NeuroEngineering Minisymposium

April 29, 2024

University of Colorado, Anschutz

Ben Nighthorse Campbell Auditorium

AGENDA

7:30 - 8:00 am	Continental Breakfast
8:00 - 8:10 am	Welcome and Introduction - Emily Gibson, PhD
	Faculty Talks
8:10 - 8:25 am	Mazen Al Borno, PhD - *Vibrotactile Stimulation for the Treatment of Neurological Disorders*
8:25 - 8:40 am	Judith Gault, PhD - *Deep Brain Stimulation for Treatment-Refractory Schizophrenia*
8:40 - 9:00 am	Cathy Bodine, PhD - *Assistive Technologies*
9:00 - 9:20 am	Daniel Kramer, MD - *Thalamic Activity During Motor Braking in Humans with Essential Tremor*
9:20 - 9:40 am	Cristin Welle, PhD - *Vagus nerve stimulation for motor learning and remyelination*
9:40- 10:00 am	Richard Weir, PhD - *Design Philosophies for Advanced Limb Replacement Systems*
10:00 - 10:30 am	Coffee break

Trainee Talks

10:30 - 10:45 am	Erin Radcliffe, BS - *Beta-correlated kinematics inform therapeutic targets and optimal neuromodulation strategies for Parkinson's disease across clinical states*
10:45 - 11:00 am	Eashan Sahai, BS - *BRAINS Board: Programmable Single and Multi Channel Neurostimulation Device*
11:00 - 11:15 am	Kathryn Mirandette, BS - *Optogenetic vagus nerve stimulation with nerve cuff for inflammation attenuation in mice*
11:15 - 11:30 am	Skylar Suarez, BS - *Two-Photon GRIN Microendoscope for Stereotactic Neurosurgery*
11:30 - 12:30 pm	Lunch

Keynote Lecture

12:30 - 1:30 pm	**Bolu Ajiboye, PhD.** *REconnecting the Hand and Arm to the Brain (ReHAB): Bi-directional neuroprostheses for sensorimotor functional restoration*
1:30 - 3:00 pm	Poster session

Co-Sponsored by:

NEUROSCIENCE INNOVATION INITIATIVE

OPEN TO ALL STUDENTS · UNIVERSITY OF COLORADO · STUDENT SENATE FUNDED · ANSCHUTZ MEDICAL CAMPUS · PROVIDED BY: STUDENT ACTIVITY FEE

Department of Bioengineering · UNIVERSITY OF COLORADO DENVER | ANSCHUTZ MEDICAL CAMPUS

NTC NeuroTechnology Center

NeuroEngineering Minisymposium

April 29, 2024

University of Colorado, Anschutz

Shore Family Forum, Nighthorse Campbell Native Health Building

POSTERS

1

Amber Bollinger
Department of Bioengineering

Analysis and Comparison of Single- vs Double-Differential sEMG Systems for Use in Prostheses

Regenerative Peripheral Nerve Interfacing (RPNI) has shown promising results in amplifying neural impulses1 through creating individual electromyography (EMG) sites. However, due to the small graft size, the surface EMG signals are still difficult to detect. Developing a system with enough spatial resolution and gain to make use of these surface electromyography (sEMG) signals could allow for improved prosthesis control. Noise and crosstalk are two factors that impact a system's ability to detect and amplify RPNI signals. Prior research has shown that double differential (DD) sEMG systems are better able to reduce crosstalk than single differential (SD) systems.2 By comparing SD- and DD-systems while varying inter-electrode distances (IEDs), this study aims to compare each system's ability to detect the individual digits' muscle signals. Preliminary results showed that the DD-system was more focal and able to reduce crosstalk, but it was unable to detect the deeper signals from the individual digits. The SD-system was less focal, but it was able to detect these deeper signals. In addition, it was also found that larger IEDs decreased noise, while smaller IEDs decreased crosstalk. Overall, the SD-system proved to be less noisy which may be related to the Common-Mode Rejection Ratio (CMRR) of each system. Both systems have benefits and drawbacks for RPNIs. Further research regarding the gain and CMRR of the systems will be conducted to determine the best approach, but preliminary results suggest the use of a SD-system with an increased gain and CMRR for detecting RPNI signals. References: [1] Vu, P. P., Vaskov, A. K., Irwin, Z. T., Henning, P. T., Lueders, D. R., Laidlaw, A. T., Davis, A. J., Nu, C. S., Gates, D. H., Gillespie, R. B., Kemp, S. W. P., Kung, T. A., Chestek, C. A., & Cederna, P. S, "A regenerative peripheral nerve interface allows real-time control of an artificial hand in upper limb amputees," Sci Transl Med, vol. 12, no. 533, eaay2857, 2020. [2] F. N. Guerrero, E. M. Spinelli, and M. A. Haberman, "Analysis and Simple Circuit Design of Double Differential EMG Active Electrode," IEEE Transactions on Biomedical Circuits and Systems, vol. 10, no. 3, pp. 787-795, 2016.

