

## Master thesis : Neuromodulation of phenomenological plasticity rules

**Auteur :** Benghalem, Nora

**Promoteur(s) :** Drion, Guillaume

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# Neuromodulation of phenomenological plasticity rules.

Nora Benghalem

*Supervisor:* G. Drion

Master in Biomedical Engineering, University of Liège

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## Abstract

Despite utterly different life courses during the day, once night appears and the calm falls over the cities and the campaigns, switch from wake to sleep is one of those things that draws individuals back together. Beyond being a time dedicated to dreams (both the good and the ugly), to unwinding and to ensuring the proper functioning of the human body, the role that sleep has on our ability to remember is now deemed to be proven. However, in practice, a complete understanding of cellular mechanisms of memory consolidation during sleep is still lacking for scientists in the field.

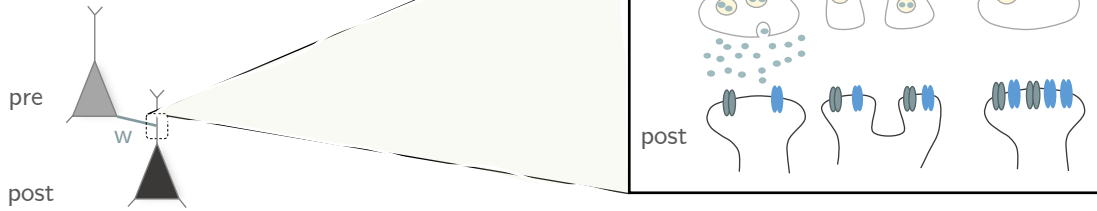
During the day, some learning takes place. At the cellular level, this takes the form of a change in the strength of the connection that binds neurons together, resulting in networks that are subject to a phenomenon known as *synaptic plasticity*. The belief that learning is enhanced, and therefore synaptic strength modulated, when neurons switch from an awake to a sleeping state is supported by the differences in rhythms between these two states, both at the organ level (cerebral waves) and at the cellular level (tonic vs. burst). Moreover, various neuromodulators such as acetylcholine, dopamine, noradrenaline and serotonin are known to be at the origin of this switch between wakefulness and sleep.

Computationally, synaptic plasticity can be modelled by biologically related rules called *calcium models* or more abstract rules called *phenomenological models*. This thesis will focus on the latter. Phenomenological models applied during arousal have proven to be good candidates to study synaptic plasticity. However, when they are applied in sleep without any modifications, they do not prove the link between memory consolidation and sleep. Indeed, [Jacquerie et al., 2022] have shown that regardless which neurons had learned more or less during the day, they all followed the same course during the night. From this observation, this phenomenon was referred to as the *homeostatic reset*.

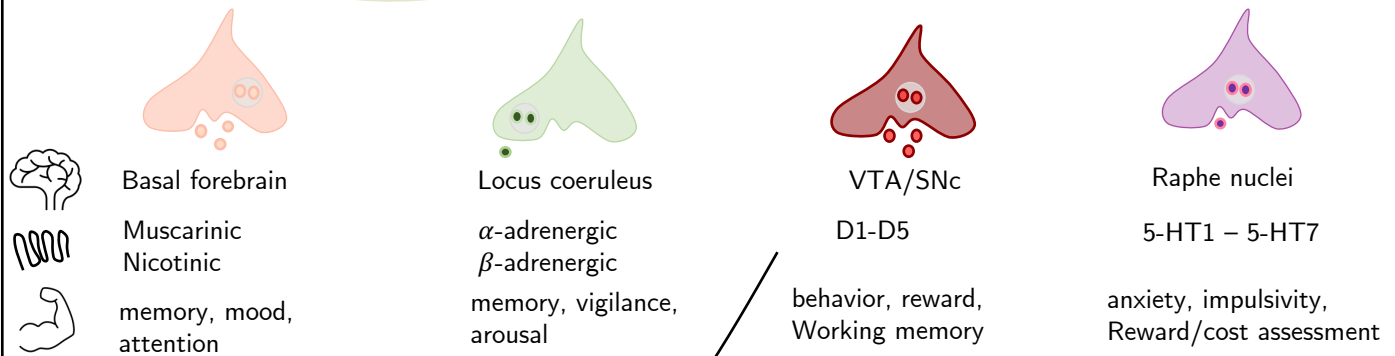
Thus, in this thesis, we integrate the effect of neuromodulators in the phenomenological rules during sleep in order to overcome this homeostatic reset. As neuromodulators are involved in the switch from wakefulness to sleep, we hope that incorporating them into the shift of phenomenological rules from one state to the other could lead to a behaviour compatible with memory consolidation. In order to achieve this goal, a review of the effects of neuromodulators on phenomenological rules during arousal and a review of papers that have implemented neuromodulated computational rules were conducted. Based on this information, computational tests have been performed in which parameters of *the pair-based model* have been modulated in order to reproduce the effect of certain neuromodulators. Some tests were unsuccessful while others were more compatible with our target scenario. However, in both cases, the gap between the computational implementation and the physiological reality and the fragility of the models have been revealed. As a perspective, we propose another way to integrate neuromodulation with the phenomenological rules of plasticity. Instead of touching the parameters of the latter, neuromodulators will tag certain synapses during the day which will allow them to be eligible for synaptic change at night. This approach would be compatible with the *synaptic tag and capture hypothesis*.

