How presynaptic release affects synaptic plasticity

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Abstract

The mechanisms by which presynaptic release influences synaptic plasticity are fundamental to understanding learning and memory processes. In this study, we employ computational modeling to explore the effects of presynaptic release dynamics on synaptic strength changes during spike-timing-dependent plasticity (STDP). Using the Tsodyks-Markram model of synaptic dynamics, we simulate the interactions between two neurons with varying presynaptic release parameters. Our findings suggest that the magnitude of presynaptic release significantly modulates the degree of synaptic potentiation and depression, highlighting the role of presynaptic dynamics in shaping synaptic plasticity. Specifically, our results show that the time constant of facilitation and recovery, as well as the magnitude of presynaptic release, are crucial in controlling the extent of synaptic changes during learning processes.

1 Introduction

Synaptic plasticity refers to the persistent changes in the structure, function, strength, and efficiency of synapses, which form the basis of neural computation and signal processing. There are various forms of synaptic plasticity, including Short-Term Plasticity (STP) and Long-Term Plasticity (LTP), categorized by the timescale of the memory trace. While LTP is often associated with long-lasting memory storage, STP occurs on much shorter timescales (milliseconds to seconds) and can involve phenomena such as paired-pulse depression (PPD), paired-pulse facilitation (PPF), and post-tetanic potentiation (PTP) [11, 8]. In addition, synaptic plasticity may manifest in forms such as Spiking-Rate-Dependent Plasticity (SRDP), Spiking-Timing-Dependent Plasticity (STDP), associative learning, and synaptic scaling [3, 1]. These mechanisms are fundamental to neural signal processing, learning, and memory formation [7].

Among the different forms of plasticity, Short-Term Synaptic Plasticity (STP) is of particular interest due to its role in shaping the temporal dynamics of synaptic transmission and the overall behavior of neural networks. STP has been observed to play a critical role in processes such as motion control, speech recognition, and working memory [14, 1]. STP can be categorized into two main types: Short-Term Depression (STD) and Short-Term Facilitation (STF). STD is typically caused by a depletion of neurotransmitters due to repetitive presynaptic activity, while STF arises from an increase in neurotransmitter release probability due to calcium influx following a presynaptic spike [12]. Both forms of STP have been extensively studied in various cortical regions [9, 5], with some synapses exhibiting a dominance of STD, others STF, and many showing a mixture of both effects.

The study of how presynaptic release affects synaptic plasticity has gained considerable attention due to its potential to explain the modulation of synaptic efficacy during learning. Presynaptic release mechanisms, including facilitation and depression, influence the synaptic weight changes during STDP. In particular, presynaptic release governs the balance between potentiation and depression, ultimately affecting the overall synaptic strength and the processing of neural information. For example, synaptic facilitation tends to enhance synaptic potentiation when presynaptic activity closely precedes postsynaptic firing, while synaptic depression may inhibit this potentiation when the presynaptic activity is excessive or poorly timed [6].

Recent computational models, such as the Tsodyks-Markram model [12], have been instrumental in understanding these dynamic processes. The Tsodyks-Markram model incorporates short-term plasticity mechanisms, where the release probability of neurotransmitters is governed by two variables: u, which represents the fraction of available neurotransmitters, and x, which represents the synaptic depression or facilitation [13]. The synaptic weight $w(t)$ is updated based on the interaction between these two variables, and the presynaptic spike train modulates their values over time.

Our study extends this model to investigate the effects of presynaptic release dynamics on synaptic plasticity during STDP. In particular, we explore how the varying presynaptic release characteristics, such as the release probability and recovery time constants, influence synaptic strength changes between two neurons. By simulating the interactions between these neurons with different presynaptic release profiles, we aim to uncover how the timing and magnitude of presynaptic activity can modulate the degree of synaptic potentiation and depression.

While the influence of presynaptic release on synaptic plasticity has been studied experimentally in several contexts [2, 10], there is still a need for computational approaches that can capture the detailed dynamics of synaptic interactions in complex neural networks. Here, we present a computational model that incorporates presynaptic release dynamics to simulate the effects of STP on synaptic efficacy during STDP. By varying key parameters of presynaptic release, such as the release probability and the recovery time constants, we explore how these factors contribute to the shaping of synaptic plasticity.

This paper provides a computational framework for studying the role of presynaptic release in modulating synaptic plasticity and contributes to our understanding of how short-term synaptic dynamics influence neural information processing. Our findings highlight the importance of presynaptic dynamics in shaping the outcome of synaptic plasticity and suggest potential avenues for further research into the functional implications of STP in learning and memory systems.

2 Method

2.1 Mathematical Model

We simulate two leaky integrate-and-fire (LIF) neurons connected via a Tsodyks-Markram synapse, which includes mechanisms for short-term facilitation (STF) and short-term depression (STD). We change the supporting Python package from NEST as in the original paper [4] to BrainPy. The LIF neuron model is governed by the following differential equation for the membrane potential $V(t)$:

$$\tau_m \frac{dV}{dt} = -(V - E_L) + RI(t)$$

where $\tau_m = 15\,\text{ms}$ is the membrane time constant, $E_L = -65\,\text{mV}$ is the resting membrane potential, and $R = 1\,\text{M}\Omega$ is the membrane resistance. The input current $I(t)$ consists of synaptic currents and external inputs, with the synaptic current described by the Tsodyks-Markram model.

