



Input Selectivity of Spiking Neurons:

Metaplasticity in a Unified Calcium- Dependent Learning Model

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Abstract

A unified, biophysically motivated calcium-dependent learning rule has been shown to account for various rate-based and spike time-dependent paradigms for inducing synaptic plasticity. Here, we investigate the properties of this model in a multi-synapse neuron that receives inputs with different spike-train statistics. In addition, we present a physiological form of metaplasticity, an activity-driven regulation mechanism, which is essential for the robustness of the model. A neuron thus implemented will be stable and develop spontaneous input selectivity.

The Unified Calcium Model

- The local $[Ca_i^{2+}]$ is the associative signal for Hebbian learning (Bear *et al.*, Science, 1987; Lisman, PNAS, 1989, Shouval *et al.*, PNAS, 2002):

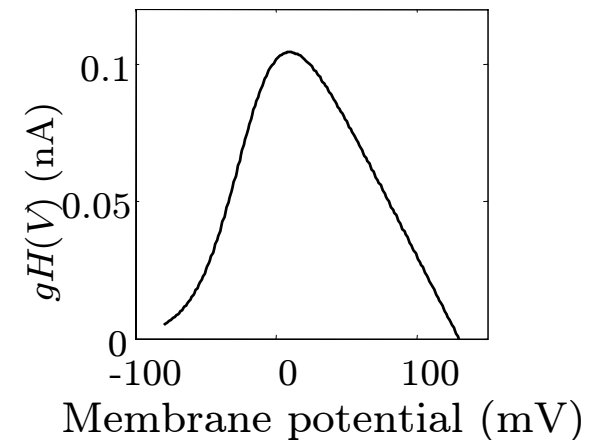
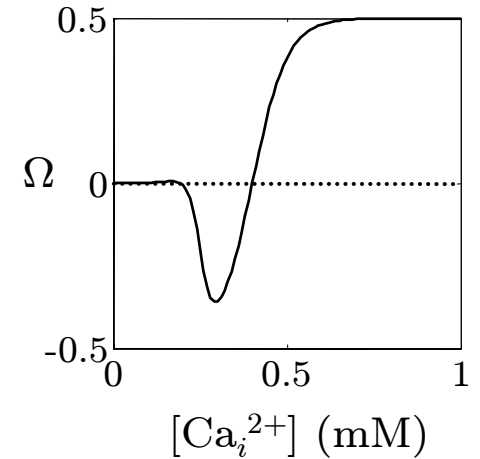
$$\dot{w}_i = \eta([Ca_i^{2+}]) \left[\Omega([Ca_i^{2+}]) - \lambda w_i \right] \quad (1)$$

- NMDA channels are the relevant sources of $[Ca_i^{2+}]$:

$$\frac{d[Ca_i^{2+}]}{dt} = I_i^{NMDA} - \frac{1}{\tau} [Ca_i^{2+}] \quad (2)$$

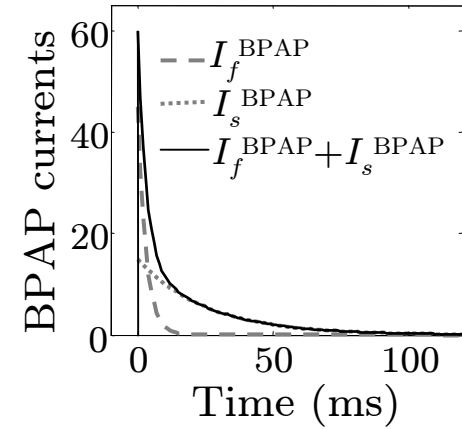
$$I_i^{NMDA} = gf(t)H(V) \quad (3)$$

$$f(t) = I_f^{NMDA} \exp\left(-\frac{t - t_{pre}}{\tau_f^{NMDA}}\right) + I_s^{NMDA} \exp\left(-\frac{t - t_{pre}}{\tau_s^{NMDA}}\right)$$



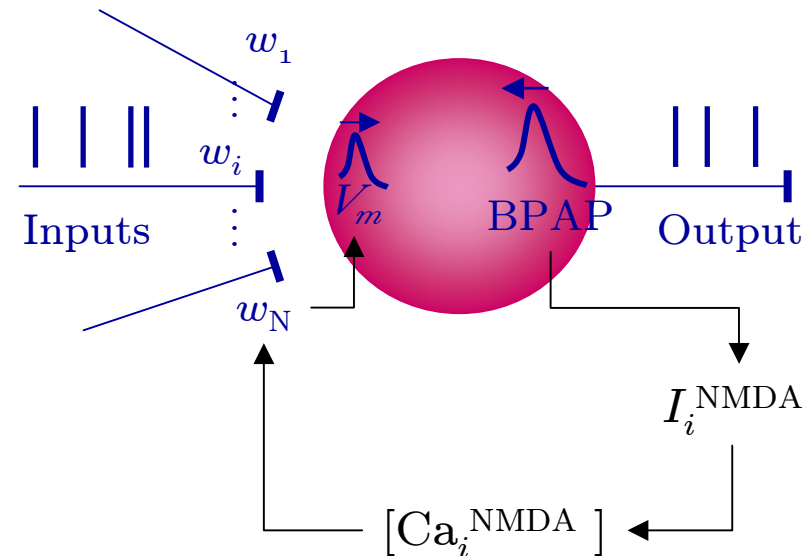
- The Back-Propagating Action Potential has a fast and a slow time constants (Magee & Johnston, Science, 1997):