2

Samuel Budoff
Physiology & Biophysics

Here there be dragons no more - Mapping retinal cells with spatial biology and neural networks

We address a critical gap in retinal neuroscience: the precise mapping of murine retinal cell types and their functional implications. Spurred by recent revelations in single-cell sequencing, which have clarified the array of retinal subtypes, and historic physiological insights, our study develops an innovative neural network strategy and methodologic approach to fill this gap in knowledge. The burgeoning understanding of retinal cell subtype spatial diversity and their influence on visual behavior shows that different retinal cell subtypes vary in their retinal distribution as well as their contribution to specific behaviors. For instance, the optic flow minimization observed in mice during hunting correlates with the high-density spatial cluster of Alpha-On sustained ganglion cells, implying a computational strategy encoded in the spatial distributions of such cells. Insights such as this underscore the necessity of detailed spatial maps to understand the retina's computational framework fully, and to predict other such behaviors. Moreover, knowledge of such distributions can be leveraged to develop novel CNN-like architectures optimized for naturalistic tasks. Unfortunately, the spatial distribution of most retinal cell subtypes is unknown. To address this need, we have utilized spatial sequencing technology, specifically the 10X Xenium platform, enabling us to map cellular distributions with unprecedented precision. Complementing this, our novel neural network approach employs gradient-based gene selection to minimize genes needed for cellular classification from transcriptomic data. The integration of spatial biology and machine learning in our study paves the way for a comprehensive understanding of retinal function. By creating detailed maps of cellular subtypes, our research illuminates how spatial variations contribute to the retina's complex computations and behavioral adaptations. This work not only fills a significant knowledge gap in retinal neurobiology, but also sets forth a new strategy for studies exploring the spatial properties of other neural tissues.

3

Nam Bui
Electrical Engineering

Dietary Sensing via Gustatory Pathway using EEG Wearable Device

Accurate, real-time monitoring of dietary intake can allow primary care physicians to make recommendations to their patients quickly and effectively. Conventional dietary monitoring measures the chewing patterns of individuals via Inertial Measurement Unit (IMU) (Wang et al., 2021), yet this method is subjective. Existing research has been able to differentiate salty and sweet tastes within participants using electroencephalogram (EEG) measurements and advanced signal processing techniques (Hashida et al., 2005). Constraints of such monitoring include the bulky nature of equipment (Casson, 2021). and financial barriers preventing access to preventative monitoring. In the pursuit of a user-friendly, generalized method of dietary monitoring, the primary aims of our project are to expand this research by utilizing our "behind-the-ear" EEG device, and to create a machine learning model used for reporting dietary information in real-time. We will record micro-voltage brain activity of cardinal tastes detectable by the human tongue (salty, sweet, sour, bitter) via our behind-the-ear EEG. The preliminary data is 20 samples of brain data of each flavor for the three researchers involved. We've created water mixtures to test with, mixing salt into water for our "salty" flavor, sugar in water for our "sweet" flavor, etc. In each instance of data collection, there are six independent trials, five trials for each flavor and one plain water trial. For each trial, participants remain motionless while holding the mixture in their mouths for one minute. The gathered data will be split into training and testing data for machine learning with a k-fold validated classification model which is used to analyze the raw data. We expect this machine learning model to classify different flavors and make predictions in real time of what the user is eating. Our method of monitoring diet may prove to be a user friendly and reliable method for qualitative dietary analysis and may advance affordable access to health monitoring devices.

