UNIVERSITY of WASHINGTON

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Online Proceedings

1B

# Unmasking Brain Function: From Single Molecules to Complex Information Processing

*Session Moderator: Tom Daniel, Biology*

**MGH 228**

*12:30 PM to 2:15 PM*

* Note: Titles in order of presentation.

**Investigating Interactions between a Presynaptic Voltage-Gated Calcium Channel and the Extracellular Matrix Protein, Laminin, in the Synaptic Cleft**

*Tinhdoan Thi (Doan) Phi, Senior, Biology (Molecular, Cellular & Developmental)*
*Mentor: Steven Carlson, Physiology & Biophysics*

At the neuromuscular synapse, the protein laminin binds the alpha subunit of the voltage-gated calcium channel (Cav2.1). Cav2.1 is a transmembrane protein of the nerve terminal; laminin is an extracellular matrix protein of the synaptic cleft. This interaction stabilizes the active zone – the cytosolic apparatus for neurotransmitter release. We hypothesize that Cav2.1 acts as an anchor for the active zone. In the B2 laminin chain, the amino acid sequence LRE plays a critical role in its interaction with the L5III extracellular loop of Cav2.1. We wish to know which amino acid residues of the L5III extracellular loop are critical for this interaction with the LRE sequence. To investigate, we are developing an assay to measure the interaction between the L5III extracellular loop, produced as a fusion protein, and a fusion protein containing the LRE sequence of the B2 laminin chain. The Cav2.1 L5III extracellular loop is laid down as a fluorescently tagged micro-patterned substrate−12 um stripes on a glass slide. Then, the slides are incubated with fluorescent beads containing the B2 laminin fusion protein with the LRE sequence. Using fluorescence microscopy, we will measure the number of beads bound to the 12 um stripes and thus measure the interaction between the two proteins. As a negative control we will use the L5III extracellular loop from Cav1.2, a calcium channel that does not bind the B2 laminin chain. By using chimeric loops containing different amounts of the Cav2.1 and Cav1.2 L5III loop sequences, we will determine which amino acid residues are critical for binding. Currently, we are using recombinant DNA methods to produce the fusion proteins for our assay. With AviTag methods we are tagging the L5III loops with biotin at a specific location which will allow us to bind the loops with a preferred orientation to a micro-patterned substrate of avidin. The active zone is critical for neuromuscular communication and our research will provide insight on the mechanism of active zone formation.

**Cervical and Thoracic Mapping of Respiratory Motor Neurons**

*Comron Nasser Ganji, Senior, Neurobiology*
*Mary Gates Scholar, UW Honors Program*
*Mentor: Michael Sunshine, Rehabilitation Medicine*
*Mentor: Chet Moritz, Physiology & Biophysics*

Respiratory dysfunction is the leading cause of death in the acute phase of high-cervical spinal cord injuries (SCIs). While survivors of high-cervical SCIs regain some of their respiratory function, many individuals require assisted ventilation. Despite the fact that there are currently many ongoing treatments, more needs to be understood about the anatomy and physiology of the respiratory pathways in the spinal cord in order to find cures for those suffering from high-cervical SCIs. Recent rodent studies using intra-spinal microstimulation (ISMS) for forelimb motor recovery has shown moderate functional recovery. In this study we mapped the motor neuron pools of three muscles used in respiration along the cervical and upper thoracic spinal cord. Additionally we explored the extent to which we can activate those muscle with ISMS in spinally intact rats.

**Encoding Properties of Moth Wing Mechanosensors are Similar to That of Haltere Neurons**

*Brandon Gene (Brandon) Pratt, Senior, Biology (Molecular, Cellular & Developmental), Neurobiology*
*Mary Gates Scholar, UW Honors Program*
*Mentor: Tom Daniel, Biology*