$$\text{BPAP}(t) = A_{bk} \left[I_f^{\text{BPAP}} \exp\left(-\frac{t - t_{post}}{\tau_f^{\text{BPAP}}}\right) + I_s^{\text{BPAP}} \exp\left(-\frac{t - t_{post}}{\tau_s^{\text{BPAP}}}\right) \right] \quad (4)$$



- Integrate-and-Fire neuron:

$$\tau_m \frac{dV_m}{dt} = V_{rest} - V_m + g_{exc}(t)(V_{exc} - V_m) + g_{inh}(t)(V_{inh} - V_m) \quad (5)$$



Plasticity-Induction Protocols

- Standard Experimental Approaches:

Rate-based protocols (Bliss & Collingridge, Nature, 1993):

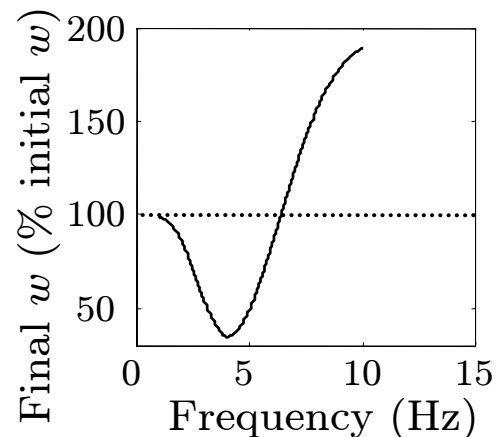
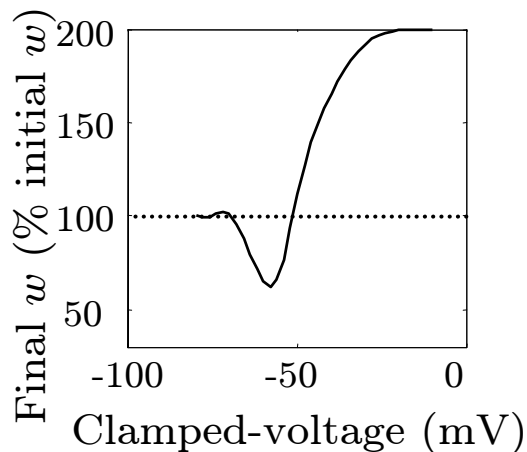
$$\begin{cases} \text{LFS} \Rightarrow \text{LTD} \\ \text{HFS} \Rightarrow \text{LTP} \end{cases}$$

Pairing protocol (Feldman *et al.*, Neuron, 1998):

LFS paired with

$$\begin{cases} \text{weak v-clamp} \Rightarrow \text{LTD} \\ \text{strong v-clamp} \Rightarrow \text{LTP} \end{cases}$$

- 1-D Simulation with the Unified Calcium Model (UCM):

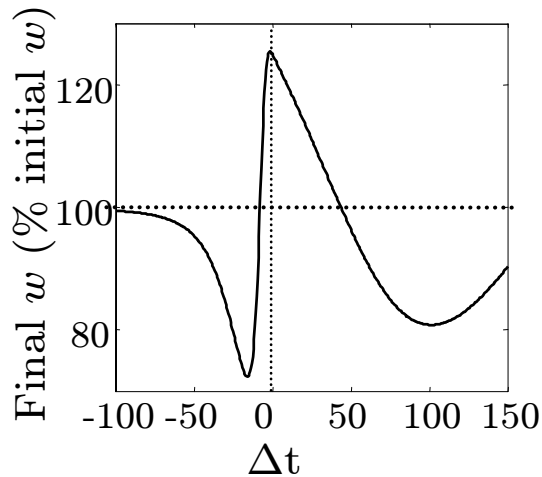


- Standard Experimental Approaches:
(cont.)

