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REVIEW

Balancing homeostasis and learning in neural circuits**

L. F. Abbott *

Volen Center and Department of Biology, Brandeis University, Waltham, USA

Summary

Neural circuits are remarkably adaptable, providing animals with the ability to modify their behavior on the basis of experience. At the same time, they are extremely robust and maintain stability despite the changes associated with adaptation. This combination of adaptability and stability is difficult to achieve, and it provides a strong constraint on any models of plasticity in neural circuits. New evidence suggests that the effect of action potential timing on synaptic plasticity may be an important element in reconciling homeostasis with adaptability. In particular, spike-timing dependent plasticity can act as both an adaptive and a homeostatic mechanism, controlling overall firing rates and distributions of synaptic efficacies while making neurons selective for certain aspects of their inputs. It can also cause networks that initially represent the present state of a stimulus to predict its future state on the basis of experience, a theoretical result supported by experimental data in behaving rats.

Key words: plasticity, homeostasis, adaptation, long-term potentiation, spike timing

Introduction

Neural circuits are both highly adaptive and sturdily robust, attributes that are difficult to reconcile with each other. Adaptation involves change, which, in learning new tasks, may have to be quite large. Maintaining the characteristics required for stable operation requires homeostatic mechanisms that resist change or, at least, tightly control it. Models of neurons and neural circuits tend to focus on one aspect or the other, that is, on learning or on homeostasis. However, a deeper understanding of neuronal circuit dynamics will require that we deal with both types of plasticity, and that we learn how they work together to produce adaptive but stable behavior.

Although mechanisms by which neurons regulate their intrinsic conductances undoubtedly play an important role in both homeostatic and adaptive processes (see, for example, Abbott and Marder, 2002), synaptic plasticity, in particular long-term potentiation and depression (LTP and LTD), has received the most attention from both experimentalists and modelers. In particular, associative forms of LTP and LTD, which follow general ideas about plasticity annunciated by Hebb and others (Hebb, 1949), have been the focus of work on learning and memory in neural circuits. An important feature of experimentally measured LTP and LTD, which has been stressed particularly in recent work, concerns the role of spike timing in its induction.

Results from a wide range of systems (reviewed in Abbott and Nelson, 2000), including rat hippocampal culture and slice preparations (Levy and Stewart, 1983; Gustafsson et al., 1987; Debanne et al., 1994; Bi and

*Corresponding author: Larry F. Abbott, Volen Center and Department of Biology, Brandeis University, Waltham, MA 02454, USA; phone: ++1-781-736-2876; fax: ++1-781-736-3142; e-mail: abbott@brandeis.edu

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Poo, 1998; Magee and Johnston, 1997; Debanne et al., 1998), neocortical slices (Markram et al., 1997; Egger et al., 1999; Feldman, 2000; Sjöström et al., 2001; Froemke and Dan, 2002), retinotectal synapses in the tadpole (Zhang et al., 1998), synapses in the lateral line lobe of electric fish (Bell et al., 1997), as well as indirect evidence from rats (Mehta et al., 1997, 2000; Allen et al., 2003), cats (Yao and Dan, 2001), and humans (Fu et al., 2002), indicate that the induction of LTP or LTD depends on the relative timing of pre- and postsynaptic action potentials. In most of these preparations, LTP arises if presynaptic action potentials precede postsynaptic action potentials by less than about 20–30 ms. LTD results if, instead, presynaptic action potentials follow postsynaptic spikes by an equivalent interval. The resulting synaptic plasticity is called spike-timing dependent plasticity, or STDP.

STDP has been the subject of a large number of theoretical studies, using a variety of techniques (Kempter et al., 1999; Song et al., 2000; Rubin et al., 2000; van Rossum et al., 2000; Kistler et al., 2000; Cateau and Fukai, 2003; Gütig et al., 2003) and applied to a variety of systems. For example, STDP-like rules have been applied to coincidence detection (Gerstner et al., 1996), sequence learning (Minai and Levy, 1993; Abbott and Blum, 1996; Roberts, 1999), path learning in navigation (Blum and Abbott, 1996; Gerstner and Abbott, 1997; Mehta et al., 2000), and direction selectivity in visual responses (Mehta et al., 2000; Rao and Sejnowski, 2000). Here the focus will be on a particular aspect of STDP, the fact that it can, at least to some degree, reconcile and unite homeostatic and adaptive effects. An additional example will show how STDP can explain modifications in the activity of neurons in behaving animals, suggesting a possible mechanism for navigation.

