Online Proceedings

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Sensory Integration, Learning, and Motor Control in Animal and Human Models

Session Moderator: Horacio de la Iglesia, Biology
MGH 231
12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

Multimodal Integration in the Disease Vector Mosquito, *Aedes aegypti*
Kennedy Keahi Stone (Kennedy) Tobin, Senior, Neurobiology
Mary Gates Scholar, UW Honors Program
Mentor: Jeffrey Riffell, Biology
Mentor: Clement Vinauger, Biology
Mentor: Chloe Lahondere, Biology

Mosquitoes transmit diseases that affect millions of people each year. As such, there is an urgent need to explore every avenue to develop efficient tools to control them. In this context, my project aims to better understand their host-seeking behavior by exploring how visual and olfactory stimuli affect the mosquito's flight response. In the Zika and yellow fever vector, *Aedes aegypti*, exposure to CO_2 triggers a strong attraction to visual features. However, the temporal and spatial features of this olfactory-gated visual response are still unknown. For my project, I seek to dive deeper into the characterization of this phenomenon. Specifically, I am interested in determining how long the effect of CO_2 lasts, and to what extent this effect is a function of the size and shape of the visual stimulus. To investigate these factors, I utilized a flight LED arena in which a tethered mosquito was presented visual stimuli and CO_2 pulses delivered at different time intervals. I recorded wingbeat frequency and amplitude, torque, head angle, and leg movements while producing 16 distinct sensory scenarios in which the size of the visual stimulus, and the timing between the delivery of pulses of CO_2 and the visual stimulus were manipulated. From this dataset, I will be able to extract the fine scale behavioral flight response to these unique sensory combinations, deepening our understanding of the complex interplay between visual and olfactory stimuli in mosquito host-seeking behavior. These results bear the potential to lead to the improvement of mosquito control strategies that target their behavioral responses to visual and olfactory stimuli.

Nocturnal Cyclic Fear Entraining Circadian Rhythms
Luis Eduardo Salazar, Sophomore, Pre-Sciences
Mary Gates Scholar
Mentor: Horacio de la Iglesia, Biology
Mentor: Miriam Ben-Hamo, Biology

Most organisms show a roughly 24-hour cycle in their physiological and behavioral processes, called circadian rhythms. Circadian rhythms are generated endogenously through the ~24-hour cyclic expression of genes known as clock genes. The expression of these genes oscillates in the master circadian clock of mammals – the suprachiasmatic nucleus (SCN) - but also in nearly every cell of the body. Typically, circadian clocks and the rhythms they sustain are 'entrained' by the 24-hour light-dark (LD) cycle. Our lab has found that fear can also act as an entraining factor; we observed that mice and rats subjected to random foot shocks during the dark phase of the LD cycle in their cages' foraging area changed from their typically nocturnal foraging pattern to a diurnal one, avoiding the fear stimulus presented during the dark. The goal of my project is to understand the neural circuits and molecular processes that are involved in fear entrainment. I have analyzed the expression of clock genes in animals that are exposed to nighttime fear or in control animals exposed to daytime fear, using a technique called *in situ* hybridization, which labels mRNA levels. This allowed me to assess the circadian rhythm of expression of clock genes of interest (Per1 and Bmal1) in the SCN and the amygdala, the region of the mammalian brain that encodes fear stimuli. Our findings could not only help elucidate the circuits that are involved in fear entrainment but also help understand the mechanisms that link fear and anxiety disorders to problems with circadian rhythms and sleep.

Exploring the Neural Mechanisms of Perceptual Rod-Cone Flicker Cancellation

Adree Songco Aguas, Senior, Neurobiology
Howard Hughes Scholar, UW Honors Program
Mentor: Fred Rieke, Physiology and Biophysics
Mentor: William Grimes, Dept. of Physiology and Biophysics

