



Calcium as the associative signal for a model of Hebbian plasticity: application to multi-input environments

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Abstract

The sign and magnitude of bi-directional synaptic plasticity have been shown to depend on: the rate of presynaptic stimulation, the level of postsynaptic depolarization, and the precise relative timing between pre- and postsynaptic spikes. It has been proposed that these different induction paradigms can coexist, and be accounted for by a single learning rule that depends on the dynamics of intracellular calcium concentration. We extend this rule to a multi-synaptic environment, where collective properties such as cooperativity, competition and selectivity can be investigated.

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1. Introduction

The intracellular ionic calcium concentration ($[Ca^{2+}]$) is known to act as a mediator of various cascades of metabolic activities in many cellular systems. In particular, it plays an important role in activity-driven synaptic changes. For example, different magnitudes and patterns of postsynaptic $[Ca^{2+}]$ can selectively induce long-term potentiation (LTP) or long-term depression (LTD) [2,8,11,19]. The functional dependence of plasticity on $[Ca^{2+}]$ has been described as U-shaped [6,7]: low levels of $[Ca^{2+}]$

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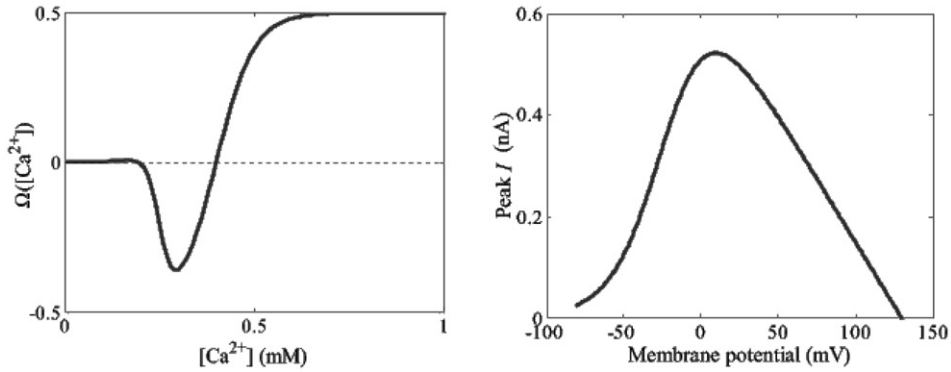


Fig. 1. Left: the shape of the learning rule. Right: the calcium current as a function of the postsynaptic potential.

induce no synaptic changes, while modest levels lead to LTD and higher ones, to LTP. The rise of $[Ca^{2+}]$ concentration depends on back-propagating action potentials (BPAPs) [9,13] in the postsynaptic cell; most interestingly, when these action potentials are paired with sub-threshold excitatory postsynaptic potentials (EPSPs), the dendritic $[Ca^{2+}]$ transient is substantially higher than the one produced by EPSPs or APs alone [12]. It is intuitive that this property should be related to the spike time-dependent type of plasticity (STDP) [3,14].

Experimental evidence, therefore, suggests a model of bi-directional synaptic plasticity that depends directly on the dynamics of $[Ca^{2+}]$. This more biophysical approach rids the model of ambiguities as to which aspects of the cellular activity (rate, depolarization or spike-timing) one should be consider in a learning rule. The model we have proposed, denoted *calcium control hypothesis* [15], describes this dependence as

$$\frac{dW_i}{dt} = \eta(Ca_i)(\Omega(Ca_i) - \lambda W_i), \quad (1)$$

where W_i is the weight of the synapse of index i , $Ca \equiv [Ca^{2+}]$, η is a calcium-dependent learning rate, Ω is a U-shaped difference of sigmoids (Fig. 1, left) and λ is the decay constant. Throughout the simulations below, $\lambda=0$, and stability is attained by the use on hard boundary conditions of W_i . These hard boundary conditions may not be necessary if metaplasticity (see Discussion) is included. We assume that the primary source of Ca influx into the spine is mediated by NMDA receptors, as described by the simple linear differential equation below

$$\frac{d(Ca_i)}{dt} = I_i(V, t) - \frac{Ca_i}{\tau_{Ca}}. \quad (2)$$

The temporal dependence of the NMDA current I describes the kinetics of the NMDA channels: it peaks at the arrival of a pre-spike and decays as a sum of two exponentials [5]. The voltage dependence is the standard function for the Mg^{2+} -block dynamics

(Fig. 1, right) [10]. Finally, V obeys the canonical non-leaking integrate-and-fire model. When a post-spike is elicited, a doubly exponential form of BPAP is added to V .