4

Tyler Currie

Bioengineering

3D Printing Optogenetic Interfaces

Optogenetics is not only a promising experimental tool for the peripheral nervous system, but also a promising neuroprosthetic in the periphery for a variety of diseases (post-traumatic stress disorder (PTSD), chronic inflammation, etc.). Traditional, electrical stimulation is non-specific, causing off-target effects that negatively affect patient populations. Optogenetics offers genetic specificity to target specific pathways eliminating complications of stimulation. Currently, there are not many options for optogenetic interfaces in the periphery and even fewer that can easily be implanted on the cervical vagus nerve of mice due to its small size (<200μm). 3D printing offers a unique advantage over traditional manufacturing (i.e. casting) by permitting rapid prototyping and enabling unique geometries. This combination allows interfaces to be quickly designed for the peripheral anatomy being targeted. To enable these interfaces, they need to be made in a material that is soft, robust, and biocompatible. Using a custom-research digital light processing (DLP) 3D printer, a polyethylene glycol diacrylate (PEGDA) resin formulation is initially examined along with a commercially available silicone. A variety of nerve cuff designs are explored with a 3D-printed, prototype, silicone cuff tested in-vivo to elicit a biological response. This technology will enable the design of optogenetic interfaces for anywhere in the periphery allowing any interesting neuromodulation or promising neuroprosthetic sites to be quickly examined.

5

Gregory Futia

Bioengineering

Opto2P-FCM: A MEMS Based Miniature Two-Photon Microscope with Patterned Optogenetic Stimulation

Miniaturized microscopes for monitoring neural activity are an indispensable tool for neuroscience research. We present a novel MEMS based miniature microscope with patterned optogenetic stimulation capabilities enabling cell-specific 2-photon optogenetics and 2-photon imaging.

6

Stephanie Lorelli

Bioengineering

Predicting Prosthetic Finger Postures Via Parallel Fuzzy C-Means Classification

Pattern recognition interprets muscle contractions so that users can intuitively switch between different motions for efficiently operating a myoelectric prosthetic hand. These can include hand open, hand close, tripod grip, or wrist rotation. However, simultaneous movement of individual fingers is lacking in current clinical standard systems for upper limb myoelectric prosthetic hands. Progress has been made through inventing a Fuzzy C-Means (FCM) parallel pattern recognition system to research if individual finger motions can be classified in parallel with an update speed of less than 100ms. This system takes in surface electromyogram data and simultaneously outputs "flexion", "off", or "extension" for each finger. The parallel classification scheme presented here is beneficial to users because the system only needs to be trained on "flexion", "off", and "extension" data for each finger; yet, without having to be trained separately, the system can classify combinations of finger motions and macro hand postures. The parallel FCM system classifies data binned at 50ms intervals at a speed of less than 10ms per bin which demonstrates that the system can be used in real-time. In addition, individual finger posture accuracies ranged from 57.84% to 99.85% with an overall mean of 89.14% and macro posture accuracies ranged from 53.63% to 99.95% with an overall mean of 87.73%. While this is a noteworthy development, further research needs to be done to increase the accuracy of the classification to be viable in a clinical setting before being made available to people using upper limb myoelectric prosthetics.

7

Michael O'Donnell
Bioengineering

Novel Adeno-Associated Viruses Target Low-Threshold Mechanoreceptors to Restore Touch in Prosthetic Systems

Sensory feedback is an important feature desired in prostheses. Optogenetic interfaces have the potential to communicate directly at single axon levels. Using optogenetics for sensory feedback requires sensory neurons to be transfected with opsin DNA. Adeno-Associated Viruses (AAVs) have different serotypes with affinities for various tissues. The DRG is composed solely of sensory axons that project from the periphery to the spinal cord. It has not been determined which serotype expresses best in murine sensory neurons after DRG-injection. We are testing four serotypes under a universal promoter to determine which expresses best in sensory neurons following direct DRG injection.

8

Samantha Olah
Pharmacology

Acute reorganization of postsynaptic neurotransmitter receptors reveals the functional impact of molecular nanoarchitecture at inhibitory synapses

Neurotransmitter receptors partition into nanometer-scale subdomains within the postsynaptic membrane that are precisely aligned with presynaptic neurotransmitter release sites. While spatial coordination between pre- and postsynaptic elements is observed at both excitatory and inhibitory synapses, the functional significance of this molecular architecture has been challenging to evaluate experimentally. Here we utilized an optogenetic clustering approach to acutely alter the nano-scale organization at inhibitory synapses and observe a correlated decrease in inhibitory currents. Our results demonstrate that acute repositioning of neurotransmitter receptors within the postsynaptic membrane profoundly influences synaptic efficacy, establishing the functional importance of precision pre/postsynaptic molecular coordination.

9

Forest Speed
BIOE

Development of the 3DFast optical interface for voltage imaging in freely moving animals

Voltage imaging enables the direct recording of individual membrane potentials across large populations of neurons in vivo. However, applications of in vivo voltage imaging are still limited to experiments with head fixed mice, as miniature microscopes are unable to reach the frame rate and illumination requirements for this modality to be used with freely moving animals. To reach this goal, the 3DFast optical interface will combine structured illumination from InGaN/GaN microLEDs with stacked BSI-CMOS technology inside of a 3D-printed miniature microscope. This

project highlights the development of this device and the data processing techniques that it will utilize.