Materials and methods

The results reported here were all obtained from mathematical models analyzed either with standard mathematical methods or by simulating them on computers. Although the work is theoretical, all the elements of the models are based on and guided by experimental data and stay faithful to those data as much as possible. Modeling approaches are extremely well suited for studies of synaptic plasticity because, although a great deal is known about LTP and LTD, it is usually obtained either from connections between individual pairs of neurons, or from stimulating numerous afferents in parallel. Although this provides the critical data on which models are built, it is not the situation that occurs in vivo, where we must analyze complex patterns of correlated and uncorrelated input across many thousands of synapses. This is precisely what modeling studies can do by extending our knowledge of synaptic plasticity, obtained under simplified conditions, to more realistic patterns of activity resembling those occurring in behaving animals.

The results shown below are based on a mathematical characterization of STDP (Song et al., 1999) used in conjunction with either integrate-and-fire or conductance-based neuron models. Details of the work can be found in the cited references.

Results

Figure 1 shows a schematic diagram of the experimental findings concerning STDP, as discussed in the introduction. The curve in this figure shows the sign and the amount of long-term synaptic modification induced by pairing pre- and postsynaptic action potentials as a function of the time between them. Action potentials that occur in rapid succession in a pre-before-postsynaptic sequence cause LTP, and those that occur in a rapid post-before-presynaptic sequence produce LTD. There is a sharp transition between these two forms of plasticity around the point of coincident pre- and postsynaptic spiking.

The results summarized in Figure 1 indicate that causality plays an important role in determining whether STDP strengthens or weakens synapses. Presynaptic

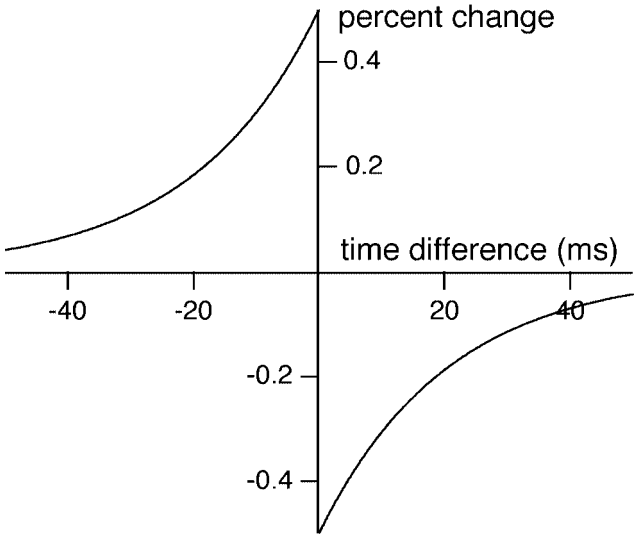

Fig. 1. Mathematical characterization of STDP. The curve shows the percent increase or decrease in synaptic strength caused by a single pairing of a presynaptic action potential separated by the specified time from an accompanying postsynaptic action potential. The left side of the plot corresponds to pre-before-postsynaptic ordering and the right side to post-before-presynaptic ordering.

action potentials that occur before the postsynaptic response, and that therefore could have contributed to evoking it, are strengthened. Presynaptic action potentials that occur in conjunction with a postsynaptic response, but that arrive too late to have evoked it, are weakened. This makes logical sense as a way of strengthening synapses that carry useful information. In the following, it will also be assumed that when pre- and postsynaptic action potentials occur in random, uncorrelated sequences, the overall effect of STDP is to weaken synapses, as has been found experimentally (Feldman, 2000).

In many ways, STDP acts as a typical Hebbian plasticity mechanism, strengthening correlated inputs, for example. However, STDP has additional homeostatic features. In the following sections, attention will be focused on aspects of plasticity exhibited by STDP that are not typically associated with Hebbian mechanisms of plasticity.

