# 12/4/2019

# Using Novel Functional Data Analysis Methods to Maximize Information from EEG Biomarkers in Autism Spectrum Disorders

## Catherine Sugar, PhD

BACKGROUND: Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental condition characterized by impairments in social behavior and communication and the presence of repetitive behaviors or restricted interests. Due to the inherent difficulty of obtaining objective and reliable measurements of symptoms and behaviors, investigators in this field are increasingly searching for translational biomarkers that will better support clinical research and practice. One of the most promising tools for biomarker development in ASD is electroencephalography or EEG. EEG can be recorded continuously, creating power spectral densities, or in response to a series of discrete stimuli, creating event-related potential (ERP) waveforms. The resulting measurements have a complex, high-dimensional structure which can be characterized as longitudinal functional data. Moreover, responses are recorded at multiple electrodes on the scalp, adding a spatial component. However, traditional EEG analyses involve multiple simplifications of this structure to increase the signal to noise ratio, effectively collapsing the functional, longitudinal and spatial components by extracting key features of the EEG signals and averaging them across time and electrodes, resulting in significant information loss. In this talk, I present ongoing work by our group to develop a methodological framework which preserves more of the structural richness of such data. The techniques, encompassing functional principal components, reliability assessment, clustering and predictive modeling, will be illustrated using examples from several collaborative studies of children with ASD and their typically developing counterparts, including the Autism Biomarkers Consortium for Clinical Trials, a major ongoing NIH initiative.

<u>BIO:</u> Dr. Catherine Sugar is a Professor in the Departments of Biostatistics, Statistics and Psychiatry at the University of California, Los Angeles. She also directs SIStat, the Biostatistics Core in the Semel Institute for Neuroscience and Human Behavior, and an equivalent unit in the Veterans Administration VISN 22 Mental Illness Research, Education and Clinical Center. Her methodological expertise is in clustering, classification and functional data analysis, all areas which focus on finding patterns in complex high-dimensional multimodal or longitudinal data. She is also extremely active in collaborative work, having been involved in projects in areas as diverse as health services research, HIV/AIDS, oncology, dentistry, cardiology, and infection control, but her primary field of application is psychiatry. She received her Ph.D. in Statistics from Stanford University, working on the development of cluster-analytic health state models for depression and schizophrenia, and remains actively involved in studies of these and other psychiatric disorders, including autism, bipolar disorder, ADHD, and drug and alcohol addiction. Dr. Sugar is an elected Fellow of the American Statistical Association and a former President of the Southern California Chapter of the ASA.

## 11/6/2019

## **Biostatistics PhD Students' Presentations**

Jinyuan Liu, Yuqi Qiu, Brian Kwan and Wenyi Lin

## 10/2/2019

## Deep Learning Approaches for Glaucoma Detection and Prediction

#### Mark Christopher, PhD

<u>BACKGROUND</u>: Glaucoma is a leading cause of blindness that affects tens of millions of people around the world. Over the past several years, the amount imaging and functional data collected by ophthalmologists to

diagnose and monitor glaucoma has exploded. Applying deep learning techniques to these large, high dimensional datasets is helping to increase our understanding of glaucoma and improve patient care.

<u>BIO:</u> Dr. Mark Christopher received his PhD in biomedical engineering from the University of Iowa. His graduate work focused on applying bioinformatics and machine learning techniques to disease prediction in ophthalmology. After graduating, he moved to UCSD where he is a post doc in the Hamilton Glaucoma Center. He is currently active in developing deep learning techniques that use ophthalmic imaging and data to identify and predict glaucoma progression.

# 5/29/2019

# Efficiency in Lung Transplant Allocation Strategies

# Jingjing Zou, PhD

BACKGROUND: Currently in the United States, lung transplantations are allocated to candidates according to the candidates' Lung Allocation Score (LAS). The LAS is an ad-hoc ranking system for patients' priorities of transplantation. The goal of our study is to develop a framework for improving patients' life expectancy over the LAS based on a comprehensive modeling of the lung transplantation waiting list. Patients and organs are modeled as arriving according to Poisson processes, patients' health status evolving a waiting time inhomogeneous Markov process until death or transplantation, with organ recipient's expected post-transplant residual life depending on waiting time and health status at transplantation. Under allocation rules satisfying minimal fairness requirements, the long-term average expected life converges, and its limit is a natural standard for comparing allocation strategies. Via the Hamilton-Jacobi-Bellman equations, upper bounds for the limiting average expected life are derived as a function of organ availability. Corresponding to each upper bound is an allocable set of (time, state) pairs at which patients would be optimally transplanted. The allocable set expands monotonically as organ availability increases, which motivates the development of an allocation strategy that leads to long-term expected life close to the upper bound. Simulation studies are conducted with model parameters estimated from national lung transplantation data. Results suggest that compared to the LAS, the proposed allocation strategy could provide a 7% increase in average total life.

