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SIAM Conference on the Life Sciences

(LS24)

IP1

Quantitative Ecology of Host-associated Microbiomes

The realization that microbiomes, associated with virtually all multicellular organisms, have tremendous impact on their host health is considered as one of the most important scientific discoveries in the last decade. The host-associated microbiomes, composed of tens to hundreds of co-existing microbial species, are highly heterogenous at multiple scales (e.g. between different hosts and within a host). In this talk, I will share our recent works on understanding the heterogeneity of complex microbial communities, and how these conceptual and technological advances in microbial ecology pave the way for precision microbiome engineering to prevent and treat diseases.

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IP2

Investigating Single-scale and Multi-scale Heterogeneous Immune Responses During Cancer Evolution

Tumour microenvironment is characterised by heterogeneity at various scales: from various cell populations (immune cells, cancerous cells, ...) and various molecules that populate the microenvironment (cytokines, chemokines, extracellular vesicles,); to phenotype heterogeneity inside the same cell population (e.g., immune cells with different phenotypes and different functions); as well as temporal heterogeneity in cells phenotypes (as cancer evolves through time) and spatial heterogeneity. In this talk we overview some mathematical models and computational approaches developed to investigate different single-scale and multi-scale aspects related to heterogeneous immune responses during cancer evolution. We also discuss the impact of this immune heterogeneity on anti-cancer therapies. Throughout the talk we emphasise the qualitative vs. quantitative results, and data availability.

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IP3

Modeling Life: A SLACers Journey

The small liberal arts college (SLAC) setting provides many opportunities to incorporate mathematical biology into the mathematics curriculum at various levels. From the scholar-teacher perspective, there are myriad ways to engage students with the breadth that math biology has to offer, while also strengthening their connection to the liberal arts paradigm. In this talk, I will discuss a more descriptive rather than prescriptive approach to leveraging the SLAC environment within mathematical biology education and vice versa.

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IP4

Role of Mathematical Modeling in Development and Roll Out of Vaccines

Mathematical modeling plays a major role in providing insights into the development of vaccines and selection of optimal vaccination strategies to control the spread of infectious diseases. For example, mathematical compartmental models provide answers to pertinent questions relating to RD decisions like progression through various phases of development given vaccine properties, vaccine dose-level and regimen, and design of clinical trials. In this talk, I will discuss some of the mathematical modeling approaches used to support these decisions as well as inform vaccine recommendations once a vaccine is licensed. Examples of a few vaccine-preventable diseases will be used for illustrative purposes.

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IP5

The Future of Pandemic Modeling in Support of Decision Making: Lessons Learned from COVID-19

The devastating global impacts of the COVID-19 pandemic are a stark reminder of the need for proactive and effective pandemic response. Disease modeling, epidemiological forecasts, and projections played an important role in this response, as they enabled forward-looking assessment and strategic planning. However, state-of-the-art predictive models repeatedly failed to give reliable predictions during key transition periods. These failures were often associated with the emergence of new variants and heterogeneity in the adoption of protective behaviors. In this talk, I will offer an overview of modeling challenges faced, lessons learned, and readiness for future pandemics. Specifically, I will discuss key challenges and considerations in epidemic modeling, with special focus on the critical gaps evident in current models. I will also emphasize the urgent need for the epidemiological modeling community to address these shortcomings in order to be better prepared for and respond to future pandemics.

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IP6

Epigenetic Cell Memory: Digital or Analog?

Epigenetic cell memory allows the cells of multi-cellular organisms to maintain distinct phenotypes, encoded by different gene expression patterns, despite a common genotype. Arguably, one of the most vexing questions in epigenetic research has been how cells ensure that these patterns persist for a lifetime. Indeed, lifetime persistence is a prerequisite for healthy state and is often compromised in disease. DNA methylation and histone modifications have appeared as key mediators of the long-term maintenance of gene expression states. Multiple experiments support that these modifications lock a gene in a silenced or active state, making long-term persistence an exclusive attribute of on and off gene states. So, is epigenetic cell memory digital? In this talk, we introduce a chromatin modification circuit model that captures the biologically possible interactions between DNA methylation and histone modifications, and predicts digital memory for sufficiently strong cross-catalysis between DNA methylation and repressive

histone marks. Surprisingly, the model predicts that when repressive histone marks do not catalyze DNA methylation, long-term maintenance of any intermediate gene expression state is also possible, thereby leading to analog memory. Experiments in engineered mammalian cell lines, in which this condition is satisfied, demonstrated for the first time analog cell memory. Our combined model and experimental results offer a new perspective on epigenetic cell memory, put under scrutiny the very concept of cell type, and more broadly challenge our current understanding of biological development.

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SP1

SIAM Activity Group on the Life Sciences (SIAG/LS) Early Career Prize Lecture - COVID-19: Why Do Some Get Sick, and Some Feel Fine?

During the height of the COVID-19 pandemic in 2020, apart from developing a vaccine, a large focus of the research community was on determining why some individuals were developing severe responses to SARS-CoV-2 infections (the COVID-19 causing virus) whereas others were asymptomatic. Given the plethora of data that was becoming available from hospitalised and non-hospitalised COVID-19 patients, we decided to see if we could use a mathematical modelling approach to answer the question: what drives severe COVID-19 disease dynamics? Using a system of delay-differential equations fit to a range of data, we created a population of virtual human patients who exhibited a range of responses from mild to severe COVID-19 disease. We then investigated what causes the disease severity seen in our virtual patients and identified one crucial biomarker. In this talk, Ill present the methods we used to tackle this project and our conclusions, which have since been verified clinically.

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JP1

LS/MPE24 Joint Plenary Presentation - Thermal Dynamics of Host-Parasite Systems: Modelling and Predicting Disease Emergence and Range Changes in a Warming Climate

Climate change is altering host-parasite dynamics globally, with changes expected to accelerate with continued warming. Predicting future impacts remains difficult, however, given multiple interacting thermal dependencies influencing dynamics, lacking data for most species, and the impossibility of empirically measuring host-parasite dynamics for yet-to-be-observed environmental conditions. Here, I will discuss how combining life-cycle-based population models with thermal performance curves based on the Metabolic Theory of Ecology provides a process-oriented approach for anticipating impacts of warming, including for data-poor species. Using well-studied model systems, I will first demonstrate the frameworks ability to predict disease emergence and geographic range changes of parasites in warming environments. To also aid predictions for data-poor species, I will then discuss ways to generalize the framework, both with respect to parameter estimates and the structure of the host-parasite dynamics. I will show how model parameters may be estimated from systematic among-species relationships of thermal sensitivity, and introduce a balance equation that reveals systematic relationships between life cycle complexity and a parasites response to warming based on the interactions of multiple thermal sensitivities through its life cycle. Together, the framework provides powerful ways for anticipating impacts of warming on parasitism, both for well-studied and data-poor systems.

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CP1

A Multiscale Vertex Modeling Framework for Simulating Biological Tissue Patterning

The spatiotemporal distribution of morphogens is important for proper development of biological tissue patterns. One means of distribution is via signaling filopodia (cytonemes), which facilitate direct long-range communication between cells. The precise mechanism by which signals are activated and transported along cytonemes is not well understood. To address this, we have developed a vertex modeling framework which allows one to control the dynamics of individual cytonemes generated from all cells within a tissue and permits the inclusion of additional models to investigate mechanisms of morphogen transport along cytonemes. We test our framework by modeling the formation of bristle cell patterns in the dorsal thorax of the fruit fly Drosophila melanoganster, which relies on Notch-Delta signaling between distant cells.

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CP1

Filopodia Dynamics and Notch-Delta Signaling in Drosophila Tissue Development

The spatiotemporal distribution of morphogens contributes to the organized development of tissues and organs. One model of morphogen distribution is active transport, which includes cell based mechanisms like signaling filopodia (cytonemes). Signaling filopodia facilitate contact between distant cells in order to allow signaling to occur, and support several cell signaling paradigms during development. Of particular interest is Notch-Delta signaling which regulates the organization of bristle cells on the thorax of Drosophila Melanogaster. Due to technical and other challenges, little is understood about how signals are activated and transported along filopodia. Our recent experiments show that basal filopodia in the fly notum are dynamic and under mechanical tension driven by myosin II contraction.

Since mechanical pulling forces are necessary for Notch activation we hypothesize that the protrusion and retraction dynamics of interacting basal filopodia generates sufficient pulling force to activate Notch. A mathematical model of the dynamics of interacting filopodia is developed and validated to test this hypothesis.

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CP1

Full Numerical PDE Bifurcation Analysis of a Cell Polarity Model

Here I investigate the non-linear dynamics of a reaction-diffusion system that models cell polarity. The model is kept generic and looks at the concentration of an active and inactive nucleation-promoting factor and the concentration of filamentous actin. I use full non-linear PDE bifurcation analysis to characterize the different types of steady state and periodic solution behaviours. This includes homogeneous steady states, periodic travelling waves, standing waves, excitable pulses, travelling fronts, and stationary solutions. For each solution type, we also characterize the linear stability along the branch of solutions and the types of bifurcations. From this, we see the coexistence of standing and travelling waves and the coexistence of travelling waves and pulses.

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CP1

The Emergence of Spatial Patterns with Diffusion-Coupled Compartments with Activator-Inhibitor Kinetics in 1-D, 2-D, and 3-D

Since Alan Turings pioneering publication on morphogenetic pattern formation obtained with reaction-diffusion (RD) systems, it has been the prevailing belief that two-component reaction diffusion systems have to include a fast diffusing inhibiting component (inhibitor) and a much slower diffusing activating component (activator) in order to break symmetry from a uniform steady-state. This time-scale separation is often unbiological for cell signal transduction pathways. We modify the traditional RD paradigm by considering nonlinear reaction kinetics only inside compartments with reactive boundary conditions to the extra-compartmental space which diffusively couples the compartments via two species. The construction of a nonlinear algebraic system for all existing steady-states enables us to derive a globally coupled matrix eigenvalue problem for the growth rates of eigenperturbations from the symmetric steady-state in 1-D, 2-D, and 3-D. We show that the membrane reaction rate ratio of inhibitor rate to activator rate is a key bifurcation parameter leading to robust symmetry-breaking of the compartments. Illustrated with Gierer-Meinhardt, FitzHugh-Nagumo and Rauch-Millonas intra-compartmental kinetics, our compartmental-reaction diffusion system does not require diffusion of inhibitor and activator on vastly different time scales. Our results reveal a possible simple mechanism of the ubiquitous biological steady and oscillatory cell specialization observed in nature.

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CP1

Modeling Interactions Between Microtubule Cytoskeleton and Insulin Granules in Pancreatic β Cells

Many models have been proposed to describe the glucose-stimulated insulin secretion (GSIS) in pancreatic β cells. Such GSIS dynamics are affected by numerous factors and the cells microtubule (MT) cytoskeleton plays a critical role in regulating insulin secretion. However, that critical role is still not fully investigated. Recent results showed the two mechanisms in which the microtubule cytoskeleton negatively regulates insulin secretion by limiting the amount of insulin near the plasma membrane and inhibiting or breaking the interactions between the plasma membrane and the remaining nearby insulin granules. In this work, we construct a computational model of the MT cytoskeleton in insulin-producing cells in 3D. Using stochastic modeling, we investigate how transport along that MT cytoskeleton influences the availability of insulin near the plasma membrane. Our study would potentially contribute to the development of an alternative therapeutic strategy for diabetes by targeting specific MT regulators.

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CP1

Active and Passive Transport in Biological Systems

Active and passive Brownian motion impacts numerous biological processes, from the microscopic motion of proteins within cells to the macroscopic foraging dynamics of animals. More often than not, the transport properties of these processes cannot be adequately explained by standard Brownian motion. Some of the most intriguing discrepancies include the presence of transient anomalous diffusion (sub- and super-diffusion) with non-Gaussian statistics that often feature non-exponential relaxation dynamics. In this talk, we will discuss a new model based on hierarchical implementation of the kinetic theory that captures most of these characteristics. In certain cases, the model can be mathematically described by a system of hierarchically coupled Ornstein-Uhlenbeck equations, which admits an analytical solution. Results on mean square displacement, non-gaussian statistics, and autocorrelation functions will be presented. We will discuss how this newly introduced model can effectively capture transient anomalous diffusion, fat-tailed spatiotemporal distributions, and slow relaxation dynamics. We will also directly compare the model's predictions to experimental findings from protein diffusion, cell migration, and animal foraging.

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CP2

A Stochastic First-Order Reaction Gene Translation and Nuclear-to-Cell Ratio Homeostasis Model

Cell size varies between different cell types, and between different growth and osmotic conditions. However, the nuclear-to-cell volume ratio (N/C ratio) is largely maintained. In this presentation, I will first introduce an osmotic pressure balance model of N/C ratio determination, which relates the N/C ratio to protein number in the nucleus and cytoplasm. Then I will present a simplified stochastic gene translation model and its corresponding chemical master equation (CME). Next, I will show how the CME can be solved analytically to obtain a joint probability distribution of the protein numbers, and how this distribution is used to calculate the mean and variance of the N/C ratio. Finally, I will present a Taylor expansion approximation of the N/C ratio, and use this approximation to show how the system size will affect the mean and variance of the N/C ratio, and how an N/C ratio homeostasis is achieved.

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CP2

The Rise of the Mini-Models

Zygotic genome activation (ZGA) in the development of flies, fish, frogs and mammals depends on pioneer-like transcription factors (TFs). Those TFs create open chromatin regions, promote histone acetylation on enhancers, and activate transcription. Here, we use the panel of single, double and triple mutants for zebrafish genome activators Pou5f3, Sox19b and Nanog, multi-omics and mathematical modeling to investigate the combinatorial mechanisms of genome activation. We first derived a transcriptional core model which can accurately describe the dynamics of the pioneer-like TF data measured in the different mutants. In a next step, the predictions obtained by the core model for the protein expression of the different TFs were used to analyse how they regulated the gene expression of 1800 genes in early zygotic development. To achieve this, 19 mini-models were built representing all possible combinations of TF performing every regulatory role and selected the mini-model which best fitted the available data for each gene. The result of that analysis was then cross-validated with an independent data-set, where open cromatine regions were measured. We found that Pou5f3 and Nanog act differently on synergistic and antagonistic enhancer types in contrast to their previosuly assumed purely synergistic action.

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CP2

Predicting the Effect of Mutation in Protein Complexes: A Mathematical Graph-Based Machine Learning Approach

Understanding the dynamics of protein-protein interactions (PPIs) is pivotal in unraveling molecular mechanisms, advancing fields like cancer research, and optimizing drug design. Mutations within PPIs can alter protein binding affinities, leading to functional changes and diseases. Predicting the impact of mutations on binding affinity remains a challenging task. In this study, we introduce a method called "GGL-PPI" that combines geometric graph representation and machine learning to address this issue. GGL-PPI employs atom-level graph coloring and multi-scale weighted colored geometric subgraphs to capture critical structural information of pro-

tein complexes. Our approach demonstrates superior predictive performance on established datasets, such as AB-Bind, SKEMPI 1.0, and SKEMPI 2.0, accurately estimating mutation-induced binding free energy changes. Furthermore, GGL-PPI's ability to generalize to blind test sets and provide unbiased predictions for both direct and reverse mutations makes it a valuable tool for enhancing our understanding of protein complexes and supporting drug design efforts.

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CP2

Gene Regulatory Networks (grns) Inference Through Optimal Transport

This talk provides an overview of using optimal transport to align single-cell datasets across different time points and its relevance in inferring gene regulatory networks (GRNs). We introduce AGW (Augmented Gromov-Wasserstein), a new formulation of the optimal transport problem that enables the simultaneous and effective alignment of both samples (cells) and features (genes) across various single-cell datasets. The applicability of this approach is demonstrated using both simulated and real datasets. Our results reconstruct the temporal sequencing of gene expression data and provide predictions for the underlying GRNs.

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CP3

Modeling the Effects of Temperature on Within-Mosquito Malaria Parasite Transitions and Sporozoite Load

Human malaria is caused by *Plasmodium* parasites and is transmitted via female *Anopheles* mosquitoes from one human to another. The asexual stage of the parasites life cycle takes place in an infected human, and the sexual stage is carried out in an infected mosquito. Several factors can inhibit or accelerate and enhance the successful completion of the parasites life cycle, which is required for malaria to be transmitted. Temperature is one of the most influential factors and is known to affect within-mosquito parasite forms and dynamics. To an existing model, we integrate experimental temperature data associated with certain transition rates of the sporogonic phase, which occurs within infected female mosquitoes. Using constructed cubic splines, we incorporate regional average monthly temperature from selected African regions by mapping the experimental temperature-dependent sporogonic traits to time-varying model parameters; we embed these converted temperature-to-time varying parameters into our mathematical model, yielding a non-autonomous system of differential equations. The system is then used to study the impact of temperature on the sporogonic malaria cycle. We also propose appropriate approximations for these constructed spline functions and investigate how the overall timeline of the sporogonic process is influenced by temperature. We conclude by discussing broader implications of rising global temperatures on malaria transmission dynamics.

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CP3

Assessing Neural Network Models of Mosquito Abundance for Vector Surveillance

Vector-borne disease outbreaks are closely tied to vector abundance, which makes knowledge of population dynamics useful in preventing future outbreaks. Here we use the Aedes-AI framework we previously developed to produce probabilistic forecasts of mosquito abundance for neighborhoods in Puerto Rico. The Aedes-AI models are a collection of neural network models of Aedes aegypti abundance [Kinney, A.C., Current, S., and Lega, J., Aedes-AI: Neural network models of mosquito abundance, PLoS Comp. Bio. (2021)]. The models are trained on synthetic data generated from a mechanistic model, in contrast to other models of mosquito abundance that rely on noisy, real world trap data for training. We previously demonstrated that the neural networks can learn the spatiotemporal features of mosquito populations. In this work, we use the Aedes-AI models to generate predictions using local weather and present a methodology of scaling the predictions and forecasting mosquito abundance based on past trap data. We assess the ability of the forecasts to capture trends in future trap data and compare them with outbreaks of mosquito-borne diseases in the region. We conclude with a discussion on how the Aedes-AI models are appealing from a public health perspective and can be used to supplement vector surveillance efforts.

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CP3

A Mathematical Model for Zika Virus Disease and Control of Affected Pregnancies

Zika virus is spread to human populations primarily by *Aedes aegypti* mosquitoes, and Zika virus disease has been linked to developmental abnormalities and miscarriage, generally coinciding with infection during early pregnancy. In this talk, we review key aspects of a modeling framework for the transmission of Zika and a range of control strategies to reduce the incidence of affected pregnancies in an outbreak. While most infectious disease models focus primarily on measures of the spread of the disease, our model is formulated to estimate the number of affected pregnancies through an outbreak scenario. The effectiveness of control measures and parameter sensitivity analysis is thus done with respect to this metric. We consider a range of intervention strategies, including the introduction of Wolbachia-infected mosquitoes into the native population. With emerging data on persistence of Zika virus in semen, the proposed model also includes a component of post-infectious males, which introduces a longer time scale for sexual transmission than the primary route. While the overall role of sexual transmission of Zika in an outbreak scenario is small compared with the more dominant human-vector route, this model predicts conditions under which subpopulations may make this secondary route more significant and durable. We also compare the well-mixed ODE framework to a network implementation with coupled randomized graph models for both human and mosquito

contact.

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CP4

Stationary & Traveling Activity in Neural Fields with Inhibition and adaptation

Neural fields are spatially-extended, nonlinear integrodifferential equations that aim to represent the large-scale dynamics of populations of neurons which are governed by synaptic interactions between neurons as well as other slow neuronal processes, e.g., adaptation. These neural field equations support a wide range of spatiotemporal dynamics, including spatially nonuniform equilibria, spatially-structured time-oscillatory patterns, and traveling waves. We discuss some recent results regarding the emergence and interaction of these different patterns of activity that arise in a family of fundamental neuronal networks on 1-dimensional and 2-dimensional spatial domains.

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CP4

Interneuron Subpopulations Modulate Noise Correlations in V1

Recent theoretical neuroscience work has advanced beyond the usual excitatory-inhibitory framework to include the diversity of inhibitory subtypes. As opposed to simply being a single class of neurons, 80% of interneurons lie in three subtypes: parvalbumin (PV)-, somatostatin (SST)-, and vasointestinal peptide (VIP)-expressing neurons, each with unique properties. Further, the differences in how these subtypes are embedded into the cortical circuit are not minor, and includes the following: 1) E neurons project onto all three subtypes, but the E to SOM connection is strongly facilitated while the E to PV connection is depressed, 2) VIP neurons project mainly onto SOM neurons, and 3) PV neurons are the only subtype to receive all of the same inputs as E neurons. In this work, we investigate how this network embedding and differences in short-term plasticity enable the different subtypes to play a particular role in establishing network dynamics in the mouse primary visual cortex. Specifically, we extend a network of exponential integrate-and-fire neurons with four subtypes to include plasticity variables as derived in Tsodyks et al. (1998). We show how the differences in the connectivity and plasticity rules of these subtypes are crucial in regulating noise correlations within the E population and can lead to new and non-intuitive results. Further, by considering inputs that mimic those received during locomotion, we show how this regulation changes between brain states.

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CP4

Identifying the Downstream Effectors of Tle4-Mediated Reprogramming

Cortical Progenitors in the ventricular zone differentiate to form the cerebral cortex, a six-layered dorsal structure involved in decision making, sensation, attention, and memory. Projection Neurons, or CPns, are a distinct class of neurons involved in communicating electrical impulses between the cerebral cortex and distal regions of the Central Nervous System (CNS). The question of how corticospinal projection neurons are involved in motor function and represents a fundamental and clinically important question in neurodevelopment. A network of transcription factors, including the transcriptional co-repressor Tle4, are central to specifying cortical projection neuron fates and identity. In this study, we investigate the role of Tle4 during embryonic development and post-natal circuit maturation. Utilizing a full stack RNA Sequencing analysis, we explore the identified transcriptional regulator Tle4 controls downstream gene patterning, causing reprogramming. Gene Ontology is later used to specify biological functions impacted by the reprogramming, and specific 4 cellular functions also impacted by reprogramming (Slit/Robo, Cadherin, Wnt Signaling, Angiogenesis). To further characterize downstream genetic patterns, we utilize a transcription factor analysis to identify motifs associated with loss of layer 6 and gain of layer 5 genes.

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CP4

Coarse-Grained Models of Cortical Circuits Via Local Dynamic Equilibria

Biologically realistic models in neuroscience are challenging to build and to simulate due to the large numbers of neurons, their complex interactions, and the large number of unknown physiological parameters. Reduced, or coarse-grained, models are more tractable, but it is not always clear how to evaluate results produced by models that are too far removed from neuroanatomy and physiology. In this talk, I will describe a coarse-graining strategy inspired by ideas from nonequilibrium statistical mechanics. The approach aims to balance biological realism and computational efficiency. I will illustrate its use on models of the primate primary visual cortex.

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CP4

Effect of Norepinephrine on Respiratory Neurons

Respiration is an essential involuntary function necessary for all living beings to survive. The preBötzinger complex (preBötC) network in the mammalian brainstem is a neuronal network that drives the inspiratory phase of the respiratory rhythm. In isolation in vitro, this neuronal network is rhythmically active and has been experi-

mentally shown to be constantly modulated by numerous neuromodulators through altering properties of the network. In this work, we integrate experimental findings with computational modeling to investigate the influence of Norepinephrine (NE) on respiratory dynamics via a focus on preBötC. Our model successfully reproduces the differential effects of NE on preBötC dynamics. Through our modeling approach and methods of dynamical systems theory, we uncover the mechanisms through which NE differentially modulates different types of preBötC neurons, providing insights into its overall impact on the network properties.

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CP4

Phase-Based Reduced Order Models of Bursting Neurons

Most formal strategies for analysis of bursting neurons exploit the separation of fast and slow timescales present in most computational models. Fast-slow decomposition in conjunction with bifurcation analysis of the fast dynamics can illuminate the mathematical mechanisms that underlie the transition between spiking and quiescence, but these general techniques are ill-suited for considering emergent behavior resulting from inter-neuron coupling and other external perturbations. This talk considers the development of accurate reduced order modeling techniques for two common topological classes of bursters in response to general perturbations such as an applied transmembrane current or synaptic current from upstream neurons. For parabolic bursters (i.e., circle/circle bursters), a persistent invariant circle allows for the application of an extended phase reduction framework. For elliptic bursters (i.e., subHopf/Fold Cycle bursters) model order reduction is accomplished by considering a carefully chosen set of reference trajectories. Mathematical analysis and accompanying numerical illustrations demonstrate the utility of the proposed approaches.

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CP5

Data Driven Model Discovery and Interpretation for Car T-Cell Killing Using Sparse Identification and Latent Variables

In the development of cell-based cancer therapies, quantitative mathematical models of cellular interactions are instrumental in understanding treatment efficacy. Efforts to validate and interpret mathematical models of cancer cell growth and death hinge first on proposing a precise mathematical model, then analyzing experimental data in the context of the chosen model. In this work, we present the first application of the sparse identification of non-linear dynamics (SINDy) algorithm to a real biological system in order discover cell-cell interaction dynamics in in vitro experimental data, using chimeric antigen receptor (CAR) T-cells and patient-derived glioblastoma cells. By combining the techniques of latent variable analysis and SINDy, we infer key aspects of the interaction dynamics of CAR T-cell populations and cancer. Importantly, we show how the model terms can be interpreted biologically in relation to different CAR T-cell functional responses, single or double CAR T-cell cancer cell binding models, and density-dependent growth dynamics in either of the CAR T-cell or cancer cell populations. We show how this data-driven model-discovery based approach provides unique insight into CAR T-cell dynamics when compared to an established model-first approach. These results demonstrate the potential for SINDy to improve the implementation and efficacy of CAR T-cell therapy in the clinic through an improved understanding of CAR T-cell dynamics.

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CP5

A Mathematical Modeling of the Mechanism Involved in Ctl-Mediated Tumor Cell Death

Advancements in cancer immunotherapy have underscored the critical role of Cytotoxic T Lymphocytes (CTLs) in eliminating tumor cells. This research presents a mathematical model aimed at elucidating the complex mechanisms governing CTL-mediated tumor cell death. The model integrates key factors such as CTL activation, migration, interaction with tumor cells, and the ensuing cytotoxic response. Through a system of differential equations, we quantify the dynamic interplay between CTLs and tumor cells, incorporating variables such as antigen recognition, effector function, and apoptotic signaling pathways. The model not only delineates the kinetics of CTL-tumor cell interactions but also explores the impact of diverse microenvironmental factors on the effectiveness of cytotoxic responses. Simulation results reveal nuanced insights into the temporal dynamics of CTL-mediated tumor cell death, highlighting the significance of factors such as antigen presentation efficiency, CTL proliferation rates, and spatial

distribution within the tumor microenvironment. Sensitivity analyses further identify key parameters influencing the robustness of the cytotoxic response and offer potential targets for therapeutic interventions. This research contributes to our quantitative understanding of the CTL-mediated immune response against tumors, providing a valuable tool for predicting outcomes under varying conditions.

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CP5

Dynamical Systems Modeling of Jak/Stat Signaling in Macrophages: Parameter Analysis to Understand Network Sensitivity to Signaling Context

Macrophages use the JAK/STAT signaling pathway to integrate cytokine cues into context-specific functional decisions. Understanding the mechanisms underlying this process is complicated by the observation that the same JAK kinases and STAT transcription factors can direct a range of gene expression programs depending on the activating cytokine. The high degree of regulatory symmetry in this pathway led us to hypothesize that the cytokine-environment controls the relative contribution of parallel network arms and that asymmetric kinetics determine its capacity to appropriately discriminate stimuli. Our group previously developed a computational workflow that links features of cytokine-induced STAT phosphorylation profiles to downstream gene expression. While the ODE model is able to recapitulate experimental observations and correctly predict the impact of JAK2 variation on gene expression, many of the 40+ model parameters are poorly constrained by the available data. Thus, our ability to understand how context-specific variation impacts signal transduction is limited. Here we present work toward optimizing parameter estimation, predicting data necessary to constrain individual model parameters, and, when individual constraint is impossible, identifying meaningful parameter relationships that determine regulatory outcome. We aim to predict the impact of network component perturbations on phospho-STAT trajectories and ultimately downstream gene expression profiles.

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CP5

Traveling Wave Speed and Profile of a go Or Grow Glioblastoma Multiforme Model

Glioblastoma multiforme (GBM) is a fast-growing and deadly brain tumor due to its ability to aggressively invade the nearby brain tissue. A host of mathematical models in the form of reactiondiffusion equations have been formulated and studied in order to assist clinical assessment of GBM growth and its treatment prediction. To better understand the speed of GBM growth and form, we propose a two population reactiondiffusion GBM model based on the go or grow hypothesis. Our model is validated by in vitro data and assumes that tumor cells are more likely to leave and search for better locations when resources are more limited at their current positions. Our findings indicate that the tumor progresses slower than the simpler Fisher model, which is known to overestimate GBM progression. Moreover, we obtain accurate estimations of the traveling wave solution profiles under several plausible GBM cell switching scenarios by applying the approximation method introduced by Canosa.

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CP5

Immune Control of the Gut Microbiota Via Avoidance and Tolerance

The mammalian gut microbiome is a complex ecosystem that provides metabolic and immunological benefits to the host. However, some gut microbes can cross the gut epithelium barrier, thereby harming the host. Furthermore, the microbe composition of the gut fluctuates in response to variations in the environment and resource availability. This ecology interacts with the host immune system, which can act as a controller, toggling between avoidance or tolerance of microbes, and their associated threats and benefits. How should the immune system monitor the gut ecology to optimize beneficial function while maintaining immunity? Using a generalized consumer-resource model coupled with a model for the tolerogenic and humoral immune responses, we investigate how host-supplied nutrients impact the composition of commensal microbes in the gut, and how in turn the microbial ecology can confer a metabolic benefit to the host. Our model sheds light on the constraints that the microbiome ecology imposes on immune control and vice versa. We also explore the hypothesis that the immune repertoire contains information about the composition-to-function mapping of the gut; for instance, identifying which compositional patterns are beneficial/harmful. We argue that since the gut microbiota is personalized amongst individuals, its specific composition is likely less important than its collective function.

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CP6

A Computational Analysis of Behavioural Phenotype: Modeling the Interaction Between the Butterfly Pieris Brasicae and Trichogramma Wasps

The diverse expression of behavioural phenotypes in a population has the potential to influence the whole population. Rather than using discrete levels of expression, we propose a model that treats the behavioural phenotype as a continuous distribution. This is more appropriate for dealing with phenotypes associated with continuous quantities, such as the amount of a pheromone secreted by a butterfly. We model the interaction of the butterfly *Pieris brasicae* and one of its predators, the *Trichogramma* wasp, using a reaction-diffusion equation coupled with an integro-differential equation with the distribution of behavioural phenotypes of the butterflies modeled as a diffusion process. The phenotypes are associated with the male butterflies' propensity to secrete a pheromone as part of the species' mating practices. We use computational methods to compute the steady states of our system and to determine their stability properties. This information facilitates a qualitative analysis of our model while avoiding the difficulties of using larger systems of equations. Our results also yield ecological inferences beyond what can be gained from merely solving the system in time.

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CP6

Early Warning Signals of a Catastrophic Collapse in a Two-Timescale Predator-Prey Mode

Identifying early warning signals for anticipating and predicting catastrophic changes in ecosystems have been crucial than ever before. Often such transitions, or more commonly referred to as the phenomenon of tipping, are preceded by long transient dynamics. In this talk, I will discuss a mathematical technique to analyze long transient dynamics preceding a catastrophic collapse in a class of singularly perturbed three-dimensional predator-prey models with explicit competition between the predators. I will address the underlying dynamical mechanism leading to the long transients and use tools from singular perturbation theory to analyze them. The analysis is then used to devise an early warning signal of a large population transition resulting in extinction of one of the predators. I will end with some preliminary analysis on extending the results to stochastic settings.

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CP6

Predicting Spotted Lanternfly Establishment Potential Based on Life Cycle Models

The spotted lanternfly is an invasive species in the Eastern United States. Compromising lumber, grape, and crop production, it has been labeled "the worst invasive species to establish in the US in a century.' We present principled mathematical models for the lanternfly life cycle and its dependence on climatic conditions, calibrated in close collaboration with lab and field ecologists. We discuss how the models, based on kinetic equations to capture the coexistence of agents at any development state, can be solved effectively to produce accurate maps of the pest's establishment potential. We also discuss how robust the lanternfly life cycle is to temperature variability and changing climatic conditions, particularly in yet unaffected but high-concern regions like California.

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CP6

The Effect of "fear" on Two Species Competition

Non-consumptive effects such as fear of depredation, can strongly influence predator-prey dynamics. There are several ecological and social motivations for these effects in competitive systems as well. In this work we consider the classic two species ODE and PDE Lotka-Volterra competition models, where one of the competitors is "fearful" of

the other. We find that the presence of fear can have several interesting dynamical effects on the classical competitive scenarios. Notably, for fear levels in certain regimes, we show novel bi-stability dynamics. Furthermore, in the spatially explicit setting, the effects of several spatially heterogeneous fear functions are investigated. In particular, we show that under certain integral restrictions on the fear function, a weak competition type situation can change to competitive exclusion. Applications of these results to ecological as well as sociopolitical settings are discussed, that connect to the "landscape of fear" (LOF) concept in ecology.

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CP6

Mathematical Models for the Spread of Spotted Lanternfly Across Multiple Scales

In 2014 the spotted lanternfly was introduced to Pennsylvania and with its ability to severely compromise lumber, grape and crop production has become a species of great concern. We present principled models for the spread of the species, capturing their hopping behavior across hosts, as observed and documented in the field. A calibrated model prototype is showcased with vineyards in mind, capturing how spotted lanternflies move between hosts in landscapes with different host geometries over the course of a season. We demonstrate how different geometries of hosts like those found in vineyards, deep forest, or edge ecosystems produce different emergent patterns of spread. We also connect the small-scale hopping model to large-scale models which forecast the spread over areas the size of the entire Northeastern US or of California.

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CP7

Modeling the Dynamics of Leptospirosis in India

Leptospirosis, a formidable zoonotic threat spawned by Leptospira, plagues tropical and subtropical realms. This study delves deep into tropical Indian states, namely, Kerala, Gujarat, Karnataka, Maharashtra, and Tamil Nadu, unraveling the dynamics of leptospirosis through a comprehensive mathematical model that embraces temperature-driven growth rates of Leptospira. Sensitivity analysis and parameter estimation techniques fortified the model's accuracy, unraveling the factors shaping leptospirosis transmission. Notably, the numerical results highlight the significant impact of rainfall, fishing, climate, mining, agriculture, and cattle farming on leptospirosis prevalence in the endemic states of India. Finally, our study urges resolute preventive action to control and combat leptospirosis in India. Strengthening surveillance, impactful awareness campaigns, targeted interventions, and improved hygiene practices among high-risk individuals are vital. Embracing these proactive strategies will alleviate the burden of leptospirosis and enhance public health in India and beyond.

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CP7

Darwinian Models for the Evolution of Resistance to Treatment

We consider a Darwinian (evolutionary game theoretic) version of a standard susceptible-infectious (SI) model in which the resistance of the disease causing pathogen to a treatment that prevents death to infected individuals is subject to evolutionary adaptation. We determine the existence and stability of all equilibria, both disease-free and endemic, and use the results to determine conditions under which the treatment will succeed or fail. Of particular interest are conditions under which a successful treatment in the absence of resistance adaptation (i.e. one that leads to a stable disease-free equilibrium) will succeed or fail when pathogen resistance is adaptive. These conditions are determined by the relative breadths of treatment effectiveness and infection transmission rate distributions as functions of pathogen resistance.

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CP7

Unveiling Global Dynamics of Monkeypox Through Deterministic and Data-Driven Models for Disease Control and Prediction

This paper thoroughly analyzes global Monkeypox (Mpox) univariate time series data, exploring disease outbreaks worldwide, including the USA, Brazil, and three continents: North America, South America, and Europe. To investigate, we developed a deterministic model integrating traditional compartmental models, deep learning techniques (1D-CNN, LSTM, BiLSTM, hybrid CNN-LSTM, and CNN-BiLSTM), and statistical time series models (ARIMA and exponential smoothing). The novelty of this study is delving into the Mpox time series data by implementing the data-driven and mathematical models concurrently an aspect not typically addressed in the existing literature. Key findings highlight the impact of vaccination rates on infected dynamics and the basic reproduction number. The study emphasizes the importance of increased vaccination among susceptible populations for effective disease control. We also employed the least square method to estimate the essential epidemiological parameters in the proposed deterministic model. The deterministic model reveals potential epidemic control by adjusting key parameters during outbreaks, particularly by reducing contact rates in high-risk groups. Data-driven models comprehensively understand disease dynamics across various locations, offering reliable short-term predictions (eight weeks). This study employs a comprehensive framework, indicating that Monkeypox is in a die-out situation, con-

sistent with real data.

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CP7

Modeling Covid-19 Transmission: Challenges of Uncertainty and Identifiability When Fitting Mechanistic Models to Time-Varying Processes

We use a compartmental model with a time-varying transmission parameter to describe COVID-19 transmission and investigate the challenges in fitting such a model to a time-varying process. We fit our model to both synthetic and real confirmed case and hospital discharge data, calculating uncertainties in the resulting parameter estimates and exploring non-identifiability within the estimated parameter set. We explore how non-identifiability between parameter estimates inflates uncertainties in the estimates of individual parameters but has a smaller impact on estimates of the basic reproduction number. Our work highlights the importance of undertaking such analyses when fitting models to data and the insights they give into how much trust we can place in parameter estimates.

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CP7

Homogenization Reveals Large-Scale Dynamics in the Spread of Chronic Wasting Disease"

Chronic wasting disease (CWD) is a neurodegenerative illness threatening cervid species such as deer and elk. It can be spread directly between infected individuals, or indirectly through environmentally deposited hazard. These transmission routes obey different dynamics, complicating our understanding of CWD spread. Additionally, small-scale variability in the landscape creates variable behaviors in hosts across space. The intersection of this variability with different transmission routes is poorly understood. We construct a model of CWD in deer on the small spatial scale of landscape variability, accounting for different movement behaviors in different types of land. Using the method of homogenization, we derive equations describing the spread of CWD on large spatial scales, which are more relevant to observation and management efforts. These equations identify direct transmission with pulled waves of CWD spread, which are driven by infectious dynamics at the leading edge. Indirect transmission is instead associated with pushed waves, in which the entire infectious population contributes to the disease's advance.

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CP7

An Epidemic Model with Infection Age and Vaccination Age Structure

A model of epidemic dynamics is developed that incorporates continuous variables for infection age and vaccination age. The model analyzes pre-symptomatic and symptomatic periods of an infected individual in terms of infection age. This property is shown to be of major importance in the severity of the epidemic, when the infectious period of an infected individual precedes the symptomatic period. The model also analyzes the efficacy of vaccination in terms of vaccination age. The immunity to infection of vaccinated individuals varies with vaccination age and is also of major significance in the severity of the epidemic. Application of the model to the 2003 SARS epidemic in Taiwan and the COVID-19 epidemic in New York State provides insights into the dynamics of these diseases. It is shown that the SARS outbreak was effectively contained due to the overlap of infectious and symptomatic periods, allowing for the timely isolation of affected individuals. In contrast, the pre-symptomatic spread of COVID-19 in New York led to a rapid, uncontrolled epidemic. These findings underscore the critical importance of the pre-symptomatic infectious period and the vaccination strategies in influencing the dynamics of an epidemic.

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CP8

Modeling the Spread of Retinal Detachment (rd) and Its Effects on the Dynamics of the Rod Outer Segment (ros) Renewal

Retinal detachment (RD) is the separation of the neural layer (NL) from the retinal pigmented epithelium (RPE) thereby preventing the supply of nutrients to the cells within the NL of the retina. In vertebrates, primary photoreceptor cells consisting of rods and cones undergo daily renewal of their outer segment through the addition of disc-like structures and shedding of these discs at their distal end. When the retina detaches, the outer segment of these cells begins to degenerate and, if surgical procedures for reattachment are not done promptly, the cells can die leading to blindness. Recent mathematical models and experimental work provide insight into how retinal detachment affects the renewal of a rod outer segment as well as the survival time of a rod cell in a detached retina. Progression of retinal detachment results in progressive loss of vision. In this work, we develop a mathematical model that combines the spatial progression of retinal detachment with the dynamics of the rod outer segment under different rates of eye movement. We use an immersed boundary method to simulate the fluid-structure interactions. Understanding the progression of retinal detachment and its effects on the population of rod cells will help predict the time frame within which retinal detachment surgery can restore vision

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CP8

A First Passage Time Approach to Assess the Influence of Ocular Geometry and Individual Variability on Intravitreal Drug Delivery and Residence Time

Standard of care for various retinal diseases involves chronic treatment with recurrent intravitreal injections. This motivates mathematical modelling efforts to identify influential factors that affect drug residence time, aiming to minimise the frequency of administration. We sought to describe the vitreal diffusion and residence time of protein therapeutics in nonclinical species frequently used during drug development for pharmacokinetic assessments. In human eyes, we investigated the impact of variability in vitreous cavity size and eccentricity on drug elimination. Using a first passage time approach, we modelled the transport-controlled distribution and elimination of standard ocular drugs. Detailed anatomical 3D geometries of mouse, rat, rabbit, cynomolgus monkey, and human eyes were constructed using ocular images and biometry datasets. A scaling relationship to calculate ocular half-lives was derived for comparison with experimental results. Model simulations revealed a dependence of residence time on ocular size and injection location. Delivery to the posterior vitreous resulted in increased vitreal half-life and retinal permeation. Inter-individual variability in human eye geometry had a significant influence on residence time, showing a strong correlation to the axial length and vitreal volume. Simulations further suggest a potential role of permeability of the posterior pathway in determining species differences in ocular pharmacokinetics.

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CP8

A Virtual Laboratory for the Simulation of Aqueous Humor Dynamics in the Eye

Glaucoma is a neuropathology of the eye representing the second major cause of irreversible blindness. Elevated intraocular pressure (IOP) is an established risk factor of glaucoma. IOP is determined by aqueous humor dynamics (AHDyn), the balance among production (Pr), diffusion (Diff) and drainage (Dr) of aqueous humor (AH), a watery transparent fluid including electrolytes and low protein concentration. Reducing AH-Pr and/or increasing AH-Dr are possible approaches to reduce IOP. Here we illustrate a virtual laboratory for the simulation of AHDyn based on reduction of (1) 3D Velocity-Extended Poisson-Nernst-Planck PDE system to model AH-Pr from the ciliary body; (2) 3D diffusion bulk flow to model AH-Diff from posterior into anterior chambers; (3) 3D poroelastic PDE system to model AH-Dr throughout trabecular meshwork (TM) and uveoscleral (Uv) pathways. Model variables represent compartment values of electric potential, ion molar densities and fluid pressure and are numerically determined by a fixed-point iteration which transforms AHDyn simulation into the successive solution of two nonlinear systems of algebraic equations, representing mass balance in AH-Pr and in AH-Diff + AH-Dr, respectively. Computational tests suggest that Na+/K+ pump and TM/Uv hydraulic conductances are the main biomarkers of a pathological increase in IOP. These results support the potential use of mathematical virtual laboratories to assist and optimize the design of IOP lowering medications

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CP8

Measuring Tumor-Associated Interstitial Fluid Flow in Vivo from Dynamic Mri with Contrast

Tumor-associated fluid flow is an important aspect of cancer physiology, informing not only how therapeutic drugs and cells may distribute within the disease site, but also how cancerous cells may invade surrounding healthy tissue. In this work, we present a novel methodology, named Lo-

calized Convolutional Function Regression (LCFR), which allows for rapid and accurate measurement of interstitial fluid flow of contrast agent from standard dynamic contrast enhanced (DCE) magnetic resonance imaging (MRI). This novel methodology, adapted for this specific application from Weak SINDy for PDEs (Messenger Bortz, 2021), is a hybrid data- and physics-informed method for simultaneous measurement of interstitial fluid flow, diffusion, perfusion, and vascular content from a single DCE-MRI acquisition. We validated this method in simulations, resulting in $< 2\%$ measurement error. We validated our methodology in porous hydrogel, resulting in velocity and diffusion measurements in line with literature of contrast agent transport in hydrogel. We tested LCFR in vivo as a method of measuring 3D flow velocity in GL261 tumors. We also utilized historic cancer data, and measured physiological differences in interstitial flow rates between breast and brain cancer. These results indicate that our methodology is both accurate, and capable of measuring physiological differences between individuals and disease types, suggesting that this methodology may be of future diagnostic and prognostic use.

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CP8

Applying Deep Learning for Accurate Analysis of Eye Tissue in Biomedical Hyperspectral Imaging

Biomedical hyperspectral imaging has emerged as a powerful tool for non-invasive examination and analysis of biological tissues. By capturing a wide range of spectral information at each pixel, hyperspectral imaging provides unique insights into tissue composition and pathology. In our research, we focus on leveraging this cutting-edge technology to enhance our understanding of ocular health. Specifically, we utilize hyperspectral images of eye tissues, including the retina, choroid, sclera, and muscle fibers, to perform precise segmentation and characterization. This segmentation task is critical for various clinical applications, such as diagnosing eye diseases and monitoring treatment responses. To tackle the challenging task of segmenting hyperspectral eye tissue images, we employ deep learning techniques, such as U-Net architectures. These methods enable us to automatically partition the hyperspectral data into distinct tissue regions, providing valuable information for ophthalmologists and researchers. Our conference talk will delve into the details of our approach, highlighting the effectiveness of deep learning in biomedical hyperspectral image analysis. By showcasing our results and insights, we aim to contribute to the growing body of knowledge in the field of ocular health and inspire further advancements in biomedical hyperspectral imaging research.

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CP9

Whole Body Physiology Model to Simulate Respiratory Depression of Fentanyl and Associated Naloxone Reversal - A Model Informed Repeat Dosing Analysis

We present here a computational model of the whole-body response to hypoxemia induced through opioid overdose. We use a physiology engine to ask the question: what are the nasal naloxone requirements to properly reverse fentanyl overdose? We investigate this question via a dynamic runtime model of the human physiology. We design a reversal scenario that considers the requirements of naloxone for a patient experiencing severe hypoxia, induced from an intravenous fentanyl bolus. We investigate a large range of possible opioid doses and for each of these doses provide goal directed naloxone reversal therapy. We show that for increasing levels of fentanyl administration to the patient, naloxone requirements also increase. The naloxone requirement displays a non-linear response to the initial opioid dose. This nonlinear response is largely logistic with three distinct phases: onset, rapid acceleration, and a plateau period for doses above 1.2mg. By designing the model to include circulation and respiration we investigate physiological markers that may be used in goal directed therapy rescue treatments. We hope that this model is the first step in further testing and requirements refinement regarding naloxone as a reversal agent. We hope that this study is the first of many to consider the needs of a fentanyl opioid overdose. Care is required to possibly change the training of first responders and to address this epidemic.