# PART I: Background

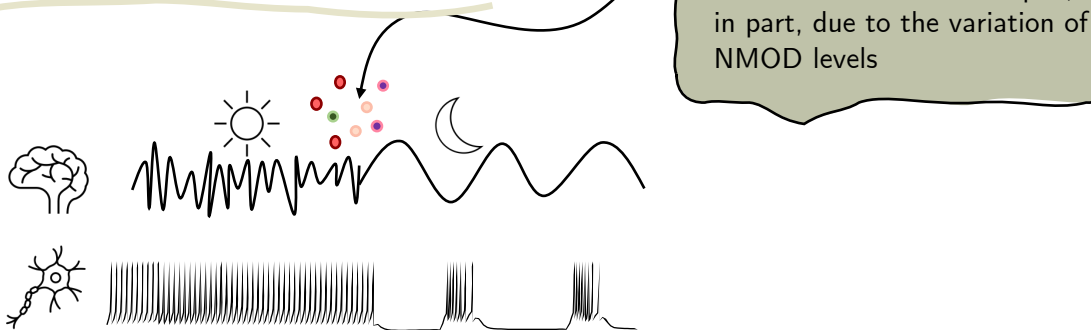
## SYNAPTIC PLASTICITY



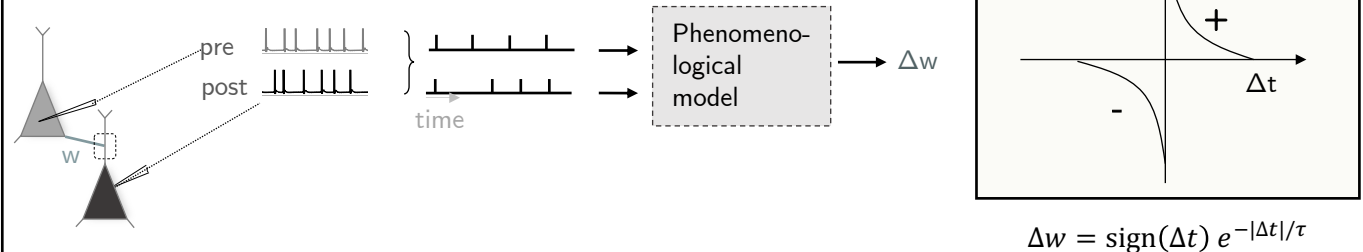
## MAIN NEUROMODULATORS



## SLEEP AND WAKE SWITCH

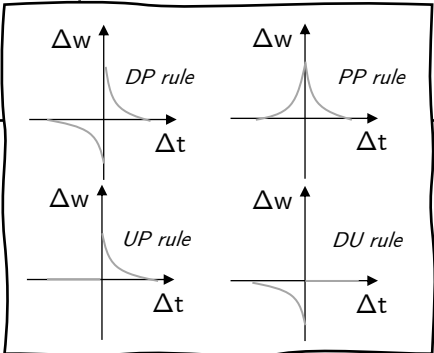
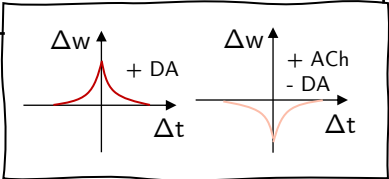
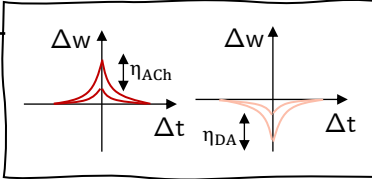


