Uncertainty Quantification for Mathematical Biology
Poster Session Abstracts
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Quantifying Uncertainty in Predictive Modeling of Brain Tumor Growth from MRI Data
Jingye Tan, Cornell University

Accurate, patient-specific prediction of brain tumor progression requires accounting for uncertainties in imaging data, tumor growth models, and tissue heterogeneity. We present a Bayesian framework to calibrate spatially-varying parameters of a biophysical tumor growth model using early-stage quantitative MRI data in a pre-clinical glioma model. Our approach incorporates atlas-based segmentation of grey and white matter to define spatial priors and region-specific parameter correlations. Using data from four rats, we calibrate the model from early tumor development and predict tumor shape at later stages. Predictions achieve high spatial accuracy (Dice > 0.89), but sensitivity analysis highlights that predictive reliability depends strongly on the number of early imaging time points. This is the first demonstration of uncertainty quantification in both tissue heterogeneity and predicted tumor morphology in this context, offering a pathway toward more robust, personalized forecasts of tumor progression.

Sex Differences and their Consequences in Oxidative Stress Management
Allison Cruikshank, Duke University

Oxidative stress, an imbalance between oxidants and antioxidants in cells, can damage cells and contribute to conditions such as metabolic dysfunction, neurological disorders, cardiovascular disease, and aging when present at high levels. Interestingly, women tend to have lower levels of oxidative stress and higher concentrations of certain antioxidants, such as glutathione, compared to men. These differences point to the important role of sex hormones in regulating oxidative stress and its effects on the body. In this work, we use mathematical modeling to uncover the mechanisms behind various experimental and clinical findings, including the complex role of estradiol in oxidative stress management. We, also, use our mathematical model to explore the mechanisms and attenuation of sex differences in Cystathionine β-Synthase Deficiency. By connecting clinical observations with mathematical modeling, this work provides insights into the underlying mechanisms and paves the way for sex- and menopausal status-specific approaches in medicine.

Uncertainty Quantification in a Cardiac Arrhythmia Model: Application to Intra-Atrial Reentrant Tachycardia
Marie Cloet, KU Leuven

Cardiac electrical excitation, which drives heart contractions, is a complex process influenced by tissue condition. While clinical software aids electrophysiologists in identifying regions of low excitability, the reliability of such algorithms remains uncertain.
Uncertainty Quantification (UQ) methods offer a pathway to address this challenge.
This in silico study aims to infer the geometry of scar tissue from synthetic recordings of electrograms (EGMs), including quantifying uncertainty in the inferred parameters.
We employ Bayesian inversion via Markov Chain Monte Carlo (MCMC) algorithms to estimate the scar geometry. Since this approach requires numerous evaluations of a cardiac electrophysiology model, the simulation setup must balance computational efficiency and accuracy. This poster presents key design decisions related to numerical methods, simulation configurations, and inversion workflows, ensuring a feasible and robust approach to scar shape inference.

Incorporating cerebral resistance response to carbon dioxide in a closed-loop cardiovascular model

Helen Harris, Virginia Commonwealth University

Cerebrovascular reactivity (CVR) is the ability of cerebral blood vessels to adapt in response to stimuli to regulate cerebral blood flow (CBF), which is crucial for sustaining life. Despite extensive research and mathematical modeling efforts, the processes contributing to CVR are still not fully understood. It is well documented that the cerebrovasculature responds to increased arterial carbon dioxide (CO2), causing blood vessels to dilate, affecting cerebrovascular resistance and CBF. Previously, Ellwein et al. modeled cerebrovascular resistance using a piecewise linear function which was parameterized empirically using available data for blood flow velocity in the middle cerebral artery, arterial blood pressure, and expired CO2. Using the existing closed-loop cardiovascular model, we have replaced this piecewise linear function with a first-order control equation for cerebral resistance and static relationship between cerebral resistance and partial pressure of CO2. Preliminary results from model simulations are comparable to those previously achieved by Ellwein et al., while the physiological fidelity of the model has improved. Ongoing modeling efforts include incorporating systemic responses to CO2 and fitting the model to additional datasets. We expect that these model adaptations will improve understanding of the mechanisms behind CBF regulation and CVR.

