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Synaptic equalization by anti-STDP

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Abstract

Experimental evidence has shown that in some neuron types, such as hippocampal CA1 neurons, distally generated excitatory postsynaptic potentials (EPSPs) are scaled up in amplitude compared to more proximally generated EPSPs such that EPSP magnitudes at the soma are approximately equal regardless of the dendritic location of origin. Using an equivalent cable model neuron, we show that a particular form of spike-timing dependent plasticity (STDP) called anti-STDP is capable of achieving this synaptic equalization. Anti-STDP equalizes synapses through the equalization of synaptic efficacies. We show this result for both a passive dendritic cable and for a cable containing a dendritic spike-initiation zone.

Keywords: Synaptic efficacy; Spike-timing dependent plasticity; Dendritic attenuation

1. Introduction

Due to the attenuation effect of dendrites, synapse location, in addition to intrinsic synaptic strength, is important in the consideration of synaptic efficacy. We define synaptic efficacy as the probability that a presynaptic spike evokes a postsynaptic action potential. A distal synapse may have to be intrinsically stronger (e.g., have a larger synaptic conductance) than a proximal synapse to have an equal impact on firing, and hence an equal efficacy. Some cell types appear to show exactly this effect, with distal synapses compensating for attenuation by being stronger than more proximal synapses [1,2,7–11]. For example, synapses at increasing distances from the soma of CA1 pyramidal neurons have been shown to generate increasingly large local dendritic excitatory postsynaptic potentials (EPSPs) but equal amplitude somatic EPSPs [9]. It has been suggested that this scaling effectively eliminates the location-dependence of

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synapses, giving distal synapses equal efficacy for the firing of the postsynaptic neuron. Here we address the question of how such a configuration of synaptic weights might arise and be maintained.

We argue that the answer lies in a particular form of spike-timing dependent plasticity (STDP). In STDP, the direction and magnitude of synaptic modification depends on the relative timing of pre- and postsynaptic action potentials. In the conventional form of STDP, pre- before postsynaptic spiking within tens of milliseconds leads to long-term potentiation (LTP), and post- before presynaptic spiking leads to long-term depression (LTD). STDP acts to enhance those inputs to a neuron that causally predict postsynaptic firing and weaken those that do not. However, it has been suggested that such a rule may have adverse consequences under some circumstances [4]. For instance, STDP may selectively strengthen proximal synapses and weaken distal ones. A different form of STDP, called anti-STDP, observed in the electrosensory lobe of electric fish has the opposite timing convention [3,5]. In particular, a spike-timing dependent LTD window for pre-before-post spiking was observed in combination with a timing-independent, nonassociative LTP [5]. Through the use of computational models, we show that this form of anti-STDP provides a homeostatic mechanism by which synapses can counteract location-dependence (for a related suggestion, see [4]).

2. The model

We used an equivalent cable model of a neuron, consisting of an active somatic compartment connected to an unbranched, passive dendritic cable. The somatic compartment contained Hodgkin–Huxley conductances for generating action potentials. One hundred excitatory synapses and 20 inhibitory synapses were distributed evenly along the dendrite. Presynaptic inputs were random Poisson processes firing with a mean rate of 10 Hz. For Figs. 2–4, the excitatory synapses were subject to an anti-STDP rule, consisting of an exponential LTD window with a 20 ms decay constant for pre-before-post spiking intervals in combination with nonassociative LTP that depended only on presynaptic firing. Specifically, the maximal synaptic conductance was decremented by the amount $-0.01\exp(T/20)$ times its initial value for $T<0$, where T is the time of the presynaptic spike minus the time of the postsynaptic spike. The maximal synaptic conductance was incremented by 0.0024 times its initial value for every presynaptic spike. Fig. 1 was generated using conventional STDP of the form: $0.01\exp(T/20)$ for $T<0$ (pre-before-post LTP) and $-0.011\exp(-T/20)$ for $T>0$ (post-before-pre LTD). Simulations were carried out using the NEURON simulation environment [6]. All simulations were initialized with equal synaptic conductances at all synapses.