10
Kira Steinke
Integrated Physiology
Employing Holographic Optogenetics to Probe the Role of Decision-Predicting Time Cells
In the United States approximately 2.55 million people were affected by a memory related disease (such as Alzheimer's) in 2017, making it the second biggest neurological burden for the country, with trends suggesting these numbers are increasing. Importantly, a hallmark of Alzheimer's is the early loss of the sense of smell, highlighting important connections between memory and olfaction. Thus, it is increasingly relevant to study the biological processes underlying memory formation and recall in olfactory settings. Previous research demonstrates a prominent role for the hippocampus, particularly dorsal CA1 (dCA1), in learning and memory, strongly suggesting a fantastic target for studying the binding of associative, episodic, and contextual information to experiences which can be retrieved as a memory. However, how these memories are stored, processed, and recalled is currently unknown. dCA1 contains both glutaminergic excitatory pyramidal cells and GABAergic inhibitory interneurons. It has been demonstrated that following olfactory discrimination learning, pyramidal cells develop selective responses to odorants as the animal becomes proficient at the go no-go task. Post hoc neural decoding of spiking patterns results in prediction of which odor was presented to the animal during a particular trial. Our recent work demonstrates that select populations of pyramidal neurons display divergent stimulus responses taking place at discrete times, thereby exhibiting 'time tiling', which can be thought of as temporally discrete divergence in activity related to stimulus valence during the go no-go associative learning task. Time tiling of these "decision-predicting time cells" (DPTCs) is reminiscent of time tiling of dCA1 "stimulus time cells" that respond to odors at discrete times between odorant application in delayed non-match to sample tasks. This work aims to probe the cellular basis of DPTCs, testing if they are a Calbindin 2 subpopulation of pyramidal cells, and test if DPTCs are necessary for correct behavioral responses in the go-no go task. Additionally, I will investigate the role that parvalbumin (PV) interneurons may play in the time tiling of DPTCs.

11
Tarah Welton
Bioengineering
Drumbeat Optogenetics: Improving the firing frequency of channelrhodopsin-2
Channelrhopsin-2 (ChR2) is still one of most reliable opsins for depolarizing a variety of cells in response to light. Unfortunately, the utility of ChR2 is limited by its slow kinetics which makes exciting action potentials at frequencies $\geq$ 40 Hz difficult. In this work, we investigated an opsin stimulation scheme called "Drumbeat Optogenetics" where optical stimulation occurs at two separate locations asynchronously in time. Theoretically, this "drumbeat" allows the opsin at one location to recover slightly while stimulation occurs at the other. Here, we tested whether drumbeat optogenetics could be used to improve the firing frequency of a peripheral nerve relative to optogenetic stimulation of a single opsin population. Loose patch clamp was used to record compound action potentials (CAPs) from the sciatic nerve of ChAT-ChR2-YFP mice ex-vivo in response to traditional one-photon optogenetic stimulation, drumbeat one-photon optogenetic stimulation, and electrical stimulation. Our preliminary results show that the drumbeat scheme does

generate CAPs with slightly higher currents than traditional optogenetic stimulation at lower frequencies (~20 Hz); however, this effect appears to be lost at higher stimulation frequencies (~40 Hz) where it would be the most helpful. Unsurprisingly, optogenetic CAPs have much smaller currents than electrically induced CAPs because ChR2 is only expressed in cholinergic neurons and only activated in a subset of the cholinergic neurons that are adequately exposed to light. Overall, this work represents progress towards a better understanding of how optogenetic stimulation generates signal in the peripheral nervous system at different stimulation frequencies while also exploring an innovative stimulation strategy to attempt to bypass the inherently limiting kinetics of ChR2.

12
Peter Pressman
Communication and Speech Analysis in Neurocognitive Disabilities Laboratory: an Overview
This poster provides an overview of the work of our lab in developing technologies to expand access to evidence-based diagnoses and therapies for neurocognitive disabilities. Projects include use of artificial intelligence techniques to analyze spontaneous speech with 95% accuracy in distinguishing healthy controls from patients with mild cognitive impairment and Alzheimer's disease, development of a Cognitive Health Review Information System to take Patient-Centered Outcome Measures (PCOMS) and translate them into preliminary diagnostic and therapeutic recommendations, and outreach and engagement to traditionally underserved populations. In this way, we aim to co-design technologies that expand access to evidence-based practices in diverse communities.