<u>BIO:</u> Dr. Jingjing Zou is currently working as a post-doctoral researcher at School of Public Health, UC Berkeley (joint with University of Cambridge), focusing on the development of statistical methods for high-dimensional medical imaging data. She received her Ph.D. in statistics from Columbia University.

# 5/1/2019

# Methodological Opportunities and Challenges with Advancing and N-of-1/Small Data Paradigm

# Eric B. Hekler, PhD

<u>BACKGROUND:</u> There is great interest in and excitement about the concept of Precision Medicine and, in particular, advancing this vision via various "big data" efforts. While these methods are necessary, they are insufficient for achieving the full promise. A rigorous, complementary "small data" paradigm that can function both autonomously from and in collaboration with big data is also needed. By "small data" I am building on Estrin's formulation referring to the rigorous use of data by and for a specific N-of-1 unit (i.e., a single person, clinic, hospital, healthcare system, community, city, etc) to facilitate improved individual-level description, prediction, and, ultimately, control for that specific unit.

<u>BIO:</u> Eric Hekler, PhD, is an Associate Professor in the Department of Family Medicine and Public Health at UCSD. He is also Director of the Center for Wireless & Population Health Systems and faculty member of the Design Lab at UCSD. His research focuses on facilitating individualized behavior change for fostering long-term health and well-being via digital health tools. Prior to UCSD, Dr. Hekler was a faculty member at Arizona

State University. He completed his postdoctoral training at Stanford University and received his Ph.D. in Clinical Health Psychology from Rutgers University.

# 2/13/19

# Adaptive Enrichment Designs for Reproducible Confirmatory Clinical Trials in the Era of Precision Medicine

# Tze Leung Lai, PhD

<u>BACKGROUND:</u> After an overview of FDA's 2012 draft guidance on enrichment strategies for clinical trials to support drug/biologic approval, we describe subsequent advances in adaptive enrichment designs in this direction. We also provide a concrete application in the enrichment design of the DEFUSE 3 trial comparing a new endovascular treatment with standard of care for ischemic stroke patients.

<u>BIO:</u> Dr. Tze Leung Lai is the Ray Lyman Wilbur Professor of Statistics and, by courtesy, of Biomedical Data Science and of the Institute of Computational and Mathematical Engineering (ICME) at Stanford University. He is also Co-director of the Center for Innovative Study Design (CISD) at the Stanford University School of Medicine. Dr. Lai has supervised 73 Ph.D. theses and seven postdoctoral trainees. He published over 300 papers, many of which are in clinical trial design and analysis, population pharmacokinetics and pharmacodynamics, survival analysis, longitudinal data analysis, multiple endpoints, biomarkers, adaptive methods, sequential analysis and time series.

# 1/9/2019

# Missing and Modified Data in Nonparametric Statistics

# Sam Efromovich, PhD

<u>BACKGROUND:</u> After a short introduction to topics in nonparametric curve estimation, covered in my new 2018 Chapman & Hall book with the same title as the talk, three specific problems will be considered. The first one is non-parametric regression with missing at random (MAR) responses. It will be explained that a complete case approach is optimal in this case. The second problem is a nonparametric regression with missing at random (MAR) predictors. It will be explained that in general a complete case approach is inconsistent for this type of missing and a special procedure is needed for efficient estimation. The last explored problem is devoted to survival analysis, specifically to efficient estimation of a hazard rate function for truncated and censored data. Time permitted, several recent results and open problems will be highlighted.

<u>BIO:</u> Dr. Sam Efromovich is the Endowed Professor of Mathematical Sciences and the Head of Actuarial Program at the University of Texas at Dallas, where he has worked since 2006. Before he was a Professor at the University of New Mexico, Albuquerque (since 1991). Sam has PhD in Information Theory and Statistics (1978) and Control Theory and Industrial Statistics (1986). He wrote more than 200 papers and two books: "Nonparametric Curve Estimation" (Springer, 1999) and "Missing and Modified Data in Nonparametric Estimation" (Chapman and Hall, 2018), which will be discussed at this seminar.