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 bidirectional synaptic plasticity are determined by the rate of presynaptic stimulation, by the level of postsynaptic potential during pairing and by the precise relative timing between pre and postsynaptic spikes. It has been proposed that these mechanisms can coexist, with a novel learning rule, dependent on the dynamics of intracellular calcium concentration. We extend this rule to a multi-synaptic environment, where collective properties such as selectivity, cooperativity and competitivity can be investigated.

Keywords: synaptic plasticity, Hebbian learning, spike timing, calcium, NMDA.

Intracellular ionic calcium concentration ($[Ca^{2+}]_i$) has long been known to act as a cellular activity signal, mediating various cascades of metabolic activities. In particular, its role in the activity-driven synaptic changes has been observed experimentally. It has been shown, for example, that different magnitudes and patterns of postsynaptic $[Ca^{2+}]_i$, can selectively induce long-term potentiation (LTP) or long-term depression (LTD) ([8], [5], [16]). The functional dependence of plasticity on $[Ca^{2+}]_i$ has been described as U-shaped ([4], [3]): low levels of $[Ca^{2+}]_i$ induce no synaptic changes, while modest levels lead to LTD and higher ones, to LTP. The $[Ca^{2+}]_i$ rise has been shown to correlate with action-potentials (APs) propagating back into the dentrites ([10], [6]), and most interestingly, when such APs are paired with sub-threshold excitatory postsynaptic potentials (EPSPs), the dendritic $[Ca^{2+}]_i$ transient is substantially higher than the one produced by EPSPs or APs alone ([9]). It is easy to guess that this property will be related to the spike time-dependent type of plasticity (STDP) ([11], [2]).

Thus, evidence suggests a synaptic plasticity model that depends directly on the dynamics of $[Ca^{2+}]_i$, rather than on the neuronal activity that elicits it. The model we use, denoted *Calcium Control Hypothesis* [13], describes this dependence as:

$$\frac{dW_i}{dt} = \eta(ca_i)\left(\Omega(ca_i) - \lambda W_i\right) \tag{1}$$

where W_i is the i-th synaptic weight, $ca_i \equiv$ local $[Ca^{2+}]_i$, $\eta(ca_i)$ is a monotonically increasing calcium-dependent modification rate, Ω is a U-shaped difference of sigmoids and λ is the stabilizing decay. Throughout the simulations below, $\lambda = 0$, since we use hard boundary conditions on W. ca

inflow is NMDA-mediated:

$$\frac{d(ca_i)}{dt} = I_i^{\mathrm{NMDA}}(t) - \frac{ca_i}{\tau_{ca}} \tag{2}$$

where the NMDA current I^{NMDA} is a separable function of time and voltage V. The time-function peaks at the arrival of a pre-spike and decays exponentially with a long tail. For the V-function we use the standard model for the Mg^{2+}-block dynamics ([7]). Finally, $V = V_{rest}$+ EPSP - IPSP + BPAP. Upon arrival of a pre-spike in the excitatory [inhibitory] synapse, an α-like function of time is added to the EPSPs [IPSPs] (excitatory [inhibitory] postsynaptic potentials); when a post-spike is elicited, a doubly exponential form of BPAP (back-propagating action potential) is added to V. Note that only the EPSPs scale, linearly, with W.

Selectivity is a general feature of neurons and underlies the formation of receptive fields and topographic mappings. A simulated neuron is called *selective* to a specific input if it responds strongly to that input and weakly to others, or equivalently, if it has a facilitated pathway for it. A simple method of analyzing selectivity is to input stimuli with different structures to different groups of synapses, and compare their final states.

We use a neuron with 1000 excitatory synapses, half of which receive Poisson spike-trains with correlated instantaneous rates with fixed mean $\overline{r}_{in} = 10$ Hz (group A), and the remaining receive uncorrelated input with the same $\overline{r}_{in}$ (group B). The instantaneous rates were generated according to the method used by [15] such that the correlation function had the same magnitude across synapses of group A, but decays exponentially in time:

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

c is the correlation coefficient and δ_{ij} is the Kronecker delta. After 100 sec of simulated time at a mid-range average input frequencies ($\approx$ 10 Hz), the synapses of group A are potentiated, while group B is depressed (not shown). This is indicates that spikes that arrive synchronously elevate cooperatively the calcium level above the potentiating threshold through spatial integration of the EPSP. However, consistent with rate-based and rate-dependent STDP protocols ([14]), for low ($\approx$ 5 Hz) and high ($\approx$ 10 Hz) enough $\overline{r}_{in}$, all the synapses are depressed and potentiated, respectively.

Eq. 1 has correctly reproduced plasticity-inducing protocols as varied as rate, voltage and spike-time based methods ([13]) in a unidimensional input space. It has as well produced promising collective features of populations of synapses which are sensitive to the structure of the input environment. Preliminary results from studies of populational dynamics of AMPA receptors, including mechanisms of insertion/depletion and phosphorilation, also indicate the necessity of plasticity equations analogous to eq. 1 ([12]). 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]. We are currently developing the appropriate form of metaplasticity for the system we described.

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