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Learning with three factors: modulating Hebbian plasticity with errors

ukasz Kuśmierz, Takuya Isomura and Taro Toyoizumi

Synaptic plasticity is a central theme in neuroscience. A framework of three-factor learning rules provides a powerful abstraction, helping to navigate through the abundance of models of synaptic plasticity. It is well-known that the dopamine modulation of learning is related to reward, but theoretical models predict other functional roles of the modulatory third factor; it may encode errors for supervised learning, summary statistics of the population activity for unsupervised learning or attentional feedback. Specialized structures may be needed in order to generate and propagate third factors in the neural network.

Address
RIKEN Brain Science Institute, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan

Corresponding author: Toyoizumi, Taro (taro.toyoizumi@brain.riken.jp)

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Introduction

Associative (Hebbian) learning indicates association between two factors (two sensory inputs or an input and an output), but such a learning is often influenced by a so-called third factor. In a very general framework of three-factor learning, plasticity is realized by changing a synaptic strength w with the following rule

$$\dot{w} = F(pre, post, g, w), \tag{1}$$

where *pre* and *post* are some functions of histories of presynaptic and postsynaptic activities, g is a third factor modulating the plasticity (Figure 1), and $\dot{w}$ denotes the time derivative of the synaptic strength w. The third factor may represent, for example, rewards, supervised errors, summary statistics, or attentional feedback, which could be used to facilitate different types of learning by providing more global information about how well the whole network is performing or how important a current situation is. Often learning rules are written in a more specific form

