




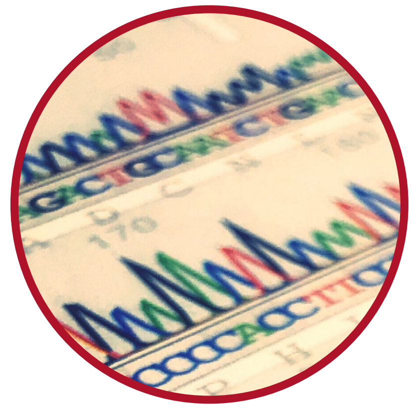
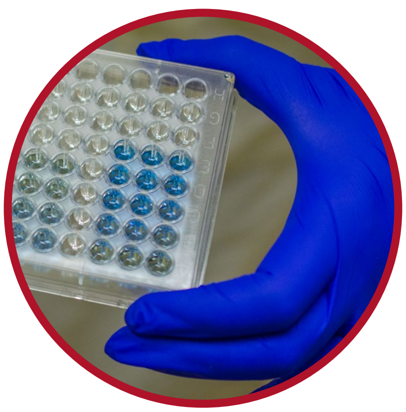

ADVANCED TOPICS IN PRECISION CARE MEDICINE

JOHNS HOPKINS UNIVERSITY
WHITING SCHOOL OF ENGINEERING

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PROGRAM INFORMATION

INTRODUCTION

PROGRAM DURATION

Four days

MODALITY

Virtual live and in-person

ACADEMIC PROGRAM DIRECTORS

Sri Sarma, PhD
Joseph Greenstein, PhD
Rai Winslow, PhD

PREREQUISITES

Helpful to have background in probability and statistics
Programming background is a plus, but not required

COURSE DESCRIPTION

In a perspective article in the *New England Journal of Medicine*, Collins and Varmus state that "what is needed now is a broad research program to encourage creative approaches to precision medicine, test them rigorously, and ultimately use them to build the evidence base needed to guide clinical practice". Computational Medicine (CM) is an emerging discipline that seeks to: develop mechanistic computational models of disease (modeling); methods for personalizing these models using data measured from individual patients (personalization); apply these personalized models to improve the diagnosis and treatment of disease (application). The course faculty, as members of the Institute for Computational Medicine (ICM), believe that CM offers one pathway to precision medicine. They are committed to training the next generation of scientists, engineers, and physicians in this approach, and doing this across all educational levels.

Class time includes lectures and tutorials covering the physiology, medicine, and engineering principles relevant to case studies that will be presented at the end of the course. Example problems will be solved using MATLAB and Python. Below is an outline of specific topics to be taught

WHO SHOULD TAKE THIS PROGRAM

- STUDENTS: Pre-med and MD students, bioengineering students who want to learn about applications of artificial intelligence, machine learning, and computational modeling in medical applications.
- DATA SCIENTISTS: Researchers in medical domain (e.g., medical device companies, pharmaceuticals, biotech, hospitals, consulting) confronting machine learning problems with clinical data sets.
- HEALTHCARE PROVIDERS: Clinicians (MDs), nurse practitioners, physician assistants, interested in precision care medicine and applications of artificial intelligence in medicine; those seeking to understand fundamental principles of biomedical data science.
- EXECUTIVES: Chief medical officers; chief strategy officers; VPs of research who seek to understand fundamentals of biomedical data science.

KEY TAKEAWAYS

BY THE END OF THIS COURSE, YOU WILL BE ABLE TO:

1. Describe foundations of predictive modeling.
2. Leverage data and personalized models to reveal and identify clinical states or phenotypes.
3. Assess risk of adverse events using models.
4. Develop predictive models to determine response to treatment.
5. Apply techniques to deal with challenges in real data sets.
6. Describe real-world applications through case studies.
7. Build your own models via a hands-on tutorial—learners will construct personalized models to solve a clinical problem based on real-world data.
8. Describe how the tools and techniques of data science are becoming integrated into the practice of medicine.

DAY 1

PROGRAM SCHEDULE

1-1 WELCOME AND OVERVIEW

Sri Sarma
Joe Greenstein

Welcome, introductions, and workshop overview. Highlight the importance of learning about the use of data science in medicine and the challenges associated with translation in precision care medicine.

1-2 REVIEW OF PROBABILITY AND STATISTICS—DISCRETE

Sri Sarma

Review discrete random variables (probability mass function (PMF), expected value, and variance).

1-3 REVIEW OF PROBABILITY AND STATISTICS—CONTINUOUS

Sri Sarma

Review continuous random variables (probability density function (PDF), expected value, and variance).

1-4 STATISTICAL MODELING

Sri Sarma

Review how to estimate underlying distributions in data using maximum likelihood estimation.

DAY 2

2-1 GENERALIZED LINEAR MODELS, PART 1

Sri Sarma	Define and provide examples of generalized linear models (GLMs) and their properties.

2-2 GENERALIZED LINEAR MODELS, PART 2

Sri Sarma Joe Greenstein	Review Bernoulli GLM, Poisson GLM, and Boosting algorithms.

