Aldwin de Guzman Abstract

In Silico phrenic nerve modeling as a tool to improve quantification of respiratory signal integration

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A significant challenge in cervical spinal cord injury (SCI) is interruption of brainstem generated signals reaching the thoracic respiratory muscles. Many research laboratories use muscle recordings or recordings of their innervating nerves in experimental animals to assess both SCI impairment and efficacy of rehabilitative therapy. The work of Eldridge and El-Bohy was a revolutionary step in quantifying neurophysiological signal integration; however, their method reports only peaks of 'integrated' activity to quantitatively assess neural output. While widely used, this method ignores signal dynamics and patterning. Our goal is to improve methods of signal quantification by accurately representing respiratory effort through examination of singular neurons and temporal patterning of ensemble signals. We hypothesize that individual neuron firing patterns, constructed with representative statistical distributions, can be merged to create an *in silico* phrenic nerve model. Using *Spike2* and *MATLAB* in all approaches, the initial methodology involved modeling the nerve signal using graphical extrapolation. Building on this, we modeled firing neurons using *in vivo* data to determine appropriate action potential timing and latency between waveforms. Our current project involves the implementation of Beta and truncated Normal distributions to obtain staggered overlap of modeled action potentials, thereby simulating actual phrenic neurograms. The constructed signals allow us to differentiate between rate changes or neuron recruitment when assessing summated signal strength. This model provides stronger alternatives to the "rectified signal", improving quantification of respiratory effort by reducing "integrated" activity peak usage, allowing better quantifying neural output, and improving methodologies for assessment of impairment and therapeutic interventions.

Vivian Zhu Abstract

A Novel Theory On Essential Hypertension: How Breathing Influences Blood Pressure

Zhu V, Samuels K, Schwanebeck K, De Guzman A, Caballero A, Sexton A, Denson H, Zubcevic J, Baekey D

One in three American adults suffer from hypertension (HTN), a condition often resulting in heart attack, stroke, and vascular disease. HTN is estimated to cost the United States $46 billion each year (Centers for Disease Control). We hypothesized that changes in the respiratory rhythmicity of sympathetic nerve activity (SNA) are fundamental in the development of essential hypertension. We investigated a proposed feed-forward pathology in which alterations in SNA upregulate microglia production in the bone marrow, triggering inflammation of hypothalamic nuclei that drives SNA. Currently, the neural circuitry underlying the relationship between breathing and HTN has not been defined. In efforts to elucidate this, we employed an in situ rodent model of Angiotensin II induced HTN and monitored both respiratory and sympathetic activity in response to intracisternal infusions of Angiotensin II. My project focuses on characterizing the changes in cardiorespiratory coupling between treated and naïve rodents. Preliminary data shows temporal changes in the relationship between respiratory efforts and SNA preceding the expression of blood pressure changes and suggest these measures may be a critical marker identifying the "prehypertensive" patient. Further experiments are underway to refine the visualization of neura plasticity in the cardiorespiratory neurological pathway.

Alexis Caballero Abstract

A Juxtacellular Silver Labeling Approach to Mapping the Spinal Respiratory Network

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Cervical spinal cord injury often results in respiratory impairment due to damage of neural pathways. While several supportive and clinical approaches are currently being developed, a poor understanding of spinal respiratory circuitry is limiting the identification of therapeutic targets. By achieving a better understanding of this respiratory neuronal circuity we hope to wean patients off ventilators, lower hospital care costs, increase hospital bed space and improve quality of life. To address this, our laboratory is using a custom multielectrode array to record ensembles of respiratory related neurons in the cervical spinal cord of naïve and SCI rats. While functional network models can be built from these recordings, determining the anatomic recording sites for each electrode presents a significant challenge. Using the technique developed by Spinelli (1975), we employed juxtacellular silver labelling to identify the location of neuron recordings and directly relate anatomic position of neurons to specific roles in the spinal respiratory network. Preliminary data confirm that electroplating silver to the tips of the electrodes does not interfere with recording capabilities while subsequent histology distinctly labels the location of each recording site. As initial imaging created silver labels spanning several neurons, we are continuing to refine the technique to achieve single cell identification. We plan to couple this technique with immunohistochemical staining to further phenotype the neurons recorded. We suggest that this combination of recording, labeling, and staining will eventually lead to more comprehensive and efficient mapping of the respiratory spine.

Kelly Schwanebeck Abstract

Defining the spinal respiratory network: interneurons recruited by intraspinal microstimulation

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The NSCISC estimates 12,000 spinal cord injuries annually in the United States. A majority occur at the cervical level with many resulting in respiratory impairment due to interference with brainstem generated ventilatory drive reaching spinal motor targets. The resulting respiratory insufficiency often leaves patients reliant on mechanical ventilation, decreasing quality of life as well as longevity. Diaphragm and phrenic nerve pacing have provided alternatives to some patients, but better technology is needed to allow for coordinated respiratory muscle activation and adaption to varying metabolic needs. To address this, our laboratory is using multielectrode arrays in a rodent model to define spinal respiratory circuitry while using intraspinal microstimulation (ISMS) to trigger coordinated activity of thoracic respiratory muscles. Examining the neural substrate responding to electrical stimulation is one aspect of the research being performed. The hypothesis for this portion of the project is that repeated electrical activation of respiratory efforts may have persistent neural effects that can be translated to therapeutic strategies. The idea of *activity dependent plasticity* is well described in several neural systems and we hope to better define its role in the spinal respiratory circuitry by monitoring ensembles of respiratory related neurons during electrical activation of the system. Initial experiments using thoracic ISMS revealed recruited cervical interneurons whose activity persisted beyond the stimulation in a dose dependent manner with respect to stimulus intensity (increased current). We suggest that these neurons are modulatory to respiration and are currently developing strategies to enhance their activity through repeated stimulus exposure.

Garrett Floyd Abstract

Using LSPR to synthesize various gold nanoparticle morphologies

Joseph Duchene, Garrett Floyd, Yueming Zhai, Ming Gao, Brendon Sweeny, Yunlu Zhang, and David Wei

The goal of this project is to demonstrate the synthesis of multiple gold nanoparticle morphologies through the use of visible light, as well as to propose an explanation for this phenomena. However, it is well known that nanoparticle crystallinity (or the arrangement of gold atoms in the nanoparticle) is instrumental in the synthesis of a given nanoparticle morphology [1]. In order to control the crystallinity of the nanoparticles we first synthesized an easily obtainable morphology with the crystal structure we desired [2, 3, 4].

Then we prepared a solution in a clear vial containing gold precursor, a growth directing agent, and a compound that assists in the addition of gold atoms to the surface of gold nanoparticles when they are exposed to the correct frequency of visible light. We then wrap the vial in tinfoil to prevent unintended light irradiation of the sample and add the oxidized nanoparticles to the solution (The bottom of the vial is not wrapped in order to allow for later light irradiation). Immediately after the addition of the oxidized particles, the vial is added to a lamp tuned to admit light at a controlled frequency [7]. The morphology of the particles were then analyzed through the use of SEM, TEM, and UV.-vis. Spectroscopy.