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## A simplified model of dopaminergic neuron Sorinel Adrian Oprisan

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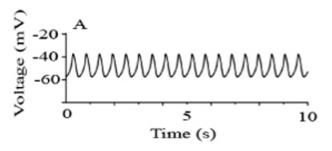
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#### Introduction

A minimal model of a dopamine cell in vitro in the presence of tetrodoxin (TTX) and tetraethyl ammonium (TEA) was developed to simulate two types of subthreshold oscillations: the slow oscillatory potential (SOP - see Figure 1A) and the square wave (Figure 1B) that can be produced by the abolition of the SOP by apamin. The L-type calcium current drives both types of oscillation. The small conductance potassium channel repolarizes the SOP, and we propose that the ether-a-go-go related potassium channel repolarizes the square wave. We further suggest that the role of this current in vivo is to relieve depolarization block. The model predicts that blocking the ether-a-go-go current will elongate the plateau of the square wave and blocking the hyperpolarization-activated potassium current shortens the period of oscillations. In addition, the model predicts that blocking the ether-a-go-go current will speed up the SOP. The model also predicts that calcium chelation converts SOPs into square waves by blocking the increase in the small conductance (SK) current. Multiple-parameter bifurcation diagrams were used to investigate the properties of the firing patterns generated by our model (Figure 2).

#### Model

The minimal model of a single-compartment Hodgkin-Huxley (HH)-type parallel conductance membrane contains the following currents: an L-type calcium current, a small conductance potassium current, a slowly-activating and fast-inactivating potassium current (tentatively identified as a ether-a-go-go current), an after-hyperpolarization current, and a linear background current (see [1,2] for detailed equations). The fast sodium current blocked by TTX and the delayed rectifier blocked by TEA are not modeled. Calcium extrusion was modeled by a nonelectrogenic pump, and buffering was modeled by assuming a fixed fraction of free calcium in the cytosol. We assumed that exogenous buffers such as BAPTA reduced this fraction [1]. We found that regardless of the values of other synaptic conductances, the model undergoes Hopf bifur-



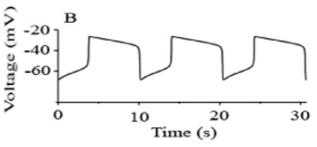
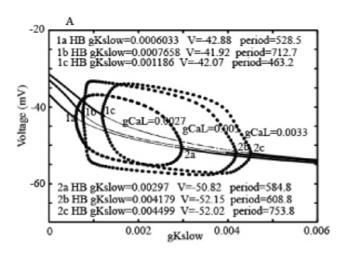


Figure I
Model-generated SOP (A) with a period of the order of 100 ms, and slow (about 10 s period) square wave oscillations (B) obtained from SOP by blocking the SK current.



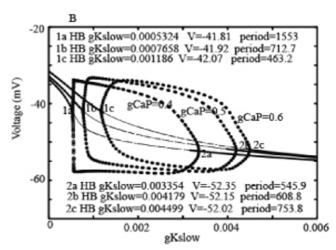


Figure 2
The bifurcation diagram for SOP reveals two Hopf bifurcation (HB) points that determine the transition to square wave oscillations. The common control parameter was the conductance of the slow potassium current and the Hopf bifurcation persisted for both L-type current variability (A) and calcium pump (B).

cations leading to a transition from a stable steady state to a stable limit cycle. The SOP period at supercritical Hopf bifurcation points is in the range of 500 to 700 ms and gradually increases to about 1500 ms.

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