Institute for Research in Statistics and its Applications (IRSA)

Neuro-Statistics: the interface between Neuroscience and Statistics

This workshop is co-sponsored by:

The International Chinese Statistical Association
The International Indian Statistical Association
Abstracts of keynote and plenary talks
Speaker: Professor Vince Clark

Brief Biography: Dr. Vince Clark obtained his PhD in Neuroscience from UCSD and his postdoctoral training at NIMH. He was recruited to New Mexico to help build and organize the Mind Research Network, eventually being promoted to Scientific Director. He is currently Professor of Psychology and Neuroscience and founding Director of the Psychology Clinical Neuroscience Center at the University. He served as an Editor for the journal, NeuroImage, and as Education Chair for the Organization for Human Brain Mapping. He also serves on the Editorial Boards of Human Brain Mapping and Brain Stimulation and is founding Chair of the annual Brain Stimulation and Imaging Meeting. His research focuses on understanding the brain basis of healthy cognition and mental illness and finding new methods for the application of neurostimulation to increase cognitive performance and treat symptoms of brain and mental illness.

Title of talk: Neuroimaging Combined with Neurostimulation: New Methods for Verifying and Utilizing the Causal Connections Between Brain and Behavior

Abstract: Neuroimaging has helped us to make great strides in understanding the mechanisms of human cognition, and for identifying differences associated with brain and mental illness. However, this work has been mostly observational, often depending on correlations that cannot be used to prove causation, and has produced few real-world benefits for cognitive enhancement or for treating mental illness. The combination of neuroimaging and non-invasive brain stimulation could lead to many advances in these endeavors, including the direct testing of causal hypotheses of brain function, a better understanding of the brain mechanisms of cognition, and developing new methods to optimize cognitive performance and treat symptoms of brain and mental illness. Examples of the combined use of neuroimaging and neurostimulation to help achieve these goals, and future directions for this area of research, will be described.
**Buehler-Martin Plenary Lecture:**

**Speaker:** Professor Martin Lindquist

**Brief Biography:** Martin Lindquist is a Professor of Biostatistics at Johns Hopkins University. His research focuses on mathematical and statistical problems relating to functional Magnetic Resonance Imaging. Dr. Lindquist is involved in developing new analysis methods to enhance our ability to understand brain function using neuroimaging. He has published over 70 articles, and serves on the editorial boards of several scientific journals in both statistics and neuroimaging. He is a fellow of the American Statistical Association.

**Title of talk:** *Brain Signatures and Models in Translational Neuroimaging*

**Abstract:** Despite the great promise in using functional neuroimaging to map brain to mind and understand human health and brain disorders, thus far it has had minimal impact on clinical practice and public health. Here, we review emerging techniques that, if used judiciously, could enable a quantum leap forward in developing translational applications. First, we review the state of translational neuroimaging and emerging techniques. Then, we outline an approach that uses these new techniques in specific ways to develop brain signatures that can be shared, tested in multiple contexts, and used in translational settings. The approach brings together ideas from statistics, ‘big data,’ replicability, and open science—ideas that, together, constitute a cultural shift in science that is bringing translational goals within reach.
**IRSA Distinguished Plenary Lecture:**

**Speaker:** Professor David Van Essen

**Brief Biography:** David C. Van Essen received his undergraduate degree from the California Institute of Technology and his doctorate from Harvard University. He was a postdoctoral fellow in Boston, Norway and England before joining the Caltech faculty in 1976. In 1992 he moved to Washington University in St. Louis and chaired the Department of Anatomy and Neurobiology for two decades. He is known for his research on the structure, function, connectivity, evolution, and development of cerebral cortex in humans and nonhuman primates. His laboratory has developed powerful methods of computerized brain mapping, with an emphasis on surface-based visualization and analysis of cerebral cortex. He has written more than 200 peer-reviewed articles and invited publications. Dr. Van Essen was a Principal Investigator of the Human Connectome Project (HCP), a highly successful endeavor to map brain function and connectivity in healthy young adults. He is currently a PI on two Lifespan HCP consortium projects. He has been a leader in two major professional societies, serves on several advisory boards, and is a Senior Editor for eLife. He is a Fellow of the AAAS and has received many awards, including several for teaching excellence.

