G.G. (2000). Stable Hebbian learning from spike timing-dependent plasticity. J. Neurosci., 20, 8812-8821.
- Sjostrom, P.J., Turrigiano, G.G. and Nelson, S.B. (2001). Rate, timing, and cooperativity jointly determine cortical synaptic plasticity. Neuron, 32, 1149-1164
- Senn W., Markram H., Tsodyks M. (2001). An algorithm for modifying neurotransmitter release probability based on pre- and postsynaptic spike timing. Neural Computation, 13, 35-67.
- Song, S., Miller, K.D. and Abbott, L.F. (2000). Competitive Hebbian learning through spike-timing-dependent synaptic plasticity. Nature Neurosci. 3, 919-926.