MMiN
International Society for
Monitoring Molecules in Neuroscience

MMiN 2024

Monday, May 13: School of Medicine

04:00 PM - 04:30 PM

MMiN 2024 Opening Session

Monday, May 13: School of Medicine

04:30 PM - 05:30 PM

Opening Plenary: Robert Kennedy

Metabolomics of the Living Brain for Phenotyping and Pharmacology

School of Medicine

Robert Kennedy
University of Michigan-Ann Arbor, Metabolomics of the living brain for phenotyping and pharmacology

Metabolomics of the living brain for phenotyping and pharmacologyChair: Sara Jones, Wake Forest University School of MedicineRobert Kennedy, Pavlo Popov, Ian Bain, Brianna Ramos, Brady AndersonUniversity of MichiganBrain extracellular space contains a wide range of molecules including neurotransmitters, neuromodulators, and metabolites. Chemicals in this space are indicative of cellular activity and are involved in regulation of that activity. Most work to date using microdialysis has focussed on measuring a small number of neurotransmitters or metabolites at a time. Recent advances in LC-MS technology and informatics have opened the possibility of identifying and tracking the concentrations of many more compounds in the brain extracellular space. The methods are also used to compare the brain chemistry of behavioural phenotypes (high responder/low responder) and effect of cocaine on brain chemistry. We further examine the possibility of monitoring selected neurotransmitters at seconds resolution using droplet fraction collection and mass spectrometry analysis.

Monday, May 13: School of Medicine

05:30 PM - 07:00 PM

Welcome Reception

School of Medicine

Tuesday, May 14: Carolina Club: Foyer Area

08:30 AM - 06:00 PM

Registration / Info Desk

Tuesday, May 14: Carolina Club: Alumni I & II

09:00 AM - 10:00 AM

Plenary 1: Paul Kenny

Molecular, cellular, and circuit mechanisms of alcohol reinforcement

Carolina Club: Alumni I & II

Paul Kenny
Icahn School of Medicine at Mount Sinai, Molecular, cellular, and circuit mechanisms of alcohol reinforcement

Molecular, cellular, and circuit mechanisms of alcohol reinforcementChair: Zoe McElligott, UNC at Chapel HillAlcohol use disorder (AUD) is a leading cause of premature death and disease in the United States. Sex differences play important roles in determining how alcohol impacts the brain and in the progression from occasion to compulsive alcohol consumption that characterizes AUD. For example, binge drinking and AUD are more common among men than women (XY vs. XX individuals, respectively), although this gap has narrowed in recent years. In other non-human mammalian species, females typically consume greater quantities of alcohol than males. Sex differences in alcohol consumption Here, were used the Visium spatial transcriptomics platform from 10x Genomics to compare the brains of adult female and male C57BL/6J mice. Specifically, the gene expression profiles of cells located in brain regions known to regulate alcohol consumption and other AUD-relevant behaviors were compared between female and male mice. This revealed that the transcriptional profiles of cells in the interpeduncular nucleus (IPn) were markedly different between females and males. Single cell RNA sequencing (scRNA-seq) confirmed that gene expression programs in IPn cells differed between females and males. Striking sex-dependent differences in gene programs involved in nicotinic acetylcholine receptor (nAChR) signaling were detected. The IPn receives massive cholinergic input from the medial habenula (MHb) and contains some of the highest densities of nAChRs in mammalian brain, particularly nAChRs containing α5 subunits (α5* nAChRs). Cell-attached recordings showed that ethanol (10-44 mM) increased the baseline firing frequency of IPn-projecting cholinergic neurons in the MHb of female and male mice, with females more sensitive to this effect. Next, we expressed a microbial periplasmic binding protein (PBP)-based acetylcholine sensing fluorescent reporter (iAChSnFR) to monitor cholinergic signaling in the IPn of freely moving female and male mice. We found that ethanol (2 g/kg) increased cholinergic transmission in the IPn of female and male mice, and that females were more sensitive to the effect. It is known α5* nAChRs play a crucial role in mediating MHb-derived cholinergic signaling in the IPn. We found that female but not male α5 nAChR subunit knockout (α5 KO) mice consumed less ethanol that their wild-type counterparts. Virus-mediated re-expression of α5 nAChR subunits in the IPn of female α5 KO mice normalized their alcohol consumption relative to wild-type female mice. Conversely, CRISPR/Cas9-mediated disruption of α5 nAChR signaling in the IPn of female mice decreased their alcohol consumption related to wild-type females. Together, these data suggest that α5* nAChR-mediated cholinergic transmission in the IPn plays a key role in sex-dependent differences in alcohol consumption.

Tuesday, May 14: Carolina Club: Alumni I

10:30 AM - 12:30 PM

S.1: Xylazine and beyond: monitoring the molecules in the unregulated drug supply

Zoe Mcelligott
University of North Carolina, Session Chair

Cassandra Gipson
University of Kentucky, Mechanisms and consequences of intravenous fentanyl use and withdrawal when xylazine is used as an adulterant
Eugene Kiyatkin
National Institute of Drug Abuse-Intramural Research Program, Xylazine, its interaction with fentanyl and heroin, and possible therapeutic strategies: direct monitoring of drug-induced brain oxygen responses
Madigan Bedard
UNC Chapel Hill, Session Chair: Xylazine is a kOR agonist and exhibits sex-specific behaviors

Nabarun Dasgupta
University of North Carolina at Chapel Hill, Understanding what's in the drug supply through community engagement

The unregulated, non-medical drug supply contains several molecular additives that may have psychotropic effects. In recent years, xylazine, a veterinary sedative and anesthetic that was principally thought to target the alpha2-adrenergic receptor, has been detected with alarming frequency in the street-drug supply, especially in samples that were thought to be heroin or fentanyl. The effects of xylazine as an adulterant are not well understood. This panel will present multiple aspects of the monitoring of xylazine. Madigan Bedard will present phamacological data in vitro cellular assays, ex vivo metrics, and in vivo mouse models demonstrating "off target" effects of xylazine, and synthesizing what this may mean for treating xylazine withdrawal. Cassandra Gipson will present data showing the effects of xylazine on fentanyl self-administration in rat models, comparing xylazine to adulteration of intravenously self-administered fentanyl with other alpha2 adrenergic agonists including lofexidine. Further, evaluations of blood glucose and sleep disruptions in the context of extended access to the xylazine/fentanyl combination will be presented. Eugene Kiayatkin will present investigations into how xylazine may potentiate fentanyl induced deficits in brain oxygenation. Nabarun Dasgupta will present on the presence of xylazine in the drug supply, and also speculate on the newer molecular substances that are impinging upon the drug supply. This student led panel will bring perspectives from individuals at different career stages, using different animal models and approaches, and will bring in a very needed public health perspective to the challenges that face the unregulated drug supply.

10:30 AM - 12:30 PM

S.2: How the gut and brain talk to influence behavior and health

Laura Rupprecht
Duke University, Session Chair

Guillaume De Lartigue
Monell/UPenn, Why do we eat foods that we know are bad for us?

Melanie Kaelberer
Duke University, A brain to gut circuit

Sarah Najjar
New York University, Pain Research Center, Sex differences in gut serotonergic signaling of visceral pain

Iris Titos
University of Utah, Department of Psychiatry, A gut feeling for behavior

Fabien Naneix
University of Aberdeen, Sex-dependent impact of high fat foods during adolescence on brain circuits of action control

OCommunication between the gut and the brain is a novel and promising target for treating neural-related disease. This panel will highlight recent study of mechanistic processes through which the gut and brain signal to influence health and disease. Will de Lartigue (Monell Center) will discuss how the gut signals onto the vagus nerve to promote overeating. He will share data showing that separate vagal neurons respond to either intestinal fat or sugar, recruiting distinct but parallel dopamine circuits to reinforce food preferences. This talk will provide insight into cellular and system level mechanisms underlying obesity. Gut afferent signals are necessary to inform the brain about the food we eat. However, emotions can influence feelings about food. Maya Kaelberer (Duke University) will discuss recent work elucidating an efferent circuit that modulates sensory transduction from brain to gut. Using novel calcium imaging and electrophysiology techniques, she will share recent work describing how molecules released from efferent vagal neurons regulate the activity of a specialized epithelial cell in the intestine. This work provides insight on brain-gut mechanisms underlying visceral hypersensitivity. Visceral hypersensitivity is associated with functional gastrointestinal disorders like IBS. Sarah Najjar (NYU) will talk about the role of intestinal serotonin (5-HT) in pain signaling and gut function. She will examine how 5-HT released from gut epithelial cells impact visceral pain and gut motility, revealing important sex differences relevant treatment for disorders like IBS. Indeed, the gut is an organ with vast therapeutic potential – even for disorders related to sleep. The final talk in the session by Iris Titos (University of Utah) will share work from fly and mouse models, demonstrating that nutrition alters sleep depth. In the gut, dietary protein causes the release of an intestinal molecule which acts on dopamine neurons in the brain to regulate sleep and amphetamine preference. Together, this panel will provide an overview on gut and brain communication, and how we might monitor and manipulate gut molecules to improve health.

Tuesday, May 14: Carolina Club: Alumni III

Lunch

12:30 PM - 01:30 PM

Tuesday, May 14: Carolina Club: Alumni I

01:30 PM - 03:00 PM

S.3: Behaviorally relevant dopamine signaling: Heterogeneity in information content, sub-regional release, and temporal dynamics

Ingo Willuhn
Netherlands Institute for Neuroscience, Mapping the striatal landscape of dopamine signaling for motivational stimuli
Talia Lerner
Northwestern University Feinberg School of Medicine, Region-specific nucleus accumbens dopamine signals encode distinct aspects of avoidance learning
Geoffrey Schoenbaum
NIH/NIDA, Striatal dopamine signals errors in cue prediction during sensory preconditioning

Arif Hamid
University of Minnesota, Wideband dopamine fluctuations for multi-timescale behavioral flexibility

It is widely accepted that dopamine signals in the striatum are critical for reinforcement learning and motivated behavior. However, several dopamine-signal features are under active debate, including their precise information content, their temporal dynamics, and their sub-regional specificity. This speaker panel will shine light on the heterogeneity of dopamine signals in the striatum regarding these features to improve our understanding of the role of the dopamine system in reinforcement learning and motivated behavior. Talia Lerner and Geoffrey Schoenbaum will contribute findings that speak to the information content of dopamine signals, where research has often focused on appetitive stimuli in general and specifically reward-prediction errors in the context of temporal difference reinforcement learning. Talia Lerner will present evidence for the involvement of dopamine in avoidance learning and sub-regional specificity of such dopamine signals within the ventral striatum. Geoffrey Schoenbaum will report evidence for prediction-error-like dopamine signals in a sensory preconditioning task. Arif Hamid will introduce an electrochemical/optical method advancement that enables the sensing of wideband dopamine fluctuations in the ventral striatum, both on fast (phasic) and slow (tonic) times scales, to tackle longstanding questions on how dopamine shapes behavior across timescales. Ingo Willuhn will present novel findings that demonstrate regional heterogeneity of behaviorally relevant dopamine signals in the ventral and dorsal striatum in response to both appetitive and aversive stimuli and associated predictive cues. Quantification of changes in the extracellular concentration of dopamine was performed using the latest technological advances in in-vivo fiber photometry and fast-scan cyclic voltammetry in unrestrained rodents performing in a variety of behavioral paradigms.

Tuesday, May 14: Carolina Club: Dowd/Harris

01:30 PM - 03:00 PM

S.4: In vivo monitoring of brain circuits during alcohol consumption

Alison Roland
University of North Carolina, Modulation of extended amygdala calcium dynamics by acute and chronic alcohol

Jacqueline Barker
Drexel University, Modulation of nucleus accumbens astrocyte calcium activity during reinstatement

Jen Rinker
Medical University of South Carolina, Prefrontal cortical calcium dynamics decode binge-alcohol drinking

Brady Atwood
Indiana University School of Medicine, Sex-dependent, lateralized engagement of anterior insular cortex inputs to the dorsolateral striatum in binge alcohol drinking

Alcohol use disorder is a chronic disease characterized by alcohol cravings, negative emotionality, and a loss of control over alcohol intake. With the development of genetic probes, there has been a resurgence of interest in understanding in vivo dynamics that underlie this disorder. This panel will present data on in vivo monitoring of neuronal and glial activity in animal models of alcohol drinking. Jen Rinker will present data on calcium activity in prelimbic (PrL) neurons during the peri-consummatory phase in response to solutions of varying hedonic value, including alcohol, sucrose, and water. Machine learning demonstrated that PrL calcium activity both predicted consumption and distinguished between solutions. PrL population activity scaled with the hedonic value of the solution, and this functional signature was disrupted by alcohol dependence. Brady Atwood will describe work on the role of anterior insular cortex inputs to the dorsolateral striatum in binge alcohol drinking. In vivo optogenetic monitoring of presynaptic calcium dynamics and direct excitation of these synapses revealed that both pre- and post-synaptic adaptations develop over the course of weeks of alcohol drinking and are related to an increased ability to control ongoing drinking behavior. Jacqui Barker will present work investigating astrocyte activity in the regulation of reward seeking following chronic intermittent ethanol. Her work identifies alterations in astrocyte calcium signaling during reward seeking, and the potential to chemogenetically target astrocyte activity to reverse dependence-induced deficits in extinction and reward seeking under conflict. Finally, Alison Roland from the Kash lab will describe her work on acute and chronic alcohol regulation of calcium dynamics in the extended amygdala. Neuronal activity in the bed nucleus of the stria terminalis and central amygdala were increased during drinking behavior, independent of fluid valence, and dynamics were influenced by stimulus novelty and chronic alcohol exposure. Together, these studies provide insight into the alcohol-induced cellular and neurocircuitry adaptations that promote pathological drinking behavior.

Tuesday, May 14: Carolina Club: Alumni III

03:00 PM - 03:30 PM

PM Break

Tuesday, May 14: Carolina Club: Alumni I **03:30 PM - 05:30 PM**

S.5: Assessing function and quantity of dynorphin peptides and kappa opioid receptors in animal models of stress and reward

Sara Jones
Wake Forest University School of Medicine, Session Chair

Huikun Wang
NIMH, Prefrontal cortical dynorphin signaling and threat processing

Gagan Deep
Wake Forest University School of Medicine, Extracellular vesicles: Liquid biopsy for molecular biomarker discovery in neurological disorders
Rohan Bhimani
University at Buffalo, Estrous-cycle dependent regulation of central catecholamine signaling in response to food and drug reward

The peptide dynorphin and its receptor, the kappa opioid receptor (KOR), are distributed widely throughout the brain and participate in a variety of processes such as stress, pain, and emotional regulation and are critically involved in reward mechanisms and alcohol/drug use disorders. Despite intense interest in dynorphin/KOR system activity, quantification of the levels and functional activity of dynorphin peptides and KORs has proven extremely difficult. This symposium will showcase several emerging techniques that are being developed for use in animal models. First, Sara R. Jones, PhD, will describe experiments with the fluorescent dopamine (DA) sensor, dLight, measuring KOR agonist-induced changes in the kinetics of spontaneously occurring DA fluctuations in freely moving mice to evaluate the functional activity of KORs in the nucleus accumbens, where DA release is inhibited and DA uptake through the DA transporter is accelerated by KOR activation. Ream Al-Hasani, PhD, will describe novel microimmuno-electrode-based detection of dynorphin as well as novel insights into dynorphin function in the neurocircuitry of reward processing. Huikun Wang, PhD, from the laboratory of Hugo Tejeda at NIMH, has explored monitoring extracellular dynorphin in the PFC using the fluorescent sensor kLight, and findings in a mouse model of fear conditioning will be preseented. To wrap up, Gagan Deep, PhD, will share how he uses blood as a "liquid biopsy" of the brain to measure KORs and other proteins in neuron-derived extracellular vesicles, or exosomes, in blood taken from socially housed rhesus monkeys.

Tuesday, May 14: Carolina Club: Dowd/Harris **03:30 PM - 05:30 PM**

S.6: Why and how a shift towards the use of data mining tools in neurochemical analysis is relevant

Sandrine Parrot
University of Lyon, Session Chair; Neurochemicals analyzed using factor analysis can be linked to psychometrical dimensions in motivated and non-motivated behaviors

Philippe de Deurwaerdere
Universite de Bordeaux, Session Chair: Forced exploration alters the correlative links between tissue neurotransmitters in mice: effect of Serotonergic 2 receptor ligands

Jesse Cushman
NIEHS, FiPhA: An open-source platform for fiber photometry analysis

Ian Bain
University of Michigan, Pairing microdialysis with droplet microfluidics and direct mass spectrometry for multiplexed, high temporal resolution neurochemical monitoring
Elena Romanova

Juliette Pelletier
Polytechnique Montreal, 3D neuronal cell culture on paper device and bioelectrochemical analysis

Neurochemists currently monitor from 1 to 4-6 parameters per individual and the statistical tools used help comparing data parameter per parameter while considering the various groups of individuals included in their studies. As many parameters can be recorded either once or using repeated measures, the classical statistical tools based on parametric or non-parametric distributions can hide some interactions between several variables. It becomes particularly pertinent when addressing the brain-wide dimension of neurotransmitter systems and their metabolism, alone or in interaction, in different cohorts of animals. In that perspective, big data tools seem to be more relevant to describe the links between variations observed in the available data by taking another look. The purpose of the symposium is to show some recent examples of the introduction of data mining in neurochemical data analysis.

Wednesday, May 15: Carolina Club: Alumni I & II **09:00 AM - 10:00 AM**

Plenary 2: Marisela Morales

Co-release of different neurotransmitters, unanticipated types of neurotransmission and future challenges

Marisela Morales
National Institute on Drug Abuse (NIDA) at the National Institutes of Health (NIH), Co-release of different neurotransmitters, unanticipated types of neurotransmission and future challenges
Co-release of different neurotransmitters, unanticipated types of neurotransmission and future challengesChair: David Lovinger, National Institute on Alcohol Abuse and Alcoholism

Wednesday, May 15: Carolina Club: Alumni I **10:30 AM - 12:30 PM**

S.7: Aptamer-based biosensors for neurotransmitter and drug monitoring

Yi Xiao
North Carolina State University, New selection methods for isolating high-quality aptamers for small molecules

Netz Arroyo
Johns Hopkins University School of Medicine, Mapping drug distribution across the brain: Aptamer-based tracking reveals significant variations in ADME
Tod Kippin
University of California, Santa Barbara, Session Chair; Elucidating the relationships between in-brain drug concentration and behavior using electrochemical aptamer-based biosensors
Anne Andrews
University of California, Los Angeles, Session Chair; Expanding the neurochemical toolbox for aptamer-FET biosensors

Nako Nakatsuka
Swiss Federal Institute of Technology Lausanne, Aptamer-modified nanopipettes for monitoring neurotransmitters at the nanoscale
Yi Zhang
U Conn, Enhancing the in vivo longevity of aptamer-based biosensors with DNase inhibitor-doped polyacrylamide hydrogel coatings

Aptamers are DNA- or RNA-based molecular recognition elements that enable high-resolution small-molecule monitoring. They overcome several key limitations associated with protein receptors or antibodies for molecular recognition. Importantly, aptamers enable, when combined with a variety of signal transduction platforms, the ability to monitor targets including neurotransmitters and drugs in high ionic strength environments in vivo or ex vivo. Brain function ultimately arises from the dynamic and complex interactions between endogenous and exogenous chemicals that impact the activity between and within neurons. Much of our understanding of these dynamics is derived from post-mortem analyses, microdialysis, or electrochemistry which, while providing critical information, also present limitations in terms of measuring the range of relevant molecules at the appropriate temporal resolution. The speakers in this symposium will focus on the latest advances in aptamer biosensing. The panel will discuss emerging aptamer-based sensing strategies aimed at monitoring molecular targets in the brain regardless of chemical class, at appropriate time scales, and in real-time. Speakers will discuss challenges and opportunities for aptamer biosensors in terms of realizing the goals of long-term stable in vivo monitoring.

Wednesday, May 15: Carolina Club: Dowd/Harris **10:30 AM - 12:30 PM**

S.8: Real-time tracking of brain neuromodulation in vivo

David Lovinger
National Institute on Alcohol Abuse and Alcoholism, Session Chair

Ozge Gunduz Cinar
National Institute on Alcohol Abuse and Alcoholism, The role of corticoamygdala endocannabinoid neuromodulation in fear extinction
Andrew Lutas
National Institute of Diabetes and Digestive and Kidney Diseases, Transient cAMP production drives rapid and sustained spiking in brainstem parabrachial neurons to suppress feeding
Jeong Oen Lee
National Institute on Alcohol Abuse and Alcoholism, A FRET-based cAMP biosensor for investigating the functional role of striatal circuitry
Tianyi Mao
Vollum Institute, In vivo imaging of intracellular signaling in response to multiple neuromodulators

Suzanne Nolan
Vanderbilt University, Session chair; Recurrent activity within microcircuits of macaque dorsolateral prefrontal cortex tracks cognitive flexibility

Recent breakthroughs in neuroscience have ushered in a new era characterized by transformative technological advancements across multiple disciplines. The symposium aims to illuminate the latest developments in molecular and optical tools, representing a cutting-edge frontier in the efficient and scalable monitoring and manipulation of neural activity in health and disease contexts. This comprehensive exploration spans various neural players, including calcium, voltage, neurotransmitters, neuromodulators, and synthetic drugs.At the molecular level, the suite of engineered tools such as optogenetics, chemogenetics, genetically encoded sensors, and other chemical tools have become pivotal in the endeavor to unravel the intricacies of neural activity, the genetic makeup of neuronal activity, and enabling real-time characterization of cellular processes in the brain. These tools allow researchers to monitor and manipulate large populations of neurons simultaneously, offering unparalleled insights into the dynamic interplay of neural networks. Synergistically, optical tools and methods have played a pivotal role in advancing our understanding of neural activity. Cutting-edge multiphoton imaging techniques, coupled with sophisticated microscopy, enable deep-tissue imaging and have allowed researchers to study neural circuits with cellular and molecular precision.In this symposium, we bring together experts from diverse disciplines, thus serving as a platform for sharing knowledge and fostering collaboration. The overarching goal is to collectively push the boundaries of what is known about neural activity, from the molecular underpinnings to the emergent properties of large-scale neural networks. Ultimately, these advancements have profound implications for our understanding of brain function in health and disease, offering new opportunities for therapeutic development and personalized interventions.

Wednesday, May 15: Carolina Club: Alumni I

01:30 PM - 03:00 PM

S.9: Cutting-edge approaches to monitor and manipulate neural activity

Ismail Ahmed
New York University School of Medicine, Session Chair

Michael Tadross
Duke University, Rewiring persistence by targeting dopamine-neuron inhibitory synaptic receptors

Ahmed Abdelfattah
Brown University, Genetically encoded voltage indicators for optical monitoring of neural activity

Christina Kim
University of California, Davis, Molecular circuits for probing activated neuronal ensembles, Session Chair

Recent breakthroughs in neuroscience have ushered in a new era characterized by transformative technological advancements across multiple disciplines. The symposium aims to illuminate the latest developments in molecular and optical tools, representing a cutting-edge frontier in the efficient and scalable monitoring and manipulation of neural activity in health and disease contexts. This comprehensive exploration spans various neural players, including calcium, voltage, neurotransmitters, neuromodulators, and synthetic drugs.At the molecular level, the suite of engineered tools such as optogenetics, chemogenetics, genetically encoded sensors, and other chemical tools have become pivotal in the endeavor to unravel the intricacies of neural activity, the genetic makeup of neuronal activity, and enabling real-time characterization of cellular processes in the brain. These tools allow researchers to monitor and manipulate large populations of neurons simultaneously, offering unparalleled insights into the dynamic interplay of neural networks. Synergistically, optical tools and methods have played a pivotal role in advancing our understanding of neural activity. Cutting-edge multiphoton imaging techniques, coupled with sophisticated microscopy, enable deep-tissue imaging and have allowed researchers to study neural circuits with cellular and molecular precision.In this symposium, we bring together experts from diverse disciplines, thus serving as a platform for sharing knowledge and fostering collaboration. The overarching goal is to collectively push the boundaries of what is known about neural activity, from the molecular underpinnings to the emergent properties of large-scale neural networks. Ultimately, these advancements have profound implications for our understanding of brain function in health and disease, offering new opportunities for therapeutic development and personalized interventions.

Wednesday, May 15: Carolina Club: Dowd/Harris

01:30 PM - 03:00 PM

S.10: Extrasynaptic volume transmission and extracellular space imaging

Paul Slesinger
Icahn School of Medicine at Mount Sinai, Session Chair

Zhenpeng Qin
University of Texas at Dallas, Session Chair

Jaume Taura Iglesias
Icahn School of Medicine at Mount Sinai

Xiaoqian Ge
University of Texas at Dallas

Lin Tian
Max Plank Florida Institute for Neuroscience

Matthew Banghart
University of California San Diego

Although quite abundant in the brain, we have a poor understanding of the ‘how, where and when’ of neuropeptide volume transmission in the brain. There is significant interest in developing new tools (sensors, nanoparticles, imaging) to study the neurobiology of peptides in the brain. This proposed symposium aims to highlight recent advances in these areas. These include new tools to measure neuropeptides in the brain with state-of-the-art sensors, photo-pharmacology, as well as to image and characterize the extracellular space that these transmission events occur. These emerging new tools start to offer a comprehensive understanding of the extrasynaptic volume transmission, and the important role of the extracellular space which serves as conduits for the extrasynaptic transmission. This symposium will bring together speakers from a range of approaches and perspectives including nanomaterials and chemistry, protein engineering, imaging, and neuroscience, to engage in cross-disciplinary conversations on this emerging topic. This symposium further provides a platform to encourage in-depth discussions among presenters and audience.

Wednesday, May 15: Carolina Club: Alumni III **03:00 PM - 03:30 PM**

PM Break

Carolina Club: Alumni III

Wednesday, May 15: Carolina Club: Alumni I **03:30 PM - 05:30 PM**

S.11: Computationally assisted multi-analyte voltammetry and its application for real-time monitoring of neurochemicals in vivo

Anne Andrews
University of California, Los Angeles, Session Chair; Expanding the neurochemical toolbox for aptamer-FET biosensors

Kenneth Kishida
Wake Forest School of Medicine, Session Chair

Cameron Movassaghi
University of California, Los Angeles

Leonardo Barbosa
Fralin Biomedical Research Institute, Virginia Tech

Kendall Lee
Department of Neurosurgery, Mayo Clinic

Sara Vettleson-Trutza
Mayo Clinic, Deep brain stimulation of ventral tegmental area modulates dopamine surge in rat nucleus accumbens following acute fentanyl administration

Fast scan cyclic voltammetry on carbon fiber microelectrodes has led the way for subsecond, real-time detection of neurotransmitters in ex vivo and in vivo paradigms for decades. Recent developments in the application of computational methods to voltametric data has opened new doors for monitoring multiple analytes simultaneously or for more reliable detection and discrimination of particular analytes of interest. These advances are creating new opportunities for work in human neuroscience and place voltammetric approaches at the forefront of methods for direct monitoring of real-time multi-analyte interactions, in situ, in humans and pre-clinical models. This symposium will introduce current state-of-the-art methods, highlight the impact these approaches are having on our understanding of voltammetry data collection and analysis – including the often-underappreciated richness of raw voltametric 'background' signals – and showcase some of the latest work being performed in human and preclinical models. The advances to be discussed include new quantitative methods for characterizing the background signal, new higher-resolution data collection protocols permitted by high-speed computer-controlled voltage clamps, advances in the use of 'black-box' artificial intelligence algorithms, but also advances in the use of interpretable models derived from supervised statistical learning methods. The motivation for developing these innovations will be exemplified by speakers' utilization of these tools in performing cutting-edge research in discovery and translational neuroscience. The panel will present and discuss applications ranging from basic science in model organisms and basic experimental studies in humans to translational work that is advancing these tools into the clinical realm for discovery and human application. We invite the audience to ask critical questions and hope for an open discussion of potential limitations and challenges with an interest in moving the field forward and thus further advancing our collective understanding of neurochemical signaling in biological systems.

Wednesday, May 15: Carolina Club: Dowd/Harris **03:30 PM - 05:30 PM**

S.12: Accumbens plasticity mechanisms regulating reward and aversion

Jessica Walsh
University of North Carolina at Chapel Hill, Repeated enhancement of serotonin via MDMA alters cortico-striatal circuits and results in a sustained rescue of social deficits
Dan Christoffel
University of North Carolina, Modulation of accumbal activity & hedonic feeding

Chase Francis
University of South Carolina, Peptidergic mechanisms of aversive learning in nucleus accumbens circuits

Sophie Cohen
Drexel University, Sleep disturbances are associated with mesolimbic dopamine dysfunction and cue-induced drug seeking during abstinence from cocaine
Elaine Grafelman
Marquette University, Aversive white noise reduces nucleus accumbens core dopamine signaling and promotes both cocaine intake and escape behavior

In any given moment, an individual may experience a vast range of stimuli with varying degrees of valence, from strongly rewarding to extremely aversive. Well-being & survival critically depend on the ability to properly identify & encode stimulus valence to prioritize resources & behave adaptively. Paradoxically, while individuals seek out pleasurable & rewarding stimuli, those that evoke aversive experiences generally ensnare attentional resources & are more easily remembered. Thus, investigating how the brain assesses the value & salience of current stimuli is pivotal to understanding the biological basis of behavior. The Nucleus Accumbens (NAc) is critical to several neural processes involved in the assessment of rewarding & aversive experiences. Frontal-striatal circuits are key regulators of decision making & action selection, whose function is often altered in avoidance & impulsive/compulsive disorders. Numerous studies reveal long-lasting changes in synaptic transmission that mediate adaptive learning, behavioral responses to stimuli of both valences & may underlie maladaptive behavior. Yet, the precise mechanisms underlying these neural adaptations are not well understood. This panel will provide insight into circuits, cell-types & neuromodulatory systems that converge in the NAc to regulate multiple distinct behaviors (social interactions, hedonic feeding & aversive response) using a wide range of modern neuroscience techniques (chemo- & optogenetics, ex vivo and in vivo neural recordings [electrical & optical] multiple behavioral paradigms). Novel findings will describe how 1) repeated enhancement of serotonin levels modulate a cortico-striatal circuit to cause lasting increases in sociability in a mouse model for autism, 2) NAc medium spiny neuron (MSN) activity regulates hedonic feeding, 3) NAc MSN plasticity driven by substance P acetylcholine release is required for cue-dependent aversive learning. Together this work sheds light on how multiple neurotransmitters modulate NAc function & provide new avenues of investigation for therapeutic development.

Thursday, May 16: Carolina Club: Alumni I & II

Plenary 3: Yulong Li

Spying on neuromodulator dynamics In vivo by constructing multi-color genetically-encoded sensors

Yulong Li
Peking University, Spying on neuromodulator dynamics in vivo by constructing multi-color, genetically-encoded sensors

The human brain consists of billions of neurons, most of which communicate with each other by releasing different kinds of neuromodulators through chemical synapses, and therefore is able to control different physiological functions like perception, motion, learning and memory. To dissect the mechanism underlying how brain take part in different physiological functions and pathological conditions, it's important to monitor the dynamics of neuromodulators in vivo. In the past few years, we and others have developed a series of multi-color GPCR-activation–based (GRAB) sensors for monitoring extracellular neuromodulator dynamics with high sensitivity, specificity, and spatial-temporal resolution in living animals. In this report, I will share our recent progress in developing sensors for monitoring monoamines, nucleotides, neurolipids and neuropeptides. With these GRAB sensors, we have monitored the dynamics of neuromodulators in mice in a wide range of physiological processes (sleep-wake cycle, motion, etc.) and pathological conditions (epilepsy, etc.).

Thursday, May 16: Carolina Club: Alumni III **10:00 AM - 10:30 AM**

AM Break

Carolina Club: Alumni III

Thursday, May 16: Carolina Club: Alumni I

10:30 AM - 12:30 PM

S.13: Probing everything everywhere all at once: Biomolecule - behavior relationships in high resolution

Eleanor Simpson
Columbia University, Session Chair

Mark Walton
University of Oxford, Session Chair

Alexxai Kravitz
Washington University, Recording global signals of dendritic calcium in the striatum

Jeffrey Markowitz
Georgia Tech and Emory University, Exploring the role of dopamine in spontaneous behavior

Mark Howe
Boston University, Trajectory error signalling in spatially organized striatal neuromodulator release

Laura Grima
HHMI/Janelia, Striatal dopamine reflects behaviour in multi-option foraging

Unraveling the neural mechanisms of behavior requires the ability to monitor molecular and cellular fluctuations with high spatiotemporal resolution. Recently developed fluorescent biosensors show huge promise to facilitate this, as they allow recording of extracellular neuromodulators and intracellular signaling molecules over ranges of space and time in diverse behavioral scenarios. A pressing challenge now is to determine how best to leverage the opportunities afforded by these advances to test understand relationships between these signals (individually or multiplexed) and increasingly rich simultaneous behavioral measures. This symposium will focus on cutting-edge approaches being developed to address this challenge including: Combining photometry with electrophysiology to determine the relationships between neuronal activity, somatic and terminal calcium dynamics and action selection (Lex Kravitz); Using multi-fiber arrays to characterize how behavior-related photometry signals are coordinated within and across brain regions (Mark Howe); Elucidating the organizational principles between striatal neurotransmission and spontaneous behavioral motifs (Jeffrey Markowitz); and Tracking dynamic dopamine signaling during foraging in naturalistic environments (Laura Grima). Each presenter will provide complementary perspectives on the overarching question of how the field can couple photometry of biosensors with other recording / manipulation techniques and rich behavioral analysis. Each will also describe important interpretational caveats when quantifying relationships between different modes of data. Finally, the Chairs will moderate an interactive exchange with the Presenters and the wider audience. Discussion will include future opportunities and areas in need of continued progress when applying quantitative approaches to different data types of interest.

Thursday, May 16: Carolina Club: Dowd/Harris

10:30 AM - 12:30 PM

S.14: Old dog, new tricks – why carbon persists as the leading material for novel technologies to detect neurotransmitters

Mei Shen
University of Illinois at Urbana-Champaign, Session Chair: Nanoscale dual-channel carbon-liquid/liquid interface probes for the simultaneous detection of acetylcholine and dopamine
Parastoo Hashemi
Imperial College London, Session Chair (S.14)

Tracy Cui
University of Pittsburgh, Carbon-based MEAs for chronic multichannel and multimodal interrogation of the brain

Jinwoo Park
University at Buffalo, Application of carbon-fiber microsensors coupled with local genetic manipulations for decoding limbic norepinephrine systems
Kalynn Turner
North Carolina State University, Real-time, voltammetric co-detection of serotonin and glucose at carbon-fiber microbiosensors

Carbon has been the material of choice for detection of neurotransmitters in biological systems for decades because this material is versatile, cheap, biocompatible and carries excellent transfer properties. A surprising facet of this material is the seemingly endless ways that carbon can be optimized and modified to fit new sensing modalities. The speakers in this session are pioneers in electrochemical detection of neurotransmitters and will present the cutting edge in new carbon sensors. Prof. Shen will discuss a rapid acetylcholine sensor based on modified ion selective carbon electrodes for in vivo sensing in mice. Prof. Hashemi will highlight a new ex vivo microfluidic platform with fast scan cyclic voltammetry - 'neuroinflammation-on-a-chip'. This device performs measurements of serotonin and histamine at exposed carbon electrodes integrated directly into the device, from cerebral organoids with potential for antidepressant drug screening. Professor Cui will introduce different ways of creating carbon-based microelectrode arrays for in vivo multichannel and multimodal interrogation of the brain and the challenges and opportunities in chronic applications. Finally, Prof. Park will showcase the ability of FSCV carbon electrodes to be coupled with neuromodulatory techniques (optogenetics and chemogenetics) for decoding brain catecholamine (norepinephrine and dopamine) circuits implicated in drug use disorders. Taken together this symposium highlights the sheer versatility and future of carbon-based sensing.

Thursday, May 16: Carolina Club: Alumni III **12:30 PM - 01:30 PM**

Lunch

Carolina Club: Alumni III

Thursday, May 16: Carolina Club: Alumni I **01:30 PM - 03:00 PM**

S.15: Monkey business: novel applications for neuroscientific methodologies in nonhuman primates

Suzanne Nolan
Vanderbilt University, Session chair; Recurrent activity within microcircuits of macaque dorsolateral prefrontal cortex tracks cognitive flexibility
Katherine Holleran
Wake Forest School of Medicine, Session Chair; Perspectives on recent advances in non human primate research

Kristen Pleil
Weill Cornell Medicine, Cornell University, Effects of sex and alcohol on neuronal function in the primate BNST

Victor Van Laar
Ohio State University, AAV-based GDNF expression in VTA prevents relapse to alcohol-drinking behavior and modifies mesolimbic dopamine function in rhesus macaques: a gene therapy approach to treating alcohol use disorder **Melanie Pina**
University of Maryland School of Medicine, Binge alcohol intake induces a cross-species loss of serotonin function in the OFC

Recent high-profile work in neuroscience has arisen from innovative methods offering unprecedented cell-specific targeting to gain insight into mechanisms responsible for the dysfunctional neurotransmission underlying neuropsychiatric conditions. For example, with the advent of optical sensors in combination with existing technique innovations, it is now possible to monitor the development of neurological dysfunction in preclinical models of neuropsychiatric conditions like substance use disorder with high spatial and temporal precision. However, the human health relevance of these findings rests on the assumption of translatability from rodent models to higher-order species like nonhuman primates, for which these tools are largely not currently available. This panel will present data exploring how novel combinations of existing tools are being applied in nonhuman primate models, thereby answering previously unanswerable questions. First, Dr. Victor Van Laar will present recently published findings exploring viral-mediated GDNF expression as a treatment for alcohol use disorder in macaques. Next, Dr. Melanie Pina will present exciting new findings regarding alcohol-induced changes in 5-HT signaling in the orbitofrontal cortex of rhesus macaques. Dr.Suzanne Nolan will then reveal novel findings on the coordination of cortical microcircuit activity using high-density calcium imaging in the primate prefrontal cortex and its relationship to behaviors like cognitive flexibility and drinking. Finally, Dr. Kristen Pleil will examine sex differences in the effects of chronic alcohol drinking on hormone dysregulation and BNST neuron physiology in rhesus macaques. Additionally, Dr. Kathleen Grant will serve as a discussant to add important context linking these findings and discuss future projections for this research area. Together, these data will illustrate how modern neuroscience tools can be leveraged in higher order species like primates to yield novel insights into the neurophysiological mechanisms underlying psychiatric disorders.

Thursday, May 16: Carolina Club: Dowd/Harris **01:30 PM - 03:00 PM**

S.16: Illuminating striatal acetylcholine-dopamine interactions: lighting up the way forward

Stephanie Cragg
University of Oxford, Session Chair

Yanfeng Zhang
University of Exeter, An axonal brake on striatal dopamine output by cholinergic interneurons

Lauren Burgeno
University of Oxford, Striatal acetylcholine reports distinct update signals during flexible multi-step decision making

Nicolas Tritsch
New York University, Intrinsic dopamine and acetylcholine dynamics in the striatum of mice

Organiser: Yanfeng Zhang, University of ExeterChair: Yanfeng Zhang, University of Exeter & Stephanie Cragg University of OxfordPresenters:Yanfeng Zhang, University of Exeter; Mark Howe, University of Oxford; Lauren Burgeno, University of Oxford; Nicolas Tritsch, NYUIndividual talk titles:Yanfeng Zhang: An axonal brake on striatal dopamine output by cholinergic interneuronsMark Howe: Coordination of striatum-wide dopamine and acetylcholine signaling during learningLauren Burgeno: Striatal acetylcholine reports distinct update signals during flexible multi-step decision makingNicolas Tritsch: Intrinsic dopamine and acetylcholine dynamics in the striatum of miceSymposium Overview: This symposium aims to showcase recent breakthroughs in the application of advanced sensors for dopamine and acetylcholine to address …

Thursday, May 16: Carolina Club: Alumni III **03:00 PM - 03:30 PM**

PM Break

Carolina Club: Alumni III

Thursday, May 16: Carolina Club: Alumni I

03:30 PM - 05:30 PM

S.17: Bioanalytical measurements for analysis of disease pathways: New molecules and methods

Parastoo Hashemi
Imperial College London, Session Chair (S.14)

Michael Johnson
University of Kansas, Unraveling zinc function in neurodegeneration with combined fast-scan cyclic voltammetry and caged-compound photolysis
Martyn Boutelle
Imperial College London, Probing neuronal recovery during advanced life support following cardiac arrest

Julie Stenken
University of Arkansas, Tailored 3D printed microsampling probes in neuroscience

Qinbo Qiao
University of Oxford, Reciprocal regulation of dopamine and serotonin release in healthy and Parkinsonian mouse striatum

Recent improvements in bioanalytical methods have greatly enhanced their sensitivity, selectivity, and applicability to human disease. This symposium highlights work from investigators who have developed enhanced analytical tools to obtain a greater understanding of human disease. These topics include using novel 3D microdialysis probes that expand the toolkit available to answer fundamental questions in neurological disease states (Stenken), single exosome electrochemical measurements and their role in intercellular chemical communication (Ewing), unraveling the role of serotonin regulation in depression (Hashemi), and dynamic measurement of metals and neurotransmitters in living brain tissue to understand mechanisms of Parkinson's disease and Alzheimer's disease (Johnson). This diverse group of speakers carry out research that is timely and relevant.

Thursday, May 16: Carolina Club: Dowd/Harris

03:30 PM - 05:30 PM

S.18: Diverse perspectives on monitoring molecules

Greatness Olaitan

Andrew Kesner
NIAAA, A role for medial septum glutamate neurons in reward-seeking: strategy switching and nucleus accumbens dopamine
Gianluigi Tanda
National Institute on Drug Abuse, Intramural Research Program, A neurochemical study of dual inhibitors of DAT and sigma receptors as potential therapeutic options for psychostimulant use disorder
Jenna Berger
North Carolina State University, Chasing the enkephalins: simultaneous co-detection of met-enkephalin and dopamine release in rat striatum
Jyoti Patel
NYU Grossman School of Medicine, Insulin targets striatal cholinergic neurons for acetylcholine and dopamine dependent nutrient sensing
Gunnar Sorensen
H. Lundbeck A/S, Within-mice comparison of microdialysis and fiber photometry- recorded dopamine biosensor during amphetamine response

Thursday, May 16: Carolina Club: Alumni I **05:30 PM - 06:00 PM**

MMiN Business Meeting

Carolina Club: Alumni I

Thursday, May 16: The Blue Zone **07:00 PM - 10:00 PM**

Banquet

The Blue Zone

Join us from 7:00PM at the Blue Zone for the Conference Banquet at the Kenan Memorial Stadium!

Thursday, May 16: The Speakeasy **09:00 PM - 11:59 PM**

KARAOKE!

The Speakeasy

🎤Join us after the banquet at The Speakeasy for Karaoke