Modeling the effects of neuropeptide C-type allatostatin (AST-C) on the cardiac ganglion of lobsters using conductance based models in xoltol

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Central pattern generators (CPGs) consist of networks of neurons that produce patterned outputs, allowing living organisms to perform essential daily tasks, such as breathing, eating, and maintaining rhythmic heart beats (Dickinson, 2006; Dickinson et al., 2018; Wiwatpanit et al., 2012). Researchers have found that CPGs are flexible and can generate motor responses without sensory input (Marder and Bucher, 2001; Cooke, 2002). The American lobster (*Homarus americanus*) contains the cardiac ganglion (CG)— a simple neuronal network that serves as a useful model of CPGs. The CG typically consists of 9 neurons including small pacemaker cells as well as large motor neurons, each contributing to heart contractions (Cooke, 2002).

While CPGs generate rhythmic bursts without sensory input, neuromodulators are required for the alteration of CPG output in response to environmental variability. These molecules— oftentimes neuropeptides— increase the specificity of motor outputs that CPGs generate (Marder and Bucher, 2001). The American lobster has been found to contain over 250 neuropeptides, which have many structural differences potentially affecting contraction outputs (Christie et al., 2010). Among the numerous neuropeptides in *H. americanus*, the allatostatins have been identified to have significant effects on contraction amplitude and frequency (Dickinson et al., 2014; Dickinson et al., 2018; Wiwatpanit et al., 2012). The C-type allatostatin (AST-C) has been shown to affect the cardiac system of *H. americanus*, serving as a circulatory hormone as well as being released locally via autocrine and paracrine signaling (Christie et al., 2010)

Over the course of this summer, I first created a simplified "conductance based" model of the CG. Conductance based models allow researchers the ability to control precise properties (i.e. time constants and activation/inactivation equations) associated with the ion channels present in many CG networks. Thus, one is able to alter the conductance properties in order to generate the neuronal network output they intend to receive. My model included one Large Cell (LC) and one Small Cell (SC), connected via an electrically coupled synapse. The electrical synapse is a biologically realistic component of neuronal networks that enables the LC and SC to burst in a synchronous fashion. By adjusting the conductances present in my cells, I was able to create a multicompartment model that mimicked physiological recordings from Ball et al. 2010 as well as Prinz et al. 2003 (this data represented output from the stomatogastric network in crabs).

Once solidifying my model simulating neuronal activity, I proceeded to model the effects of AST-C modulation on the CG. In order to induce a drastic decrease in contraction frequency— one of the neuronal network outputs associated with AST-C— I methodically altered certain ion channel properties of my conductances (i.e. time constants and activation/inactivation equations). Furthermore, by significantly increasing the maximal conductance of my A-Type potassium conductance— a channel property involved in the time period between bursting activity of the neuron— I was able to generate a decrease in contraction frequency by approximately -33% (Wiwatpanit et al., 2012). In addition, I was able to generate alternative outputs in other burst parameters including an increase in the number of spikes per burst as well as a slight increase in burst duration. While CG output in conjunction with AST-C modulation has been found to be rather inconsistent, I was able to match the heart preparations that generated a consistent decrease in contraction frequency.

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Citations

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