A Calcium-Based Model Of Spike-Timing Dependent Plasticity

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Spike-Timing Dependent Plasticity and memory

- Learning and memory associated with synaptic plasticity
- Hebb’s postulate
- Importance of the timing and the order (pre-post or post-pre)
- $\Delta t = t_{Post} - t_{Pre}$
Spike-Timing Dependent Plasticity and memory

- Learning and memory associated with synaptic plasticity
- Hebb’s postulate
- Importance of the timing and the order (pre-post or post-pre)
- $\Delta t = t_{Post} - t_{Pre}$

[Fieldman, 2012, Neuron]
Anti-Hebbian STPD in cortico-striatal synapses

\[ \text{STDP} = \Delta t \times N_{\text{Pairings}} \times \text{Freq} \]

Introduction

Model

Simulations

Conclusion

Stimulation

Recording & stimulation

Cortex

Striatum

\[ \text{Normalized EPSC (\%)} \]

\[ \text{Time (min)} \]

\[ \text{N=100 pairings} \]

\[ 100x (-30 < \Delta t < 0 \text{ms}) \]

\[ (n=10) \]

\[ 100x (0 < \Delta t < +30 \text{ms}) \]

\[ (n=7) \]

[Cui et al, 2015, J. Physiol.]
Anti-Hebbian STPD in cortico-striatal synapses

\[ STDP = \Delta t \times N_{Pairings} \times Freq \]

- Pre-post pairings lead to LTD
- Post-pre pairings lead to LTP

[Anti-Hebbian learning rule]

[Introduction
Model
Simulations
Conclusion]

[Cui et al, 2015, J. Physiol.]
Importance of the number of pairings

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Different models of STDP

\[ \text{STDP} = \Delta t \times N_{\text{Pairings}} \times \text{Freq} \]

- Several biophysical models explain STDP curves as [Graupner and Brunel, 2012, PNAS] based on the post-synaptic calcium trace.
- Anti-Hebbian STDP curve

[Graupner and Brunel, 2012, PNAS]
Different models of STDP

\[
STDP = \Delta t \times N_{Pairings} \times \text{Freq}
\]

Different models of STDP

\[ STDP = \Delta t \times N_{Pairings} \times Freq \]

- Influence of the number of pairings in [Graupner and Brunel, 2012, PNAS]
- Monotonic variation of the STDP curve as a function of the number of pairings

[Graupner and Brunel, 2012, PNAS]
Problematic and goals of the study

[Cui et al, 2016, eLife] : a biophysical model explaining this dependence but a complex model

How to implement this plasticity rule with a minimal model that explains all the experimental data and that could be implemented in a network?

- Develop a simple phenomenological model taking into account the different mechanisms and dependence on the number of pairings
- Find parameters that would reproduce [Cui et al, 2015, J. Physiol.] data
- Test the stability of this model
Different mechanisms for calcium-based STDP

Inspired from [Cui et al, 2016, eLife]
Different mechanisms for calcium-based STDP

\[
\tau \frac{d \rho_{eCB}}{dt} = -\rho_{eCB} (1 - \rho_{eCB}) (\rho^* - \rho_{eCB}) + \gamma_{eCB LTP} (1 - \rho_{eCB}) \Theta [C^a (t) - \theta_{eCB LTP}] - \gamma_{eCB LTD} \rho_{eCB} \Theta [C^a (t) - \theta_{eCB LTD}] + \text{Noise}_{eCB} (t)
\]

\[
\tau \frac{d \rho_{NMDA}}{dt} = -\rho_{NMDA} (1 - \rho_{NMDA}) (\rho^* - \rho_{NMDA}) + \gamma_{NMDA LTP} (1 - \rho_{NMDA LTP}) \Theta [C^a (t) - \theta_{NMDA LTP}] + \text{Noise}_{NMDA} (t)
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**Introduction**

**Model Simulations Conclusion**

\[ \tau \frac{d \rho_{eCB}}{dt} = -\rho_{eCB} (1 - \rho_{eCB})(\rho_* - \rho_{eCB}) \]

\[ + \gamma_{eCB \ LTP} (1 - \rho_{eCB}) \Theta [C'a(t) - \theta_{eCB \ LTP}] \]

\[ - \gamma_{eCB \ LTD} \rho_{eCB} \Theta [C'a(t) - \theta_{eCB \ LTD}] \]

\[ + \text{Noise}_{eCB} (t) \]

\[ \tau \frac{d \rho_{NMDA}}{dt} = -\rho_{NMDA} (1 - \rho_{NMDA})(\rho_* - \rho_{NMDA}) \]

