Modeling Substantia Nigra Pars Reticulata Responses to Pallidal and Striatal Inputs Using a Two Compartment Model

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Introduction

- In the brains of vertebrates, a subcortical region called the *basal ganglia* (**BG**) is thought to be involved in decision making and action selection.
- Within the rodent brain, the *substantia nigra pars reticulata* (**SNr**) serves as the primary output nucleus of the basal ganglia.
- The SNr receives converging $GABA_A$ mediated inputs from the direct and indirect pathways within the BG.
- We modeled the integration of these converging GABA dynamics by SNr neurons.

Methods

- We devised and analyzed a computational model of an SNr neuron that includes somatic and dendritic compartments, relevant GABAergic inputs, and other pertinent factors including intracellular chloride dynamics.
- Our model is built upon the Hodgkin-Huxley framework, where I_{APP} is the applied current, I_x is the current generated by a channel for the ion x, and V_S and V_D are the membrane potentials and C_S and C_D are the capacitances for the somatic and dendritic compartments respectively:

$$C_S \frac{dV_S}{dt} = -\left(\Sigma_{n \in S^*} I_n\right) + I_{APP},$$

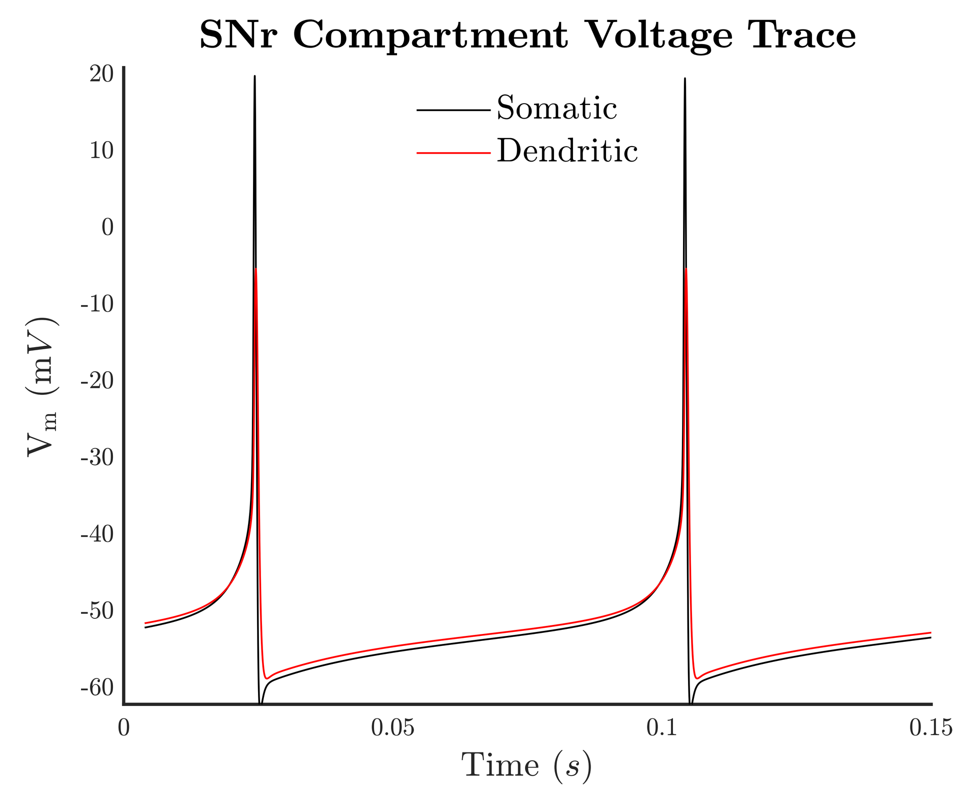
$$S^* = \{\text{Na, NaP, K, Ca, SK, Leak, GABA, DS}\}$$