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CP9

Mathematical Models of HBV Infection

Nearly 300 million of people are chronically infected with hepatitis B virus (HBV). Currently no cure has been developed, leading to more than 800,000 HBV-related deaths annually. The focus of therapies is on eliminating the template for HBV replication, i.e. covalently closed circular DNA (cccDNA). However, HBV surface antigens (HBsAg) derive also from integrated DNA (iDNA). The presence of HBsAg activates the immune response, which leads to an inflammatory state and eventually to liver damage. Our collaborators at the Viral Hepatitis Center of John Hopkins University considered a cohort of 10 HBV-HIV co-infected participants on nucleos(t)ide analogue (NUC) therapy for a short or long time (from a few weeks to almost 12 years). Liver biopsies were obtained from each individual at 2 time points and single cell analysis was performed, measuring the genetic material inside each cell. First, we quantify the decay/growth of the number of cells with viral genetic material, and its timescale, with the aim of understanding how NUC therapy affects this dynamics. Then, we build a stochastic model that accounts for hepatocytes spatial distribution to study the distribution of infected cells and how the viral genetic material accumulates inside each cell.

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CP9

Forecasting Drug Overdose Mortality by Age in the United States at the National and County Levels

The drug overdose crisis in the United States continues to intensify. Fatalities have increased five-fold since 1999 reaching a record high of 108,000 deaths in 2021. The epidemic has unfolded through distinct waves of different drug types, uniquely impacting various age, gender, race and ethnic groups in specific geographical areas. One major challenge in designing effective interventions is the forecasting of age-specific overdose patterns at the local level so that prevention and preparedness can be effectively delivered. We develop a forecasting method that assimilates observational data obtained from the CDC WONDER database with an age-structured model of addiction and overdose mortality. We apply our method nationwide and to three select areas: Los Angeles County, Cook County and the five boroughs of New York City, providing forecasts of drug-overdose mortality and estimates of relevant epidemiological quantities, such as mortality and age-specific addiction rates.

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CP9

Modeling Hypothermia with a Multiscale Model Coupling Partial Differential Equations for Blood Flow and Temperature with Ordinary Differential Equations.

We present a computational model simulating body temperature in extremities subject to extreme cold (hypothermia). The phenomenological description of the problem is that the body responds to hypothermia by vasoconstriction, whereby the body restricts blood flow to the extremity, preserving core body temperature even at the expense of sacrificing tissue in the extremity. Our model includes several elements: (i) a parabolic partial differential equation (PDE) with an energy exchange term modeling blood perfusion through tissue, and this term is derived by multiscale analysis. In turn, (ii) blood flow is modeled by a network model. Our model also includes (iii) a constrained ODE representing the bodys metabolic and vasoconstrictive responses. We approximate the solution to the model with a mixed finite element method on Cartesian grid for the parabolic PDE with an immersed boundary approach to handle complex geometries, coupled to the blood flow and ODE models. We present analyses and simulation results.

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CP9

Time-Dependent Antibody Kinetics for Previously Infected and Vaccinated Individuals Via Graph-Theoretic Modeling

Modeling the deterioration of antibody levels is paramount to understanding the time-dependent viral response to infections, vaccinations, or a combination of the two. These events have been studied experimentally, but also benefit from a rigorous mathematical underpinning. Disease or vaccination prevalence in the population and time-dependence on a personal scale simultaneously affect antibody levels, interact non-trivially, and pose considerable modeling challenges. We propose a time-inhomogeneous Markov chain model for event-to-event transitions coupled with a probabilistic framework for post-event antibody kinetics. This approach is ideal to model sequences of infections and vaccinations, or personal trajectories in a population. We demonstrate the modeling process as well as estimation of transition probabilities. This work is an important step towards a comprehensive understanding of antibody kinetics that will allow us to simulate and predict real-world disease response scenarios.

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CP10

Capturing Spatiotemporal Signaling Patterns in Cellular Data with Geometric Scattering Trajectory Homology

Cell signaling plays a critical role in orchestrating complex processes required for the development and normal functioning of organisms. To facilitate quantitative understanding of the dynamics of cellular signaling, we developed Geometric Scattering Trajectory Homology (GSTH), a novel framework that integrates geometric scattering and topological data analysis. GSTH comprises of four steps: (1) creation of a cell adjacency graph to model spatial connectivity with the timelapse signal as vertex features, (2) featurizing the graph signal using the geometric scattering transform, a discretization of the wavelet transform, (3) dimensionality reduction using tPHATE, a manifold learning technique, and (4) computation of topological properties of the resulting low dimensional embedding using persistent homology. We tested GSTH using a variety of computational models and experimental data. Our findings demonstrate that the shape of GSTH embeddings reveal the degree of synchrony, speed, and quasi-periodicity of the underlying signaling pattern. GSTH also enables data-driven modeling, through the recovery of model parameters using neural networks trained on GSTH embeddings of data.

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CP10

Modelling Glucose Regulation: Lipotoxicity and the Progression to Type 2 Diabetes

As an individual moves from healthy to pre-diabetic to diabetic, there are many physiological changes that occur, but it is not known which of these changes are the main drivers of the progression to type II diabetes. In this talk, I will describe a simple model for glucose regulation and how modeling can help determine which of these physiological changes are capable of pushing an individual from healthy to diseased. By framing this problem in terms of bifurcations, we can find models that create qualitative changes to the system that allow for movement between healthy and diseased states. We will examine a model that includes the toxicity of lipids in the pancreas, and find a bifurcation that describes the progression to type II diabetes.

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CP10

Modeling Antibiotic Resistance Via Horizontal Gene Transfer and Antibiotic Dosing

In this talk we will present models for in-vivo transfer of antimicrobial resistance and determine efficient antibiotic regimens in the presence of drug resistant bacteria. We consider models of resistance acquisition involving horizontal transfer of resistant genes from a resistant to a susceptible strain which has been identified as primary mechanism for in-vivo drug resistance. We consider models where resistance is acquired via conjugation, transformation, and transduction. We show that periodic dosing at a constant level may not always be successful in eradicating the bacteria. We use a numerical optimization algorithm to determine the best antibiotic dosing strategy. We study the effects of varying different model parameters on the qualitative behavior of the optimal dosing.

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CP10

Understanding Stacked Trimer Assembly

Cells employ large macromolecular machines for the execution and regulation of many vital processes for cell and organismal viability. Interestingly, cells cannot synthesize these machines as functioning units. Instead, cells synthesize the molecular parts that must then assemble into the functional complex. An extremely common motif is a stacked ring-like topology. Thus, understanding how stacked trimers assemble is crucial for our understanding of how complexes are regulated. Here, we developed a mathematical model of stacked trimer assembly that accounts for different binding affinities between and within rings. Our main finding is that deadlock a severe form of kinetic trapping can be extremely long, lasting for days or longer. Deadlock is worst when all the interfaces have high binding affinities. So, we predict that evolutionary pressures select against stacked trimers having strong binding affinities throughout. We tested our prediction by analyzing solved stacked trimer structures; we found that indeed the majority if not all of the stacked trimers did not contain very strong interactions. Finally, to better understand the origins of deadlock, our pathway analysis show that when all the binding affinities are strong, many of the possible pathways are utilized, consuming subunits, and creating high levels of deadlock. In sum, our work provides critical insight into the evolutionary pressures that have shaped the assembly of stacked rings.

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CP10

Numerical Simulation of Whole Cell Calcium Signaling in Detrusor Smooth Muscle

Urinary incontinence, also known as involuntary leakage of urine, is usually the result of overactivity of the urinary bladder smooth muscles (UBSM), which control the bladder. The intracellular calcium (Ca2+) dynamics play an essential role in the contraction and relaxation of the UBSM cell. This study establishes a whole-cell Ca2+ model based on the numerical simulation of the UBSM cell concerning experimental data. Simulation of electrophysiology and intracellular Ca2+ dynamics in UBSM comprises fast stochastic dynamics in tiny sub-compartments, partial differential equations (PDEs) with stochastic source terms for concentration fields, and the globally coupling membrane potential. A set of reaction-diffusion equations describes the behavior of the intracellular concentration fields on length scales from tens of nanometers to cell size (tens of micrometers) and milliseconds to tens of seconds. Detailed highly stochastic Ca2+ release units (CRUs) models drive source functions in the PDE model. The timescale separation between fast stochastic CRU dynamics and slower PDE dynamics limits efficiency with traditional approaches. We developed an efficient adaptive finite element simulator interface for the numerical simulation of this multi-physics and multiscale problem. In this work, we have presented an efficient and novel computational approach for the simulation of intracellular Ca2+ dynamics in UBSM tissues.

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CP10

Understanding and Quantifying Network Robust-

ness to Stochastic Inputs

A variety of biomedical systems are modeled by networks of deterministic differential equations with stochastic inputs. In some cases, the network output is remarkably constant despite a randomly fluctuating input. In the context of biochemistry and cell biology, chemical reaction networks and multistage processes with this property are called robust. Similarly, the notion of a forgiving drug in pharmacology is a medication that maintains therapeutic effect despite lapses in patient adherence to the prescribed regimen. What makes a network robust to stochastic noise? This question is challenging due to the many network parameters (size, topology, rate constants) and possible types of noisy inputs. In this paper, we propose a summary statistic to describe the robustness of a network of linear differential equations (i.e. a first-order mass-action system). This statistic describes the variance of a certain conditional last passage time on the network. This statistic can be quickly computed on a modern computer, even for networks with thousands of nodes. Furthermore, we use this statistic to prove theorems about how certain network motifs increase robustness. Importantly, our analysis reveals the essential reason why a network is or is not robust to noise. We illustrate our results in several examples of networks and classes of stochastic inputs.

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CP11

Travelling Waves in Phenotypically Structured Models of Cell Migration into Extracellular Matrix

Collective cell motility is a widely observed phenomenon in many biological scenarios, particularly developmental biology and medicine. A range of modelling approaches have been employed to study this, but they rarely take into account population heterogeneity, which is associated with treatment failure and the recurrence of cancerous tumours. To model this, we consider a system of non-linear cross-dependent partial differential equations that represent the evolution of multiple populations in space and time, which take the form of reaction-diffusion equations. We first consider a homogeneous cell population where cells can degrade extracellular matrix (ECM), divide and move, before comparing this to a population consisting of 2 distinct cell phenotypes: where one has the ability to degrade the ECM and move and the other, to proliferate. We show that the system displays multiple spatially homogeneous steady states and that the phenotypic structure of the invading cell population depends largely on the environmental and density dependence of the switching mechanisms of the cells. Beyond providing insight into the qualitative behaviour of cell invasion models when cells are able to switch phenotypes, these models could also be used to guide future developments of treatments for related diseases.

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CP11

Biologically Mediated Precipitation in a Biofilm System

Microbial life on Eart prevalently evolves in the form of biofilms, which are colonies of microorganisms embedded in a self produced matrix interacting with the surrounding environment. Mathematical modeling of biofilm systems is essential to investigate microbial life evolution and related interactions with the media in which they evolve. In particular, inorganic particles, such as trace metals, are able to interact with this living systems and affect all biofilm biotechnological applications. This work presents a mathematical model able to describe the growth and evolution of a multispecies biofilm in a trace metals rich environment. The work focuses on the precipitation phenomenon, occuring in the inner part of the biofilm when specific environmental conditions occur. The availability of space in the biofilm structure and the physico-chemical characteristics of the surrounding environment are the main factors affecting the biologically mediated precipitation process. The general formulation of the model includes: a system of first order quasi-linear hyperbolic equations that describes the growth of the biofilm components; a system of diffusion-reaction equations for soluble compounds; a nonlinear ordinary differential equation for the biofilm thickness, which represent the free boundary evolution of the biofilm domain. Numerical applications highlight the model accuracy in reproducing the accumulation of precipitates in real case biofilm systems.

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CP11

A Multiscale Model for Biofilm Matrix Structure and Rheology

Biofilms are initiated by polymer-producing bacteria that undergo a phenotypic switch and produce various types of extracellular polymeric substances (EPS). Some bacteria mutants produce enzymes necessary for EPS components production while also consuming a shared resource (public good), and some mutants solely consume the public good without contributing to EPS components production. The EPS form a matrix of polymeric network combined with the fluid solvent creating a gel-like fluid that exhibits rheo-

logical behavior. The cooperation and communication between multispecies bacterial communities control the concentration of the EPS constituents, which influence the viscoelastic behavior of biofilm. We developed a mathematical model to understand the mechanism of biofilm formation and the physics of biofilm rheology at different scales, from EPS production to biofilm rheological behavior as a soft matter and to the spatiotemporal organization of biofilm structure. Using linear viscoelastic models and a multiphase solver, we characterized the viscoelasticity of various biofilm variants and described the structure of biofilm matrix components that are produced by bacterial communities. These results provide valuable insights into the complex nature of biofilm heterogeneity and variability, controlling chronic biofilm infections, and effective biofilm removal strategies.

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CP11

Modeling of Lophotrichous Bacteria

Bacterial swimming mediated by flagellar rotation is one of the most ubiquitous forms of cellular locomotion, and different flagellated bacterial species exhibit several distinct motility patterns. In this talk, we introduce a mathematical model of a bacterium swimming in a fluid. We particularly focus on a model for lophotrichous bacteria whose swimming patterns involve a recently reported wrapping mode. We also investigate how the material and physical properties of bacterial flagella affect their swimming patterns.

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CP11

Modelling Drinking Water Biofilms: Bacterial Adhesion and Legionella Pneumophila Necrotrophic Growth

A mathematical model is presented to simulate the establishment and growth of a drinking water distribution system biofilm, with a specific emphasis on the influence of ionic strength on bacterial adhesion and persistence of *Legionella pneumophila*. We consider how ionic strength affects interaction energies during the initial phase of biofilm formation, incorporating this dependence into the attachment flux. Specifically, we introduce a novel function of ionic strength, calibrated based on experimental literature results, into the formulation of the attachment rate, which is modelled as a first-order linear rate with respect to free-floating cells. The model also includes a novel necrotrophic kinetics to simulate the *Legionella pneumophila* metabolism. The biofilm is modelled as a 1D free boundary domain, and its evolution is governed by hyperbolic-parabolic PDEs. The initial attachment phase is modelled by assuming a vanishing initial value for the free boundary. Through numerical simulations, we explore the impact of the necrotrophic kinetic parameters, the role of ionic strength on the initial stage of biofilm formation through bacterial attachment, and the effects of nutrient level variations on system dynamics. The numerical results demonstrate that ionic strength mainly governs bacterial adhesion for young biofilms and highlight that the ecology of this biofilm system may be strongly affected by ionic strength even in the presence of a biocide.

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CP12

Partially Functional Resistance in Gene Drive Control

Gene drives (GDs) allow scientists to spread a genetic cargo into a target population. GD technology has immense promise in the control of pest species. To spread, GDs exploit DNA repair mechanisms to duplicate themselves at the expense of a target gene. However, faulty repair can produce GD-resistant alleles. Resistance is one of the greatest threats to GD use in the wild and is difficult to study at appropriate scales within laboratory experiments. Current approaches to studying resistance rely on a binary paradigm: resistant alleles are either functional or nonfunctional. In this work, we move beyond this paradigm and study partially functional resistant alleles. Partially functional resistance occurs when an allele restores somebut not allgenetic function to the organism. Even if these alleles are deleterious, spread of the GD can select for the spread of the resistance allele, threatening control failure. Using a coupled genetic population dynamics model, we study GD performance in a population with partially functional resistance. We pay particular attention to GD performance in certain mosquito species of interest, such as the malaria mosquito Anopheles gambiae, and the dengue mosquito Aedes aegypti. We study the roles played by certain DNA repair mechanisms so that our findings can be applied to other target organisms. Our work will inform the development of GDs going forward to mitigate the risk

of control failure due to resistance arising in target populations.

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CP12

Early Warning Signals for Dynamics on Networks

Complex dynamical systems in biological domains often show sudden major changes, or tipping points, as the system gradually changes. Examples include mass extinctions in an ecosystem, deforestation, and aggressive progression of a disease in a human body. Exploiting critical slowing down phenomena among other things, various early warning signals that anticipate tipping events before they occur have been developed. Complex dynamical systems for which we want to anticipate sudden regime shifts often form a heterogeneous network. We propose methods to select sentinel nodes in a given network to construct informative early warning signals given that the network may be heterogeneous and show multistage transitions [MacLaren, Kundu & Masuda, Journal of the Royal Society Interface, 20, 20220743 (2023)]. We show that small subsets of nodes can anticipate transitions as well as or even better than using all the nodes under the proposed node selection method. We also present mathematically supported sentinel node selection methods along the same idea.

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CP12

Modeling a Novel Gene Drive Targeting Immune Responses to Increase Confidence in Local Confinement

Gene drive technologies have the potential to combat invasive pests, preventing the spread of diseases and protecting local ecosystems and agriculture. However, this potential cannot be realized until they are made safe enough to release. One major concern preventing drives from being released is whether they will remain locally confined. Invasion thresholds are the most common strategy to accomplish this by taking advantage of unstable equilibrium points in allele frequency, below which the drive will not spread. This maintains local confinement by preventing migrants from spreading the drive in surrounding populations. This strategy has found limited success in suppression gene drives because of the drives high fitness costs which lead to unfeasibly high release ratios to pass the threshold. We circumvent this issue by designing a novel suppression drive system that targets the immune response of an organism to a local stressor (i.e., endemic virus, fungus, or a specialized parasitoid). The drive system increases the target organisms susceptibility to the stressor by increasing the likelihood of acquiring the infection or the impact of infection on the organism. This means that the drive systems fitness cost is dependent on the abundance of the stressor. We model several drive systems with several stressors to consider the efficacy of the system. Using successful combinations, we investigate the ability of the drive to stay locally combined using spatial models.

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CP12

Environmental Feedback Allows Escape from the Prisoner's Dilemma

The prevalence of cooperative behavior is a fundamental problem in evolutionary biology. Cooperative behaviors impose a cost, so cooperative individuals are vulnerable to exploitation by Defectors that do not contribute and instead benefit from the cooperation of others. Bacteriophage ϕ_6 shows strategies of cooperation and defection during infection: ϕ_6 phages produce essential proteins in the host cell cytoplasm. Because coinfection is possible, a phage does not have exclusive access to its own products. Cooperator phages produce products while Defector phages produce less and instead steal from Cooperators. Previous work found that ϕ_6 is trapped in a prisoners dilemma, predicting that Defectors will replicate faster than Cooperators and out-compete them; cooperation is doomed. Still, cooperative ϕ_6 exist, so there must be a mechanism that maintains cooperation. Defectors are advantaged when coinfection is common and there is opportunity to extort Cooperators, while Cooperators are advantaged when single infection is common. The rates of single versus coinfection are modulated by the densities of hosts and viruses. We propose that environmental feedback, or the interplay between viral and host densities, maintains cooperation in ϕ_6 populations. We develop and analyze a mathematical model that incorporates environmental feedback and find that environmental feedback leads to the co-existence of Cooperators and Defectors.

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CP13

Exploring the Impact of the Extracellular Space Geometry in the Egg Chamber

Cell migration plays a pivotal role in fundamental biological processes such as development, tissue repair, immune responses, and cancer metastasis. Understanding the mechanisms governing cell migration is crucial for devising treatments for diverse diseases. Despite extensive studies on individual cell movements, there has been limited attention to the collective migration of cell clusters through intricate extracellular environments. Our approach utilizes techniques from reducing domain methods to phase field methods to mathematically model cluster cell migration, accounting for the extracellular space within the egg chamber. By recreating the architecture of the egg chamber, our model incorporates different cell types, considering cell-cell adhesion, repulsion forces, and epithelial layer substrate. This research aims to characterize the biological mechanisms associated with clustered cell migration. This research was funded in part by NSF-DMS #1953423, B.E. Peercy, and the MERCK Graduate Science Research Scholarship to N. Akhavan.

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CP13

Foraging and Decision-Making in *C. Elegans*: a

Biophysical and Data-Driven Model of Neural Network Dynamics

C. elegans produce many behaviors, such as foraging, by switching between forward and reversal states with turns ending reversals. While experimentalists have identified subsets of neurons that drive forward and reversal states, these premotor neurons are highly integrated into a larger network whose collective dynamics ultimately determine which behaviors are sustained and terminated. Analyzing collective network dynamics presents a major challenge in *C. elegans* and other biological networks where a subsystem of interest is embedded in a complex larger system. In this talk, I will introduce a dynamical systems model of the *C. elegans* neural network that is amenable to analysis and treats subnetworks relevant to behavior as perturbed holistic components. Our model elucidates how nonlinear intrinsic dynamics in conjunction with connectivity structure may produce stochastic switching activity underlying foraging behavior and highlights different roles for gap junctions and synaptic connections.

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CP13

Analysis and Simulations of a Free Boundary Problem Modelling Phototrophic Granular Systems

In recent years, phototrophic granular systems have become increasingly popular in the field of wastewater treatment. In such a system, free-living cells agglomerate around spherical wireless light emitters, leading to the formation of light-dependent granules. The attached species proliferate by consuming dissolved substrates diffusively transported from the bulk liquid within the granules and by using light as a source of energy. In this context, a model is proposed to simulate a case of biological and engineering interest. The granule is modelled as a free boundary domain with radial symmetry. The free boundary evolution is described by an ODE, accounting for microbial growth, as well as attachment and detachment fluxes. The dynamics of the microbial cells, both in sessile and suspended form, and substrates are governed by systems of PDEs. Additionally, a light-dependent function is introduced to account for the influence of light on the attachment of specific photo-dependent species in the presented application. The work focuses on the quantitative and qualitative analysis of the model. Numerical simulations describing the initial formation of a light-dependent granular biofilm on a wireless light emitter are presented. By using the method of characteristics, the equations are converted into an equivalent integral system. Existence and uniqueness of solutions are discussed and proved for the attachment regime using fixed point strategies.

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CP13

Mathematical Topology and Geometry-Based Classification of Tauopathies

Neurodegenerative diseases, like Alzheimer's, are associated with the presence of neurofibrillary lesions formed by tau protein filaments. While it is known that different morphologies of tau filaments characterize different neurodegenerative diseases, there are few metrics of global and local structure complexity that enable to quantify their structural diversity rigorously. By using cryo-electron microscopy structures of tau filaments that are available in the Protein Data Bank, we employ for the first time mathematical topology and geometry to classify neurodegenerative diseases and also to identify specific sites of interest such as the PHF6 motifs and the 301 mutation site, and other aspects of their filament structure relevant to experiments. Our results reveal a hierarchy of classification from global to local topology and geometry characteristics. In particular, we find that tauopathies can be classified with respect to the handedness of their global conformations and the handedness of the relative orientations of their repeats. Progressive supranuclear palsy is identified as an outlier with an observable knotoid structure. This topological characteristic can be attributed to a pattern of the beginning of the R3 domain that is present in all tauopathies but at different extent. Our results also reveal that topology and filament structures alone also predict sites with twice as high probability of mutation that leads to aggregation as reported in the literature.

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CP13

Algorithmic Foundations for Colocalization in Single-Molecule Localization Microscopy

The orchestration of intricate cellular activities is facilitated by the interaction between biological macromolecules. Single-molecule localization microscopy (SMLM) offers a powerful approach for the direct visu-

alization of molecular positions, achieved through fluorescently labeling two presumed interaction partners and subsequent localization at the nanoscale. Colocalization, as implied by its name, investigates the spatial proximity between these two kinds of molecules. Nevertheless, traditional approaches to colocalization analysis predominantly rely on heuristic insights such as correction relation. Here we formulate it as algorithmic questions that are mathematically tractable, propose a new probabilistic algorithm to infer the amount of coupling from noisy measurements of molecular positions. The approach is robust across a wide range of molecular densities and localization precisions. We have demonstrated the use of the framework via both simulations and experiments of equilibrium and dynamical biochemical reactions. We further formulate this as a learning problem and explore the statistical and algorithmic limitations.

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MS1

Modeling cell packing and flexural rigidity of pattern in the embryonic notochord

The notochord is the defining feature of chordates, and during development it lengthens the embryo, provides structural support, and in many organisms acts as a template for spine development. It consists of inner, vacuolated cells (chordocytes) surrounded by epithelial sheath cells (chordoblasts). To investigate the effect of differing ratios of cortical tension between these two cell types on overall morphometry and biomechanics of the embryonic notochord as a whole, we model the notochord using foam physics and elastic membrane physics, respectively. Under these two modeling frameworks, we propose a relationship between cortical tension and packing pattern, and further quantify the resultant flexural rigidity, which depends on pattern and orientation, for finite notochords of varying length.

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MS1

Mechanical Perturbations and Branching Morphogenesis: Findings from Mathematical Modeling and Laboratory Experiments

Branching morphogenesis governs the formation of tree-like organs such as the mammary glands and lungs. Defects in branching morphogenesis may lead to poor organ function. Understanding the mechanisms that generate branched organs could potentially advance knowledge for regenerating organ function and/or creating artificial organs as a means to combat diseases. Mechanical signaling is believed to regulate branching morphogenesis but how this occurs is not well understood. In particular, how mechanical forces affect branch distributions/organization is not well understood. A holistic approach is essential to understand the intricate interactions that coordinate the formation of branched organs. In this talk, I will describe how we are using combinations of laboratory experiments, digital image analysis, agent-based models and multifractal models to shed light on the effect of mechanical forces on branching morphogenesis.

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MS1

Differential Growth in Stomach Bending

The mechanisms by which the vertebrate stomach undergoes its evolutionarily conserved leftward bending remain incompletely understood. Although the left and right sides of the organ are known to possess different gene expression patterns and undergo distinct morphogenetic events, the physical mechanisms by which these differences generate morphological asymmetry remain unclear. We have developed a suite of continuum models for asymmetric stomach morphogenesis. Using a morphoelastic framework, we investigate the morphogenetic implications of a variety of hypothetical, tissue-level growth differences between the left and right sides of a simplified tubular organ. Simulations reveal that, of the various differential growth mechanisms tested, only one category is consistent with the leftward stomach curvature observed in wild-type embryos: equal left and right volumetric growth rates, coupled with transversely isotropic tissue thinning on the left side. Simulating this mechanism in a defined region of the model over a longer period of growth leads to mature stomach-like curvatures.

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MS1

Toward a Shear-Dependent Platelet Aggregation Model

Blood clotting is an intricate biological response that is triggered following vascular injury to prevent excessive bleeding at the site of an injured blood vessel. The hemostatic system is composed of three fundamental components: platelet aggregation, coagulation, and fibrinolysis. Platelet aggregation involves a primarily physical process wherein platelets adhere to the injured vessel wall, become chemically activated, recruit additional platelets, and form a platelet plug. In recent years, increased attention has been given to the pivotal role of von Willebrand Factor (vWF), a multimeric glycoprotein in the bloodstream, in mediating platelet aggregation. Understanding the intricate mechanisms of vWF-platelet interactions is essential for comprehending the complex dynamics of clot formation and identifying potential targets for therapeutic interventions in bleeding disorders such as von Willebrand disease. This work presents a novel shear-dependent platelet aggregation model that incorporates shear-dependent activation, adhesion, and cohesion mechanisms mediated by vWF. The model is validated with data produced from in vitro microfluidic experiments where agonists such as ADP and Thromboxane A2 were systematically inhibited to determine the parameters associated with vWF-mediated ad-

hesion and cohesion.

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MS2

Sex Differences in Glutathione Metabolism and Acetaminophen Toxicity

Clinical and experimental evidence has shown that females in humans and other mammals have higher glutathione (GSH) levels than males, which are caused by higher levels of estradiol. Understanding how hepatic GSH level and synthesis velocity depend on the sex hormones is important since oxidative stress contributes to risk for heart disease and cancer, and oxidative stress is reduced by GSH. We use mathematical models for hepatic glutathione metabolism including one-carbon metabolism and acetaminophen detoxification to investigate how the activation of certain enzymes by estradiol creates dramatic changes in reaction velocities and metabolite concentrations. The models explain why women of child-bearing age have higher glutathione than men. During the menstrual cycle the GSH concentration changes daily but over surprisingly narrow range. We explain how this dynamic homeostasis depends on the biochemical network that produces GSH. The model also explains why female mice are less susceptible than males to hepatotoxicity due to acetaminophen overdose and suggests that this might also be true for humans.

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MS2

Parameter Identifiability of a Respiratory Mechanics Model in a Preterm Infant

The complexity of mathematical models describing respiratory mechanics has grown in recent years, however, parameter identifiability of such models has only been studied in the last decade in the context of observable data. This study investigates parameter identification of a nonlinear respiratory mechanics model tuned to the physiology of 1 kg preterm infant, using global screening and local deterministic sensitivity analyses together with gradient-based optimization and model reduction. The model predicts airflow and dynamic pulmonary volumes and pressures under several clinically relevant levels of continuous positive airway pressure (CPAP) and a range of parameters characterizing key pulmonary mechanical attributes. Results indicate that the sensitivity of model parameters varies with level of CPAP, suggesting that diagnosis and treatment of respiratory mechanics issues must account for the effects of mechanical ventilation imposed upon patient.

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MS2

Modeling at the Intersection of Ovulation and Metabolism

Endocrine physiology is a complex system of crosstalk between hormones in various tissues. Reproductive hormone dysregulation may disrupt ovulation and may be exacerbated by metabolic abnormalities. Racial and ethnic disparities are also prevalent at the intersection of metabolic and ovarian dysfunction. Here we discuss a mathematical model of the human ovulatory cycle and consider mechanisms of disruption to characterize ovulatory phenotypes. We also consider how model-based phenotypes interact with glucose metabolism and health disparities.

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MS2

Virtual Clinical Trial Simulations Using a Quantitative Systems Pharmacology (qsp) Model of Cdk Inhibitors in Breast Cancer Patients

Breast cancer (BC) is the most commonly diagnosed cancer worldwide and a major area of emphasis for the development of novel treatments. Cyclin Dependent Kinase 4/6 (CDK4/6) inhibitors, in combination with Endocrine Therapy (ET), are a standard of care for ER+/HER2- metastatic BC. In this work, we present a Quantitative Systems Pharmacology (QSP) platform model to support the development of next-generation CDK inhibitors. QSP models can be leveraged to quantitatively explore mechanistic hypotheses around drug mechanism of action and enable systematic extrapolation of optimal dose and regimen for novel therapies. These models also provide an in-silico hypothesis testing framework that integrates preclinical and clinical data sources. Virtual population (Vpop) methods are computational approaches that fit QSP models to clinical datasets through selection of virtual patients for a virtual trial. We have leveraged internal preclinical data along with historical and emerging clinical data to develop virtual clinical trial simulations that can project the efficacy of next-generation CDK inhibitors in clinically relevant patient populations. We will specifically highlight an example Vpop developed using historical data from a Phase 3 clinical trial and demonstrate how the QSP model connects a mechanistic model of CDK protein signaling to clinical efficacy endpoints such as progression-free survival (PFS) and objective response rate (ORR).

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MS3

Understanding Communication Between Biological Cells Triggered by a Diffusing Extracellular Signal

We developed and analyzed a cell-bulk coupled reaction-diffusion system, motivated by quorum-sensing and diffusion-mediated behavior in microbial systems, that characterizes communication between localized spatially segregated biological cells. Each cell secretes a signaling chemical into the extracellular environment (bulk region) at a constant rate and receives feedback of the bulk chemical from the entire collection of cells. This global feedback, which activates signaling pathways within the cells, modifies their intracellular dynamics according to the external environment. We analyzed the model in the limit of O(1) and large bulk diffusivity using the method of matched asymptotic expansions and Sel'kov reaction kinetics. The

effect of cell membrane permeability, intracellular reaction kinetics, bulk diffusivity, and the spatial configuration of cells on both the emergence and synchronization of oscillatory intracellular dynamics, as mediated by the bulk diffusion field, was investigated.

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MS3

Cover Times of Many Stochastic Searchers

Many cellular systems can be modeled by searchers moving through a domain. For example, the immune system hunts pathogens, and the airinemes in zebrafish pattern formation detect mislocated cells. The timescale of detection can be understood by using the cover times that measure the exhaustive search for an entire spatial domain. Most of the prior work has generally studied cover times of a single searcher, or a "small number" of multiple searchers. In this talk, we discuss the cover times of many random walkers on both continuum domains and networks in a general framework. We derive the asymptotic form for the cover times as the number of searchers increases and explain which spatial domain features matter for the leading order behavior of the spread time. This is a joint work with Sean Lawley at the University of Utah.

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MS3

Heterogeneity and Bursting in Spatial Patterns of Stochastic Gene Expression

Advances in microscopy can now provide snapshot images of individual RNA molecules within a nucleus. Decoding the underlying spatiotemporal dynamics is important for understanding gene expression, but challenging due to the static, heterogeneous, and stochastic nature of the data. I will write down a stochastic reaction-diffusion model and show that observations of this process follow a spatial point (Cox) process constrained by a reaction-diffusion PDE. Inference on this data resembles a classical inverse problem but differs in the observations of individual particles rather than concentrations. We perform inference using variational Bayesian Monte Carlo with promising results. However, many open computational and modeling challenges remain in the development of scalable and extendable techniques for this inverse problem. This work is in collaboration with the Fangyuan Ding lab of Biomedical Engineering at UCI and Scott McKinley at Tulane.

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MS3

Precision Limits to Cellular Sensing of Fluid Flow

Reliable sensing is crucial for cell survival, and many cellular sensors have evolved to be as precise as physically possible. Understanding these precision limits can therefore give important insights into the mechanisms and capabilities of cell sensing. Cancer cells have been shown to use self-guided chemotaxis to migrate downstream in fluid flow. At the same time, they use pressure sensing to migrate upstream, and the two mechanisms compete. We use stochastic analysis to address the question of whether the competition is decided by sensory limits or by internal decision-making. This approach reveals the stochastic processes that constrain cell behavior.

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MS4

Negotiating the Tug-of-War in the Migration of Cell Doublets

Collective cell migration plays a crucial role in fundamental physiological processes including embryonic development, wound healing, and regeneration upon injury. Here, we focus on how coordination of the front-to-rear polarity axes are established in a cell doublet, the simplest example of a cell collective. In a theoretical setting, we demonstrate that mechanical forces at the cell-cell junction are a necessary and sufficient condition to establish biochemical synchronization. We further show the implications of this finding in establishing a chirality bias in the spotaneous otation of two epithelial cells placed on an adherent substrate.

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MS4

Modeling the Influence of ECM on Immune Cell Migration by Bridging Artificial Life and Spatial Imaging

Direct observation of immune cell trafficking patterns in clinical tumors is challenging, but computational simulations based on clinical data provide valuable insights. Collagen, a fundamental component of the ECM within the tumor microenvironment, plays a crucial role in regulating T cell-mediated killing of cancer cells by influencing migration. In vitro studies suggest that T cells preferentially migrate along collagen fibers. We evaluated collagen density and alignment using Second Harmonic Generation (SHG) imaging of head and neck squamous cell carcinomas. Measures of collagen density and alignment were incorporated into our artificial life framework to model the gradient field under the influence of artificial immune cells. We examined two hypothesized modes of immune-collagen interaction: perpendicular or parallel immune migration with respect to collagen fibers. By simulating immune cells distributed evenly on the domain edge, our model predicts that the parallel mode exhibits a stronger anti-correlation between immune coverage and disease stage, where late-stage disease corresponds to lower immune coverage. We expanded the model to include tumor-immune-collagen interactions and observed how collagen in late-stage tumors facilitates immune escape. The integration of computational modeling with experimental data enhances our understanding of how microenvironmental factors shape immune responses

in cancer progression.

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MS4

The Role of Local Cortical Stress Generation and Cortex-Membrane Interaction in Cell Swimming

The actin cytoskeleton, the primary force generating machinery in the cell, is organized into a variety of structures, including the cell cortex. The cell cortex is a thin layer of crosslinked actin that underlies and is connected to the plasma membrane of the cell. The material properties of the actin cortex and its ability to locally exert tension on the cell membrane are mediated through localized activity of a variety of accessory proteins such as Arp2/3, myosin, and cofilin. In addition, the mechanical properties of the ERM proteins that connect the cortex to the plasma membrane are not well understood. What has been observed is that the cortex can generate membrane tension gradients that have been shown to result in unconfined cell swimming in a fluid (Wang and Othmer, 2015; Wu et al, 2018). To better understand how the local rheological properties of the cortex and the nature of the membrane-cortex adhesions affect membrane tension and movement through a fluid, we present a two-dimensional model of a swimming cell whose membrane and cortex are each modeled as discrete, piecewise linear structures and the cell interior and exterior are both treated as Newtonian fluids. By globally and locally modifying the rheological properties of the cortex and cortex-membrane adhesions, we analyze how membrane tension and curvature, cortical flow, and cellular swimming velocities are affected.

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MS4

Computational Modeling of Adhesion-Independent Confined Cell Migration

Cell migration is critical for many vital processes, such as embryogenesis and tissue repair, as well as harmful processes, such as cancer cell metastasis. Recent experiments highlight the diversity in migration strategies employed by cells in physiologically relevant environments. In 3D fibrous matrices and confinement between two surfaces, some cells migrate using round membrane protrusions, called blebs. In bleb-based migration, the role of substrate adhesion is thought to be minimal, and it remains unclear if a cell can migrate without any adhesion complexes. We present a 2D computational fluid-structure model of a cell using cycles of bleb expansion and retraction in a channel with several geometries. The cell model consists of a plasma membrane, an underlying actin cortex, and viscous cytoplasm. Cellular structures are immersed in viscous fluid which permeates them, and the fluid equations are solved using the method of regularized Stokeslets. We find that cells are able to migrate in rigid channels if actin turnover is included with a viscoelastic description for the cortex. The model is then used to simulate investigate conditions for migration in different channel geometries.

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MS5

The Stochastic Dynamics of the Morris-Lecar Elliptic Burster

The Morris-Lecar burster, a model of e.g. a thalamic relay neuron, consists of three o.d.e's: for voltage, for a "recovery" variable, and for a very slowly alternating current, which moves the dynamics defined by the first two equations through a repeating cycle of firing and quiescence. The model was proposed and developed by Rinzel and others in a series of papers beginning in the 1980's. It has been further developed through the 2000's by Izhikevich and others. It is known that in the deterministic model, as the slow current moves, the onset of firing or "stability loss" is delayed beyond the bifurcation point of the model, whereas the inclusion of stochasticity causes the delay to be reduced or eliminated. Using a simple picture of how the null-clines move with the slow current, we explore this delay and how the burster reacts to a broad range of noise intensities. This is joint work with Peter Rowat of UCSD.

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MS5

Exopolymeric Substances and Algal Bloom Dynamics in Sea Ice

The ecosystem of the Arctic Ocean relies heavily on sea ice, which serves as a habitat for microbes living within its brine inclusions. Algae living with the ice form the foundation of the polar marine food web, are imperative to the organisms that live below, above, and inside sea ice, and play a vital role in nutrient cycling inside the polar marine ecosystem. To protect them from the extreme, potentially harmful environment inside sea ice, these algae secrete gelatinous exopolymeric substances(EPS). This process creates a biophysical feedback loop where the EPS secreted by algae accumulates, altering the brine inclusions, and increasing the systems tortuosity. This alteration changes the physical properties of sea ice, possibly impeding fluid flow through the brine microstructure and thus potentially reducing the rate of nutrient replenishment in the system ultimately impacting the habitability of sea ice for the algae. The algae are inadvertently affected by

the consequences of their thriving presence. We develop a dynamical systems model to characterize the dynamic relationship between EPS, algae, and nutrients within sea ice. With this model, we address the following questions: How does EPS affect algal bloom dynamics? Does EPS accumulation ever reach levels that inhibit algal growth, i.e., are algae ever victims of their own success? We will first discuss the bifurcation structure of the dynamical system, followed by an examination of transient algal bloom dynamics.

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MS5

Covid-19 Variants Wave Dynamics

Our study aims to predict the amplitude of forthcoming COVID-19 variant waves using statistical modelling and a unique global dataset from throughout the pandemic. Utilizing publicly available datasets, we compiled relevant features such as demographics, geographic distribution, mobility patterns, epidemiological data, immunity levels, and viral genomic characteristics, which influence the spread and severity of COVID-19 waves. To train our model, we used the amplitude of consecutive COVID-19 waves, specifically Delta, BA.1, and BA.2 waves. For feature selection, we employed elastic net regression, given the models effectiveness in handling diverse and multi-scale data types, emphasizing predictive accuracy. We implemented a leave-one-out cross-validation strategy that respects the time series nature of the data from each country. We then applied a random forest model using the same cross-validation strategy. Our preliminary findings indicate a slight overestimation of subsequent peaks in countries with a smaller BA.1 compared to Delta and a smaller BA.2 compared to BA.1, while a slight underestimation of the subsequent peaks in countries with larger ones. Addressing this underestimation is our current focal point, as it could potentially diminish the predictive utility of our model in critical situations. These observations guide ongoing refinements to our approach as we continue to investigate the complex dynamics involved in predicting COVID-19 variant waves.

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MS5

An Inter-Spike-Interval Study of the Stochastic Elliptic ML Burster

The bivariate Morris Lecar (ML) neuron firing model, parameterized by input I, has a bistable range with a stable limit cycle (firing), and a stable fixed point (quiescence). In our paper Rowat, Greenwood 2011, we studied the stochastic dynamics of a related stochastic ML neuron. A stochastic ML burster is obtained by adding to the bivariate dynamics a third, slow, process which moves the parameter, I, cyclically, back and forth across the phase plane. After a review, we present histograms of the inter-spike and inter-burst interval distributions from long simulations of the stochastic ML burster at various noise levels. The histograms show interesting patterns of fluctuation, which we are able to interpret in terms of noise-dependent addition/deletion of fast cycles ("spikes") from a burst, and noise-dependent extensions/reductions of the quiescent intervals.

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MS6

Measuring Pandemic Inequality in Heterogeneous Populations

Four years into the COVID-19 pandemic, the question of how mandated interventions impact heterogeneous populations remains open due to the lack of suitable measures of pandemic inequality and nonlinear effects. We addressed this question by introducing pandemic Lorenz curves to measure the unequal distribution of pandemic severity across local areas, using a large-scale agent-based model (ABM). The ABM matched census-based demographics of Australia and considered complex COVID-19 pandemic scenarios, simulating two most recent Australian census years (2016 and 2021), three variants of concern (ancestral, Delta and Omicron), and five representative intervention policies. Our results quantified nonlinear effects of population heterogeneity on the pandemic severity, highlighting that the pandemic impacts are distributed unequally across local areas. We also examined and delineated the effects of urbanisation on pandemic severity, distinguishing between urban and regional waves. Our findings suggest that public health response to long-lasting pandemics must be regularly reviewed and adjusted to demographic changes.

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MS6

Modeling the Coevolution of Epidemics and Infodemics

Vaccine hesitancy, resulting from misinformation and distrust, threatens the possibility of ending the COVID-19 pandemic through mass vaccination. The COVID-19 pandemic coincides with an overabundance of controversial information regarding disease transmission and public health mitigation approaches. The rapid spread of information, or *infodemic*, significantly changes the population's behavior that promotes or reduces the spread of infection. We investigate an infodemic model with an evolutionary game theoretical framework to help understand how the spread of information and vaccination impact disease transmission. We show the interplay between the epidemic, and infodemic leads to stable infection states or periodic cycles of epidemic outbreaks. Even when the perceived risk of vaccination is low, and the vaccine efficacy is as high as 90%, the epidemic can persist with widespread misinformation. Our results suggest that countering misinformation is necessary to control the pandemic.

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MS6

An Overview for Computing $\mathcal{R}_0$ in Metapopulation Models

Mathematical models are an essential tool for understanding how an infectious diseaseprogresses in a population. We formulate epidemiologicalmodels with the intent to extract key features such as the number of infections, the time to peak, the final size of the epidemic, and the basic reproduction number. All of these measures provide useful information about the characteristics of an infectious disease and can help mitigate the next outbreak. The challenging aspect comes when we cannot compute these measures explicitly due to the complexity of the model. In this talk, we will discuss how to approximate $\mathcal{R}_0$ for metapopulationmodels. We will proceed through several examples to observe how the methodology is applied to disparate model structures.

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MS6

A State-of-the-art Epidemic Simulator and Web App for Viral Transmission in Indoor Spaces

During COVID-19, policymakers and managers of indoor spaces were tasked to take fast decisions to mitigate its transmission, often without any scientific input available. New computational tools are urgently required to prevent or quickly mitigate future epidemics. We have developed a novel agent-based simulator - a modelling framework that integrates the schedule and movements of individuals in an indoor space, information about the air flow and ventilation as well as detailed architectural design. We accurately capture the architectural design through the topologicpy software developed by W. Jabi. The simulator accurately predicts the virus concentration and the spatiotemporal infection risk each individual agent experiences while moving in the space and can compare mitigations. We have validated the model using data from real case studies. This work is in collaboration with policymakers who have directed our focus to three priority settings: care homes, educational settings and supermarkets. We have also developed a user-friendly web app that allows quick exploration of several scenarios of interest and visualises the simulations, so that policymakers, architects, and space managers can easily assess an indoor space and formulate recommendations for mitigating the infection risk from a viral disease. The app will be also made available to the public. (The work is funded by a UKRI Impact Acceleration Account grant.) Key references: Lau et al, 2022; Moore et al, 2021

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MS8

Exploring Multiple Patterns in Biological Systems with Neural Networks

The investigation of nonlinear Partial Differential Equation (PDE) systems from modeling complex dynamical systems in biology has intrigued researchers, particularly in discovering solution structures like pattern formation. This talk will cover computational methods for computing multiple solutions of nonlinear PDEs based on neural networks. We will explore the efficacy of neural networks by coupling them with homotopy continuation, a powerful approach for computing multiple steady states of nonlinear differential equations. Through several benchmark problems, we will demonstrate the effectiveness of neural networks in learning and predicting various patterns in biological systems.

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MS8

Reconstructing Transition Dynamics from Static Single-Cell Genomic Data

Recently, single-cell transcriptomics has provided a powerful approach to investigate cellular properties in unprecedented resolution. However, given a small number of temporal snapshots of single-cell transcriptomics, how to connect them to obtain their collective dynamical information remains an unexplored area. One major challenge to connecting temporal snapshots is that cells measured at one temporal point may divide at the next temporal point, leading to growth and differentiation in the system. Its increasingly clear that without incorporating cellular growth dynamics, the inferred dynamics often becomes incomplete and less accurate. To fill these gaps, we present a novel method to reconstruct the growth and dynamic trajectory simultaneously as well as the underlying gene regulatory networks. A deep learning-based dynamic unbalanced optimal transport is developed to infer interpretable dynamics from high-dimensional datasets.

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MS8

Physics-Informed Energetic Variational Models for Tumor Growth

In this talk, we introduce an energetic variational approach for modeling tumor growth. Tumor tissue, like many biological systems, behaves like active complex fluids, where different mechanical and chemical mechanisms interact and compete across various spatial and temporal scales. Developing a thermodynamically consistent mathematical model for such systems is often challenging. The idea of the energetic variational approach is to model these chemomechanical couplings by considering their free energy and the rate of energy dissipation. An advantage of this approach is that physical constraints, such as conservation laws, frame indifference, and thermodynamic consistency, are satisfied automatically. Moreover, the resulting model often has a smaller number of parameters and is easier to calibrate using experimental data.

