BMC Neuroscience



Poster presentation

Open Access

Database analysis of a computational model of an elemental oscillator in the leech heartbeat neuronal network

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from Eighteenth Annual Computational Neuroscience Meeting: CNS*2009 Berlin, Germany. 18–23 July 2009

Published: 13 July 2009

BMC Neuroscience 2009, 10(Suppl 1):P263 doi:10.1186/1471-2202-10-S1-P263

This abstract is available from: http://www.biomedcentral.com/1471-2202/10/S1/P263

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Background

The rhythmic activity of the heartbeat neuronal network of the leech is based on pairs of inhibitory interneurons that make reciprocal spike-mediated and graded synapses across the ganglion midline [1]. In this work, we modeled such a pair of HN(4) reciprocally inhibitory interneurons (Figure 1) with a half-center oscillator (HCO) model. We aim to investigate the changes in this model's oscillatory activity and bursting characteristics based on cellular and synaptic parameters. To achieve this, we varied selected parameters in all combinations by using a brute-force approach and built a database of the resulting model characteristics following earlier work [2,3].

Methods

We represented the individual neurons as single isopotential compartments with Hodgkin and Huxley type intrinsic and synaptic membrane conductances. The model differential equations were integrated by using the exponential Euler method with a time step of 0.1 ms [1]. For our parameter search, we varied eight parameters in both neurons: the maximal conductances of the spike-mediated synapse, graded transmission synapse, and of the persistent Na⁺, slow Ca²⁺, leak, hyperpolarization-activated (*h*), and persistent K⁺ currents, across of 0, 25, 50, 100, 125, 150, and 175 percent of their canonical values, and the leak reversal potential across -0.07 V, -0.065 V, -0.06 V, -0.055 V, and -0.05 V, resulting in a parameter space of 10,485,760 models. After changing a parameter, a model was run for 100 s to allow the system to establish stable

activity, and then, it was run for another 100 s, from which the data were recorded and analyzed. The cycle period was measured as the time between the middle spikes of two consecutive bursts. The HCO model was classified as either bursting, spiking or silent.

Results

We performed all the simulations. However, as a preliminary step in the analysis of the model database, we selected a random subset of 10,000 simulations from the entire set, for which we build a SQL database table [2,3]. Approximately 37% of these simulations have both cells as being silent, 30% of them have both cells spiking, and 17.5% have both cells bursting with standard alternating HCO activity. The rest of the simulations do not have symmetric activity in the two model cells. We will now use this sample and then the entire database to ask fundamental questions about HCO activity. For example, we will subdivide the bursting HCOs in to those in which the component cells are intrinsically silent, spiking or bursting, and then, ask whether oscillators of these different types respond to parameter changes similarly. We will be particularly interested in parameter changes that correspond to known neuromodulations such as the modulation of *h* current by myomodulin [4].

Acknowledgements

This work was supported by the National Institute of Neurological Disorders and Stroke Grant NS024072 to R.L.Calabrese.

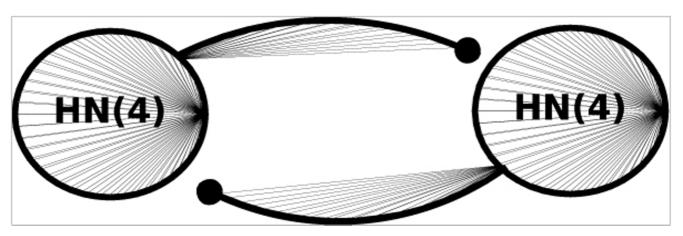


Figure I Elemental Oscillator Model.

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