Over the course of a natural day-night cycle, mean luminance levels can span ten log units or more. Mammalian retinas effectively encode visual information over this vast range, in part, by cone photoreceptors in bright conditions. These visual signals, regardless of their origin, must pass through a common set of retinal ganglion cells- thus creating opportunities for signal interactions. The overarching goal of this research is to understand how the retina behaves under intermediate lighting conditions (e.g. dawn and dusk) when both rods and cones are active, and to relate the circuit-level retinal processing of rod and cone signals to human perception. Previous human perceptual experiments have revealed interactions between flickering rod and cone stimuli that are thought to occur in the retina. Here we explore the neural basis of rod-cone flicker interference in On and Off ganglion cells that project to the primate magnocellular visual pathways. Our recordings (from *in vitro* non-human primate retina) reveal a strong, suppressive interaction between rod and cone signals. The dependence of this interaction on the frequency and phase of the temporal modulation is similar to that observed in perceptual measurements from human subjects. This destructive interference between rod and cone signals appears to reflect a linear combination of kinetically-distinct rod and cone signals upstream of the ganglion cell synaptic inputs. Using our empirically-derived data as a foundation, we construct a mathematical model that captures known rod-cone interactions and accurately predicts retinal output in response to arbitrarily time-varying rod and cone stimuli.

Shape Selectivity in V4 Using Novel Time Dynamic Stimuli

Alex Paul (Alex) Rockhill, Senior, Neurobiology, Applied & Computational Mathematical Sciences (Biological & Life Sciences)
UW Honors Program
Mentor: Wyeth Bair, Biological Structure
Mentor: Anitha Pasupathy

We hypothesize that neurons in the visual cortical area V4 have a distinct temporal integration time on the order 40 to 100 milliseconds that is required to perceive rapidly moving or changing shapes. If this is true, then we should be able to characterize these neurons using fast streams of dynamic stimuli. To test this, we created stimuli that change their boundary features rapidly by presenting different shapes in immediate temporal progression at various durations for visual fixations lasting just over one second. The duration for which each of the shapes was presented within the sequence was held constant for each fixation trial and varied randomly across trials for durations of 40, 80, 160 and 320 milliseconds. To access which shape durations were sufficient to cause differential, shape-tuned responses, we constructed tuning curves of the mean firing rate as a function of the duration of shape presentation. Our results suggest that shape tuning is consistent across durations from 80 to 320 milliseconds and exists at a lesser amount at 40 milliseconds. This raises the possibility that our future experimental design can involve showing stimuli for shorter durations, allowing us to characterize shape tuning for 3D stimuli, which requires the presentation of a greater number of stimulus images. It also suggests that V4 neurons may play an important role in encoding dynamic scenes as objects change shape or move or rotate with respect to the observer.

Does Cerebellar Variability Compensate for Variable Motor Commands?

Dorothy Anne (Dorothy) Cabantan, Senior, Neurobiology
UW Honors Program
Mentor: Farrel Robinson, Biological Structure
Mentor: Amy Nowack, Otolaryngology

Normally, repeated voluntary movements to the same target are nearly identical to one another. If, however, the cerebellum is damaged, then repeated movements to the same targets have variable trajectories and end in different places. To investigate why cerebellar damage makes movements variable, we record in a rhesus monkey from the type of neurons in the cerebellum that we know most about, those that influence rapid eye movements (saccades). These neurons are in the medial nucleus of the cerebellum and send their axons to the saccade control center in the brainstem. The burst of action potentials fired by a single saccade-related cerebellar neuron can be long, short, fast, or slow. How do these variable signals from the cerebellum help create identical saccades? One commonly accepted idea is that the variability for each cerebellar neuron is not correlated with the variability of other cerebellar neurons. The uncorrelated variability of many cerebellar neurons produces a consistent summed signal that produces identical saccades. If this is true, then why are saccades variable when we damage the cerebellum? We propose an alternative hypothesis: the variability of saccade-related neurons is correlated. This correlation produces a variable summed output from the cerebellum for identical saccades. We think that the saccade-to-saccade variability of cerebellar output compensates for variability in the motor commands from the cerebral cortex. The signals from both the cerebellum and the cortex vary but their sum is consistent because they vary in opposite directions. Without cerebellar output, only the variable motor command from the cortex drives saccades. Variable commands make variable saccades. To test our proposal, we record from several cerebellar neurons si-

multaneously to measure how correlated their variability is. If our proposal is correct, then the variability of cerebellar neurons is not random. It serves a previously unsuspected function to create consistent saccades.

