
Master thesis : Neuromodulation of calcium-based plasticity rules

Auteur : Ponnet, Juliette

Promoteur(s) : Drion, Guillaume

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Neuromodulation of calcium-based plasticity rules.

Juliette Ponnet

Supervisor: G. Drion

Master in Biomedical Engineering, University of Liège

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Abstract

In the age of navigation systems, online reminders, and calendars, there is little room left for our memory capacity. Once disconnected from these tools, we constantly check our pockets and wonder: *how do I get to that friend's house again?* Due to this more-than-connected world, it sometimes becomes difficult to even take the time to sleep. However, many people know that sleep is one of the keys to our well-being. But what if sleep was actually our secret memory weapon?

During learning, neurons are able to rewire their neuronal connection to encode and store information, a property known as synaptic plasticity. While during wakefulness thalamic neurons are activated according to tonic firing pattern to process information, during sleep there is a change in neuronal firing pattern and these neurons are bursting. Experimental studies provide evidence of the link between this switch in brain neuronal patterns and the memory function of sleep. It has been shown that during sleep following learning, neurons in specific areas of the brain are activated. This activity remodels the neuronal connections (*i.e.*, synaptic plasticity) that mediate the formation and storage of memories. Despite ample evidence pointing to the role of sleep in memory consolidation, the detailed cellular mechanisms remain to be understood.

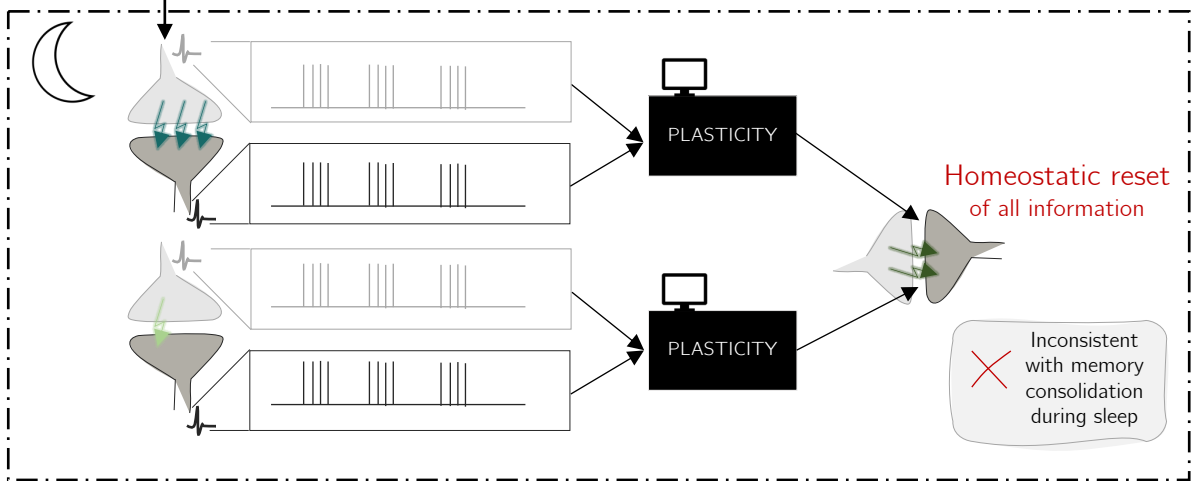
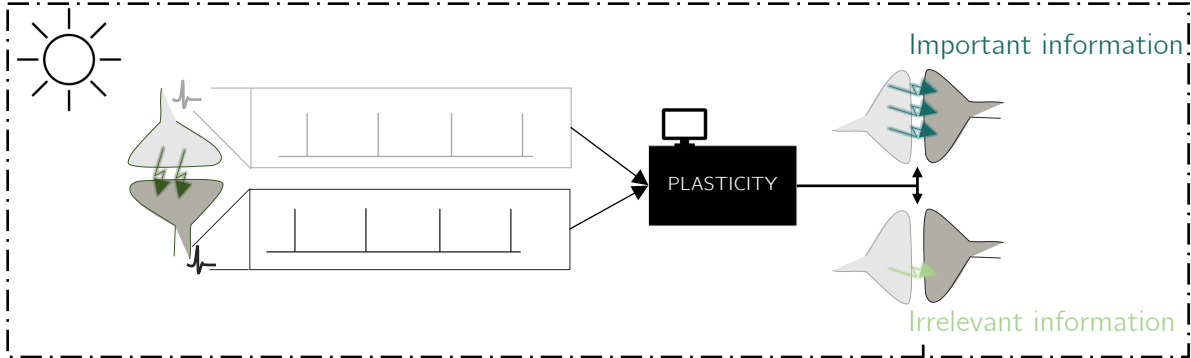
Different approaches can be taken to understand how sleep shapes our memories. In this thesis, we apply a computational approach to model the evolution of the synaptic strength. These synaptic plasticity rules are divided into two categories: *phenomenological* models and *biological* models. We focus on biological rules that are based on calcium dynamics (*i.e.*, calcium-based plasticity rules) to predict the direction of the synaptic plasticity (*i.e.*, strengthening or weakening of neuronal connections). While these models accurately describe the dynamics of neuronal components during wakefulness, they are not adapted to changes in neuronal firing patterns that take place during the switch from wake to sleep state as shown by [Jacquerie et al., 2022]. They observed that, no matter how important a piece of information is received during the day (important vs irrelevant), it is consolidated in the same way during sleep. They named this phenomenon, which is inconsistent with memory consolidation, the "*homeostatic reset*".