Animals and humans collect and process information from their environment using a host of sensory modalities to maintain control of movement. Such integration of information

is exceedingly challenging for the control of flight in insects, which is inherently unstable. We use insects as a model system for understanding how multiple sensory inputs influence flight control. While vision is necessary for flight, its processing time is too slow for effective fight control. Thus insects use a faster sensory modality that encodes mechanical information (inertial forces). We use a combination of experimental and theoretical approaches to reveal the precision, sensitivity, and rapid processing speeds of inertial sensors in flying insects. In particular, we suggest that wings not only serve a role as propuslors, but by virtue of the mechanosensory neurons in them, provide a key sensory role for inertial forces. We hypothesize that the wing mechanoreceptors of the hawkmoth (Manduca sexta) rapidly and precisely extract mechanical information necessary for flight control. We further hypothesize that such encoding properties are similar to those in wing evolutionary predecessors, halteres (a sensory organ that is known to be a gyroscopic organ) in flies. To test our hypotheses, we recorded the electrical activity of wing neurons subject to a mechanical stimulus. We used methods from computational neuroscience to characterize the encoding properties (the stimulus features that drive neural responses). We found that nearly all neurons respond rapidly with 5 ms precision and they are extremely selective for the temporal pattern of the stimulus. These results are similar to those found for halteres, and suggest a novel finding that wings serve the dual function of both actuation and sensing. These results reveal a new interpretation of movement control in animals and can serve as inspiration for the next generation of flight systems.

**Circadian Modulation of Neuromotor Control**

*Jazmine Guadalupe Perez, Senior, Gender, Women, and Sexuality Studies, Biology (Physiology)*

*Levinson Emerging Scholar, Mary Gates Scholar, Undergraduate Research Conference Travel Awardee*
*Mentor: Horacio de la Iglesia, Biology*

Motor behavior is the result of neural programs emerging from the Primary Motor Cortex (PMC). To generate behavioral outputs the PMC integrates exogenous and endogenous sources of variance. Electrical activity from the PMC has been effectively used to operate minimally invasive brain-machine interfaces (BMIs) that can operate prosthetic limbs to achieve basic motor outcomes such as operating a joystick. Further development of neuroprosthetic technology will rely on a deep understanding of sources of variance to the PMC and how the PMC compensates for this. The circadian system regulates physiology and behavior within the 24-hour time frame and it represents a predictable source of endogenous variance for the generation of motor behavior. The specific pathways by which the circadian clock(s) may modulate PMC motor programs is not understood, but preliminary results from our lab show that the circadian system modulates the PMC electrical activity associated with wheel running in mice. We implanted electrocorticographic (ECoG) electrodes onto the PMC of mice and recorded electrical activity while they ran on a wheel at different circadian times. This showed that the PMC electrical signals associated with wheel-running are modulated in a predictable manner by the circadian system. I propose to replicate these experiments in mice with a malfunctioning circadian clock. I hypothesize that the canonical molecular circadian clock is essential for this modulation. To test this hypothesis, I used ECoG electrodes to record PMC electrical activity of Bmal1$^{-}/-$ mice, which have no copies of the clock gene BMAL1, and their wildtype (Bmal1$^{+}/+$) littermates. This determines whether the circadian modulation of the PMC depends on an intact molecular circadian clock. Understanding the regulatory effects of the circadian system on PMC brain wave activity is crucial for the design of BMIs and their effective operation throughout the 24-hour day.

**Neurobiological Basis of Menopausal Hot Flashes**

*Alejandra Cabrera, Non-Matriculated, Integrative Biology , University of Washington*

*UW Post-Baccalaureate Research Education Program*
*Mentor: Robert Steiner, Obstetrics And Gynecology*
*Mentor: Don Clifton, Obstetrics And Gynecology*
*Mentor: Ashley Krull, Neuroscience*
*Mentor: Sarah Larsen, Ob/Gyn*