2-3 RANDOM FORESTS

Tony Wei	Present the random forest technique and how it is used in solving binary classification problems.

2-4 BINARY CLASSIFICATION, PART 1

Joe Greenstein	Present the following concepts and techniques: static threshold classifiers, confusion matrices, construction of receiver operating characteristic (ROC) curves, area under the curve (AUC), other performance metrics (sensitivity, specificity, PPV, NPV).

DAY 3

3-1 BINARY CLASSIFICATION, PART 2

Tony Wei

Define and present the following concepts: class imbalances, feature selection & evaluation, methods for feature pruning, lasso regulation (GLMs), SHAP analysis.

3-2 EARLY DETECTION OF ADVERSE EVENTS, PART 1

Joe Greenstein

Propose the "Transitional Sub-state Hypothesis" and the subtleties of determining clinical state labels using case examples. Describe detection rules (e.g., threshold on risk score).

3-3 EARLY DETECTION OF ADVERSE EVENTS, PART 2

Joe Greenstein

Present the following concepts and techniques: spectral clustering applied to risk scores, universally sudden nature of the transitional event, patient-specific positive predictive value.

3-4 EXPLORATORY DATA ANALYSIS, PROCESSING AND REDUCTION TECHNIQUES

Joe Greenstein

Present the following concepts and techniques: clustering (k-means), Principal Components Analysis (PCA), supervised feature reduction methods, correlation matrices, and the method of building a model one feature at a time.

DAY 4

4-1 CASE STUDIES

Sri Sarma Joe Greenstein	Faculty will present two case studies of techniques covered in the workshop.

4-2 CASE STUDIES

Sri Sarma Joe Greenstein	Faculty will present two case studies of techniques covered in the workshop.

4-3 IN-CLASS STUDY

Sri Sarma Joe Greenstein Tony Wei	Faculty will present a clinical data set and pose prediction problems for attendees to work on.

4-4 IN-CLASS STUDY

Sri Sarma Joe Greenstein Tony Wei	Attendees will perform data analysis and modeling on the clinical data set. This session will be facilitated by workshop faculty and teaching assistants.

LIST OF PROJECTS AND PIs DISCUSSED IN THE COURSE

1. **Computational Signatures for Post-Cardiac Arrest Trajectory Prediction: Importance of Early Physiological Time Series**
   (Biomedical PIs: Robert Stevens, Jose Suarez, Christian Storm;
   Engineering PIs: Raimond Winslow, Joseph Greenstein)

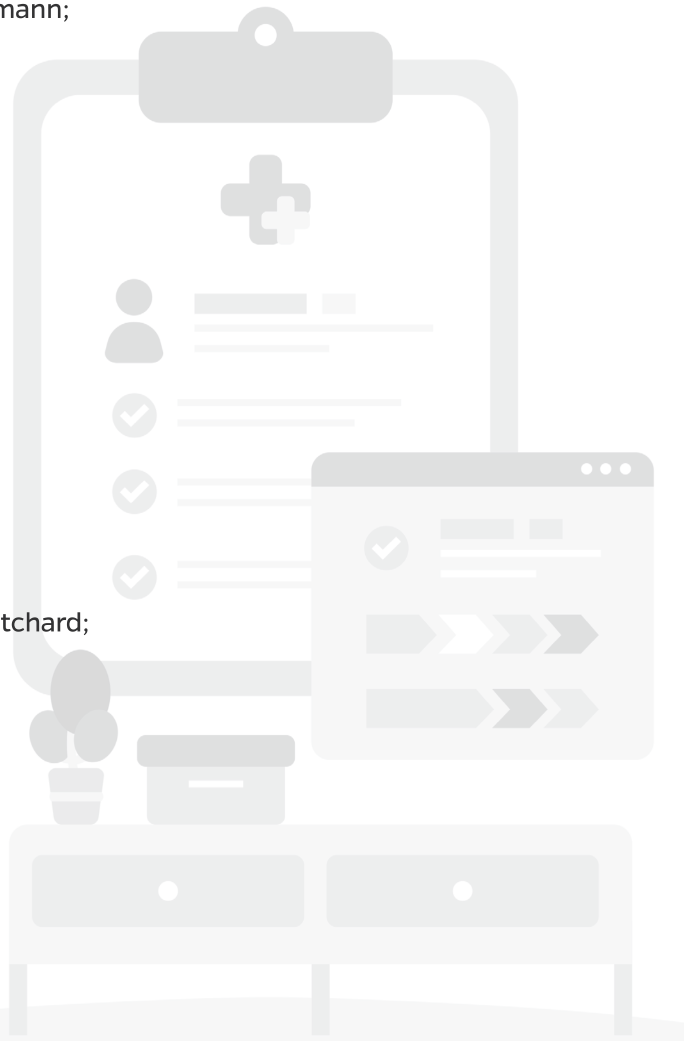
2. **Predicting Flow Rate Escalation for Pediatric Patients on High Flow Nasal Cannula Using Machine Learning**
   (Biomedical PIs: Jim Fackler, Anthony Sochet, Jules Bergmann;
   Engineering PIs: Raimond Winslow, Joseph Greenstein)