Since we want to observe a behavior that is consistent with memory consolidation during sleep (*i.e.*, memorization of important information and forgetting of irrelevant ones), this thesis aims at adapting the calcium-based plasticity rules to bypass this "*homeostatic reset*". With this aim in mind, we ask whether, during sleep, neuromodulators could act as regulators of synaptic plasticity and affect the different signaling cascades linked to it to allow the consolidation of important information. To this end, we conduct a literature review detailing the role of principal neuromodulators on synaptic plasticity and related signaling cascades. Then, based on these biological facts, we suggest modification of computational biological plasticity rules that are inconsistent regarding memory consolidation due to the "*homeostatic reset*". While the outcomes are convincing, they prove to be fragile and artificial. Finally, insights are given regarding another approach that would instead benefit from the "*homeostatic reset*" rather than trying to overcome it.

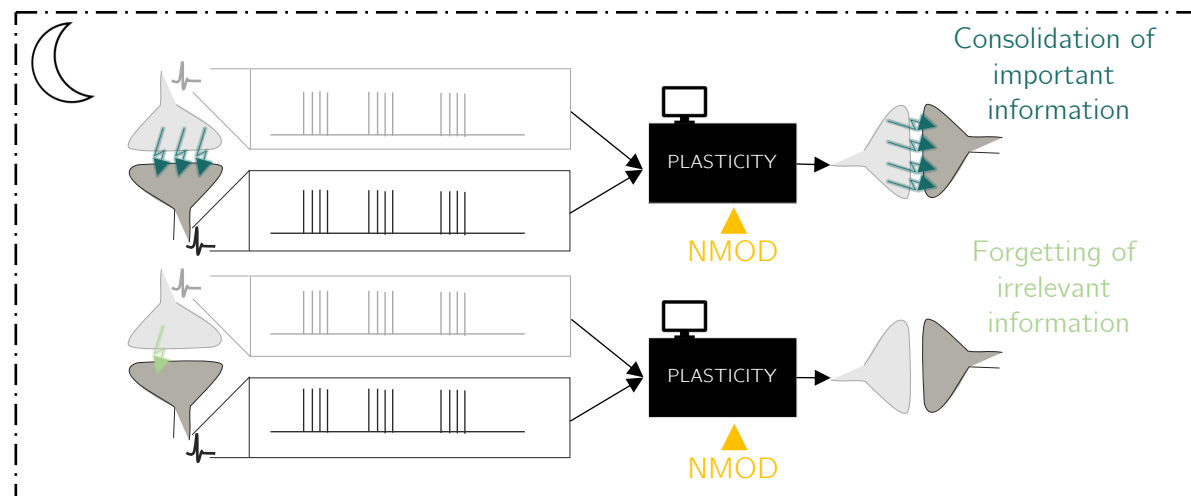
Motivation and the scope of this thesis

Problematic

[Jacquerie-Minne, 2022, in progress]

