Competition and timescale separation in calcium-based plasticity

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Among existing formulations, the calcium-based model of early long-term plasticity introduced by Graupner and Brunel in 2012 [1] is still widely used [2], [3] and serves as a foundational reference for describing synaptic potentiation and depression. However, the model exhibits limitations such as abrupt changes, slow drift toward extreme potentiation or depression in the absence of calcium, and instantaneous molecular signaling from calcium concentration to synaptic changes, thus neglecting timescale separation and competing signaling mechanisms between potentiation and depression. Building on this seminal work, we propose a minimal and general framework for the signaling pathways underlying synaptic changes, which addresses the issues of the original model. Consistent with Graupner and Brunel's philosophy, our approach avoids committing to specific physiological mechanisms, which is advantageous given their substantial variability across brain regions and cell types. By introducing timescales for potentiation and depression pathways, our model strengthens the robustness and memory dependence of synaptic modification, and shares similarity with the sliding threshold model of Bienenstock, Cooper and Munro [4]. Greater timescale separation shifts the Spike-Timing-Dependent Plasticity (STDP) kernel upward, allowing us to set a much higher potentiation threshold than in previous studies. Conversely, increased competition lowers the STPD kernel in regimes where the timescale separation is not too strong. Our formulation improves both the biological plausibility and stability of the synaptic model, while offering a flexible framework for future extensions, e.g. adding pathways with distinct timescales to capture short-term and late long-term plasticity within a unified model.