Homeostatic effects of STDP

As mentioned above, models allow us to examine how STDP acts when a large number of inputs interact. Figure 2 shows histograms of the strengths of synapses obtained from simulations in which a large number of excitatory synapses, subject to STDP, drove the responses of a model neuron (Song et al., 1999). Because STDP is a Hebbian form of plasticity, we would expect that it would tend to either maximally strengthen or maximally weaken synapses. This is because Hebbian mechanisms make strong synapses stronger and weak synapses weaker. The horizontal scales in Figure 2 run from the minimum (zero) to the maximum allowed synaptic strength. The bimodal form of the histograms indicates that this intuition is correct, but it does not fully describe what is going on.

Although the synapses described by the histograms in Figure 2 fall into either weak (near zero) or strong (near the maximum) categories, as would follow from a destabilizing "learning" form of plasticity, there is also a homeostatic element in their overall distribution. As further analysis has shown (Song et al., 1999), the synapses in this case divide themselves into weak and strong groups in such a way that the postsynaptic response is regulated in a homeostatic manner. For Fig. 2A, the synaptic inputs to the model neuron were each firing at 10 Hz. This produced a roughly equal division between weak and strong synapses, as indicated by the histogram in Fig. 2A. When the input firing rates were increased by 3 Hz, STDP produced the histogram of Fig. 2B, in which a larger percentage of the synapses are in the weak group. Thus, STDP reduces the overall drive to the neuron, which compensates for the increase in input firing rate, a typical homeostatic function. In fact, over a wide range of input firing rates, STDP can homeostatically regulate and buffer both the overall postsynaptic firing rate and aspects of its variability (Song et al., 1999; Kempter et al., 2001).

It is surprising to see a Hebbian form of plasticity performing a homeostatic function. In most models of Hebbian plasticity, constraints must be introduced to perform the required homeostatic adjustments to maintain reasonable levels of activity (Miller and MacKay, 1994). STDP can, at least in part, perform these homeostatic functions itself, while retaining the desirable features of Hebbian plasticity, such as producing selectivity in individual neurons and activity-dependent maps of selectivity in neuronal populations (Song and Abbott, 2001).

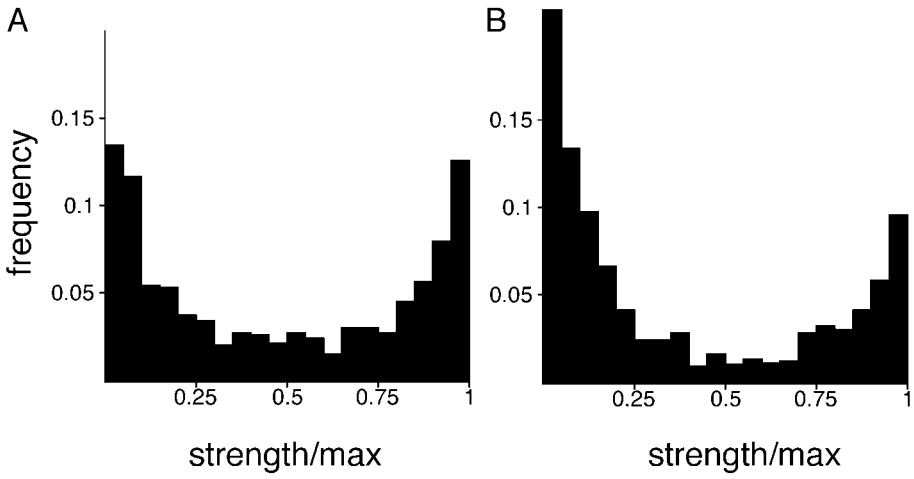

Fig. 2. Histograms of the strengths of multiple synapses onto a single model neuron in the case of low- (**A**) and high- (**B**) frequency input. The horizontal axis indicates the strength of a synapse divided by the maximum allowed strength, and the vertical axis corresponds to the fraction of such synapses that appear after STDP has equilibrated. STDP produces a bimodal distribution of synaptic strengths, with the percentage of strong and weak synapses varying to compensate for modifications in total synaptic input.