## PHENOMENOLOGICAL MODEL: PAIR-BASED STDP



PART II: neuromodulation of synaptic plasticity rules											
Neuromodulator/ neurotransmitter	Area of the brain	Type of receptor	Activation	Inhibition	Effect on STDP					Paper	
					Polarity		Time window	Magnitude			
					tLTP	tLTD	tLTP	tLTP	tLTD		
Noradrenaline	Hippocampus	$\beta$ -adrenergic	×							[Lin et al., 2003]	
		$\beta$ -adrenergic	×							[Seol et al., 2007]	
	Cortex	$\alpha$ -adrenergic	×								[Seol et al., 2007]
		$\alpha$ -adrenergic + $\beta$ -adrenergic	×								[Guo et al, 2012; Huang et al., 2014]
Dopamine	Hippocampus	$D_1$ -like	×								[Brzosko et al., 2015]
		$D_1$ -like	×								[Brzosko et al., 2015]
	Cortex	$D_1$ -like + $D_2$ -like	×								[Xu and Yao, 2010; Ruan et al., 2014]
	Striatum	?									[Pawlak and Kerr, 2008]
	Amygdala	$D_2$ -like	×								[Bissière et al., 2013]
Acetylcholine	Hippocampus	Muscarinic	×								[Zheng et al., 2012]
		Muscarinic		×							[Sugisaki et al., 2011, 2016]
		Muscarinic + Nicotinic	×								[Tsubokawa and Ross, 1997]
	Dorsal cochlear nucleus	Muscarinic	×								[Zhao and Tzounopoulos, 2011]
	Cortex	Muscarinic + Gs	×								[Seol et al., 2007]
		Muscarinic or Nicotinic	×								[Zaitsev and Anwyl, 2012]
		Nicotinic	×								[Couey et al., 2007]
		Nicotinic	×								[Goriounova and Mansvelder, 2012]
Serotonin	Cortex	5-HT	×							[Song et al., 2015]	
BDNF	Hippocampus	/									[Lu et al., 2014]
	Cortex	/									[Pattwel et al., 2012]
Glutamate	Cortex	/									[Rodriguez-Moreno and Paulsen, 2008]
	Striatum	/									[Valtecheva and Venance, 2016]
GABA	Hippocampus	GABA <sub>A</sub>		×							[Paille et al.,2013]
	Striatum	GABA <sub>A</sub>		×							[Valtecheva et al., 2017]

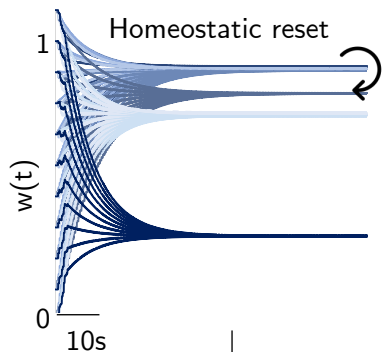
## PART II: Neuromodulation of phenomenological plasticity rules

Authors Year	Pedrosa et al. 2017	Zannone et al. 2018	Ang et al. 2021
Motivation	Review the possible effects of neuromodulators on cortical plasticity using a simple computational model.	Demonstrate that neuromodulation of plasticity allows flexible learning.	Test the predictions of the model developed by Zannone et al. in 2018.
Area of the brain Neuromodulator	Visual cortex Mainly acetylcholine (ACh) and noradrenaline (NA)	Acetylcholine (ACh) and dopamine (DA) mainly	Hippocampus Acetylcholine (ACh)
Methods	STDP: pair-based model	Sequentially neuromodulated plasticity (Sn-plast) i.e. a combination of a modified STDP rule and an eligibility trace	Sn-Plast (see [Zannone et al., 20218])
			