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MS8

Phase Field Model of Dictyostelium Discoideum Chemotaxis

A phase field approach is proposed to model the chemotaxis of Dictyostelium discoideum. In this framework, motion is controlled by active forces as determined by the Meinhardt model of chemical dynamics which is used to simulate directional sensing during chemotaxis. Then, the movement of the cell is achieved by the phase field dynamics, while the reaction-diffusion equations of the Meinhardt model are solved on an evolving cell boundary. This task requires the extension of the usual phase-field formulation to allow for components that are restricted to the membrane. The coupled system is numerically solved by an efficient spectral method under periodic boundary conditions. Numerical experiments show that our model system can successfully mimic the typically observed pseudopodia patterns during chemotaxis.

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MS9

Mathematical Modeling of Osteoporosis Due to Surgical Menopause

Osteoporosis, characterized by decreased bone mass and structural deterioration, results from an imbalance in the bone tissue's metabolic processes. In the adult skeleton, bone is remodeled regularly due to dynamic interactions between several bone cell types: osteoclasts, osteoblasts, osteocytes, and their precursors. It is known that estrogens affect bone remodeling in both biological sexes. Specifically, postmenopausal bone loss results from estrogen deficiency in older women. Estrogen deficiency has a sudden onset when the ovaries are surgically removed, and osteoporosis risk is higher in these patients than for those experiencing natural menopause. We have developed a mathematical model for the bone cell dynamical responses to estrogen deficiency during the surgical menopausal transition using information about the key impacts observed in female mice and humans after ovary removal. We build upon an existing model for osteoporosis due to aging. Our new model considers the role of embedded osteocyte cells in regulating enhanced osteoclast formation, inducing enhanced bone resorption after surgical menopause. With two new adjustable parameters, the model fits clinical bone mineral density decreases. Other parts of the model results will be compared to various in vivo clinical and animal studies. The impacts of hormone replacement therapy on surgical menopause in silico scenarios will also be simulated and discussed.

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MS9

Mathematical Modeling of Tissue Specific Insulin Resistance in Adolescent Girls with Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) affects approximately 12% of reproductive-aged women and is associated with impaired metabolic health. Characterizing tissue-specific insulin resistance (IR) in adolescent girls with PCOS is vital to understanding disease progression and guiding early interventions. The gold standard for quantifying tissue specific IR, the multistage hyperinsulinemic euglycemic clamp, is labor intensive and does not represent physiological glucose-insulin dynamics. The oral glucose tolerance test (OGTT) is more physiologic and easier to administer, but mathematical modeling, such as the Production and Disposal Oral Minimal Model for Glucose (OMMPD),

is necessary to optimally interpret tissue-specific IR from OGTT data. OMMPD provides a differential-equations based methodology for estimating hepatic and adipose insulin sensitivity (SI*) from OGTT data involving two stable isotope tracers. We discuss methods for overcoming nonsteady state errors to enable reliable quantification of SI* using a dual tracer protocol in an IR cohort of obese adolescent girls with PCOS. Improved methodology for estimating SI* using OMMPD will contribute to the characterization of the metabolic phenotype of PCOS and facilitate the identification of effective therapeutic interventions.

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MS9

Discussion: Future Directions and Challenges Facing Researchers in Mathematical Approaches to Womens and Childrens Health

The session will conclude with a discussion that looks to the future of the field. Emerging motivation for new work in mathematical approaches to womens and childrens health will be discussed, including healthcare challenges and an explosion of available data. We will discuss the advantages of current approaches, including their ability to develop large-scale predictions, patient-specific recommendations, and clinical software. The limitations of available methods, such as a lack of current understanding of biology or physiology, data storage challenges, and privacy concerns, will be discussed, with an opportunity to generate solution ideas. This look at the future of the field will be viewed through both theoretical and applied lenses. The session organizers will moderate the discussion.

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MS9

Studying the Effects of Oral Contraceptives on Coagulation Using Mathematical Models

The use of oral contraceptives (OCs) is known to increase the risk of thrombosis, but the mechanisms underlying this risk and the determinants of the tests that assess this risk are not fully understood. In this study, we used a mathematical model to study the effects of an OC containing levonorgestrel (lev) on blood clotting. Lev is reported to change the plasma levels of blood clotting factors. The mathematical model used in this study simulates coagulation reactions in a small injury under flow, takes clotting factors as inputs and outputs time courses of the coagulation enzyme thrombin. To study the effects of lev, we created a virtual patient population with factor levels before and after lev use based on published patient data and conducted simulations to predict thrombin response for each individual virtual patient. After analyzing the simulated thrombin, we found that changes in factor levels due to lev increased the amount and speed of thrombin generation for all virtual patients. This suggests that factor level changes alone can heighten the prothrombotic state of the model system. We extended the model to include generation of the inhibitor activated protein C (APC) and test the effects of lev on the systems sensitivity to APC. In line with literature reports, the use of lev increased the APC sensitivity resistance, which correlates with increased thrombosis risk.

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MS10

The Impact of Endoplasmic Reticulum Morphol-

ogy on Ire1 Protein Clustering and Signaling

The endoplasmic reticulum (ER) is an organelle composed of a connected network of sheets and tubes. The ER is a key site of protein synthesis and folding and harbours many unfolded proteins, which in excess disrupt cell activities. Unfolded proteins in the ER activate the signaling protein IRE1, which then forms dimers, oligomers, and clusters with activity that initiates the unfolded protein response (UPR) to return the ER to a healthy level of unfolded proteins. Experiments show IRE1 clusters with complex shapes, including wrapping around ER tubes, and dynamics consistent with coarsening behaviour. We quantitatively modeled IRE1 protein cluster dynamics on a tubular surface as a lattice gas, simulated with a kinetic Monte Carlo algorithm. We show that ER tube diameter controls whether clusters transition from roughly round to a conformation that wraps around the tube and grow without unfavourable interface length increases, with narrow tubes promoting wrapping. We find that wrapped clusters on narrow tubes grow more rapidly, evaporate more slowly, and are stable at lower protein concentrations compared to equal-sized round clusters on wider tubes. This suggests that cluster wrapping, facilitated by narrower tubes, may be an important factor in the growth and stability of IRE1 clusters, impacting UPR persistence. This work may tie into cell and human health, as UPR signaling persistence and dysfunction is associated with pathologies such as cancer and neurodegeneration.

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MS10

Mathematical Models of Plasticity and Drug Resistance in Cancer

Non-genetic mechanisms of drug resistance are increasingly recognized as a major cause of treatment failure in cancer. These mechanisms often result in phenotypic plasticity in which the drug-response characteristics of individual cells may evolve stochastically or in response to environmental signalling. In this talk I will discuss some mathematical models of phenotypic plasticity in drug-response, and explore how these phenomena may impact treatment optimization.

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MS10

Can We Get Rid of Menopause? Stochastic Modeling of Ovarian Aging and Procedures for Menopause Delay

Ovarian tissue cryopreservation is a proven tool to preserve ovarian follicles prior to gonadotoxic treatments. What if this procedure is applied to healthy women to delay or eliminate menopause? In this talk, we will present a mathematical model to predict the efficacy of this procedure and optimize its implementation. The theory relies on a recent stochastic growth activation model for how dormant primordial follicles in the ovarian reserve decide to grow.

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MS10

Modulation of Antigen Discrimination by Duration of Immune Contacts in a Model of T Cell Activation with Extreme Statistics

T Cells must reliably recognize the presence of pathogens through noisy surface interrogation of antigen presenting cells. In this talk I will present a perspective on this important problem via extreme statistics. The central premise is that while a single stochastic interaction may exhibit large variability (unreliable), the extrema of multiple independent interactions has a remarkably tight distribution (reliable). In a mathematical model of immune recognition based on kinetic proofreading, we show that extreme statistics provide an amplification effect that can bypass traditional tradeoffs between sensitivity and selectivity. In addition, we show that extreme statistics amplify the role that the duration of immunological contacts plays in positive signaling outcomes.

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MS11

Cell Entrainment in a Mechano-Chemical Model of Collective Cell Migration

Small GTPases, such as Rac and Rho, are well known central regulators of cell morphology and motility, whose dynamics also play a role in coordinating collective cell migration. Experiments have shown GTPase dynamics to be affected by both chemical and mechanical cues, but also to be spatially and temporally heterogeneous. While progress on understanding GTPase dynamics in single cells has been made, a major remaining challenge is to understand the role of GTPase heterogeneity in collective cell migration. Motivated by recent one-dimensional experiments (e.g. micro-channels) we introduce a one-dimensional modelling framework allowing us to integrate cell bio-mechanics, changes in cell size, and detailed intracellular signalling circuits (reaction-diffusion equations). Using this framework, we build cell migration models of both loose (mesenchymal) and cohering (epithelial) tissues. We use numerical simulations, and analysis tools, such as bifurcation and local perturbation analysis, to provide insights into the regulatory mechanisms coordinating collective cell migration. We show how feedback from mechanical tension to GTPase activation lead to a variety of dynamics, including collective and individual cell migration phenotypes.

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MS11

Hybrid Modeling of Cell Migration in Viral Tissue Infection and Tumor Immune Microenvironments

Cell migration is a critical feature of health and disease conditions. During infection and disease, immune cells migrate to affected sites to clear the diseased cells and repair the tissue microenvironment. However, the aberrant influx of immune cells and persistent microenvironment remod-

eling can lead to inflammation and the spread of diseased cells to other body parts. Here, we developed two agent-based models of cell migration during viral infection and cancer migration to understand the effects of migration on disease progression and severity. In the viral tissue infection model, we considered intracellular viral replication, infection of epithelial cells, and host immune response in lung tissue. We identified M2 macrophage migration at damaged sites due to extracellular cues as the primary contributor to higher collagen area fraction in the tissue, which leads to aberrant tissue repair and fibrosis. In a separate model, we considered the interactions between cancer cells and surrounding tissue microenvironments. The model simulated the migration of cancer cells due to the degradation and crosslinking of collagen fibers in the tissue. We observed a reduced invasion rate with randomly distributed collagen fibers and enhanced migration efficacy with increasing fiber density. The computational models give us a better understanding of how cell migration and interaction between cell and extracellular matrix lead to tissue microenvironment remodeling and disease severity.

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MS11

Dynamics of Fibril Collagen Remodeling by Migrating Tumor Cells

Progression of benign breast cancer to an invasive tumor involves changes not only in the tumor cells, but also in the surrounding stroma, including modification in the extracellular matrix (ECM) fibril patterns. We used a combination of mathematical modeling (silicoDCIS model) and image analysis techniques to identify the rules of tumor cell-stroma interactions that guide the emergence of three tumor associated collagen signatures (TACS) previously observed in laboratory experiments. The TACSs are correlated with tumor behavior, such as benign growth or invasive migration, however, it is not fully understood how one specific fibril pattern can be dynamically remodeled to form another alignment. Here, we propose the rules of cellECM physical interplay and feedback that guided the emergence and transition among various TACSs. This integrated approach provides an in silico tool for testing biomechanical hypotheses of tumor cell-tumor matrix interactions that leads to tumor cell migration and formation of microinvasions.

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MS11

A Contact Mechanics Model to Predict the Effect of Vascular Geometry, Cell and Matrix Mechanics on Vessel Leakiness

The microvasculature, far from being just a conduit for blood flow, is a dynamic organ that controls the transfer of nutrients and immune cells. This involves a two-way interaction between immune and blood vessel cells, influencing immune cell movement into tissues. This process is disrupted in conditions like atherosclerosis and cancer, where cancer cells mimic immune cells in vascular navigation. The vasculature's behavior is also shaped by physical factors like extracellular matrix properties, vascular cell forces, and vascular network geometry. We introduce a mathematical model that integrates physical, molecular, and cellular factors to explain vascular dynamics, gap formation between cells, and the movement of immune or cancer cells. Based on continuum mechanics, this model incorporates a new traction-separation law to describe the complex interactions at cell-cell and cell-matrix adhesions. Using this model, we analyze how forces differ in 3D microvasculature versus 2D monolayers, affecting gap creation, leakiness, and cell migration. We examine how physical aspects like matrix stiffness and vessel size impact these processes. Importantly, we explore how these factors influence cancer cell migration and metastasis potential.

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MS12

Life History Speed, Population Disappearances, and Noise-Induced Ratchet Effects.

Nature is replete with variation in the body sizes, reproductive output, and generation times of species that produce life history responses known to vary from small and fast to large and slow. Although researchers recognize that life history speed likely dictates fundamental processes in consumer-resource interactions like productivity and stability, theoretical work remains incomplete in this critical area. Here, we examine the role of life history speed on consumer-resource interactions by using a well used mathematical approach that manipulates the speed of the consumers growth rate in a consumer-resource interaction. Importantly, this approach holds the isocline geometry intact allowing us to assess the impacts of altered life history speed on stability (coefficient of variation, CV) without changing the underlying qualitative dynamics. Although slowing life history can be initially stabilizing, we find that in stochastic settings slowing ultimately drives highly destabilizing population disappearances, especially under reddened noise. Our results suggest that human-driven reddening of noise may decrease species stability because the autocorrelation of red noise enlarges the period and magnitude of perturbations, overwhelming a species natural compensatory responses via a ratchet-like effect. This ratchet-like effect then pushes species population dynamics far away from equilibria, which can lead to precipitous local extinction.

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MS12

Model Free Method of Predicting Transient Dynamics

Transient dynamics are referred to as those dynamics that

happen on ecologically relevant timescales, in which classical modelling techniques often fail to capture. Due to the ever changing environments and ecosystems, increased interest has been placed on the study of transient dynamics. However, many of the advances made towards understanding transients are fundamentally mathematical and beg to be connected to ecology and ecological data. In this talk I will show how uniting the underlying theory of dynamical attractors and empirical dynamical modelling we can understand when an ecological system is in a transient state based solely on ecological time series data. We further show that several metrics can be used to predict when a transient event is coming to an end. This work connects the mathematical literature on transient dynamics to the real-world application of understanding transients and short term changes in ecological systems.

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MS12

Driving Change: How Do Change-Points in Animal Movement Behaviour and Measured Landscape Productivity Correlate

In animal movement ecology, studies often look first at the qualities of the environmental landscape to interpret changes in movement behaviour patterns, for example by using step selection analysis. But this method starts with the environment and looks for behaviour switches second. Due to limitations in GPS data collection, the two or three dimensional nature of movement, and impacting missing values, there is a gap in ecology for identifying change points for movement strategies. We attempt to first identify points in time where animals change their movement behaviour, and then look at the environment for characteristics that maybe correspond to such changes and resulting patterns. The methods described are applied to grizzly bear (Ursus arctos horribilis) telemetry data in southwestern Alberta from 2001 to 2018. Such techniques could allow deeper insight into many species and the hidden forces behind movement decisions.

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MS12

Uncertainty Quantification for Optimal Control in the Face of Climate Change

Markov Decision Processes (MDPs) are widely used for optimal control of natural resources, from managing hunting or harvest quotas to determining the best conservation action from a set of options. However, historical management problems have been formulated with the assumption that the system itself is stationary, with no explicit time dependence. An area of current research is how to best account for the nonstationary nature of climate change in these optimal control problems. Under stationary conditions, these models already often have a considerable number of parameters, many of which are difficult or impossible to estimate precisely. Climate change introduces considerable additional uncertainty. There is uncertainty in the magnitude and rate of change of the environment, and there is uncertainty in how sensitive the population or community is to these changes. In this talk, we demonstrate how Uncertainty Quantification (UQ) methods can be used to understand the relative importance of these various uncertainties. We show how UQ methods can be used to incorporate climate change forecasts into natural resource management, helping to identify the most important sources of uncertainty. We also discuss how UQ methods can be used to guide both model refinement and data collection, improving our ability to effectively use optimal control methods for natural resource management in our rapidly changing world.

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MS13

Modeling Malaria Across Scales

Malaria, a disease on the rise due to global warming, puts at risk half the world's population. Malaria is caused by a protozoan parasite with multiple life stages in the host and the vector, making it several orders of magnitude more complex than viral and bacterial diseases. In this talk, we will discuss how molecular phenomena emerge as epidemiological trends that can best be explained with the harmonization of data across scales.However, the skill set necessary to undertake this type of study is vast. We will explore the use of generative artificial intelligence in conjunction with adaptive learning to aid in the exploration of multi-omic multi-scale data. The tool is ALICE, Adaptive Learning for Interdisciplinary Collaborative Environments, an open-source web-based information system funded by NSF and NIH.

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MS13

Linking Mosquito Trap Data with Mathematical Models

Aedes aegypti is responsible for a few arbovirus transmissions. In this talk, I will present how we connect differential equation parameters with the mosquito trap data collected from 2017 to 2019. We specifically will talk about parameter identifiability and model comparison problems we encountered during our fitting. The model is then used to compare the Ae. aegypti population and evaluate the impact of rainfall intensity in different urban built environments. Our results show that rainfall affects the breeding sites and the abundance of Ae. aegypti more significantly in tourist areas than in residential places. In addition, we apply the model to quantitatively assess the effectiveness of vector control strategies in Miami-Dade County in South Florida, USA.

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MS13

Assessing the Impact of the Wolbachia-based Control of Malaria in Endemic Setting

Malaria remains a significant infectious disease globally, causing hundreds of thousands of deaths each year. Traditional control methods, such as disease surveillance and

mosquito control, along with the development of malaria vaccines, have made strides in reducing the disease's impact. Wolbachia is a natural bacterium that can infect mosquitoes and reduce their ability to transmit diseases. While initially used to control dengue fever, recent research has explored its potential for malaria control. In this study, we develop and analyze a novel mathematical model to assess the potential use of Wolbachia-based strategies for malaria control in endemic regions. The model describes the complex Wolbachia transmission dynamics among mosquitoes and incorporates key features of malaria transmission in humans with dynamical immunity feedback. We derive the basic reproduction number of the malaria disease transmission, which depends on the prevalence of Wolbachia in mosquitoes. Our findings reveal bifurcations in both Wolbachia transmission among mosquitoes and malaria transmission in humans, suggesting the potential for malaria elimination through Wolbachia-based interventions.

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MS15

Integrating Machine Learning with Pharmacokinetics-pharmacodynamics Models to Identify Therapeutic Windows for New Oral Anticoagulants

Determining the optimal dosage of novel oral anticoagulants (NOACs) presents a challenge due to their diverse mechanisms of action and variability among patients. Despite advancements in developing computer models for coagulation, these are rarely utilized in clinical settings because of their significant computational demands and the complexity of integrating them with pharmacokinetic models and patient-specific data. To address these issues, we used deep learning algorithms trained on synthetic data generated from a validated model that simulates clot formation under venous flow conditions. These surrogate models were integrated with pharmacokinetic models describing NOAC concentrations and pharmacodynamic models that relate these concentrations to their effects on thrombin generation. This framework allows us to identify patient profiles that respond optimally to various NOAC regimens. Subsequently, we propose an algorithm that adjusts treatment protocols based on individual thrombin generation kinetics, optimizing treatment efficacy, including strategies that involve combinations of NOACs. Upon further validation, this algorithm can serve as a proof-of-concept for a diagnosis tool which can be easily deployed in clinical settings to help medical practitioners determine optimal NOAC therapy regimens for specific patients.

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MS15

Modeling Single-cell and Spatial Transcriptomic Data with Optimal Transport

Single-cell and spatial transcriptomics data examines high-throughput gene expression profiles at fine resolutions providing an unprecedented opportunity to elucidate the underlying complex biological processes. Optimal transport has proven to be an effective tool for various applications with such data, such as multi-omics integration. In this talk, we will discuss several optimal transport variants motivated by the biological applications, where there are detailed application-specific constraints, multiple distribution species, and multiple embedding spaces of the same system. We will illustrate the applications of these tools for addressing multi-compatible molecular species in cell-cell communication analysis and devising coherent trajectories of the same biological system from multi-omics datasets.

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MS15

Multiscale Modeling and Topological Data Analysis in Artificial Intelligence-driven Biology

Artificial intelligence (AI) has emerged as a pivotal tool in biology, revolutionizing data analysis at both large-scale and single-cell levels. However, the lack of interpretability in AI poses challenges in extracting intricate functions and dynamics from high-dimensional, complex heterogeneous, and noisy biological data. In this talk, we aim to address these challenges by investigating dynamics and topology of data via multiscale modeling and topological data analysis. First, we will discuss our approaches for deciphering cellular spatio-temporal dynamics, focusing on the interplay between gene regulation, spatial signals, and intercellular mechanical interactions. Our approaches include stochastic simulations, the subcellular element method, and reaction diffusion equations. Building upon this foundation, we have developed a deep learning-based dynamical model using unbalanced dynamic optimal transport to connect time-course single-cell transcriptomic snapshots and interrogate underlying gene regulatory networks. Lastly, we will discuss AI models designed to expedite protein design that incorporate a persistent spectral Laplacian method, large language models, and a hierarchical clustering-based Bayesian optimization approach.

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MS15

A Noise Guided Learning from Observation of Stochastic Collective Dynamics

We present a series of methods to learn the drift as well as the nose term from observation of stochastic collective dynamical systems. Our methods can handle high dimensional observation data as well as unknown correlated noise. We show extensive numerical tests to support our theoretical claims over various different dynamical systems.

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MS16

Parameterization and Uncertainty Quantification in a Mathematical Model of Brain Tumors under Treatment

This talk describes efforts to parameterize and quantify the predictive accuracy, over time horizons of one to three months, of treatment response and tumor recurrence in patients with glioblastoma multiforme (the most common type of primary brain cancer in adults). Three hundred magnetic resonance (MR) scans from 22 unique patients, each of whom had suffered a recurrence following initial surgery and chemoradiation, were incorporated into this modeling study, which attempted to predict tumor progression from one patient scan time to the next. A Latin hypercube design was applied to initialize and parameterize a simplified reaction-diffusion model, developed by the authors, from clinical imaging. The model attempts to distinguish between proliferating and necrotic cells. Prediction accuracy for each patient is assessed by comparing model output to observed tumor in the subsequent scan. An initial set of model simulations over 72 different scan intervals has found that prediction accuracy is fair to good in about two-thirds of the cases. In the remaining cases, the observed tumor either grew much more quickly than the model suggested, or treatment response (as observed on imaging) was better than the model predicted. The talk also describes efforts to incorporate MR perfusion data, which distinguishes between regions of actively growing tumor and regions where the tumor cells are largely quiescent or necrotic as a consequence of treatment.

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MS16

Estimating Treatment Sensitivity and Resistance in Tumor Growth with a Random Differential Equation Model

Resistance to treatment, which comes from the heterogeneity of cell types within tumors, is a leading cause of poor treatment outcomes in cancer patients. Previous mathematical work modeling cancer over time has neither emphasized the relationship between cell heterogeneity and treatment resistance nor depicted heterogeneity with sufficient nuance. To respond to the need to depict a wide range of resistance levels, we develop a random differential equation model of tumor growth. In the inverse problem, we aim to recover the sensitivity to treatment as a probability distribution. This allows us to observe what proportions of cells exist at different sensitivity levels. After validating the method with synthetic data, we apply it to monoclonal and mixture cell population data of isogenic Ba/F3 murine cell lines, as well as multiple myeloma patient samples, to uncover each tumor's levels of sensitivity to treatment.

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MS16

Application of a Nonlinear Mixed-Effects Droop Model to Understand Prostate Cancer Dynamics under Androgen Deprivation Therapy

The characteristics of an individual relevant to the determination of cancer dynamics, often under treatment, are presumed to be represented by a subset of parameters in mathematical models. Thus, the estimation of these parameters is crucial to gain greater insights and to make appropriate predictions in practice. However, model parameters often have no direct link to measurable biological quantities, resulting in large and unconstrainable uncertainty on their estimated values. Furthermore, when a model is fitted to the data of each individual, there can be orders of magnitude difference in the estimated parameters between different individuals, which may have no biological meaning. In this talk, I will present a modeling framework for prostate cancer with rigorous biological, mathematical, and statistical foundation to address both of the aforementioned issues. The mathematical model is formulated based on a series of previous modeling studies that used the Droop cell quota concept. The model is fitted to data from a clinical trial of intermittent androgen deprivation therapy for prostate cancer using nonlinear mixed-effects population fitting. This approach allows for robust parameter estimations for all individuals. Moreover, when there are substantial variations in some parameter, this set of parameters may be used as a classifier of treatment outcome.

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MS16

Image-Guided Mathematical Modeling for Patient-Specific Prediction and Optimization of Breast Cancer Response to Neoadjuvant Therapy

Neoadjuvant therapy (NAT) is the standard-of-care of locally advanced breast cancer (BC). However, pathological complete response (pCR) rate in BC patients to current NAT regimens is less than 50%. Aside from the need to develop new therapies with higher efficacy, a critical barrier to improving BC response is the lack of rigorous ways to tailor therapeutic regimens. We seek to address this challenge by integrating mathematical modeling with longitudinal clinical images. A triple-negative breast cancer cohort ($n = 37$)

from the ARTEMIS trial is used for this study. Each patient received the standard-of-care chemotherapies for NAT and longitudinal MRIs were collected before and during the treatment. A mechanism-based model is established based on a reaction-diffusion equation that describes tumor cell migration, proliferation, and drug-induced death. The model is calibrated with MRIs of an individual patients and used to predict patient-specific response. Our model achieved high accuracy (AUC= 0.89) in predicting patient response to the actual treatment. Moreover, with investigating 128 clinically reasonable NAT schedules, we observed that without changing the total dose, shortening the duration of NAT administration increased the treatment efficacy; 8 out of 18 actual patients who had non-pCR to their actual treatment were predicted to achieve pCR with the dense-dose NAT. Our image-guided model provides a unique opportunity of optimizing patient-specific BC response to NAT.

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MS17

Modelling Optogenetic Control of Cellular Motility and Shape Dynamics

I will present my investigations on the role of filamentous actin (F-actin) in cell motility, focusing on the regulation of Rac GTPases through optogenetics. Collaborating with Orion Weiner's lab, we propose testing their hypothesis of the presence of a local Rac inhibitor using a 2D moving cell computational model developed in the open-source software Morpheus. Preliminary results demonstrate the model's capability to simulate Rac activity and cell responses, aligning with Weiner's experimental data. This model-experiment cycle aims to uncover insights into the flexible modulation of Rac activity and its impact on cell motility. The study's approach complements and extends existing models within the Keshet group, contributing to a broader understanding of GTPase networks and their influence on cell shape and motility.

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MS17

A Dynamical Systems Approach to Modeling Cell Morphology and Migration

Modeling and understanding cell shape and motility is often thought of as a pattern formation problem. In this talk, I will reframe a few questions in this area in terms of dynamical systems and demonstrate how the use of a new class of pseudo-analytic PDE bifurcation analysis tools can yield new mechanistic insights. I will discuss two specific projects from this perspective. First, Ill discuss our recent efforts to understand what might be responsible for the development of the discrete but complex landscape of broad cell shapes that migratory cells exhibit. This work is motivated by recent imaging classification showing that cells exhibit 6 or 7 distinct shapes and can transition between those shapes. Using new approaches to PDE bifurcation analysis, we demonstrate that simple biochemical interactions between cytoskeletal regulators can explain this discrete heterogeneity. Second, Ill discuss recent work using similar approaches to model the interactions between cytoskeletal regulation, actin growth, and cell tension. Our results here demonstrate that feedback between mechanics and regulation may provide cells with a form of mechanochemical adaptation (which is distinct from other commonly discussed forms of adaptation) that allows cells to robustly migrate in a wide range of different chemoattractant concentrations.

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MS17

Bayesian Parameter Identification Applied to the Gef Rho-Myosin Model

Cellular signalling pathways regulate various cellular processes, including cell motility, proliferation, and responses to external stimuli. To unravel the complex dynamics governing these pathways, we adopt an innovative approach that combines Bayesian parameter estimation and bifurcation analysis. Parameter identification, involves gaining insights into model parameters based on experimental measurements, by aligning mathematical models with experimental data. Analytical parameter identification is a rarity, and many parameters lack direct experimental measurement or well-defined physical interpretations. Our proposed approach not only aids in allocating parameters to specific regions of interest but also assists experimentalists in refining hypotheses, particularly pertinent in the context of Rho-Myosin dynamics modelling. By deducing the probability distribution for model parameters through a synthesis of prior knowledge and experimental observations, we establish a robust foundation for our study. The sample drawn from this distribution represents a set of parameters for the mathematical model of the GEF-Rho-Myosin interaction network. In this talk, I will describe an experimentally-driven mathematical model of GEF-Rho-

Myosin signalling. Additionally, I will describe the steady state continuation method and how it is used in the description of model prior. Finally I will describe some numerical results.

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MS17

Spatio-Temporal Dynamics of Rho-Gef-Myosin Signaling Network in a Conserved System with a Quasi-Steady State Approximation

Experimental observations have revealed that local cell contraction pulses are regulated by the Rho-GEF-Myosin based activator inhibitor signaling network, This network generates oscillatory and excitable system dynamics via positive and negative feedback loops, In this talk, I will 1. Utilize existing experimental observations to motivate a coupled system of ODEs. 2. Analyze the temporal dynamics of the system 3. Derive the conditions for diffusion-driven instability to the spatial system. 4. illustrate some Turing parameter spaces for the system. Finally, I will illustrate some numerical solutions using MATLAB package pdepe in 1D

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MS18

The Role of Sensing for Collective Behavior in the Presence of Geometrical Obstacles

While prodigious research has been devoted to particle models of collective behavior that capture the synchronous motion characteristic of animal groups like bird flocks and fish schools, almost all of this work has been devoted to environments where the domain is homogeneous and free of obstacles and sometimes even boundaries. In this talk, we abstract the idea of collective motion in a complex environment through a simulation study of the canonical Vicsek flocking model. We show that the presence of obstacles in the domain dramatically impacts the ability of flocking particles to coordinate their motion, and this influence is regulated by the ratio between the size of obstacles and each particles sensing range. We further this understanding from performing an empirical study from a swarm of echolocating grey bats (*Myotis grisescens*) navigating through obstacles.

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MS18

Data-Driven Modeling of Bacterial Aggregation

The soil bacterium *Myxococcus xanthus* is a model organism with a set of diverse behaviors. These behaviors include the starvation-induced multicellular development program, in which cells move collectively to assemble multicellular aggregates. After initial aggregates have formed, some will disperse, with smaller aggregates having a higher chance of dispersal. Initial aggregation is driven by two changes in cell behavior: cells slow down inside of aggregates and bias their motion by reversing direction less frequently when moving toward aggregates. However, the cell behaviors that drive dispersal are unknown. Using agent-based modeling combined with data from florescent microscopy, we show dispersal is predominantly generated by a change in bias, which is strong enough to overcome slow-down inside aggregates. Notably, the change in reversal bias is correlated with the nearest aggregate size, connecting cellular activity to previously observed correlations between aggregate size and fate.

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MS18

Multiple Sensing Modalities and Emergent Collective Behavior

Many collective behavior models assume individuals communicate primarily through visual sensing modalities. However, certain social animals, like bats and dolphins,

rely on alternative modalities such as audition. The literature lacks comprehensive models incorporating these diverse sensing modalities. This study explores the influence of combining information from different modalities, for example, audition and vision, on emergent group-level behavior. We conduct simulations to understand how the relative strength of these sensory cues influences group behavior, measured in terms of different order parameters. Our findings suggest that integrating sensory cues allows systems to attain collective behavior that they would otherwise not be able to achieve with a single sensory modality.

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MS18

Infering Structures of Biological Systems from Partial Measurments.

Many biological systems exhibit stochastic dynamics. Observational data, coupled with advancements in data science, play a crucial role in unraveling biological mechanisms across various scales. It is sometimes difficult to distinguish between stochastic dynamical states from measurements, deceiving us into incorrect models and flawed understanding of natural phenomena. Here, we propose a model-free, statistical framework, grounded in network and control theory, to estimate the number of states of a stochastic system from perceptible dynamics. The framework extends previous techniques for deterministic systems, based on the rank of ancillary matrices. Our method reliably estimates the correct number of dynamical states, allowing us to determine whether a single observed state corresponds to multiple indistinguishable states. Additionally, the method can assist in pinpointing external, unmeasured variables. We demonstrate our approach in various life science domains, including biophysics, physical chemistry, epidemiology, and collective behavior.

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MS19

Modeling the Effects of Rapid Cellular Disposition on Drugs with Fast Clearance: Impact of Uncertainty in Recording Observational Times

The two-compartment pharmacokinetic (PK) model which typically accounts for drug elimination mechanisms and its distribution into tissues and organs, is inadequate to describe the PK of drugs which are cleared by atypical pathways, e.g., via cellular disposition. Using a dynamical systems approach, we propose a model to describe the observed PK behavior and explore the properties of the model to understand and elucidate the reasons behind the large observed inter-individual variability of such atypically eliminating compounds. Furthermore, using uncertainty analysis of the underlying dynamical system we explore the implications of the uncertainty in the reported sample times and the time elapsed between the sample collection and bioanalysis. We show that for molecules that are eliminated rapidly (nominal half-life ¡ 10 minutes) this can result in poor estimates of the true clearance, inter-individual variability, and residual error. Finally, we showcase the utility of our modeling approach to reconcile some of the observed interindividual variability in proteasome inhibitors and provide a possible way to model the observed clinical PK of such drugs. Our work can pave the way to establish improved methods to model drugs with atypical metabolism and elimination pathways.

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MS21

A Mesoscopic Compartmental Approach for the Modeling of Vaccine Hesitancy

We propose a mesoscopic viewpoint for understanding the link between opinion formation phenomena and epidemic dynamics. The recent pandemic has brought to light that vaccine hesitancy can present different phases and temporal and spatial variations, presumably due to the different social features of individuals. The emergence of patterns in societal reactions permits to design and predict the trends of a pandemic. This suggests that the problem of vaccine hesitancy can be described in mathematical terms, by suitably coupling a kinetic-like compartmental model for the spreading of an infectious disease with the evolution of the personal opinion of individuals, in the presence of leaders. The resulting model makes it possible to predict the collective compliance with vaccination campaigns as the pandemic evolves and to highlight the best strategy to set up for maximizing the vaccination coverage. We conduct numerical investigations which confirm the ability of the model to describe different phenomena related to the spread of an epidemic. This is a joint work with Giuseppe Toscani and Mattia Zanella.

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MS21

Improving the Effectiveness of Water, Sanitation, and Hygiene Interventions: a Mechanistic Modeling Approach to Generalizing the Outcomes of Intervention Trials

Recent large-scale trials have revealed that interventions improving water, sanitation, and hygiene (WASH) in low-income settings may not confer the expected health gains for young children; evidence-based guidance is needed to inform programs and future studies. We developed a mechanistic infectious disease transmission model to account for multiple environmental pathways, multiple interventions applied individually and in combination, adherence to interventions, and individuals not enrolled in the study. Leveraging a set of mechanistic parameter combinations

fit to the WASH Benefits Bangladesh trial (n=17,187 individuals) using a Bayesian sampling approach, we simulated trial outcomes under counterfactual scenarios to estimate how changes in intervention completeness, coverage, adherence, and efficacy, as well as baseline WASH conditions and disease burden, impacted intervention effectiveness. Increasing community coverage was associated with the greatest impact on intervention effectiveness, but its impact depended on the fraction of transmission that was along pathways modified by the interventions. Intervention effectiveness was reduced in counterfactual simulations with lower levels of preexisting WASH conditions or increased baseline disease burden. Next-generation WASH programs must address coverage and completeness and account for the fact that effect of individual-level WASH improvements will be blunted the further the community is from achieving herd protection.

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MS21

Multi-Agent Simulation and Reinforcement Learning for Public Health Decision Analyses

A significant challenge in intervention decision analyses for the control of infectious diseases is identifying an optimal intervention policy specific to each population while considering the cross-over effects from other populations. Taking HIV as a case study, the U.S. 'Ending the HIV Epidemic' initiative aims to reduce HIV incidence, nationally, by 90% by 2030. Because of disparities in infections across geography, one policy is not suitable for all, and because of geographical dynamics of infection spread, analyses to identify optimal policies cannot be conducted independently in each jurisdiction. To address this, we implemented a multi-agent reinforcement learning (MARL) algorithm to identify jurisdiction-specific optimal policies, using an environment that simulates a national population as a composition of 96 interacting sub-jurisdictions. We evaluate alternative objective functions, minimizing costs and disease burden, and minimizing disease burden. We discuss the development of the simulation environment, the implementation of MARL, and preliminary findings.

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MS21

Incorporating Population Heterogeneity Into ODE Models via the Generalized Linear Chain Trick.

Multi-agent systems with structured populations are often modeled with ODEs. These often (implicitly) assume times spent in a state (dwell times) are exponentially distributed. In practice, other distributions may be desired: Delay differential equations can incorporate fixed delays, and integral equations (IEs) can allow for any dwell time distribution. But, the flexibility of IEs comes with more difficult simulation and analysis. One compromise is the classical "linear chain trick" to build ODEs with Erlang dwell times (i.e., Gamma distributions with integer shape parameters) equivalent to analogous IEs. We have extended this technique to a more flexible family of distributions known as "phase-type distributions" which are the absorption time distributions for continuous time Markov-chains (CTMCs). This generalized linear chain trick (GLCT) allows modelers to quickly develop ODEs that incorporate Gamma, hypo- and hyper-exponential, and Coxian distributed dwell times (and others), without the need to derive them from integral equations. An additional benefit the GLCT is that the resulting matrix-form of the ODEs can yield analytical expressions interpretable using stochastic processes theory (e.g., formulas for mean absorption times or absorption probabilities). I will summarize this approach, demonstrate a basic reproduction number calculation for a very general family of SEIRS models, and given an example incorporating a time-varying delay in a COVID-19 model.

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MS22

Mathematical Modeling of the Intrinsic Pathway of Blood Coagulation

Thrombotic disorders caused by pathological activation of the blood coagulation system represent a leading cause of death worldwide. The contact pathway of coagulation, activated by exposure of blood to negatively charged surface, has been identified as a key driver of pathological coagulation. Critically, the contact pathway of coagulation appears to play a relatively minor role in mediating essential hemostatic processes. As a result, there has been considerable interest in targeting this pathway for development of safe and effective anticoagulant strategies. We contend that such efforts are limited by an incomplete understanding of how activation of the contact pathway is regulated. We will introduce a preliminary computational model for the contact pathway of coagulation, which has been validated and calibrated using experimentally acquired thrombin generation data. Additionally, we will outline a hypothesis driven by the model, proposing a novel potential target for anticoagulation.

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MS22

Towards a Mathematical Model of Aggregate Growth Mediated by Vwf

In this talk, we will discuss ongoing work towards a simplified model of platelet aggregation to inform PDE models and efficiently determine essential pathways involved in platelet aggregate formation. High shear rate conditions in arterial blood flow occur naturally in various regions of the body and pathological conditions such as stenoses. In these environments, the mechanically sensitive protein Von Willebrand Factor (vWF) mediates the initial deposition of platelets to the wall or pathological structure. While CFD simulations provide a highly detailed description of the process, computational complexity limits our ability to examine various physiological conditions that could impact aggregation, like shear rate, vessel geometry, and injury size. This modeling framework incorporates an averaged flow through porous media, imparting a drag force that is balanced by crosslink bonds which break in a force-dependent manner. We will show how the inclusion of vWF is essential to aggregation at high shear rate by changing the primary pathway to initial platelet cohesion and activation. We will also investigate how the properties of vWF affect the growth rate and stability of the aggregate. These results have implications for aggregation in stenotic regions as well as in disease states such as Von Willebrands Disease.

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MS22

Improvements and Extensions of a Stochastic Clot Lysis Model

Understanding the breakdown of blood clots inside the circulatory system is of critical importance to treating stroke, deep vein thrombosis, and many other life-threatening conditions. A multi-level, stochastic computational model of the basic processes of fibrinolysis [B. E. Bannish, J. P. Keener, and A. L. Fogelson, *Math. Med. and Bio.*, 31 (2014), pp 1744] has made contributions to the field, but accumulated technical debt has hampered further development and the involvement of other researchers. We discuss the model, and recent extensions and additions, that are enabling new insights. These include consideration of the role played by fibrin degradation products and the enlargement of pores in the fibrin mesh. Additionally, we will cover the parallel project which has facilitated this work, comprising user interface upgrades, high-performance computing tools, data classification and storage standards, and re-implementation of code in more modern languages.

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MS22

Reevaluating TFPI Mechanisms of Action With Bayesian Inference and Analysis of the Inhibition of Factor X Activation Under Flow

Blood coagulation is a vital physiological response involving a complex network of biochemical reactions that form a clot to repair vessel injuries. It unfolds in three stages–initiation, amplification, and propagation–culminating in thrombin formation. Tissue factor pathway inhibitor (TFPI) is an important inhibitor of the initiation phase, where it inhibits the activation of factor X. Despite its crucial role, the specific mechanisms by which TFPI inhibits the activation of factor X remain poorly understood. It has been hypothesized that TFPI acts through two distinct mechanisms: direct and indirect, but many mathematical models consider only the indirect mechanism. In this study we investigate the inhibitory mechanisms of TFPI by revisiting a comprehensive mathematical model that incorporates both hypothesized mechanisms of TFPI action, and secondly, the inhibition of factor X activation due to flow by extending the model to account for blood flow. Through Bayesian inference, we refined our model parameters based on posterior distributions that best fit the empirical data from static experimental studies of factor X activation under varied TFPI and TF:VIIa concentrations. Our results indicate that both TFPI mechanisms are necessary to align with experimental data. Upon extending our model to account for blood flow, we found that significant TFPI inhibition under flow conditions is only possible when the direct TFPI binding mechanism is considered.

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MS23

Comparative Analysis of Reprogramming Methods: a Model-Based Study

Experimental studies have shown that chromatin modifiers have a critical effect on cellular reprogramming, i.e., the conversion of differentiated cells to pluripotent stem cells. Here, we develop a model of the OCT4 gene regulatory network that includes genes expressing chromatin modifiers TET1 and JMJD2, and the chromatin modification circuit on which these modifiers act. We employ

this model to compare three reprogramming approaches that have been considered in the literature with respect to reprogramming efficiency and latency variability. These approaches are overexpression of OCT4 alone, overexpression of OCT4 with TET1, and overexpression of OCT4 with JMJD2. Our results show more efficient and less variable reprogramming when also JMJD2 and TET1 are overexpressed, consistent with previous experimental data. Nevertheless, TET1 overexpression can lead to more efficient reprogramming compared to JMJD2 overexpression. This is the case when the recruitment of DNA methylation by H3K9me3 is weak and the methyl-CpG-binding domain (MBD) proteins are sufficiently scarce such that they do not hamper TET1 binding to methylated DNA. The model that we developed provides a mechanistic understanding of existing experimental results and is also a tool for designing optimized reprogramming approaches that combine overexpression of cell-fate specific transcription factors (TFs) with targeted recruitment of epigenetic modifiers.

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MS23

Modeling Epigenetic Landscape of Cellular Aging and Reprogramming

Waddington's landscape serves as a potent metaphor that encapsulates the process of cellular differentiation. It illustrates how chemical and environmental stimuli reshape the epigenetic landscape, consequently directing the cell's developmental trajectory towards a variety of cell fates. Quantifying the landscape has been done by the construction of an energy-like function from stochastic gene regulatory networks. Experimental evidence shows that overexpressing key regulators that maintain pluripotency leads to the resetting of the chromatin state, resulting in a small subpopulation regaining stemness. In this research, we combine tools from dynamical systems and statistical mechanics to decompose the high-dimensional epigenetic landscape, revealing the structure of the cellular trajectories. We construct a minimal epigenetic network and show how multiplicative noise arises from its master equation may lead to different outcomes of cellular reprogramming.

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MS23

Discovery and Analysis of Cell-Fate Landscape Underlying Single-Cell Transcriptome Data

Single-cell sequencing technologies provide unprecedented resolution for studying the dynamic process of cell-state transitions during development and complex disease. These transitions can be modeled and understood as a multi-scale, stochastic dynamical system on a cell-fate landscape. However, analyzing high-dimensional, static single-cell RNA-sequencing data with such models can be challenging due to the curse of dimensionality. In this talk, I will discuss how machine learning has enabled us to overcome the challenge and use statistical mechanics techniques to analyze scRNA-seq data. I will first introduce the MuTrans algorithm, which uses a low-dimensional dynamical manifold to identify attractor basins and transition probabilities in snapshot data. I will also present the scTT (single-cell transition tensor) and spliceJAC algorithms, which use non-equilibrium dynamical theory to analyze attractor stability within the landscape and identify transition-driving genes in gene expression and splicing processes. Finally, I will discuss our efforts to construct a time-varying landscape, which interpolates non-stationary time-series scRNA-seq data using Wasserstein-Fisher-Rao metric, unbalanced optimal transport and its neural network-based partial differential equation implementations. Overall, these approaches bridge the model-based and data-driven methods in the physical modeling and analysis of single-cell biology.

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MS24

Equivariant Neuronal Representations: Insights from Mouse Visual Cortex

To facilitate reasoning about visual scenes, brains must convert complex visual inputs to relevant neuronal representations. One main source of complexity of visual inputs is that they typically undergo geometric transformations, e.g. rotations. We study whether image rotations are imprinted as group representations in the structure of neuronal responseswe call such structure rotation-equivariance. Rotation-equivariance shapes the image manifold that is formed by the neuronal responses to an image and all its rotational transforms. We find that an eigendecomposition of the matrix representation identifies orthogonal neuronal subspaces where image manifolds either collapse to points or to concentric circles. To study how the brain represents image rotations across different stages of visual processing, we performed large-scale Calcium-imaging across multiple visual cortical areas in mice while presenting a variety of rotated images. Primary and higher-order visual areas showed strong evidence for rotation-equivariance, but their equivariant structure differs. In particular, collapsed image manifolds of various images cause a larger fraction of variance in higher-order areas, potentially to extract image identity. In contrast, deep convolutional neural networks that have been used to model neurons in the visual cortex are not rotation-equivariant. Our findings show that symmetries of sensory inputs structure neuronal representations through equivariance.

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MS24

Adding Spikes in the FitzHugh-Nagumo Model with Low-Frequency Periodic Forcing

Oscillations are a ubiquitous feature of neural activity at multiple scales in the brain. The FitzHugh-Nagumo (FHN) model is a simplified mathematical model for neuron action potentials that exhibits fast-slow dynamics. Fast mechanisms drive rapid jumps in phase space (spikes), and slow mechanisms contribute to the recovery between spikes. Augmenting the FHN model with additional slow dynamics can induce bursting, oscillatory patterns characterized by repeated spikes interleaved with periods of quiescence. In this study, we investigate the bursting behavior of the FHN model under low-frequency external forcing, which simulates low-frequency communication between brain regions. Using geometric singular perturbation theory and numerical simulation, we examine how the number of spikes in the bursting oscillation changes as the amplitude and frequency of the input vary. We identify and describe the interaction of two mechanisms for adding spikes as these parameters change: folded-node and folded-saddle canards. Canards are solutions that remain near unstable regions of the phase space on the slow timescale, and we find their existence contributes to both the onset and termination of bursts. Our findings provide insights into the role of low-frequency external forcing in modulating the oscillatory behavior of the FHN model.

