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Inst, IUPUI and Indiana Univ School of Medicine, 402 N. Blackford Street, Indianapolis, IN 46202, and Karen A Sigvardt, Center for Neuroscience and Dept of Neurology, University of California, Davis, 1544 Newton Ct, Davis, CA 95616. Modeling pathophysiology of motor symptoms in Parkinson's disease.

The origin of the motor symptoms in Parkinson's disease (PD) remains a poorly understood subject in spite of extensive studies of basal ganglia and other brain structures in PD patients and animal models of PD. In the present work we consider the development and dynamics of mathematical models for the major symptoms of PD: akinetic behavior (slowness of movement) and rest tremor. The goal of this project is to develop a biophysically based mathematical model of the basal ganglia-thalamocortical networks that integrates available biological data and helps to understand cellular and networks mechanisms underlying major symptoms of the disease. Based on the available experimental data on basal ganglia anatomy and physiology and using conductance-based models of basal ganglia neurons (i.e. systems of ordinary differential equations) we consider the minimal networks, which may be involved in the generation of motor symptoms. We study how tremor and akinesia arises due to the pathological properties of these networks, and how the symptoms depend on the cellular and network parameters. These models suggest biologically plausible mechanisms for the origin of the akinetic behavior and tremor and allow to make testable predictions with potential implications for treatment strategies. (Received August 26, 2006)