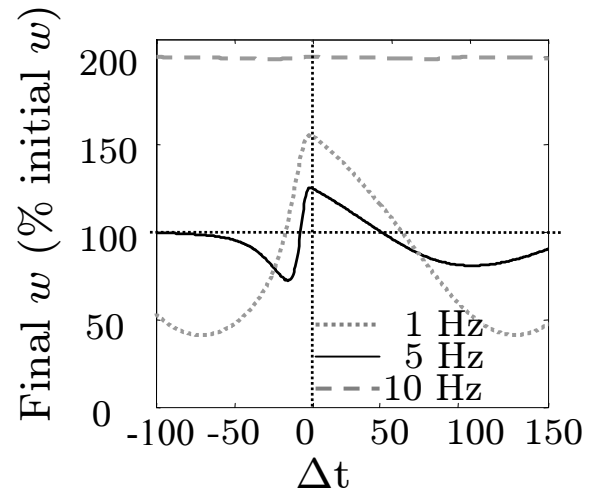
Spike Time-Dependent Plasticity (Markram *et al.*, Science, 1997;
Bi & Poo, Science, 1997):

$$\begin{cases} \Delta t < 0 \Rightarrow \text{LTD} \\ \Delta t > 0 \Rightarrow \text{LTP}, \quad \Delta t = t_{\text{post}} - t_{\text{pre}} \end{cases}$$

- 1-D Simulation with the UCM:
new predictions



New pre-before
-post region



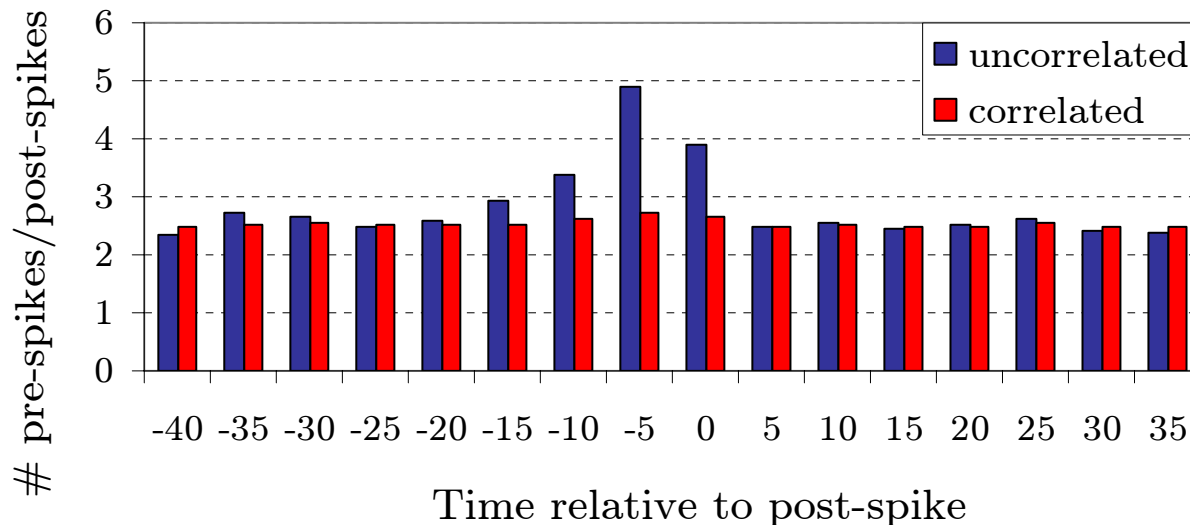
Rate-dependent
STDP window

Spike-Train Correlation

- Input environment: 100 excitatory and 20 inhibitory synaptic connections.

Synapses 1 through 50: Correlated Poisson spike train with mean rate r (see methods).

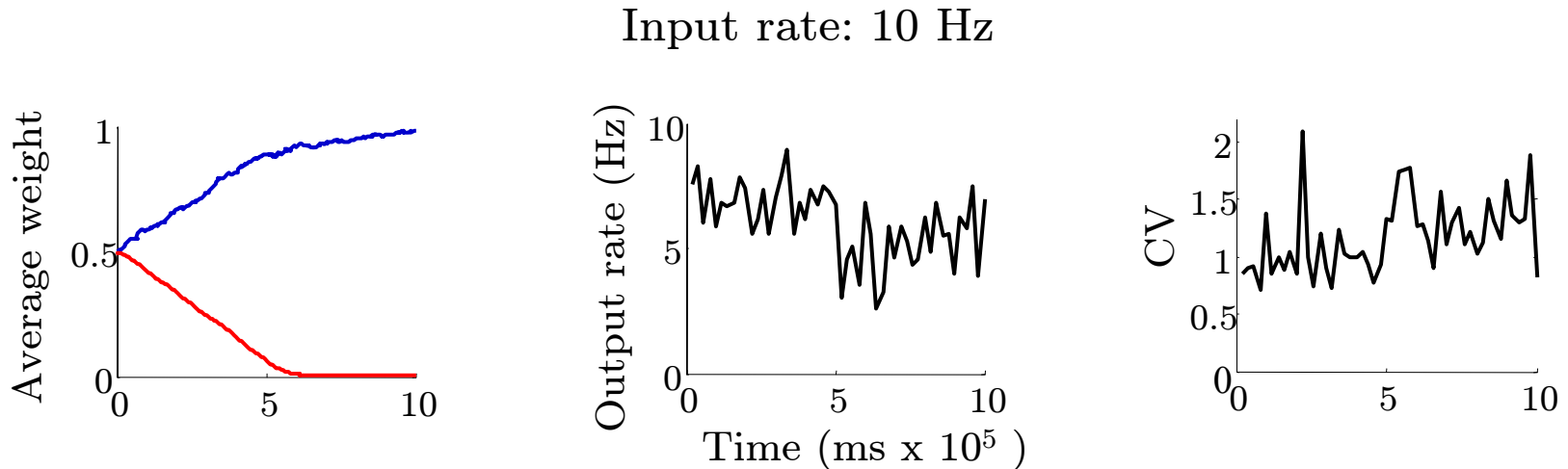
Synapses 51 through 100: Uncorrelated Poisson spike train with same mean rate.