The synaptic dynamics are described by:

$$\frac{du}{dt} = \frac{U_{\text{max}} - u}{\tau_{\text{rec}}} - u \cdot \left(\sum_i \delta(t - t_i) \right)$$

$$\frac{dx}{dt} = \frac{1 - x}{\tau_{\text{fac}}} + x \cdot \left(\sum_i \delta(t - t_i) \right)$$

$$w(t) = A_{\text{max}} u(t) x(t)$$

Where:

- $u(t)$ represents the recovery variable, which decays over time with a time constant τ_{rec},
- $x(t)$ represents the facilitation variable, which grows and decays with a time constant τ_{fac},

- $w(t)$ is the synaptic weight, and
- $\delta(t - t_i)$ is the Dirac delta function that accounts for the arrival times of presynaptic spikes.

Here, the synaptic strength $w(t)$ depends on both the facilitation and recovery variables, with each presynaptic spike inducing a transient change in the neurotransmitter release probability, modeled by these variables.

2.2 Simulation Setup

Two neurons are modeled using the LIF neuron equations. The presynaptic spike trains are modeled using Poisson processes, with each spike train defined by an exponential distribution for interspike intervals. The simulation includes two current inputs to the neurons:

$$I_1(t) = \begin{cases} 500\,\text{pA}, & 50 \leq t \leq 51 \\ 0, & \text{otherwise} \end{cases}$$

$$I_2(t) = \begin{cases} A_2\,\text{pA}, & 50 + \Delta t \leq t \leq 51 + \Delta t \\ 0, & \text{otherwise} \end{cases}$$

where A_2 represents the magnitude of the second current injection, and Δt is the time difference between the two presynaptic spike events. This configuration allows us to manipulate the timing of the inputs and explore their effects on synaptic plasticity.

2.3 Data Collection and Analysis

The synaptic weight $w(t)$ is tracked during the simulation, with a focus on changes in synaptic strength over time. We calculate the synaptic weight for different values of Δt, alpha, and beta, and monitor how changes in presynaptic release parameters influence the synaptic efficacy during STDP. We average the synaptic weight over the first and last 50 ms of the simulation to capture the initial and final stages of synaptic change.

3 Results

The simulations reveal a clear relationship between presynaptic release dynamics and synaptic plasticity. The presynaptic release magnitude, represented by A_2, and the timing between presynaptic and postsynaptic spikes, significantly influence the synaptic potentiation and depression observed during STDP.

As shown in the figure, the synaptic weight increases when presynaptic facilitation dominates, particularly when the timing of the postsynaptic spike closely follows the presynaptic spike (i.e., smaller Δt). On the other hand, when the presynaptic spikes are poorly timed or excessive, synaptic depression dominates, and the synaptic weight is reduced.

Additionally, we found that the facilitation time constant τ_{fac} plays a crucial role in enhancing synaptic potentiation. Increasing τ_{fac} led to larger synaptic potentiation, while increasing the recovery time constant τ_{rec} reduced the potentiation effect.

4 Conclusion

In this study, we presented a computational model to investigate how presynaptic release dynamics influence synaptic plasticity during STDP. Our results demonstrate that the presynaptic release parameters, such as the magnitude of release and the facilitation and recovery time constants, significantly shape the synaptic strength changes between two neurons. The Tsodyks-Markram model provided an effective framework to explore these interactions, revealing the importance of presynaptic dynamics in determining synaptic potentiation and depression.

Our findings suggest that presynaptic release mechanisms play a key role in synaptic computation, with potential implications for learning and memory processes. Future work should explore the effects