3. Results

Fig. 1 shows the result of a simulation using the conventional form of STDP, where pre-before-post spiking generates LTP, and post-before-pre generates LTD. The out-

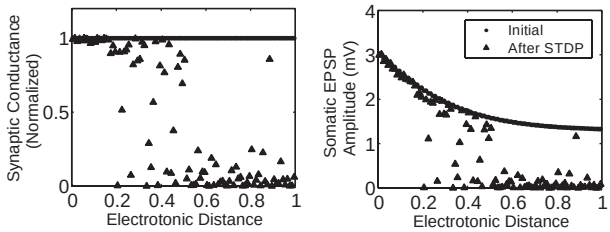

Fig. 1. STDP increases the disparity between proximal and distal synapses. Maximal synaptic conductance, normalized to the initial value of synaptic conductance, and somatic EPSP amplitude are plotted for each synapse as a function of the distance of the synapse from the soma (in units of the electrotonic length constant).

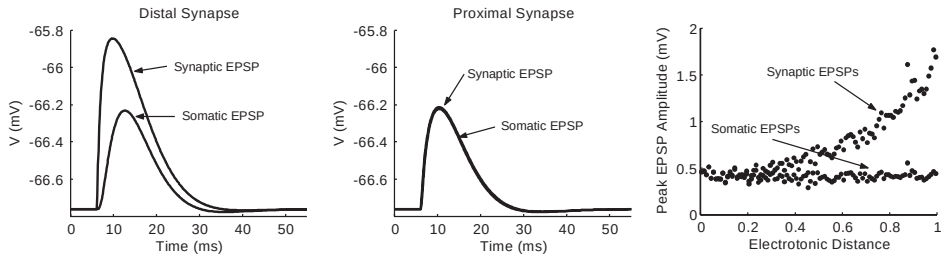

Fig. 2. Anti-STDP equalizes synapses. The left and middle plots show sample EPSPs for a distal and a proximal synapse both at the site of the synapse and at the soma. The plot on the right shows EPSP amplitude as a function of electrotonic distance for all synapses. Dendritic EPSPs increase with distance, but somatic EPSPs are equal in amplitude.

come, if all synapses are initialized to the same strength, is that the distal synapses are all weakened while the proximal synapses remain strengthened. This occurs because, as a competitive learning rule, STDP strengthens the most effective synapses (in this case, the synapses closest to the soma) at the expense of the least effective, or distal, synapses.

On the other hand, anti-STDP leads to a rather different result. Fig. 2 shows the resulting EPSPs when the simulation is run to equilibrium using anti-STDP rather than conventional STDP. In this case, EPSPs at distal synapses have larger amplitudes than do EPSPs at more proximal synapses. At the soma, however, EPSPs have the same amplitude regardless of synaptic distance. This figure is strikingly similar to the experimental result described in Ref. [9].

How does this combination of spike-timing dependent LTD and activity-dependent LTP achieve such synaptic equalization? It does so by equalizing the synaptic efficacies, where efficacy refers to the probability that a presynaptic spike induces a postsynaptic spike. One way to measure synaptic efficacy is to calculate the pre–

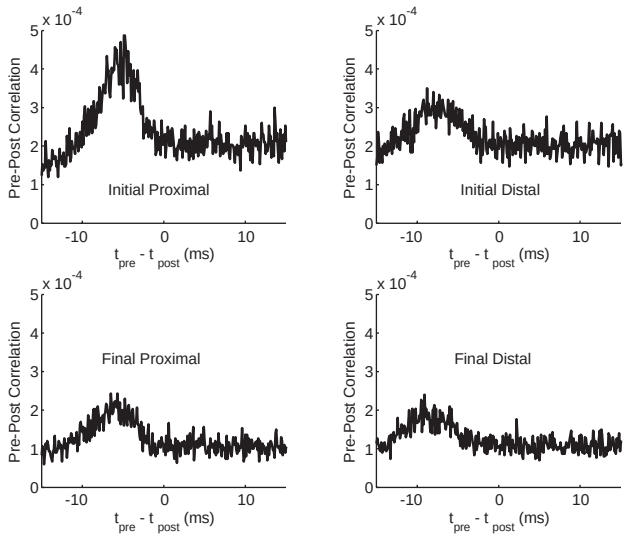

Fig. 3. Anti-STDP equalizes synaptic efficacies. Sample pre–post cross-correlograms are shown for a proximal and a distal synapse both initially (when all synapses are at the same synaptic strength) and at equilibrium after allowing anti-STDP to modify synapses. Although the proximal synapse initially has a much larger correlation, or efficacy, than the distal one, anti-STDP acts to equalize their efficacies.