- There are more pre-spikes arriving before a post-spike in the correlated group.

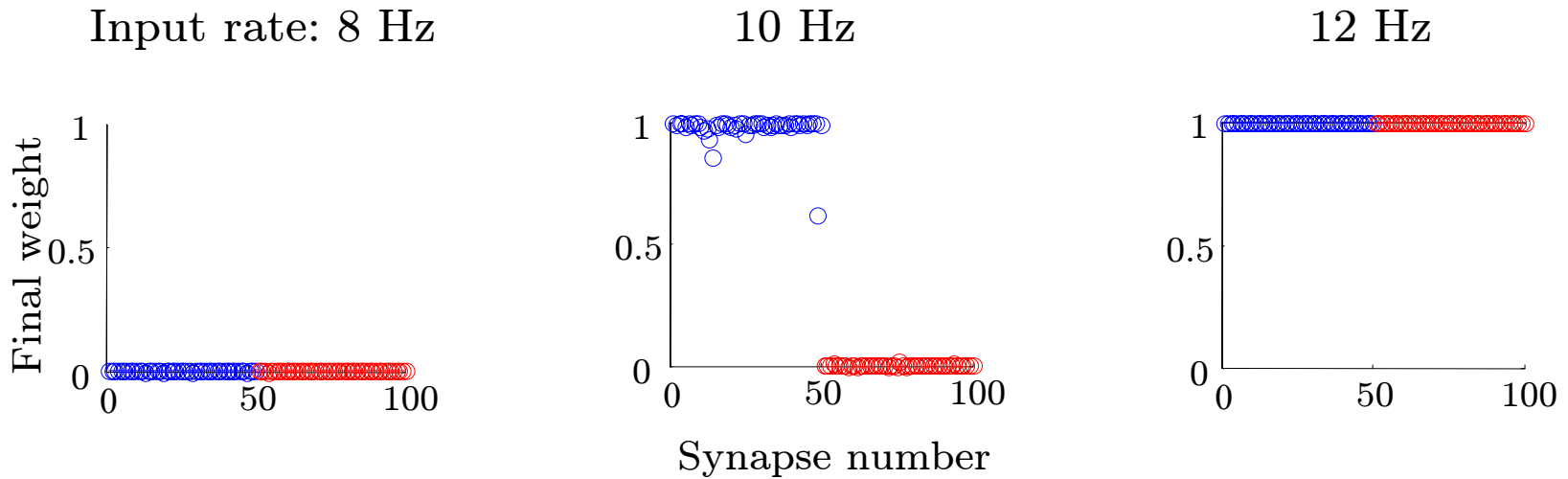
- Pre-before-post generates higher calcium influx (see slide 4).

- RESULTS:



- The system selectively potentiates the synapses that received correlated inputs while depressing synapses receiving uncorrelated ones, in agreement with previous results from additive STDP learning rules (Song *et al.*, Nature Neurosci., 2000).
- As in linear STDP rules, this model requires upper and lower saturation limits to ensure stability.
- When segregation occurs, the output rate is stable and the output spike train is highly variable.

- The segregation is due to collaborative firing of the correlated group and temporal competition between the two groups; and depends on the balance between the NMDA and the non-NMDA (scaled by w_i) conductances.

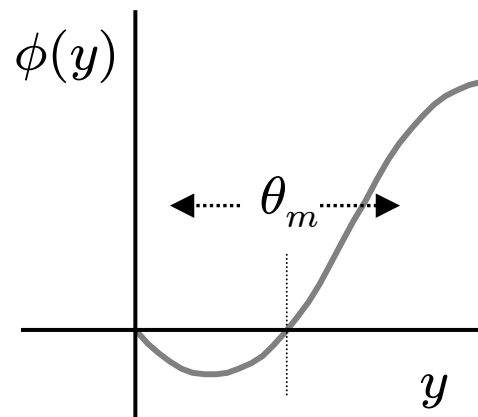


- However, the results are very sensitive to simulation parameters.