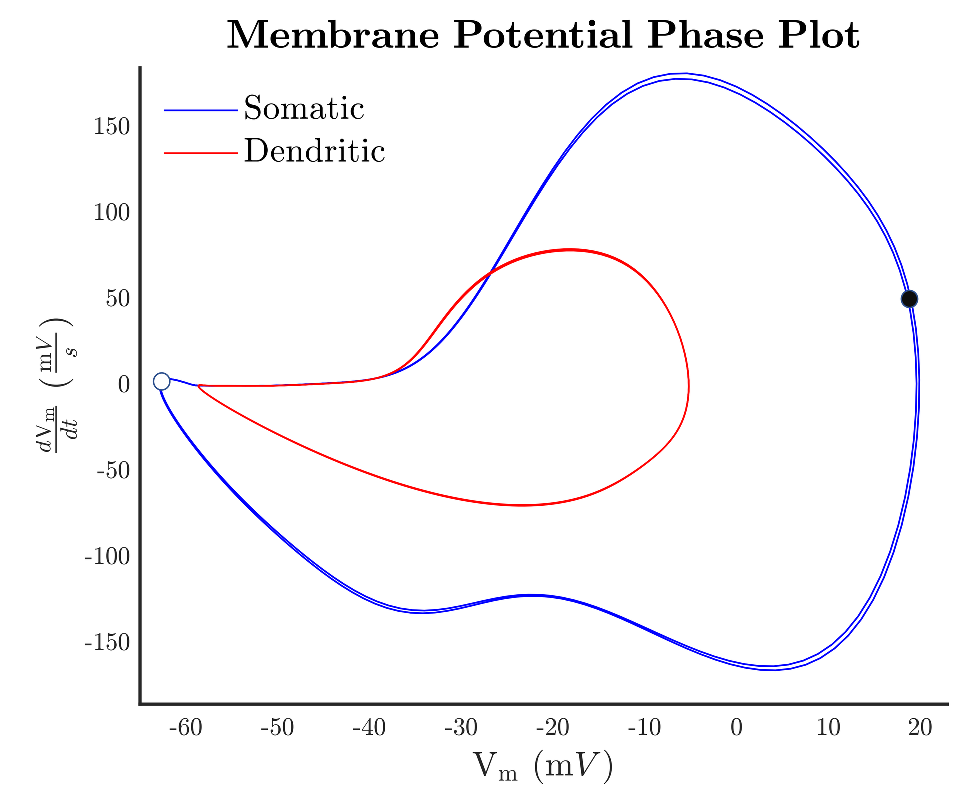
$$C_D \frac{dV_D}{dt} = -\left(\Sigma_{n \in D^*} I_n\right),$$

$$D^* = \{\text{TRPC3, GABA, SD}\}$$

- Parameters and their values, as well as gating equations and additional differential equations are not included.