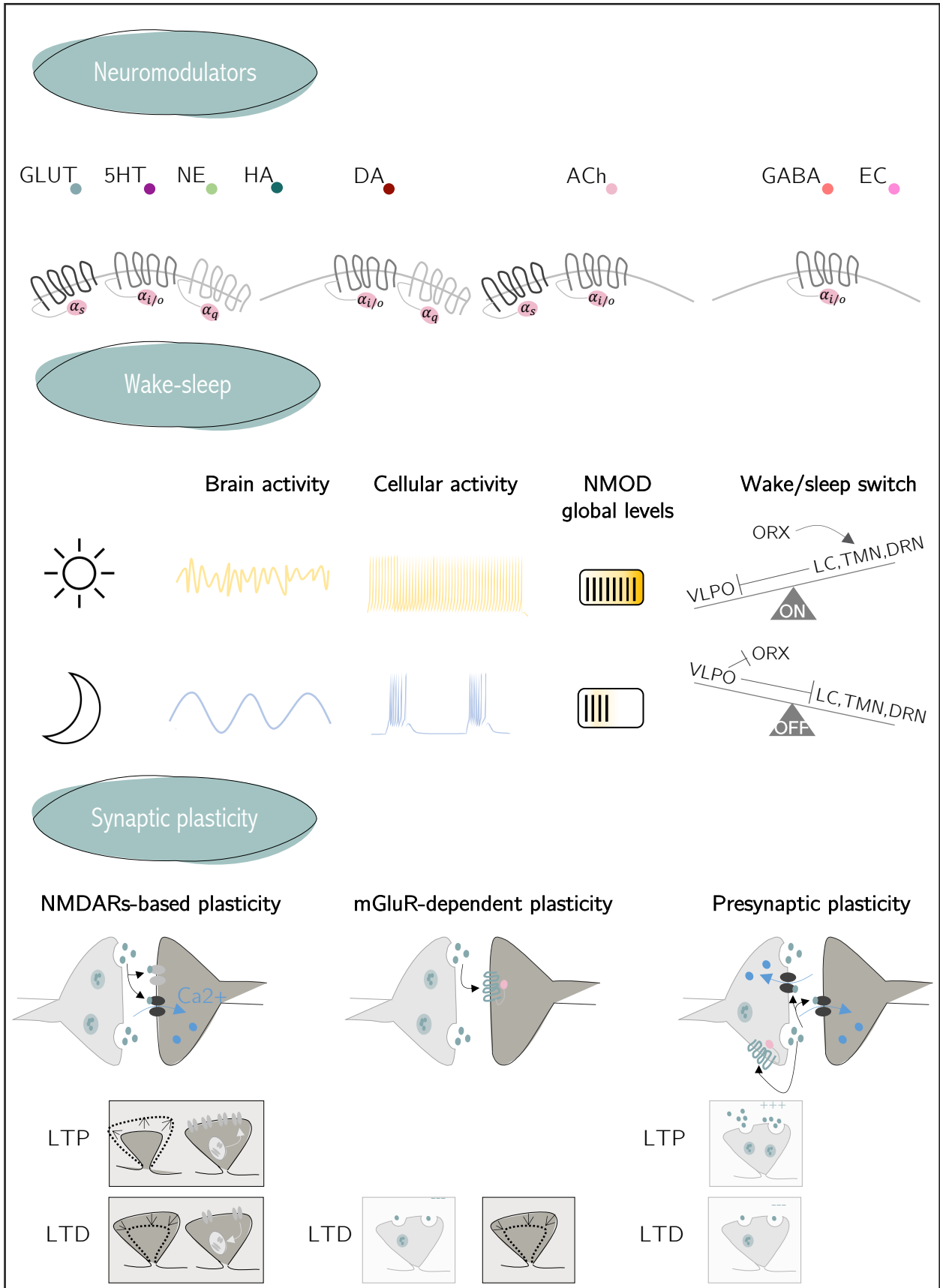


Aims



2.5 Summary

Elements of neurophysiology



3.4 Summary

Calcium-based plasticity rules

Model 1

[Shouval et al., 2002]

$\tau_w([Ca])\dot{w} = \Omega([Ca]) - w$

Model 2

[Graupner et al., 2016]