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MS24

Activity Patterns of A Two-Timescale Neuronal Ring Model with Voltage-Dependent Piecewise Smooth Inhibitory Coupling

We present an analysis of activity patterns in a neuronal network that consists of three mutually inhibitory neurons with voltage-sensitive piecewise smooth coupling. One of the observed propagating solutions appears to be contrary to the network architecture and is characterized by a sudden turn-around of trajectories during fast transitions between quasi-stable states. Standard fast-slow analysis fails to describe the mechanism underlying this activity pattern due to the voltage-sensitive nature of the coupling. We exploit the piecewise smooth nature of the coupling and consider a sequence of fast subsystems defined in a piecewise way. Our analysis shows that there are three possible scenarios during fast jumps, which may depend on both the fast dynamics and the slow dynamics. First, the fast dynamics may succeed to equilibrate at (or near) a critical manifold, after which the slow dynamics relaxes to its own fixed point. Second, while the fast dynamics tries to equilibrate to a critical manifold, the slow dynamics may push the fast system through a bifurcation, which forces a second fast jump to a new critical manifold. Third, the presumed critical manifold may be lost prior to fast subsystem equilibration, through effects that may relate to either the slow dynamics or the fast dynamics, in which case the fast dynamics is forced to approach a new critical manifold directly. In the second and third cases, we observe the sudden turn-around during fast jumps.

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MS24

Strong Symmetry Breaking in Coupled, Identical Slow/fast Oscillators

We study pairs of symmetrically-coupled, identical slow/fast oscillators, where the coupling can be through the fast and/or slow variables. We find a plethora of strong symmetry breaking rhythms, in which the two oscillators exhibit qualitatively different oscillations, and their amplitudes and frequencies can differ by as much as an order of magnitude. Such differences in amplitude and frequency can be associated with different functional states, such as unihemispheric slow-wave sleep in certain marine animals and birds during which one hemisphere exhibits large-amplitude, low-frequency oscillations characteristic of sleep while the other exhibits small-amplitude, high-frequency oscillations associated with a wakeful state. Geometric singular perturbation analysis of the coupled system shows that a key folded node singularity, located off the symmetry axis, is the primary mechanism responsible for the strong symmetry breaking. Passage through the neighborhood of this folded node can result in splitting between the amplitudes of the oscillators, with one constrained to remain of small amplitude while the other makes a large-amplitude oscillation or a mixed-mode oscillation.

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MS25

Evolutionary Dynamics on Switching Temporal Networks

Population structure has been known to substantially affect evolutionary dynamics. In constant-selection dynamics, with which the fitness of an individual only depends on its type but not on its neighbors, networks that promote the spreading of fitter mutants are called amplifiers of selection, and those that suppress the spreading of fitter mutants are called suppressors of selection. It has been discovered that most networks are amplifiers of selection under the Birth-death updating combined with uniform initialization, which is a standard condition assumed widely in the literature. We extend the Birth-death processes to temporal (i.e., time-varying) networks. For the sake of tractability, we restrict ourselves to switching temporal networks, in which the network structure alternates between two static networks at constant time intervals. We show that, in a majority of cases, switching networks are less amplifying than both of the two static networks constituting the switching networks. Furthermore, a substantial fraction of small switching networks are suppressors, which contrasts to the case of static networks. Additionally, we also study weighted networks under both the Birth-death updating and the death-Birth updating rules. We discovered that random assignment of weights suppress the selection of a fitter mutant with a high probability under both the updating rules.

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MS25

Negative Frequency-dependence is Not a Mechanism of Coexistence in Spatially Fragmented Populations

Across scales of organization, understanding the mechanisms that shape and maintain diversity in a population remains a fundamental challenge and there exists a large literature in evolutionary biology describing the processes that can account for persistent coexistence within populations. At their core, the theoretical frameworks are grounded in balancing selection, including negative frequency-dependent (NFD) selection, spatial or temporal habitat heterogeneity, and heterozygote advantage. In particular, NFD selection, by favoring rare types, is often suggested as the main selective force for biodiversity and polymorphism in natural populations. In this talk I will describe an evolutionary model in which, unintuitively, the opposite occurs: NFD selection decreases coexistence relative to neutrality, for certain spatial population structures. We call this the spatial speedup effect and, using a combination of mathematical analysis and simulation, we find that the condition for this effect depends critically on the spatial arrangement of the population. We show that spatial speedup is specifically shaped by the algebraic connectivity of the population: a measure of spatial fragmentation that derives from spectral graph theory. I will discuss how spatial speedup in fragmented populations can significantly impact biodiversity over evolutionary and ecological timescales by analyzing fixation times and species richness as the respective proxies for coexistence.

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MS25

Can Indirect Reciprocity Maintain Cooperation When Reputations Are Privately Held?

Indirect reciprocity refers to a mechanism of human cooperation, where a donor of a help receives reciprocation from a third party. It has been theoretically known that indirect reciprocity can sustain cooperation if individuals in the population share the same reputation about a focal individual. It has been, however, largely underexplored whether cooperation can be maintained if they do not necessarily share the same opinion. In fact, some previous works have shown negative results for the cases where reputations are privately held. Here we develop a new analytical machinery to tackle this question and study if indirect reciprocity can evolve even if people can have different opinions on the same individual. We have shown that indirect reciprocity can be sustained as an evolutionarily stable strategy if individuals adopt a specific rule of reputation assignment. Specifically, we have found that the rule called Simple Standing is able to sustain cooperation, whereas the rule called Stern Judging fails completely. Our results suggest that consensus in opinions among individuals is not necessarily needed to sustain indirect reciprocity.

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MS26

Towards a Predictive Framework for Cytokine Release Syndrome (CRS): Linking Clinical CRS Grading and Mechanistic Modeling

T-cell engagers (TCEs) represent a transformative approach in cancer therapy, designed to redirect the immune system to selectively target cancer cells. Despite their promising efficacy, the activation of immune system poses the risk of rapid release of cytokines, leading to occurrence of Cytokine Release Syndrome (CRS), potentially leading to severe concerns around patient safety. In this work, we will introduce a two-step predictive framework for predicting CRS in TCE therapy. The core of the framework is a mechanistic model capturing the homeostatic dynamics and the interplay between the immune system, TCE dosing, and cancer cells. The key output of this module is the time course of cytokine release and can provide the predictions on the cytokine peaks and its feedback on the immune system, overcoming the typical limitations of clinical observations. This information then feeds into a data driven statistical classifier that employs a machine learning approach, linking drug exposure metrics, baseline factors, and cytokine peaks for prediction of incidence of clinical CRS. We showcase the utility of our approach using example data across various TCEs and cancer indications. Recognizing CRS as a limiting factor for TCE development, this work highlights a practical tool for strategic model-based optimization of TCE therapy.

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MS26

Predicting the Optimal Cut-Off Date in Prospective Clinical Trials Based on Weakly-Supervised Virtual Populations

Predicting survival in oncology clinical trials is crucial for oncology drug development. However, traditional survival modeling has certain limitations. Firstly, it requires ongoing clinical trials with sufficient data collected. Secondly, commonly used survival frameworks such as the Cox proportional hazard framework fail to account for how the treatment effect may vary over time, often quantified as a hazard ratio (HR). In this study, we propose a novel methodology that addresses these limitations by transferring virtual population dynamics learned from historical trials combined with a time-dependent survival framework. Our virtual populations are generated from a quantitative systems pharmacology (QSP) model, which accurately cap-

tures the intricate cellular dynamics and drug interactions within the biological system. This innovative approach enables us to predict optimal cut-off dates of prospective clinical trials, thereby maximizing the likelihood of their success. We will present several examples based on real clinical trials of cancer immunotherapies in non-small cell lung cancer (NSCLC) to illustrate the strength and scope of our method.

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MS26

Mechanistic Tumor Modeling and the Recist Criteria of Disease Progression

Quantitative systems pharmacology models are based on biological mechanisms and their interactions. In oncology, these mechanisms–uncontrolled cell division, angiogenesis, hormonal promotion of tumor growth, and others– constitute or promote the growth of individual tumor volumes. And standard treatments– radiation therapy, chemo, BiTEs, antiangiogenics, checkpoint inhibitors–all act to diminish the growth rates of individual tumor volumes. However, the standard clinical measure of tumor burden, the RECIST 1.1 criteria, characterizes disease progression by a sum of lesion diameters. In this talk we will discuss tumor modeling at Eisai, and the problem of relating RECIST measures to tumor volumes and its implications for oncological QSP.

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MS26

Model-Based Meta-analysis for cross-indication and cross-endpoint bridging to accelerate clinical development

In several disease areas like immunology or oncology, the same treatment is studied in and approved for multiple disease indications. For example, interleukin inhibitors are approved for use in several indications like psoriasis, psoriatic arthritis and inflammatory bowel disease, and PD-1 inhibitor compounds are approved for multiple oncology indications like melanoma and non-small cell lung cancer. There is a large corpus of published results from clinical trials of such compounds that can provide information for development of novel therapies in indications that benefit from the same mechanism of action. Model-Based Meta-analysis (MBMA) is a method used to integrate aggregate-level data from multiple published clinical studies using mathematical models to quantitatively describe the effect of treatments on clinical endpoints. Specifically, MBMA can be used to quantify relationships between clinical endpoints within and across different disease indications by leveraging information across compounds, clinical endpoints, and indications. MBMA-derived quantitative relationships between early and late endpoints, or between clinical endpoints in different indications can provide data-informed insight for clinical trial design and decision making. In this talk, we will explore MBMA methods to bridge between clinical endpoints within and across indications and discuss applications, advantages and limitations of these methods.

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MS27

Undergraduate Research in Computational Psychiatry Through the Madison Experimental Mathematics Lab

Each semester, undergraduates at University of Wisconsin - Madison have the opportunity to apply to work in teams with other undergraduates, a graduate student, and a professor for a research project through the Madison Experimental Mathematics Lab (MXM). Cross-disciplinary projects are highly appealing to students, but the variations in student backgrounds make them more challenging to complete in one semester. A balance must be struck between enough background outside of math to situate the work in existing knowledge, without detracting from their chance to learn and create new math. Our team strove to design a task that is practical for both humans and computers to complete, in order to discriminate between model-based and model-free learning. The students had to master the techniques necessary to work with Markov Decision Processes, a framework wherein an agent iteratively interacts with an environment to learn what actions to take, how computer science and psychology view model-free and model-based learning, and the constraints involved in making tasks practical for use with humans. In this talk I will discuss what we learned from working with a diverse group of students on a project with such a vast body of prior related works, as well as the structure of the Madison Experimental Mathematics Lab.

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MS27

Inclusive by Design: Expanding the Cure Framework to Accommodate a True Interdisciplinary Research Experience

Mathematicians with limited biological background frequently collaborate with biologists who have little mathematical experience to address problems in biology. Though there are challenges inherent to such interdisciplinary collaborations undergraduate programs rarely include specific training to address them. One way to offer direct research experience to students is through a Course-based Undergraduate Research Experience (CURE); however, full implementations of the standard CURE framework used in most laboratory science courses are notoriously difficult in mathematics. We describe an Expanded CURE framework that allows for partial implementation of research projects and offer early evidence that the expanded ver-

sion shares many of the benefits of full CUREs, including in measures of equity. We then discuss how we used this expansion to design a senior-level, one-semester, interdisciplinary mathematical biology CURE course for both mathematics majors with little biology background and biology students with limited mathematics background and report some outcomes of the first run of that course.

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MS28

A Data-Driven Kinetic Model for Opinion Dynamics with Social Network Contacts

Opinion dynamics is an important and very active area of research that delves into the complex processes through which individuals form and modify their opinions within a social context. The ability to comprehend and unravel the mechanisms that drive opinion formation is of great significance for predicting a wide range of social phenomena such as political polarization, the diffusion of misinformation, the formation of public consensus, and the emergence of collective behaviors. In this paper, we aim to contribute to that field by introducing a novel mathematical model that specifically accounts for the influence of social media networks on opinion dynamics. With the rise of social-media platforms such as X, Facebook, and Instagram and many others, social networks have become significant arenas where opinions are shared, discussed, and potentially altered. To this aim after an analytical construction of our new model and through incorporation of real-life data, we calibrate the model parameters to accurately reflect the dynamics that unfold in social media, showing in particular the role played by the so-called influencers in driving individual opinions towards predetermined directions.

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MS28

A Kinetic Model of Epidemic Dynamics Influenced by the Spread of Opinions on Social Media

As recent Covid-19 outbreaks have shown, opinions about the use of nonpharmacological protective measures are crucial in influencing individual behavior, and in an age when social media dictates how we think, opinions can be strongly influenced by what is shared on social networks. In this paper we aim to present a novel approach to modeling infectious disease dynamics by incorporating the dynamics of social media opinions and contacts into a kinetic epidemiological framework. The proposed model extends the conventional SEIR framework to account for the evolution of opinions and the impact of social media on them, emphasizing in particular the role of popular users and their potential in influencing public opinion and driving the adoption of protective measures. We also performed some numerical simulations to confirm the plausibility of our model and its ability to describe different epidemiological phenomena.

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MS28

Manipulating Opinions: A Kinetic Model on a Social Network

In this talk we propose a kinetic model for opinion formation over a large online social network; in particular, we leverage graphons (graph functions) to be able to fruitfully incorporate the adjacency relation between people over a large network. (Weighted) graphons are defined as a well-posed limit of a sequence of graphs when the number of vertices tends to infinity, this allows to work on measurable functions rather than with large matrices. Moreover, we propose an optimal control problem in which the goal is not to steer the opinion of the population towards a target, but rather to prevent people's opinions to cluster. This control problem is presented both in the homogenoeus case and in the case of a network-mediated interaction among people.

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MS28

Unraveling Spillover Effects in Multi-Population Models: Mathematical Approaches and Insights

For many public health challenges, the burden of morbidities is not uniform across all populations due to longstanding systemic inequities. Interventions focusing on priority populations can help reduce disparities and ensure effective use of limited public health resources. Using mathematical models to aid in planning and evaluating such intervention strategies requires structured, multi-population models capturing the necessary population stratifications. Due to varying interactions among different groups, benefits from interventions serving certain groups may also affect outcomes in other groups (spillover effect). While spillover effects have important public health implications, their direct mathematical analysis is challenging, given their inherently nonlinear, time-dependent nature. Thus, standard analytical techniques based on linearization are ineffective. We examine this issue by mathematically formalizing the notion of spillover effects and exploring different approaches for their analysis. For smaller models, we discuss direct approaches and formally establish several results. For larger-scale models, we discuss data-driven methods based on polynomial chaos expansion. We will use models of HIV transmission as illustrative examples, however, the concepts discussed also apply more generally.

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MS29

A Computational Model for Occlusive Arterial Thrombosis

The generation of occlusive thrombi in stenotic arteries involves the rapid deposition of millions of circulating platelets under high shear flow. The process is mediated by the formation of molecular bonds of several distinct types between platelets; the bonds capture the moving platelets and stabilize the growing thrombi under flow. We investigated the mechanisms behind occlusive thrombosis in arteries with a two-phase continuum model. The model explicitly tracks the formation and rupture of the two types of interplatelet bonds, the rates of which are coupled with the local flow conditions. The motion of platelets in the thrombi results from competition between the viscoelastic forces generated by the interplatelet bonds and the fluid drag. Our simulation results indicate that stable occlusive thrombi form only under specific combinations for the ranges of model parameters such as rates of bond formation and rupture, platelet activation time, and number of bonds required for platelet attachment.

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MS29

Modeling the Role of Protein S in Coagulation

Anticoagulant proteins regulate blood coagulation, protecting against unnecessary and pathological clotting. Protein S (PS) is an important anticoagulant. For instance, a type of pathological clotting known as deep vein thrombosis is associated with deficiencies in PS. Nevertheless, much remains unknown about PS. We study a notable anticoagulant function of PSits enhancement of the activity of the α-isomer of tissue factor pathway inhibitor (TFPIα), where TFPIα inhibits the procoagulant protein known as factor Xa (fXa). This enhancement due to PS likely arises because in the presence of PS, TFPIα binds more effectively to phospholipid membranes than otherwise, thereby bringing TFPIα in close proximity to fXa on phospholipid membranes. However, since blood flow tends to wash away unbound proteins, and since PS anchors TFPIα to phospholipid membranes, we hypothesize that flow critically regulates anticoagulant interactions involving PS and TFPIα. Hence, we turn to an established model of coagulation under flow. The model consists of a system of several hundred ordinary differential equations based on mass-action kinetics with experimentally-determined parameters. To account for PS in the model, we incorporate new terms describing the enhancement of TFPIαs inhibition of fXa on phospholipid membranes and in the tissue factor-factor VIIa-fXa complex; as well as interactions between factor V isomers, TFPI and PS.

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MS29

A Mechanistic Model of Emicizumab

Emicizumab is a bispecific antibody that brings together activated Factor IX and Factor X, replacing the missing Factor VIII in hemophilia A patients. Although widely used, the lipid-surface dependence of emicizumab is not well understood. A key mechanistic difference between emicizumab and FVIII is that emicizumab does not bind directly to the lipid surface, while FVIII does. In biochemical assays, emicizumab has been shown to inhibit FX activation by TF:VIIa a lipid-surface dependent reaction. Previously, we developed and validated a mathematical model that uniquely captured the lipid-surface dependence of TF:VIIa activation of FX. In this work, we expand the model to include emicizumab and consider all plausible biochemical mechanisms. As emicizumab does not bind TF:VIIa, this tests interaction of emicizumab and FX alone, a one arm interaction. We calibrate the model with experimental data under several conditions and explore two sets of kinetic parameters previously reported. Results agree with experiments and capture the inhibitory effect of high concentrations of emicizumab on FX activation. Through parameter exploration, we determine the mechanism of the interaction and discover that kinetic rates derived from surface plasmon resonance (SPR) measurements may be inaccurate. Future directions include expansion of the study to fully understand the effects of surfaces on the efficacy of emicizumab via the inclusion of FIXa, a two arm interaction.

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MS29

Parallel multiscale 3D simulations of thrombus growth under flow

We have developed a 3D multiscale framework to simulate thrombus growth under flow comprising four individually parallelized and coupled modules: a data-driven Neural Network (NN) that accounts for platelet calcium signaling, a Lattice Kinetic Monte Carlo (LKMC) simulation for tracking platelet positions, a Finite Volume

Method (FVM) simulator for solving convection-diffusion-reaction equations describing agonist release and transport, and a Lattice Boltzmann (LB) flow solver for computing the blood flow field over the growing thrombus. Parallelization was achieved by developing in-house parallel routines for NN and LKMC, while the open-source libraries OpenFOAM and Palabos were used for FVM and LB, respectively. Importantly, the parallel LKMC solver utilizes particle-based parallel decomposition allowing efficient use of cores over highly heterogeneous regions of the domain. The parallelized model was validated against a reference serial version for accuracy, demonstrating comparable results for both microfluidic and stenotic arterial clotting conditions. Moreover, the parallelized framework was shown to scale essentially linearly on up to 64 cores. Overall, the parallelized multiscale framework described here is demonstrated to be a promising approach for studying single-platelet resolved thrombosis at length scales that are sufficiently large to directly simulate pathophysiologically relevant blood vessels.

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MS30

Controlling Cell Fate Transitions: Landscape and Path of Gene Networks

Cellular functions in biological systems are regulated by the underlying gene regulatory networks. How to investigate the dynamics and stochasticity in cell fate transitions of gene networks is a challenging problem. In this talk, I will present some approaches we recently developed, i.e., the dimension reduction of energy landscape, the transition path, and the landscape control approach, to study the stochastic dynamics of gene networks. The basins (attractors) on the landscape characterize different cell types (stable states), with the barrier heights between stable states quantifying the relative stability of different cell fates. The transition paths based on the minimum action principles quantify the transition dynamics between different cell states. We also developed a landscape control approach to control cell fate transitions in gene regulatory systems. I will also discuss some applications of these approaches in various biological systems, including cell cycle, cancer network, and neural dynamics.

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MS30

A Statistical Physics Approach to the Coordination and Multistability of Cell States in Tissue

Multicellular organisms exhibit a variety of cell types supporting numerous tissue functions, yet it remains unclear how interacting cells can precisely coordinate their gene expression during tissue self-organization. We develop a generalized model of multicellular gene expression that includes intracellular and intercellular gene interactions in tissue-like collectives. We represent multistable cellular phenotypes by mapping the binarized transcriptional patterns of individual cells onto Hopfield networks, and incorporate cell-cell signaling by coupling transcriptional cell states on a graph. We show how tuning the intercellular signaling strength results in a cascade of transitions toward different collective states with emergent single-cell phenotypes. We find that disordered intercellular signaling tends to stabilize a surprisingly small number of compositionally and spatially simple tissue types. These results establish a theoretical framework to investigate how cell collectives self-organize into distinct stable patterns, and to study reprogramming at both the cellular and tissue levels.

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MS31

Dynamics of Sleep-Wake Regulation Across Early Childhood Development

Sleep-wake patterns exhibit great variability across early childhood development. The transition from a biphasic pattern, consisting of a midday nap and a nighttime sleep, to a monophasic pattern of consolidated behavior is an important milestone for young children. In this talk, we present a physiologically-based mathematical model of the sleep-wake regulatory network, that also includes feedback from the circadian system and the homeostatic sleep drive. By integrating observational and experimental data from preschool-aged participants, we identify parameter sets that accurately reflect the sleep behaviors of 2-year-olds (napping) and 5-year-olds (non-napping). We vary a subset of six model parameters associated with the dynamics and sensitivity to the homeostatic sleep drive based on different evolution trajectories, and thus, generate diverse bifurcation sequences that represent varying ages of transition onset, transition durations, and transitional sleep patterns. Time-permitting we will discuss the effect of light exposure on the sleep-wake patterns generated during this transition.

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MS31

Exploring the Impact of Calcium Buffering on Spike Frequency Adaptation Linked to Neuropathic Pain

Parvalbumin-expressing interneurons (PVINs) within the dorsal horn of the spinal cord play a crucial role in preventing touch inputs from activating pain circuits. During nerve injury, however, PVINs' output decreases via mechanisms that remain not fully understood. We recently showed that PVINs from nerve-injured male mice change their firing pattern from tonic to adaptive. To examine the ionic mechanisms responsible for this decreased output, we used a reparametrized Hodgkin-Huxley type model of PVINs to predict that this transition in firing pattern occurs due to an increase in the contribution of small conductance calcium-activated potassium (SK) channels, enabled by impairment in intracellular calcium buffering systems. Analyzing the dynamics of the Hodgkin-Huxley type model demonstrated that a generalized Hopf bifurcation differentiates between the two types of state transitions observed during adaptation in PVINs. By embedding the PVIN model within a neuronal circuit model of the spinal dorsal horn, we further showed how this adaptation allows for an increase in circuit output responsible for generating neuropathic pain. These predictions were all validated experimentally. In this talk, I will provide an overview of the methods applied and the results obtained.

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MS31

The Effect of Short Term Plasticity on the Synchrony and Rhythms of Hippocampal Interneurons

Neurons in hippocampus have been shown to coordinate their activity to form coherently firing networks at physiological frequencies. Interneurons (relatively few in number) are thought to provide a base non-plastic rhythm that can drive excitatory neurons (more numerous). Interneuron microcircuits in vitro, in vivo, and in silico have thus been extensively studied, with an emphasis on synchronous firing assemblies at gamma frequencies. More recently, the possibilty neuromodulation of interneurons in hippocampus has been experimentally studied, with evidence that PV+BCs do allow for neuromodulation through short term plasticity mechanisms at the presynaptic membrane. A model of the mechanism was parameterized from this data (leading to depression), which can be tuned to also apply to other types synapses (facilitating or mixed). In this talk we examine the effect of adding STP on interneuron microcircuits, both computationally and analytically. Small numbers of PV+BCs are studied, and their behavior is compared with large network simulations, and a mean-field approximation of the latter.

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MS32

Bystander Effect as an Emergent Property of Individual Psychological Prospects

The bystander effect is a sociological phenomenon in which individuals are less likely to help a person in need if there are others present. Sociologists and psychologists have proposed multiple plausible reasons for the bystander effect, from ambiguity and group cohesiveness to diffusion of responsibility and mutual denial. We build a dynamical systems model based on these sociological and psychological hypotheses, along with ideas borrowed from behavioral economics; in particular, we use prospect theory to predict an individuals decision to take action or not. With this model, we find the conditions under which a bystander effect emerges from these individual decisions, and we validate with experimental and observational data from social psychology studies.

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MS32

A Mechanistic Model of Gossip, Reputations, and Cooperation

Social reputations facilitate cooperation by indirect reciprocity: someone who behaves altruistically improves their reputation, which makes others more likely to help them in the future. But when people hold private views of one another, reputation-based indirect reciprocity breaks down because disagreements can lead to perceptions of unjustified behavior that ultimately undermine cooperation. Theoretical studies often assume full agreement about reputations, invoking rapid gossip as an endogenous mechanism for reaching consensus. However, the theory of indirect reciprocity lacks a mechanistic description of how gossip generates consensus. We develop a mechanistic model of gossip-based indirect reciprocity that incorporates two forms of gossip: exchanging information with randomly selected peers or consulting a single gossip source. We show that these two gossip processes are mathematically equivalent under an appropriate transformation of parameters. We then derive an analytical expression for the minimum amount of gossip required to stabilize cooperation and discuss how this critical gossip duration depends on model parameters. Finally, we show that biased gossip can either facilitate or hinder cooperation, depending on the direction (positive or negative) and magnitude of bias. Our results contribute to the growing literature on cooperation facilitated by communication and highlight the need to study strategic interactions and information spread in a coupled context.

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MS32

Mutation-selection Dynamics: Progress and Challenges

In evolutionary game theory, many studies focus on processes with little or no strategy mutation. While this assumption is justified in many settings, there are others in which the transmission of traits from parent to offspring is less faithful. One example is when strategies are spread through imitation (rather than reproduction) and mutation is interpreted as exploration. I will discuss a standard approach to modeling mutation-selection dynamics, along with some recent results for how to evaluate mean frequencies in spatially-heterogeneous populations. I will conclude with an outlook for future directions, aimed at describing more realistic populations, which current models fail to capture.

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MS32

Reasoning About Errors and Reputations Within Indirect Reciprocity

Indirect reciprocity serves as a pivotal mechanism in fostering cooperative behaviour within social groups. However, challenges arise in maintaining its effectiveness due to errors in assessments and actions, leading to disagreements on reputations and an unravelling of cooperation. To address these challenges, we explore two cognitive mechanisms, Bayesian and abductive reasoning. By considering the probabilities of errors along with prior beliefs about the prevalence of good and bad individuals, observers employ reasoning to aide in evaluating the reputations of others. Under Bayesian reasoning, this is an application of Bayes' rule. While under abductive reasoning, individuals' beliefs and observations are combined to infer reputations. Further, abductive reasoning is in a sense "lazy" since it only considers the simplest explanations when accounting for errors. We assess the effectiveness of such reasoning on promoting cooperation under various conditions. We find that Bayesian reasoning generally undermines cooperation relative to the non-reasoning and abductive reasoning models, expect for the Scoring norm. Abductive reasoning generally outperforms the non-reasoning and Bayesian reasoning models but may undermine cooperation in high-error situations. Further, we find that a slight pessimism about the reputations of others or a resistance to changing reputations can benefit cooperation.

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MS33

A Network Model for Phenotypic Switching in Bacterial Populations

Bacterial populations can consist of several isogenic subpopulations known as phenotypes. Individuals in a bacterial population can switch from one phenotype to another to adapt to changing environments. Kussell et. al. [*Science*, 2075, (2005)] studied a model of a bacterial population with inter-phenotypic switching, consisting of n phenotypes and n environments. They derived an analytical expression for the "Lyapunov exponent", which is a measure of the asymptotic growth rate of the total population. We study a network of n nodes in which some of the inter-phenotypic switching rates are zero and thus the network representing the bacterial population is not a complete graph. We compute the Lyapunov exponent of bacterial populations corresponding to different network models, both numerically and analytically via modifications to the originally derived analytical expression. We find that the approaches that we consider in this work can be used to compute the Lyapunov exponent in a parameter regime where the original expression cannot be used.

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MS33

A Data-Driven Model of Portland Policing

This talk introduces a mathematical model examining the association between policing dynamics and criminal behavior in Portland, Oregon. Using offense statistics and police presence data, a 1st-order non-linear system of differential equations is constructed to capture key variables, including the number of offenders, victims, police presence, and reported crimes. The study assumes homogeneously well-mixed populations, with results suggesting individuals susceptible to offenses may become offenders, victims represent those engaged in meaningful social interactions with offenders, and individuals can report offenses through police encounters. The findings elucidate the dynamics of neighborhood populations interacting with the police, addressing the decision to report crimes, and exploring underreporting dynamics influenced by social factors. The talk summarizes successful data combination, model formulation, and parameter fitting per neighborhood, aligning with average trends in police dispatches and crime reports. The results bear significance in understanding how neighborhood populations interact with local law enforcement. Future work is proposed to adapt the model for various crime types, considering economic and social factors.

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MS33

Inclusivity in Mentorship: Engaging Undergraduates in Exploring Computational Fluid Dynamics and Marine Organism Movement

Exploring fluid-structure interaction simulations of biological organisms can pose a significant challenge for undergraduate researchers, especially those without prior fluids coursework or substantial coding experience. This talk will focus on a recent project that has included undergraduate researcher collaboration, numerical simulations of swimming blue blubber jellyfish. Despite their large lobed oral arms and staccato-like bell pulsation, blue blubber jellyfish have relatively high propulsive efficiency. Typically, oral arms and tentacles are neglected in numerical simulation, the novelty in this work is the inclusion of varying biologically informed oral arm morphologies. This research area might seem unsuitable for undergraduates due to the complexity of the governing equation, the incompressible Navier-Stokes equations, and the computational

demands for solving them in a three-dimensional domain. Additionally, the organisms' elasticity requires specialized numerical methods for handling fluid-structure interface boundary conditions. To address these challenges, I've incorporated inclusive mentorship practices. The talk will first present the research aims and outcomes from the blue blubber simulations, offering insights into new findings and the project's complexities. The second part will outline mentoring approaches used in this and other collaborations with undergraduate students.

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MS33

Ola I Ka Aina: An Ecosystem Revitalization Guided by Native Hawaiian Knowledge

This is an exploration of an innovative project centered on the revitalization of a fish pond ecosystem, guided by Native Hawaiian indigenous knowledge, through an integrated approach that leverages applied mathematics and ecology. The initiative seeks to harmonize traditional wisdom with modern quantitative tools to restore and sustainably manage a fishpond. The project is leaning into Native Hawaiian traditional methods of caring for the land, and is employing mathematical models, statistical analyses, and ecological principles. The goal is to optimize the balance between biodiversity and water quality, and more importantly, to build trust between traditional ecological knowledge practitioners and western scientists. This holistic approach not only addresses the ecological challenges but also respects and integrates the rich heritage of Native Hawaiian wisdom. This will serve as a model for fostering sustainable ecosystem management that bridges the gap between ancient traditions and contemporary science.

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MS34

Organelle Size Scaling and Fluctuations Within a Stochastic Gene Expression Model of Cell Growth

The size of the nucleus scales robustly with cell size so that the nuclear-to-cell sizethe N/C ratiois maintained during growth in many cell types. To address the fundamental question of how cells maintain the size of their organelles despite the constant turnover of proteins and biomolecules, we model the synthesis of macromolecules during growth using a simplified stochastic gene translation model and its corresponding chemical master equation (CME). We show how the CME can be solved analytically to obtain a joint probability distribution of the protein numbers, and how this distribution is used to calculate the mean and variance of the N/C ratio.

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MS34

Predicting Noise-Induced Calcium Waves

We employ Large Deviations Theory to predict the most likely means that noise can induce cell-wide waves of calcium. To do this, we outline a microscopic model consisting of N stochastic calcium channels coupled with a PDE governing the concentration of calcium and other signalling molecules. We estimate the relative likelihood of different solution trajectories using the theory of Large Deviations. The equations yielding the optimal trajectory are determined using the calculus of variations. Finally our results are compared with experimental data from the lab of Gaetan Barbet.

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MS34

Effect of Noise on Intracellular Transport of Intermediate Filaments

Noise affects all biological processes from molecules to cells, organisms and populations. Although the effect of noise on these processes is highly variable, evidence is accumulating which shows natural stochastic fluctuations (noise) can facilitate biological functions. Herein, we investigate the effect of noise on the transport of intermediate filaments in cells by comparing the stochastic and deterministic formalizations of the bidirectional transport of intermediate filaments. Intermediate filaments are long elastic polymers transported along microtubules within cells by antagonistic motor proteins. By numerically exploring discrepancies in timescales and attractors between both formalizations, we characterize the impact of stochastic fluctuations on the individual and ensemble transport. Noise is found to promote the collective movement of intermediate filaments by reducing the impact of initial distributions of motor proteins in cells and increase the efficiency of the transport regulation by the biochemical properties of motor-cargo interactions.

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MS35

Exploring Regulation of the Molecular Motor Myosin Across Scales of Complexity

The inside of a cell is both incredibly crowded and highly organized. It is this organization that allows it to be an exciting environment capable of the functions associated with life. Important players in a cells ability to maintain an ordered state are motor proteins. These microscopic engines allow a cell to transport, compartmentalize, and arrange its components by generating force and creating motion. In this talk, I will discuss work to understand how the motor protein myosin is regulated in a cell. I will highlight studies and associated models that span scales of size and complexity, from single motor studies of purified proteins (nanometer-scale) to studies of ensembles of motors working together in phagocytosis (micrometer-scale) to in-

vestigations of the mechanical properties of muscle fibers (millimeter-scale). Uniting these studies is a focus on understanding how forces can regulate motor function.

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MS35

Cover Times Under Stochastic Resetting

Cover times indicate the time taken to comprehensively search a region of space with examples in biology ranging from immune system defense to animals scavenging for food. However variable in spatial and temporal scale, such search processes are ubiquitous in nature and warrant rigorous and generalizable mathematical treatment. In this talk, we consider cover times associated with a wide class of stochastic search processes under frequent stochastic resetting. By assigning to a searcher a detection radius, we define the cover time of a target region as the first time that all of the region has been detected. Using recent results on the corresponding first hitting time problem, we determine the full distribution and moments of cover times in the frequent resetting limit. Our results depend only on two measurable system parameters: searcher diffusivity and a geodesic length between the resetting and target regions. In contrast to simulation, applying our analytical results to specific systems is straightforward.

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MS35

Modeling the Mechanics of Actomyosin Structures

Many essential cellular processes depend on subcellular structures capable of generating active forces. One such structure is the stress fiber (SF), composed of actin filament bundles with force-generating myosin motor proteins. These fibers can adhere to the cellular environment and have a contractile tension along their length which is harnessed by the cell for functions such as migration and mechanotransduction. While there have been studies on the rheology and assembly of individual SFs, how embedding them in the cytoplasm impacts subcellular flows and forces is still not well understood. It is also unknown how these flows and forces scale with cell shape and size, or fiber orientation, position, and density. To address these questions, we model stress fibers as 1D viscoelastic contractile structures, embedded in a compressible, potentially contractile, viscous fluid representing the cytoskeletal mesh. We simulate the system with the immersed boundary method, varying the SF mechanical properties, position, and density to investigate the emergent subcellular flows and forces. We show that our model reproduces classical experimental results, e.g. SF response to laser ablation, and then use the model to further predict the role of stress fibers and how their effects scale with cell size and geometry. Our work highlights the relevance of hydrodynamic interactions between stress fibers and other higher-order contractile actin structures which make up the cytoskeleton.

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MS35

Bridging the Molecular to Cellular Scale of Molecular Motor-Based Intracellular Transport with a Combination of Mathematical Modeling and Biophysical Experiments

Intracellular transport starts when molecules are packaged into vesicles. Then, molecular motors diffusing on the vesicle surface bind to and "walk" along the cytoskeleton, the network of protein filaments spanning the cell interior. Much is known about how single molecular motors move along a single protein filament. Less is known about how multiple motors navigate a vesicle through the cytoskeleton. To bridge this gap, we made a mathematical model, which keeps track of the position and orientation of the vesicle, and the position of and forces on each motor. Using parameters from single motor measurements, the model updates the position and state of each motor. In collaboration with an experimental lab, we defined model parameters, validated its predictions, and reproduced measurements of multiple myosin Va molecular motors transporting vesicles through 3D networks of actin filaments. We then used the model to determine how actin filament density affects transport through a randomly oriented actin network. With increased actin density, vesicles transition from directed transport on single actin filaments to an apparent random walk, resulting from a mixture of transport and tug-of-wars. This phase transition arises from a percolation phase transition at a critical number of accessible actin filaments, N_c. N_c is a geometric property of the actin network that depends only on the position and polarity of the actin filaments, transport distance, and vesicle diameter.

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MS36

Toward an Electro-Fluid-Mechanical Model of the Human Heart

We present a model of the human cardiac conduction system, governed by monodomain equations. Electrical activation begins at the sinoatrial node (SAN) in the right atrium, modeled as a one-dimensional structure. Signals then propagate through a three-dimensional atrial model. A one-dimensional tree represents the atrioventricular node (AVN), bundle of His, and Purkinje network, connecting atria and ventricles. Coupling meshes with different codimensions is achieved via an operator splitting algorithm. Monodomain equations are solved using implicit-explicit methods, and explicit methods solve ionic models. Developing human cardiac electrophysiology models presents challenges, requiring fine meshes for wave propagation resolution. Additionally, the absence of human ionic models for specific cell types, such as the AVN, is a significant obstacle. Often, human phenomenological or biophysically detailed models from other species are used. Moreover, coupling meshes with different codimensions necessitates care-

ful parameter selection due to varying resting potentials in different heart regions. We will address these challenges through the lens of our patient-specific model. Finally, we will explore the potential integration of our model with a comprehensive fluid-structure interaction (FSI) model of the human heart. The FSI model, based on the immersed finite element-difference method, extends the immersed boundary method.

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MS36

Modeling Thrombosis on Moving Structures

Blood clotting is a complex phenomenon which involves interplay between biochemistry and fluid-structure interactions. A complicated set of protein interactions must occur in order to activate platelets and promote the formation of platelet-subendothelium and intraplatelet bonds, which form the bulk of the initial thrombus. The thrombus behaves as a porous viscoelastic material whose properties and size evolves with the flow. Herein we present a model of porous, viscoelastic growth in the presence of a moving structure. While we approach the model from the perspective of thrombosis on moving structures, e.g. on the aortic valve, our approach can be extended to model other systems that involve deposition and growth of a viscoelastic material.

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MS36

Patient-Specific Models of Transcatheter Aortic Valve Replacement Using the Immersed Finite Element-Difference Method

Transcatheter aortic valve replacement (TAVR) is the implantation of an artificial aortic heart valve without an open-heart surgery. Computer modeling and simulation is an important tool in the process of transcatheter aortic valve (TAV) device design, regulatory approval, and indication in the care of specific patients, since there are still many open questions surrounding post-implantation complications. Improved computational models beyond those in the existing literature have the ability to provide more accurate performance predictions for individual patients. We present computational fluid-structure interaction models of TAVs using the immersed finite element-difference method. We perform dynamic simulations of crimping and deployment of the devices as well as their behavior across the cardiac cycle in a patient-specific aortic root anatomy reconstructed from CT image data. These IFED simulations incorporate biomechanics models fit to experimental tensile test data and automatically capture the contact within the devices and between the stents and native anatomies. We apply realistic driving and loading conditions based on clinical measurements of human ventricular and aortic pressures and flow rates. Our models provide informative clinical performance predictions, such as pre- and post-procedure transvalvular pressure differences, detailed flow patterns, leaflet dynamics, and valve orifice areas.

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MS36

Fluid Dynamics of Tubular Hearts

The vertebrate embryonic heart first forms as a valveless, tubular pump, and several different pumping mechanisms have been suggested to drive blood flow in these tubular hearts. The particular pumping mechanism employed is significant because it changes the force patterns that act on the cardiac wall, which in turn affects the proper development of the heart tube into the fully developed adult chambered heart. First, we explore a 2-point dynamic suction pumping heart tube model. The heart and circulatory system is modeled as a closed "racetrack" with two actuation points along a section of straight elastic tube. The immersed boundary method is used to solve the fully-coupled

fluid structure interaction problem of an elastic, valveless tubular heart immersed in a viscous and incompressible fluid. We analyze flow behavior and wall movement in immersed boundary simulations of our heart tube model for a range of parameters of interest. Our preliminary results suggest that both Womersley number and pumping phase difference play a significant role in the effectiveness of the 2-point dynamic suction pumping mechanism.

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MS37

Efficient Methods for Generating Virtual Populations with Applications for Infectious Diseases

Virtual patient cohorts (VPCs) are computer-generated representations of patients that mirror real-world populations employed to study biomedical problems for several compelling reasons. For instance, VPCs allow for the comprehensive exploration of disease mechanisms and therapeutic responses at low-cost and no burden to patients. Our lab has recently used VPCs in a variety of applications to, for example, distinguish the mechanisms driving severity in immunosuppressed and cancer patients with COVID-19. However, a knowledge gap exists in the generation of such VPCs when clinical outputs (e.g., cytokine and cellular concentrations) display overlapping distributions, making it difficult to discriminate between the patients of those groups. Our focus is the implementation of Approximate Bayesian Computation (ABC), which leverages Bayesian inference to estimate posterior distributions of parameters for simulation-based models, while integrating Markov Chain Monte Carlo (MCMC) techniques in ABC to enhance efficiency of VPC generation. Our primary goal is to apply the ABC- MCMC method to distinguish parameters from overlapping output distributions. The findings of this research will be applied in the study of infectious diseases. With the help of VPCs, we can test different drug combinations and treatment plans before performing clinical trials using virtual clinical trials, which enables the customization and personalization of treatment plans for different patient groups.

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MS37

Virtual Trial Simulations to Support Dose Optimization in Oncology Drug Development

While the field increasingly recognizes the importance of developing mechanistic models aligned with biological processes and drug mechanisms, akin to systems biology and quantitative systems pharmacology, this presentation takes a statistical approach to highlight the value of employing statistical sampling strategies in virtual trial simulations to assess the likelihood of tumor response to a given treatment and dose-response relationship. This talk delves into response variations and dose dependency across patients and clinical scenarios, with calibration against clinical data. Notably, the empirical statistical models, even without detailed considerations of tumor biology, prove to be valuable in predicting the statistical probability of a tumor lesion responding to treatments. In a case study utilizing statistical sampling strategies, we synthesize clinical trials to predict the optimal doses of targeted therapies and how we can use virtual trial simulation to support the selection of optimal doses. We contend that statistical models, offer a complementary "top-down" method to extract insights from clinical observations and inform the likelihood of a patient responding to treatments and potential dose-response relationships.

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MS37

Digital Twins Enabled Partial Pediatric Extrapolation

Quantitative systems pharmacology (QSP) models are promising approaches that aim to mechanistically combine representations of key pathophysiology and the mechanism of action of a drug. QSP models are increasingly applied in drug discovery and clinical development to aid in the understanding of the interactions between disease biology and the drugs effect. These models are particularly useful in representing monogenic diseases where there is a clear understanding of the etiology of dysfunction. Virtual patient populations (VPs) are collections of simulated patients generated by sampling distributions of relevant QSP model parameters, allowing the representation of diverse patient subgroups and recapitulating the observed biological variability that exists in the disease being modeled. QSP models informed by clinical data can simulate the effect of a drug in a sub-population of patients that may not be feasible to include in a clinical trial. These predictions of drug efficacy are possible due to the QSP models mechanistic representation of the new virtual population with the knowledge gained from previous clinical trials. In this study, we applied this approach to partially extrapolate the efficacy of olipudase alfa from adult to pediatric acid sphingomyelinase deficiency (ASMD) patients. Our results suggest that QSP models can be a useful tool for exploring the potential effects of drugs in vulnerable patient sub-populations.

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MS37

Do Digital Twins Need Qsp-Based Pharmacometric Vaccinations?

This presentation will start with definitions, use cases, and challenges for digital twins and their cousins, virtual populations. Applications and impact of QSP and virtual populations will be presented, focusing on how they can help enable execution, innovation, and earlier decision-making while mitigating risk. Examples may include: ? supporting vaccine RD decisions like dose-level and regimen through compartmental models; ? an approach to mitigate the surprisingly large potential impact (on efficacy estimation and clinical trial duration) of false positive and false negative sample-testing errors; ? model-based meta-analysis (MBMA) methods and their application for decision support for RSV and COVID vaccines; ? how MBMA models (1) enabled prediction of efficacy (RSV prophylaxis for infants) of maternal RSV vaccination and of a monoclonal antibody; and (2) improved interpretation of the immunogenicity of pneumococcal conjugate vaccines ("PCVs"), en-

abling better prediction of the potential public health impact of novel PCVs on breakthrough invasive pneumococcal disease; and ? methods using subject-level data to estimate risk curves as a function of immunological measures of response to vaccination (e.g., serum neutralizing titer) and to estimate efficacy, and effects of demographic subgroups (e.g., age group, past infection).

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MS38

Non Linear Metric and Machine Learning Methods for Partial 3D Registration and Automating Atomic Model Building in Cryo-Em

Recent advances in microscopy and techniques for extracting biological shapes, from the atomic to the cellular scales, have led to a surge of data with new mathematical and computational challenges associated with it. In this context, my group recently developed several computational methods that take advantage of non-linear metrics in shape space, with a focus on studying 3D maps of biomolecules imaged from single particle cryogenic electron microscopy (cryo-EM). As aligning maps remains challeng- ing in the presence of a map that only partially fits the other (e.g. one subunit), we propose a new procedure for partial alignment of 3D maps that first finds a coupling between 3D point-cloud representations associated with their so-called unbalanced Gromov Wasserstein divergence, and second, uses this coupling to find an optimal rigid body transformation. We further use this framework to develop new algorithms for automating and optimizing atomic model building, and develop new metrics for learning continuous conformational heterogeneity. Our method generally outperforms standard linear methods for aligning subunits of a protein complex and fitting atomic models to a density map, suggesting potential applications of Partial Optimal Transport for improving Cryo-EM pipelines.

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MS38

Constraining Generative Molecular Models with Human Physiology

Realizing the full potential of modern biotechnology requires integration of advanced experimental and computational tools. This talk will describe our approach to integrate in data-driven and systems modeling approaches that empower biological discovery and design for biological design problems. To bridge the gap between molecular structure and the constraints of human physiology, we use a language model, which is pretrained on extensive databases of molecular sequences, to design of drug-like molecules whose properties meet the demands of human pharmacokinetics.