Equalization of synaptic efficacy by anti-STDP

Synapses on many types of neurons appear to be adjusted in strength to compensate for distance-dependent attenuation; in particular they appear to grow stronger the further out they are on the dendrite in such a way that somatic postsynaptic potentials are roughly equalized (Iansek and Redman, 1973; Jack et al., 1981; Anderson et al., 1980; Triller et al., 1990; Stricker et al., 1996; Magee and Cook, 2000; Smith et al., 2003). Recent work (Rumsey and Abbott, 2003; see also Goldberg et al., 2002) has shown that a form of STDP seen in electric fish (Bell et al., 1997), called anti-STDP, can produce this result.

The timing-dependent plasticity seen in synapses between electrosensory neurons in electric fish is a weakening of synapses (LTD) when pre- and postsynaptic action potentials are paired in the pre-before-post ordering. This is the opposite of what is seen in most preparations, which accounts for the name anti-STDP. In addition, there is a non-associative form of LTP seen at these electric-fish synapses, which plays an important role in the effect described below.

To examine the effect of anti-STDP on the synaptic strengths of distal and proximal synapses, a multi-compartment model of an extended neuronal dendritic cable was coupled to a spiking soma model (Rumsey and Abbott, 2003). Initially, all the synapses of the model were given the same intrinsic strength, which, due to attenuation, produced the steadily attenuating somatic excitatory postsynaptic potentials (epsps) seen in Fig. 3A. At this point, a steady 10 Hz input was simulated on all synapses and anti-STDP adjusted synaptic strengths on the basis of the pre- and postsynaptic activity at each synapse. After the synaptic strengths reached equilibrium values, the intrinsic strengths of the synapses increased steadily as a function of distance along the dendritic cable. As a result, the somatic epsps evoked by stimulating each synapse independently, as measured from the soma, achieved equal values (Fig. 3B). This form of synaptic equalization is similar to what has been seen experimentally (see, for example, Cook and Magee, 2000).

Anti-STDP is a homeostatic form of plasticity, so the fact that it regulates synaptic strengths, rather than forcing them to extreme values, is to be expected. The novel feature in this example is that synaptic strengths compensate for attenuation. This represents a connection between the local factors that determine the efficacy of a synapse, namely its intrinsic strength, and the global factors that modify this efficacy, such as attenuation along dendritic cables. The ability of anti-STDP to compensate local and global elements affecting synaptic efficacy suggests that it may be an important element of homeostatic synaptic regulation.

STDP and hippocampal place cells

The previous examples stressed the role of STDP (or anti-STDP) in homeostatic regulation because this is a