$\tau_w\dot{w} = \gamma_p(1-w)\Theta([Ca] - \theta_p) - \gamma_d w\Theta([Ca] - \theta_d)$

Construction of a model equivalent to model 2 written in the format of model 1

[Jacquerie-Minne, 2022, in progress]

Model 3

$[Ca] < \theta_d \quad \tau_w^0\dot{w} = \Omega^0 - w$

$[Ca] \in [\theta_d, \theta_p] \quad \tau_w^d\dot{w} = \Omega^d - w$

$[Ca] > \theta_p \quad \tau_w^p\dot{w} = \Omega^p - w$

Fitting model 3 on wakefulness experimental data

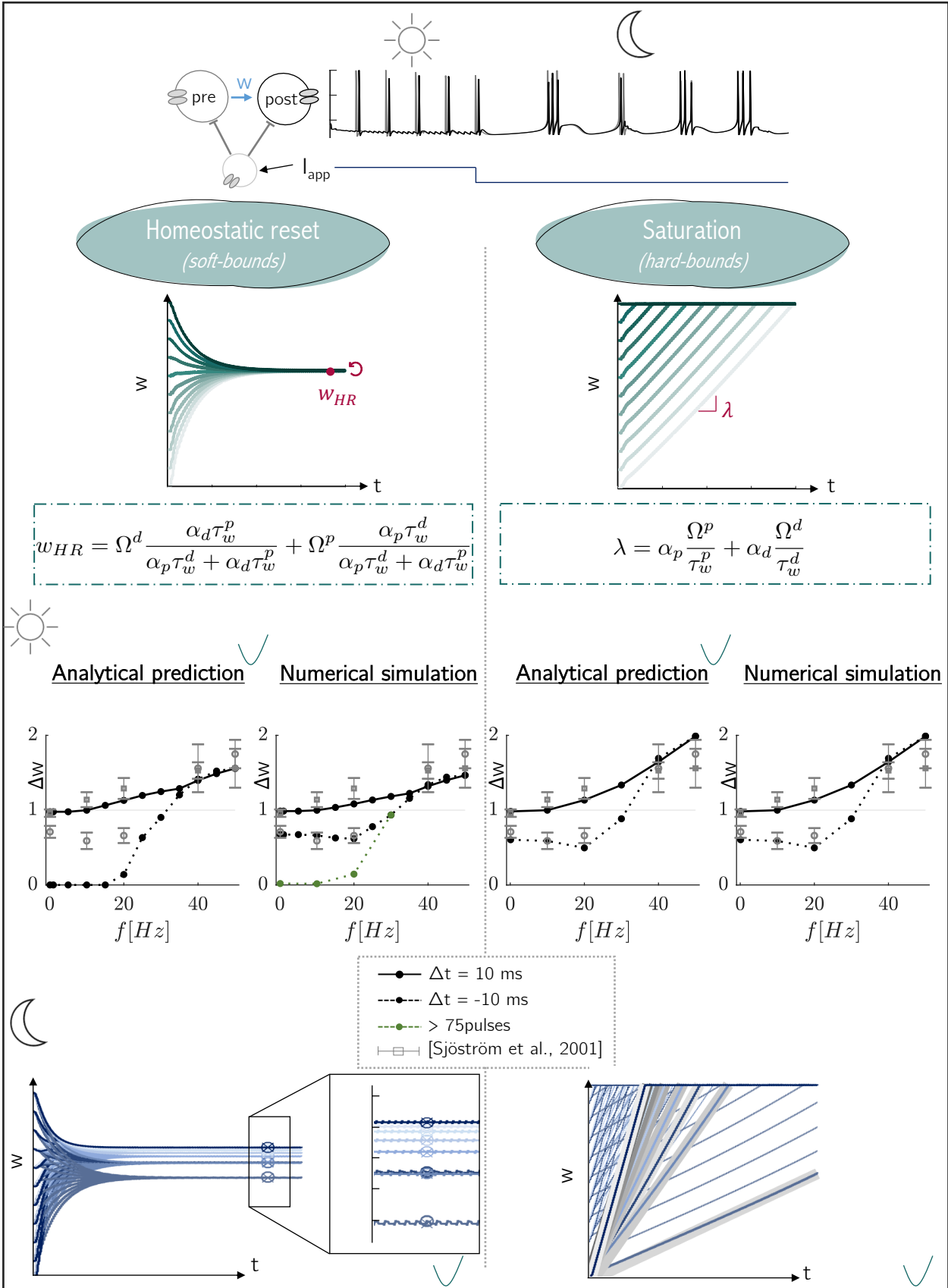
[Jacquerie-Minne, 2022, in progress]