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MS38

Novel Topological Metrics of Protein Structure Complexity

Understanding the interplay between sequence, structure and function of biopolymers is a major problem in Biology and Bioengineering, at the core of protein folding, protein aggregation and cell nucleus organization and function. The single, pairwise, or multi-chain characterization of entanglement complexity becomes rigorous in the context of mathematical topology. A biopolymer can be seen as a simple mathematical curve in 3-space, which can attain many different conformations. Mathematical curves in 3-space are studied in Knot Theory, however, biopolymers are, in principle, not mathematical knots, since they have open ends. In this talk we will introduce a rigorous and general topological approach to analyze the structures of such macromolecules using new methods in knot theory. We will apply our methods to proteins and show that these can be used to characterize all protein structures and that experimental folding rates correlate with the conformational complexity that these measures capture, in the absence of knotting. By analyzing structures in the Protein Data Bank we can obtain a representation of the native topological landscape of proteins that provides a new way of understanding their structures. When applied to the SARS-CoV-2 spike protein, we see that the local native topological landscape can predict residues where mutations can have an important impact on protein structure and possibly in viral transmissibility.

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MS38

Automated Analysis of Nmr Data with Bayesian Nonparametric Statistical Learning

The faithful interpretation of nuclear magnetic resonance (NMR) data is central to Biophysics and Biochemistry. Unluckily, the analysis of NMR data, especially data from complex biomolecular systems, presents a significant challenge as it requires accurate characterization of individual resonances which is most often obscured not only by noise, but also by chemical exchange and structural uncertainties in the probed systems. For instance, raw NMR signals often capture an unknown set of resonances and/or resonances with unknown features such as chemical shifts, relaxation, and exchange rates. In addition to these challenges, manual analyses of NMR signals are also hindered by overlapping resonances and vast amounts of data that remain inconclusive without efficient processing. In this talk I will present a comprehensive mathematical framework for fully automated NMR data analysis. Our approach relies on nonparametric data representations and Bayesian parameter estimation techniques that allow for: identification and characterization of every resonance in an NMR dataset, noise deconvolution, and extensions to multidimensional NMR data or data from specialized protocols. Our work offers a promising avenue for automated in-depth analysis of complex NMR datasets.

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MS39

Social Dilemmas of Sociality Due to Beneficial and Costly Contagion

Levels of sociality in nature vary widely from solitary species to complex multi-family societies. Increased levels of social interaction can allow for the spread of useful innovations and beneficial information, but can also facilitate the spread of harmful contagions, such as infectious diseases. In this talk, we will explore how coupled contagion processes can help shape the rules for interaction in complex social systems. We consider a model for the evolution of sociality strategies in the presence of both a beneficial and costly contagion, and study dynamics of this model at multiple timescales. We use a susceptible-infectious-susceptible (SIS) model to describe contagion spread for given sociality strategies, and then employ the adaptive dynamics framework to study the long-time evolution of the levels of sociality in the population. For a wide range of assumptions about the benefits and costs of infection, we identify a social dilemma: the evolutionarily-stable sociality strategy (ESS) produced by adaptive dynamics is distinct from the collective optimum. In particular, the ESS level of social interaction is greater (respectively less) than the social optimum when the good contagion spreads more (respectively less) readily than the bad contagion. Our results shed light on how contagion shapes the evolution of social interaction, but reveals that evolution may not necessarily lead populations to social structures that are good for any or all.

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MS39

Within-Host Dynamics of Sars-CoV-2: Parameter Estimates, Identifiability, and Modelling De Novo Mutant Generation and Transmission

Despite a relatively low mutation rate, the large number of SARS-CoV-2 infections has allowed for substantial genetic change, leading to a multitude of variants of concern. Utilizing recently determined mutations rates (per site replication), as well as within-host parameter estimates for hospitalized SARS-CoV-2 infections, we applied a stochastic transmission bottleneck model to describe the survival probability of rare de novo SARS-CoV-2 mutations. In the first part of this talk I will briefly discuss the significance and relevance of our within-host infection parameters. I will then discuss our work on SARS-CoV-2 within-host evolution where we compute the survival probability of neutral mutations (no phenotypic effect), and various mutations affecting viral life history. We examine transmission bottlenecks of varying sizes, estimating which mutations are most likely to occur de novo and be transmitted during a single infection. This work offers both a null model for SARS-CoV-2 substitution rates and predicts which aspects of viral life history are most likely to successfully evolve, despite low mutation rates and repeated transmission bottlenecks.

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MS39

The Effect of Climate Change on Vector-Host Populations in West Nile Virus Modeling

Over the past 25 years, three mosquito-borne diseases were introduced to the Americas and quickly spread within a matter of months. The expansion and spread of mosquito-borne diseases continues to be a concern due to the continued effects of climate change. Mosquito biology and vector epidemiological processes are heavily influenced by environmental factors, such as temperature and precipitation. This talk will introduce a three population partial differential equations model for West Nile Virus (WNV) transmission the most common vector-borne disease in the continental US between mosquito vectors, bird hosts, and human hosts. The model includes time and temperature dependence on demographic and epidemiological processes, and considers infection-age structure for mosquito vector and bird host populations. We describe how we connect experimental infection and epidemiological data to infection-age dependent processes, and parameterize the model to human WNV case data from the Greater Toronto Area. We further show a range of scenario analysis projections under the RCP 4.5 and RCP 8.5 climate change scenarios to quantify the increased risk and variability for future WNV prevalence.

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MS39

Scaling Metabolic Models Describing Host-parasite Dynamics from Individuals to Populations

Temperature has strong effects on ectotherm diseases, leading to potentially complex effects of a changing climate. A challenge is that pathogens and their hosts each have temperature-dependent physiological responses, such that pathogen growth in or on hosts depends on thermal mismatches between pathogen and host thermal performance curves (TPCs). However, parameterizing predictive models based on vertical mismatches between pathogen and host TPCs is difficult due to inseparability of key parameters when fitting models to infection data. A proposed solution is to describe pathogen and host TPCs

using models based on the metabolic theory of ecology (MTE). These models assume that pathogen infectivity and host resistance are physiological rate processes governed by organism metabolic rates, allowing partial model parameterization using separately measured proxies of pathogen and host metabolic rates. We tested whether this approach could successfully describe temperature-dependent infection in a chytridiomycosis (Bd)-frog system using data from controlled-temperature infection experiments and metabolic proxies for the pathogen (e.g., zoospore swimming speed) and its frog host (respiration rate). This approach successfully described temperature-dependent growth rates and equilibrium dynamics of Bd on frogs and yielded biologically reasonable parameters and predictions, regardless of which organisms metabolic proxy (host or pathogen) generated our initial parameter estimates. Additionally, we conducted a mesocosm experiment to quantify the temperature dependence of this system in small populations of susceptible hosts. Remarkably, our MTE-based approach also provides good temperature-dependent predictions of pathogen load when scaling to these small populations, even when experimental results at this scale yield unexpectedly higher pathogen loads than in individuals.

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MS40

The Effect of Model Structure and Data Availability on Usutu Virus Dynamics at Three Biological Scales

Understanding the epidemiology of emerging pathogens, such as Usutu virus infections, requires systems investigation at each scale involved in the host-virus transmission cycle, from individual bird infections, to bird-to-vector transmissions, and to Usutu virus incidence in bird and vector populations. In this talk, I will present mathematical models for the within-host scale, bird-to-vector transmission scale, and vector-borne epidemiological scale investigating the dynamics of two strains of Usutu virus. I will use individual within-host infectious virus data and percent mosquito infection data to predict USUV incidence in birds and mosquitoes. I will address the dependence of predictions on model structure, data uncertainty, and experimental design.

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MS40

Mathematics of Malaria Transmission Dynamics: The Renewed Quest for Eradication

Malaria, a deadly disease caused by protozoan Plasmodium parasites, is spread between humans via the bite of infected adult female Anopheles mosquitoes. Over 2.5 billion people live in geographies whose local epidemiology permits transmission of P. falciparum, responsible for most of the life-threatening forms of malaria. The wide-scale and heavy use of insecticide-based mosquito control interventions, notably long-lasting insecticidal nets and indoor residual spraying), during the period 2000-2015, resulted in a significant reduction in malaria incidence and burden in endemic areas, prompting a renewed quest for malaria eradication. Numerous factors, such as Anopheles resistance to the currently-available insecticides used in mosquito control and anthropogenic climate change, potentially pose important challenges to the eradication efforts. In this talk, I will discuss a genetic-epidemiology mathematical modeling framework for assessing the combined impacts of insecticide resistance and climate change on distribution and burden of malaria mosquitoes and disease. Specifically, questions on whether eradication can be achieved using existing insecticide-based control resources will be addressed.

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MS40

Exploring Immune Responses to SARS-CoV-2 with an Agent-based Model

Affinity maturationthe process by which produced antibodies increase in affinity for antigenoccurs during the course of an immune response. Repeated exposures to the same antigen will produce antibodies of successively greater affinities, however, as antigen move away (in antigenic distance) from the initial strain, the ability of the body to cross-reactively neutralize the antigen decreases. This is a concern in the face of successive variants of concern (VOC) of SARS-CoV-2 that demonstrate an increase in antigenic distance from the original strain. Such VOCs would be less susceptible to any immune protection gained from vaccination and prior infection. We modeled adaptive immunity using an agent-based model (ABM) that considers B cells (nave, plasma, memory), antibodies, and antigens. We represent receptor (B cells, antibodies) and epitope (antigens) proteins in Euclidean shape space, simulating binding between these agents based on Hamming distance. We also consider the formation of immune complexesfree antibodies bind to antigen which limits the antigens ability to infect more cells. In this talk, we will present preliminary results

from our ABM including the examination of potential immune responses when presented with various VOCs and differing immune imprinting.

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MS40

Structural and Practical Identifiability Analysis of a Multiscale Immuno-epidemiological Model

We perform the identifiability analysis of a multiscale model of seasonal influenza with multiscale data. We show that the well studied target cell limited within-host model is not structurally identifiable. So, we reformulate the model and work with a scaled within-host model which is structurally identifiable. We find that the scaled within-host model is practically identifiable with respect to two distinct viremia data sets while fitting with weighted or unweighted least squares. We introduce a methodology on how to study the structural identifiability of multiscale epidemic models specifically nested immuno-epidemiological models. All parameters of the multiscale model are practically identifiable. Furthermore, we find that the practical identifiability of the multiscale model is significantly better when fitted to viremia and incidence data as opposed to when fitted to viremia and cumulative incidence data. Comparing first and second order numerical methods for solving the partial differential equations suggests that using a higher order numerical method does not affect the identifiability of the parameters. Further simulations suggest that the choice of the linking functions has some impact on identifiability when viremia and incidences are fitted but no impact when viremia and cumulative incidences are fitted.

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MS41

Stability-flexibility Dilemma in Individual and Social Cognition

Cognitive stability and flexibility are key ingredients of goal-directed behavior. In this talk we will discuss how a simple dynamic model of cognitive processing provides a mechanistic insight into the tradeoff between stability and flexibility in human goal-directed behavior, connecting theoretical insights from dynamical systems theory to data from task switching experiments. We will then discuss extensions of this model to the multi-agent setting in which we will explore the effects of heterogeneity in cognitive stability and flexibility across individuals on group performance in collaborative task switching.

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MS41

Cognitive Strategies for Hierarchical Inference

Decision in dynamic environments benefit from knowing the underlying change rate, which allows for efficient discounting of evidence based on the perceived relevance to the current state. To learn the latent change rate, an observer can track changes in the environmental state. With an ideal observer, simultaneously learning the change rate and identifying the current state take the form of a hierarchical inference process, whereby the believed change rate determines how past evidence should be used to infer the current state and observed changes in state update the believed change rate. However, it is not known whether humans perform hierarchical inference in dynamic environments, learning the latent environmental features, or rely on alternative suboptimal strategies. This work addresses the performance and associated strategies of human subjects presented with a decision-making task in a dynamic environment. In this task, subjects are asked to attune to different environmental features (e.g., state or change rate) to probe their ability to utilize underlying environmental features in their decision strategies. These responses are compared to the ideal observer and deviations in performance and their implications for human decision strategies in dynamic environments will be presented.

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MS41

Contributions of Sensory Adaptation and Pupil-linked Arousal to Adaptive Decision-making in Non-human Primates

Animals can make decisions using flexible forms of evidence accumulation that adapt to the demands of dynamic, changing environments. However, the neural implementation of this adaptive evidence-accumulation process is not well understood. We trained two rhesus monkeys on a random-dot motion task in which we manipulated environmental stability via change-points, or abrupt switches in motion direction. We recorded activity of motion-sensitive neurons in the middle temporal area (MT) of extrastriate visual cortex as well as pupil diameter, a non-invasive measure of arousal state. We found that for monkeys, like for humans, context stability affected the dynamics of the evidence-accumulation process. Specifically, in more unstable contexts, monkeys showed smaller gains in perceptual sensitivity as a function of viewing duration, consistent with a normative change in the time constant governing the integration process. Additionally, we found that these context-dependent behavioral adjustments were reflected in both the dynamics of sensory adaptation in MT and the magnitude of pupil-linked arousal responses. These results suggest that two complementary mechanisms underlie adaptive decision-making: (1) bottom-up, stimulus-dependent adjustments to the dynamics of adaptation in neurons that encode sensory evidence; and (2) top-down, context-dependent modulations of the temporal dynamics of the evidence-accumulation process by pupil-linked

arousal systems.

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MS42

Necrotic Cores in Atherosclerotic Plaque

Solid cancer tumors and atherosclerotic plaques are both observed to develop necrotic cores: internal regions of necrosis where cells have undergone non-apoptotic cell death. Hypoxia can cause necrosis in both advanced atherosclerotic plaques and cancer tumors. In these cases, the shape, location, and distribution of the cores is determined by the transport properties of oxygen within the tissue. In this presentation, we propose a quantitative framework to describe the evolution of atherosclerotic plaque. We use partial differential equations (PDEs) with macrophages, necrotic cells, oxidized lipids, oxygen concentration, and PDGF as primary variables coupled to a biomechanical model to describe vessel growth. A feature of our method is that it outputs color-coded vessel sections corresponding to regions of the plaque that are necrotic and ?brous, qualitatively similar to images generated by enhanced intravascular ultrasound.

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MS42

Parameter Estimation from Single Sample Cancer Recurrence Data

We develop consistent estimators for crucial parameters that govern the dynamics of tumor cell populations when subjected to pharmacological treatments. While these treatments often lead to an initial reduction in the abundance of drug- sensitive cells, a population of drug-resistant cells frequently emerges over time, result- ing in cancer recurrence. Samples from recurrent tumors present an invaluable data source that can offer crucial insights into the ability of cancer cells to adapt and withstand treatment interventions. To effectively utilize the data obtained from recur- rent tumors, we derive several limit theorems in the limit of a large initial population. These theorems then serve as the foundation for constructing novel statistical estimators. A distinguishing feature of our approach is that our estimators only require data from a single tumor sample, thereby enhancing the practicality of our approach and enabling the understanding of cancer recurrence at the individual level.

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MS42

The Heart of the Matter: Cardiotoxicity and Chemotherapy

Despite significant advances in cancer treatment, cancer remains the second leading cause of death in the United States and will lead to an estimated 609,820 deaths in 2023. Chemotherapy induced cardiotoxicity is an important contributor to treatment related morbidity and mortality and can occur through a variety of biological mechanisms. For example, anthracyclines are well known to cause cardiotoxicity in a cumulative dose-dependent manner through direct damage to cardiomyocytes resulting in left ventricular dysfunction. This type of irreversible cardiomyopathy is seen across many traditional classes of cytotoxic chemotherapies through a variety underlying biological mechanisms of action resulting in both early and late clinical presentations of cardiotoxicity. Newer targeted therapies can also cause both direct cardiotoxicity through biological action on cardiomyocytes and indirect cardiotoxicity through secondary effects on the heart such as increased risk of hypertension or thromboembolism. Finally, immune checkpoint inhibitors, which have recently emerged as a breakthrough treatment across a variety of cancer subtypes, can cause immune related cardiotoxicity which manifests in a range of cardiac pathologies including myocarditis, myocardial infarction, and arrhythmia. This talk is intended to provide an accessible review of clinically relevant mechanisms and manifestations of chemotherapy induced cardiotoxicity.

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MS42

Who Is at Risk of a Drug-Induced Arrhythmia? Exploiting Machine Learning to Predict Susceptible Individuals

Many drugs used to treat cancer can cause cardiotoxicity as a serious adverse event, and this can limit the usage of these otherwise-effective drugs. We sought to better understand cardiotoxicity caused by cancer therapeutics through a combination of transcriptomic measurements, mathematical modeling, and physiological measurements. Cardiomyocytes were differentiated from induced pluripotent stem cells, treated with 30 FDA-approved cancer drugs, and drug-induced changes in gene expression were quantified with mRNA sequencing. These results were integrated into mechanistic mathematical models to generate predictions, and optical measurements of action potentials and intracellular calcium were performed to test key modeling predictions. Results showed not only that modeling predictions were mostly accurate, but also that models could be used to accurately predict the response to the secondary insult of hypokalemia. Surprisingly, the results also showed differences in arrhythmia susceptibility between cell lines from different individuals, in both simulation and experimental results. Overall, the work demonstrates how large-scale screening data can be integrated with existing mechanistic models, and it provides insight into differences between individuals in adverse event risk.

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MS43

A Mathematical Model of Analog Epigenetic Cell Memory

Epigenetic cell memory is the property that allows multicellular organisms to keep different cell phenotypes despite a common genotype. Covalent modifications to DNA and histones have appeared as key mediators of the long-term maintenance of gene expression patterns that define cell type. Experiments in semi-synthetic genetic systems indicate that these modifications silence and reactivate a gene in an all or none fashion, thereby suggesting that long-

term maintenance is an attribute of extremal gene states. This digital epigenetic memory hypothesis is also consistent with a number of in vivo experimental observations. Here, we introduce a mathematical model that combines histone modifications and DNA methylation to demonstrate that the experimental observations of the probability distribution of gene expression, used to argue for digital memory, are also compatible with analog memory. That is, they are compatible with a scenario where cells can maintain any initially set gene expression level, not just the silenced and active ones. The model reveals that intrinsic noise combined with an ultrasensitive response between the level of DNA methylation writer DNMT3A and DNA methylation grade at a gene causes the potential ambiguity. The model thus suggests key experiments to perform in order to distinguish between digital and analog memory, thereby offering a tool for interrogating the very essence of epigenetic cell memory.

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MS43

Stochastic Switching of Delayed Feedback Suppresses Oscillations in Genetic Regulatory Systems

Delays and stochasticity have both served as crucially valuable ingredients in mathematical descriptions of control, physical and biological systems. In this work, we investigate how explicitly dynamical stochasticity in delays modulates the effect of delayed feedback. To do so, we consider a hybrid model where stochastic delays evolve by a continuous-time Markov chain, and between switching events, the system of interest evolves via a deterministic delay equation. Our main contribution is the calculation of an effective delay equation in the fast switching limit. This effective equation maintains the influence of all subsystem delays and cannot be replaced with a single effective delay. To illustrate the relevance of this calculation, we investigate a simple model of stochastically switching delayed feedback motivated by gene regulation. We show that sufficiently fast switching between two oscillatory subsystems can yield stable dynamics.

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MS43

Stochastic Modeling of Retinal Degeneration: Insights into Pathological Mechanisms and Interventions

Cell degeneration, including that resulting in retinal diseases, is linked to metabolic issues. In the retina, photoreceptor degeneration can result from an imbalance in lactate production and consumption as well as disturbances to glucose and pyruvate levels. We analyze a novel mathematical model for the metabolic dynamics of a cone photoreceptor, which accounts for energy generation from fatty acid oxidation of shed photoreceptor outer segments. We have published work on deterministic (ODE) versions of this model, and I will discuss preliminary work on investigating the impacts of intracellular noise in this system. This will include noise driven by stochastic interactions between discrete biomolecules as well as temporally fluctuating extracellular influences.

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MS44

Time Series Analysis of Motor-Cargo Complexes from In Vivo Experiments

A significant amount of knowledge about molecular motor-based transport, primarily driven by kinesin and dynein, has been obtained from in vitro experiments using experimental tools such as fluorescence microscopy, laser traps, and others. Within-cell observations of time-course data introduce a number of challenges, especially with the significant density of microtubules allowing for multiple switches of the motor-cargo complexes between microtubules. Here, we will present stochastic process models and accompanying statistical methodology to extract meaningful biological information from such data.

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MS44

Stochastic Fountain Dynamics and Associated Challenges for Inference

In the last couple of years, I have noticed an emerging theme in my work. Across multiple biological systems, colleagues and I have articulated models that involve particles that (1) emerge at random times from a fixed source-location distribution; (2) move throughout a local environment randomly (either diffusing, or switching between deterministic states); and (3) are removed from the system due to state-switching or escape from some predefined region. I am tentatively calling these systems stochastic fountains, and have been studying what these systems look like when you only have access to partial information. For example, what if you only have a snapshot of particles at one instant in time? Or, what happens if you can only observe particles at the moment they leave the domain? The associated inference problems arise naturally in mathematical biology applications, and are a fascinating example of how statistical (Fisher) information can be used to assess the quality of data in partially observed systems.

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MS44

Multiscale Modeling of Microtubule and Protein

Dynamics Following Neuronal Axotomy

Microtubules are dynamic intracellular filaments which provide structure to cells and facilitate cargo transport. While cargo transport on stable microtubules has been previously studied, the impact of dynamic microtubules on transport as well as the reciprocal signaling effects of cargo localization on microtubule growth remain open questions. These topics are of particular interest in neuronal injury where microtubule dynamics and cargo localization are key to the cellular response which promotes regeneration in peripheral nervous system cells after axon severing. Motivated by experiments in sea slugs, this project uses multiscale modeling to couple microtubule dynamics with cargo transport to test cellular mechanisms which are hypothesized to facilitate neuronal regrowth.

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MS44

Organization of Plant Cortical Microtubules

The self-organization of ordered cortical microtubule arrays plays an important role in the development of plant cells. This is observed to emerge from a combination of various factors such as microtubule-microtubule interactions, nucleation, and localization of microtubule-associated proteins. Distilling this process into the interaction of one-dimensional bodies on the two-dimensional cortex, quantitative models have been proposed to emulate array formation. Modelling microtubules as thin elastic rods constrained on a surface, it has been found that microtubule shapes resulting from curvature minimization may differ significantly from the previously assumed geodesic paths. We implement this in an agent-based, event-driven simulation. In our preliminary work, we find that this curvature mechanics provides a strong influence for directional alignment. This simulation provides the opportunity for further exploration into mechanical influences on array formation and their regulation through microtubule-associated proteins, with their associated model parameters.

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MS45

Computational Modeling of Mechanosensation and Spinal Injury Recovery in Swimming Lampreys

Spinal cord injuries in many vertebrates, including mammals, often result in a permanent loss of function. Other vertebrates, such as lampreys, can partially or wholly recover locomotor functions following severe spinal injuries. The exact mechanism by which recovery occurs is not well understood. One hypothesis is that function may recover through amplified proprioceptive (body-sensing) feedback. Lampreys serve as model organisms for vertebrate neurophysiology and swimming studies. In this work, we implement a multiscale, integrative, computational model of an anguilliform (eel-like) swimmer fully coupled to a viscous, incompressible fluid in an immersed boundary framework and examine the effects of mechanosensory input on swimming performance and injury recovery. Our results show that feedback amplification below a spinal lesion is sometimes sufficient to partially or entirely restore normal swimming behavior.

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MS45

Pulsating Soft Corals

Soft corals of the family Xeniidae have a pulsating motion, a behavior not observed in many other sessile organisms. We are studying how this behavior may give these corals a competitive advantage, especially by allowing their symbiotic algae to photosynthesize to a greater extent. We will present numerical methods and computational simulations of the pulsations of the coral. Direct numerical simulations of the pulsating corals and the resulting fluid flow by solving the Navier-Stokes equations coupled with the immersed boundary method will be discussed. We will present results of how the mixing created by the corals is modified as we vary parameters of the fluid flow and the pulsating motion. Furthermore, we will discuss the coupling of the fluid flow with a simplified photosynthesis model of the algae and resulting simulations.

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MS45

Using Shape Mode Analysis to Analyze Active Forces in Microswimmers

Microswimmers, such as sperm and Chlamydomonas reinhardtii, move in fluids using flagella, which are thin, threadlike filaments that enable these organisms to swim in fluids. These flagella move in a wavelike motion where the shape of the flagellar waveform emerges from interactions with the surrounding fluid, which depends on the fluid rheology; from passive mechanical properties, like extensional and bending forces; and active motor forces. It is thought that the mechanical feedback on the molecular dynein motor proteins in the flagella is responsible for the spatiotemporal coordination among motors. However, the means of mechanochemical feedback are not well understood, since the motor forces cannot be measured directly. We develop a computational model using experimental data of flagella in different types of fluids to extract information about how motor forces change in response to external forces and different fluid rheologies.

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MS45

Flows Generated by Jellyfish with Prominent Oral Arms

Our study simulates the blue blubber jellyfish, Catostylus mosaicus, using a three-dimensional model based on the immersed boundary method, focusing on its unique swimming mechanics and the energetics of its oral arms. These arms, rarely included in jellyfish simulations, are key in understanding the species feeding and mixing processes, which are vital for both individual survival and broader ecosystem dynamics. This approach draws parallels with recent studies on Mastigias sp., emphasizing Darwin's mechanisms of biogenic mixing. Our model, validated against empirical data, reveals insights into the swimming kinematics and vortex structures of C. mosaicus, offering a novel perspective on the ecological role of jellyfish movements.

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MS46

Methodological Challenges in Selecting and Interpreting Virtual Populations for Oncology

Simulations from virtual populations are increasingly being used to guide development decisions in industry. While there are range of approaches for selecting virtual populations, most rely on using some weighted selection or sampling of parameter values to allow mechanistic QSP models to match the diverse responses observed in real clinical populations. Due to the computational challenges in selecting populations for large models, much effort has been focused on creating efficient computational methods for virtual population generation. Fewer works have focused on best practices for assessing the quality of a virtual population and identifying likely numerical or computational pitfalls that can result in bias or poor predictive performance. In this talk I will review some proposed approaches and outline some major challenges for assessing the quality of virtual populations. Questions about quality depend centrally on how prior parameter bounds, non-identifiability and population variability interact within the sampling procedure. Taking these factors into account can help derive a better set of quality criteria for virtual population selection, which in turn can help guide numerical developments and improve stopping criteria. I will use some simplified models as well as real examples drawn from virtual population work in oncology to demonstrate this analysis.

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MS46

Systems Modelling of Adoptive T Cell Pharmacology

Engineered T cells have emerged as highly effective treatments for hematological cancers. Hundreds of clinical programs are underway in efforts to expand the efficacy, safety, and applications of this immuno-therapeutic modality. A primary challenge in developing these living drugs is the complexity of their pharmacology, as the drug product proliferates, differentiates, traffics between tissues, and evolves though interactions with patient immune systems. While the data generated from clinical studies is typically quite sparse, the information content can be enhanced using both systems modelling and machine learning methods that incorporate established immuno-biology. Using publicly available clinical data from Chimeric Antigen Receptor (CAR) T cells, Ill demonstrate how such approaches can be used to quantify the relationships between product characteristics, patient physiology, pharmacokinetics and clinical outcomes. As scientists work to develop next-generation cell therapy products, biologically informed mathematical models will be integral for contextualizing data and facilitating the translation of product designs to clinical strategy.

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MS46

QSP Digital Twins to Address Phase 1 Biological Variability for CD20/CD3 Bispecific Antibody Mosunetuzumab

Phase 1 oncology clinical trials often comprise a limited number of patients representing different disease subtypes who are divided into cohorts receiving treatment(s) at different dosing levels and schedules. To address this, we have developed a novel workflow to generate digital twins for each patient in the trial, which together form a virtual population (VPOP) that represented variability in biological, pharmacological, and tumor-related parameters from the phase I trial. The digital twins were generated for a previously developed QSP model for CD20/CD3 T-cell engaging bispecific antibody, mosunetuzumab. The mosunetuzumab QSP digital twin VPOP was used to characterize the clinical dose/exposure-response relationship. Furthermore, the QSP digital twin approach allows the identification of biological determinants of clinical response. Notably, the inferred digital twin parameters from clinical responders and nonresponders show that the potential biological difference that can influence response include tumor parameters (tumor size, proliferation rate, and baseline T-cell infiltration) and parameters defining the effect of mosunetuzumab on T-cell activation and B-cell killing. In the absence of a large sample size from the clinical trial, the dose/exposure-response predicted by the QSP model identified using the QSP digital twin VPOP can supplement empirical modeling approaches during dose escalation to inform dose optimization.

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MS46

Immunogenomics-Guided Virtual Patient Generation Using a QSP Model in Immuno-Oncology

Cancer is a leading cause of death worldwide with over 19 million estimated new cases and nearly 10 million deaths in 2020. While the number of clinical trials has increased over the past decades, the success rate of oncology trials remains the lowest among all therapeutic areas. This challenge necessitates the development of computational tools to predict the effectiveness of drugs of interest and identify predictive biomarkers for various treatment combinations. In model-informed drug discovery and clinical trial design, quantitative systems pharmacology (QSP) models have begun to play crucial roles due to their ability to integrate mechanistic knowledge from cancer biology and pharmacology into a quantitative framework. I will present a modular QSP platform for immuno-oncology (QSP-IO) that describes the cancer-immunity cycle, which allows for varying degrees of complexity based on our research goals. When parameterized to non-small cell lung cancer, the model was used to generate a virtual patient population that statistically matched the immune subset ratios from immunogenomic analysis. The model predicted a response rate of 18.6% (95% bootstrap confidence interval: 13.3–24.2%) and identified Treg/CD8 ratio as a potential predictive biomarker in addition to PDL1 expression and tumor mutational burden. I aim to demonstrate that publicly available genomic data served as a reliable resource for virtual patient generation techniques in immuno-oncology using QSP models.

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MS47

A PNP Ion Channel Deep Learning Solver with Local Neural Network and Finite Element Input Data

In this talk, a deep learning method for solving an improved one-dimensional Poisson-Nernst-Planck ion channel (PNPic) model called the PNPic deep learning solver, is presented. In particular, it combines a local neural network scheme with a PNPic finite element solver. With two PNPic coarse grid solutions generated by the solver as the input data, the neural network scheme can be trained much faster than a global neural network because it only needs a much smaller amount of training data and its input data involves a small local patch of coarse grid solutions. After proper training, it can output a predicted PNPic solution with much higher accuracy than the low-cost coarse grid solutions. Moreover, it can be trained using finite element solutions reflecting different perturbation cases on the parameters, ion channel subregions, interface and boundary values, etc. To this end, the PNPic deep learning solver can generate a numerical solution with high accuracy for a family of PNPic models. As an initial study, two types of numerical tests were done in this work by perturbing one and two parameters of the PNPic model, respectively, and the tests were done by using a few perturbed interface positions of the model as training samples. Even so, numerical results demonstrate that the PNPic deep learning solver can generate highly accurate PNPic numerical solutions.

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MS47

Geometric and Topological Data Analysis in Biology Applications

This talk will discuss geometric and topological data analysis in biology applications and focus on the recent developments. The multiscale analysis of graph neural network and the de Rham-Hodge theory provides a unified paradigm for the evolving manifolds constructed from filtration, which induces a family of evolutionary complexes. While the present evolutionary de Rham-Hodge method can be easily applied to close manifolds, the emphasis is given to more challenging compact manifolds with 2-manifold boundaries, which require appropriate analysis and treatment of boundary conditions on differential forms to maintain proper topological properties. Meanwhile, we will discuss the the multiscale graph neural network in the modeling of biomolecules.

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MS47

BAYESIAN APPROACHES to DATA INTERPRETATION in INTEGRATIVE BIOPHYSICAL INVESTIGATIONS

Understanding cystic fibrosis (CF) pathology involves the interplay of genetic mutations, drug efficacy, and the dynamic function of the cystic fibrosis transmembrane conductance regulator (CFTR) channel. CFTR mutations cause a hereditary disorder with dense mucus production, leading to airway obstruction, lung damage, and digestive issues. The varying efficacy of medications in restoring specific mutant CFTR forms emphasizes the need for understanding mutation and drug impacts on CFTR function for targeted therapeutics. Structural studies reveal CFTR channel conformations, but the mechanism governing transitions between open and closed states is unclear. This research uses ensemble functional measurements, smFRET, electrophysiology, and kinetic simulations to unveil NBD dimerization preceding channel opening, elucidating the allosteric gating step. Kinetic simulations replicate smFRET and electrophysiology data, exposing rate-limiting conformational changes in NBD-dimerized channels and potentially identifying therapeutic targets. Initial results on the inverse problem approach to extract CFTR function from multi-perspective data will be presented. If time allows, the presentation will shift to photophysical modeling of dye pairs in smFRET experiments for precise FRET

measurements. References Jesper Levring, Daniel Terry, Zeliha Kilic, Gabriel Fitzerald, Scott Blanchard, Jue Chen, "Single-molecule analysis of allostery in CFTR gating and pharmacology", Nature, 2023

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MS47

Prediction of Mutation-Induced Protein-Protein Binding Free Energy Changes Based on Computational Topology and Machine Learning

Vaccines and antibody drugs are essential in the fight against COVID-19; however, the vast number of mutations distributed throughout the entire genome makes vaccine development a complicated endeavor. As a result, it becomes a time-consuming and costly process for wet labs to verify the potential impact of these mutations and design corresponding vaccines and drugs. Therefore, exploring alternative, efficient computational methods to better understand the mutational impact, would greatly contribute to the development of more targeted and effective vaccines. In this talk, I will introduce how Computational Topology and Machine Learning help to predict the binding free energy change, BFE change, of the virus Spike and ACE2 or antibody, which is induced by mutations. This research has the potential to reveal the virus's infectivity and the effectiveness of antibody treatments, thus paving the way for designing more targeted and potent vaccines and antibody treatments.

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MS48

A Review of Mechanistic Learning in Mathematical Oncology

In the past, knowledge-driven mechanistic mathematical modeling and data-driven machine and deep learning models have been embraced by different communities. Today, "mechanistic learning integrates these concepts. It is of particular promise for clinical applications where challenges such as limited data, and the demand for model interpretability are immanent. We present a review of the current status of the research direction of mechanistic learning. We emphasize the synergistic potential of knowledge- and data-driven approaches by drawing attention to similarities and differences in model complexity, data requirements, generated outputs, and interpretability of algorithms and results. We propose four flavors of mechanistic learning: sequential, parallel, intrinsic, and extrinsic. Examples from oncology applications are showcased, such as physics-informed neural networks, surrogate model learning, and digital twins. As machine learning continues to gain widespread usage and influence, there is a growing need to incorporate it into the study of mathematical oncology. Mechanistic learning offers a practical avenue for this integration. As mechanistic learning evolves, we envision this review and the proposed categorization framework to foster collaboration between data science and mathematical modeling, thereby contributing to the resolution of key challenges in oncology, such as limited data availability, model transparency, and complex input data.

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MS48

Optimization of a Single Cell Bioprinting and Agent-based Modeling Pipeline by Spatiotemporal Representation Learning

Tissue-scale dynamics of cancer arise from the behavior of individual cells within the tumor microenvironment (TME). One tool for understanding the TME is Agent-based modeling (ABM), which simulates entities and their interactions within a user-defined environment. Current limitations include controlling for biological variables (i.e., genetic alterations) and reliance on costly biological validation solely of endpoints. Single cell bioprinting spatially arranges cells with precise control and reproducibility. Printing cells engineered with specific alterations can efficiently create reductionist models (RMs) of biological systems. ABMs can be seeded with imaging from RMs and calibrated by grid-search of parameter values to match RMs at each timestep. Applied iteratively, these methods can build more complex ABMs. The spatiotemporal quality of TME ABMs, however, may render governing equations that capture the nonlinear system dynamics and emergent properties intractable. Here, we employ representation learning to learn the structure and parameters of the system from the results of grid-search. We aim to derive governing equations with minimal terms necessary to describe system dynamics; identify critical drivers of tumor growth and behavior; and facilitate design of new biological experiments or RMs. This pipeline lays the foundation for developing ABMs initialized from a patients data as a high-throughput assay platform to inform personalized anti-cancer therapies.

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MS48

Patient-specific, Imaging-informed Forecasting of Prostate Cancer Progression in Active Surveillance

Active surveillance (AS) is a standard management option for newly-diagnosed prostate cancer (PCa), which usually exhibits low to intermediate clinical risk. During AS, patients have their tumor monitored via multiparametric magnetic resonance imaging (mpMRI), serum prostate-specific antigen (PSA) tests, and biopsies. If these exams reveal tumor progression towards an increased clinical risk, the patient is prescribed a curative treatment. However, current AS protocols rely on an observational population-based approach, which complicates the personalization of monitoring plans and the early detection of tumor progression. To address these issues, we propose to forecast PCa growth using personalized simulations of an mpMRI-informed biomechanistic model solved over the 3D anatomy of the patient's prostate. We describe PCa growth in terms of the spatiotemporal dynamics of tumor cell density as a combination of tumor cell mobility and net proliferation. Model calibration and validation rely on assessing the mismatch between model predictions and mpMRI-based measurements of tumor cell density. We also build a logistic classifier of PCa risk using model-based biomarkers calculated from the model forecasts at the times of histopathological assessment (i.e., biopsy, surgery). Our results suggest that, while further improvement and testing in larger cohorts are required, our forecasting technology has potential to predict PCa progression and personalize clinical decision-making in AS.

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MS48

Data-Driven Investigations Lead to Hypothesis Generation for Modeling Dynamic Microbiome-Immune Interactions in Mice

The gut microbiome plays important roles in the development and function of the immune system, including vaccine efficacy. However, understanding the relationship between a microbiome and its host is challenging due to a lack of understanding of different pathways impact on immune function. To address this, we analyze high-dimensional metagenomic and metabolomics data from two mouse models: wild-type (complex microbiome) and gnotobiotic (simplified microbiome). We used dimensionality reduction techniques and information gain to identify relevant features. Relationships between these features are then used as hypotheses to form dynamic mechanistic models. Furthermore, this comparative data-driven pipeline helps produce hypotheses that are simplified enough for targeted experimentation and generating data to build dynamic mechanistic models. We are incorporating structural and functional features of the microbiome, including shotgun sequencing, metabolic pathways, metabolites, along with responses of adaptive and innate immunity from the host. Initial efforts using the Gini index have focused on the identification of metabolite signatures that show distinct differences between the two cohorts of mice. This interwoven approach of combining a data-driven approach with mechanistic modeling represents key steps toward understanding the microbiome's mechanistic role in shaping host immunity and vaccine efficacy.

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MS49

Mathematical Insights into Hiv and Nutrition: Immunological and Epidemiological Perspectives

HIV continues to be a significant global health issue, having claimed millions of lives in the last few decades. While several empirical studies support the idea that proper nutrition is beneficial in the fight against HIV, very few studies have focused on developing and utilizing mathematical modeling approaches to assess the association between HIV, the human immune response to the disease, and nutrition. In this presentation, we introduce a novel within-host model for HIV that captures the dynamic interactions among HIV, the immune system, and nutrition. We explore the relationship between serum protein levels and key parameters such as viral loads, viral production rates, and the enhancement rate of protein by the virus in HIV-infected individuals. Additionally, we will discuss the correlation between dietary protein intake and serum protein levels in individuals with HIV. We will conclude the presentation with the introduction of a novel epidemiological model on HIV, which can be integrated with the aforementioned within-host model, considering economic and nutritional aspects.

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MS49

Modeling the Impact of Vaccination on Covid-19 Dynamics in St. Louis

We investigate how human mobility, vaccination, and time-varying transmission rates influenced COVID-19 transmission in five counties in the St. Louis area. A COVID-19 model with a system of ordinary differential equations was developed to illustrate the dynamics with a fully vaccinated class. Using the weekly number of vaccinations, cases, and hospitalization data from five counties in the greater St. Louis area in 2021, parameter estimation for the model was completed. The transmission coefficients for each county changed four times in that year to fit the model and the changing behavior. We predicted the changes in disease spread under scenarios with increased vaccination coverage. SafeGraph local movement data were used to connect the forces of infection across various counties.

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MS49

Jorge Velasco-Hernandez's Talk Title

We present a description of the distribution of dengue cases in Mexico from 2014-2022 according to several criteria including municipality, state and hidrological basin. Then

we intriduce a matematical model for the description of dengue dynamics.

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MS50

Introducing Thermodynamic Corrections to Aceto- and methanogenesis Kinetics in an ADM1-based Model for Spatially Resolved Reactor Geometries

Mathematical modeling of biochemical reaction rates in the multistage process of anaerobic digestion may be described using Monod-type kinetics with empirically determined parameters. Despite recent models, among them the established Anaerobic Digestion Model No. 1, taking various inhibitory mechanisms into account, the complex endeavor of incorporating thermodynamic constraints was not attempted but referenced as alternative to direct hydrogen inhibition. Based on previous proposals of thermodynamically modified reaction rates and a coupled transport-reaction system, our model introduces a thermodynamic approach dependent on Gibbs free energies in a spatially resolved reactor model. It has been applied to experimental data of laboratory reactors in stable and unstable phases including process collapse. Results show that in some model applications the thermodynamic approach to modeling is necessary to reflect the accumulation of longer chain acids indicating process instability. Furthermore, it suggests that inhibition by overall acid concentration could be the triggering cause of process collapse in systems where pH remains relatively stable.

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MS51

Knot Data Analysis for Biomolecular Interactions Using Multiscale Gauss Link Integral

Over the past decade, topological data analysis (TDA) has become a powerful tool in data science, with its main technique being persistent homology. This method tracks topological properties as point cloud data evolves, using algebraic topology. Despite the significance of knot theory and related mathematical subjects, their practical applications have been limited due to localization and quantization challenges. To address these issues, we introduce knot data analysis (KDA), a new approach that incorporates curve segmentation and multiscale analysis into the Gauss link integral. This results in the multiscale Gauss link integral (mGLI), which not only reveals global topological features of knots and links at an appropriate scale but also provides multiscale feature vectors to capture local structures and connections within each curve segment at different scales. We demonstrate its representative ability on biomolecules and molecular interactions through protein flexibility analysis and protein-ligand binding affinity predictions. The proposed mGLI significantly outperforms other state-of-the-art methods including earlier persistent homology based methods. Our approach enables the integration of artificial intelligence (AI) and KDA for general curve-like objects and data.

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MS51

Data-Driven Identification of the External Communication Signals and Analysis of Their Associated Signaling Networks Using Exfinder

Cells make decisions through their communication with other cells and receiving signals from their environment. Different computational tools have been developed to infer cellcell communication through ligands and receptors using single-cell transcriptomics. However, the existing methods only deal with signals sent by the measured cells in the data, the received signals from the external system are missing in the inference. This presentation will commence with an introduction to exFINDER, a computational approach designed to identify external signals received by cells in single-cell transcriptomics datasets. It further delves into the analysis of associated ligand-target signaling networks. Additionally, we will demonstrate the integration of exFINDER with other computational methods to infer cell lineages.

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MS51

Emerging Mathematics and Deep Learning Models in Drug Design

The intersection of mathematics and artificial intelligence (AI) has ushered in a new era of drug design, offering unprecedented accuracy and efficiency in ranking drug potency. Building on our previous work, in which we showcased the superiority of our mathematical models for binding affinity prediction tasks, this talk delves deeper into the emerging mathematical techniques and deep learning models that are revolutionizing drug discovery. We will discuss the latest advancements in differential geometry, persistent spectral graphs, and large language models, all of which have proven instrumental in characterizing biomolecular and molecular interactions. A standout feature of our approach is its scalability, which accommodates diverse molecular representations, and its robustness, especially when handling low-quality data. These strengths have catapulted our models to the forefront, as evidenced by our top-tier performance in the CASF benchmarks, protein-protein interactions, and the D3R grand challenges. This presentation will offer insights into the future trajectory of drug design, where the synergy of mathematics and AI is set to redefine the boundaries of what is achievable in pharmaceutical research.

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MS52

The Effect of Inertia on the Hydrodynamic Perfor-

mance of Swimming Protist Colonies

The transition from unicellular to multicellular organisms marks a crucial evolutionary event in Metazoan history. For multicellular colonies to evolve and thrive, selective pressures must favor this transition, especially if it confers a fitness advantage over unicellular counterparts. To understand the hydrodynamics of swimming protist colonies, a detailed model that can capture cell morphology and flagellar dynamics would be ideal, although the computational cost can be high. Here we examine a colony comprised of reduced models of individual cells, where the reduced model of a cell has been calibrated by its far-field velocity computed using a detailed model. Choanoflagellates, model protists sharing ancestry with animals, provide insights into the evolution of multicellular behavior. Although the typical length scales and speeds are small enough that the Stokes equations apply, PIV images from Koehl Lab - UC Berkeley reveal large flow velocities near the colony, resulting in a higher Reynolds number in those regions. This suggests that inertial effects may contribute to the local dynamics of the colony. Our previous work used a regularized force dipole reduced model in the Stokes regime that best fit an averaged far-field flow. In this study, we include inertia and propose a reduced model that has similar behavior as the regularized force dipole. We present how inertial effects influence the hydrodynamics of the colony.

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MS52

A Reduced Model of Swimming Microorganisms Based on Regularized Stokeslets

A single particle representation of a self-propelled microorganism in a viscous incompressible fluid is derived based on regularized Stokeslets in three dimensions. The formulation is developed starting from two regularized Stokeslets of equal and opposite strength and different size regularization parameters. The model is the result of taking the limit as the two forces approach each other and the regularization parameters approach a common value. A parameter that captures the size difference in regularization provides the asymmetry needed for propulsion. We show that the resulting limit is the superposition of a regularized stresslet and a potential dipole. The model parameters and choice of regularization function provide a length scale of the organism, its swimming speed, and the swimming mode (puller or pusher). Similarities with other models will be discussed and the collective dynamics of dilute concentrations of particles will be presented.

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MS52

Computational Methods for Microorganism Swimming in Complex Fluids

Many important biological functions depend on microorganisms' ability to move in viscoelastic fluids such as mucus and wet soil. The effects of fluid elasticity on motility remain poorly understood, partly because, the swimmer strokes depend on the properties of the fluid medium, which obfuscates the mechanisms responsible for observed behavioral changes. We develop computational models that use experimental data from the undulatory motions of *C. elegans* and mammalian sperm as well as the breast stroke motion of the algae *C.reinhardtii* to explain experimental observations and to explore the effects of fluid elasticity on swimming. We review numerical methods for simulating microorganism swimming in complex fluids. We focus on the immersed boundary method with different means of driving the motion including: prescribed active forces, prescribed kinematics, and multiscale models of molecular motors in which the coordination is emergent. We use these different types of models to (1) disentangle these affects by changing the gait and fluid rhology independently and to (2) examine how the swimmer gait emerges from the properties of the environment.