Eq. (1) has correctly reproduced the traditional experimental plasticity-inducing protocols in a one-dimensional input space [15]. Here, we extend this to a multidimensional environment. This allows us to examine receptive field formation and its significant biological implications.

2. Selection of correlated inputs

Selectivity is a general feature of many cortical neurons, and underlies the formation of receptive fields and topographic mappings. Therefore, a biologically plausible learning rule must be able to account for the formation of selective receptive fields. A simulated neuron is called *selective* to a specific input if it responds strongly to that input and weakly to others. We have chosen to induce selectivity in our simulated neuron by choosing different spatiotemporal structures for different groups of input neurons.

We use a neuron with 100 excitatory synapses, half of which receive Poisson spike-trains with correlated instantaneous rates with fixed mean $\bar{r} = 10$ Hz (group A), and the remaining receive uncorrelated input with the same \bar{r} (group B). The correlation function had the same magnitude across synapses of group A, but decays exponentially in time [18]:

$$\langle r_i(t)r_j(t') \rangle = \bar{r}^2 + \bar{r}^2(\sigma^2\delta_{ij} + (1 - \delta_{ij})c^2)e^{-|t-t'|/\tau_c} \quad \text{if } i, j \in A, \quad (3)$$

where c is the correlation coefficient and δ_{ij} is the Kronecker delta. In addition, this neuron receives 20 inhibitory uncorrelated Poisson inputs with the same \bar{r} .

After 100 s of simulated time, we observe that, for 10 Hz inputs, the synapses of group A are potentiated, while group B is depressed (Fig. 2, center). This indicates that spikes from the correlated group cooperatively elevate the calcium level above

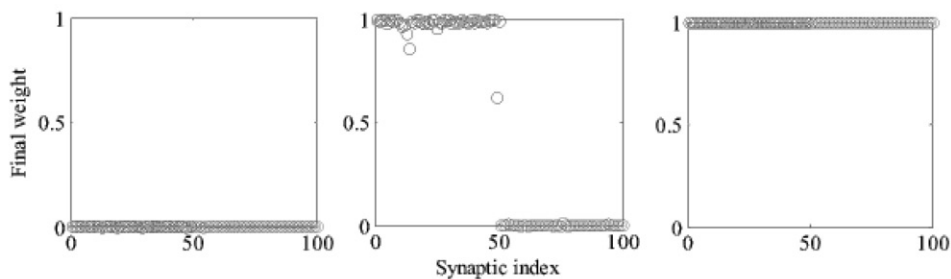


Fig. 2. Input selectivity at various stimulation frequencies: left, 8 Hz; middle, 10 Hz and right, 12 Hz. Group A (the righter half of each histogram) is the group with input correlation; group B (the lefter half of each histogram) is the group with no correlation.

the potentiating threshold, through spatial and temporal integration of local depolarizations. Furthermore, such depolarization increases the probability of causally eliciting a postsynaptic spike, which will associate with the presynaptic spike through the BPAP in a Hebbian manner. It was observed that, when segregation occurs, the postsynaptic spiking rate is stable, and has a high degree of variability (coefficient of variation ≈ 1 , not shown).

However, consistent with the rate-based and the rate-dependent STDP protocols [17], for low and high enough \bar{r} , all the synapses are depressed and potentiated, respectively.

3. Discussion

Both simulations [15] and biophysical analysis [16] lead us to a learning model of the form of Eq. (1). Our previous work, however, assumed a simplified, one-dimensional input space. In this paper, we show that this learning rule can give rise to selective receptive fields in a more realistic multidimensional input space. However, this selectivity is highly sensitive to the model parameters, and for low input rates all synapses are driven to their lower saturation limit, whereas for high input rates they are driven to their upper limit. Metaplasticity, the activity-dependent modification of the functional form of synaptic plasticity, has successfully added robustness in other systems, as described by the BCM theory [1,4]. We are currently developing the appropriate form of metaplasticity for the system we described.

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