

Poster presentation

Characterizing the heterogeneity of globus pallidus neuron behavior by comparing a real neuron database with model databases of varying conductance parameters

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Background

The function of brain networks is highly dependent on the dynamical properties of single neurons, whose activity ranges from complex spontaneous activity patterns such as oscillations and bursting, to a variety of synaptic response patterns serving functions such as coincidence detection or rebound firing. These dynamical properties vary in time through modulation and plasticity, and are also heterogeneous across individual neurons of the same type. Commonly, neurons show two to five-fold variability in the density of voltage-gated conductances, which accounts for large variations in dynamical behavior.

The globus pallidus (GP) is dominated by a single morphological type of GABAergic projection neuron, which shows patterns of spiking ranging from strongly bursting to more regularly firing *in vivo*. The activity of different neurons is uncorrelated in normal animals, but in Parkinsonian states, activity switches to synchronous bursting. The degree to which single neuron properties contribute to the diseased activity pattern has not been addressed.

We study the composition of intrinsic properties that yields the electrophysiology recorded from rat GP neurons in slice. The GP population provides heterogeneous electrophysiology that can be addressed by modeling. Finding intrinsic properties of GP neurons and their distribution is a crucial step in understanding larger-scale

phenomena such as network oscillations and inter-nuclei synchronization.

Methods

We use the PANDORA Matlab Toolbox to automatically determine electrophysiologic measures of real and model GP neurons from voltage traces. These measures are collected in databases (DBs), allowing quantitative comparisons between neurons (e.g., between model and real neurons). The physiology DB (physDB) contains recordings from 146 real GP neurons. The model DBs contain variations of our GP model that consists of 500 – 600 compartments in three different morphological reconstructions, where each compartment has 9 conductances. Each conductance can be scaled using a maximal conductance parameter, and its dynamics are governed by activation, inactivation and time constant curve parameters. In earlier work, we analyzed a ~100,000-model DB by varying the maximal value of the model's nine conductances (mcDB). In the present study, we compare earlier results with a model DB obtained by varying the half-activation voltage parameter of selected conductance activation and inactivation curves (haDB). We used a brute-force approach to scan the entire parameter space to identify all regions that give physiologically realistic models and understand parameter effects throughout the specified range. mcDB was obtained by choosing 3 – 4 levels of each of the nine maximal conductances in a geometric scale, whereas haDB was obtained by shifting the curve

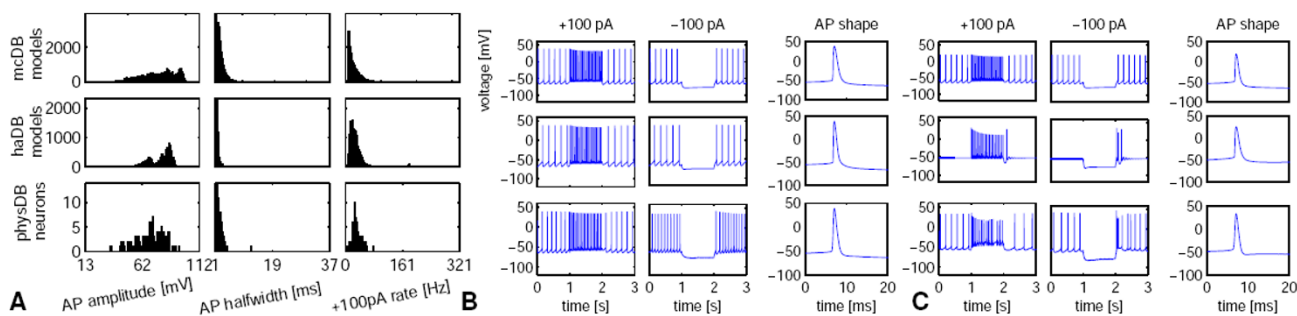


Figure 1

Matching real and model neuron traces. **(A)** Action potential (AP) amplitude, width, and firing rate measure distributions from the two model neuron DBs are similar and match distributions from real neurons. **(B)** Raw traces of matching real and model neurons. **(C)** A model in the haDB is superior in matching AP amplitude decay.

half-activations by +/- 5 mV. The measures of models in both model DBs are matched against the measures of neurons in physDB. Each model DB is evaluated for its quality of representing the electrophysiological heterogeneity found in real GP neurons.

Results and conclusion

Preliminary analyses revealed that distribution of model measures obtained by shifting the half-activation and by varying maximal conductance were similar (Fig. 1A), and both manipulations provided good matches to the electrophysiological characteristics of the recorded GP neurons (Fig. 1B). A formal analysis of the relationship between the conductance and half-activation parameters was consistent with the view that these parameters cause common effects within limited ranges of membrane voltage. We found specific cases where each manipulation had its advantages in obtaining realistic behavior (Fig. 1C). We conclude that it is equally possible that GP heterogeneity is caused by a continuous distribution of either maximal conductance (ion channel density) or half-activation curve shifts (change in ion channel voltage-sensor sites).

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