Metaplasticity

Metaplasticity is the activity-dependent modulation of synaptic plasticity. Different forms of metaplasticity can stabilize Hebbian learning in the absence of hard boundaries on the synaptic weights.

- In BCM theory: it has been shown that metaplasticity is necessary for robustness and introduces temporal competition into a learning system (Bienenstock *et al.*, J. Neuroscience, 1982).

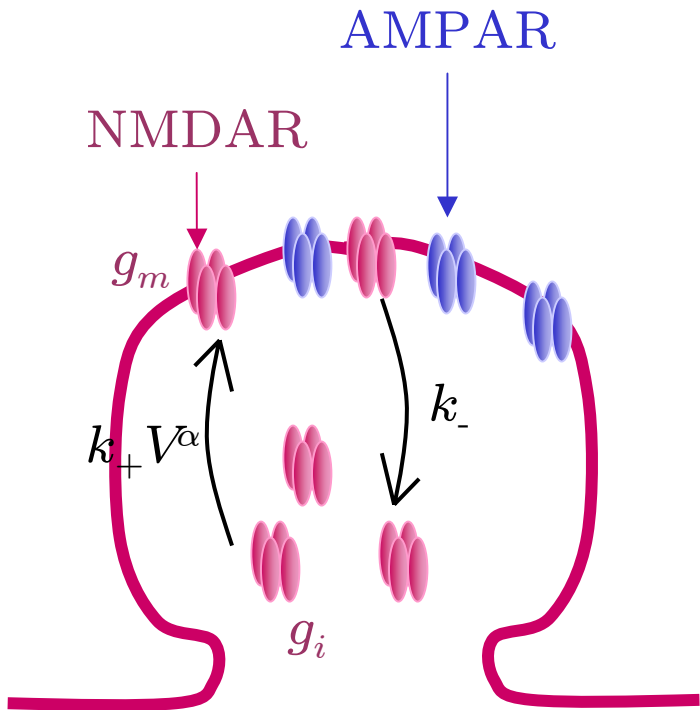


$$\begin{aligned} \dot{\vec{w}} &= \phi(y, \theta_m) \vec{x} \\ \theta_m &= \langle y^2 \rangle_t \end{aligned}$$

(6), where:

$$\begin{cases} \vec{x} = \text{input vector} \\ y = \text{output} \\ \theta_m = \text{threshold between LTP and LTD} \end{cases}$$

- Physiological formulation: insertion and removal of NMDA channels to and from the membrane (Carmignoto & Vicini, Science, 1992; Watt *et al.*, Neuron, 2000; Shouval *et al.*, Biol. Cybern., 2002).



- Kinetics depends on post-synaptic voltage to the α th-order.

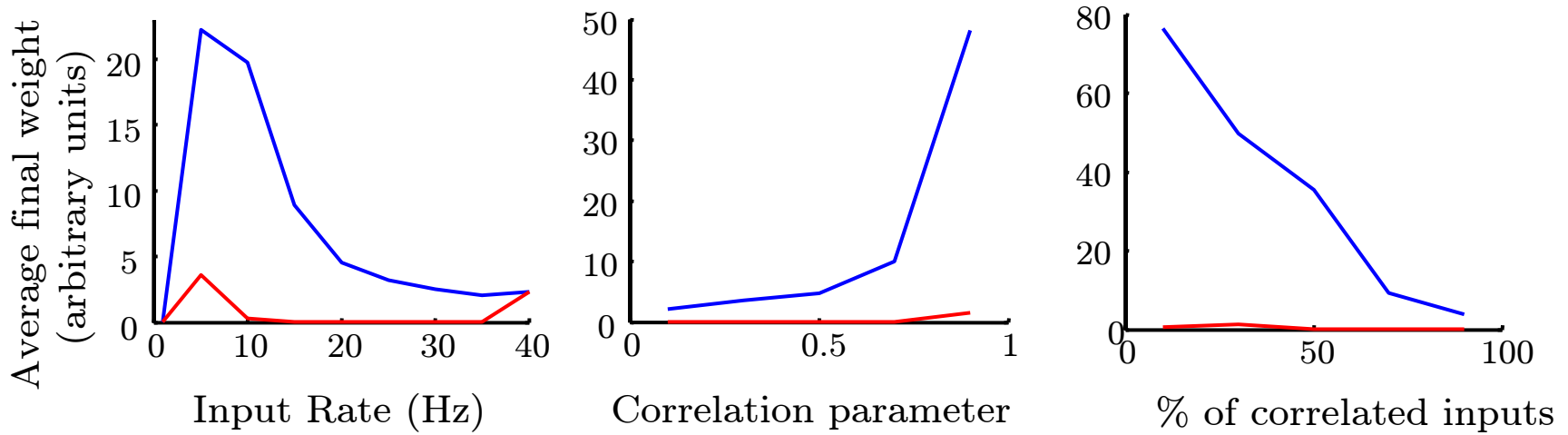
- Fixed point:

$$g_m \xrightarrow{\tau_m} \frac{g_t}{1 + \frac{k_-}{k_+ V^\alpha}}$$

(7), where

$$\begin{cases} g_t = g_m + g_i \\ \tau_m = \frac{1}{k_- + k_+ V^\alpha} \end{cases}$$