3. **Predicting Flow Rate Escalation for Pediatric Patients on High Flow Nasal Cannula Using Machine Learning**
   (Biomedical PIs: Robert Stevens, Jose Suarez;
   Engineering PI: Sri Sarma)

4. **Predicting Acute Kidney Injury After Surgery**
   Biomedical PIs: Lee Goeddel;
   Engineering PIs: Raimond Winslow, Joseph Greenstein)

5. **Delirium Subtype Identification and Prediction**
   (Biomedical PIs: Robert Stevens, Jose Suarez;
   Engineering PIs: Raimond Winslow, Joseph Greenstein)

6. **Diagnosing ADHD Using Pre-diagnostic Questionnaires**
   (Biomedical PIs: Calliope Holingue, Luther Kalb, Alison Pritchard;
   Engineering PIs: Sri Sarma, Joseph Greenstein)



INSTRUCTORS

SRI SARMA

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Sarma received a BS in Electrical Engineering from Cornell University in 1994, and an MS and PhD in Electrical Engineering and Computer Science from Massachusetts Institute of Technology (MIT) in 1997 and 2006. From 2000 to 2003, she took a leave to start a data analytics company. From 2006 to 2009, she was a postdoctoral fellow in the Department of Brain and Cognitive Sciences at MIT. An associate professor in the Department of Biomedical Engineering, she is associate director of the Institute for Computational Medicine. Her research includes modeling, estimation, and control of neural systems using electrical stimulation. She is cofounder of Neurologic Solutions, Inc. that develops EEG analytics tools for brain disorders. Sarma teaches courses in precision care medicine, systems and control, and networks. She is a recipient of the Burroughs Wellcome Fund Careers at the Scientific Interface Award, the Krishna Kumar New Investigator Award from the North American Neuromodulation Society, and a recipient of the Presidential Early Career Award for Scientists and Engineers, and the Whiting School of Engineering Robert B. Pond Excellence in Teaching Award.

JOSEPH GREENSTEIN

JGREENST@JHU.EDU

Greenstein received a BS in Biomedical Engineering from Boston University in 1995 and a PhD in Biomedical Engineering from Johns Hopkins University in 2002. After a brief stint at a drug discovery company, he returned to Johns Hopkins and joined the Institute for Computational Medicine. His research aims at understanding healthy and diseased cardiac function over a broad range of biological levels spanning from molecular interactions to cardiac tissue, with a focus on the development and analysis of mathematical and computational models of physiological function to address unanswered disease-related questions about biological mechanisms—an approach now known as multi-scale modeling. In recent years, he has focused on a new area of computational healthcare research that leverages the physiological patient data collected from monitors in critical care settings to develop statistical models of patient state for the purpose of early prediction of actionable clinical state changes, e.g., impending sepsis or septic shock, respiratory failure, or oxygen desaturation.

TONY WEI

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Tony Wei received his BS in Biomedical Engineering and BS in Applied Mathematics and Statistics from the Johns Hopkins University. He is a third year PhD candidate in Biomedical Engineering at Johns Hopkins University in Sridevi Sarma's Neuromedical Control Systems Lab. His past research includes designing and coding GUIs for diagnosis and treatment of obstructive sleep apnea patients at the Johns Hopkins Bayview Medical Center, and applying reinforcement learning for semi-autonomous delivery of anesthetics for the FDA Center for Devices and Radiological Health. He has been a team leader and teaching assistant for the Precision Care Medicine course at Johns Hopkins. His research interests include neural signal processing, machine learning applications in neuroscience, and chronic pain. For his PhD, he is collaborating with Dr. Latremoliere and Dr. Alexandre from the Neurosurgery Pain Research Institute at Johns Hopkins to identify an EEG neuropathic pain biomarker from mice fronto-parietal brain activity during sleep.

RAI WINSLOW

RWINSLOW@JHU.EDU

Winslow is the Raj and Neera Singh Professor of Biomedical Engineering at the Johns Hopkins University School of Medicine. He is the founding director of the Institute for Computational Medicine (established in 2005) at the Johns Hopkins University School of Medicine and Whiting School of Engineering. In collaboration with colleagues at Hopkins and around the world, he has contributed to the emergence of the discipline of Computational Medicine. His research is focused in two areas. The first is use of computational modeling to understand the molecular mechanisms of cardiac arrhythmias and sudden cardiac death. The second is use of statistical and dynamical systems modeling methods to predict the temporal evolution of patient clinical state and to predict the impending occurrence of significant changes in patient state before they occur. He holds joints appointments in the departments of Electrical and Computer Engineering, Computer Science, and the Division of Health Care Information Sciences at Johns Hopkins University.

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for the completion of Advanced Topics in Precision Care Medicine workshop

February 2022

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Sri Sarma, Ph.D.
Program Director
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