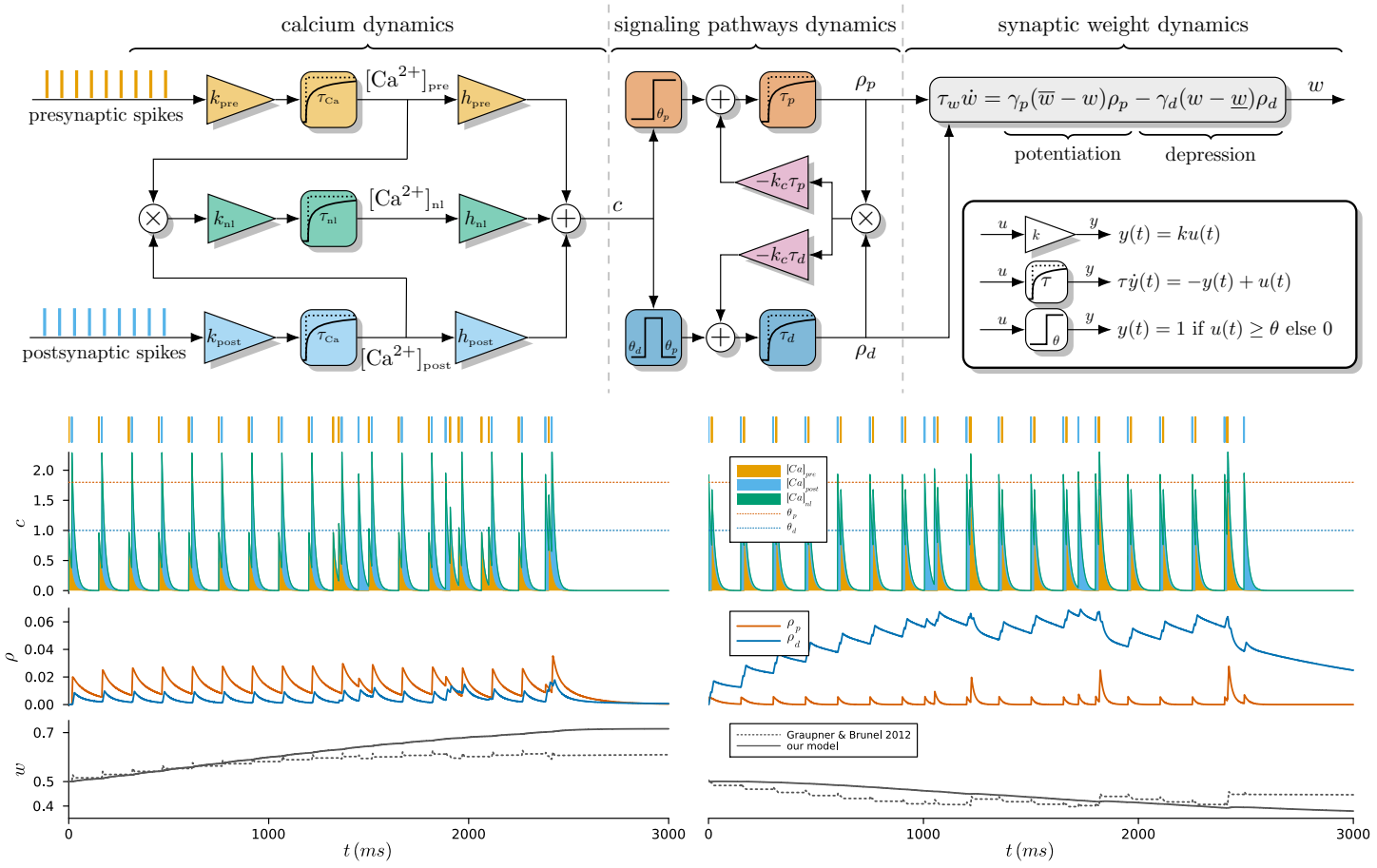

Fig. 1: **Top**: Block diagram of the spike-driven and calcium-based model of synaptic weight changes. The signaling pathways (in the center) represent the main contribution of this work. It incorporates distinct timescales for potentiation (fast τ_p) and depression (slow τ_d), and features a competitive mechanism (the negative feedback in purple) that reduces one pathway's activity when the other is active. **Bottom**: Temporal dynamics of c, ρ_p, ρ_d, and w in response to a noisy potentiation (left) and depression (right) stimulation protocol. The stimulation protocol consists of pre-synaptic (in yellow) and post-synaptic (in light blue) spike pairs with $\Delta T = \pm 15$ms repeated every 150ms over 2.5s. 6 random spikes are triggered between 1s and 2.5s. The synapse is simulated with $k_{\text{pre}} = 1, k_{\text{post}} = 2, k_{\text{nl}} = 0.01, \tau_{\text{Ca}} = \tau_{\text{nl}} = 15, h_{\text{pre}} = h_{\text{post}} = h_{\text{nl}} = 1, \theta_d = 1, \theta_p = 1.8, \tau_p = 200, \tau_d = 1000, k_c = 1, \tau_w = 5000, \gamma_p = 85, \gamma_d = 13, \overline{w} = 1, \underline{w} = 0, w^* = 0.5$.

Graupner and Brunel's model. The original model consists of a differential equation which links an aggregated calcium concentration at the synapse c to changes in the synapse's capacity to transmit electrical information, quantified by a synaptic weight w.

$$\tau_w \dot{w} = \gamma_p(\overline{w} - w)\Theta(c - \theta_p) - \gamma_d(w - \underline{w})\Theta(c - \theta_d) + (\overline{w} - w)(w - \underline{w})(w - w^*) \tag{1}$$

τ_w is the plasticity timescale; γ_p and γ_d are the potentiation and depression rate of the synapse; $\overline{w}$, $\underline{w}$ represent the maximum and minimum synaptic weight, and w^* delimits their basins of attraction; finally Θ is a threshold function ($\Theta(c-\theta) = 1$ if $c \geq \theta$, and $\Theta(c-\theta) = 0$ otherwise) with θ_p, θ_d the potentiation and depression thresholds.

Our Model. We introduce two activity variables, ρ_p and ρ_d, which represent the activity level of the signaling pathway for early long-term potentiation and depression respectively. Both pathways are driven by the aggregated calcium concentration c. The change of synaptic weight is then governed by ρ_p and ρ_d rather than by c.

$$\tau_p \dot{\rho}_p = -\rho_p \; -k_c \tau_p \rho_p \rho_d \; +\Theta(c - \theta_p) \tag{2a}$$

$$\tau_d \dot{\rho}_d = -\rho_d \; -k_c \tau_d \rho_p \rho_d \; +\Theta(c - \theta_d)\Theta(\theta_p - c) \tag{2b}$$

$$\tau_w \dot{w} = \gamma_p(\overline{w} - w)\rho_p - \gamma_d(w - \underline{w})\rho_d \tag{2c}$$

