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

{Georgios.Detorakis, Antoine.Chaillet }@lss.supelec.fr

Introduction

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 some 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 nonlinear dynamics involved, 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 showing that a stimulation proportional to STN activity efficiently disrupts pathological oscillations in a delayed neural field model of the STN-GPe network.

The STN-GPe Network Model

We describe the spatiotemporal dynamics of STN-GPe network using the following coupled neural field equation (for a survey of neural fields see [2]):

$$\tau_1 \frac{\partial z_1}{\partial t} = -z_1 + S_1\left(\sum_{j=1}^{2}\int_{\Omega} w_{ij}(r,r')z_j(r',t-d_j(r,r'))dr' + I_1(r,t) + u(r,t)\right) \quad (1a)$$

$$\tau_2 \frac{\partial z_2}{\partial t} = -z_2 + S_2\left(\sum_{j=1}^{2}\int_{\Omega} w_{ij}(r,r')z_j(r',t-d_j(r,r'))dr' + I_2(r,t)\right), \quad (1b)$$

where $z_1(r,t)$ and $z_2(r,t)$ indicate the instantaneous activity at position $r \in \Omega$ of STN and GPe respectively. Ω is a compact set, $I_1(r,t)$ is the cortical input to STN and $I_2(r,t)$ is the striatal input to the GPe. w_{ij} are the synaptic strength functions and we assume that they can be described by Gaussian functions, except w_{11} which is zero. The axonal delays d_j are described by $d_j(r,r') = \frac{|r-r'|}{c_j}$, where c_1 and c_2 are the axonal conduction velocity of STN and GPe neurons, respectively. Functions S_1 and S_2 are sigmoidal activation functions of STN and GPe neural populations, respectively.
The proposed closed-loop stimulation signal on STN is given by:

$$u(r,t) = -k_c\alpha(r)\big(z_1(r,t) - z_{ref}(r)\big), \quad (2)$$

where k_c is a positive control gain, $\alpha(r)$ is a function that defines the photosensitization of STN neurons and $z_{ref}(r)$ is a prescribed rate for the rate activity of STN. A schematic representation of our model is depicted in **Figure 1**.

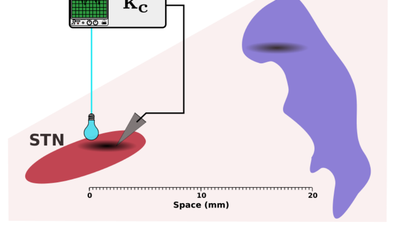

Figure 1

Theoretical Results

Theorem 1 *Consider any admissible target pattern $z_{ref}(r)$. For each $i \in \{1,2\}$, let S_i be any bounded, increasing and ℓ_i-Lipschitz function. Assume that the lateral synaptic weights in the uncontrolled population satisfy*

$$\ell_2\|w_{22}\| < 1, \quad (3)$$

and that the function α satisfies $\inf_{r\in\Omega}\{\alpha(r)\} > 0$. Then, for any $k_c > 0$ sufficiently large, the neural fields (1) *under closed-loop stimulation* (2) *is stable and, from almost all admissible initial conditions[a], its solutions exponentially converge to an equilibrium pattern [b].*

Physical interpretation Our theoretical result, Theorem 1, reveals that we can disrupt pathological oscillations in the STN-GPe network, if the intralaminar GPe neural synaptic strengths are not strong. In addition,

- The proposed closed-loop stimulation relies on STN measurements only. No real-time information about GPe is required.
- Any large gain k_c works and thus
- there is no need for precise parameter values and fine tuning.

[a] When the activations functions are bounded, we call *admissible* any initial condition that lies within their ranges.

[b] The proof is based on [4]

Simulation Details

In order to put to the test our model and our theoretical results, we conduct four numerical experiments. First of all, we discretize equation (1) using 15 nodes for the STN and 15 for the GPe. STN neurons are placed $10mm$ away from GPe neurons. Each, STN and GPe, structure has a spatial dimension of $2.5mm$, modeling a part of STN and GPe according to neurophysiological evidence [8]. In every numerical experiment, we solve numerically equations (1) to (2) and conditions proposed by **Theorem 1** are satisfied, meaning that $l_2||w_{22}|| = 1 \times 0.95 < 1$.

Numerical Experiments

Oscillations disruption

The first protocol has to do with the disruption of pathological oscillations of β-band. As it is depicted in **Figure 2** on left panel, when we apply the proposed closed-loop stimulation (at $0.5s$), pathological oscillations are disrupted. On the right panel is illustrated the control signal $u(r,t)$. These results confirm that the proposed closed-loop technique suppresses sustained oscillations.

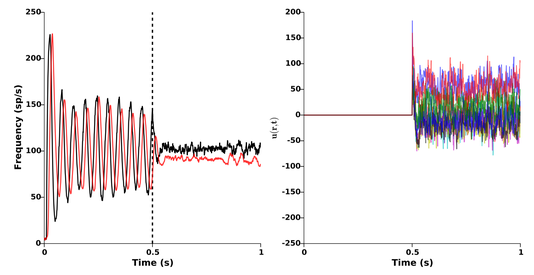

Figure 2

Effect of poor photosensitization

Next we investigate the case when only a part of the STN neurons is photosensitized. To this end we randomly stimulate 50% of STN neurons only illustrated in **Figure 3** (left panel), the oscillations are not entirely disrupted. The middle panel of the same Figure shows the spatiotemporal evolution of the neural activity of SNT-GPe network and the right panel depicts the amplitude of oscillations when we vary the percentage of photosensitized neurons. The smaller the percentage of photosensitized neurons the bigger the amplitude of oscillations.

