Analyzing how varying neuronal parameters influence network activity using a database of computational models of a half-center oscillator

Anca Doloc-Mihu*, and Ronald L. Calabrese

1 Department of Biology, Emory University, Atlanta, USA

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. Here, we modeled such a pair of HN(4) reciprocally inhibitory interneurons, known as a half-center oscillator model [1]. We aim at investigating 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.

For our parameter search, we varied eight parameters in both neurons: the maximal conductances of the spike-mediated and of graded transmission, and of the persistent Na\(^+\), slow Ca\(^{2+}\), 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 \(-70\) mV, \(-65\) mV, \(-60\) mV, \(-55\) mV, and \(-50\) mV, 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.

We performed all the simulations and we built a SQL database table for their firing characteristics [2,3]. We used the entire database to ask fundamental questions about the activity of half-center oscillators. First, we subdivided the models in to those in which the component cells are intrinsically silent, spiking or bursting, and then, asked whether or not oscillators of these different types responded to parameter changes similarly.

The results we have so far show that in approximately 36.46% (3,823,240 simulations) of the models both cells were silent, in 27.72% (2,906,249) of them both cells were spiking, and in 22.03% (2,310,359) both cells were bursting. The rest of the simulations (13.79% or 1,445,912) did not have symmetric activity in the two model cells. Out of the bursting models, in 18.96% (438,041) both cells showed irregular activity, in 18.19% (420,307) the component cells produced spikeless plateau potentials, in 8.18% (189,041) the two cells showed asymmetric bursting activity, and in 54.67% (1,262,970) both cells were bursting with standard bursting activity. We will now use this last sample of bursting models and then the entire database to ask mechanistic questions about their alternating activity. We will be particularly interested in parameter changes which correspond to known neuromodulations such as the modulation of h current by myomodulin [4].

Supported by NS024072.