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Synaptic modifications depend on synapse location and activity: a biophysical model of STDP

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Abstract

In spike-timing-dependent plasticity (STDP) the synapses are potentiated or depressed depending on the temporal order and temporal difference of the pre- and post-synaptic signals. We present a biophysical model of STDP which assumes that not only the timing, but also the shapes of these signals influence the synaptic modifications. The model is based on a Hebbian learning rule which correlates the NMDA synaptic conductance with the post-synaptic signal at synaptic location as the pre- and post-synaptic quantities. As compared to a previous paper [Saudargiene, A., Porr, B., Worgotter, F., 2004. How the shape of pre- and post-synaptic signals can influence stdp: a biophysical model. Neural Comp.], here we show that this rule reproduces the generic STDP weight change curve by using real neuronal input signals and combinations of more than two (pre- and post-synaptic) spikes. We demonstrate that the shape of the STDP curve strongly depends on the shape of the depolarising membrane potentials, which induces learning. As these potentials vary at different locations of the dendritic tree, model predicts that synaptic changes are location dependent. The model is extended to account for the patterns of more than two spikes of the pre- and post-synaptic cells. The results show that STDP weight change curve is also activity dependent.

Keywords: Spike-timing-dependent plasticity; Synaptic modifications; Hebbian learning; Back-propagating spike; Dendritic spike; Neuronal activityss

1. Introduction

It is believed that learning and memory in biological neurons are based on the modifications of the synaptic strengths (Benett, 2000). Synapses are weakened or strengthened depending on the order and temporal difference of the pre- and post-synaptic activity. If the pre-synaptic spike precedes the post-synaptic spike ($T > 0$), the synapse is potentiated, while it is depressed if the temporal order is reversed ($T < 0$). This phenomenon is called spike-timing-dependent plasticity (Markram et al., 1997; Bi and Poo, 2001).

However, recent physiological experiments suggest that the properties of synaptic modifications may depend not only on timing, but also on the location of the synapse (Golding et al., 2002). For example, synaptic strength is regulated by local learning rules. This assumption is supported by the fact the signals which drive synaptic plasticity strongly depend on

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the location at the neuron where a synapse is located (Haüsser and Mel, 2003; Golding et al., 2002). Close to the soma back-propagating or, more distally, dendritic spikes provide the necessary post-synaptic depolarisation (Magee and Johnston, 1997; Golding et al., 2001, 2002; Larkum et al., 2001).

The natural activity of biological neurons is much more complex than that used in the experimental conditions of STDP induction. In these experiments, the synaptic inputs are paired with post-synaptic action potentials (Magee and Johnston, 1997; Markram et al., 1997; Bi, 2002) or a synapse is stimulated with low or high frequency inputs (Bear, 1995). In natural conditions of learning, multiple pre- and post-synaptic spikes may occur within milliseconds and bursting is observed (Paulsen and Sejnowski, 2000; Bi, 2002). How such neuronal activity influences synapse potentiation and depression still remains under debate (Bi, 2002). It has been argued that the spike pairs may cause independent effects (Kempter et al., 1999; Song et al., 2000; van Rossum et al., 2000) or interact with each other (Froemke and Dan, 2002; Eisele and Miller, 2002) such that the contribution of one given spike pair depends on the presence of other spikes. For example, it was observed that the first spike pair diminishes the influence of the following spike pair in layers 2 and 3 Pyramidal neurons (Froemke and Dan, 2002) implying that synaptic modifications are activity dependent.

In this study, we present a biophysical model of STDP which can account for more realistic spiking patterns and capture the dependence of synaptic changes on the shapes of the pre- and post-synaptic signals. The model correlates the NMDA synaptic conductance and a post-synaptic signal, dependent on the post-synaptic depolarisation at the location of the synapse. The influence of the activity of the pre- and post-synaptic cells is incorporated in the model by introducing efficacies of each spike. In this study we use real neuronal signals and triplets of spikes as compared to another recent paper (Saudargiene et al., 2004) where the simulations were based on artificial signals and only spike pairs were considered. Also the learning rule differs. Here we will show that the new model reproduces the generic STDP weight change curve and is sensitive to the shapes of the post-synaptic membrane potential, responsible for learning induction. As this signal varies along the dendritic tree, the model predicts that STDP is location dependent. We find that the most pronounced differences in synaptic modification rules should be in proximal and distal dendrites—anti-symmetrical STDP versus symmetrical weight change curve where only potentiation is observed, respectively. Moreover, we note that STDP characteristics are influenced by the the spiking pattern of the pre- and post-synaptic cells.

2. Biophysical model of STDP

The biophysical model of STDP implements a dendritic compartment with a plastic synapse which consists of NMDA and AMPA channels (Fig. 1).

The AMPA channels are the ones that mainly *express* the plasticity by changing the synaptic strength ρ (Lisman, 1994). Our model is concerned with plasticity induction, therefore, no steps have been undertaken to explicitly model processes that modify AMPA channels.

The NMDA channels are essential for plasticity induction as their blockage to a large degree prevents STDP (Nishiyama et al., 2000; Golding et al., 2002). First, they serve as a coincidence detector between the pre- and post-synaptic activity (Markram et al., 1997). Second, open NMDA channels enable Ca^{2+} ion influx into the post-synaptic cell. It is believed that NMDA channel-mediated Ca^{2+} influx triggers complex chain reactions involving CaMKII, calmodulin, calcineurin and results in plasticity (Lisman, 1994; Bi, 2002).

In our model we associate the pre-synaptic signal with the time- function of the NMDA synaptic conductance given by:

$$g(t) = \bar{g}c_N(t) = \bar{g}\frac{e^{-t/\tau_1} - e^{-t/\tau_2}}{1 + \kappa e^{-\gamma V_m(t)}}, \quad (1)$$

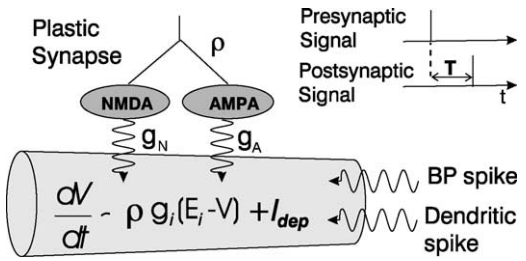

Fig. 1. Schematic diagram of the biophysical model. A plastic synapse consists of NMDA and AMPA channels and has the strength ρ. The source of depolarisation which removes Mg^{2+} block from the NMDA channel may take the form of a BP or dendritic spike.