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Computing the delay margin of the subthalamopallidal feedback loop

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In the last ten years, several models of basal ganglia dynamics have been proposed in order to explain the abnormal neural oscillations that appear in Parkinson's disease. Recently, Nevado Holgado et al. [1] have shown that a two-dimensional nonlinear model of the subthalamopallidal feedback loop, which interconnects the subthalamic nucleus (STN) and the external part of the globus pallidus (GPe), exhibits oscillations in the beta band when the parameters of the model are those of the pathological state. They proposed, moreover, a simplified model for which the condition for oscillations can be computed analytically. In our work, we consider a slightly more general model of the subthalamopallidal feedback loop, that includes a self-excitation loop of the STN onto itself and allows more general activation functions. It coincides with the model of Wilson and Cowan [2], with the difference that interconnection delays are included and that the refractory period is neglected.

Our approach [3] to obtain existence conditions for neural oscillations can be separated in two steps. In a first step, the existence of equilibrium points is studied. In the absence of delays, our method gives a necessary and sufficient condition for the existence of a unique stable equilibrium, independently of the level of external inhibition applied to the system (this condition excludes the possibility of having multiple equilibria [2]). In this case, the system can be linearized around its equilibrium. In a second step, Nyquist's stability criterion is applied to the feedback loop. This criterion gives directly the maximal admissible delay in the loop. When the internal delays of the STN and of the GPe are neglected, our stability condition can be computed analytically. Otherwise, a transcendental equation must be either solved numerically or approximated. In any case, existence conditions for oscillations are obtained, without the need of integrating numerically the differential equations associated to the model.

Comparing our method to that proposed by Nevado Holgado et al., we have found that when the internal delays are small our zero self-delay approximation gives an improved analytical condition for the existence of oscillations. If the value of the internal delays is close to that of the external ones, the method of [1] gives more precise results. More surprisingly, it appears that when the gain that describes the excitation level from the STN to the GPe is small the method of [1] gives very good results, even in the absence of internal delays. Another observation that comes out from our study is the influence of the STN's self-excitation gain on stability. This gain was not considered in [1]. It appears, however, that it has an impact on the existence of multiple equilibria (a point that was already observed in [2]) and on the delay margin of the system.

[1] A. Nevado Holgado, J. Terry, and R. Bogacz. Conditions for the generation of beta oscillations in the subthalamic nucleus-globus pallidus network, *The Journal of Neuroscience*, Vol. 30, No. 37, 12340-12352, 2010.

[2] H. Wilson and J. Cowan. Excitatory and inhibitory interactions in localized populations of model neurons, *Biophysical Journal*, Vol. 12, No. 1, 1-24, 1972.

[3] W. Pasillas-Lépine. Equilibrium, stability, and delay margins of Wilson and Cowan's time coarse graining model. Submitted to *Neural Information Processing Systems*, 2011. Preprint available upon request.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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