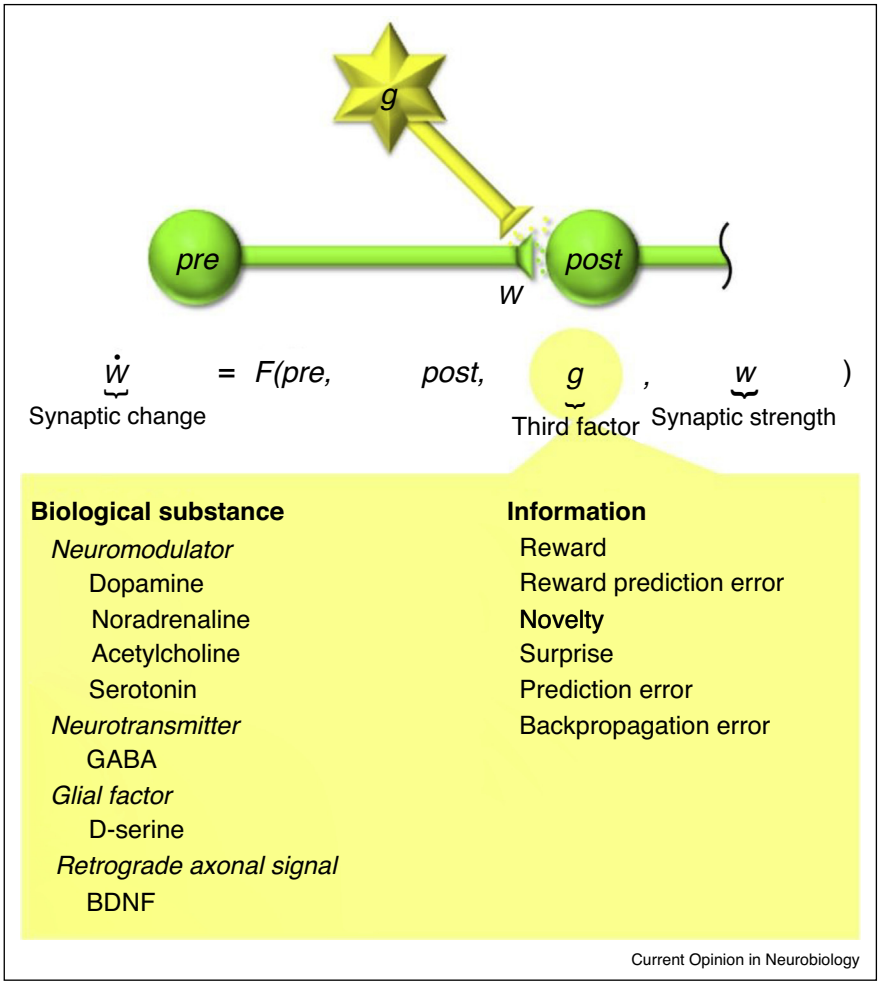
$$\dot{w} = gH(pre, post), \tag{2}$$

where H is a generalized Hebbian term, which includes some measure of correlation between presynaptic and postsynaptic activities. As a simple example, the classical Hebbian learning assumes a rate model of neurons, wherein the activities are described by real valued firing rates f_{pre} and f_{post}. The Hebbian plasticity term then simply involves a product of those firing rates ('fire together wire together').

In more detailed, biologically plausible models, the activity of each neuron is approximated by a point process, that is, it is fully determined by a set of times at which the neuron generated action potentials (spike train). When both *pre* and *post* are given by the spike trains of the corresponding neurons, the learning rule based on H(*pre*, *post*) is called spike-timing-dependent plasticity (STDP) [1,2]. In the simplest scenario STDP is described by pairwise interactions, that is, it depends only on the relative timing of pairs (*pre–post*) of individual spikes [3,4]. Function H(*pre*, *post*) can be in this case determined by the learning window (also STDP function), that is, one dimensional function of the relative time between presynaptic and postsynaptic spikes. In the standard STDP, long-term potentiation (LTP, the connection is strengthened) is observed if the presynaptic spike precedes (in some short time window) the postsynaptic spike (pre-before-post), whereas long-term depression (LTD, the connection is weakened) is observed if the postsynaptic spike precedes the presynaptic spike (post-before-pre). This temporally asymmetric STDP is an extension of the original Hebb's postulate and in some limits simplifies to the classical Hebbian term ($f_{pre} f_{post}$). Note that Equation 2 can describe more complicated STDP rules that may involve more than two spikes [5] or more biophysical calcium-based plasticity rules if the calcium concentration is primarily determined by the presynaptic and postsynaptic activity [6,7].

A possible biological implementation of the three-factor learning is provided by neuromodulators. Multiple *in vitro* experimental studies have shown that neuromodulators modulate Hebbian plasticity in various ways. In hippocampus, the activation of the D_1 subunit dopamine receptor reverses LTD to LTP and extends the LTP

Figure 1



A schematic image of modulations of Hebbian plasticity by third factors.

part of the STDP time window [8], leading to temporally symmetric STDP function (LTP for both pre-before-post and post-before-pre). In contrast, the activation of the α subunit adrenaline receptor reverses LTP to LTD [9]. In addition, modulations of synaptic plasticity occur with various neuromodulators, including dopamine [10], noradrenaline [11], acetylcholine [12], and serotonin (5-HT) during the developmental stage [13]. Another biological mechanism that can implement the three-factor learning is inhibition. Recently, it was reported that GABAergic inhibition directly suppresses local dendritic Ca^{2+} signaling and promotes spine shrinkage and elimination of hippocampal dendritic spines [14], and such suppression of dendritic Ca^{2+} is sensitive to precise timing (<5 ms) of inhibitory input [15]. In corticostriatal synapses, with intact physiological GABAergic transmission, the pre-before-post stimulation induces LTD, while the post-before-pre stimulation induces LTP [16]. However, blockade of $GABA_A$-receptors converts LTD into LTP, and vice versa [17]. In addition, glial cells may also modulate and coordinate Hebbian plasticity [18].

In this manner, the third factor modulates the original associative learning in various ways, which must play roles in different brain functions. Note that the multiplicative relationship between the third factor and the Hebbian term in Equation 2 is a useful mathematical simplification. The biological third factors described above can, in addition, directly modulate the presynaptic or postsynaptic activities. In the rest of the paper we list some of the hypothetical roles of the third factor proposed in the theoretical literature, as well as possible computational mechanisms of their generation and propagation. Although many of these functions were proposed based on theoretical considerations, the underlying algorithms