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Half-center oscillator computational models: the influence of neuronal parameters

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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 ganglionic midline. Here we build upon our previous research, where 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 eight parameters in all combinations by using a brute-force approach, which resulted 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.

We performed all the simulations and we built a SQL database table for their firing characteristics [2,3]. Now, we use the entire database to ask fundamental questions about the activity of half-center oscillators. First, we subdivide the models into those in which the component cells are intrinsically silent, spiking or bursting, and then, ask whether or not oscillators of these different types respond 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) 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 show symmetric activity in the two model cells. Out of the bursting models, in 18.96% (438,041) both cells showed irregular activity (Figure 1 A), in 18.19% (420,307) the component cells produced spikeless plateau potentials (Figure 1 B), 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 (Figure 1 C). We will now use this last sample of bursting models and then the entire database to ask mechanistic questions about their alternating

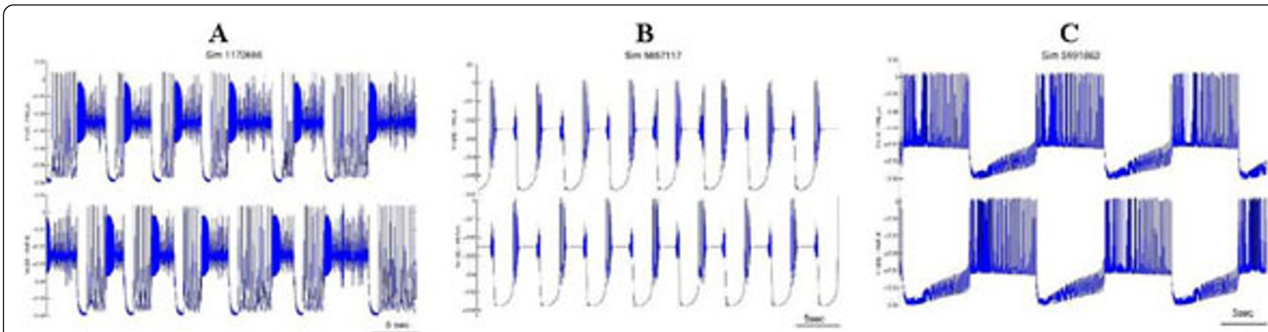

Figure 1 Half-center computational models.A. Irregular; **B**. Plateau; **C**. Regular.

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activity. We will be particularly interested in parameter changes which correspond to known neuromodulations such as the modulation of h current by myomodulin [4].

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