Computational Modeling of the Regulation of Pacemaker Frequency in Dopamine Neurons

Marco Huertas and Carmen Canavier

Department of Cell Biology and Anatomy, LSU Health Sciences Center, New Orleans

Midbrain dopamine neurons are important for motivation and movement . Abnormal dopaminergic signaling has been implicated in many diseases including Parkinson's, schizophrenia, bipolar disorder, attention deficit disorder and drug addiction. The firing pattern of dopamine neurons in behaving animals has been linked to reward-related signals. Therefore it is important to understand how the firing pattern in these neurons is generated. These neurons are pacemakers when isolated from their normal synaptic inputs, and can be modeled as nonlinear oscillators due to their complement of ionic conductances with a nonlinear dependence on membrane potential. We use the simulator package NEURON to simulate the electrical activity of dopamine neurons with spatially extended dendritic processes under various experimental conditions. This includes data gathered by blocking the native fast sodium conductance and replacing it with a virtual conductance using a real time interface between a computer and a living neuron. We show that the subthreshold component of the sodium current contributes to setting the pacemaking rate, and that this current must be distributed over the dendritic tree in order to replicate the experimental data.