Closed-loop regulation of the activity of delayed neural fields with only partial measurement and stimulation

Georgios Is. Detorakis, L2S, Univ. Paris Sud, Supélec, georgios.detorakis@lss.supelec.fr
Antoine Chaillet, L2S, Univ. Paris Sud, Supélec, antoine.chaillet@supelec.fr

The main motor symptoms of Parkinson's disease (PD) can be treated by the Deep Brain Stimulation (DBS) treatment, which consists in a permanent stimulation of targeted brain structures through implanted electrodes [1]. While it is known [5] that PD motor symptoms are linked to persistent beta oscillations in the subthalamic nucleus (STN), the DBS action mechanism is not yet fully understood. Several attempts have been made to optimize DBS, by relying on real-time measurements of the brain activity: see [3] for a recent survey.

Among these attempts, a firing-rate regulation strategy has been adopted in [7]: it consists in injecting a stimulation signal proportional to the low frequencies of the STN activity. This closed-loop DBS strategy was shown to effectively disrupt pathological oscillations in the basal ganglia model proposed in [6]. Nonetheless, three important practical features were neglected in that work, namely the spatial heterogeneity of the activity within basal ganglia, the impossibility to measure the activity at each point of the targeted structure, and the local nature of the influence of the stimulation signal.

In this work, we aim at deepening the analysis of this closed-loop DBS strategy by modeling the two neural populations involved, namely the STN and the external part of the globus pallidus (GPe), as neural fields. Due to its integro-differential structure, the neural field equation describes the evolution of the neural population activity not only in time, but also in space. It also takes into account the time needed for axonal transport by involving position-dependent delays. According to this model, the activity x_i of the population $i \in \{1, 2\}$ (either STN or GPe) at time t and position $r \in \Omega$ is ruled by

$$\tau_i \frac{\partial x_i(r,t)}{\partial t} = -x_i(r,t) + f_i\Big(\sum_{j=1}^{2} \int_\Omega w_{ij}(r,r') x_j(r', t - d_j(r,r'))dr' + I_i^{\text{ext}}(r) + \alpha_i(r)u(r,t))\Big), \tag{1}$$

where f_i is the activation function, $w_{ij}(r,r')$ is the synaptic weight from the position r' in population j to the position r in population i, $d_j(r,r')$ is the time needed for the activity of the j-th population at r' to reach position r due to axonal delays, and I_i^{ext} is the external input to the i-th neural population (e.g. from other brain areas). Neural fields have been used in several studies (see [2] for a survey), and a theoretical framework to study their stability has been proposed in [4] based on Krasovskii-Lyapunov functionals.

The peculiarity of the model above is that it explicitly takes into account the control signal $u(r,t)$ that arises from the implanted electrode. Since the DBS signal does not impact the whole neural population in a homogeneous manner (for instance, due to medium resistivity), it is multiplied by a function $\alpha_i(r)$, which can vanish on some portions of the population if they are situated too far from the stimulation point. We also assume that only the STN population is targeted by the DBS signal, meaning that $\alpha_2(r) = 0$ for all $r \in \Omega$ if population 2 denotes the GPe.

Similarly to [7], we take the closed-loop DBS signal proportional to the STN activity, meaning that

$$u(r,t) = -k_c(x_1(r,t) - x_1^{\text{ref}}(r)), \tag{2}$$

where k_c denotes a positive gain and x_1^{ref} is a targeted rate distribution. We stress that the implementation of this DBS signal does not require any measurement in GPe.

Our main result states that, by picking the feedback gain k_c sufficiently large, the closed-loop DBS strategy (2) globally stabilizes the nonlinear delayed neural field (1), thus impeding sustained oscillations, provided that the unmeasured and unactuated population (GPe) does not generate endogenous oscillations on its own. The latter assumption is reasonable as PD pathological oscillations are believed to be induced by too strong synaptic gains between STN and GPe, rather than by a spontaneous generation within any of these populations [6]. Numerical simulations confirm these theoretical expectations, by showing that pathological oscillations in (1) are efficiently counteracted once the closed-loop DBS signal (2) is activated.

Acknowledgement: This work has received support from ANR JCJC SynchNeuro and from the iCODE institute project funded by the IDEX Paris-Saclay, ANR-11-IDEX-0003-02.

References

[1] A.L. Benabid, P. Pollak, C. Gervason, D. Hoffmann, D.M. Gao, M. Hommel, J.E. Perret, and J. de Rougemont. Long-term suppression of tremor by chronic stimulation of the ventral intermediate thalamic nucleus. *The Lancet*, 337:403–406, 1991.

[2] Paul C Bressloff. Spatiotemporal dynamics of continuum neural fields. *Journal of Physics A: Mathematical and Theoretical*, 45(3):033001, December 2011.

[3] R. Carron, A. Chaillet, A. Filipchuk, W. Pasillas-Lépine, and C. Hammond. Closing the Loop of Deep Brain Stimulation. *Frontiers in Systems Neuroscience*, 13(112):1–18, 2013.

[4] G. Faye and O. Faugeras. Some theoretical and numerical results for delayed neural field equations. *Physica D*, 239(9):561–578, 2010.

[5] C. Hammond, H. Bergman, and P. Brown. Pathological synchronization in Parkinson's disease: networks, models and treatments. *Trends in Neurosciences*, 30(7):357 – 364, July 2007. INMED/TINS special issue–Physiogenic and pathogenic oscillations: the beauty and the beast.

[6] A.J. Nevado Holgado, J.R. Terry, and R. Bogacz. Conditions for the Generation of Beta Oscillations in the Subthalamic Nucleus-Globus Pallidus Network. *Journal of Neuroscience*, 30(37):12340, 2010.

[7] W. Pasillas-Lépine, I. Haidar, A. Chaillet, and E. Panteley. Closed-loop deep brain stimulation based on firing-rate regulation. In *Proc. 6th IEEE EMBS Conf. on Neural Engineering*, San Diego, USA, 2013.