post cross-correlogram for a particular synapse. The excess correlation above baseline for pre-before-post timing intervals corresponds to presynaptic spikes that contributed to postsynaptic firing and thus represents the efficacy of the synapse. As shown in Fig. 3, when all the synapses are initialized to the same strength, a proximal synapse has a much larger pre–post correlation than does a distal synapse. After allowing the anti-STDP rule to act on the synapses, however, the pre–post correlation is equalized for proximal and distal synapses. This occurs when an equilibrium condition is reached, at which time the synaptic weakening due to the LTD interactions balances the continuous synaptic strengthening of the nonassociative LTP.

This equalization of efficacy will occur regardless of the precise dendritic morphology or the presence of active conductances in the dendrites. Factors such as active conductances will alter the specific distribution of synaptic weights required to achieve this equalization but will not change the equalization itself. An illustration of this is shown in Fig. 4 for a simulation in which a secondary spike-initiation compartment was added to the distal end of the dendritic cable. Unlike the previous case, now the most distal synapses initially have high efficacy because they are effective at inducing action potentials in the distal compartment, which can then propagate to the soma. This results in a U-shaped profile for the initial efficacies when all synapses have the same strength. At equilibrium though, the efficacies are again equalized due to an inverse U-shaped profile of synaptic strengths.

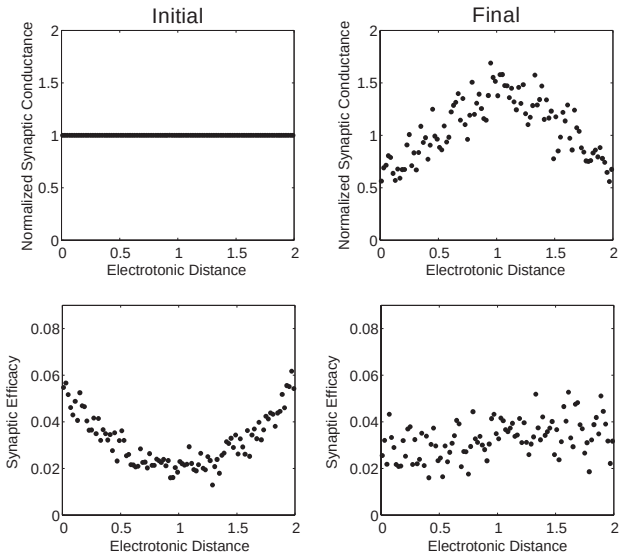

Fig. 4. Anti-STDP equalizes synaptic efficacies in a model containing a distal dendritic spiking compartment. The addition of a spike-generation zone to the distal end of the cable results in an initial efficacy distribution that is U-shaped. At equilibrium, the synapses show an inverse U-shaped profile of synaptic weights (normalized conductances) that equalizes the efficacies.

4. Conclusions

In general, spike-timing plasticity rules are a useful means for measuring the efficacy of synapses because they distinguish between those presynaptic spikes that are causally related to postsynaptic action potentials and those that are not. How this measure is used at a synapse depends on the particular form of spike-timing plasticity. In the case of conventional STDP, the efficacy measure is used to strengthen the most effective synapses and weaken the least effective. On the other hand, anti-STDP acts in a homeostatic manner to equalize the efficacies of synapses and is capable of achieving the type of distance-dependent synaptic scaling that is observed experimentally.

As illustrated by Fig. 4, anti-STDP equalizes efficacies regardless of the presence of active conductances in the dendrite. In a very long passive cable, distal synapses might have to be potentiated to unrealistically large levels in order to achieve equalization with proximal synapses. Active dendrites or the presence of dendritic spiking zones alleviate this problem by increasing the initial efficacy of distal synapses. In this case, anti-STDP can equalize efficacies across very long dendrites without requiring unrealistic synaptic strengths.

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