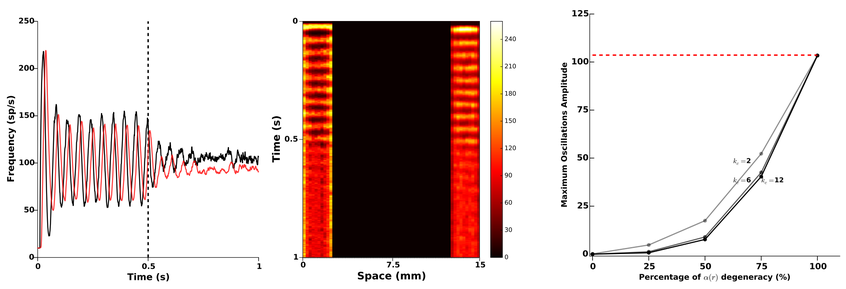

Figure 3

Single light source

In this third experiment we stimulate all the STN neurons using only one single light source. Again in this case the model is able to cope with suppressing sustained oscillations as **Figure 4** shows (left panel). This means that our proposed closed-loop method is able to work if we replace the original $u(r,t)$ signal by $u(r,t) = -k_c\int_{\Omega_1}(z_1(r,t) - z_{ref}(r))dr$, where Ω_1 is the spatial domain corresponding to STN.

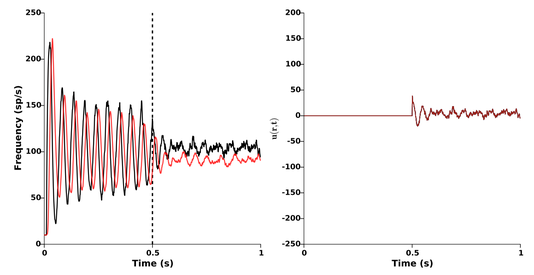

Figure 4

Effect of acquisition and processing delays

The last protocol demonstrates how acquisition and processing delays affect the proposed closed-loop DBS technique. Therefore, we introduce a processing delay of $5ms$ and a second one of $10ms$. For a $5ms$ delay, the proposed stimulation signal manages to alleviate oscillations (central panel of **Figure 5**). On the other hand, a delay higher than $8ms$ renders the stimulation unable to attenuate pathological oscillations (see the left panel). The right panel shows how different delays and different loop gains affect the amplitude of oscillations. It is apparent that a choice of large k_c provide less robustness to acquisition and processing delays. In addition long delays contribute to an enhancement of sustained oscillations.

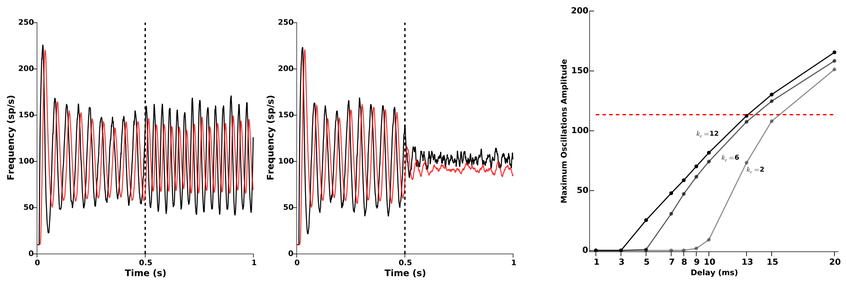

Figure 5

Conclusions

In this work we introduced a closed-loop deep brain stimulation method based on optogenetics. We showed that when the synaptic strengths of GPe neurons are not strong, we can disrupt pathological oscillations of β-band by applying a photostimulation on STN neurons. We devised four different numerical experimental protocols, where we put to the test our delayed neural field model. The stimulation is able to cope and to eliminate pathological oscillations. However, when delays coming from on-line processing and acquisition, the method may lose its therapeutic ability.

References

[1] Benabid, A.L., Pollak, P., Hoffmann, D., Gervason, C., Hommel, M., Perret, J.E., De Rougemont, J. and Gao, D.M. *Long-term suppression of tremor by chronic stimulation of the ventral intermediate thalamic nucleus*, The Lancet, 337(8738), pp.403-406, 1991.

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

[3] Carron, R., Chaillet, A., Filipchuk, A., Pasillas-Lépine, W. and Hammond, C., *Closing the loop of deep brain stimulation*, Frontiers in systems neuroscience, 7, 2013.

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

[5] Hammond, C., Bergman, H. and Brown, P., *Pathological synchronization in Parkinson's disease: networks, models and treatments*, Trends in neurosciences, 30(7), pp.357-364, 2007.

[6] Holgado, A. J. N., Terry, J. R. and Bogacz, R. *Conditions for the generation of beta oscillations in the subthalamic nucleus–globus pallidus network* The Journal of Neuroscience, 30 (37) pp. 12340–12352, 2010.

[7] Pasillas-Lépine, W., Haidar, I., Chaillet, A. and Panteley, E. *Closed-loop deep brain stimulation based on firing-rate regulation* Neural Engineering (NER), 2013 6th International IEEE/EMBS Conference on, pp. 166–169, 2013.

[8] Zaidel, A., Spivak, A., Grieb, B., Bergman, H. and Israel, Z, *Subthalamic span of β oscillations predicts deep brain stimulation efficacy for patients with ParkinsonâĂŹs disease*, Brain, 2010.