Sensory and Memory in Foraging Behavior: A Comparative Analysis in Humans and Rodents

Gusti Lulu (Lulu) Fatima, Senior, Biology (Molecular, Cellular & Developmental)

Levinson Emerging Scholar, UW Honors Program

Mentor: David Gire, Psychology

Mentor: Brian Jackson

Foraging behavior in mammals requires the integration of various sensory cues to allow the subject to navigate through the environment. When the search becomes predictable and repetitive, memory can be used to enhance the sensory cues. To model the dynamic interactions between sensory and memory, we performed a comparative analysis on rats and humans by designing a two-stage task paradigm: search and return. The subjects were trained to search for rewards in a confined space with limited sensory cues. After the end of each trial, they were trained to return to the start position. The rat task was performed in an automated arena that allowed the rats to follow the reward's olfactory cues but prevented visual and hearing cues. Similarly, the human task simulated the paradigm using a computer game that allowed the subjects to search and return in a virtual room with limited visual cues. We predict that sensory cues have a more significant impact on the search strategies compared to the return strategies. If the reward locations are fixated in every trial, we also expect the subjects to increasingly rely on memory for both the search and return strategies. Our research will provide insight on the tracking methods and analysis in studying the roles of sensory and memory in complex foraging behavior.

Fluid Intelligence Raised through Electrical Stimulation Tested on Ravens Matrices

Stephanie Ai Mizuno, Freshman, Pre-Sciences

Mentor: Andrea Stocco, Department of Psychology

Fluid intelligence is defined as the ability to solve reason and solve novel problems independent from previous knowledge. Fluid intelligence is typically tested with Raven's Progressive Matrices (RPM), a non-verbal test of logical and abstract reasoning. Previous studies have shown that fluid intelligence and performance on the RPM test rely on various brain regions, especially the left inferior parietal lobule (IPL) and the left middle frontal gyrus (MFG). In this study, we tested the hypothesis that artificially increasing the activity of these regions using Transcranial Alternating Current Stimulation (tACS) would improve RPM performance during stimulation. In the experiment, 16 naïve participants were tested with a within-subject design while they solved RPM problems of varying complexity. Each participant was tested under four conditions. In the two experimental conditions, tACS stimulation was applied to either the middle frontal gyrus or the inferior parietal lobule. Stimulation was administered using an HD-tACS system at 0.5 mA and 40 Hz, in a configuration with a central cathode and four surrounding anodes. In the remaining two control conditions, sham stimulation was applied to the same regions. Preliminary analysis suggests that stimulation resulted in a significant decrease in response times, especially for the most difficult problems. The results of this study could pave the way for future applications in cognitive rehabilitation, progression in the understanding of the neural signature of fluid intelligence, and improving cognitive performance.

Adolescent Alcohol Abuse Produces Sexually Dimorphic Effects in Later Adult Decision Making

Sophia Jiahn (Sophia) Weber, Senior, Biology (Physiology)

Mentor: Jeremy Clark, Psychiatry and Behavioral Sciences

Alcohol abuse is a major public health problem, particularly during adolescence given the propensity towards risky behavior during this time period. Throughout this developmental period, the brain is highly susceptible to environmental insults, including alcohol. Preclinical research has shown that alcohol intake in adolescent rats leads to risk preference and suboptimal decision making when tested later in adulthood. However, these experiments were carried out exclusively in male animals, therefore I decided to explore whether adolescent alcohol abuse induces deficits in risk-based decision-making in a sexually dimorphic manner. In order to test this question, I provided female rats with access to 10% ethanol in a gelatin matrix for 20 days. Following a prolonged period of abstinence from alcohol, I accessed the effects of the alcohol exposure using a probability-discounting task, which assesses risky decision-making. Briefly, this task involves the presentation of two levers, one of which is associated with a guaranteed low reward of 2 sucrose pellets, while the other represents a risky but high reward of 4 pellets. The riskiness associated with the high reward lever increased daily over a five day period beginning with 100% reward delivery and then decreasing by 25% each day until the high reward lever had a 0% chance of delivery of the 4 sucrose pellets. Compared with male rats that had previously undergone the same alcohol exposure paradigm, female rats consumed significantly more ethanol gelatin; furthermore, the female rats exposed to ethanol displayed reduced risky behavior compared to controls, unlike ethanol-exposed male rats who exhibited an increase in risky behavior. These data have broader implications for how we view the long terms effects of adolescent alcohol abuse in men and women in order to create more effective therapeutic treatments.