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Systematic computational exploration of the parameter space of the multi-compartment model of the lobster pyloric pacemaker kernel suggests that the kernel can achieve functional activity under various parameter configurations

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The pyloric network in the lobster stomatogastric ganglion (STG) produces rhythmic activity generated by a pacemaker group of electrically coupled neurons AB (anterior burster) and PD (pyloric dilator). The AB neuron is an intrinsic burster and is smaller than the two PD neurons, which can either spike tonically or burst if isolated from AB. We explored the 23-dimensional parameter space of a 4-compartment model of this pacemaker kernel to examine why it includes two types of neurons with different properties, and how its behavior depends on their cellular and synaptic properties. The model consisted of one AB coupled to one PD model neuron, each with a somato-neuritic and an axonal compartment. Our computational exploration started with a hand-tuned pacemaker model [1] and systematically varied maximal conductances of membrane currents, axial conductances, and the electrical coupling strengths. To reduce computation time, the parameter space of each individual neuron was first explored separately. Every parameter set for an individual model neuron was simulated and classified as functional if it produced biologically feasible spiking or bursting (for PD) or bursting (for AB) activity. Specifically, we were looking at the period, amplitude, burst duration, number of spikes per burst, and spike frequency, 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 (also determined in our experiments). Functional single neuron parameter combinations were then joined with a range of coupling strengths and again tested with current injections and model deafferentation. Many different parameter sets performed successfully under all tested conditions. This suggests that the properties of a pacemaker kernel with multiple neurons do not have to be narrowly tuned to achieve functional and robust pacemaker output. Furthermore, our step-by-step approach to selection of "good" models, allowed us to determine criteria that are crucial for classification (*e.g.*, proper activity with and without neuromodulation) and others that seem redundant (*e.g.*, response to current injections).

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References

1. Soto-Treviño , *et al.*: **Computational model of electrically coupled, intrinsically distinct pacemaker neurons.** *J Neurophysiol* **94**:590-604.