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MS52

Microswimmers in Dissipative Vortices: Studies of Collective Interactions

Microswimmers in nature often need to navigate vortical background flows. The theoretical Burgers' vortex provides a rich model for such flows with vortex diffusion and stretching. We propose several approaches using regularized fundamental solutions of the Stokes equations to model Burgers-like vortical structures at the low Reynolds number limit. Using these vortices as background flows, we test microswimmer-vortex interactions both for an individual swimmer and for a collective. First, we investigate the changes in swimming modes and vortex-induced shape deformations for a filiform swimmer for different vortex strengths using a Kirchhoff Rod-Regularized Stokeslet Segment framework. For the multi-swimmer collective interactions, we choose a minimal model where every swimmer is characterized by a regularized force dipole, comprised of

a stresslet and a potential dipole. The parameters of this force dipole are optimized to reproduce a flow field similar to that generated by an actual organism in free space.

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MS53

Modeling Mechanisms of Length and Polarity Regulation in Neuronal Microtubules

Microtubules are protein polymers which are known to be stable and to have specific orientations in neurons. This is crucial, since key proteins get transported along these polarized microtubules, which ensures long-term survival of neurons. But microtubules also need to be dynamic and reorganize in response to injury events. How this balance is achieved remains an open question. Using information from experimental measurements and a stochastic mathematical model, we first seek to understand mechanisms that control microtubule length in dendrites of fruit fly neurons. The modeled mechanisms include limited tubulin availability and the dependence of shrinking events on microtubule length. We also develop a reduced deterministic model that validates and guides our choices of parameters for the more complex stochastic model. Insights from these models of microtubule dynamics can then be used to understand how the microtubule filaments collectively organize into polarized structures in neurons.

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MS53

Transduction of Chirality from Intracellular to Multi-Cellular -Experiments and Models

Many externally bilaterally-symmetric animals, including both vertebrates and invertebrates, have an internal left-right asymmetry that is established during embryo development. This asymmetry can be critical for proper organ function (e.g. the mammalian heart). In *C. elegans*, left-right asymmetry (chirality) arises during cell division at the four-cell stage and eventually manifests in a consistent handedness in the twisting of intestine and gonad in the adult. In collaboration with the Sugioka Lab, we are developing models to explain the onset of chirality at the multicellular scale. Chirality appears intracellularly during cell division in the form of chiral flow of the actomysosin cortex. We hypothesize that this flow induces friction forces between neighbouring cells mediated by adhesions. The model takes the form of force balance differential equations and does well in comparison with quantitative data extracted from live-cell and *in vitro* imaging. This work is an early step in mapping out the process of the transduction of chirality from molecular to multicellular scales.

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MS53

G Mediated Diffusive Coupling Synchronizes Actin Oscillators in Cell Migration

At the cortex of Dictyostelium, the actin cytoskeleton localizes in discrete patches which have been shown to oscillate at different phases. Recent findings suggest that the spatial coordination of actin oscillators is regulated by the G protein subunit Gβ, which diffuses rapidly throughout the cell. G sequestration impairs directional migration of D. discoideum cells and drives large-scale oscillations of cortical F-actin. Here we compare Kuramoto-type models for coupled oscillations between actin sections, and a reaction-diffusion model, where within each sector, actin dynamics is governed by an excitable activator-inhibitor model with diffusive coupling by a chemical species that diffuses between actin cortex sectors.

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MS53

Understanding the Biased Distribution in Traction Forces in Cooperative Cell Motility

Streams of migratory *Dictyostelium* cells are initiated by the formation of tandem pairs of cells connected head to tail to which other cells and subsequently adhere. Interestingly, when cells migrating in tandem pairs the dynamics of the traction forces exhibit two distinct patterns with a significant bias in their occurrences. In about 80% of the time each cell in the migrating tandem pairs generates a contractile traction force dipole, maintaining the traction force signature of the single cell case. In about 20% of the time the two cells fuse into a single contractile traction force dipole. Although previous experimental works suggested linking the pair mechanically, it remains unclear what are the contributing factors that lead to this bias. In this work, we develop a model to explain the emergence of the biased distribution traction forces mechanistically. As the mechanism at the cell-cell junction with the environment in *Dictyostelium* cells is unknown, we will use both a 2D model and a simplified model to reveal the mechanical coupling at the cell-cell junction that gives rise to this bias.

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MS54

Clone Size Statistics of Tumor-inhabiting Bacteria

Bacteria inhabit different areas of the human body and perform essential functions. Increasing evidence of bacterial effects on cancer progression has brought interest to tumor-inhabiting bacteria. However, it is not understood how bacteria affect the tumor, nor how the tumor environment affects bacterial dynamics. Recent experiments, done with barcoded bacterial colonies, show that clone sizes of bacteria inhabiting tumors in mice exhibit universal statistical patterns. The patterns are robust across experiments and collection times, and unique to bacteria grown in the tumor environment rather than in liquid culture. We find that the liquid experiments can be explained by a simple birth-death process that cannot capture the observed statistics in the tumor. In this work, we develop a mechanistic understanding of the microecological dynamics of tumor-inhabiting bacteria. We present a physical model that captures the observed statistics with simple assumptions and explains the uniqueness of this observation to the tumor environment.

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MS55

Birth-Regulated Vs Death-Regulated Interactions in a Heterogenous Population

In this talk, we will consider a stochastic model of a two-type heterogeneous population splitting and dying according to density-dependent rates. In applications, these subpopulations interact with each other, and that interaction can manifest through the birth dynamics, the death dynamics, or some combination of the two. We propose an inference method for disambiguating the type of interaction and understanding the birth and death processes by looking at time-series data of the population sizes. The inter-species interactions considered can be competitive, antagonistic, or mutualistic. In the specific example of sensitive and resistant cancer cells, the method also gives insight into the effects of different drug treatments. This is joint work with Heyrim Cho and Linh Huynh.

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MS55

A Stochastic Model of Relapse in Drug Addiction

A large percentage of individuals recovering from substance use disorder relapse within one year of abstinence. A primary role in relapsing, even after long periods without using drugs, is played by experiencing stressful experiences and being exposed to external stimuli associated with past drug-taking. Stressors and cues elicit memories of drug-induced euphoria and the expectation of relief from current anxiety, igniting an intense craving to use again. Positive experiences and supportive environments may instead act as protective factors. We present a mathematical model of relapse in drug addiction that draws on known psychiatric concepts and where relapsing depends on external factors (intensity and timing of life events) as well as individual traits (mental responses to these events). We study which combinations and ordering of stressors, cues and positive events lead to the largest relapse probability and illustrate best interventions to alleviate the likelihood of relapse.

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MS55

The Dynamics of Particles with Ligand-Receptor Contacts

One way to glue objects together at the nanoscale or microscale is by ligand-receptor interactions, where short sticky hair-like ligands stick to receptors on another surface, much like velcro on the nanoscale. Such interactions are common in biology, such as white blood cells, virus particles, cargo in the nuclear pore complex, etc, and they are also useful in materials science, where coating colloids with single-stranded DNA creates particles with programmable interactions. In these systems, the ligand-receptor interactions not only hold particles together, but also influence their dynamics. How? I will introduce our modelling and experimental efforts aimed at understanding the coarse-grained dynamics of particles with ligand-receptor interactions. Our models proceed by averaging over the fast, small-scale, stochastic dynamics of the ligand-receptor pairs, to obtain effective dynamics for the particle on longer timescales. This approach predicts that ligand-receptor interactions can change the particles' effective diffusion by orders of magnitude. Our experiments, using DNA-coated colloids, verify this dramatic dynamical slowdown, but also show other dynamical features not yet captured by our model, which suggest new avenues for exploration.

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MS55

Can a Small Group of Passive Agents Cause Lasting Chaos?

We consider a lattice model of active matter with exclusion and derive its hydrodynamic description exactly. The hydrodynamic limit leads to an integro-differential equation for the density of particles with a given orientation. Volume exclusion results in nonlinear mobility dependent on spatial density. Such models of active matter can support motility-induced phase separation, which occurs despite the absence of attractive interactions. The addition of passive particles animates the clusters, creating stable travelling fronts. We study the onset of phase separation with linear stability analysis and numerical simulations and classify stationary states by deriving coexisting phase densities.

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MS56

Global Sensitivity Analysis of Epidemiological Agent-Based Models to Inform Calibration Priorities

Global sensitivity analysis (GSA) apportions the sources of model input uncertainties to obtain the relative influence each source of uncertainty has on a target outcome of a computational model. GSA is an essential preliminary analysis for calibration, used to identify and prioritize important parameters for large scale models. Focusing on a Department of Energy exascale-ready epidemiological agent-based model, we will present the requirements to provide proper treatment of GSA. A practical implementation will be introduced with a tiered sampling scheme so that the variability in model initialization is captured and distinct from the propagation of the parameter uncertainties. Setting a fixed seed, that controls the reproducibility of the model, we then implement a classic variance-based approach to derive the Sobol indices for the model parameters. Varying the seed and continuing to calculate the Sobol indices for each seed, results in the uncertainty of the Sobol indices. This provides a rich analysis space to better understand the variability of the model and prioritization of parameters for calibration. A further deep dive into the interpretation of the results will be provided. Ultimately this presentation will provide a practical application of GSA to inform calibration priorities for stochastic agent-based models while outlining challenges and opportunities for applying GSA to complex systems modeling.

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MS56

Modeling Growth Dynamics and Survival of Liberibacter Crescens Bt-1

Liberibacter crescens is the only cultured member of its genus, which includes the devastating plant pathogen Candidatus Liberibacter asiaticus, associated with citrus greening/Huanglongbing (HLB). L. crescens is currently the best model organism available for these pathogens. It grows slowly and dies rapidly under current culture protocols and this extreme fastidiousness makes it challenging to study. We experimentally determined that a major cause of rapid death of L. crescens in batch culture is increase in pH of the medium. Under stress, bacterial cells shut down their metabolism to survive in a stationary but recoverable state. We formulated a set of differential equations to model populations of cells in different metabolic states, treating stress as a continuous variable. We conducted experiments to test the model prediction that controlling the pH will significantly affect recoverability of cells from 10-day cultures. We conducted global sensitivity analysis using Sobol indices to determine sensitivity of bacterial growth to experimental conditions over a course of 10 days. Our results also suggest that growth-dependent pH alteration that overcomes medium buffering should always be considered when growing fastidious bacteria.

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MS56

Into the Jungle: Using Sobol Indices to Disentangle the Ecology of Emerging Sylvatic Cycles

Endemic transmission cycles of arboviruses such as dengue virus (DENV), Zika virus (ZIKV), or yellow fever virus (YFV) in non-human primates are known as sylvatic cycles, and these sylvatic cycles maintain permanent reservoirs of these pathogens, complicating disease control efforts. While YFV, which originates from Central Africa, was able to establish a sylvatic cycle in the Americas following its introduction by humans, it remains unclear whether DENV or ZIKV will similarly establish in non-human primates. During disease emergence, the number of infections in a population is often small, and subsequently, stochastic fluctuations become prominent. Stochastic compartmental models are a common tool from mathematical epidemiology used to deal with these fluctuations, and one that has been used to investigate the sylvatic cycle of arboviruses.

Global sensitivity analysis of these stochastic models is essential to disentangle which processes are more important than others to the underlying biological problem. However, global sensitivity analysis of stochastic models poses more challenges than sensitivity analysis of deterministic models. Here, we construct a stochastic model of the sylvatic cycle in the Americas, and we perform a global sensitivity analysis using a generalization of Sobol indices to understand which ecological factors are most important in the establishment of DENV or ZIKV in non-human primates in the Americas.

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MS56

A Model of Gastric Mucosal PH Regulation: Extending Sensitivity Analysis Using Sobol' Indices to Understand Higher Moments

Several recent theoretical studies have indicated that a relatively simple secretion control mechanism in the epithelial cells lining the stomach may be responsible for maintaining a healthy pH adjacent to the stomach wall, even in the face of enormous electrodiffusive acid transport from the interior of the stomach. Subsequent work used Sobol' Indices (SIs) to quantify the degree to which the wall pH is held neutral as mathematical parameters vary. However, questions remain regarding the nature of the control that specific parameters exert over the maintenance of a healthy stomach wall pH. One limitation of analysis based on SIs is that they provide little or no information regarding the higher moments of the model output distribution. In this work, we define γ-indices to quantify sensitivity of variance, skewness, and kurtosis to the choice of value of a parameter, and we propose an efficient strategy that uses both SIs and γ-indices for a more comprehensive sensitivity analysis. Our analysis uncovers a control parameter which governs the "tightness of control' that the secretion mechanism exerts on wall pH, which we use as a surrogate for gastric health. Finally, we show how uncertainty in this unidentifiable parameter can be reduced using expert information about higher moments, and speculate about the physiological advantage conferred by this control mechanism.

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MS57

The Effect of Vaccination of the Competitive Advantage of Two Strains of An Infectious Disease

We investigate how a population's natural and vaccine immunity affects the competitive balance between two strains of an infectious disease with different epidemiological characteristics. We focus specifically on the case where one strain is more transmissible while the other strain is more immune-resistant. Our analysis shows that, in this scenario, vaccination can have a significant effect on the competitive balance between two strains. Specifically, as a population's effective vaccination level is increased, the competitive advantage can flip from one strain to the other. We also show that which strain gains an advantage depends on the nature of integration of natural and vaccine immunity.

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MS57

Machine Learning Approaches for Sars-CoV-2 Lineage Frequency Forecasting

With dozens or hundreds of minor variants of SARS-CoV-2 circulating in the global population, there is an urgent need for predicting the scale and the rate of the spread of a new variant when it emerged in the population. This would allow for more focused experimental efforts and for timely formulation of new vaccines. To address this need, we constructed a machine learning model, based on the transformer architecture (used in modern language processing models), and trained the model using existing lineage frequency time series. We show that our machine learning model out-competes existing approaches, and this model could predict the frequency of a newly emerged lineage 2 months into the future with a high level of accuracy. Overall, the model represents promising new methods utilizing genomic data for SARS-CoV-2 lineage monitoring and forecasting.

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MS57

Optimizing Antiviral Treatment of SARS-CoV-2 Infections

Chronic SARS-CoV-2 infections can persist in immunocompromised individuals for months or even years. Effective treatment for these cases is essential from both a clinical care and public health perspective because examples of significant within-host viral evolution marked by mutations congruent with variants of concern have been reported among chronic infections. Several antiviral drugs have demonstrated efficacy against SARS-CoV-2 infection by lowering viral load and preventing hospitalization and death in the general population. Clinical trials are currently underway exploring modifications to antiviral monotherapy protocols for treating immunocompromised patients, including longer duration of therapy. We have calibrated ODE models combining within-host viral dynamics and drug pharmacokinetics to recapitulate the results of clinical trials for three SARS-CoV-2 antivirals: nirmatrelvir/ritonavir, molnupiravir, and remdesivir. We used this modeling framework to explore the impact of changing the dose level, timing of doses, and duration of therapy on treatment outcomes for both healthy and immunocompromised populations.

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MS57

Immune Uncertainties, Individual Behavior, and the Dynamics of Covid-19

As has been illustrated by SARS-CoV-2, a number of characteristics can affect disease dynamics. In this talk, I will highlight the potential effects of remaining immune uncer-

tainties on the future immuno-epidemiological dynamics of SARS-CoV-2. I will also examine the dynamics of individual decision-making with respect to adherence to an intervention. Throughout, I will use simple models to qualitatively examine these dynamics.

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MS58

Personalized Mathematical Models for Cancer Early Detection

Many aggressive cancers are treated best when they are discovered early, while still confined to their primary organ of origin. Early detection of cancer is possible using imaging-based strategies such as mammography and ultrasound, but imaging is expensive and not always accessible or feasible for frequent screening. A more cost-effective screening strategy uses simple blood tests to measure abnormal levels of proteins, nucleic acids or other cancer biomarkers that are shed from a patients tumor into blood. Abnormal levels of these blood biomarkers frequently correlate with cancer state, but the mathematical relationship between a patients longitudinal blood measurements and aggressive tumor growth is not well understood. Here, we present mechanistic mathematical models of tumor growth and biomarker shedding to better understand the biology underlying blood-based cancer screening and a patients personal risk for aggressive cancers. The models are fitted to experimental time-course biomarker data to estimate individual tumor growth rates and to predict the presence of aggressive vs. indolent tumors. The predicted tumor growth rate is then used to optimize a patients cancer screening frequency. Our modeling framework can be adapted for virtually any solid cancer and associated biomarkers shed to establish effective personalized screening schedules customized for individuals of any age or cancer risk level.

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MS58

Mathematical Methods in Evolution and Medicine

Evolutionary dynamics permeates life and life-like systems. Mathematical methods can be used to study evolutionary processes, such as selection, mutation, and drift, and to make sense of many phenomena in the life sciences. How likely is a single mutant to take over a population of individuals? What is the speed of evolution, if things have to get worse before they can get better (aka, fitness valley crossing)? Can cooperation, hierarchical relationships between individuals, spatial interactions, or randomness influence the speed or direction of evolution? Applications to biomedicine will be discussed.

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MS58

Early ctDNA Kinetics as a Dynamic Biomarker of Treatment Response

Next-gen sequencing (NGS) has made it possible to collect and sequence circulating tumor DNA (ctDNA) from longitudinal blood samples. While ctDNA data continues to be collected on a wide variety of cancers and treatment types, it is still unclear what ctDNA biomarkers are most indicative of treatment success or failure. We present models for ctDNA shedding under targeted therapy, chemotherapy, surgery, and radiotherapy. We use ctDNA metrics to define dynamic biomarkers of treatment efficacy and show that they outperform existing ctDNA biomarkers. Our work demonstrates ways in which early ctDNA can be used to quickly and reliable predict treatment response or lack thereof.

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MS59

Cardiac Fluid-Structure Interactions

Fluid-driven material damage and failure are significant in many engineering and industrial fields, such as tissue failure, fracking, and blasts on structures. However, conventional continuum-based methods have challenges in simulating such failure processes. In this work, we introduce an extension of the immersed boundary frameworks called an immersed peridynamics method to simulate soft material damage and failure by integrating an immersed-type method with peridynamics. Numerical examples demonstrate constitutive correspondence with classical continuum mechanics for non-failure cases along with essentially grid-independent predictions of fluid-driven soft material failure.

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MS59

Methods for Mixing Analysis for Pulsing Xeniid Corals

A unique pulsating movement is observed in the sessile soft corals belonging to the Xeniidae family. Experiments and numerical results suggest that the energetically expensive behavior facilitates the oxygen-limited photosynthesis of the symbiotic algae by decreasing the oxygen buildup around the tentacles. Analyzing and quantifying this mixing of the fluid by the pulsing action can provide insight into the effects of climate change on the species and in the development of industrial or engineering pulsing mechanisms for facilitating mixing. To this end, we present numerical methods used to analyze and quantify this mixing using a three-dimensional Navier-Stokes simulation of a pulsing coral whose kinematics emerge from a prescribed active tension. We also present results demonstrating the

effects varying parameters on the amount of mixing seen.

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MS59

Flow Through the Oral Arms of Upside Down Jellyfish

Rising ocean temperatures have led to an increase in invasive jellyfish populations, notably the Cassiopea sp. (upside-down jellyfish), which thrives in warmer waters. This study focuses on understanding their unique interaction with local flows. Cassiopea, distinguished by their inverted posture with their bells resting on the ocean floor and oral arms extended upwards, create distinctive flow patterns crucial for feeding, nutrient exchange, and waste removal. Contrary to previous research that often overlooks the oral arms, our model integrates these structures and includes their porosity. I will present our novel modeling approach, highlighting how the complex structure of Cassiopea's oral arms significantly influences the surrounding water flow.

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MS59

Exploring the Fluid Dynamics of Establishing Symbiosis in the Bobtail Squid

The bobtail squid Euprymna Scolopes employs counter-illumination to protect itself from predation, a process crucial to its survival. For this, it must successfully extract the bioluminescent bacteria, Aliivibrio fischeri, from its environment. This capture process takes place largely on the surface of a specialised organ within the squid, known as the light organ, which co-evolved to support the bacterial colonisation of the squid. Fluid-structure interactions at the surface of the light organ and bacterial chemotaxis facilitate this process. By combining techniques from low Reynolds number fluid dynamics and sensitivity analysis within numerical simulations, we will explore how the geometry of the light organ impacts the ability of the squid to capture and select its bacterial partners.

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MS60

Mechanistic Insights into the Fluidity and Rheological Behavior of Epithelial Tissues Using Biophysical Models

During embryonic development, tissues experience significant reshaping to create functional organs. Adult animals also face ongoing mechanical stresses and deformations in their cells and tissues to maintain physiological functions. The ability of cells to resist these mechanical forces, as well as to flow collectively, is crucial for both embryonic development and adult physiology. These mechanical changes can be self-generated at the cellular level or imposed externally by adjacent tissues and organs. Past research in tissue mechanics has often focused either on how tissues respond to external forces or on the internal stresses generated within the cells. In contrast, our study integrates both aspects using a 2D active vertex model of confluent tissue. We investigate how external forces applied across the tissue interact with internal stresses arising from cellular movements. Specifically, we explore how the balance between external and internal forces influences the overall mechanical behavior of the tissue. Our focus is on tissues that are near a transition point between behaving like a solid or a fluid, known as the jamming/unjamming transition. In such tissues, we identify a range of intriguing rheological properties, including yielding, shear thinning, continuous shear thickening (CST), and discontinuous shear thickening (DST). Our model offers a comprehensive framework for understanding the complex, nonlinear rheological behaviors observed in living tissues.

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MS60

Tgf-Beta Signaling and the Epithelial Mesenchymal Transition: An Interdisciplinary Approach

The epithelial mesenchymal transition (EMT) is a process by which cells gain the migratory properties associated with mesenchymal cells. This transition allows cells to migrate away from a tumor while maintaining this invasive behavior, suggesting that there is a bistable switch between the epithelial and mesenchymal phenotypes. Here, we present an interdisciplinary approach to understanding EMT. Using biological experiments (protein extractions, flow cytometry, and qPCR), we found evidence of this bistability in the MCF7 cell line. Using this data, we created a simple mathematical model that examines the relationship between E-cadherin, a protein associated with the epithelial phenotype, and Slug, a transcription factor upregulated during EMT, in response to pro-epithelial and pro-mesenchymal factors, cell-cell contact and TGF-b, respectively. We propose a reversible bistable switch in response to a loss of cell-cell contact but an irreversible switch when the cell is exposed to TGF-b. Taken together, this model shows that acquiring invasive behavior in cells with high levels of cell-cell contact is not impossible but depends on the cooperation between the two switches. Ultimately, our model works well to predict E-cadherin and Slug mRNA expression in low confluence experiments, while also highlighting issues that arise when comparing experimental results to theoretical predictions.

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MS60

Statistical Physics of Embryonic Transcriptomes Reveal Map of Cellular Interactions

Starting from one totipotent cell, complex organisms form through a series of differentiation events, resulting in a multitude of cell types. Conceptualizing this process as a single cell differentiating in response to external signals neglects the interconnected nature of development; cells must coordinate within an embryo and differentiate in a spatially robust manner. Using recent single-cell sequencing data of early ascidian embryos, we leverage natural variation together with techniques from statistical physics to investigate development at the level of a complete interconnected embryo. After robustly identifying distinct transcriptomic states or cell types, a statistical analysis reveals correlations within embryos and across cell types beyond mean expression levels. From these intra-embryo correlations, we infer minimal networks of cell-cell interactions using regularization and the principle of maximum entropy, revealing spatial connections that are of key importance in development.

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MS61

Affinity-dependent Mutation Rate Leads to Efficient Germinal Center Reaction

B cells producing high-affinity antibodies are generated through a dynamic evolutionary process known as affinity maturation, which takes place in a specialized microenvironment called a germinal center. Affinity maturation is driven by cycles of T cell mediated selection and clonal expansion of B cells expressing high-affinity antibodies. During cell division of selected B cells, antibody diversity is generated through somatic hypermutation (SHM), where the mutation rate per division is believed to be fixed. However, as SHM is random, deleterious mutations occur much more frequently than affinity enhancing mutations, which is especially counterproductive for B cells expressing high-affinity antibodies. How can SHM drive efficient affinity maturation despite producing mostly deleterious mutations? In this work, we present a model and supporting experimental data suggesting that affinity maturation is optimized by modulating the rate of SHM depending on affinity.

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MS61

Evolution-Based Treatment Strategies in Cancer

Evolution-informed therapies exploit ecological and evolutionary consequences of drug resistance to inhibit the expansion of treatment-resistant populations and prolong time to progression. In the first part of the talk, we focus on conceptual development of alternative treatment strategies that leverage the principles of evolution to mitigate treatment resistance. We introduce this broad class of drug scheduling strategies known as evolutionary therapies and explain how mathematical modeling can aid by providing patient-specific predictions as a decision-support tool for providing clinical insight. Next, we explore a practical implementation of an evolutionary therapy within an in vivo model of non-small-cell lung cancer treated with ALK inhibitors. Treatment-naive tumors are associated with more convex exposure-response curves (low doses provide sufficient response) while evolved-resistance tumors are generally more concave (requiring high doses for equivalent response). We explore the practicality of guiding treatment scheduling based on convexity (or concavity). Concave exposure-response functions predict that the daily administration of a dose of x may be less efficacious than a regimen that switches equally between 120% of x and 80% of x (every other day). Convex exposure-response provide the opposite prediction (continuous dosing is best). We validate the effectiveness of this approach in non-small cell lung cancer in vivo models by comparing response predictions based on the convexity of dose response (ALK-inhibitors) for both continuous versus high / low dosing schemes. However, treatment fails due to the gradual evolution of treatment resistance, as tumors acquire cooperating genetic and epigenetic adaptive changes. Using mathematical modeling, we can predict the dose-dependent rate of resistance onset. Drug holidays have recently been suggested for their potential re-sensitization effect in tumors. Indeed, the mathematical modeling here also predicts a second-order trade-off between maximizing response (continuous protocols) and maintaining drug sensitivity (high / low protocols), suggesting re-sensitization is possible. Thus, we propose alternative switching treatment protocols to balance this trade off: continuous followed by high / low (or vice versa). Mathematical modeling predicts the optimal switching time point, which is subsequently validated by measuring response and sensitivity to treatment under these protocols in vivo. This integrative mathematical-experimental approach to treatment scheduling illustrates the effectiveness of incorporating second-order effects into protocol design. This framework also validates a promising switching approach to mitigating the evolution of resistance by initial continuous treatment followed by a switch to high / low intermittent dosing.

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MS62

Stochastic Analysis of Chromatin Modification Circuits That Control Epigenetic Cell Memory

Epigenetic cell memory, the inheritance of gene expression patterns across subsequent cell divisions, is a critical property of multi-cellular organisms. It was previously found via simulations of stochastic models that the time scale separation between establishment (fast) and erasure (slow) of chromatin modifications (such as DNA methylation and histone modifications) extends the duration of cell memory, and that different asymmetries between erasure rates of chromatin modifications can lead to different gene expression patterns. We provide a mathematical framework to rigorously validate these computational findings using stochastic models of chemical reaction networks. For our study of epigenetic cell memory, these are singularly perturbed, finite state, continuous time Markov chains. We exploit special structure in our models and extend beyond

existing theory to study these singularly perturbed Markov chains when the perturbation parameter is small. We also develop comparison theorems to study how different erasure rates affect the behavior of our chromatin modification circuit. The theoretical tools developed in our work not only allow us to set a rigorous mathematical basis for highlighting the effect of chromatin modification dynamics on epigenetic cell memory, but they can also be applied to other singularly perturbed Markov chains beyond the applications in this work, especially those associated with chemical reaction networks.

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MS62

Asymptotic Analysis of First Hitting Times with Lvy Flights

How long will a confined Brownian particle take to first hit a small target? It is well known that as the target size decreases the mean-first-hitting-time (FHT) diverges in dimensions two and greater, whereas it remains bounded in one dimension. What happens if the particle instead exhibits Lvy flights? In this talk I will describe how asymptotic techniques can be used to characterize the mean-FHT for a Lvy flight in a periodic one-dimensional domain. These asymptotic results illustrate that as the stability index of the Lvy flight is decreased we recover behavior that is qualitatively similar to that of a one-, two-, and higher-dimensional Brownian particle. We conclude with a brief discussion of the "optimality' of Lvy flights.

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MS62

Conditional Stochastic Extinction in Population Models

A fundamental question in population ecology concerns the likelihood of persistence of two or more interacting species and, conversely, the risk of extinction of one or more of these species. The importance of quantifying this extinction risk can be observed in models of cancer immunotherapy, where treatment success is described by an extinction event. While it is well understood that the mean-field description fails to capture species extinction, stochastic simulation reveals trajectories resulting in extinction events before entering a metastable state. Our analysis shows that these trajectories occur with high probability and, unlike previous studies, require only small fluctuations from the mean-field trajectory. We derive a modified boundary condition to the Fokker-Planck approximation describing the probability of extinction prior to entering the metastable state. Our analysis of this model allows us to quantify extinction risk, and reveals the important role of initial population size.

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MS62

From Formulas to Futures, Mathematical Insight into Endosomal Escape

The research project focuses on developing a new method to measure the endosomal escape following the successful delivery of siRNAs (small interfering RNAs) into ovarian cancer cells using fusogenic peptides. The objective is to counteract the rapid degradation of siRNAs in the endosome, a problem that the specially designed fusogenic peptides address. These peptides, created by Dr. Alexander-Bryant, attach to siRNAs and facilitate their movement from the endosome into the cytosol. Our goal here is to develop and optimize statistical models to quantify the endosomal escape of siRNAs in cancer cells.

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MS63

Impacts of Behavioral Adaptation Assumptions on Disease Prevalence Forecasts

Forecasting the prevalence of an infectious disease requires making assumptions about how individuals social distancing behavior will change over time in response to both extrinsic factors (e.g., policy, seasonal changes) and intrinsic factors (e.g., compliance fatigue, fear of the disease). Further, bias or delays in prevalence estimates derived from testing, hospitalization, or mortality data may impact social distancing behavior. In this talk, we will examine how social distancing behavior is expected to change over time assuming: (1) full compliance with an optimal social distancing strategy imposed by a central planner, (2) myopic decision-making with perfect knowledge of disease prevalence, (3) myopic decision making with imperfect knowledge of disease prevalence resulting from reporting bias or delays. We will compare the total cost of the epidemic (including social distancing and infection costs) under the optimal, myopic - perfect information and myopic biased/delayed information scenarios. Finally, we will examine how a mis-match between the true and assumed behavioral adaptation impacts the accuracy of near-term disease prevalence forecasts.

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MS63

Impact of Antibody Waning on Estimated SARS-CoV-2 Cumulative Incidence and Severity Risk

Serology assesses antibody levels following infection, allowing inference of cumulative incidence and fatality or hospitalization risk from infection (IFR and IHR, respectively). Waning of antibody titers against SARS-CoV-2, the viral cause of the COVID-19 pandemic, can bias these inferences. This seroreversion bias varies by immunoassay. We, however, know of no systematic, quantitative assessment of how assay characteristics impact seroreversion risk. We quantify the contribution of immunoassay design and antigen target to seroreversion bias, facilitating assay-specific seroreversion adjustments. Lateral flow assays, though cheaper and easier to use in the field, suffered greater seroreversion risk than laboratory enzyme-linked immunosorbent assays. Greater seroreversion also occurred for antibodies against the nucleocapsid protein concealed within SARS-CoV-2 than for antibodies against the spike protein on the viral surface where the spike remains exposed to antibodies and to antibody-producing cells. Seroreversion adjustment reduced differences in estimated cumulative incidence, IFR, and IHR between serology studies that used assays at greater seroreversion risk compared to studies that used assays with less seroreversion risk. And seroreversion more strongly skewed studies with later sampling dates, exaggerating calculated IFR and IHR with time, including for longitudinal studies. These results may inform seroreversion modeling during future pathogen outbreaks.

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MS63

Facets of Measure Theory: Diagnostics, Prevalence Estimation, and Uncertainty Quantification

Diagnostic testing and prevalence estimation have become increasingly important aspects of measurement science that inform public health decisions. These tasks also play critical roles in surveillance of wildlife populations for identification of pathogen reservoirs and detection of emerging diseases. Notably, the types of data available data for estimating prevalence varies wildly between these contexts, making it difficult to pin down mathematical principles that inform them all. In this talk, I consider how basic ideas from probability and specifically a measure-theoretic perspective thereof unify disparate problems in wildlife and human serology, and surprisingly, also make rigorous connections to uncertainty quantification. I begin with a prototypical two-cave problem, wherein we only are given serology measurements on bats from two different caves, each having a different but unknown seroprevalence of antibodies against a disease (e.g., Ebola). I then derive: (i) a one-to-one mapping between optimal methods for classifying a bat as belonging to cave 1 or cave 2 and the corresponding optimal solution for seropositive and seronegative populations; (ii) a system of non-linear equations whose solution is the true prevalence of seropositive individuals in each cave. Finally, I consider how the analysis motivates a re-interpretation of classification in terms of relative probability level sets and suggests novel methods for uncertainty quantification in diagnostics.

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MS63

Equitable Access to Vaccines Makes a Life-Saving Difference to All Countries

Vaccine inequity is a major challenge for the global response to the COVID-19 pandemic, as it leads to high rates of infections and deaths in low- and middle-income countries (LMICs) and the emergence and spread of new variants that may evade existing vaccines. We use a multistrain metapopulation model to show that equitable vaccine allocation strategies can substantially curb the spread of new strains, while vaccine inequity provides only limited and short-term benefits to high-income countries (HICs). We also propose AI tools that can predict and prevent genetic mutations that may cause disease or escape from immune recognition, and can help design more effective and precise vaccines. By using these solutions, we can achieve a more equitable, effective, and sustainable response to the current and future health crises.

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MS64

Leveraging Wastewater Surveillance to Understand Multi-Strain Dynamics

Wastewater-based surveillance (WBS) emerged during the COVID-19 pandemic as a promising complementary tool to monitoring disease burden in communities. WBS offers unprecedented insight into viral evolution and multi-strain dynamics. We integrate wastewater data with disease transmission models in order to study competition in the context of two strains circulating within a population and use this data to validate our models.

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MS64

Your Guide to Cleverly Introducing New Data Streams into Nonlinear Odes

Identifiability refers to the ability to recover unknown parameters uniquely from measured input-output data for a given model. Systems analysis and research using nonlinear ordinary differential equations (ODEs) is influenced greatly by this property. When unique parameter estimates cannot be obtained for a model, there are potentially real-world consequences: misplaced supplies, poorly designed experiments, or unrealistic predictions. Methods have been developed to algebraically and numerically determine the identifiability of a model, as well as some tools to resolve unidentifiability issues. These solutions, such as re-parameterizing or collecting more data, can be potentially costly or impractical. We present an alternative method for resolving unidentifiability in a system by introducing a new data stream correlated with a parameter of interest. First, we demonstrate how and when non-constant input data streams can be introduced into any nonlinear ODE system. Then, we prove when these input functions improve structural and potentially also practical identifiability for a given model and relevant data streams. By utilizing pre-existing data streams, these methods can potentially reduce experimental costs, while still answering key questions.

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MS64

Investigating Heterogeneity in HIV Viral Rebound Times

Antiretroviral therapy (ART) effectively controls HIV infection, suppressing HIV viral loads to levels undetectable by commercial tests. While typically suspension of therapy is rapidly followed by rebound of viral loads to high, pre-therapy levels, observations from the last decade give nuance to that statement: in a small fraction of cases, rebound may be delayed by months, years, or even possibly, permanently. We will discuss modeling to investigate that heterogeneity in outcome of treatment suspension, focusing on time to viralrebound. We will first discuss our data-validated, mechanistically-motivated survival function for time-to-rebound using time-inhomogeneous branching processes. We show good agreement with data for both rapid and significantly delayed viral rebound. We will then use this model to characterize the impact of covariates such as treatment initiation time and pre-ART drug regimen on time to rebound.

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MS64

Tissue-Specific Control of T Cell Responses to Optimize Trade-Offs in Immune Pathologies

T cells must mount destructive responses to eliminate threats from the host while simultaneously not compromising essential tissue functions during inflammatory responses. How the proper balance between host defense and tissue integrity is set remains poorly defined, especially considering that different tissues exhibit disparate properties, including host critical functions, selection pressures, and regenerative capacities. These varying properties and constraints suggest that tissues must manage distinct trade-offs between collateral damage and destructive T cell responses to systemically protect the host. Thus, we hypothesize that the parameters governing T cell immune interactions vary naturally throughout the host, optimally adjusting T cell control on a tissue-specific basis to reflect distinct trade-offs between host protection and collateral damage. To explore this hypothesis, I employ high-resolution multiplexed microscopy to quantify immune parameter variations in different tissue contexts coupled with mathematical modeling to understand the dynamics and control of tissue-specific T cell regulation. We pose tissue-specific trade-offs as multi-objective optimization problems and show that our mathematical immune model helps explain our in vivo imaging results.

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MS65

A Predictive Tool for the Expansion of Tumor Infiltrating Lymphocytes in Patients Bladder Tumor

The first clinical trial with adoptive T cell therapy (ACT) that uses bladder cancer patients autologous tumor-infiltrating T lymphocytes (TILs) recently opened at Moffitt. In this work, we present a machine learning predictor of expansion of tumor-infiltrating lymphocytes (ML-PETIL) that uses 102 retrospectively collected patient tumor data with 16 commonly collected features in the clinic that are either demographic, clinical, or biological sample-related. The proposed method consists of a suite of algorithms: (i) the random forest (RF) method was applied to the internal training/testing cohort to identify robust predictive features, (ii) the support vector machine (SVM) was used to learn the optimal classification hyperparameters based on the training cohort with an internal 10-fold cross-validation, (iii) Mathews correlation coefficient (MCC) was used to determine the decision boundary threshold (Yes TILNo TIL) that accounts for the imbalances in the training dataset. The MCC method produced a decision boundary threshold of 0.613. This optimal SVM-MCC model was then verified on the testing cohort yielding an accuracy of 0.72, specificity of 0.667, sensitivity of 0.75 and AUC=0.778 and validated on the external validation cohort with an accuracy of 0.8, specificity of 0.75, sensitivity of 0.812, and AUC=0. 828. This computational predictor can be used as a clinical supportive tool to stratify patients eligibility for an immune-based therapy, such as the ACT-TIL.

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MS65

Micro-Environmental Modulation and Optimal Control in the Tumor-Immune Interaction

There are different types of cancer dormancy, including cellular and immune-mediated dormancy. The balance between pro-tumor and anti-tumor immunity plays a critical role in cancer elimination or progression, resulting in cancer escape, elimination, or equilibrium. This equilibrium phase is associated with immune-mediated dormancy, where T cell killing matches the cancer division rate. However, previous mathematical models using ordinary differential equations (ODEs) have limitations, including neglecting the distributional behavior of cells and the probability of extinction at low population sizes. To address these limitations, this talk will present a new stochastic model based on non-linear birth-death processes to more accurately describe dormancy dynamics. The model assumes a cancer population undergoing stochastic birth and death with an exponential growth rate, modified by an immunomodulation function that depends on the population size and an inhibitory element. This modeling framework can be used to identify the immunomodulatory effects of cancer therapy. We expand on this framework to describe micro-metastatic dormancy as an optimal control problem where the tumor population has some degree of control over modulating their birth and death rates via their apoptosis signaling pathway. We analytically approach this control problem to find a optimal policy for the tumor dormancy from the perspective of the tumor.

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MS65

Personalized Predictions of Glioblastoma Infiltration: Mathematical Models, Physics-Informed Neural Networks and Multimodal Scans

Predicting the infiltration of Glioblastoma (GBM) from medical MRI scans is crucial for understanding tumor growth dynamics and designing personalized radiotherapy treatment plans.Mathematical models of GBM growth can complement the data in the prediction of spatial distributions of tumor cells. However, this requires estimating patient-specific parameters of the model from clinical data, which is a challenging inverse problem due to limited temporal data and the limited time between imaging and diagnosis. This work proposes a method that uses Physics-Informed Neural Networks (PINNs) to estimate patient-specific parameters of a reaction-diffusion PDE model of GBM growth from a single 3D structural MRI snapshot. PINNs embed both the data and the PDE into a loss function, thus integrating theory and data. Key innovations include the identification and estimation of characteristic non-dimensional parameters, a pre-training step that utilizes the non-dimensional parameters and a fine-tuning step to determine the patient specific parameters. Additionally, the diffuse domain method is employed to handle the complex brain geometry within the PINN framework. Our method is validated both on synthetic and patient datasets, and shows promise for real-time parametric inference in the clinical setting for personalized GBM treatment.

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MT1

Parameter Inference

Input your abstract, including TeX commands, here. The abstract should be no longer than 1500 characters, including spaces. Only input the abstract text. Don't include title or author information here.

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MT1

Parameter Inference

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MT2

Sensitivity Analysis in the Life Sciences

Sensitivity analysis (SA) describes a host of methods to assess the impact of variations in parameters, initial conditions, and other factors on model predictions. While used extensively in engineering applications to aid in design, uncertainty, and robustness measures, SA has different nuances in life science applications. For example, the sources of parameter variations are quite different in biological applications due to intrinsic variations in living organisms rather than variations due to production that can be better controlled. Additionally, the goal of SA can be much more flexible in biological applications and be geared towards understanding optimal control, experimental design and model robustness. The goal in this mini-tutorial is to give an overview of several classes of SA, show some relatively straightforward Python/Matlab implementations, and examples drawn from classical life-sciences applications. This will provide a framework for determining the most appropriate method and implementation depending on the needs. We will also spend some time discussing how the three topics of SA, uncertainty quantification and parameter identifiability are inter-related.

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MT3

Evidence Integration and Decisions on Social Networks

See tutorial description.

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MT4

Stochastic Simulation Algorithms for Biochemical Systems with Non-Markovian and Non-Elementary Reactions

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PP1

Simulating Biological Patterning Using Vertex Models

Repeating patterns, such as hair follicles and bristles play important roles in the lives of animals. These structures help animals to optimally sense their environment. Notch signaling is known to control these patterns. Primarily, Notch signaling is a local communication between neighboring cells in contact (signal-sending and signal-receiving cells). The local communication between cells in contact is not able to explain all the complex biological patterns observed. Further studies reveal long-range communication between cells using actin-based filopodia called cytonemes. The precise understanding of how cells communicate through their filopodia on a long range is unclear. In this work, we develop a mathematical model to help unravel the mystery of this long-range communication between cells.

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PP1

A Machine Learning Framework for Efficient classification of Bristle Cell Patterns in Fruit Flies

Repeating patterns are important for epithelia that sense the environment. Optimizing the organization of these tissues helps them to function normally. A major challenge for researchers is the ability to quantify and classify complex cell and tissue patterns across wild type and perturbed conditions. We study this problem in the fruit fly Drosophila melanogaster, where the organization of sensory bristles on its thorax contributes to the proper function of its peripheral nervous system. A well-known perturbation in bristle cell organization is density, which has been found to increase in certain fly mutants. It is unclear if this density phenotype is shared by other mutants and whether additional pattern features beyond density exist that can be used to distinguish bristle patterns. In this study, we investigate the utility of clustering features of bristle organization in distinguishing between wildtype and perturbed patterns. The K-means algorithm is used to identify and quantify clusters. Our study finds that perturbed patterns generated through various genetic knockdowns show better organized clusters than wild type patterns.

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PP1

Dynamic Modeling of Gene Regulatory Networks

Understanding the intricate dynamics of gene regulatory networks (GRNs) is crucial for unraveling the complexity of cellular processes and their dysregulation in diseases. This research focuses on the dynamic modeling of GRNs, employing advanced computational techniques to simulate

and analyze the temporal aspects of gene expression. The study explores the impact of time-dependent factors, such as feedback loops, delays, and stochasticity, on the behavior of GRNs. By employing dynamic models, we aim to capture the nuanced interactions among genes and their regulatory elements, shedding light on the temporal orchestration of cellular events. The research also investigates the implications of dynamic modeling in predicting system responses to perturbations and external stimuli, contributing to the understanding of robustness and adaptability in gene networks. The findings from this study not only enhance our comprehension of fundamental biological processes but also have potential applications in fields such as systems biology, drug discovery, and personalized medicine.

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PP1

A Model for Bleb-Based Chemotaxis Using the Level Set Method

Cells utilize blebs as one of the primary structures for migration. Blebs, which are spherical cell membrane protrusions, are driven by intracellular fluid pressure to propel the membrane forward. Many questions remain unanswered regarding the physical and chemical mechanisms governing bleb-based motility. Particularly intriguing is the role of membrane-to-cortex binding proteins in regulating bleb size and frequency, as well as how cells translate mechanochemical cues into coordinated movement. In this work, we present a model for bleb-based chemotaxis, simulated using the level set method [Liu Yang, Janet C Effler, Brett L Kutscher, Sarah E Sullivan, Douglas N Robinson and Pablo A Iglesias, Modeling cellular deformations using the level set formalism]. We use this model to explain recent experimental data from Dictyostelium discoideum cells which show that loss of Talin A reduces the size and frequency of blebs.

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PP1

Modeling Stage-Specific Effects of Induced Resistance on Herbivore Population Growth

Herbivorous insects have negative effects on the growth of plants. In response, plants can produce chemical defenses that slow insects rates of feeding, growth, or reproduction. Many models have looked at how feedback through this induced resistance affects herbivore population dynamics. These models typically assume uniform population structures, despite models from other areas suggesting that stage structure can be important. Insects have discrete life stages with different growth rates, feeding rates, and sensitivities to diet quality. We aimed to determine whether including stage structure in models of induced resistance would change model behavior, particularly when including time lags in induced resistance. We used a general discrete-time difference equation model to address how insect stage structure and induced resistance affect insect populations. The model has five distinct insect size classes, from egg to adult, and plant quality depends on insect density. Increasing the time lag in the plants induction response creates a Hopf bifurcation by varying insect sensitivity to plant quality, leading to cycles in insect density. However, cycles only appear when pupal emergence is relatively synchronized. These results suggest that population cycles may only be possible in a narrow region of parameter space and that changes to pupal emergence patterns, such as those caused by variation in climate, may affect whether cycles are seen in natural populations.

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PP1

Microbiome Profiling of St. Lawrence River Data and Its Relationship with Water Quality Measures Using Bayesian Regression Analysis

This study explores the intricate relationship between the microbiome profile of the St. Lawrence River and key water quality measures through the application of Bayesian regression analysis. Leveraging advanced microbial sequencing technologies, we conducted a comprehensive assessment of microbial communities within the river ecosystem. Concurrently, various water quality parameters were measured, including Total phosphorus level, Chloride level, Sulfate level, Optical Brightener(OB) .The Bayesian regression analysis employed in this research allows for a nuanced understanding of the complex interplay between microbial diversity and water quality. By integrating high-throughput sequencing data with Bayesian normal regression methods, we aim to identify significant microbial taxa associated with specific water quality indicators. The findings from this study contribute to a more profound comprehension of the ecological dynamics within the St. Lawrence River, providing valuable insights for environmental monitoring and sustainable water management practices.