**Title of talk:** Human Cerebral Cortex: Structure, Function, Connectivity, Development, and Evolution

**Abstract:** The cerebral cortex is the dominant structure of the mammalian brain that plays critical but diverse roles in cognition, perception, emotion, and motor control. This lecture will review progress in elucidating the structure, function, connectivity, development, and evolution of cerebral cortex in humans and nonhuman primates. Underlying methodological themes will include the power of surface-based analysis and visualization and the importance of user-friendly data sharing for accelerating progress in exploring these issues. Consideration of cortical development will include questions of why the cortex is a sheet whose convolutions vary across species and across individuals. Advances in elucidating functional organization include a recent multimodal human cortical parcellation, based on data from the Human Connectome Project (HCP), that reveals 180 distinct areas in each hemisphere. The ability to accurately parcellate the cortex in individual subjects will enable systematic analyses of individual variability in relation to many neurobiologically informative features as well as hundreds of behavioral measures that are part of the freely shared HCP data. Comparisons with nonhuman primates, including chimpanzees as well as macaque monkeys, provide intriguing evolutionary insights regarding the expansion of neocortical regions associated with higher cognition in the human lineage.
Abstracts of invited talks
**Speaker:** David Darrow

**Title of talk:** *Statistical Challenges in the Neuromodulation Parameter Space*

**Abstract:** There are now many applications of various types of neuromodulation, ranging from epilepsy to depression. Each type of neuromodulation possesses increasing capacity to adjust therapy through a growing parameter space, providing a method of fine-tuning therapy for each patient. The resulting combinatorial expansion of the parameter space for most modern devices provides a new challenge for clinical patient care and clinical trials. To date, most devices operate through an open loop design, requiring manual adjustment of stimulation settings by a clinician to personalize therapy. I will briefly discuss the plethora of neuromodulation devices and diseases, while focusing on a single clinical trial we designed to address a large parameter space with few patients. Even more recent work on newer trial designs and statistical approaches will be discussed.
Speaker: Mark Fiecas

Title of talk: *Modeling Longitudinal Functional Connectivity Networks in fMRI*

Abstract: Motivated by longitudinal neuroimaging studies, in this talk we discuss a framework for modeling functional connectivity networks in functional magnetic resonance imaging (fMRI) data that accounts for multiple sources of variation and covariation, including temporal autocorrelation inherent in fMRI, the heterogeneity across subjects, and within-subject covariation that arise from repeated measures of each subject. We show how to account for temporal autocorrelation in a nonparametric and subject-specific manner, and how to estimate the other sources of variation and covariation using a one-step estimator. We give an empirical illustration of our method by analyzing a subset of the ADNI data set to show the impact of Alzheimer’s disease on functional connectivity networks. This is joint work with Brian Hart (University of Minnesota, Division of Biostatistics) and Ivor Cribben (University of Alberta, School of Business).
Speaker: Apostolos Georgopoulos

Title of talk: Time Series Analysis of Multimodal Neural Data

Abstract: A frequent focus of functional neuroimaging and neurophysiological studies is on determining associations between recorded time series (e.g. BOLD fMRI, magnetoencephalographic [MEG] signal, local field potentials, etc.) and/or between such series and time series of behavioral measures. The validity of the results obtained, and, hence, of claims about functional connectivities and neurobehavioral relations, critically depend on the proper preprocessing of the time series, lack of which typically leads to spurious outcomes and false claims. In this talk I will discuss statistical properties of time series, how they impinge on determining true associations between series, and how pitfalls can be avoided by the proper preprocessing of the time series. I will illustrate those points from published papers in neuroscience.

References
Speaker: Nathaniel Helwig

Title of talk: Modeling Longitudinal Change of Brain Signals in Twins

Abstract: Longitudinal studies of brain functioning can offer unique insights into how the brain develops. In this talk, we explore the use of nonparametric mixed-effects regression approaches for modeling longitudinal changes in event-related potential (ERP) data. We apply the approach to ERP data collected as a part of the Minnesota Twin Family Study, which has been conducting repeated assessments of 1,522 twin participants. Specifically, we use the approach to examine how an individual’s ERPs change across the ages 11, 14, 17, 20, and 24, an important developmental period spanning the onset of adolescence to early adulthood and characterized by significant changes in brain structure and function. This is joint work with Jeremy Harper and Steve Malone.
**Speaker:** Esther Krook-Magnuson

**Title of talk:** *Finding Precision to Harness Diversity in Temporal Lobe Epilepsy*

**Abstract:** Temporal lobe epilepsy is the most common type of epilepsy in adults and notoriously pharmacoresistant. There are a number of hurdles to better understanding this neurological disorder and thus to the informed design of new treatment strategies. Techniques for selective manipulation of neuronal circuits including on-demand optogenetics enable improved dissection of neuronal circuits in epilepsy and identification of intervention targets. Novel analysis and data science methods are important to continue to move the field forward. Dr. Krook-Magnuson’s talk will focus on recent work using on-demand optogenetics in rodents to gain circuit-level insights into the disorder, and will highlight some open data analysis issues.
**Speaker:** Christophe Lenglet

**Title of talk:** *Brain Microstructure Characterization using Sparse Bayesian Inference and Multi-compartment Models Estimation*

**Abstract:** First, we demonstrate how sparsity can be introduced into a recent multi-resolution algorithm (RubiX) to estimate white matter fiber orientations from compressed (under-sampled) diffusion MRI (dMRI) data. A sparse Bayesian algorithm combines data acquired at different spatial resolutions via a dictionary representation and priors which leverage the dependence between fiber orientations, and the spatial redundancy in data representation. Second, we introduce a data fitting procedure for biophysical models which relate quantities such as axonal radius and density to the dMRI data by predicting signal in the intra- and extra-axonal compartments. Using variable projection and stochastic global search algorithms, we present an efficient and robust method to estimate axonal radii and densities from non-invasive dMRI data.
**Title of talk:** *Is Adolescent Brain Development Impacted by Substance Use? Insights to be Gained from the Adolescent Brain and Cognitive Development (ABCD) Project*

**Abstract:** Substance use, particularly use of alcohol, in excessive quantities has deleterious effects on brain structure and behavior in adults and during periods of rapid neurodevelopment. Whether similar outcomes characterize other developmental periods, such as adolescence, and in the context of less extensive use is unknown. Recent cross-sectional studies and a small number of longitudinal studies suggest that binge drinking as well as alcohol use disorders in adolescence are associated with disruptions in regional white matter microstructure, gray matter volumes, functional connectivity, and task-based neural function. However, a number of confounding factors limit the extent to which cause-effect conclusions can be drawn. This work will be summarized, and the framework of the newly launched Adolescent Brain and Cognitive Development (ABCD) Consortium project will be described. Implications for our understanding of neurodevelopment and clinical outcomes will be discussed.
**Speaker:** Theoden Netoff

**Title of talk:** Optimizing Deep Brain Stimulation with Noisy and Non-Stationary Responses

**Abstract:** Deep brain stimulation using high frequency electrical pulses is currently used to treat Parkinson's Disease and Epilepsy. Implantable devices that deliver the therapy are tuned by the clinician to select the stimulation frequency and amplitude to maximize therapy while minimizing side effects. The Netoff lab focuses on developing algorithms for automated tuning of parameters based on neural biomarkers and symptoms borrowing from traditional systems engineering approaches. However, finding the optimal parameters are hindered by the fact that neural signals are noisy and non-stationary over time. Our goal is to develop robust algorithms simple enough that even a neurosurgeon could use them.
Speaker: Gülin Öz

Title of talk: Applications of High Field Magnetic Resonance Spectroscopy in Neurodegenerative Diseases

Abstract: Neurochemical profiles obtained by in vivo magnetic resonance spectroscopy (MRS) are increasingly used to monitor diseases of the central nervous system. The sensitivity and resolution advantages at high and ultra-high magnetic fields (3T and above) allows reliable quantification of neurochemical profiles that consist of up to 18 metabolites, including neuronal and glial markers, neurotransmitters and antioxidants, in brain regions that are involved in various neurological disorders. This presentation will share examples of utilizing MRS in clinical populations with neurodegenerative diseases and the statistical approach we took to combine neurochemical profile data obtained from multiple brain regions.
Speaker: Jörg Polzehl

Title of talk: Towards In-Vivo Histology of the Brain

Abstract: Recent advances in neuroimaging attempt to enable in-vivo histology of the brain. Doing so requires increased spatial resolution up to a situation where the signal meets the noise floor. The talk will cover research conducted at WIAS, in collaboration with MR physicists, on statistical issues in modeling imaging data characterized by low signal-to-noise ratio (SNR).

I'll cover several specific, but interrelated problems:
- characterization of the signal distribution in MR experiments,
- effects of preprocessing on the signal distribution,
- estimation of the noise profile in MR images,
- use of spatial information for variance reduction in (collections of) MR images,
- bias due to incorrect modeling in MR experiments.

I'll consider two specific imaging experiments to illustrate problems, effects and solutions:
- diffusion weighted MR, with an analysis based on data of the Human Connectome Project,
- multi-parameter mapping, using data measured at the Wellcome Trust Center for Neuroimaging, London.

Literature:

- K. Tabelow, Ch. D'Alonzo, L. Ruthotto, M. F. Callaghan, N. Weiskopf, J. Polzehl and S. Mohammadi: Removing the estimation bias due to the noise floor in multi-parameter maps, accepted for *ISMRM annual meeting 2017.*
Speaker: Sophia Vinogradov

**Title of talk:** Using Data-Driven Bioinformatics Approaches to Understand Puzzling Patterns in our Clinical Trial Data

**Abstract:** The identification of meaningful treatment response patterns in schizophrenia that are sensitive induced to well-defined interventions may deepen our understanding of underlying pathophysiology and generate new hypotheses about successful treatment mechanisms. Conventional intent-to-treat analyses of data from our trials of neuroscience-driven cognitive training in schizophrenia have yielded interesting but puzzling patterns of results. By combining data sets from four separate trials that used similar study designs, and by employing principal components analysis and topological data analysis, we identified discrete response patterns in clinical and cognitive symptom profiles that were associated with a precisely defined cognitive training intervention vs. a computer games control condition. These response patterns suggest important avenues for further investigation into the heterogeneity of schizophrenia.