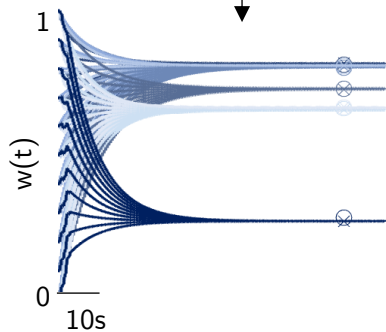
# PART III: computational study



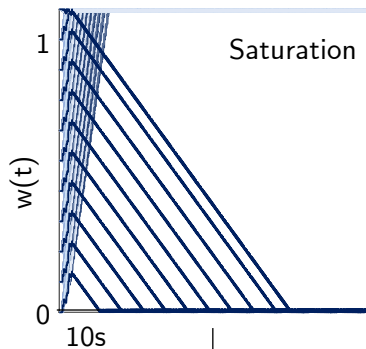
## Soft-bounds



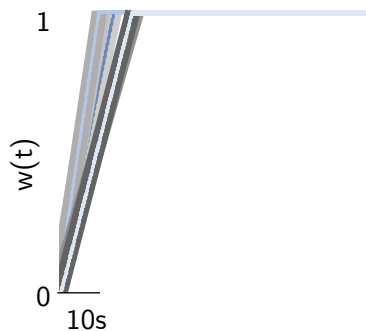
$$w_{HR} = \frac{A_+ c_+}{A_+ c_+ + A_- c_-}$$



## Hard-bounds

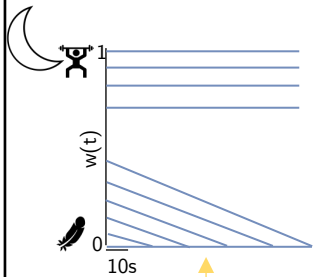


$$\dot{w} = A_+ c_+ - A_- c_-$$

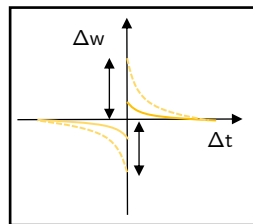
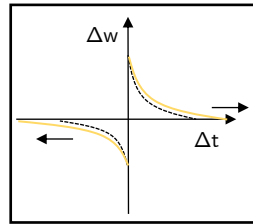
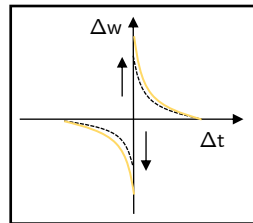
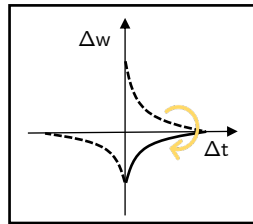


# PART III: computational study

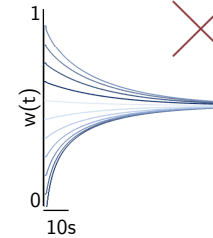
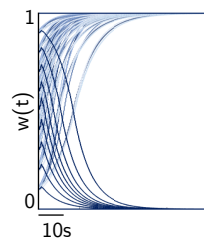
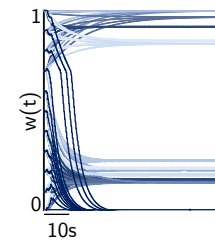
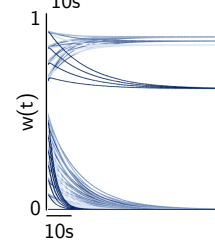
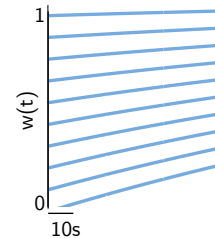
## GOAL



## METHODS



## RESULTS



## CONCLUSION

The neuromodulation of the amplitude of the potentiation and depression window used in the pair-based model is the only parameter modulation that allows to conclude to memory consolidation during sleep

The neuromodulation of the pair-based STDP model as conducted in this work does not lead to the confirmation of memory consolidation during sleep.