# Basal Ganglia Model Network for Motor Control in Healthy Subjects and Parkinsonian Patients.

**Leonid L. Rubchinsky[1], Nancy Kopell[2], Karen A. Sigvardt[3]**

[1] Center for Neuroscience, University of California, 1544 Newton Ct., Davis, CA 95616
lrubchinsky@ucdavis.edu
[2] Center for BioDynamics and Department of Mathematics, Boston University, Boston, MA 02215
nk@bu.edu
[3] Center for Neuroscience and Department of Neurology, University of California, Davis, CA 95616
kasigvardt@ucdavis.edu

## Abstract

We propose a model of basal ganglia network for control of motor programs. The network organization corresponds to the hypothesis that the basal ganglia facilitate the desired motor program and inhibit competing motor programs that interfere with the desired movement. Such a framework is supported by data from numerous experimental studies. The network consists of subthalamic and pallidal (both external and internal segments) units, with inputs from the cortex and the striatum. Inputs from the striatum and cortex are represented as external signals to our model network. Network organization includes functional units within the basal ganglia nuclei that correspond to the desired motor program and the unwanted motor programs. A single compartment conductance-based model represents each unit. Dynamics of the model network is examined and the relationship between these dynamics and the motor behavior observed in normal subjects and the hypokinetic behavior in parkinsonian patients is considered.

## Summary

Current paradigmatic models of Parkinson's disease motor symptoms ("standard model") are steady-state models based on the hypothesized action of the "direct" and "indirect" anatomical pathways. The explanatory and predictive power of these models has acknowledged limitations (Obeso et al., 2000; Bar-Gad and Bergman, 2001; Bergman and Deuschl, 2002). Development of computational models of the basal ganglia to date have focused primary on higher-level models of the role of the basal ganglia in reinforcement learning. The present work develops a biophysically motivated dynamic model of basal ganglia networks responsible for control of motor programs and for its pathology in Parkinson's disease.

The standard model of the basal ganglia is a so called "box-and-arrow" model. It includes the direct inhibitory pathway from striatum to internal segment of Globus Pallidus (GPi), which is inhibitory, and the indirect pathway from striatum through external segment of Globus Pallidus (GPe) to subthalamic nucleus (STN) to internal segment of pallidum, which is excitatory. Activation of the appropriate motor program would occur when the thalamus is released from its tonic inhibition by GPi, allowing facilitation of the

appropriate region of cortex. According to the model, the release of dopamine has opposing modulatory effects on cortical excitation of the two subpopulations of striatal neurons, facilitating the striatal neurons in the direct pathway via D1 receptors and inhibiting the striatal neurons in the indirect pathway via D2 receptors. The deficient initiation and slow execution of motor tasks would then result from an imbalance between the two pathways due to the loss of dopamine, underactivity of the direct pathway and overactivity of the indirect pathway. The overall effect would, therefore, be hyperactivity in GPi and a consequent increase in inhibition of the thalamus.

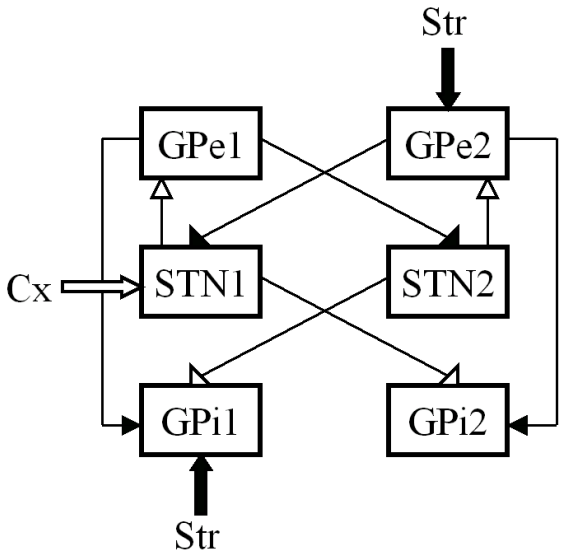
The standard model is attractive because it provides a unified framework for understanding both hyperkinetic (e.g. Huntington's Disease) and hypokinetic (e.g. Parkinson's disease) extrapyramidal disorders. However, the model fails in a number of ways. For example, the model correctly predicts that a lesion to GPi in parkinsonian patients would enable movement by removing the supranormal inhibition of the thalamus exerted by GPi. But the model also predicts that lesions in GPi in normals would produce dyskinesias. However, lesions in GPi in humans and in normal monkeys do not result in dyskinesia. And in patients with Parkinson's disease, lesions in GPi reduce L-DOPA induced dyskinesias. More importantly, the standard model does not connect the cellular properties of basal ganglia nuclei with its dynamics and does not explain how its function corresponds to behavior. The aim of this work is to develop a modeling approach that will help answer these questions.

The proposed network is motivated by the hypothesis that the basal ganglia focuses disinhibition of the thalamus, facilitating desired movement, and controls competing motor programs, inhibiting those that can interfere with the voluntary movement being executed (e.g., Mink and Thach, 1993; Mink, 1996). More recent experiments support this framework (Wenger et al., 1999; Boraud et al., 2000). Direct and indirect pathways remain in our network, but our focus is on function. The model builds on the idea of sets of cells whose activation corresponds to wanted and unwanted movements, cell assemblies that change dynamically in time.

The organization of the network is presented in the Figure below. The network consists of GPe, STN and GPi units, with inputs from the cortex and the striatum. The cortex and striatum determine which cells in their target structures are to be activated or not. Inputs from the striatum and cortex are represented as external signals to our model network with assigned timing and spatial distributions appropriate to its state and are not derived from self-consistent modeling.

For the functional units of GPe, STN and GPi, wegroup together those cells, which are, at that moment, chosen to participate in some motor program (wanted) and those that are not (unwanted). The connectivity of the circuit is based on the known anatomy and connectivity of BG. What we have added to this proposed circuit is the way in which the wanted and unwanted subsets of each structure are connected to one another. That is, the circuit represents our current hypothesis of how the flow of signals goes through these

structures. The connections are chosen so that the distinction between wanted and unwanted functional units in the network will be sharpened.




Every functional unit of the basal ganglia model network is represented by conductance-based models of subthalamic and pallidal cells. These conductance-based models are based on models developed by Terman and colleagues (2002) for modeling studies of activity patterns in basal ganglia. Besides standard sodium, potassium and leak currents, the model incorporates low threshold T-type calcium current, high-threshold calcium current, and calcium-activated voltage independent afterhyperpolarization potassium current, which are responsible for the oscillatory properties of the cells in *in vitro* experiments with isolated cells (Bevan and Wilson, 1999) and cellular cultures (Plenz and Kitai, 1999).

We studied how the proposed basal ganglia model network behavior is consistent with the hypothesis of facilitation of "wanted" motor program/inhibition of "unwanted" motor programs. Modification of the network, that can model the parkinsonian basal ganglia (characterized by the loss of specificity of neuronal responses), can lead to abnormal patterns of activation of GPi functional units - simultaneous inactivation of conflicting units would correspond to the parkinsonian symptom of rigidity, and delayed deactivation would correspond to akinetic behavior. Switching between motor programs in model network for normal and parkinsonian basal ganglia are compared with experimental data obtained from normal subjects and parkinsonian patients.