Mechanisms of Stretch Feedback and Interactions with Neuromodulators in the Cardiac Ganglion of the American Lobster, *Homarus americanus*
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**Central Pattern Generators**

Organisms produce rhythmic behaviors through neural networks, which control rhythmic motor behaviors. These complex behaviors can be modulated through multiple levels, including the pattern generator itself, sensory feedback, and the response of the muscle to a given pattern of motor output. The cardiac ganglion (CG) of the American Lobster, *Homarus americanus* is a central pattern generator that consists of two oscillatory groups of neurons: 4 pacemaker cells and 5 or motor neurons, which are electrically and chemically coupled (Hartline, 1967).

**Stretch Response**

The degree of stretch upon heart muscle contraction (the feedback information) is sent to the CG through stretch sensitive dendrites and acts through the motor neurons and the pacemaker cells. Since the CG causes the heart to contract, it determines the whole heart contraction cycle period. Therefore, previous experiments found that tonic stretch elicits a decrease in contraction cycle period in the majority of whole hearts. However, stretch occasionally actually increases cycle period in some lobster hearts. Therefore this stretch feedback is more complex than expected (Harmon, 2014).

**SGRN**

In addition to this intrinsic stretch modulation, neuropeptides, such as SGRNFLRFamide (SGRN), modulate the neurogenic lobster heartbeat as well. SGRN is interesting in specific because the peptide has opposing effects on cycle frequency in the whole heart and the isolated CG. At lower concentrations the heartbeat tends to increase the cycle frequency in the whole heart, while having minimal effects on the isolated CG. At higher concentrations, it still tends to increase the frequency in the whole heart, but also decreases the frequency of firing in the CG (Dickinson et al., 2014).

**Research Question:** I examined the role of stretch and the interaction between SGRN and stretch in modulating the neurogenic lobster heartbeat.

**Methods**

I isolated the CG of *Homarus americanus* hearts, keeping the posterior muscles surrounding the small cells intact. With small hooks, one end of the intact muscles is attached to a motor, which applies computerized stretched, and the other to a force transducer, which measures the force of the applied stretch. While stretching the muscles, I recorded intracellularly from motor neurons of the CG. Since stretch is computer controlled, I modulated stretch parameters including rate, extension distance, repeated short stretches, and duration. Then I can measure the response to a variety of patterns of stretch. After I tested the CG response to stretch in saline, I then perfused the heart with different concentrations of SGRN.

**Preliminary Results and Future Directions**

During tonic stretch, driver potential and frequency of the heartbeat increased as a function of force, but only in CGs with long baseline burst durations. Since, in reality, the feedback from the heartbeat’s contraction act as series of short repeated stretches, I examined the ability of the heartbeat to match, or entrain to, a range of these applied stretches. When phasic stretches were applied, the range of periods over which stretch could entrain a heartbeat appeared to be dependent on baseline duration of the driver potential and the CG’s ability to shift their burst cycle. Additionally, previous data found that when the CG was perfused with 10-9 M SGRN, the range over which entrainment was successful decreased (Dickinson et al., 2015). This summer, I perfused the CG with a concentration of 10-8 M SGRN, which resulted in conflicting responses, and further supports the huge variability between individual lobsters.

Throughout the rest of the summer and into the fall, I will further explore these trends through conducting more experiments and analyzing data. This will hopefully lead to identifying the mechanisms of these modulators on the rhythmic behavior of the lobster heartbeat.

**Modeling**

In addition to experimentally identifying the mechanism of stretch modulation, I will be continuing to computationally studying the mechanism in collaboration. To determine the consequences of this variability, in collaboration with Matt Gorroff, we added a stretch component to a model of the CG, which is built off a pair of Morris-Lecar oscillators coupled by electrical and excitatory synapses (Williams et al., 2013).

We first ran this preliminary model with the stretch reversal potential around -35mV because we hypothesized that the stretch effects stretch sensitive chloride channels that have a reversal potential around -35mV. However, since we don’t actually know which ion channels are involved, we ran the same model many times, only changing the reversal potential parameters to correlate with different ion channels. Many of the simulations behaved like the experimental results. This variability may critically determine how the network behaves in response to manipulation.

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References:


