The role of synaptic and structural plasticity in the long-term desynchronization effect by coordinated reset stimulation

THANOS MANOS

Laboratoire de Physique Théorique et Modélisation, CNRS, UMR 8089
CY Cergy Paris Université, Cergy-Pontoise Cedex, France
thanos.manos@cyu.fr ● https://sites.google.com/site/thanosmanos/

Mathematical modelling is an important tool in understanding the basic mechanisms of the human brain. Such models, based on ordinary differential equations can capture and describe the underlying dynamical evolution of interactions between a relatively small number of neurons within certain brain areas. In this study, we focus on pathological neural activity which is characterized by abnormally strong neuronal synchrony and is known to be associated with Parkinson's disease. Coordinated Reset (CR) stimulation was computationally designed to specifically counteract abnormal neuronal synchronization processes by desynchronization [1,2]. In the presence of spike timing-dependent plasticity (i.e., short-term synaptic weight changes) this leads to a decrease of synaptic weights and ultimately to an unlearning of abnormal synaptic connectivity and abnormal neuronal synchrony [3-5]. The long-lasting desynchronizing impact of CR stimulation has been verified in pre-clinical and clinical proof of concept studies [6]. To date, computational models were not able to reproduce the clinically observed increase of desynchronizing effects of regularly administered CR stimulation intermingled by long stimulation-free epochs. In this talk, I will discuss how this clinically important phenomenon can be computationally reproduced by also considering structural plasticity (SP) [7]. SP refers a mechanism that deletes or generates synapses to homeostatically adapt the firing rates of neurons to a set point-like target firing rate in the course of days to months (i.e., long-term changes in the number of synapses between neurons). This study highlights the crucial role of stimulation- and dosing-induced modulation of homeostatic set points in therapeutic processes [8].

References

[1]   P.A. Tass, *Biol. Cybern.* **89**, 81 (2003).
[2]   P.A. Tass, *Prog. Theor. Phys. Suppl.* **150**, 281 (2003).
[3]   M. Ebert, C. Hauptmann, P.A. Tass, *Front. Comput. Neurosci.* **8**, 154 (2014).
[4]   T. Manos, M. Zeitler, P.A. Tass, *PLoS Comput. Biol.* **14**, e1006113 (2018).
[5]   T. Manos, M. Zeitler, P.A. Tass, *Front. Physiol.* **9**, 376 (2018).

[6]   K.J. Pfeifer, J.A. Kromer, , A.J. Cook, T. Hornbeck, E.A. Lim, B. Mortimer, et al., *Front. Physiol.* **12**, 200 (2021).

[7]   S. Diaz-Pier, M. Naveau, M. Butz-Ostendorf, A. Morrison, *Front. Neuroanat.* **10**, 57 (2016).

[8]   T. Manos, S. Diaz-Pier, P.A. Tass, *Front. Physiol.* **12**, 716556, (2021).