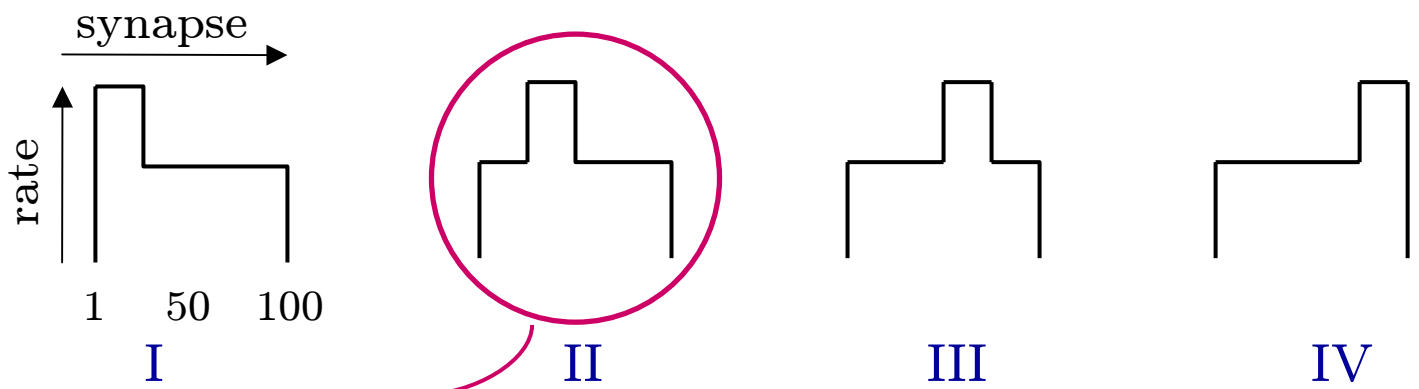
• RESULTS:



- Metaplasticity significantly widens the range of parameters for stable selectivity.
- Strengthening the correlation increases segregation, suggesting that cooperativity enhances potentiation, as shown before (slide 7).
- Increasing the fraction of correlated inputs weakens the final weight of the correlated group, suggesting that less potentiation is needed to control the output spike-timing.
- In the presence of metaplasticity, no upper saturation limit is required.