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PP1

Mathematical Models of Autistic Aging Using The Virtual Brain

The Virtual Brain (TVB) is a model simulation platform for creating full-brain dynamic models that simulate neuroimaging data. TVB constructs a graph of a parcellated brain based on structural and functional data, where vertices (or nodes) and edges of the graph represent brain regions and axonal connections between regions. A system of ordinary differential equations is used to simulate neuron population activity within nodes (Sanz-Leon et al, 2015). TVB has been used to study aging and neurodegenerative brains to gain insight into pathology (Stefanovski et al, 2019; Zimmerman et al, 2018; Nakagawa et al, 2013). Recent studies suggest that people with autism have higher risk of experiencing neurodegenerative diseases (Vivanti et al, 2021; Starkstein et al, 2015). In this study, we use brain data from aging autistic and neurotypical adults to create personalized brain models in TVB. Following previous

studies, the reduced Wong-Wang model is used to represent the coupled excitatory and inhibitory populations (Sanz-Leon et al, 2015) to simulate neuron population activity in each node, which is transformed to simulated fMRI data. Four key model parameters are optimized through statistical comparison of simulated and empirical data (Klein et al, 2021; Aerts et al, 2020; Zimmerman et al, 2018; Adhikari et al, 2015). We compare optimized parameters between groups to categorize possible differences between aging autistic and neurotypical brain connectivity.

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PP1

A Mathematical Modeling Reveals Crizotinib, a Class of Medication for Metastatic Non-Small Cell Lung Cancer Causes Cardiac Toxicity

Purpose: Crizotinib is orally used as a multitargeted receptor tyrosine kinase inhibitor for the treatment of metastatic non-small cell lung cancer (NSCLC). The purpose of this study is to investigate the propensity of Crizotinib to modulate cardiac electrophysiological properties using a mathematical model. Methods: The sinoatrial node (SAN) cell is described as an equivalent electrical circuit with ion channels, which are established using the ordinary differential equations in HH formalism. The biophysically altered funny current is integrated into the single SA node electrophysiological model to investigate Crizotinib's modulating properties. Results: The resting membrane potential (RMP) is set at -80mV. A current pulse of 2 nA for 10 ms is injected to evoke the AP. The steady-state value of the activation parameter of the funny current (if) is shifted to the negative side after applying Crizotinib of 1 μmol/L. The action potential timing is altered when we incorporate the biophysically modified funny current. The results show that the modified funny current plays an important role in reducing the frequency of the spontaneous action potentials at the SA node. Conclusions: Our simulations suggest that Crizotinib reduces the frequency rate of the spontaneous action potential firing by reducing the funny current density. Therefore, the dosage of Crizotinib should be controlled to avoid cardiac toxicity.

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PP1

Modeling Collective Symmetry Breaking in Cells

Collective cell migration is necessary in several important physiological processes including embryonic development and immune system response. Prior to migration, a cell must break its symmetry and establish a front-to-rear directional axis. There are several theories proposed for symmetry breaking, including Turing pattern formation [Goryachev AB, Leda M, Many roads to symmetry breaking: molecular mechanism and theoretical models of yeast cell polarity, 2017]. Here, we use an established model that couples the kinetics of a biochemical network to the dynamics of mechanical structures in cells [Copos C, Mogilner A, A hybrid stochasticdeterministic mechanochemical model of cell polarization, 2020]. In the model, chemicals and mechanical structures simultaneously segregate leading to symmetry breaking in a single cell. But how do groups of cells synchronize this process so that their directional axes point in the same direction? We extend the existing framework to investigate the specific interactions in the cell-cell region that ensures both cells directional axes align parallel to each other. We test over 100 interaction rules by modifying the reaction rates in the biochemical networks or the growth rates of the mechanical structures. We find that interaction rules which regulate the signaling kinetic rates differentially and dependently on the local mechanical forces are the most successful in achieving high probability of co-aligned directional axes in the paired cells.

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PP1

Phase Response Properties of Relaxation Oscillators in Their Singular Limit: Implications for Coordination in Neural Central Pattern Generators

Relaxation oscillations arise naturally in many neural central pattern generating circuits. They are characterized by periodic oscillations that switch between long relaxation (ON/OFF) intervals of slowly evolving dynamics and short transition intervals of rapidly evolving dynamics. If slow dynamics occur on time scale t, fast dynamics occur on the timescale of $\bar{t} = t/\epsilon$ with $0 < \epsilon << 1$. Phase response curves (PRCs) describe the change in phase of an oscillator in response to small abrupt perturbations. PRCs play an important role in understanding how oscillators respond to continuous external input and how networks of couple oscillators coordinate their activity. Previously, Itzikevitch (2000) analytically derived approximations for the phase response curves of relaxation oscillators in the singular limit, i.e., $\epsilon \to 0$. Here, we reexamine this case and explicitly include corner-layer dynamics that Itzhikevitch omitted in his analysis. The corner-layers are associated with the shift from the slow dynamics to the fast dynamics in which the system evolves at an intermediate timescale $\hat{t} = t/\epsilon^{\frac{2}{3}}$. Importantly, we show that the primary sensitivity of relaxation oscillators in response to perturbations to the fast variable occurs in the corner-layer and that the sensitivity in the other intervals are negligible. We then show how this influences the coordination of activity in neural central pattern generators.

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PP1

Assessing the Impact of Seasonality on Wolbachia-Based Controls for Mosquito-Borne Diseases

Wolbachia infection in *Aedes Aegypti* mosquitoes can render mosquitoes less capable of spreading mosquito-borne diseases, such as dengue and Zika. We developed and analyzed a mechanistic compartmental ordinary differential equation model to evaluate the effectiveness of *Wolbachia*-based vector control strategies among these wild mosquitoes in Australia, where ongoing field trials are implemented for dengue control. The model tracks the mosquito life stages, including egg, larva/pupa, and adult (male and female), and we aim to understand how seasonality affects the spread and the establishment of stable *Wolbachia* infection among *Aedes Aegypti* mosquitoes. We incorporated time-varying parameters to account for the impact of seasonal climate (i.e. temperature and humidity) on mosquito life traits. These include mosquito death rates at different life stages, female reproduction rates, development rates, and carrying capacity for the larval stage. Taking this into account, we identified a threshold release number of infected mosquitoes needed to establish a stable *Wolbachia* prevalence in the field. We further studied how this threshold may vary given the seasonality and explored the optimal time window for *Wolbachia* releases.

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PP1

Characterization of Tumor Microenvironment Using a Heterogeneous Model: A Simulation Study Based on Combined Cellular Automation and Diffusion-Reaction Model

Prior computer simulations to characterize tumor growth within a host microenvironment have incorporated tumor vasculature, viable tumor and necrotic cells, and fluctuations of H+ and glucose concentrations to provide a simulation-based characterization of tumors during early tumor growth. Here, we extend this approach to incorporate into the model, 1) heterogeneous vascular features, 2) irregular cellular spatial structures, 3) metabolic alterations including acidosis, hypoxia, and nutrient stress which are reflective of tumors during advanced stages of growth. We evaluate the impact of these alterations on the clonal evolution of cancer. In this work, we develop a computational model of the tumor microenvironment using a hybrid multiscale mathematical model to characterize vascular, cellular, and metabolic heterogeneity within the tumor microenvironment. The hybrid model is formed with a combination of cellular automatic to characterize cell-cell interaction and differential equations to describe metabolic concentrations. The impact on tumor growth was evaluated with a range of parameter settings to characterize vascular, cellular, and metabolic heterogeneity. We model aggressive tumors by incorporating vascular and cellular heterogeneity, acidosis, glycolysis, blood flow, oxygen, and nutrient supply into the combined cellular automation and diffusion-reaction model.

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PP1

Zigzag Persistence for Coral Reef Resilience Using a Stochastic Spatial Model

A complex interplay between species governs the evolution of spatial patterns in ecology. An open problem in the biological sciences is characterizing spatio-temporal data and understanding how changes at the local scale affect global dynamics/behaviour. Here, we extend a well-studied temporal mathematical model of coral reef dynamics to include stochastic and spatial interactions and generate data to study different ecological scenarios. We present descriptors to characterize patterns in heterogeneous spatio-temporal data surpassing spatially averaged measures. We apply these descriptors to simulated coral data and demonstrate the utility of two topological data analysis techniquespersistent homology and zigzag persistencefor characterizing mechanisms of reef resilience. We show that the introduction of local competition between species leads to the appearance of coral clusters in the reef. We use our analyses to distinguish temporal dynamics stemming from different initial configurations of coral, showing that the neighbourhood composition of coral sites determines their long-term survival. Using zigzag persistence, we determine which spatial configurations protect coral from extinction in different environments. Finally, we apply this toolkit of multiscale methods to empirical coral reef data, which distinguish spatio-temporal reef dynamics in different locations, and demonstrate the applicability to a range of datasets.

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PP1

An Extended Atom Type System for Algebraic Graph-Based Machine Learning Model for Blood-Brain Barrier Permeability Prediction

In the complex realm of drug discovery, a crucial challenge is predicting whether a drug-like molecule can cross the blood-brain barrier (BBB). This prediction is vital for developing central nervous system drugs, as it accelerates the discovery and validation of neuroactive agents. Recent advancements in biomolecular sciences have seen the rise of algebraic graph-based models for accurate representation of molecular properties and BBB permeability prediction. Our novel approach, AGL-BBB-Score, utilizes these models along with extended atom types in multiscale weighted colored subgraphs. These graphs effectively capture the interactions that influence BBB permeability, based on key physicochemical properties. When combined with the gradient-boosting decision tree (GBDT) algorithm, AGL-BBB-Score demonstrates superior performance in predicting BBB permeability compared to existing models. This innovative method streamlines the drug development process, especially in neuropharmacology, by providing a more efficient and cost-effective approach to evaluating BBB permeability of drug candidates.

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PP1

Infection Induced Increases to Population Size During Cycles in a Discrete-Time Epidemic Model

One-dimensional discrete-time population models, such as those that involve Logistic or Ricker growth, can exhibit periodic and chaotic dynamics. Expanding the system by one dimension to incorporate epidemiological interactions causes an interesting complexity of new behaviors. Here, we examine a discrete-time two-dimensional susceptible-infectious (SI) model with Ricker growth and show that the introduction of infection can not only produce a distinctly different bifurcation structure than that of the underlying disease-free system but also lead to counter-intuitive increases in population size. We use numerical bifurcation analysis to determine the influence of infection on the location and types of bifurcations. In addition, we examine the appearance and extent of a phenomenon known as the 'hydra effect,' i.e., increases in total population size when factors, such as mortality, that act negatively on a population, are increased. Previous work, primarily focused on dynamics at fixed points, showed that the introduction of infection that reduces fecundity to the SI model can lead to a so-called 'infection-induced hydra effect.' Our work shows that even in such a simple two-dimensional SI model, the introduction of infection that alters fecundity or mortality can produce dynamics can lead to the appearance of a hydra effect, particularly when the disease-free population is at a cycle.

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PP1

Coupled Pump-Leak Equation System for Modeling of Ion and Cell Volume Stabilization

The Donnan effect is characterized by the presence of impermeant molecules within a cell, leading to an increased cell volume due to water influx. Animal cells counteract this effect through a Pump-Leak Mechanism (PLM), utilizing Na^+-K^+ ATPase (NKA) pump to actively transport Na^+ out and K^+ into the cytoplasm. The Pump-Leak Equations (PLE) model these processes as a system of algebraic-differential equations, accounting for water fluxes across the membrane, membrane potential, and intracellular ion concentrations (Na^+, K^+, and Cl^-). This study extends the PLE to coupled systems, which are critical for modeling complicated biological structures such as epithelia. These systems involve a second compartment coupled to the first, with ion transport occurring across the shared membranes and along the membrane adjacent to the extracellular space. The objectives of this project are (i) derive analytical results for the equilibrium in passive systems and the steady-states in active systems, (ii) conduct sensitivity analysis to define parameter spaces for coupled PLE models, and (iii) explore control techniques for volume regulation under parameter perturbations.

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PP1

Merging Traditional Scientific Computing with Data Science to Develop a New Prediction Engine for Brain Cancer

Glioblastoma multiforme (GBM) is one of the fastest-growing brain tumors and it has very low survival rates. Mathematical modeling can be used to predict the growth and treatment of brain cancer. However, one of the difficulties lies in the ability to estimate patient-specific parameters in the mathematical model from magnetic resonance imaging (MRI) data. We constructed a numerical solver to simulate tumor growth over a realistic 3D brain geometry derived from segmented-MRI. Then, using information about the size of the different glioma sub-regions, we are developing a method that estimates the patient-specific model parameters to inform the forward simulation. Ultimately, we hope to predict the overall survival of a patient from a single pre- operative scan.

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PP1

Machine Learning and Food Web Dynamics

Ecologists use a variety of synthetic food webs for different theoretical studies. These food webs, which capture key structural properties of complex food webs, are topological in nature and do not include dynamics. The goal of this work is to incorporate dynamics into synthetic food webs, and to investigate how dynamics affect the food web's structure. We show that the food webs are inherently unstable in the sense that incorporating dynamics, even deterministic dynamics, causes many species to go extinct. Using analytical and numerical methods, we investigate the influence of initial conditions, dynamical rates, and predation efficiency on species persistence. Additionally, we utilize a neural network model to predict extinctions, derive an analytical expression to elucidate the sequence of species extinctions, and employ clustering methods to unveil the role of rates in food web persistence. The results underscore the need for ecologists to exercise caution when infusing dynamics into structural food webs.

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SIAM Conference on Mathematics of Planet Earth

(MPE24)

IP1

Tipping Points in Coupled Human-environment Systems

Humans and the environment form a single complex system where humans not only cause ecosystem impacts, but also react to them. Coupled human-environment system (CHES) mathematical models are essential to understand the impacts of social behaviour and interventions and their potential to avoid catastrophic environmental events. Sustainable trajectories on multi-decadal timescales can be explored with relatively simple models. These models demonstrate how social parameters, as well as the degree of human influence on environmental systems can profoundly affect the number and type of tipping points that may occur via bifurcations to alternative stable states. Additionally, the efficacy of early warning signals can be altered through this coupling, with potential for the monitoring of environmental systems through social data. Coupled study systems presented here include forests and land use, coral reefs and fishing, and invasive species models.

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IP2

AI for Climate: A Call for Application-driven Innovation

Machine learning is increasingly being used to help tackle climate change, from optimizing electrical grids to emulating climate models and monitoring biodiversity. As such applications grow, however, it is becoming clear that high-powered ML tools often fall short. Methods designed using standard benchmarks may fail to capture the constraints or metrics of specific real-world problems, while a one size fits all approach ignores useful auxiliary information in specific applications. In this talk, we show how problem-centered design can lead to ML algorithms that are both methodologically innovative and highly impactful in the fight against climate change.

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IP3

Process and Data Informed Models: New Approaches, Old Ideas, and Challenges

In the last couple of years, process (physics)-informed neural models have become ubiquitous across many areas of science due to the necessity of adding process-based information (e.g., fluid dynamics) inside the neural network black box. In many scientific applications where there is substantial a priori process knowledge, incorporating this knowledge can improve model efficiency. The notion of including process knowledge in data-driven models is not new (e.g., data assimilation, physical-statistical modeling, etc.), yet some of the lessons from such endeavors are sometimes ignored, and many approaches do not provide adequate uncertainty quantification (UQ) across. This talk presents an overview of some general approaches for hybrid modeling that accommodate process knowledge and data-driven parameter/process estimation, with a focus on flexible models that can also provide uncertainty quantification. The talk will include numerous examples and present some challenges.

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IP4

Evaluating Forecasts of Extreme Events

Predictions for events with significant inherent uncertainty should be probabilistic in nature to convey information on the uncertainty associated with the outcome. This holds, in particular, for settings where the prediction is subsequently used by many different users to derive further predictions for both expected outcomes and associated risks. Examples of such predictions include weather and climate forecasts such as predictions of extreme precipitation and flooding. We thus take a probabilistic view and assume that forecasts are given as predictive distributions. Evaluation of extreme forecasts then falls in three distinct categories, depending on the question being asked: 1. A probabilistic forecast is issued for the extremes only and we want to know how good it is. 2. A probabilistic forecast is issued for every type of outcome, and we want to know how good it is at predicting extreme outcomes. 3. A probabilistic forecast is issued for every type of outcome, and we want to know how well certain tail properties or functionals of the predictive distribution match those of the true data distribution. When predicting extreme events and assessing risk, the evaluation of the forecasts is additionally complicated by a lack of substantial observation set due to the rarity of the outcome of interest. We discuss how to perform the evaluation for all three categories above under these constraints within the frameworks of proper scoring rules and consistent scoring functions, and review the available literature on these topics.

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SP1

Activity Group on Mathematics of Planet Earth (SIAG/MPE) Early Career Prize Presentation, and the SIAG/MPE Prize Lecture - A Circuitous Journey of Computational Science around the Earth

This session will include the SIAM Activity Group on Mathematics of Planet Earth Prize (SIAG/MPE) Lecture, as well the SIAG Early Career Prize presentation to recipient Johannes Lohmann, University of Copenhagen, Denmark. Earth and its component systems are complex, multiscale, and interconnected. Properly recreating and predicting its behavior as more carbon is released into the atmosphere is a grand challenge that requires teams of scientists with backgrounds that span the different Earth science domains, computer scientists, software engineers, and applied mathematicians. This talk will present several examples of efforts to address accuracy and time to solution via faster and more scalable algorithms in multiple Earth system model components. Just as critical, we have focused on expanding testing capabilities to perform robust verification and validation during model development to quantify the effects of algorithmic as well as more general performance changes across the full software infrastructure and time scales of simulations. Incorporating the statistical nature of Earth system outcomes into our testing strategy

allows us to evaluate the quality of deterministic or machine learning based models and design metrics that track both scientific and computational performance. We will discuss how further progress in Earth system prediction requires attention to the efficiency, scalability, and accuracy of its algorithms even as the models in which they are implemented and the target computational platforms on which they will run are increasing in complexity.

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JP1

LS/MPE24 Joint Plenary Presentation - Thermal Dynamics of Host-Parasite Systems: Modelling and Predicting Disease Emergence and Range Changes in a Warming Climate

Climate change is altering host-parasite dynamics globally, with changes expected to accelerate with continued warming. Predicting future impacts remains difficult, however, given multiple interacting thermal dependencies influencing dynamics, lacking data for most species, and the impossibility of empirically measuring host-parasite dynamics for yet-to-be-observed environmental conditions. Here, I will discuss how combining life-cycle-based population models with thermal performance curves based on the Metabolic Theory of Ecology provides a process-oriented approach for anticipating impacts of warming, including for data-poor species. Using well-studied model systems, I will first demonstrate the frameworks ability to predict disease emergence and geographic range changes of parasites in warming environments. To also aid predictions for data-poor species, I will then discuss ways to generalize the framework, both with respect to parameter estimates and the structure of the host-parasite dynamics. I will show how model parameters may be estimated from systematic among-species relationships of thermal sensitivity, and introduce a balance equation that reveals systematic relationships between life cycle complexity and a parasites response to warming based on the interactions of multiple thermal sensitivities through its life cycle. Together, the framework provides powerful ways for anticipating impacts of warming on parasitism, both for well-studied and data-poor systems.

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CP1

Efficient Bayesian Data Assimilation Schemes for Multi-Timescales One-Way Coupled Dynamical Systems

Dynamical systems play an important role in transporting a variety of natural quantities (e.g. aerosols, pathogens, water masses, plankton, sediments, etc.) and artificial materials (e.g. pollutants, floating debris, search and rescue, etc.). A robust scheme to assimilate Lagrangian data allows us to infer key characteristics of the flow. We propose an assimilation scheme for multi-timescales and one-way coupled dynamical systems in general and specifically for the Eulerian-Lagrangian dynamical system which efficiently and robustly deals with the (i) high dimensionality of the gridded Eulerian data by using DO-based state space reductions, (ii) high computational cost of running stochastic ocean models by optimally minimizing resampling of Eulerian state space variables, (iii) nonlinear and non-Gaussian nature of Lagrangian dynamics by using a GMM-based description of joint pdfs, and (iv) chaotic nature of Lagrangian dynamics by updating Lagrangian conditional posteriors at a much higher frequency than their Eulerian counterparts.

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CP1

Towards Predictive Uncertainty Quantification in Space Weather Simulations Through Surrogate Models for Dynamical Systems

Space weather events such as fast-moving Coronal Mass Ejections (CMEs) result in geomagnetic storms that can damage critical infrastructure on Earth such as the electric power grid and break down radio communications. While predictive models built from first principles have been successfully validated against remote and in-situ observations of CMEs, long-term forecasts for new events remain challenging and require systematic Uncertainty Quantification (UQ) and Data Assimilation. Here, we consider the problem of forward UQ via surrogate models/emulators that approximate the dynamics. The high cost of Sun-to-Earth simulations and high-dimensional parameter space limit our access to a few hundred simulations that are conducted using the Space Weather Modeling Framework (SWMF) for a particular event. These arise from uncertain flux rope parameters that describe the shape and strength of a CME. The leading edge of the CME is extracted using synthetic white light images obtained from the simulations. Its evolution is approximated via emulators such as Proper Orthogonal Decomposition (POD), Operator Inference (OpInf) and Neural Ordinary Differential Equations (NODEs). The final surrogate model can evolve the leading edge based on test initial conditions and supply predictive uncertainties for the same, through the framework of conformal prediction. This also has the potential to accelerate subsequent inverse UQ steps for constraining the free parameters.

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CP1

A New and Fast Physics-Informed Data-Driven Approach for the Atmospheric Radiative Transfer Equation

FORUM (Far-infrared Outgoing Radiation Understanding and Monitoring) is the ninth Earth Explorer mission se-

lected by the European Space Agency in 2019. It will provide interferometric measurements in the Far-InfraRed (FIR) spectrum, constituting 50% of Earth's outgoing longwave flux. Accurate Top Of the Atmosphere measurements in the FIR are crucial for improving climate models. Existing instruments are inadequate, necessitating new computational techniques. In the mission's early stages, an End-to-End Simulator (E2ES) was developed to demonstrate proof-of-concept and evaluate the impact of instrument characteristics on reconstructed atmospheric properties. The E2ES includes modules simulating the measurement process, addressing both the radiative transfer equation (direct problem) and its inversion (retrieval problem). The ill-conditioned inverse problem requires the Optimal Estimation approach, a Bayesian Tikhonov regularization scheme. However, the computational cost of such methods make them impractical for Near Real-Time (NRT) data analysis, an important goal for next-gen satellites and climate models. The development of faster models is therefore essential to advance NRT technology. To this end, we propose a physics-informed machine learning approach combining data-driven operator learning with a neural-network based Tikhonov regularization. We show that our methods can produce high-quality reconstructions of atmospheric quantities with low computational cost.

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CP1

Big Data Technology Demonstration: 4-Dimensional Visual Delivery of Big Climate Data

This presentation is a demonstration of the 4-Dimensional Visual Delivery (4DVD) technology www.4dvd.org, which is a software system to visually deliver big climate data at an extremely fast speed. The system visualizes and delivers netCDF climate data in a 4-dimensional (x, y, z, t) space-time domain. It allows users to quickly visualize the data before making a download for further analysis. Numerous graphics options help a user identify desired climate dynamics patterns. Data can eventually be downloaded for a spatial map of a given time and a historical climate time series of a given location after the map and time series are identified to be useful. In this way, the 4DVD software enables a user to quickly reach the key climate features without downloading the entire dataset in advance. This not only saves time and storage space, but also can deliver the real climate data to classrooms and households. The fast speed of the 4DVD software system is achieved through optimally harnessing the cutting-edge technologies of distributed computing and our proprietary database indices for fast queries. We will use data from (i) NOAA's 20th Century Reanalysis model and (ii) our NSF AI Institute stochastic models (NSF award # 2324008) as examples to show the fields of temperature, U-wind, V-wind, precipitation rate, and more. We will show that 4DVD is an efficient tool for research, education, and public outreach.

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CP1

Physics-Informed Neural Networks for Modeling Atmospheric Radiative Transfer

Aerosols and clouds play a crucial role in Earths radiative budget, influencing the radiative balance through the scattering and absorption of solar radiation. Yet, modeling of their radiative effects imposes significant uncertainties in climate forcing estimates. This results in part from large uncertainties that exist in determining their optical and physical properties over the globe, at different spatial and temporal scales. Global remote-sensing measurements are conducted by spaceborne or ground-based sensors to assess the impact of clouds and aerosols on solar radiation. Aerosol and cloud properties are estimated through an inverse-modeling retrieval approach utilizing the remote-sensing measurements within an atmospheric radiative transfer model that is often poorly constrained or ill-posed. In our presentation, we will showcase a novel approach to modeling atmospheric radiative transfer by leveraging a Physics Informed Neural Network (PINN) model. Our proposed method enables forward radiative transfer simulations by integrating physical principles within a neural network framework. It offers valuable insights into how aerosol or cloud properties affect the measured radiance, and a theoretical analysis of the solution error bounds. Unlike most forward solvers, PINN allows fusion of measurements within the solution process, reducing errors and enabling the simultaneous retrieval of optical parameters.

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CP2

A Coupled Social-Climate Model with Multiple Populations

Recent work has shown that the inclusion of human behavioural aspects in mathematical models of climate change can significantly affect the outcomes predicted by these models. We further work in this area by constructing a coupled social-climate model with social dynamics across multiple populations. We incorporate projections of renewable energy costs and economic damages associated with climate change, along with a description of social norms, into a dynamic learning-based behavioural model. This 'social component of the model is then coupled to a simplified earth-system model, representing two-way feedback processes between the two sub-components. Through our results we aim, primarily, to gain an understanding of how heterogenous social dynamics across multiple populations could influence climate change outcomes at a global scale. We seek to establish estimates of the range of impacts social processes in our model have on climate change projections, as well as to study the nature of interactions between different behavioural and socio-economic factors

in the context of climate change mitigation.

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CP2

Beyond Echo Chambers: Modeling Misperception of Public Support for Climate Policy

Since the late 1980s, climate change has become a strongly polarizing issue in the United States. However, overall support for climate policy is high, with 66-80% of Americans supporting climate policies. Curiously, 80-90% of Americans underestimate public support for these policies, estimating the prevalence of support to be as low as 37-43% [Sparkman et al., Americans experience a false social reality, *Nature communications* 13.1 (2022): 4779]. The implications of such widespread misperception range from individual behaviors to legislative outcomes. Here we present an agent-based social-network model of public perception of support for climate policy grounded in previous empirical studies. We find that homophily effects alone do not explain widespread misperception. However, our network analysis suggests that disproportionate representation of opposition to climate policy among central nodes can offer a potential explanation for underestimation of public support. In order to assess the validity of this assumption in the real world, we explore the coverage of climate policy in U.S. news media. We couple our analysis of media coverage of climate policy with existing opinion survey data in order to inform our model.

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CP2

Climate Denying Rumor Propagation in a Coupled Socio-Climate Model

Individual attitudes vastly affect the transformations we are experiencing and are vital in mitigating or intensifying climate change.We developed a socio-climate model by coupling a model of rumor dynamics in heterogeneous networks to a simple Earth System model in order to analyze how rumors about climate change impact individuals' opinions when they may choose to either believe or reject the rumors they come across over time.Our model assumes that when individuals experience an increase in the global temperature, they tend to not believe the rumors they come across.The rumor rejectors limit their CO_2 emissions to reduce global temperature.Our numerical analysis indicates that, over time, the temperature anomaly becomes less affected by the variations in rumor propagation parameters and having larger groups is more efficient in reducing temperature(by efficiently propagating rumors)than having numerous small groups.We also observed that decreasing the number of individual connections does not reduce the size of the rejector population when there are large numbers of messages sent through groups.We found that mitigation strategies considered by the rejectors are highly influential. The absence of mitigative behavior in rejectors can cause an increase in the global average temperature by 0.5C.Our model indicates that rumor propagation in groups has the upper hand in controlling temperature change compared to individual climate-denying propagation.

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CP2

A Random Kick-Flow Model of Self-Organized Vegetation Patterns in Drylands

Banded patterns of vegetation, on gentle slopes, can be found in certain dryland regions. The soil water and biomass dynamics act on a slow timescale, and infrequent rainstorms inject water into the system on a fast timescale. We model the slow subsystem as the time-evolution of a reaction-diffusion equation, and we treat the storms as instantaneous kicks of added water. This water is deposited inhomogeneously due to differences in the infiltration rate and downhill flow speed in areas with dense biomass versus bare soil. Specifically, biomass impedes the downhill flow of surface water and increases infiltration, which leads to the surface water left by a storm being concentrated in the soil near the uphill edge of a vegetation band. We explore the effect of storm variability by introducing randomness into the timing and the total amount of water deposited by storms. We are particularly interested in how storm variability affects the resilience of the vegetation patterns compared to the idealized case of identical, regularly-timed storms, as this may give insight into potential risks of ecosystem collapse due to increased variability brought about by climate change.

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CP2

Tech-Enhanced Agriculture: Crafting Innovative Substrates for Soilless Growth

The FAO report The future of food and agriculture: alternative pathways to 2050 emphasizes the imperative to enhance agricultural production and minimize ecological impact in tackling the challenge of feeding nearly 10 billion people by 2050. Soilless cultivation can play a key role in this context, aiding in meeting food demands while widely reducing land use, water consumption and fertilizer supply. This presentation introduces a novel method to craft from scratch 3D lattice materials, designed for soilless growing media. The aim is to replicate the main properties of existing organic/inorganic substrates such as perlite, peat, rockwool, coco. Lattice materials are obtained by the periodic repetition of a specific unit cell. In particular, the physical properties (at the macro-scale) are determined by the specific topology of the unit cell (at the micro-scale). We present an automated process for identifying the unit cell topology, ensuring desired mechanical, fluid dynamics, and chemical properties for the lattice. From a methodological viewpoint, the proposed approach relies on the homogenization theory, which provides a straightforward link between the macroscopic material behavior and the periodic microstructure, and on 3D topology optimization, to shape the new unit cell. The resulting process is enriched by the adoption of a smart computational 3D mesh that allows us to sharply design the lattice structure within a finite element discretization framework.

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CP2

Swarm Performance Impact of Instabilities in Multi-Agent Transportation Systems

Multi-agent systems are ubiquitous, both natural (schools of fish, flocks of birds) or human-made (vehicular traffic flow or swarms of robots). We study, via models that connect the microscopic agent interactions with the macroscopic emergent patterns, the impact of dynamic instabilities on relevant swarm performance metrics. A key example is the impact of phantom traffic jams and traffic waves on traffic safety and system-level energy consumption. Analogous systems in higher dimensions, such as multi-vehicle off-road transportation, are also showcased.

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CP3

New Developments in Nonsmooth Control Methods: from Climate Models to Wind Turbine Power Systems

Nonsmooth systems are seen in many applications such as climate models and wind turbine power system (WTPS) models. Some approaches, such as smoothing approaches, were developed to overcome challenges associated with nonsmooth systems, but such approaches suffer limitations. Hence, generalized derivatives-based methods, such as the lexicographic differentiation (LD) approach, were introduced to treat nonsmooth functions directly. We present two different applications where the LD approach was used. The first application is a climate model (the Stommel box model) where the models identifiability and observability are studied. Our work extends traditional methods, developed to study identifiability and observability only for smooth systems, by using the LD approach, so we can study the nonsmooth Stommel box model. The second application is an optimal control problem, where we use the sequential optimal control method in a nonsmooth setting to determine the optimal trajectory for the pitch angle controller of a WTPS. For this problem, we use a nonlinear well-posed WTPS differential algebraic model, with an objective functional aiming to maximize the power output of the WTPS, without exceeding the rated power of the grid. The novelty of our work is that both the objective functional and the dynamics of the WTPS include nonsmooth functions that unify the model over all ranges of wind speed. Hence, we apply the LD-based sequential method to overcome this nonsmoothness challenge.

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CP3

Collection-Time Optimal Path Planning in Dynamic Flows on Planet Earth

Increasingly, autonomous vehicles that optimally collect/harvest external fields from highly dynamic environments have grown in relevance for Planet Earth. This includes path planning for optimal energy harvesting (solar, wind, wave, thermal, etc.) or optimal cleanup or collec-

tions in dynamic environments. In this work, we develop an exact partial differential equation-based methodology that predicts collection-time optimal paths for autonomous vehicles navigating in dynamic environments. The governing differential equations solve the multi-objective optimization problem of navigating a vehicle autonomously in a highly dynamic flow field to any destination to minimize travel time while also maximizing the collected amounts of fields harvested by the vehicle. Using Hamilton-Jacobi theory for reachability, our methodology computes the exact set of Pareto optimal solutions to the multi-objective path planning problem. Our approach applies to path planning in various environments; however, we primarily present examples of navigating in dynamic ocean flows. First, we validate our methodology using steady and unsteady benchmark cases. We then showcase optimal fish growth paths for moving fish farms, optimal algae growth and collection paths for autonomous carbon capture, and optimal plastic collection paths for marine cleanup. Overall, we find that our exact planning equations and efficient schemes are promising to address several pressing challenges for our planet.

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CP3

Stable and Unstable States of the Atlantic Ocean Circulation

Various large-scale elements of the Earth system may lose stability and undergo catastrophic transitions as a result of future climate change. In addition, already at present-day conditions, spontaneous transitions to an undesired state may be induced by stochastic fluctuations, if any of those elements occupy a multi-stable regime. For instance, the Atlantic Meridional Overturning Circulation (AMOC) may undergo a transition to a stable collapsed state. Along with such an undesired stable state there also exists an additional unstable state. This so-called edge state anchors the basin boundary separating the desired and undesired regimes, and it lies at the heart of the path taken by the system during a noise-induced transition between two stable states. Here we construct the stability landscape of a global ocean model under North Atlantic freshwater forcing. The model features various co-existing stable states with a vigorous and collapsed AMOC. This indicates that the path towards a collapsed AMOC may consist of a series of step-wise changes, which could depend sensitively on intial condition and the rate of climate change. Further, using an edge tracking algorithm, an edge state lying between the vigorous and collapsed AMOC regimes is computed, and its physical characteristics are analyzed. This can be useful to detect if a spontaneous collapse of the AMOC is underway. Finally, we compare the edge state to transition paths driven by finite-amplitude noise.

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CP3

Sensitivity Analysis of a Permafrost Model Responding to Surface Temperature Variations in Variable Topography

We consider a computational model for energy equation in permafrost soils extending [Bigler, Peszynska, Vohra, 2022] using data and constitutive parameters from [Ling, Zhang 2003]. Our focus is on the dependence of model results on several model parameters including the thermal conductivity, volumetric heat capacity, and the dependence of surface boundary conditions on the albedo which varies in various regions such as (snow, vegetation, wildfire-affected vegetation, desert, river). Next, we evaluate the response of the model to these parameters. To this end, we set up the sensitivity equation as well as Sobol indices sensitivity framework. Our results allow to assess the robustness of our computational model as well as to understand the uncertainty associated with the parameters and the model itself. Our simulations and analyses help to determine the response of the soils in the Arctic to the changing climate and to assess the reliability of the model.

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CP3

Probabilistic Attribution and Time Series Analysis to Investigate Atmospheric Drivers of Precipitation-Induced Disasters

Mechanisms of atmospheric moisture transport, such as atmospheric rivers (ARs) and extratropical cyclones, are primary drivers of heavy precipitation in the mid-latitudes. While crucial for freshwater supply, they also trigger precipitation-induced disasters (PIDs) such as floods and landslides. Here, we introduce a methodological approach that combines stochastic climate theory and time series analysis to quantify the strength, directionality, and significance of the non-linear relation between atmospheric moisture transport events (AMTEs) and PIDs. Employing probabilistic attribution, we reveal the spatial extent over which AMTEs cause precipitation upon landfall. Subsequently, we use event coincidence analysis, a non-linear measure specially tailored for event time series, to quantify the precedence relation between precipitation released by AMTEs and PIDs. We determine the significance of our findings through Monte Carlo experiments, hypothesis testing, and sensitivity analysis. Applying our methodological approach, we demonstrate that precipitation from land-falling ARs was the primary trigger of precipitation-induced landslides in Western North America between 1996 and 2018. Our approach, extendable to broader regional and global analyses, is a robust tool for exploring land-atmosphere couplings and precipitation-induced hazards, contributing crucial insights to improve forecasting accuracy and bolster mitigation strategies.

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CP3

Reflection/transmission of Plane Waves at the Interface of An Inviscid Fluid and a Rotating Transversely Isotropic Thermoelastic Diffusion Solid Half-Space in a Fractional-Order Thermo-Elasticity

In this research, the problem of reflection and transmission of a plane wave incident obliquely at a plane interface between thermal inviscid fluid half-space and a rotating transversely isotropic thermoelastic diffusion solid half-space in a fractional-order thermo-elasticity is studied. The energy distribution among the reflected and transmitted waves is the investigated. The governing partial differential equations and the expression for reflection coefficient and energy ratios are formulated. Results are verified for particular material and effect of rotation and diffusion are depicted graphically.

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CP4

Monitoring a Ground Source Heat Pump System in the Mediterranean Climate of Cyprus

European Union (EU) has developed energy strategies and has invested in new energy technologies to ensure higher energy efficiency of buildings. The Ground Source Heat Pump (GSHP) system is one of the most well-known geothermal systems and renewable energy technologies for heating and cooling of buildings due to its high efficiency (see Coefficient of Performance COP) and its environmental friendliness. GSHPs make use of Ground Heat Exchangers (GHEs), which are designed to cover the energy demand both in summer and winter. Such geothermal systems can be controlled by a remote monitoring system (building management systems BMS). In this study the evaluation of a GSHP/GHE system performance regarding the use for heating and cooling in the building where the University Municipal Library of Limassol (Cyprus) is housed. The system (GSHP controlled by the BMS) acts as a research and educational laboratory. The GSHP system includes vertical GHEs with various specifications and two open loop (well) systems. A theoretical and experimental investigation is needed to evaluate the performance of the different parts of the geothermal system and give recommendations for improving its efficiency. The entire GHE system is constantly monitored by a digital program that records the energy, flow, volume, incoming and outgoing temperature at each installed HP. The general three-dimensional convection-diffusion equation is used to model the individual GHEs. In addition, based on data collected for several summer and winter months, (i) the electrical power into the system, (ii) the power absorbed /rejected by/to the system, and (iii) the COP of the whole system (including all installed GHEs) are estimated and compared. By studying the obtained results, several suggestions regarding the operation and the optimization of the GSHP as well as the BMS systems will be discussed.

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CP4

Automating Wildfire Identification from Remote Sensing Data Using Distributed Memory, GPU-Parallel Support Vector Machines

Timely and synoptic mapping of wildfires could enable better understanding of forest carbon balance and impacts on ecosystems, but involves intensive labor: the United States Monitoring Trends in Burn Severity product lags present day by about two years and ignores small fires, which may be very important due to their frequency. We describe PermonSVM a distributed memory parallel Support Vector Machine (SVM) implementation, built on top of the Portable, Extensible Toolkit for Scientific Computation (PETSc) and its application to identification of wildfire-affected areas in large remote-sensing data sets. Our aspirational goal is to enable synoptic mapping of fires across North America. In experiments so far, we have achieved good classification performance and believe that our we are effectively identifying smaller fires missing from the MTBS layers. Leveraging recent developments for GPU support in PETSc, we have achieved significant speedup for the SVM calculations on both NVIDIA, AMD, and Intel GPU-powered supercomputers, and are actively working to further improve computational efficiency. Recent algorithmic improvements we are developing and evaluating include improved duality gap-based stopping criteria, novel approaches for stabilizing the underlying quadratic optimization algorithm, using Platt scaling to get probabilistic output from the classifiers, and GPU-friendly compact-dense formulations of quasi-Newton updates.

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CP4

Stochastic Modeling and Learning for Sea Ice Dynamics

Accurate sea ice models are essential to predict the complex evolution of rapidly changing sea ice conditions and study impacts on climate and wildlife. However, numerical sea ice models contain various uncertainties associated with initial conditions and forcing (wind, ocean), as well as with parameter values, functional forms of the constitutive relations, and state variables. Additionally, there is loss of accuracy due to unresolved subgrid-scale processes. In this work, we develop new stochastic partial differential equation (PDE)-based Sea Ice Dynamically Orthogonal equations and schemes for efficient uncertainty propagation and probabilistic predictions. These equations and schemes preserve nonlinearities in the underlying dynamics and evolve the non-Gaussianity of the statistics with a lower computational cost than Monte Carlo methods. We use the Gaussian Mixture Model (GMM)-DO filter for Bayesian nonlinear data assimilation and learning. Assimilating noisy and sparse measurements, we provide posterior probability distributions for the sea ice velocities, thickness, and concentration, external forcing, parameters, and even functional forms of the model. We also explore neural network-based closure models that learn missing physics and subgrid-scale processes, and augment low-fidelity numerical sea ice simulations. Finally, we highlight the principled joint nonlinear inference and learning of the sea ice state and dynamics.

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CP5

Using Variational Data Assimilation with Acoustic Observations Within a General Circulation Model

Direct ocean observing systems are a scarce set of data that build the backbone for understanding the current state of the ocean. These systems are limited in areas of high variability in temperature and salinity. Pioneering work of Munk and Wunsch (1979) proposed efforts to extract detailed hydrographic information using sound propagation through the ocean, providing the scaffolding to improve our understanding of the ocean's interior. The integrated nature of such measurements makes acoustic tomography a powerful application for monitoring regional to basin-scale hydrographic changes in the ocean, a measurement that is difficult to achieve by canonical oceanographic measurements alone. In this talk, equations to resolve regional ocean dynamics and underwater acoustic propagation are summarized featuring results for modeled travel times. This work then develops a simple expansion to a well established adjoint model used in ocean state estimation, taking into account tomographic travel times as a novel set of observations. The updated framework is employed for a study on sensitivity of the hydrographic state due to acoustic measurements as applied on a regional ocean general circulation model.

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CP5

Wave and Balanced Motions in Rotating, Stratified, Non-Hydrostatic Fluids

Oceanic flows are dominated by rotation and non-constant stratification, which leads to motions with balanced (low frequency) and unbalanced (high frequency) components. The balanced components are associated with slow quasi-geostrophic large-scale flows while the unbalanced components correspond to fast small-scale inertia-gravity waves. In this talk, we will analyze properties of both components in the context of rotating fluids with non-constant stratification. Exact analytical expressions for available potential energy density (APE) and available potential vorticity (APV) will be derived from first principles. In addition to their intuitive appeal and simplicity, the new APE and APV expressions are easily implemented in numerical computations of Boussinesq dynamics with non-constant stratification. This is joint work with Jeffrey J. Early, Leslie M. Smith and M.-Pascale Lelong.

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CP5

The Complex Interaction Between Divergence, Vorticity, and Deformation Rates at the Submesoscales in the Ocean

Ocean flows are generally described in terms of velocities, but to understand the redistribution of floating material the velocity gradients play a more significant role. In particular, dispersion and accumulation result from path-integrated divergence and deformation rates. Here we report on a study of the solution space of the nonlinearly coupled system of differential equations describing the Lagrangian (i.e., along-path) evolution of divergence, vortic-

ity, and normal and shear deformation rates under steady forcing in the submesoscale regime. Even with linearized forcing, the resulting 8-dimensional parameter space is huge. Exploiting symmetries and other patterns, we characterize time series of divergence, vorticity, and deformation rates, their stability, and associated phase space trajectories. As the underlying motivation is to improve the understanding and interpretation of observed Lagrangian time series of these kinematic quantities from drifter data, the realism of possible solutions is also addressed.

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CP5

Utilization of Hydroacoustic-Scholte Waves for Persistent, Long-Term Measurement of Climate-Relevant Ocean Properties

With the goal of assisting climate-change research through long-term, persistent sensing of ocean variables, this work investigates an approach to energy conversion and sensor utilization at the seafloor. Present focus is on the mathematics of energy transfer from second-order interactions in stationary random multi-directional surface wave fields to groups of hydroacoustic-Scholte waves propagating through the coupled water-column-seafloor system. Energy balance relations are derived for propagating wavenumber frequency spectra of free and forced hydroacoustic-Scholte waves, relating them to the interface boundary conditions (and dispersion relations). Energy transfer is appreciable at resonance, when the forced hydroacoustic-Scholte wave frequency and wavenumber lie on a dispersion surface for the two-media system. Mild nonuniformities in the media are accounted for, and expressions for available deep-water power densities in watts/seafloor area are derived, along with a relation that allows combined use of seismometer and pressure transducer measurements to infer local acoustic phase speeds in the water column as proxy for density, temperature and salinity. Long-term observation of seawater acoustic speeds over sub/mesoscale areas could refine tracking of the effects of future global warming on the deep ocean. Also discussed will be extensions of the theory to near-shore depths, to provide energy for persistent sensing of dissolved carbon-dioxide in the surf zone.

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CP5

Generalized Neural Closure Models for Ocean and Chaotic Dynamical Systems

Our generalized neural closure models (gnCMs) based on unified neural partial differential equations (PDEs) are applied to ocean, sea ice, and chaotic systems. We augment existing/low-fidelity dynamical models directly in their PDE forms with both Markovian and non-Markovian neural network (NN) closures. The melding of the existing models with NNs in the continuous spatiotemporal space followed by numerical discretization automatically allows for generalizability. The Markovian term is designed to enable extraction of its analytical form and thus provides interpretability. The non-Markovian terms allow accounting for inherently missing time delays needed to represent the real world. Our flexible gnCMs provide full autonomy for the design of the unknown closure terms such as using any linear-, shallow-, or deep-NN architectures, selecting the span of the input function libraries, and using either or both Markovian and non-Markovian closure terms, all in accord with prior knowledge. We apply the gnCMs to learning experiments with advecting nonlinear waves, shocks, ocean acidification, ocean submesoscales, and sea ice models. We highlight applications to chaotic systems, emphasizing the need for adaptive learning schemes. Our learned gnCMs discover missing chaotic physics, find leading numerical error terms, discriminate among candidate functional forms in an interpretable fashion, achieve generalization, and compensate for the lack of complexity in simpler models.

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MS1

Parameter Calibration and Uncertainty Quantification from Climate Statistics

Process-based climate models are a collection of partial differential equations that must represent dynamics across many spatial and temporal scales. The physics at the smallest scales is represented by empirical or data-driven parameterization schemes that link what is unresolvable to variables resolved on the grid scale. A large source of uncertainty in climate prediction comes from the calibration of parameters in such parameterization schemes. Despite access to observational data, and high-resolution simulations, uncertainties are not quantified in practice due to the large computational expense of running PDE models. In this talk we demonstrate successes with an approach to learn a suitable parameter distribution from indirect time-averaged statistical data. Our method, Calibrate-Emulate-Sample (CES), combines ensemble Kalman processes, machine learning, and statistical sampling tools applied in a black-box (i.e. derivative-free) fashion to obtain approximate posterior distributions. The method accelerates this task, requiring 1000s of times fewer evaluations of models that classical approaches. Besides acceleration, the method is parallelizable, scalable to moderately high input and output dimensions. Time permitting, we shall explore some successes of this approach in idealized aquaplanet simulations, and from climate model components developed at the Climate Modelling Alliance.