Enhancing Clinical Hypoxemia Forecasting through Uncertainty Quantification and Personalized Modeling

Rowan Barker-Clarke, Cleveland Clinic

Postoperative hypoxemia is a frequent and clinically significant complication, yet standard clinical monitoring may miss early warning signs. While machine learning models show efficacy in forecasting hypoxemic events, they often lack mechanisms to express confidence in their predictions. These problems can undermine trust in potential clinical decision-support tools, particularly through alarm fatigue if these tools generate multiple false positive alarms.
Objective: To improve the interpretability and clinical robustness of hypoxemia prediction models by integrating uncertainty quantification (UQ) strategies and personalized SpO_2 thresholds.
Methods: Building on prior work using Random Forests (RF) and statistical features derived from SpO_2 time-series data, we implemented two forms of UQ: Prediction intervals from quantile RF and posterior probability analysis from Gaussian mixture models (GMMs). We generated empirical prediction intervals (5th–95th percentiles) from RF outputs to quantify model uncertainty per forecasted window. Prediction width was used to identify low-confidence predictions. For each patient, SpO_2 values were also modeled using GMMs ($G = 2$ or 3), and personalized desaturation thresholds were defined at the intersection of posterior distributions. Cluster membership uncertainty was calculated to identify patients near risk boundaries.
Results: Prediction intervals successfully flagged unstable or borderline windows, aligning with clinical patterns of intermittent desaturation. GMM posterior uncertainty identified patient subgroups with ambiguous thresholds, and is related to clinical features including high BMI and derivative STOP-BANG score. Preliminary integration of these UQ features into the RF model suggests a potential reduction in false positive alerts without compromising sensitivity.
Conclusion: Incorporating uncertainty quantification into hypoxemia forecasting models enhances interpretability and patient-specific risk assessment. Future work will explore real-time integration of confidence metrics into clinical alerts and EHR dashboards to improve decision support.

Towards Predictive Digital Twins with Applications to Precision Oncology

Graham Pash, Oden Institute

Well calibrated mathematical and computational models enable the prediction and control of complex systems. These models can be utilized to design engineering systems or to develop treatment protocols. In contrast to one-size-fits-all approaches that seek to mitigate risk at the population level, digital twins enable personalized modeling that seeks to improve decisions at the level of the individual to improve cohort outcomes. This tailored approach is crucial in applications such as precision oncology. In particular, high grade gliomas exhibit significant heterogeneity in physiology and response to treatment that result in low median survival rates despite an aggressive-standard-of-care. We develop a computational pipeline that utilizes longitudinally collected MRI data to generate a patient-specific computational geometry and estimate the tumor cellularity. The data are then used to inform the spatially varying parameters of mathematical models for tumor growth through the solution of an inverse problem. The high-consequence nature of downstream decisions prompts a rigorous approach to uncertainty quantification. We utilize a Bayesian framework with a focus on scalable and efficient methods to characterize the uncertainty in the model inputs from the sparse, noisy imaging data. Furthermore, we show promising results for therapy planning using a risk-based formulation for optimization under uncertainty.

Long-term homeostasis in microbial consortia via auxotrophic cross-feeding

Amanda Alexander, University of Houston

Multicellular organisms, as well as systems like the microbiome, perform extremely complex biological functions that are not fully understood. One aspect of this functionality is division of labor between cell types and regulation of relative proportions of each cell subpopulation. To learn how this regulation occurs, synthetic microbial communities can be studied as models of natural multicellular systems in an experimentally controllable setting. Our collaborators have developed one such community: two auxotrophic cell types whose population ratios can be tuned using cross-feeding in continuous coculture. Here we present a data driven mathematical model that is needed to gain insights into the mechanisms underlying observed cell population ratios. The model accurately predicts the population ratio given specific nutrient concentrations, which enables experimental control of this ratio via nutrient addition. This auxotrophic microbial community serves as a foundation to design systems with increasingly complex abilities, such as differentiation and cell to cell adhesion. Pairing experimental design with data driven modeling allows for understanding and control of increasingly sophisticated synthetic systems for medical applications and the study of multicellular organization.