**Physiological and mathematical investigations of the modulation of cell types in the lobster cardiac ganglion using calcitonin-like diuretic hormone**

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The cardiac neuromuscular system of the American lobster, *Homarus americanus*, provides a strong model for investigating central pattern generators. Central pattern generators (CPGs) can be characterized as neural networks that drive any number of rhythmic movement patterns (e.g., heartbeat, breathing, or locomotion). These rhythmic patterns are often characterized by wave-like ‘bursts’ of action potentials, followed by periods of quiescence. A burst of action potentials refers to the rapid activation patterns of neurons in the central nervous system when they ‘communicate’ with nearby cells. These rhythmic patterns can become flexible via neuromodulation. Neuromodulation is any process by which a neuron’s physiological activity is altered when confronted with a stimulus, such as a chemical agent, and neuromodulation can alter wave properties like amplitude (the height of an action potential), burst frequency (how often rapid activity occurs during a given period of time), and burst duration (how long rapid neural activity lasts). A classic example of this ‘flexible nature’ of ‘rhythmic movement’ in a neuronal network can be seen in a heartbeat. A heart can beat either more quickly or more slowly, relative to some defined resting rate, but will still retain its pulsating behavior: this change in speed points to the flexibility of the neuronal outputs that drive the behavior, but the overall pattern of beating is still repetitive in nature. Understanding the mechanisms that cause neuronal firing patterns has larger implications in helping to characterize macro-level behaviors influenced by neuromodulation.

The lobster’scardiac neuromuscular system provides an invaluable model for understanding these modulatory mechanisms through its simplicity and manipulability. The cardiac ganglion (CG) consists of just nine cells: five anterior motor neurons (“large cells”) and four posterior pacemaker neurons (“small cells”) (Cooke 2002). It has been established that these two classes of cells are electrically and chemically coupled, resulting in coordinated bursting activity (i.e., cells are ‘in-phase’) (Cooke 2002). Though great progress has been made in understanding the physiological mechanisms of the CG in the American lobster, few computational models exist to help explore and predict the complex behavior of the CG, especially when considering neuromodulation.

This summer, a two-cell (large cell and small cell) computational model of the cardiac ganglion was constructed, drawing on a computational model of the stomatogastric ganglion (STG) in the spiny lobster, *Panulirus interruptus* (Soto-Treviño et al. 2005). The model was then confronted with physiological data from the CG of the American lobster, which would then allow for the exploration of neuromodulation on the heart, specifically the CG, of the American lobster (Cooke 2002). Two neuromodulatory conductances were modeled: proctolin and calcitonin-like diuretic hormone.

Calcitonin-like diuretic hormone (CLDH) is a powerful modulator of cardiac output in the American lobster, but little is known about its function in the cardiac ganglion as a whole; CLDH was first identified in decapods in 2010 and it was shown to qualitatively increase the frequency and amplitude of firing in the lobster heart (Christie et al. 2010). One of the unique features of CLDH is that it is the first intrinsic modulatory peptide identified in the CG; it is released from the large cell in the network. A peptide is essentially a very small protein. Proctolin is another powerful modulator of cardiac output and is known for its ability to excite the CG by increasing burst amplitude and frequency, similar to that of CLDH and other excitatory peptide modulators (Swensen and Marder 2000).

In completing this summer’s work, we created the first computational model to explore CLDH in any decapod and the first model to explore the possible interaction of CLDH and proctolin in the American lobster. The model predicts that the intrinsic modulator CLDH and the external modulator proctolin, when released, interact to produce a complex, non-linear output in the heart that increases the amplitude, burst frequency, and burst duration in the two-cell model. Future research will explore what conductances CLDH specifically modulates to produce the increase in burst amplitude and frequency; we also look to investigate the release patterns of proctolin and CLDH.

**Faculty Mentors: Patsy Dickinson, Ph.D., Mary Lou Zeeman, Ph.D., and Daniel Powell, Ph.D.**

**Funded by the Henry L. and Grace Doherty Charitable Foundation Coastal Studies Research Fellowship**

**References:**

Christie AE, Stevens JS, Bowers MR, Chapline MC, Jensen DA, Schegg KM, Goldwaser J, Kwiatkowski MA, Pleasant

TK Jr, Shoenfeld L, et al. 2010. Identification of a calcitonin-like diuretic hormone that functions as an intrinsic modulator of the American lobster, Homarus americanus, cardiac neuromuscular system. J Exp Biol. 213(1):118–127.

Cooke IM. 2002. Reliable, responsive pacemaking and pattern generation with minimal cell numbers: the crustacean cardiac ganglion. Biol Bull. 202(2):108–136.
Soto-Treviño C, Rabbah P, Marder E, Nadim F. 2005. Computational model of electrically coupled, intrinsically distinct pacemaker neurons. J Neurophysiol.

94(1):590–604.
Swensen AM, Marder E. 2000. Multiple peptides converge to activate the same voltage-dependent current in a central pattern-generating circuit. J Neurosci.

20(18):6752–6759.