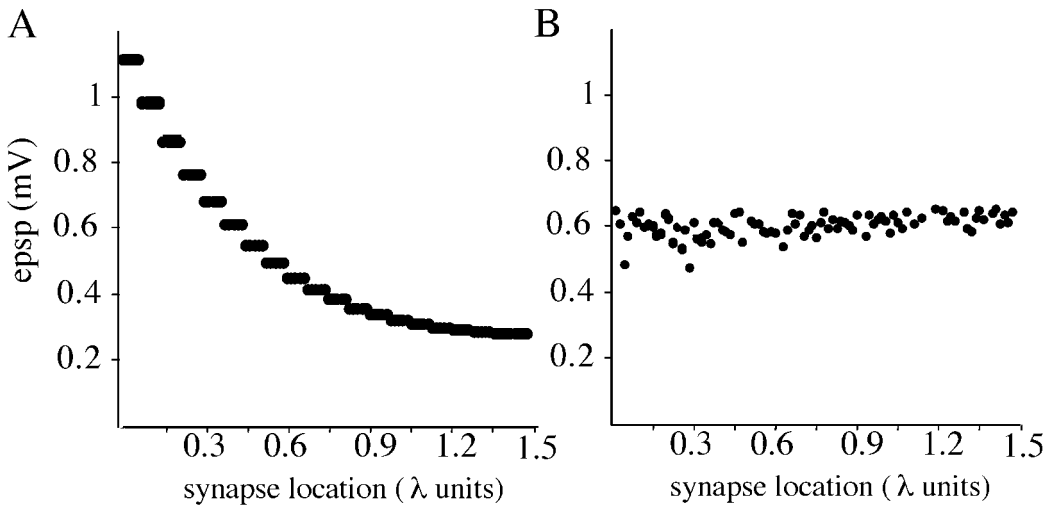

Fig. 3. Equalization of synaptic efficacy by anti-STDP. Both plots show the magnitudes of epsps, measured at the soma of a model neuron, produced by synapses at varying distances along a dendritic cable (each dot corresponds to a different synapse). The distance from the synapse to the soma, indicated along the horizontal axis, is given in units of the electrotonic length constant of the dendritic cable (λ units). (**A**) Initially, proximal synapses produced larger epsps than distal synapses. The steps in these results reflected the compartmental structure of the dendritic cable. (**B**) After anti-STDP has modified synaptic strengths, epsp magnitudes are equalized for proximal and distal synapses.

somewhat surprising feature (especially in the case of STDP). A final example, given in this section, shows how STDP can act in a more usual Hebbian learning capacity, except with the added wrinkle of its timing dependence. This produces an interesting effect that allows networks that initially provide a representation of a stimulus parameter to predict future values of that parameter on the basis of previous experience (Abbott and Blum, 1996). The particular example, hippocamal place cells, is chosen because evidence of the predicted effects of STDP has been seen in this system (Mehta et al., 1997, 2000).

Hippocampal place cells fire action potentials at a rate that depends on the location of the rat within its environment. Using models of STDP, it is possible to compute the effects that the activity of place cells has on the synapses between them (Blum and Abbott, 1996). Furthermore, because place cell activity is correlated with an animal's locomotion, it is possible to assess the effect that previous behavior has on place cell activity through timing-dependent synaptic plasticity. Finally, theoretical predictions of place cell modification by previous experience can be tested experimentally due to the extensive recording done of place cell activity in behaving animals.

Consider the situation depicted in Fig. 4A, which shows two place cells that are reciprocally connected by excitatory synapses that are subject to STDP. Suppose that a rat walks along a path that sequentially activates the neurons shown in Figure 4 in the order cell 1 followed immediately by cell 2. In other words, these two neurons have place fields (the area in the environment that evokes place cell activity when occupied by the rat) in neighboring regions of space, and the rat moves through these regions in a direction that caused neuron 1 to fire and then neuron 2 to fire. In this example, the two reciprocal synapses initially have the same strengths (Fig. 4A). If the rat moves repeatedly through its environment along the postulated path, neurons 1 and 2 will repeatedly fire sequentially and, through STDP, the synapses between them will be modified. Because this direction of motion produces a specific order of firing, the synapse from neuron 1 to neuron 2 will be strengthened by this process, while the synapse from neuron 2 to neuron 1 will be weakened (Fig. 4B).

As a result of the synaptic modification shown in Fig. 4B, neuron 2 may, after STDP has occurred, fire in response to the excitation coming from neuron 1 through the strengthened synapse. From the point of view of someone recording the activity of neuron 2, this has the effect of expanding its place field in a direction opposite to the direction of motion of the rat during the "training" period. Of course, there are many more than two place cells in the rat hippocampus but, using computational methods, it is possible to compute the effect of large numbers of place cells and synapses on place field size and shape (Blum and Abbott, 1996). A result of such a calculation is shown in Figure 5. The thinner line in this plot shows the activity of a model place cell prior to the experience that modifies its shape. The place field, in this example, is the region of space covered by the response "tuning curve", which is a Gaus-

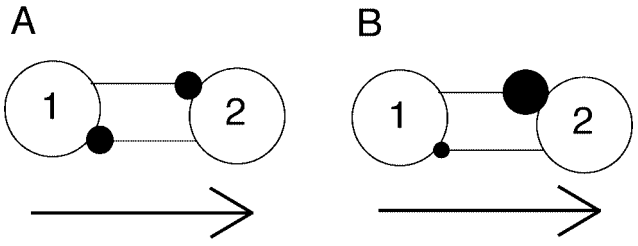

Fig. 4. Effect of locomotion on synaptic connections between place cells. The two open circles in each figure represent two hippocampal place cells. The two filled circles indicate reciprocal synapses between these two neurons, with the size of the filled circle representing the strength of the synapse. The arrows indicate that a rat is moving in a direction that causes sequential activation of neuron 1 followed by neuron 2. (**A**) Before locomotion, both synapses have equal strength. (**B**) After repeated locomotion in the direction indicated by the arrow, STDP strengthens the synapse from neuron 1 to neuron 2 and weakens the synapse from neuron 2 to neuron 1.

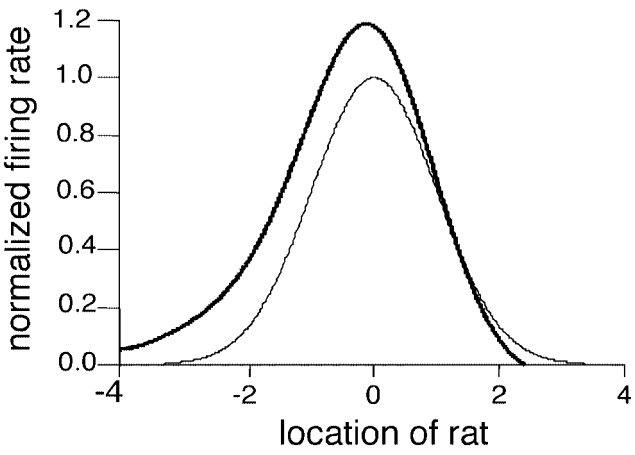

Fig. 5. Predicted place field shift. Activity of a model place cell is plotted as a function of the position of the rat in its environment. Firing rate is normalized to a maximum of one for the initial firing rate curve. The thinner line shows the firing rate as a function of position prior to training experience. The thicker line is the firing rate of the same neuron after repeated network activity corresponding to motion of the rat from left to right along the horizontal axis. The resulting shift arises from modification due to STDP of the strengths of synapses onto this neuron from other place cells.

sian function of the location of the rat. The thicker line is the response tuning curve of the same neuron calculated after experience modifies its shape through STDP. The "experience" here corresponds to motion of a rat from left to right in Figure 5. Notice that after this experience, the place field is expanded in an asymmetric way, primarily in the direction opposite to that traversed by the rat.

Such place field shifts, initially predicted from mathematical calculations (Blum and Abbott, 1996), have been seen in experiments involving repeated traversal (in a single direction) of a rat around a closed-loop path (Mehta et al., 1997, 2000). The shape and direction of place field shifts seen in the data match those of the prediction. This provides strong, though indirect, evidence that spike-timing dependent mechanisms are active in behaving animals. Furthermore, the place field shift seen in Figure 5 has interesting functional implications. Before the experience, place field activity provides an internal, neuronal representation of the location of the rat in space. After the experience-induced changes in place field shape take place, the activity of the population of place cells that initially reported the current location of the rat now represents a prediction of the future location of the rat on the basis of the training experience (Blum and Abbott, 1996; Gerstner and Abbott, 1997). In a more general context, STDP provides a way for neural circuits to develop predictive representations of quantities with behavior relevance.

Discussion

Synaptic plasticity is viewed primarily as a mechanism for enhancing the selectivity of a neuron through Hebbian learning. However, important homeostatic processes are also required to make a neuron function properly. Among these is regulation of total excitatory synaptic strength and synapse equalization, which means that distal synapses have, at least potentially, an equal chance of controlling postsynaptic firing as proximal synapses. Reconciling the homeostatic and learning functions of synaptic plasticity is difficult but, in some instances, STDP, or its reverse anti-STDP, can serve these homeostatic functions. STDP can act as both an adaptive and a homeostatic mechanism, controlling overall firing rates and distributions of synaptic efficacies while making neurons selective for certain aspects of their inputs. It can also cause networks that initially represent the present state of a stimulus to predict its future state on the basis of experience, a theoretical result supported by experimental data in behaving rats. An appropriate combination of STDP and anti-STDP has the potential of providing both homeostatic and learning functions.

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References

Abbott, L.F. and K.I. Blum. 1996. Functional significance of long-term potentiation for sequence learning and prediction. Cereb. Cortex 6: 406–416.

Abbott, L.F. and E. Marder. 2002. Activity-dependent regulation of neuronal conductances. In: The Handbook of Brain Theory and Neural Networks (M. Arbib, ed.). Bradford MIT Press, Cambridge, pp. 85–87.

