Competition and timescale separation in calcium-based plasticity

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Graupner and Brunel's Model

The calcium-based model *Graupner et al. 2012* is a foundational reference for synaptic plasticity. The original formulation links calcium c directly to the synaptic weight w:

$$\tau_w \dot{w} = \gamma_p(\overline{w} - w)\Theta(c - \theta_p) - \gamma_d(w - \underline{w})\Theta(c - \theta_d)$$

- τ_w is the plasticity timescale;
- γ_p, $\overline{w}$ and θ_p are the gain, the maximum synaptic weight, and the threshold for **potentiation**;
- γ_d, $\underline{w}$ and θ_d are the gain, the minimum synaptic weight, and the threshold for **depression**.

Limitations:

- **No timescale separation**: Instantaneous molecular signaling from calcium concentration to synaptic weight;
- **Lack of memory dependence**: Blind to past synaptic activity after calcium has decayed;
- **Lack of noise robustness**: A single spike can trigger potentiation or depression;
- **Difficulty with data fitting**: Potentiation and depression thresholds are typically very close to each other (*Chindemi et al. 2022*).

Our Model: Signaling Pathways

We introduce activity variables ρ_p and ρ_d to represent **signaling pathway kinetics** driven by calcium concentration c:

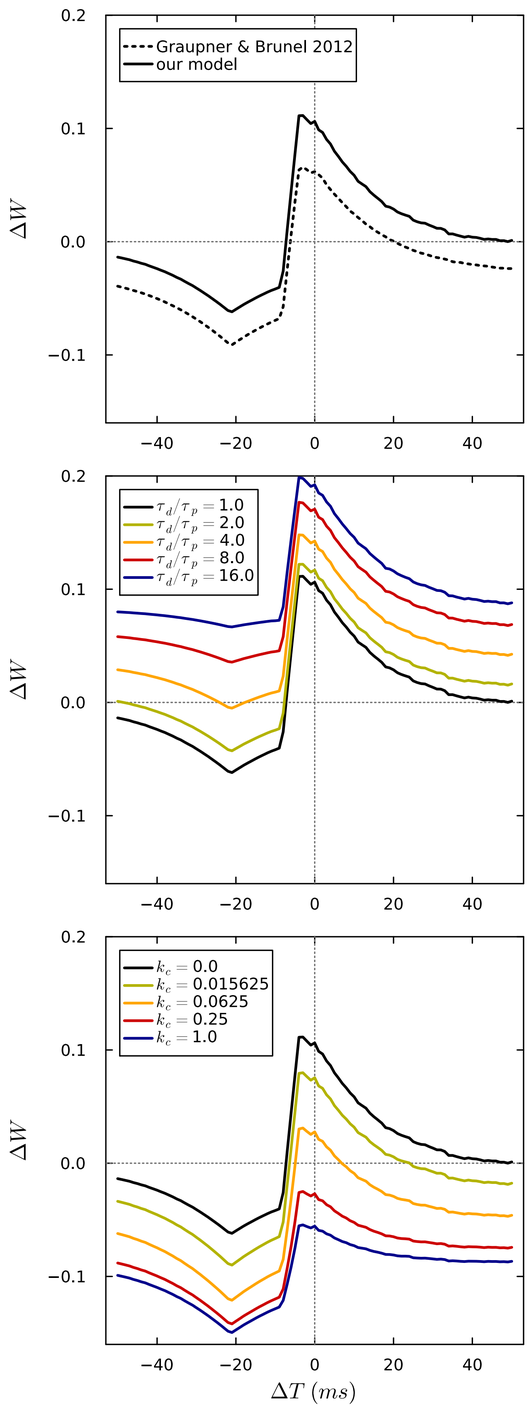
$$\tau_p \dot{\rho}_p = -\rho_p - k_c \tau_p \rho_p \rho_d + \Theta(c - \theta_p)$$
$$\tau_d \dot{\rho}_d = -\rho_d - k_c \tau_d \rho_p \rho_d + \Theta(c - \theta_d)\Theta(\theta_p - c)$$
$$\tau_w \dot{w} = \gamma_p(\overline{w} - w)\rho_p - \gamma_d(w - \underline{w})\rho_d$$

Innovations:

- **Potentiation Pathway:** Fast signaling timescale τ_p, active only for $c \geq \theta_p$;
- **Depression Pathway:** Slow signaling timescale τ_d, active only for $c \in [\theta_d, \theta_p]$;
- **Competition Mechanism:** Incorporates a dynamical **negative feedback** of gain k_c between the two signaling pathways.

Our approach **strengthens robustness** and the **memory dependence** of synaptic modification, similar to the BCM sliding threshold model of *Bienenstock et al. 1982*.