Two Compartment SNr Model Neuron Produces Appropriate Dynamics

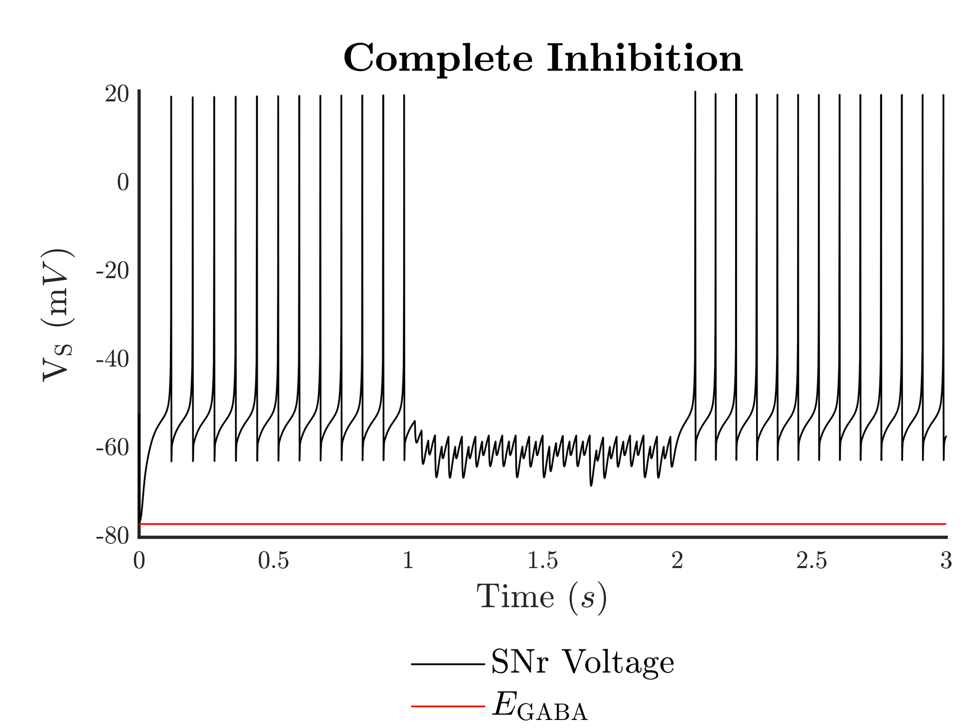


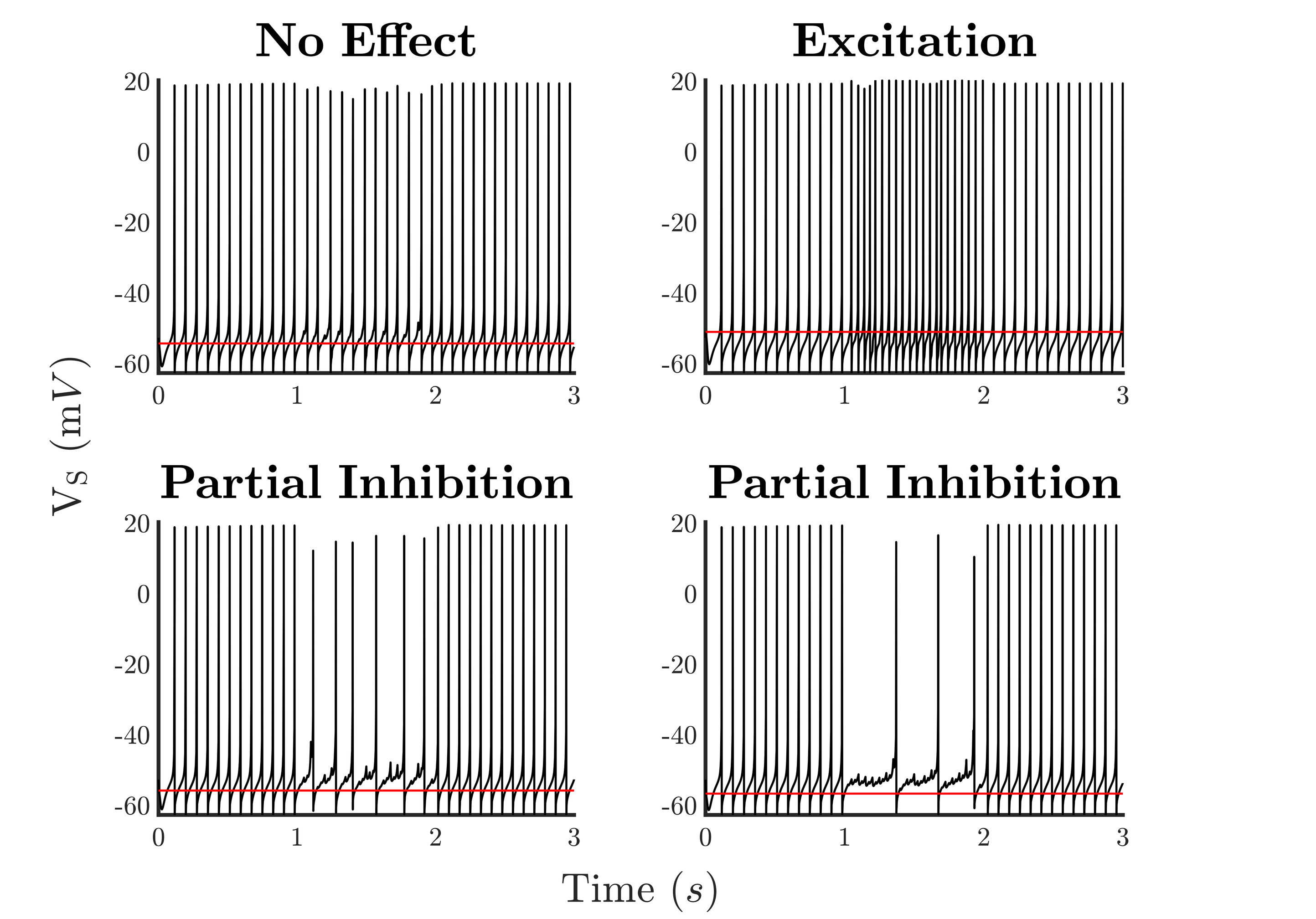


- These two plots show the model exhibits the expected behavior of an action potential.
- In the membrane phase plot, the white dot is the point *afterhyperpolarization* (**AHP**). The black dot is *spike height* (**AP Peak**).

GPe Stimulation Affects Firing Rate Based on E_{GABA} & Cl^-

- The *globus pallidus* (**GPe**) is a segment of tissue within the BG that connects to the soma of SNr neurons and is responsible for the indirect pathways in the BG.
- We simulated optogenetic stimulation of the somatic synapses of the SNr neurons by the GPe for the duration of one second at 40 Hz.
- The effect of this stimulation on the SNr neuron's somatic behavior depended upon the value of E_{GABA} and the intracellular Cl^- levels.
- g_{KCC2} and g^{Tonic}_{GABA} are the conductances associated with a tonic chloride load and the extrusion capacity of Cl^- respectively. The figure to the right shows the result of low E_{GABA}, small Cl^- conductance, and high Cl^- extrusion. The neuron is unable to fire.





- The four plots above show four different possibilities as a result of GPe stimulation and differing parameters.
- These reaffirm that stronger somatic chloride presence and greater GABA potential increase the compartment firing rate.

Future Directions

- We are interested in how identical populations of SNr neurons can maintain differing firing rates without continuous input. Our next steps are to add synaptic coupling to this model, specifically looking at two coupled SNr neurons.
- We will analyze the effects of a shift in E_{GABA} in the two-neuron model and see whether this results in a difference in firing rate for the two neurons.
- Validate model by measuring intracellular Cl^- and E_{GABA}.

Acknowledgements

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