INSTITUTE for COMPUTATIONAL MEDICINE

# Computational Medicine Night

Wednesday, March 24, 2021

**PROGRAM OF EVENTS**

5:30 – 5:50 PM

**COMPUTATIONAL MEDICINE INFORMATION SESSION**
**Raimond L. Winslow, PhD,** Raj & Neera Singh Professor,
Department of Biomedical Engineering
Director, Institute for Computational Medicine

5:50 – 6:20

**STUDENT RESEARCH PRESENTATIONS**

**Jacob Desman**, BME Senior, CM Minor
Mathematical Analysis of NeuroImaging of the Cerebral Brain Lab

**Chloe Paris**, BME Junior, CM Minor
Computational Design of Therapeutics Lab

**Precision Care Medicine Team Emerald**:
**Michael Ainsworth**, BME MSE Student
**Alex Hepp**, BME Senior, CM Minor
**Zachary Murphy**, BME MSE student
**Varun Naga**, BME Senior
**Athena Olszewski**, BME Junior

**Precision Care Medicine Team Coquelicot**:
**Timothy Bedard**, BME Senior, CM Minor
**Yunru Chen**, BME MSE student
**Andy Ding**, BME MSE student
**Madi Kusmanov**, BME MSE student
**Morgan Sanchez**, BME Senior
**Shreyash Sonthalia**, BME MSE student

6:20 – 6:30

**PRECISION CARE MEDICINE Q & A**

6:30 – 7:00 PM

**ICM RESEARCH AREA BREAKOUT SESSION**
Visit Zoom breakout rooms to meet ICM's students and trainees, learn about the research of ICM's labs, and ask questions.

## ABOUT ICM

Biological research has entered a new and exciting phase, one in which computational methodologies and modeling plays a critical role in revealing the causes and treatment of human disease. At the forefront of this evolution in medical research and treatment is the Institute for Computational Medicine (ICM).

The Institute represents a first of its kind interdivisional initiative that builds on groundbreaking research at both the Whiting School of Engineering and the School of Medicine.

ICM's mission is to develop quantitative approaches for understanding the mechanisms, diagnosis and treatment of human disease through applications of mathematics, engineering and computer science. Personalized patient data and In Silico model simulations are then used to help physicians tailor therapies to meet the needs of the individual.

## UNDERGRADUATE MINOR IN COMPUTATIONAL MEDICINE

The ICM offers an undergraduate minor in Computational Medicine, the first educational program in CM. Like the ICM, the Undergraduate Minor in Computational Medicine is integrative and multidisciplinary. With a minor in CM, students will have a solid grounding in the development and application of computational methods that are essential to the advancement of modern medicine, and are prized both in academic research and industrial research.

The courses and research opportunities available in the CM minor will place students at the forefront of the application of mathematics, computing and engineering to human health. Whether you go on to medical school, graduate research, or biomedical industries, the comprehensive quantitative training and exposure to cutting edge CM techniques will give you a competitive advantage for working in the medicine of tomorrow – which will be data-driven, predictive, personalized and preventative.

## STUDENT RESEARCH PRESENTATIONS (5:50 – 6:20 PM)

***Investigating Bok's Hypothesis Via Normal and Equivolumetric 3D Coordinate Systems for Cortical Areas***

**Jacob Desman**, BME senior, CM minor
**PI:** Tilak Ratnanather, DPhil, Associate Research Professor, BME

**Abstract:** In 1929, Bok published the observation that folding in the cortical ribbon composed of layers in the brain seems to adjust layer thickness in order to preserve layer-specific volume. Image-based methods have modeled this equivolumetric principle. However, there is no unique solution to the arrangement of these layers, thereby causing different implementations to result in different layering schemes. Furthermore, many of such analyses compare these methods against 2D histological sections. Advances in neuroimaging datasets, particularly the BigBrain dataset, have allowed high resolution 3D surfaces and layer segmentations to be generated across the entire brain. This allows for verification in 3D against such cortical layer segmentations. Here, we explore using a method by Ratnanather et al. which utilizes diffeomorphic evolution in 3D from the gray/white matter surface to the pial surface while enforcing the equivolumetric constraint. Additionally, normal lines are developed orthogonally to the white matter surface to mimic cortical columns resulting from embryonic neuron growth. We seek to verify these theories on neurological development by incorporating these constraints and comparing against individual 3D layer segmentations. Disruptions in cortical layer growth and folding are known as possible causes of some neurological disorders. Therefore, accurately estimating layers in cortical regions will provide a foundation for better understanding neurological development and disease.