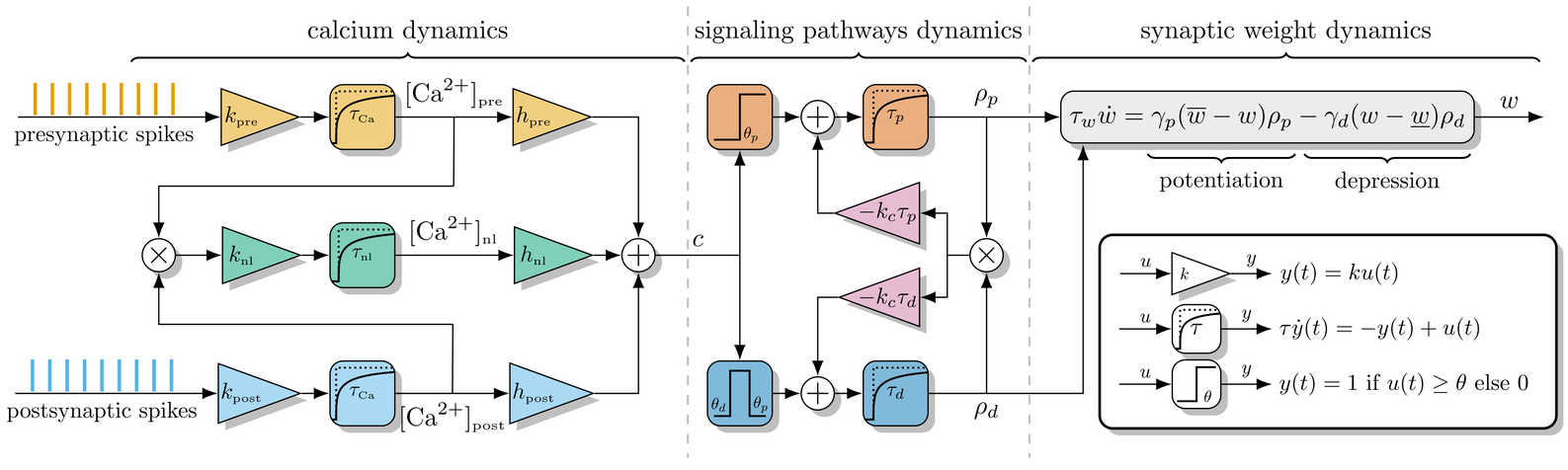
STDP Kernel Modulation



- **Top:** Baseline with zero competition and timescale separation;
- **Middle:** Increased timescale separation favors **potentiation**;
- **Bottom:** Increased competition favors **depression**.

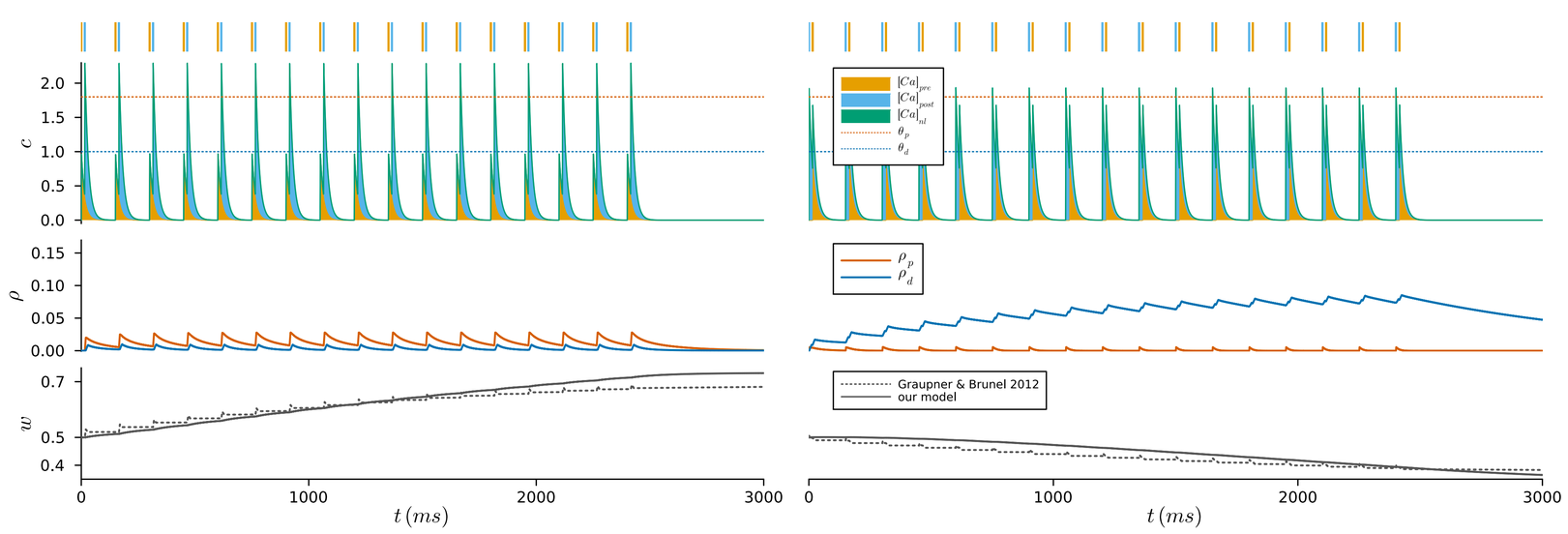
Tuning is achieved without modifying the **calcium thresholds**!