\[ + \gamma_{NMDA \ LTP} (1 - \rho_{NMDA \ LTP}) \Theta [C'a(t) - \theta_{NMDA \ LTP}] \]

\[ + \text{Noise}_{NMDA} (t) \]
Different mechanisms for calcium-based STDP

Introduction
Model
Simulations
Conclusion

\[ C_{\text{hel}} = \frac{S_{NMDA} \times S_{eCB}}{a \times b} \]

\[ \tau \frac{d \rho_{eCB}}{dt} = -\rho_{eCB} (1 - \rho_{eCB}) (\rho^* - \rho_{eCB}) + \gamma_{eCB} \text{LTP} (1 - \rho_{eCB}) \Theta [C^a (t) - \theta_{eCB \text{LTP}}] - \gamma_{eCB \text{LTD}} \rho_{eCB} \Theta [C^a (t) - \theta_{eCB \text{LTD}}] + \text{Noise}_{eCB} (t) \]

\[ \tau \frac{d \rho_{NMDA}}{dt} = -\rho_{NMDA} (1 - \rho_{NMDA}) (\rho^* - \rho_{NMDA}) + \gamma_{NMDA \text{LTP}} (1 - \rho_{NMDA \text{LTP}}) \Theta [C^a (t) - \theta_{NMDA \text{LTP}}] + \text{Noise}_{NMDA} (t) \]

Inspired from [Cui et al, 2016, eLife]

Change in synaptic efficacy = \( S(NMDA) \times S(eCB) \)

With S a sigmoid function
Dependence on the number of pairings

\[ \tau \frac{d \rho_{\text{eCB}}}{dt} = -\rho_{\text{eCB}} (1 - \rho_{\text{eCB}}) (\rho_* - \rho_{\text{eCB}}) \]
\[ + \gamma_{\text{eCB LTP}} (1 - \rho_{\text{eCB}}) \Theta \left[ C_a(t) - \theta_{\text{eCB LTP}} \left( \int_{t_0}^t C_a(t') dt' \right) \right] \]
\[ - \gamma_{\text{eCB LTD}} \rho_{\text{eCB}} \Theta \left[ C_a(t) - \theta_{\text{eCB LTD}} \left( \int_{t_0}^t C_a(t') dt' \right) \right] \]
\[ + \text{Noise}_{\text{eCB}}(t) \]

\[ \tau \frac{d \rho_{\text{NMDA}}}{dt} = -\rho_{\text{NMDA}} (1 - \rho_{\text{NMDA}}) (\rho_* - \rho_{\text{NMDA}}) \]
\[ + \gamma_{\text{NMDA LTP}} (1 - \rho_{\text{NMDA LTP}}) \Theta \left[ C_a(t) - \theta_{\text{NMDA LTP}} \left( \int_{t_0}^t C_a(t') dt' \right) \right] \]
\[ + \text{Noise}_{\text{NMDA}}(t) \]
Dependence on the number of pairings

Introduction

Model

Simulations

Conclusion
Theoretical solution using a mean-field approach

- Mean-field approach as in [Graupner and Brunel, 2012, PNAS] for each independent mechanism

\[ d\rho_t = (\alpha(t)\rho_t + \beta(t)) \, dt + \sigma(t) \, dB(t) \]

- Resolution with Ito formula

- \( \rho \) as a Gaussian distribution, computation of its mean and variance

- Fit to the experimental data using Python scipy library
Application to anti-Hebbian STDP

Introduction

Model

Simulations

Conclusion

Number of pairings

Change in synaptic efficacy

$N_{\text{pairings}} = 14$

$N_{\text{pairings}} = 45$

$N_{\text{pairings}} = 100$
Comparison to experimental data

$$STDP = \Delta t \times N_{Pairings} \times Freq$$
How do the different mechanisms participate?

- **a** Only NMDA
- **b** Only endocannabinoids

![Graphs showing the change in synaptic efficacy](image)

- **Change in synaptic efficacy**
- **Number of pairings**
- **Δt (s)**

**Legend:**
- Red indicates a greater change in synaptic efficacy.
- Blue indicates a lesser change in synaptic efficacy.

**Introduction**

- **Model**
- **Simulations**
- **Conclusion**
Influence of frequency

\[ STDP = \Delta t \times N_{Pairings} \times Freq \]
- A simple model with few parameters and 2 equations that reproduces experimental data of STDP

- Predictive model for frequency dependence

[Feldman, 2012, Neuron]
- A simple model with few parameters and 2 equations that reproduces experimental data of STDP

- Predictive model for frequency dependence

Future:

- Compare this model to other experimental situations in other parts of the brain

- Implement this STDP rule in networks
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