Patterns of Rate Distribution

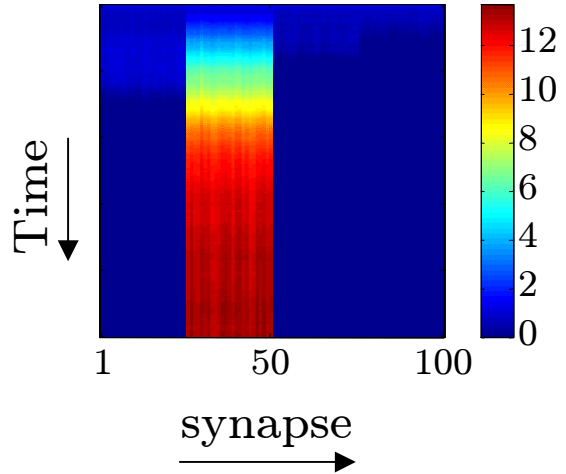
- Input environment: 4 square patterns



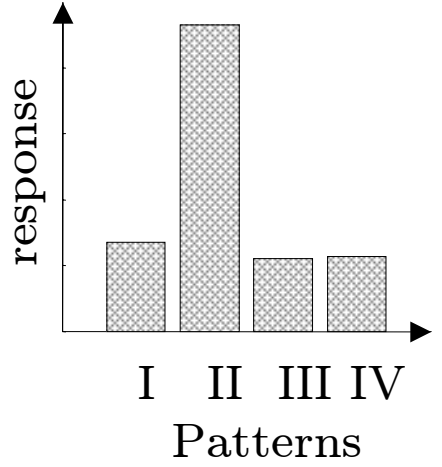
Input Patterns

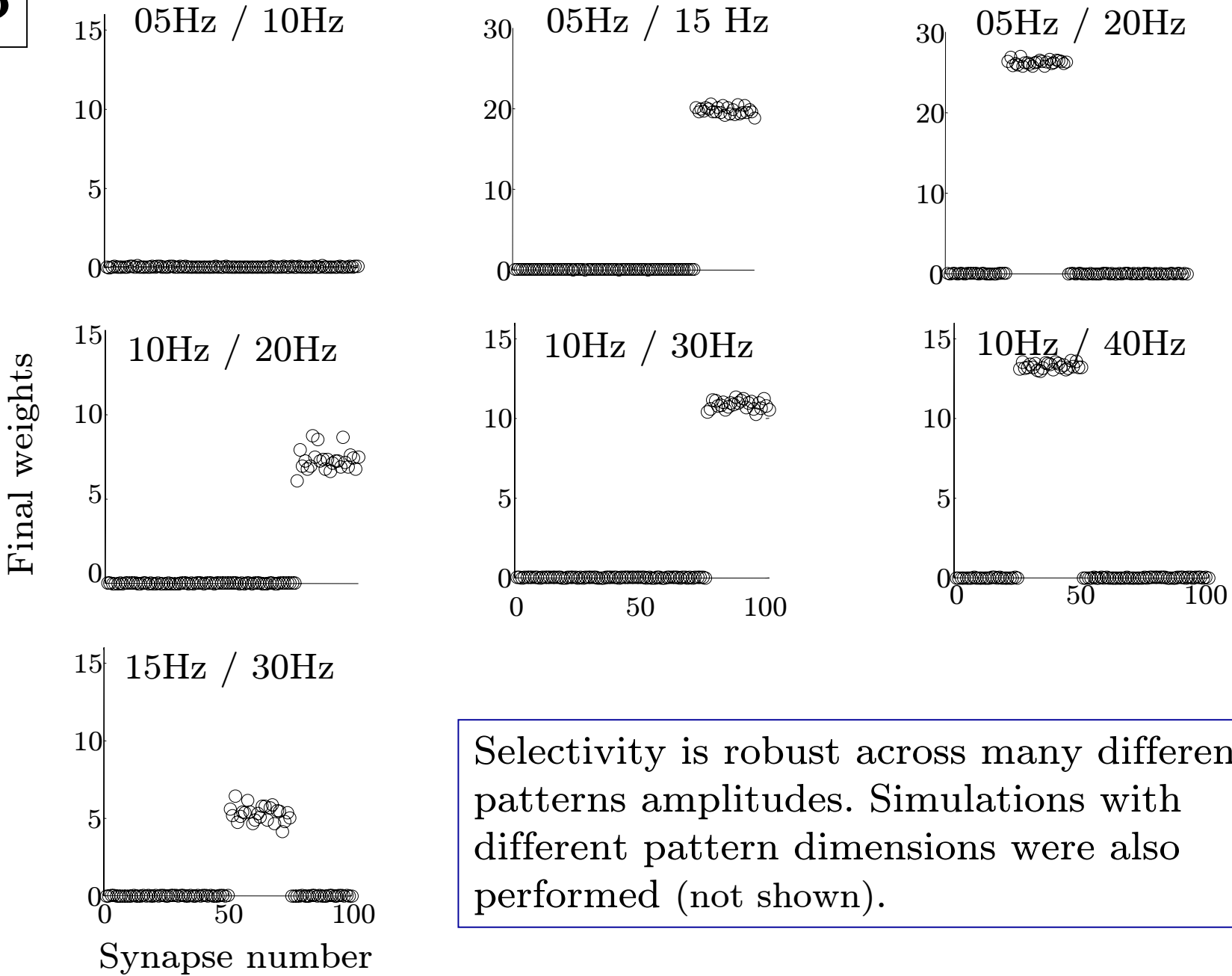
selective

Synaptic weight evolution



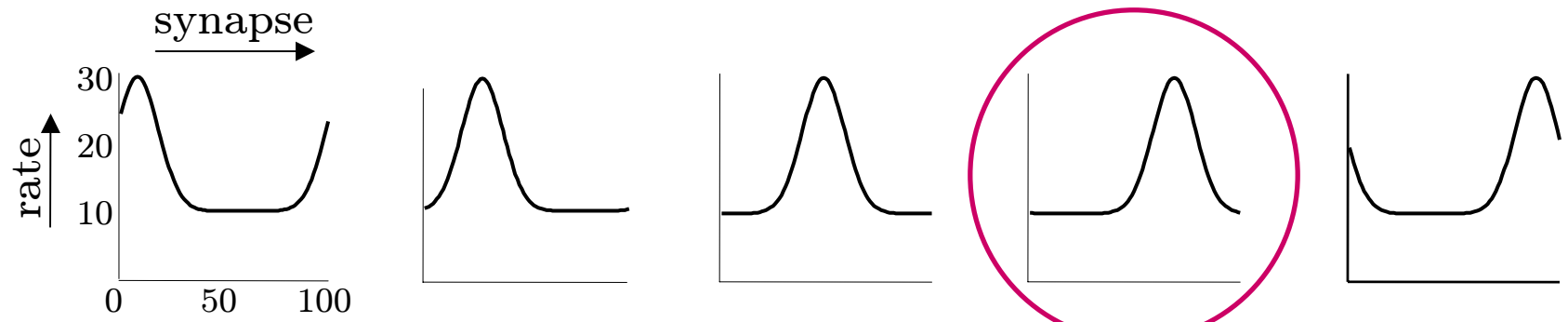
Output





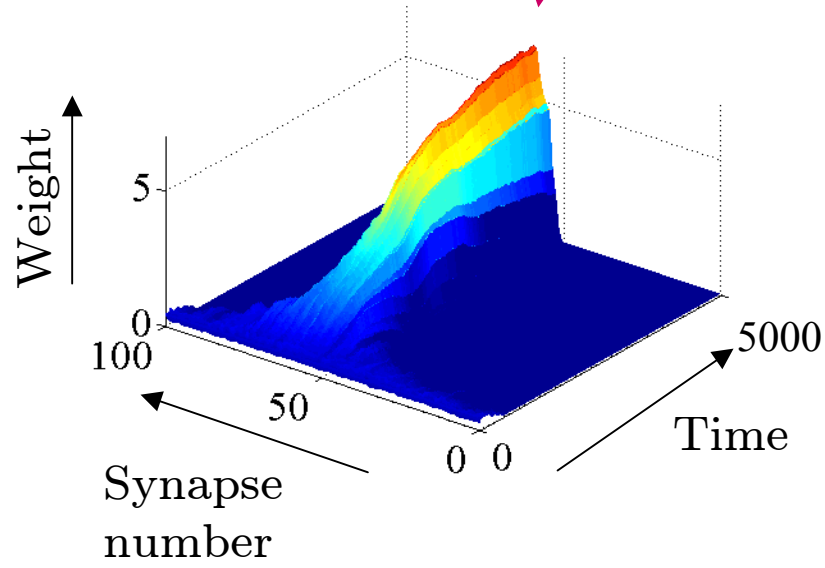
Selectivity is robust across many different patterns amplitudes. Simulations with different pattern dimensions were also performed (not shown).

- Input environment: 5 gaussian patterns



Input Patterns I II III IV V

Synaptic weight evolution



Conclusions

- Spontaneous development of selectivity to inputs with different spike-train statistics is achieved using the Unified Calcium Model (UCM).
- Such selectivity is attained because the model favors cooperativity and temporal competition. However, the results are not stable.
- Incorporation of a physiological mechanism as a possible basis for the BCM-type metaplasticity enhances robustness of the model.
- The UCM and metaplasticity jointly accounts for selectivity in a rate-based environment, where training is performed with different patterns of input rate distribution.
- Further study include development of receptive fields in more complex input environments and network properties of the model.

Methods

- **Learning Rule:** We simulate a single neuron with 100 plastic excitatory synapses and 20 non-plastic inhibitory synapses. The excitatory synapses undergo Eqn. (1). H is a linear function of the local calcium $[Ca_i^{2+}]$ and Ω is a difference of sigmoids: $\Omega = \sigma([Ca_i^{2+}], a_1, b_1) - \sigma([Ca_i^{2+}], a_2, b_2)$, where $\sigma(x, a, b) := \exp(b(x-a))/[1 + \exp(b(x-a))]$.