Contrary to (1), the pathways of potentiation and depression now have their own respective timescale, τ_p and τ_d, with typically $\tau_d > \tau_p$; in (2b), the depression pathway is triggered if $c \in [\theta_d, \theta_p]$ rather than if $c > \theta_d$; finally, a dynamical competition mechanism between the potentiation and depression pathways is incorporated (in purple) with a gain k_c. Consistent with recent literature [2], [3], the nonlinear term in (1) is removed in (2c). The block diagram of the full model is reported at the top of Fig. 1.

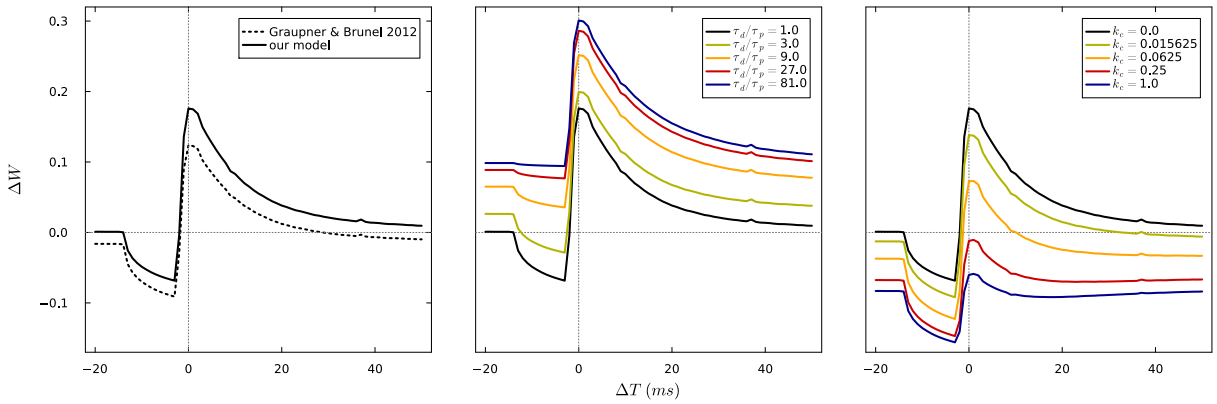

Fig. 2: STDP kernels showing synaptic weight change $\Delta W = w(1000\text{ms}) - w(0\text{ms})$ induced by pre–post spike pairs with interval ΔT, repeated every 150ms over 750ms. **Left**: the synapse is simulated with $k_{\text{pre}} = 1, k_{\text{post}} = 2, k_{\text{nl}} = 0.05, \tau_{\text{Ca}} = \tau_{\text{nl}} = 20, h_{\text{pre}} = 0, h_{\text{post}} = h_{\text{nl}} = 1, \theta_d = 1, \theta_p = 1.8, \tau_p = \tau_d = 200, k_c = 0, \tau_w = 5000, \gamma_p = 150, \gamma_d = 20, \overline{w} = 1, \underline{w} = 0, w(0) = w^* = 0.5$. **Middle**: increasing the depression timescale τ_d. **Right**: increasing the competition gain k_c.

Findings. Our proposed model (2) produces smoother synaptic weight dynamics and removes the sporadic abrupt transitions between potentiation and depression which occurred with (1). As synaptic changes accumulate during prolonged potentiation and depression protocols, the enhanced dependence on past synaptic activity in (2) compared to (1) reduces sensitivity to noise and diminishes the efficacy of subsequent changes if they oppose the prior ones. These findings are illustrated at the bottom of Fig. 1. The STDP kernels of (1) can be readily recovered; however, because (2b) does not induce depression above the θ_p threshold, our STDP kernel lies slightly above that of (1). Increasing k_c favors depression while increasing τ_d favors potentiation, enabling STDP tuning without altering the thresholds θ_d and θ_p, so θ_p remains sufficiently larger than θ_d. These findings are illustrated in Fig. 2.

References

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