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***Developing Personalized Mechanistic Computational Models of Menstrual Cycle Hormones***

**Chloe Paris**, BME Junior, CM Minor
**PI:** Feilim Mac Gabhann, PhD, Associate Professor, BME

**Abstract:** The monthly cycle of ovarian follicular development and menstruation is a complex interplay of interdependent hormones and tissue changes. To better understand such complex systems and to predict how best to design therapies or interventions, mechanistic computational models have become essential. Furthermore, the observed variability from cycle to cycle and even from person to person, points to a need for a computational model that can simulate not just a typical or average person, but also many individuals and patient populations. My research has focused on developing such a population - a group of personalized computational models simulating different individuals over time. The hormone and tissue network is represented by a coupled set of ordinary differential equations, and using sensitivity analysis and optimization techniques I identify different parameter sets to act as the individual menstruators. I have shown that because of these different parameter values, these virtual individuals have different hormone levels, cycle lengths, and even differences in how stable the cycles are. I am using this virtual patient population to understand which parameters, and therefore which biological processes, most result in the variability of the menstrual cycle. Currently, I am working on exploring the effect of perturbations to the system by simulating birth control therapies on the virtual patient population and observing the diversity of responses across this large group of menstruators.

## STUDENT RESEARCH PRESENTATIONS CONTINUED (5:50 – 6:20 PM)


Clockwise from top left: Zachary Murphy, Michael Ainsworth, Varun Naga, Athena Olszewski, Alex Hepp

***Predicting Hospital Outcomes in Stroke Patients using Hemodynamic Features***

**Team Emerald**, Precision Care Medicine
**Clinical PIs:** Mona Bahouth, MD, Assistant Professor, SOM Neurology; Besty Zink, MS, Clinical Nurse Specialsit, JHMI Neuro CCU

**Abstract:** Stroke is a leading cause of death and disability worldwide. In the acute post-stroke phase, there is a disruption of the blood-brain barrier and cerebral blood flow autoregulation, which exacerbates the impact of hemodynamics on brain perfusion and recovery. Better understanding trends in these hemodynamic parameters could provide predictive insight into patient outcomes. Particularly, predicting length of stay would assist in continuity of care and act as a rough measure of recovery.

Using data from the Johns Hopkins Hospital electronic health record for 2,101 patients we created models to predict whether a patient admitted for acute stroke will have a prolonged hospital stay using time-series data from the first 24 hours of admission including pulse, temperature, blood pressure, and oxygen saturation as well as demographic and comorbidity data. With an XGBoost classifier (AUC = 0.834), we obtained an optimal operating point for predicting a <7 day stay with precision of 0.70 and recall of 0.77. This demonstrates a decent ability to predict length of stay using data from the first 24 hours of admission. Future work will extend this approach to predict other outcomes at discharge, such as mobility and functional status, mental status, and discharge location.

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**Clockwise from top left:** Andy Ding, Madi Kusmanov, Morgan Sanchez, Timothy Bedard, Shreyash Sonthalia, Yunru Chen

***Prediction of Physiological Deterioration and Mortality in Mechanically Ventilated Patients Admitted to the ICU***

**Team Coquelicot**, Precision Care Medicine
**Clinical PI:** Pedro Mendez-Tellez, M.D., Assistant Professor, Anesthesiology and Critical Care Medicine, Johns Hopkins Medicine

**Abstract:** Ventilator-induced organ damage has been associated with the delivery of high tidal volumes and, more recently, with the delivery of high mechanical power (MP) by the ventilator, which describes the energy transferred from the ventilator to the lung tissue per unit time. This study aims to build machine learning models that leverage knowledge of ventilator settings and other patient features to predict physiological deterioration and mortality in mechanically ventilated patients. To this end, patient data from the Phillips eICU Database were used to build predictive models. Inclusion criteria include age ≥18 years, ICU stay duration ≥48 hours, volume- or pressure-controlled mechanical ventilation, and ventilation duration ≥48 hours. Physiological deterioration was defined as any increase in the daily Sequential Organ Failure Assessment (SOFA) score between days 3–7 from initiation of mechanical ventilation. Classification models including logistic regression, random forest, and support-vector machines were evaluated for predicting mortality and physiological deterioration using area under the receiver operating characteristic curve (AUC). Using these models, we show predictive power for mortality (AUC: 0.76) and for overall physiological deterioration using total SOFA scores (AUC: 0.65). We have also shown predictive power for organ-specific deterioration, specifically for renal (AUC: 0.76) and pulmonary systems (0.73), using their respective SOFA subscores as outcome measurements. Inclusion of additional physiological data as well as patient-related comorbidities may further improve the performance of these models.