- **Calcium transients:** The local calcium concentration varies through Eqn. (2). Upon pre-spike, f reaches its peak value. A fraction I_f^{NMDA} of it decays with the fast time constant τ_f^{NMDA} , and the rest (I_s^{NMDA}) decays with slow time constant τ_s^{NMDA} . $H(V)$ is the magnesium-block dependence on the postsynaptic depolarization (Carmignoto & Vicini, Science, 1992).
- **Excitability and membrane potential dynamics:** The input is a Poisson spike train feeding into an Integrate-and-Fire neuron according to Eqn. (5). If V_m reaches the firing threshold V_{thrsh} a post-spike is generated and the BPAP reaches its peak A_{bk} according to Eqn. (4). A fraction I_f^{BPAP} of it decays as τ_f^{BPAP} , and the rest (I_s^{BPAP}) decays as τ_s^{BPAP} . The total voltage is thus $V = V_m + \text{BPAP}$.

- **Correlation:** We adopt the method used by Rudolph & Destexhe (J. Comp. Neurosci., 2001). At each time step $N_0 = N + \sqrt{c} (1-N)$ Poisson-distributed random synaptic events are generated and randomly redistributed among N synaptic channels, $N_0 < N$.
- **Rate distribution:** The time intervals were generated according to an exponential distribution of mean τ_c . At each interval, a pattern of rate distribution is randomly assigned to the synapses.
- **Metaplasticity:** The NMDA conductance was implemented as a function of the time average of the membrane potential according to eqn. (7).

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