Hot flashes (HF) are acute vasomotor disturbances that cause facial flushing and sweating. They commonly occur in menopausal women as a result of a decreased production of estradiol from the aging ovary, which triggers an acute malfunction in the brain's control of body temperature. However, the molecular and cellular mechanisms that generate HF are poorly understood. Recent studies suggest that superactivation of KNDy neurons in the hypothalamus, which occurs in response to either reduced levels of estradiol or artificial stimulation, can disrupt thermoregulatory centers in the brain. To test this, we are developing an optogenetic animal model for HF aimed at understanding their physiological origins and enabling preclinical testing of potential therapeutics. We have created a transgenic mouse that has a light-sensitive membrane channel (channelrhodopsin-2) inserted into KNDy neurons, which can be activated with a fiber optic probe inserted into the brain. Selective activation of KNDy neurons and the subsequent behavioral response of the animal along a thermal gradient allow us to explore the role of KNDy neurons in thermoregulation. We hypothesize that following activation of KNDy neurons, the thermoregulatory set-point for excess heat perception will be lowered, so the animal will move to a cooler place along the gradient. We have preliminary evidence to suggest that when activated with a different technology (Designer Receptor Exclusively Activated by Designer Drugs) animals do, in fact move to cooler temper-

atures. Testing this hypothesis is our primary objective. We believe development of an animal model for hot flashes will aid our understanding of their neurobiological basis and foster development of better and safer therapeutic options for treatment.

**Shape Selectivity in V4 for Three-Dimensionalized Shapes**

*Alex Paul (Alex) Rockhill, Senior, Neurobiology, Applied & Computational Mathematical Sciences (Biological & Life Sciences)*

*UW Honors Program*

*Mentor: Wyeth Bair, Biological Structure*

Area V4 is a cortical region that carries out intermediate visual processing along the ventral ("what") visual pathway. It integrates information about boundary and surface features from the primary visual cortex and sends signals downstream to the inferior temporal cortex, which supports complex object recognition. Neurons in area V4 have been shown to encode the boundary curvature of 2-dimensional (2D) shapes in an object-centered coordinate system. For example, a neuron may prefer a wide variety of stimuli that have a protrusion (convexity) to the upper right. Our goal is to determine whether this type of boundary representation along 2D boundaries also applies in three dimensions (3D). We also aim to determine whether the same V4 neurons that encode 2D shapes also encode 3D form, or whether there might be separate populations activated by 2D and 3D form. To address this, we created a set of images of spheres that are deformed by the addition of a dent or protrusion. We varied the pose and the direction of lighting. The images were based on wire-frame models created in Blender. We recorded responses from single neurons in the fixating macaque monkey using a novel set of 156 3D images and a set of 230 2D images have been studied in previous experiments. We found that our 3D stimulus set elicited robust differential responses from V4 neurons. Some neurons responded better to 2D shapes without surface shading, while others preferred 3D shapes. Our next steps are to determine whether responses 2D and 3D shapes can be explained with one unified model. Ultimately, we want to understand how neurons encode natural scenes, and studying responses to such parametric, naturalistic stimuli brings us closer to achieving that goal.

**Characterization of TMS-Induced Percepts for Advanced Brain-to-Brain Transmission of Complex Visual Information**

*Darby Michael (Darby) Losey, Senior, Neurobiology, Computer Science*

*Levinson Emerging Scholar, Mary Gates Scholar, UW Honors Program*

*Mentor: Andrea Stocco, Department of Psychology*

Phosphenes are temporary visual percepts which can be elicited via transcranial magnetic stimulation (TMS) of the visual cortex. Often described as flashes or blobs of light, phosphenes usually occupy a small subset of the visual field and can be consciously perceived and described by a human subject. In order to investigate the relationship between phosphene characteristics and the methods in which they are elicited, subjects were asked to draw the phosphenes they perceive in response to different stimulation intensities, locations, and orientations. This information was then used for direct brain-to-brain communication of simple images. Functional magnetic resonance imaging (fMRI) was utilized to decode information from the brain of one human ("the sender") and TMS was used to encode that information into the brain of another human ("the receiver"). Namely, the image that the sender viewed was determined by monitoring oxygenated blood flow patterns in the brain and transmitted directly to the brain of the receiver. The receiver "saw" the image viewed by the sender through TMS-induced phosphenes which were elicited by stimulating with parameters determined during the mapping stage. This brain-to-brain interface allows for the successful transmission of complex visual information directly from one human brain to another and does so through noninvasive methods.