Architecture



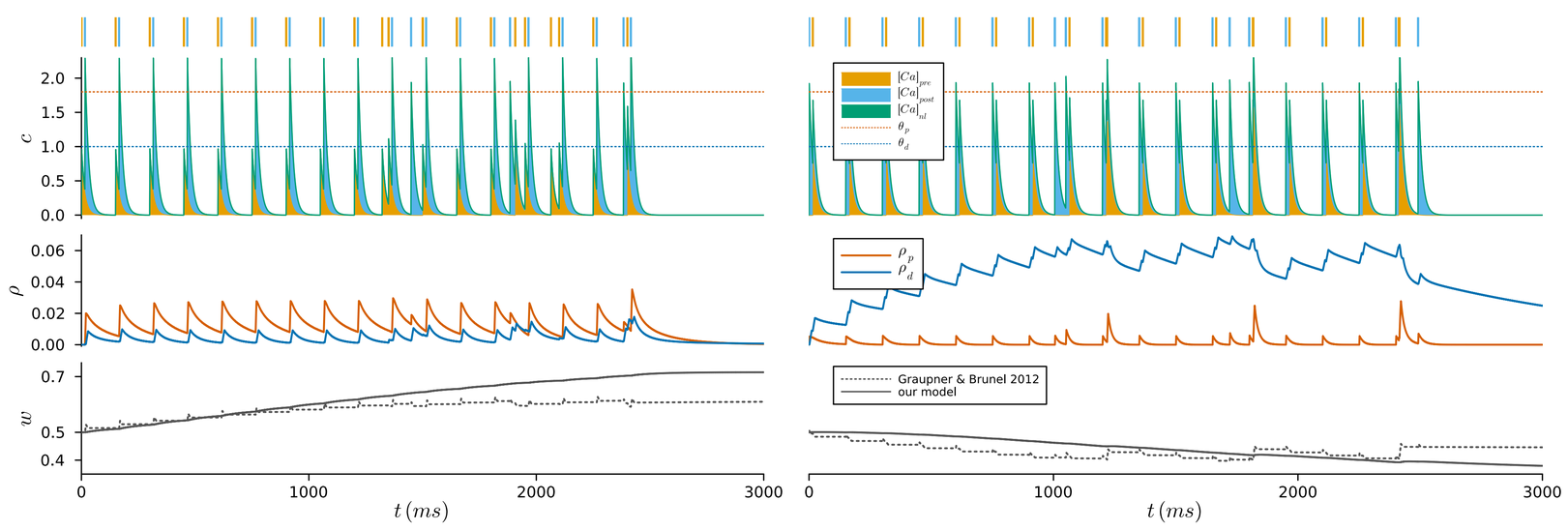
- The **calcium dynamics** low-pass filter **pre-synaptic** and **post-synaptic** spikes and their **coincidence** before combining them through a weighted sum. In contrast, *Graupner et al. 2012* first sums the spikes and then applies a single low-pass filter.
- The **signaling dynamics** integrate **potentiation** and **depression** pathways with distinct timescales. A **competitive mechanism** ensures nonlinear mutual suppression, leading to more stable weight dynamics where one pathway dominates the other. This part of the model is our main contribution; it is absent from *Graupner et al. 2012*.
- The **synaptic weight dynamics** combines the activity of the potentiation and the depression pathways following the saturating model of *Graupner et al. 2012*.

Model Response to Potentiation and Depression Protocols



Our pathways activity variables ρ_p and ρ_d act as **integrators**. This ensures only **consistent stimulation** triggers changes, while **isolated noise spikes** have a much weaker influence. This is consistent with recent experimental findings *Inglebert et al. 2020*.

Model Response to Noisy Potentiation and Depression Protocols



Adding random spikes disrupts *Graupner et al. 2012*'s model. However, the stronger dependence on **past synaptic activity** of our model reduces **noise sensitivity** and weakens subsequent changes that oppose earlier ones.

Conclusions and perspectives

Our proposed model produces smoother synaptic weight dynamics and removes the sporadic abrupt transitions between potentiation and depression which occurred with *Graupner et al. 2012*. As synaptic changes accumulate during prolonged potentiation and depression protocols, the enhanced dependence on past synaptic activity reduces sensitivity to noise and diminishes the efficacy of subsequent changes if they oppose the prior ones. The STDP kernels of *Graupner et al. 2012* can be reproduced. Increasing competition favors depression while increasing timescale separation favors potentiation, enabling STDP tuning without altering the thresholds θ_d and θ_p, so they remain well-separated.

Perspectives

Our formulation improves both the biological plausibility and the stability of the synaptic model, while providing a flexible framework for future extensions. For example, additional pathways with distinct timescales could be incorporated to capture both short-term and late long-term plasticity within a unified model. This framework remains to be experimentally validated and evaluated on larger neuronal networks.

References

Bienenstock, EL et al. (Jan. 1982). "Theory for the development of neuron selectivity: orientation specificity and binocular interaction in visual cortex". In: *The Journal of Neuroscience* 2.1, pp. 32–48.

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