Abbott, L.F. and S.B. Nelson. 2000. Synaptic plasticity: taming the beast. Nature Neurosci. 3: 1178–1183.

Allen C.B., T. Celikel and D.E. Feldman. 2003. Long-term depression induced by sensory deprivation during cortical map plasticity in vivo. Nat. Neurosci. 3: 291–299.

Anderson P., H. Silfvenius, S.H. Sundberg and O. Sveen. 1980. A comparison of distal and proximal dendritic synapses on CA1 pyramids in guinea-pig hippocampal slices in vitro. J. Physiol. 307: 273–299.

Bell, C.C., V.Z. Han, Y. Sugawara and K. Grant. 1997. Synaptic plasticity in a cerebellum-like structure depends on temporal order. Nature 387: 278–281.

Bi, G.-Q. and M.-M. Poo. 1998. Activity-induced synaptic modifications in hippocampal culture, dependence on spike timing, synaptic strength and cell type. J. Neurosci. 18: 10464–10472.

Blum, K.I. and L.F. Abbott. 1996. A model of spatial map formation in the hippocampus of the rat. Neural Comp. 8: 85–93.

Cateau, H. and T. Fukai. 2003. A stochastic method to predict the consequences of arbitrary forms of spike-timing-dependent plasticity. Neural Comp. 15: 597–620.

Debanne, D., B.H. Gahwiler and S.M. Thompson. 1994. Asynchronous pre- and postsynaptic activity induces associative long-term depression in area CA1 of the rat hippocampus in vitro. Proc. Natl. Acad. Sci. USA 91: 1148–1152.

Debanne, D., B.H. Gahwiler and S.M. Thompson. 1998. Long-term synaptic plasticity between pairs of individual CA3 pyramidal cells in rat hippocampal slice cultures. J. Physiol. 507: 237–247.

Egger, V., D. Feldemeyer and B. Sakmann. 1999. Coincidence detection and efficacy changes in synaptic connections between spiny stellate neurons of the rat barrel cortex. Nature Neurosci. 2: 1098–1105.

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. and Y. Dan. 2002. Spike-timing-dependent synaptic modification induced by natural spike trains. Nature 416: 433–438.

Fu Y.X., K. Djupsund, H. Gao, B. Hayden, K. Shen and Y. Dan. 2002. Temporal specificity in the cortical plasticity of visual space representation. Science 296: 1999–2003.

Gerstner, W. and L.F. Abbott. 1997. Learning navigational maps through potentiation and modulation of hippocampal place cells. J. Computational Neurosci. 4: 79–94.

Gerstner, W., R. Kempter, J.L. van Hemmen and H. Wagner 1996. A neuronal learning rule for sub-millisecond temporal coding. Nature 383: 76–78.

Goldberg, J., K. Holthoff and R. Yuste. 2002. A problem with Hebb and local spikes. Trends in Neurosci. 25: 433–435.

Gustafsson, B., H. Wigstrom, W.C. Abraham and Y.-Y. Huang. 1987. Long-term potentiation in the hippocampus using depolarizing current pulses as the conditioning stimulus to single volley synaptic potentials. J. Neurosci. 7: 774–780.

Gütig R., R. Aharonov, S. Rotter and H. Sompolinsky. 2003. Learning input correlations through nonlinear temporally asymmetric Hebbian plasticity. J. Neurosci. 23: 3697–3714.

Hebb, D.O. 1949. The Organization of Behavior: A Neuropsychological Theory. Wiley, New York.

Iansek, R. and S.J. Redman. 1973. An analysis of cable properties of spinal motoneurones using a brief intracellular current impulse. J. Physiol. 234: 613–636.

Jack J.J.B., S.J. Redman and K. Wong. 1981. The components of synaptic potentials evoked in spinal motoneurones by impulses in single group 1a fibres. J. Physiol. 321: 65–96.

Kempter R., W. Gerstner and J.L. van Hemmen. 1999. Hebbian learning and spiking neurons. Phys. Rev. E 59: 4498–4515.

Kempter R, W. Gerstner W and J.L. van Hemmen. 2001. Intrinsic stabilization of output rates by spike-based Hebbian learning. Neural Comp. 13: 2709–2741.

