Synaptic Equalization by Anti-STDP

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The impact of an individual synapse on the firing pattern of a neuron depends not only on its intrinsic strength, but also on its dendritic location in relation to the overall morphology and conductance profile of the neuron. We define synaptic efficacy as the probability that a particular input to a neuron evokes an action potential. Because of attenuation along dendritic cables, a distal synapse may have to be intrinsically stronger (i.e. have a larger synaptic conductance) than a proximal synapse to have an equal effect on firing, and hence an equal efficacy. Some cell types appear to show exactly this effect, with distal synapses compensating for attenuation by being intrinsically stronger (Magee and Cook, 2000; Stricker et al., 1996; Jack et al., 1981; Anderson et al., 1980; Iansek and Redman, 1973). Synapses at increasing distances from the soma of CA1 pyramidal cells have been shown to generate increasingly larger local dendritic excitatory postsynaptic potentials (EPSPs) but equal amplitude somatic EPSPs (Magee and Cook, 2000). It has been suggested that this scaling effectively eliminates the location-dependence of synapses, giving distal synapses equal efficacy for the firing of the postsynaptic neuron. Here we address the question of how such a configuration might arise and be maintained. In other words, how do local synaptic plasticity mechanisms account and compensate for global factors, such as synaptic location, that have a powerful effect on functional synaptic efficacy?

We argue that the answer lies in a particular form of spike-timing dependent plasticity (STDP). STDP, in which the direction and magnitude of synaptic modification depends on the relative timing of pre- and postsynaptic action potentials, has been observed experimentally in a number of forms (see Abbott and Nelson, 2000). In the usual form of STDP, pre- before postsynaptic spiking within tens of milliseconds leads to long-term potentiation, and post- before presynaptic spiking leads to long-term depression. 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 (Goldberg et al., 2002). 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 (Bell et al., 1997) has the opposite timing convention. Through the use of computational models, we show that anti-STDP provides a homeostatic mechanism by which synapses can counteract location-dependence (for a related suggestion see Goldberg et al., 2002).

The ability of anti-STDP to compensate for attenuation results from its sensitivity to synaptic efficacy. This allows efficacy, which is a global property of the neuron, to guide the local processes at individual synapses that control synaptic strength. In particular, using statistical arguments, we show that synapses being modified by anti-STDP

equilibrate at a strength that sets their efficacy equal to a fixed number, which is the same for every synapse regardless of its location. This requires, in addition to the anti-STDP process, a global form of plasticity that regulates the postsynaptic firing rate, and we use a form of synaptic scaling (Turrigiano et al., 1998) for this purpose.

The figure below shows the results of using an equivalent cable model of a neuron to explore the implications of anti-STDP. A somatic compartment was connected to a multi-compartment, unbranched cable designed to simulate an equivalent cable for an extended dendritic tree. Excitatory and inhibitory synapses were located along the length of the dendritic cable, and excitatory synapses were subject to an anti-STDP rule. Although the proximal synapses initially have a much higher efficacy than the distal ones, anti-STDP acts to equalize efficacies across the length of the dendrite, in striking agreement with the experimental results of Magee and Cook (2000). This equalization is stable over time. Further mathematical analysis has been used to reveal the conditions that are necessary for this effect of efficacy equalization to occur.

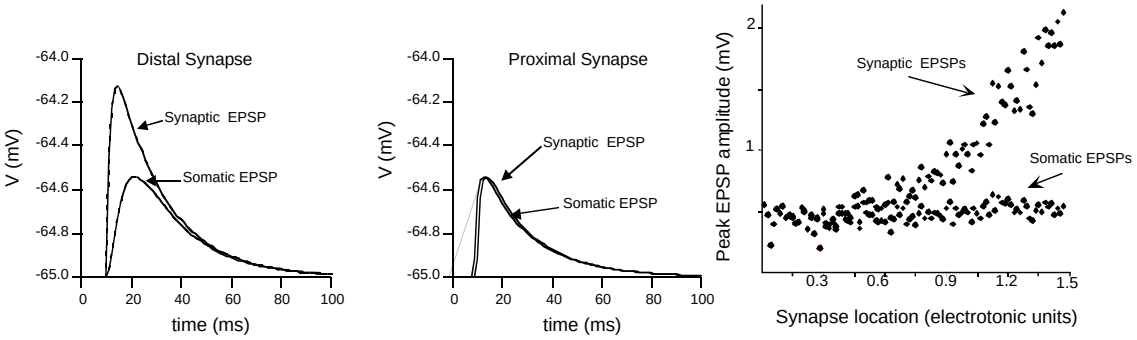

Figure: Results of a cable simulation of the equalizing effects of anti-STDP. The left and center panels show EPSPs "recorded" at the site of the synapse and in the soma for a distal (left) and a proximal (center) synapse. Although the distal synapse shows attenuation and the proximal does not, both produce the same size EPSP at the soma. The right panel shows EPSP amplitudes measured locally and at the synapses for all the synapses in the model, revealing the equalization effect.

References

Abbott LF, Nelson SB (2000) Synaptic Plasticity: Taming the Beast. Nature Neurosci 3:1178-1183.

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

Bell CC, Han VZ, Sugawara Y, Grant K (1997) Synaptic plasticity in a cerebellum-like structure depends on temporal order. Nature 387:278-281.

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

Iansek R, Redman SJ (1973) The amplitude, time course and charge of unitary post-synaptic potentials evoked in spinal motoneurone dendrites. J Physiol 234:665-688.

Jack JJB, Redman SJ, Wong K (1981) The components of synaptic potentials evoked in cat spinal motoneurones by impulses in single group Ia afferents. J Physiol 321:65-96.

Magee JC, Cook EP (2000) Somatic EPSP amplitude is independent of synapse location in hippocampal pyramidal neurons. Nat Neurosci 3:895-903.
Stricker C, Field AC, Redman SJ (1996) Statistical analysis of amplitude fluctuations in EPSCs evoked in rat CA1 pyramidal neurones in vitro. J Physiol 490:419-441.
Turrigiano, GG, Leslie KR, Desai, NS, Rutherford LC, Nelson, SB (1998) Activity-dependent scaling of quantal amplitude in neocortical neurons. Nature 391:892-896.