[Sjöström et al., 2001]

Fitting completed ✓

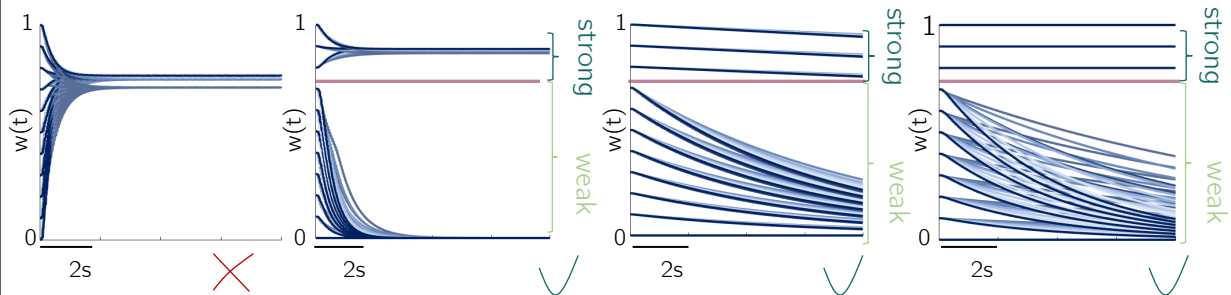
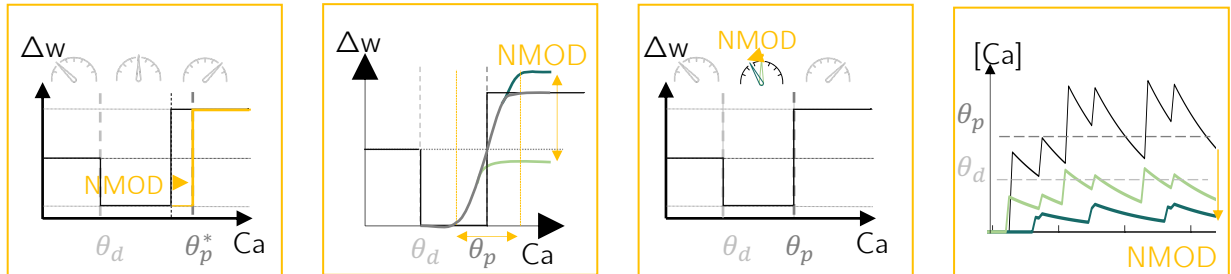
5.3 Summary

Analytical prediction of the homeostatic reset



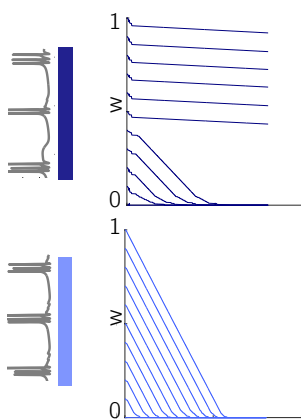
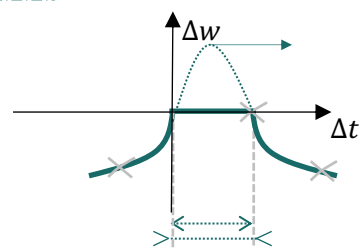
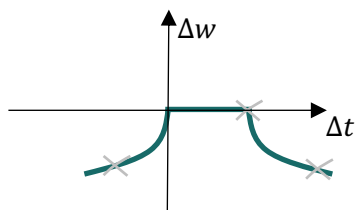
Neuromodulation of calcium-based synaptic rules during sleep

Hand-tuning of calcium-based rules



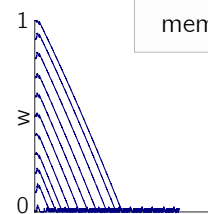
[González-Rueda et al., 2018] in calcium-based rule

✗ Experimental data



✓ Consistent with memory consolidation

✗ Not robust to variability



✗ Not consistent with memory consolidation