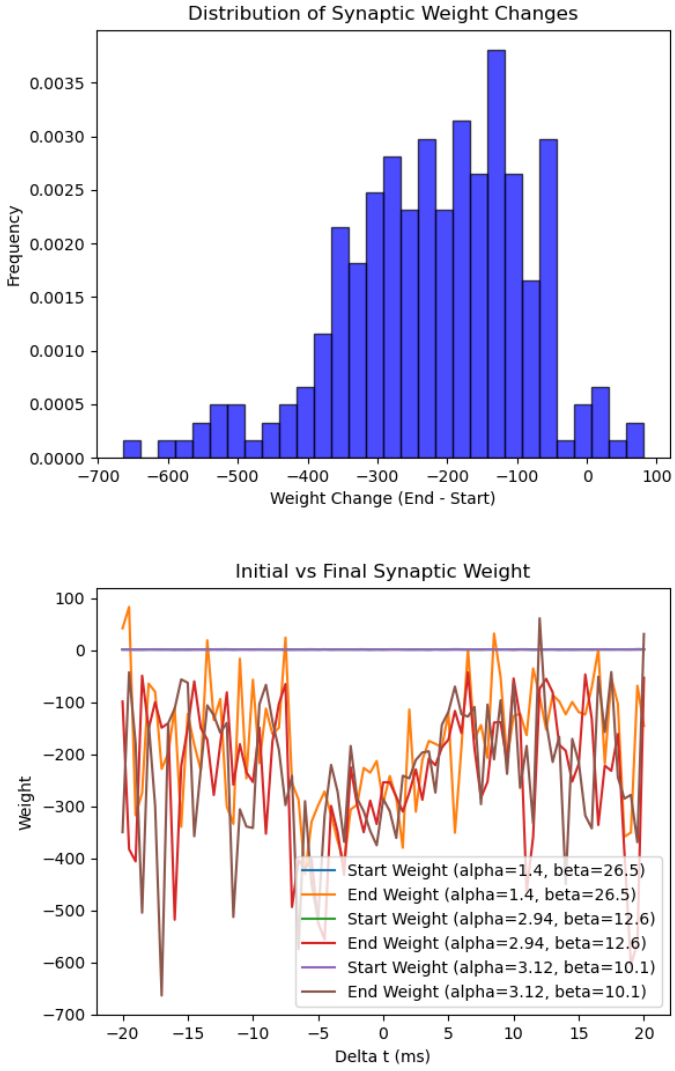

Figure 1: Synaptic weight changes over time for different presynaptic release profiles.

of more complex neural network architectures, as well as the role of these dynamics in other forms of plasticity, such as associative learning and memory consolidation. Further investigation into how presynaptic release interacts with other synaptic processes could provide a deeper understanding of how the brain encodes and processes information. Additionally, exploring the functional consequences of presynaptic dynamics in larger, more biologically realistic networks could offer valuable insights into the role of synaptic plasticity in cognitive processes.

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References

[1] L. F. Abbott and Wade G. Regehr. Synaptic computation. *Nature*, 431(7010):796–803, 2004. doi: 10.1038/nature03010. 1

[2] L. F. Abbott et al. Synaptic depression and cortical gain control. *Science*, 275(5297):221–224, 1997. doi: 10.1126/science.275.5297.221. 2

[3] G. Bi and M. Poo. Synaptic modification by correlated activity: Hebb's postulate revisited. *Annu. Rev. Neurosci.*, 24:139–166, 2001. 1

[4] Peter H Chipman, Chi Chung Alan Fung, Alejandra Pazo Fernandez, Abhilash Sawant, Angelo Tedoldi, Atsushi Kawai, Sunita Ghimire Gautam, Mizuki Kurosawa, Manabu Abe, Kenji Sakimura, Tomoki Fukai, and Yukiko Goda. Astrocyte glun2c nmda receptors control basal synaptic strengths of hippocampal ca1 pyramidal neurons in the *stratum radiatum*. *eLife*, 10: e70818, oct 2021. ISSN 2050-084X. doi: 10.7554/eLife.70818. URL `https://doi.org/10.7554/eLife.70818`. 2

[5] J. S. Dittman, A. C. Kreitzer, and W. G. Regehr. Interplay between facilitation, depression, and residual calcium at three presynaptic terminals. *J. Neurosci.*, 20:1374–1385, 2000. 1

[6] G. et al. Fuhrmann. Coding of temporal information by activity-dependent synapses. *J. Neurophysiol.*, 87:140–148, 2002. 1

[7] M. S. Goldman, P. Maldonado, and L. F. Abbott. Redundancy reduction and sustained firing with stochastic depressing synapses. *The Journal of Neuroscience*, 22(2):584–591, 2002. 1

[8] H. Markram and M. Tsodyks. Redistribution of synaptic efficacy between neocortical pyramidal neurons. *Nature*, 382(6594):807–810, 1996. doi: 10.1038/382807a0. 1

[9] H. Markram, J. Lübke, M. Frotscher, A. Roth, and B. Sakmann. Regulation of synaptic efficacy by coincidence of postsynaptic aps and epsps. *Science*, 275(5297):213–215, 1997. 1

[10] R. Rosenbaum, J. Rubin, and B. Doiron. Short term synaptic depression imposes a frequency dependent filter on synaptic information transfer. *PLoS Computational Biology*, 8(6):e1002557, 2012. doi: 10.1371/journal.pcbi.1002557. 2

[11] C. F. Stevens and Y. Wang. Facilitation and depression at single central synapses. *Neuron*, 14 (4):795–802, 1995. doi: 10.1016/0896-6273(95)90223-6. 1

[12] M. Tsodyks and H. Markram. The neural code between neocortical pyramidal neurons is based on short-term synaptic plasticity. *Science*, 275(5297):213–215, 1997. 1, 2

[13] M. Tsodyks, K. Pawelzik, and H. Markram. Neural networks with dynamic synapses. *Neural Computation*, 10(4):821–835, 1998. doi: 10.1162/089976698300017502. 2

[14] R. S. Zucker and W. G. Regehr. Short-term synaptic plasticity. *Annual Review of Physiology*, 64(1):355–405, 2002. doi: 10.1146/annurev.physiol.64.092501.114547. 1