Kistler W.M. and J.L. van Hemmen. 2000. Modeling synaptic plasticity in conjunction with the timing of pre- and postsynaptic action potentials. Neural Comp. 12: 385–405.

Levy, W.B. and D. Steward. 1983. Temporal contiguity requirements for long-term associative potentiation/depression in the hippocampus. Neurosci. 8: 791–797.

Magee, J.C. and D.A. Johnston. 1997. Synaptically controlled, associative signal for Hebbian plasticity in hippocampal neurons. Science 275: 209–213.

Magee J.C. and E.P. Cook. 2000. Somatic EPSP amplitude is independent of synapse location in hippocampal pyramidal neurons. Nat. Neurosci. 3: 895–903.

Markram, H., J. Lubke, M. Frotscher and B. Sakmann. 1997. Regulation of synaptic efficacy by coincidence of postsynaptic APs and EPSPs. Science 275: 213–215.

Mehta, M.R., C.A. Barnes and B.L. McNaughton. 1997. Experience-dependent, asymmetric expansion of hippocampal place fields. Proc. Natl. Acad. Sci. USA 94: 8918–8921.

Mehta, M.R., M.C. Quirk and M. Wilson. 2000. Experience dependent asymmetric shape of hippocampal receptive fields. Neuron 25: 707–715.

Miller, K.D. and D.J.C. MacKay. 1994. The role of constraints in Hebbian learning. Neural Comp. 6: 100–126.

Minai, A.A. and W.B. Levy. 1993. Sequence learning in a single trial. INNS World Congress of Neural Networks II: 505–508.

Rao, R. and T.J. Sejnowski. 2000. Predictive sequence learning in recurrent neocortical circuits. In: Advances in Neural Information Processing Systems 12 (S.A. Solla, T.K. Leen and K.-B. Muller, eds.). MIT Press, Cambridge MA.

Roberts, P.D. 1999. Computational consequences of temporally asymmetric learning rules, I. Differential Hebbian learning. J. Computational Neurosci. 7: 235–246.

Rubin, J., D.D. Lee and H. Sompolinksy. 2001. Equilibrium properties of temporally asymmetric Hebbian plasticity. Phys. Rev. Lett. 86: 364–367.

Rumsey, C. and L.F. Abbott. 2003. Synaptic equalization through anti-STDP. J. Neurophysiol. (in press). Sjöström P.J., G.G. Turrigiano and S.B. Nelson. 2001. Rate, timing, and cooperativity jointly determine cortical synaptic plasticity. Neuron 32: 1149–1164.

Smith M.A., G.C.R. Ellis-Davies and J.C. Magee. 2003. Mechanism of the distance-dependent scaling of Schaffer collateral synapses in rat CA1 pyramidal neurons. J. Physiol. 548: 245–258.

Song, S. and L.F. Abbott. 2001. Column and map development and cortical re-mapping through spike-timing dependent plasticity. Neuron 32: 339–350.

Song, S., K.D. Miller and L.F. Abbott. 2000. Competitive Hebbian learning through spike-timing-dependent synaptic plasticity. Nature Neurosci. 3: 919–926.

Stricker C., A.C. Field and S.J. Redman. 1996. Statistical analysis of amplitude fluctuations in EPSCs evoked in rat CA1 pyramidal neurons in vitro. J. Physiol. 490: 419–441.

Triller A., T. Seitanidou, O. Franksson and H. Korn. 1990. Size and shape of glycine receptor clusters in a central neuron exhibit a somato-dendritic gradient. New. Biol. 2: 637–641.

van Rossum M.C., G.-Q. Bi and G.G, Turrigiano. 2000. Stable Hebbian learning from spike timing-dependent plasticity. J. Neurosci. 20: 8812–8821.

Yao H. and Y. Dan. 2001. Stimulus timing-dependent plasticity in cortical processing of orientation. Neuron 32: 315–323.

Zhang, L.I., H.W. Tao, C.E. Holt, W.A. Harris and M.-M. Poo. 1998. A critical window for cooperation and competition among developing retinotectal synapses. Nature 395: 37–44.