BMC Neuroscience

Poster presentation

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Systematic selection of model parameter values matching biological behavior under different simulation scenarios

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from Seventeenth Annual Computational Neuroscience Meeting: CNS*2008
Portland, OR, USA. 19–24 July 2008

Published: 11 July 2008

BMC Neuroscience 2008, **9**(Suppl 1):P53 doi:10.1186/1471-2202-9-S1-P53

This abstract is available from: http://www.biomedcentral.com/1471-2202/9/S1/P53

In this work, we systematically explore a 12-dimensional parameter space of a 2-compartment model of the AB (anterior burster) neuron, which is one of the two cells that form the pacemaker kernel in the pyloric network in the lobster stomatogastric ganglion (STG). Our computational exploration started with a hand-tuned AB model [1] and systematically varied maximal conductances of membrane currents. Every parameter set for an individual model neuron was simulated and classified as functional if it produced biologically realistic bursting activity. Specifically, we were looking at the period, burst duration, spike and slow wave amplitude, number of spikes per burst, spike frequency, and after-hyperpolarization potential, which all had to be within limits determined in our physiological experiments. Furthermore, in order to be classified as "good," the models had to exhibit proper responses to STG deafferentation (*i.e.*, neuromodulator deprivation) as well as current injections both in the presence and in the absence of neuromodulation. The above selection criteria were applied in a step-by-step fashion, meaning that only the models deemed "good" in the previous step were tested in the next. After applying all the criteria, not only have we determined that many different parameter sets performed successfully under all tested conditions, but we have also found that application of just a subset of the selection criteria was often enough to almost fully constrain the model parameters and application of additional criteria did not significantly reduce the extent of the model's solution space. In order to further analyze this "saturation effect," rather than utilizing the step-by-step approach, we have re-simulated models in our database for all testing criteria. This allowed us to draw conclusions about the relative selectiveness of particular criteria as well as to analyze overlapping regions between subsets of models that simultaneously fulfilled some, but not all, conditions. Due to this approach, we were able to pinpoint parameter values that are crucial for a proper functioning of a model under each of the simulation scenarios separately, which helps explain which maximal conductances of particular membrane currents are important for a given type of activity.

Acknowledgements

Support contributed by: Burroughs-Wellcome Fund CASI Award to AAP. NIH MH60605 to FN.

References

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