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MS1

Quantification of Structural and Parametric Uncertainty in Cloud Microphysics Parameterizations with Bayesian Statistics, Physics, and Machine Learning

Bayesian parameter inference solves a major challenge in atmospheric model parameterization development: estimating optimal parameters for a given set of target performance metrics. While atmospheric models are too computationally expensive for direct application of Bayesian inference methods such as Markov Chain Monte Carlo (MCMC), machine learning can overcome this limitation. Here, we use machine learning-enabled Bayesian parameter inference to constrain parameters of a structurally flexible cloud microphysics parameterization (BOSS: Bayesian Observationally constrained Statistical-physical Scheme). Specifically, we constrain BOSS parameters in a large-eddy simulation (LES) via target performance metrics from the same LES with a more complex microphysics scheme and in a atmospheric general circulation model via target performance metrics from satellite observations. We perform this parameter inference for a number of different BOSS structural designs and performance metrics to quantify parameterization structural and parametric uncertainty.

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MS1

Autocalibration of the E3SM Version 2 Atmosphere Model Using a PCA-Based Surrogate for Spatial Fields

Global Climate Model (GCM) tuning (calibration) is a tedious and time-consuming process, with high-dimensional input and output fields. Experts typically tune by iteratively running climate simulations with hand-picked values of tuning parameters. We present a practical rigorous calibration approach on the atmosphere-only model of the Department of Energys Energy Exascale Earth System Model (E3SM) version 2. Our approach can be summarized into two main parts: (1) the training of a surrogate that predicts E3SM output in a fraction of the time compared to running E3SM, and (2) gradient-based parameter optimization. To train the surrogate, we generate a set of designed ensemble runs that span our input parameter space and use polynomial chaos expansions on a reduced output space to fit the E3SM output. We use this surrogate in an optimization scheme to identify values of the input parameters for which our model best matches gridded spatial fields of climate observations. To validate our choice of parameters, we run E3SMv2 with the optimal parameter values and compare prediction results to expertly-tuned simulations across 45 different output fields. This flexible automated approach is straightforward to implement, and we demonstrate that the resulting model output matches present day climate observations as well or better than the corresponding output from expert tuned parameter values and operating in a fraction of the time.

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MS1

E3SM Uncertainty Quantification Using Surrogate Neural Networks

Large-scale global climate models like the Department of Energys E3SM (Energy Exascale Earth System Model) require immense super-computing resources for high resolution simulations. However to account for uncertainty in the physics model parameters, these simulations need to be run many times with different climate model parameters, which will require expert climate domain knowledge and significant computational time. Our work aims to speed up the model parameter tuning of E3SM by creating a surrogate Machine Learning model that approximates E3SM. We then use Optimal Experimental Design to perform the climate model parameter tuning on this surrogate, which is less computationally expensive. In this talk we demonstrate the construction of such a surrogate model using a neural network that takes in the E3SM model parameters and predicts climate metrics on a global map, introducing PCA based prediction dimension reduction and optimization for experiment design. We also cover the introduction of stochasticity in last layer of the surrogate neural network where we use Markov Chain Monte Carlo (MCMC) to help quantify the uncertainty of our predictions. We then explore different approaches to calculate Expected Information Gain from incrementally adding data points, and use

that to conduct Optimal Experimental Design to select the optimal next model parameters.

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MS2

Lessons Learned When Using a Tiered Verification Process for Climate Data Analytics

A key framework to quantitatively assess performance of Earth System Models, ESMs, is the Model Intercomparison Projects, MIPs, for which simulation and output design are specified ensuring that spread in outcome between models is due to the characteristics of the models themselves. Just as ESMs embed key assumptions, have tunable parameterizations, and possess biases requiring MIPs to expose them, so to do many of the advanced tools used on climate datasets. In fact, the most common technique used to identify natural modes in the climate, PCA, has been shown to only be effective for one dominant mode (Fulton Hegerl, 2021). We believe there is a need for benchmarks designed to evaluate the efficacy of methods before they are used to explain physical processes, diagnose emergent properties, attribute impacts, or derive other understandings just as each MIP is designed to address specific science questions in order to evaluate ESM performance against observation (known truth) and enable refinement. Since advanced methods are designed to accomplish distinct goals, it is expected that the benchmark datasets may possess distinct characteristics. In this talk, we will discuss a process of tiered verification, which uses benchmark datasets of increasing complexity, used by a variety of methods to identify and address weaknesses where appropriate, and provide quantitative evaluation of their accuracy before being applied on fully coupled ESM simulations.

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MS2

Inverse Optimization Enabled by Operator Learning: Benchmarks, Limitations, and Opportunities

Inverse problems arise when quantities of interest cannot be measured directly but rather are estimated by observing another quantities which are related through a mathematical model. Traditional approaches to solve inverse problems, such as inverse optimization, are infeasible for earth system models due to the computational cost of the model evaluations. Hence, surrogate models are needed. Many traditional surrogate modeling approach exists; however, recent advances in operator learning introduce new opportunities for high-dimensional approximation which better captures spatio-temporal dynamics. Such advances can enrich the inversion capability by leveraging spatially resolved data such as satellite measurements. Nonetheless, many challenges arise related to training, robustness, and interpretability of the models, particularly in a limited data setting. In this presentation we will consider a sequence of synthesized inverse problems with increasing complexity to understand the capabilities and limitations of operator learning in the service of atmospheric source inversion.

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MS2

AI Attribution Benchmarks: Do We Gain the Correct Insights When Employing Explainable AI Tools?

The so-called eXplainable Artificial Intelligence (XAI) aims to explain how artificial neural networks (NNs) make decisions by highlighting which variables in the input contribute the most to a prediction. XAI has increasingly seen application to geoscience, providing insights about how NNs decide, which help scientists calibrate model trust and/or learn new science. However, many of these methods have been shown to face non trivial limitations in specific problem setups, while the assessment of their fidelity is typically on subjective criteria. The lack of a ground truth to assess an explanation has the risk of cherry-picking specific methods and reinforcing individual biases. With the aim of adding more objectivity in the assessment of XAI, here, we provide a general framework to generate attribution benchmark datasets for regression or classification problems, where the ground truth of the explanation/attribution is known a priori. Based on our framework, we generate long datasets and train a network to learn the underlying function that was used for simulation. We then use the ground truth of the attribution to assess the fidelity of different XAI methods and identify systematic strengths and weaknesses. Our work shows that there is room towards more objective assessment of XAI methods that may be of great importance for attribution studies and further application of NNs in geoscience.

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MS2

Confirming Climate Relationships Using Local Feature Importance on Echo State Networks

As policy-makers continue to discuss climate change mitigation strategies such as stratospheric aerosol injections,

there is a need to develop methods that characterize the potential downstream impacts of such actions. Of particular interest is understanding the connection between a locally sourced injection of aerosols and resulting changes to temperature at various locations across the globe. We develop a deep learning approach that combines an echo state network (ESN) with spatio-temporal feature importance to quantify changes over time in the relationship between relevant climate variables and future values of stratospheric temperature. By using locally defined radial basis functions as the dimension reduction technique in our ESN, our method allows for inference from local sources to local impacts. We validate the location-specific inference obtained from feature importance with the data-generating mechanism from simulated climate models. We further demonstrate our method on reanalysis data containing the eruption of Mount Pinatubo, an observed stratospheric aerosol injection event. SNL is managed and operated by NTESS under DOE NNSA contract DE-NA0003525

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MS3

Forecasting Fire and Smoke Hazard on Subseasonal to Seasonal Timescales

Identifying the evolving niche of catastrophic wildfires across different climate zones is of the utmost importance for devising fire management and adaptation plans at multiple spatiotemporal scales. Traditional tools widely used for assessing fire potential, such as the Canadian Fire Weather Index (FWI) suffer from two main limitations: a) they often rely on parametric relationships of daily scale atmospheric predictors while ignoring any fuel information and seasonal scale land-atmosphere interaction effects, and b) they need to be tuned for applicability in heterogeneous landscapes with different fuel composition than their calibration area. Here I introduce a new fire hazard index (FHI), constructed using weekly-scale fire weather predictors, remotely sensed vegetation indices and soil moisture, along with different natural and human-related ignition predictors. The FHI is developed for each 12km (1/8 degree) grid cell in several fire prone regions, namely western United States, Mediterranean Europe, and southern Australia. Using a symbolic regression algorithm, we derive approximate functional forms of the FHI, accounting for the influence of seasonal scale antecedent climate on fuel availability and moisture content for each plant functional type in different biomes. Our robust, interpretable FHI framework underscores the promise of machine learning in forecasting wildfire risk, assessing impacts of extreme events, and building fire-resilient communities.

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MS3

Sensitivity of Simulated Wildfire Spread to Parameter Uncertainty and Spatial Resolution of Terrain and Fuel Maps

This study presents a critical analysis of the ELMFIRE wildfire behavior model, focusing on its sensitivity to environmental parameters and fire physics. Through rigorous testing using Latin Hypercube and Sobol Sequence Sampling, the research explores the impact of diverse environmental variables and physical parameters on wildfire simulation accuracy. Key aspects such as spotting dynamics, wind speed, and fuel moisture are extensively examined to assess their influence on fire propagation. The integration of remote sensing data, particularly from the VIIRS instrument, provides a benchmark for validating ELMFIRE's predictive capabilities. Results demonstrate significant variations in model performance based on environmental settings, underscoring the crucial role of precise parameter configuration. Advanced statistical tools, including ANOVA and Sobols Sensitivity Analysis, quantify the impact of each parameter, revealing essential insights into the factors driving wildfire behavior. The findings highlight the complex interplay between environmental variables and fire physics, emphasizing the need for accurate parameter tuning in wildfire modeling for enhanced prediction and management.

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MS3

Using Machine Learning to Understand the Drivers of Wildfires and Their Past and Future Changes

Wildfire is a complex system controlled by multiple environmental and anthropogenic factors. This poses significant challenges for understanding and modeling wildfires and their past and future changes. Given sufficient training data, machine learning (ML) can be used to model the relationships between wildfires and their predictor variables. Using Extreme Gradient Boosting (XGBoost) and artificial neural network (ANN), we have developed ML models that are skillful in predicting wildfire extent and wildfire emissions across the contiguous US. Using explainable artificial intelligence (XAI), the ML model predictions can be interpreted to provide insights on the drivers of wildfires. I will present examples of using ML and XAI to understand several aspects of wildfires including their spatiotemporal variability and long-term trends, revealing the drivers of large fire emissions and extension of the peak fire emissions from summer to fall in the western US during last few decades. Combining the ML models with meteorological and vegetation changes projected by an ensemble of climate models allows us to project future changes in fire emissions and understand the key factors driving the changes. Lastly, ML models can also be used to diagnose the biases of wildfire simulations produced by physics-based fire models, providing insights on modeling aspects that may be improved in the future.

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MS3

Multi-fidelity Coupled Fire/Atmosphere Modeling to Support Proactive Approaches to Wildland Fire

As the fire community looks towards more aggressive fire management or more proactive approaches to address the

growing challenges of wildland fire, the importance of science-based decision support increases. Progress in these arenas involves a different decision space from those associated with simply trying to put out every fire while it is small or predicting the general direction and speed that the fire will travel. When, attempting proactive unconventional management or there is an expectation that decision makers have weighed the pros and cons of their action (or lack of action) and are optimizing their actions to meet objectives, reducing costs, and avoiding unintended consequences. Whether it is assessing possible benefits of fuels treatments or planning and analyzing prescribed fires, next generation coupled fire atmosphere models can contribute to the science basis for land management decisions. The requirements on these models are that they capture the influences of the heterogenous and dynamic fire environment on fire behavior with sufficient detail to enable decision makers to understand the consequences of the various possible decisions. Continual improvement of the science basis and availability of decision support requires a multi-fidelity modeling approach where detailed, faster running models can continuously help us increase our understanding of the relationship between fire behavior and its environment in current or future climate scenarios.

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MS4

Coastal Dynamics in Monterey Bay, CA: Mimetic Curvilinear Coastal Ocean Model (mccom)

Accurate fluid dynamics modeling over complex bathymetric features necessitates terrain-following curvilinear coordinate grids. Solving the Navier-Stokes equations on a 3D curvilinear grid is programmatically and computationally intricate. The physical characteristics of a terrain-following curvilinear grid transform into a rectilinear logical coordinate system, and a numerical method is applied to solve the system, with the solution then converted back into physical space. This research streamlines the programming of a Navier-Stokes solution on a curvilinear grid using mimetic operators from the Mimetic Operator Library (MOLE). Mimetic operators, discrete analogs of traditional calculus operators, maintain accuracy up to boundaries and are implemented as sparse matrix-vector products, aligning well with modern computer capabilities. MOLE's implementation yields solutions in seconds, capitalizing on computational features and achievable on a personal computer. This high-speed mimetic approach is central to the Mimetic Curvilinear Ocean model. Our presentation elaborates on curvilinear grid components, explains computational efficiency gains, and outlines current and potential advancements and challenges, particularly in modeling internal seiches in the Monterey Canyon system.

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MS4

Model Based Simulation of Geophysical Flows

Depth-integrated free-surface flow models are successfully applied in many geophysical applications like river floods, tsunami modeling, sediment transport or debris flows. The *shallow water* model is the most well-known system of equation for such models with many adaptations and alternatives that have been developed for specific application areas with additional requirements. The *shallow moment* method is one such specimen that incorporates information about the bottom shear stress and the vertical velocity profile by depth-averaged the Navier-Stokes equations under certain geophysical reasonable assumptions. The governing model now raises several interesting questions: Boundary conditions and closure relations can be inferred directly from the three-dimensional setting. Can this be used to replace heuristically relations like a Manning-friction model that is typical the *shallow water* equations? While 'enhanced' depth-averaged methods like the *shallow moment* model introduce more physical information compared to the *shallow water* model, does this also positively impact the propagation of uncertainties for real-world applications? In this talk, we want to present our findings on these questions based a comparison of the *shallow water* and *shallow moment* equations for differently relevant test cases.

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MS4

Modeling Sediment Transport Using Shallow Water Moment Equations

Sediment transport in shallow-water environments is a complex phenomenon with significant implications for coastal morphology, environmental sustainability, and infrastructure management. In this talk, we will introduce a novel sediment transportation model through the development and implementation of the Shallow Water Moment Model (SWME). The SWME is based on a comprehensive theoretical framework that integrates principles from fluid dynamics and sediment transport. The new model represents a paradigm shift in sediment transport modeling, departing from traditional shallow flow methods by incorporating a polynomial expansion of the horizontal velocity profile in a vertical direction. In addition to the usual shallow water equations, the expansion coefficient equations provide a hierarchical system that improves accuracy when more equations are considered. By coupling with the Exner and sediment concentration equations, the general derivation of the model accommodates both bedload and suspended load transport, addressing a wide spectrum of sediment transport scenarios in shallow water bodies. We will discuss the theoretical analysis of the 1D model, and lastly, we will further highlight the accuracy improvements with respect to standard shallow water equations using a tailored numerical scheme.

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MS4

Towards a Practical Application of the Dispersive Shallow Moment Equations

Shallow Water Moment Models can be seen as generalizations of the classical shallow flow equations that preserve information on the vertical profile of the flow variables. A further extension includes a nonhydrostatic pressure component that enables dispersive effects in the flow. In this talk we will see a framework for the systematic derivation of Dispersive Shallow Water Moment models (DSM). The derivation from a set of balance laws is based on a splitting of the pressure followed by a same-degree polynomial expansion of the velocity and pressure fields in vertical direction. Dimensional reduction follows via Galerkin projections with weak enforcement of the boundary conditions at the bottom and at the free surface. After a quick look at the dispersive properties of the resulting equation systems, we will look into numerically solving the equations in one and possibly two horizontal dimensions. The special structure of the equation systems makes a splitting technique necessary where a Poisson equation has to be solved in every step. We will discuss simulation results for the stationary case on a finite domain with a set of mixed boundary conditions and results for the instationary case on a periodic domain.

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MS5

Generative Super Resolution for Estimating Climate Change Impacts on Power Systems and Communities

As climate change progresses, high-resolution climate-change-impacted weather data is crucial for assessing the impacts on power systems and communities. We introduce methods using generative adversarial networks (GANs) to downscale global climate model (GCM) data, achieving enhanced spatiotemporal resolutions suitable for power system and community analysis. We have effectively downscaled key power system modeling inputs, including wind, solar, temperature, and humidity, to 4km hourly resolutions. This advancement facilitates more nuanced power system analysis and better adaptation planning. Similar methods combine satellite imagery and human settlement layers to generate 1-km hourly urban heat island estimates. These estimates are crucial for evaluating heat risk and resilience in urban areas, especially during future extreme events impacted by climate change. By leveraging GANs, our approach significantly improves climate data resolution at low computational cost, offering new insights into the impacts of climate change on power infrastructure and urban communities, thus aiding in the development of more informed and resilient adaptation strategies.

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MS5

Exploring Pathways to Decarbonize Building Energy Needs Using Surrogate Modeling

The building and construction sector is responsible for 40% of worldwide carbon emissions, 65% of it is for the energy operation alone. Three central concepts to decarbonize building energy needs are the reduction of demand, a greater penetration of renewable energy and a more flexible energy consumption. In the Energy in Cities group at UVic, several projects develop surrogate models with machine-learning (ML) techniques to assist the rapid implementation of these concepts. Surrogate models are rapid data-driven models built from applications of slow and complex common design tools. By leveraging the power of ML and precision of complex tools, they help making informed decisions at early design stage, explore broader design spaces and find synergies within energy systems. In this talk, we present our work on surrogate models for building energy simulation tools to assist the design and selection of thermal retrofit solutions, and our work to evaluate surrogate model capabilities in demand-side management tasks using pre-cooling. The talk also focuses on a project investigating potential synergies between energy carriers, loads and storage at building and district level. This project explores the possibilities to bring surrogate modeling and the energy hub concept together. We further discuss how these examples illustrate commonalities, insights and pitfalls in the development strategy of surrogate models.

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MS5

Modeling and Operation of Power Distribution Grids using Real Utility Data and Artificial Intelligence

This talk will introduce two use cases of leveraging smart meter data to improve power distribution grid modeling and operation. The first use case is to estimate grid voltages. The previous studies on this topic mainly focus on primary distribution networks, which ignore secondary distribution networks where DERs are connected to and overlook extreme DER penetration cases. We will present a customized physics-inspired neural network (PINN) model whose structure is inspired by a derived coupled power flow model of primary-secondary distribution networks. The PINN's "structure-mimetic" design enables superior extrapolation for unseen scenarios and enhances physical information awareness. The effectiveness and advantages of the proposed PINN model are validated using real utility data. The second use case is a data-driven approach to identify service transformer-customer connectivity in low-voltage distribution grids by using only smart meters without any prior knowledge of transformer quantities. A weighted derivative dynamic time warping (WDDTW) method is proposed to calculate the pair-wise similarity of time-series voltage profiles, which is scalable and robust to

missing data.

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MS6

Synthesizing Data Products, Mathematical Models, and Observational Measurements for Lake Temperature Forecasting

We present a novel forecasting framework for lake temperature profiles using Gaussian process (GP) surrogates. Lake temperature forecasting is crucial for managing lake ecosystems and drinking water resources. The General Lake Model (GLM), a 1D process-based model, has been widely used for this purpose, but it requires a large number of input variables, many of which are stochastic; presents challenges for uncertainty quantification (UQ); and exhibits noticeable model bias. To address these issues, we propose a GP surrogate-based forecasting approach that efficiently handles large, high-dimensional data and accounts for input-dependent variability and functional output. The framework also includes a mechanism to account for systematic model bias. We validate the proposed approach and compare it with other forecasting methods, including a climatological model and raw GLM simulations. Our results demonstrate that the bias-corrected GP surrogate (GPBC) outperforms competing approaches in terms of forecast accuracy and UQ.

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MS6

Statistical Physical Frameworks

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MS6

Modeling Permafrost Thaw with Non-Equilibrium Models and Data from Mixed Sources

Permafrost soils respond to the daily, regional, and long-term atmosphere temperature variations through the heat conduction in its active layer. The thermal model is a nonlinear parabolic PDE which features a free boundary and is coupled to a flow model which describes the surface water(s); our computational model is conservative with sequential coupling of otherwise fully implicit components. However, the material properties of this active layer, the thermal conditions at the bottom as well as the actual surface temperature boundary conditions are generally not well known, and may vary substantially in a typical 40 km^2 cell of global predictive models. More generally, the slow response of the soil to these time varying inputs calls for the use of non-equilibrium models. In the talk we describe our efforts to use computational experiments to build and calibrate a non-equilibrium look-up table for the quantities of interest such as the increasing depth of the active layer. This is joint work with students and collaborators to be named in the talk.

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MS7

Enhancing Climate Model Calibration Through History Matching

Calibrating complex and computationally expensive simulators is a highly challenging task in climate science modeling. In this work, we tackle this challenge by employing the history matching approach, which explores the parameter space and identifies plausible regions where the simulated data matches the observed data. History matching (HM) rules out regions of the parameter space that lead to simulations deviating from the observed data, thereby narrowing down the search for plausible model parameter configurations. We demonstrate this approach using the Lorenz96 example, which is a simple yet benchmark model for complex climate dynamics. Our results show a significant reduction in the parameter space. Additionally, we extend our approach by implementing Markov Chain Monte Carlo (MCMC) on this reduced space to obtain the posterior distribution of the parameters. The emulator constructed in the history matching framework allows us to examine the obtained posteriors at each iteration of the history matching approach. Through comparisons with existing approaches, we highlight the advantages of our extended methodology in enhancing the efficiency of climate model calibration.

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MS7

Covariance Estimation for High Dimensional Geophysics Problems

Covariance estimation is a fundamental task in Earth science and a key step in many algorithms for uncertainty quantification, data assimilation, and machine learning. In Earth science applications, where state spaces are typically high-dimensional and sample sizes often small, covariance estimation is challenging. The sample covariance is known to be a poor estimator, and a number of different estima-

tion techniques have been proposed to address this issue. In this talk, we review a variety of different covariance estimation techniques for high-dimensional, low sample size problems, compiling methodologies from across the Earth sciences and statistics. In our review, we perform a comparative study of these methods on standard test problems from statistics and atmospheric science. We discuss how each method relies on a different set of assumptions, which in turn defines their applicability, scalability, and practically to high-dimensional, Earth science applications.

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MS7

Efficient Sampling of Climate Models Using Bayesian Optimal Experimental Design

Modeling, simulating, and predicting Earth's climate is essential for anticipating and quantifying the effects of climate change in the near and long term. However, current earth climate models require costly calibration efforts, usually done by hand tuning parameters, whenever new data or physics models are introduced. To speed this up, surrogate models are used, but these surrogate models require training data from computationally expensive climate models. To reduce the computational expense and maximally utilize simulation information, we seek to utilize Bayesian optimal experimental design (OED) to credibly select training data for the surrogate model. Using the Bayesian paradigm allows us to model the uncertainty of the surrogate model and to design experiments to optimally reduce this uncertainty. The fitted surrogate model with its reduced uncertainty can then be used for calibration of the climate models. This abstract presents work using Bayesian OED for training a Gaussian Process model of the Lorenz 96 model. Bayesian calibration using the BOED-trained Gaussian process model compared to using the high-fidelity Lorenz 96 model will be shown.

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MS8

Characterizing Buoyant Flow Instabilities for Wind-Driven Fires

The emergence of counter-rotational vortices in the velocity fields generated by both wildland fires and laboratory-scale experimental fires is a well-documented but relatively poorly understood phenomenon. The structures formed by these vortices, sometimes called towers and troughs, are an important mechanism of heat transfer in flaming fires. A deeper understanding and mathematical description of the physical mechanisms underlying the formation of these structures would aid in the development of faster, more accurate models of fire spread. We hypothesize that towers and troughs emerge due to thermally driven buoyancy and independent of fuel consumption, a theory supported by previous experimental work. When viewed this way, the formation of counter-rotational vortices looks very similar to the formation of convective cells in Rayleigh-Bnard convection. To exploit this analogy, we formulate the Boussinesq equations for fluid flow over a hot plate in a moving frame corresponding to a constant horizontal wind velocity and analyze the instabilities that emerge in the resulting system of PDEs. We extend the study by running a series of numerical experiments using FIRETEC, a full-fidelity landscape-scale wildland fire model, to understand the effects of various environmental factors on the frequency and magnitude of the towers and troughs pattern.

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MS8

Data Assimilation for Wildfire Predictions via Deep Generative Models

Increased wildfire prevalence has led to the development of sophisticated coupled atmosphere-wildfire spread models. Additionally, advances in the use of geostationary and polar orbiting satellites for wildfire detection provide multiple sources of measurement data which can be used to improve model forecasts through data assimilation. Performing data assimilation for coupled atmosphere-wildfire models requires a detailed time-history of the initial fire trajectory, which is used to initialize the wildfire and atmosphere states. This history is encoded in the high-resolution (60 m) fire arrival time, which provides the time fire reaches any location in the domain. Additionally, satellite measurements provide sparse and noisy measurements of the arrival time at much coarser resolutions (0.3-2 km). In this talk we describe how, by posing this problem as a probabilistic inverse problem, we can combine measurements from various sources with a physics-driven wildfire simulator to obtain a high-resolution probabilistic version of the fire arrival time. To do this, we develop an approach using deep conditional generative algorithms to sample from the desired conditional distribution, given measurements. The algorithm is trained with solutions from a coupled atmosphere-wildfire model, along with corresponding measurements obtained by applying a measurement operator to these solutions.

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MS8

Efficient Algorithms for Continuous Maxent Models with Applications to Wildfire Science

Maximum entropy (Maxent) models are a class of statistical models that use the maximum entropy principle to estimate probability distributions from data. Historically used in physics, engineering and statistics applications, Maxent models are now frequently used in machine learning to estimate probability distributions for big data applications. Recent advances in algorithmic techniques have made it feasible to train Maxent models on big data sets robustly and efficiently, provided the underlying Maxent distributions are discrete. In several applications, however, the underlying Maxent distributions cannot be approximated as discrete due to the curse of dimensionality. Even when possible, this discretization remains an often undesirable approximation and is often used only to make the problem amenable to numerical algorithms. In this talk, I will present a novel approach for training Maxent models with continuous probability distributions on large-scale data sets. I will illustrate my results on the WUMI wildfire data set to estimate the probability of fire occurrences as a function of ecological features.

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MS8

Data-Driven Hybrid Mechanistic/Neural/Statistical Models for Wildfire Propagation with Uncertainty Quantification

Spatio-temporal data are ubiquitous in the sciences, medicine, and engineering, and their study is important for understanding and predicting a wide variety of processes. One of the difficulties with statistical modeling of spatial processes that change in time is the complexity of the dependence structures that must describe how such a process varies, and the presence of high-dimensional complex datasets and large prediction domains. It has long been the case that deep (hierarchical) statistical models have proven helpful for such data, yet these models can be difficult to implement for various reasons. Incorporating mechanistic processes within the hierarchical modeling framework has proven helpful. Increasingly, black-box neural (AI) models are being used for spatio-temporal data as well, capitalizing the strength of those models to learn complex dependence structures. The downside of such models is the requirement for large amounts of training data, interpretability, and uncertainty quantification (although, there are solutions to each of these issues). It is natural to consider hybrid models that address some of these issues. Here, I illustrate by example that combines a level-set mechanistic formulation and reservoir computing neural model within a hierarchical statistical framework to model wildfire front propagation. This approach allows for hybrid mechanistic/neural models an uncertainty quantification.

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MS9

Bayesian Filtering via Projected Transport Maps

In Bayesian filtering, the goal is to sample from the distribution of the state of a dynamical system given past observations. Here we are interested in sampling from filtering distributions associated with high-dimensional chaotic systems, such as turbulent flows. This is a problem of sampling from a high-dimensional Bayesian posterior that is often non-Gaussian and singular. Several transport-based methods for sampling and Bayesian inference that are based on a variational principle – minimizing the distance from a pushforward of a source distribution to the target – have become recently popular. Here we introduce a new principle – infinite-dimensional score-matching – from which to derive a transport map. Unlike traditional transport methods, the new transport map exhibits fast convergence like a Newton-Raphson method, and can more effectively handle multimodality in the target. We develop a method to project this transport map algorithm, called Score Operator Newton or SCONE, on the unstable manifold of the underlying chaotic dynamics. Such a projection leads to a filtering algorithm whose cost only scales with the unstable dimension as opposed to the overall system dimension. This scheme is applicable to complex, singular filtering distributions that have absolutely continuous conditionals on the unstable manifold.

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MS9

Large Ensemble Forecasting, Interpretability, and Data Assimilation with Deep Learning Weather Models

Sampling extreme and rare events in weather forecasting is frustrated by the computational cost and complexity of producing a large enough ensemble of individual forecast trajectories using traditional NWP. Over the last year deep learning (DL) weather models have shown promising competitiveness versus traditional weather models at a fraction of the computation time. With the ability to incorporate statistical randomness through model uncertainty, along with traditional initial condition and state perturbation, generating a large number of ensembles forecasts from DL models has become an appealing methodology to

probe extreme and rare events. In this talk we explore the challenges of understanding the calibration of these deep learning weather models and some methods useful for exploring their learned dynamics. Results show 1000 member ensemble predictions of weather extremes, such as heat waves, atmospheric rivers, and tropical cyclones. Probabilistic metrics like CRPS, spread skill ratio and extreme forecast index are examined and the implications of different perturbation methods on the predicted variables are discussed in light of these results.

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MS10

Ai for Managing Water Quality in Water Systems

Controlling water quality in water supply systems is crucial for ensuring public health, preventing disease outbreaks, and maintaining environmental sustainability. This presentation will provide an overview of the recent advances in multiscale modeling and optimization techniques to enable real-time management and control of water quality in drinking water supply systems. The presentation will focus on 3 interconnected research topics: (1) the development of data-driven optimization frameworks for optimizing the placement of water quality sensors to maximize network-wide observability of water quality indicators, and to enable model-predictive water quality control; (2) the application of Bayesian optimization techniques to optimize water treatment processes to optimize the dosing of chlorine-based disinfectants to maintain sufficient protections against microbial contamination, both accidental and intentional; and (3) the application of AI/ML approaches for the early detection of contamination events, rapid identification of contamination sources, and optimization of contamination response strategies, which includes the isolation and containment of contaminants entering the supply system, as well as water quality restoration through automated flushing and emergency disinfection. This work aims to support water supply utilities in maintaining high water quality in drinking water systems.

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MS10

Observationally-Constrained Predictions of the Time to Exceed Policy-Relevant Global Warming Thresholds: A Non-Crossing Quantile Regression Neural Network Approach

The Paris Agreement is an international treaty established in 2015 by world leaders to address anthropogenic climate change. The main goal is to significantly reduce global greenhouse gas emissions so as to limit global warming to well below 2 C, while also striving to limit warming to 1.5 C. If global temperatures exceed 2 C warming, the risks of climate extremes are projected to be far greater for a larger portion of the Earth than with a 1.5 C increase. A non-crossing quantile regression neural network for the full quantile regression process is used to make probabilistic predictions of the time remaining before global warming thresholds are exceeded. The model 1) allows data for multiple warming thresholds and scenarios to be combined into a single model; 2) incorporates global surface air temperature (GSAT) warming rate as an additional predictor; and 3) accounts for the assessed likely range of equilibrium climate sensitivity (ECS) when making model predictions. Out-of-sample robustness is tested using realizations from climate models not included in training, and by making predictions for the known time-of-exceedance of the 1.05 C threshold using historical observations and the assessed distribution of Earth's climate sensitivity. Finally, the machine learning model is interrogated using explainable artificial intelligence techniques to see if a robust, interpretable relationship with a plausible mechanism of operation emerges.

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MS10

Towards Science Foundation Models for Complex Energy Systems

Foundation models are revolutionizing language and vision processing. These models, which are trained on lots of broad data and can be applied across a wide range of contexts, are often used as"noisy idea generators. That is, they can rapidly generate new data or make predictions on novel inputs when prompted, which vastly reduces the time and expertise needed to train specialized models catered to each specific task of interest. This presentation will begin by motivating science foundation models designed to address computational challenges in the design, analysis, and management of complex energy systems. Then, the BuildingsBench platform for researching science foundation models will be introduced. BuildingsBench facilitates studying large-scale pretraining with simulated time series data in conjunction with fine-tuning on real data in the setting of building short-term load forecasting. Next, this talk will describe a new framework for developing language-guided surrogate models of complex energy systems. Language guidance, which can improve the interpretability, controllability, and usability of data-driven surrogate models, is achieved by leveraging concepts from multi-modal machine learning and pretrained large language models. Finally, a roadmap of future work will be provided to conclude the presentation.

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MS10

Optimizing Dual-Ring Traffic Signal Controller with Deep Reinforcement Learning

Traffic signal control problems have been formulated as explicit optimization models. The assumptions behind such models are that traffic can be modeled as functions, i.e., the mappings from input to output are one-to-one mappings. However, from either the random behavior of drivers or the stochasticity in the macroscopic observations, with one input (state or control), the resulting output could be a random variable of a certain joint distribution. Recent research has shown that reinforcement learning (RL) can solve traffic control problems effectively due to its ability to learn policies from stochastic simulation episodes. During the RL training process, reward at every time step is used to incrementally improve the RL policy. In the literature, most actions are taken within a control cycle and formed acyclic controls. These actions within a cycle may

not be technically achievable. The cyclic control, i.e., assigning green times for all phases in a cycle, is seen more in stage-based control (i.e., one-ring control) while dual-ring control is widely applied in the U.S. In this study, we propose a framework that enables RL to be applied in dual-ring controllers by constructing a differentiable convex optimization layer at the end of a neural network to ensure that the output actions of RL comply with the constraints defined by National Electrical Manufacturers Association (NEMA) standards. We found that RL-based controls can reduce the delay of an intersection by over 50%.

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MS11

Fully Well-Balanced Semi-Implicit Schemes for Shallow Water Equations: Integrating Splitting and Relaxation Techniques

This work focuses on the design of fully well-balanced semi-implicit schemes for one-dimensional shallow water equations, ensuring preservation of all steady states, not just water-at-rest equilibria. The proposed methods outperform standard explicit schemes in the low-Froude regime, where celerity is larger than fluid velocity, avoiding the need for many iterations on large time intervals. Employing splitting and relaxation techniques, the approach yields both first and second-order schemes. Unlike recent Lagrangian-based methods, this technique maintains all steady states while avoiding complexities tied to Lagrangian formalism

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MS11

High-Order Fully Well-Balanced Methods for the Shallow Water Equations with Horizontal Temperature Gradients

In this work, we consider the shallow water equations with horizontal temperature gradients, which can be seen as a particular case of a general family of systems of balanced laws that also includes the compressible Euler system with gravity. Our goal is to obtain high-order numerical methods that preserve all the stationary solutions that represent fluid at rest, i.e., hydrostatic stationary solutions. However, the above task is not trivial due to the existence of infinite hydrostatic stationary solutions. A previous methodology to develop high-order methods that exactly preserve a two-parameter family of non-moving stationary solutions will be extended.

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MS11

Fully Well-Balanced Methods for Shallow Water Linearized Moment Model with Friction

In this research, our focus lies in the numerical investigation of hyperbolic shallow water moments equations introduced in [Koellermeier, J., Pimentel-Garca,Steady states and well-balanced schemes for shallow water moment equations with topography, (2022) Applied Mathematics and Computation, 427, 127166], considering smooth bottom topographies and friction terms. We introduce first- and second-order well-balanced methods designed to preserve all stationary solutions of the system. These methods are based on fully well-balanced reconstruction operators which combine specifics collocation methods and quadrature formulas. To validate their accuracy and well-balanced characteristics, we present numerical tests demonstrating their performance.

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MS12

Data-Driven Parameterization of Un(der)-Resolved Gravity Wave Momentum Fluxes for Atmospheric Modeling

Atmospheric gravity waves on scales of 10^2 to 10^5 meters play an important role in the global circulation by transporting momentum from the surface to the free atmosphere. The position and strength of the jet streams (and hence the track of winter storms) depends critically on these waves. This poses a problem to atmospheric modeling: large scale features that require a global model depend on fine scale phenomena that we simply cant simulate on such a domain. This closure problem requires an estimate, or parameterization of the missing momentum fluxes based on the resolved scale flow and information about sub-grid scale wave sources (e.g., topography and convection). I will detail novel data-driven strategies to overcome this challenge. The process involves two components. First, the missing waves must be estimated from high resolution simulations capable of accurately capturing all the relevant scales. Second, machine learning techniques are used to capture the missing momentum transport. We explore differing strategies, contrasting brute force approaches, where we let machine learning crunch the solutions, hoping to learn the statistics from the data alone, vs. hybrid approaches, where we couple machine learning with physics-based closures. The latter strategy involves an inverse problem: what are the optimal gravity wave sources, and machine learning: how to estimate them from available source indicators.

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MS12

Long-Term Instabilities and Physical Inconsistencies of AI Weather Models

A number of fully data-driven weather models (FourCastNet, Pangu, GraphCast), which have been trained on just 40 years of reanalysis data, have shown remarkable short-term forecast skills (10-day lead times). However, when integrated for longer times (weeks and months), these models go unstable or produce unphysical circulations. Here, we discuss a major cause of these problems: the spectral bias. This bias, which is an optimization issue, hinders the learning of small-scale dynamics by these models, which manifests itself as long-term instabilities or unphysical drifts. We will discuss the theoretical aspects of this bias and solutions to reduce it.

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MS12

Data-Driven Deterministic and Stochastic Subgrid-Scale Parameterization in Atmosphere and Ocean Models: A Pattern-Based Approach

Data-driven deterministic and stochastic subgrid modeling schemes for atmosphere and ocean models are discussed. This is a hybrid modeling setting in which a physics-based model is augmented with data-driven elements. A novel pattern-based approach is taken where pairs of patterns in the space of resolved variables, or physically meaningful functions of these, and in the space of the subgrid forcing are identified and linked in a predictive manner. On top of this deterministic part of the subgrid scheme the subgrid patterns may be forced stochastically with white or red noise. Both the deterministic and the stochastic scheme may be further constrained by physically motivated conservation laws, such as momentum conservation or (kinetic) energy conservation but enstrophy dissipation. The schemes are machine learning style, but unlike black-box approaches such as neural networks the present methodology still allows to understand and interpret the subgrid model. The subgrid modeling schemes are implemented in an intermediate-complexity atmospheric model with realistic mean state, variability and regime behavior. The model at a high horizontal resolution is regarded as reference against which coarser-resolution versions, equipped with the subgrid modeling schemes, are compared. The configurations are tested in long-term simulations as well as in an ensemble prediction setting.

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MS12

Probabilistic and Generative Machine Learning Based Modeling of Earth System Processes

We focus on the use of probabilistic and ensemble machine learning (ML) methods to facilitate the modeling of Earth system processes. The techniques we consider range from generative ML models such as conditional versions of generative adversarial networks (GAN) and variational autoencoders (VAE) to transformers and Bayesian neural networks and ensemble versions of reservoir computing, Given the nonlinear and multiscale nature of various Earth system processes, in one application, we focus on inferring a stochastic closure to represent the effect of unobserved (unresolved) small scale processes on observed (resolved) large scale processes conditioned on the latter. In a second application, we focus on the large scales of the climate system: Predictability typically arises from deterministic dynamics, dynamical symmetries and their associated invariants, and various linear, nonlinear and emergent oscillations/patterns (e.g., in the climate system, the annual seasonal cycle, Rossby waves, the North Atlantic Oscillation, the El Nino Southern Oscillation, the Atlantic Meridional Overturning Circulation, etc.). However, the inevitable problem of model bias prevents comprehensive first-principles based climate models from being able to model such variability skillfully. As such, we focus on reduced-dimensional, data-driven predictive, spatiotemporal modeling of such natural variability using probabilistic and generative ML techniques.

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MS13

The Role of Turbulence in Wildland Fire Behavior and Ember Transport

Fire suppression activities in the past few decades in North America have led to higher fuel accumulations, which coupled with shifting hydroclimatic patterns has led to an increase in frequency and severity of wildland fires. Prescribed fires and fuel treatments such as mechanical thinning are deemed to be effective tools for managing fuel loads. However, assessing the effectiveness of fuel treatments is rendered complicated due to several factors such as wind, fuel moisture, and fire-atmospheric interactions at the fine scales. Detailed analyses on turbulent heat and energy exchange are conducted to understand the fundamental processes governing varying regimes of fire intensity, fire spread, ember transport, and fuel consumption under different conditions of fuel moisture and treatment. The conclusions are generalized to highlight the importance of considering vegetation response to hydrometeorological events, coupled with fine-scale fire-atmosphere interactions while managing wildland fire behavior. On the other hand, wildland fires themselves are characterized by their own weather which is driven by both shear and buoyancy-driven turbulence. In this talk, we will explore the complex turbulent dynamics of wildfire propagation using the tools of boundary layer physics and turbulent fluid dynamics. Insights into the energetics of turbulent exchange processes during fire propagation will lead to a better understanding and improved models for wildland fire behavior.

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MS13

Learning Fire Models with Noisy Data

Describing the complex dynamics in fire science remains a challenge because of multiscale and multiphysics processes involved. For example, characterizing the turbulent atmospheric environment is key to describe ember flight trajectories. While physics-based models relying on fundamental principles such as conservation of mass and momentum result in differential equations, learning these models is challenging, especially because real data in fire science is inherently noisy. I will present a data-driven approach to learn the governing equations directly from noisy fire data.

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MS13

High-Fidelity Ensemble Simulations of Large-Scale Wildfires for Fire-Impact Assessment

With the increasing severity and frequency of large wildfires, there is a critical need for improved modeling capabilities to inform mitigation plans for fire management and risk mitigation. In particular, high-fidelity modeling tools are needed to provide reliable predictions of fire-spread behavior to support scientific inquiry and fire-risk assessment, as well as landscape management at an early stage. However, because of the computational complexity, physics-based models are largely limited to simulating a few conditions. We present a high-fidelity simulation framework that takes advantage of emerging programming paradigms, novel computing hardware architecture, and ensemble calculations for simulating large-scale wildfires scenarios at affordable cost, thereby enabling the parametric study and statistical analysis of wildfires scenarios under consideration of changing environmental conditions, ignition probabilities, and vegetation and fuel-moisture regimes. We discuss details of the simulation framework that is based on TensorFlow and the utility of ensemble simulations to examine fire-spread behavior in the presence of coupled wind-slope conditions that remain an outstanding scientific challenge for fire-spread predictions.

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MS13

Modeling the Hourly Growth of Large California Wildfires with a Suite of Meteorological, Human, and Land-Based Controls

Recent fire seasons, such as in California in 2020 and 2021, included dozens of megafires that lasted for weeks and had periods of explosive growth. The monitoring and predictive modeling of extreme fire spread are important tasks for protecting communities and allocating firefighting resources. Here we develop the GOES-Observed Fire Event Representation (GOFER) algorithm to derive the hourly fire progression of large wildfires and create a product of hourly fire perimeters, active fire lines, and fire spread rates. Using GOES-East and GOES-West geostationary satellite detections of active fires, we test the GOFER algorithm on 28 large wildfires over 50,000 acres in California from 2019-2021. Based in Google Earth Engine, the GOFER algorithm includes parameter optimizations for defining the burned-to-unburned boundary and correcting for the parallax effect from elevated terrain. We then use GOFER with XGBoost to predict the fire-wide growth in area. We train the model using 2019-2020 fires and test the prediction on 2021 fires. Our preliminary model using the active fire line length, vapor pressure deficit, wind speed, and topography as predictors explains 40% of variance in the fire-wide growth in area in the test dataset. In summary, we built a temporally-resolved fire progression database for large California fires and find that active fire lines are a key control on fire growth with potential use cases for fire spread forecasts and improving atmospheric models.

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MS14

A Possible Hysteresis in the Arctic Ocean Due to Release of Subsurface Heat During Sea Ice Retreat

The Arctic Ocean is characterized by an ice-covered layer of cold and relatively fresh water above warmer and saltier waters below. It is estimated that enough heat is stored at depth in the Arctic Ocean to melt all the Arctic sea ice many times over. But this heat has historically remained trapped at depth: the seawater density differences are dominated by salinity, making the vertical stratification stable, and the sea ice cover damps wind-generated internal waves that could otherwise mix the warm waters up to the surface. In this talk, I will discuss a positive feedback process involving the release of subsurface heat in the Arctic Ocean as the sea ice retreats. I will present idealized model results showing that this feedback process can give rise to a hysteresis window bounded by saddle-node bifurcations, featuring an abrupt "tipping point" under global warming when the bifurcation point is crossed. The hysteresis occurs for only a limited range of plausibly realistic parameters, however, and questions remain regarding the likelihood that this potential tipping point could occur under global warming during the coming century. Nonetheless, even in the absence of a tipping point, this positive feedback could substantially accelerate the melt of Arctic sea ice.

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MS14

Homogenization for Convection-Enhanced Thermal Transport in Sea Ice

Polar sea ice is an essential moderator of heat exchange at the Earths ocean-atmosphere interface. As such, the effective thermal conductivity of sea ice is a key parameter in models of heat transport in the climate system. At the same time, measuring and predicting the effective thermal conductivity is challenging due to its sensitive dependence on temperature, salinity, and fluid flow through the brine microstructure. Despite the development of models for thermal diffusion through sea ice, advective contributions to fluid flow have not been considered theoretically. In this talk, we consider the homogenization of a multiscale advection-diffusion equation which models thermal transport through porous sea ice when fluid flow is present. We present rigorous bounds on the effective thermal conductivity both with respect to the Péclet number and temperature. These bounds reflect an enhancement in thermal transport due to fluid convection and capture field measurements and numerical simulations.

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MS14

Well-Posedness of Hibler's Sea Ice Model

We establish the local-in-time well-posedness of solutions to an approximating system constructed by mildly regularizing the dynamical sea-ice model of W.D. Hibler, Journal of Physical Oceanography, 1979. Our choice of regularization has been carefully designed, prompted by physical considerations, to retain the original coupled hyperbolic-parabolic character of Hiblers model. Various regularized versions of this model have been used widely for the numerical simulation of the circulation and thickness of the Arctic ice cover. However, due to the singularity in the ice rheology, the notion of solutions to the original model is unclear. Instead, an approximating system, which captures current numerical study, is proposed. The well-posedness theory of such a system provides a first-step groundwork in both numerical study and future analytical study.

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MS14

Arctic Marginal Ice Zone Dynamics Captured by Ocean-Scale Mushy Layer Model

The Arctic marginal ice zone (MIZ) is the transition region between dense pack ice to the north and open ocean to the south, and has widened by 40% over the satellite era, impacting climate dynamics, ecological processes, and human accessibility to the Arctic. The MIZ also undergoes dramatic annual cycles, widening by a factor of four while seasonally migrating more than 1,600 km poleward in the Bering-Chukchi Sea sector. Here we showcase a transformative mathematical modeling approach to understanding changes in MIZ location and width. We consider the MIZ as a liquid-solid phase transition region on the scale of the Arctic Ocean. Invoking the physics of phase changes, temperature in the ocean surface layer is described by a nonlinear heat equation with effective parameters obtained using homogenization theory for a random medium of ice floes in sea water. This model captures 96% of the annual cycle of MIZ location and 78% of the annual cycle of MIZ width.

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MS15

Fast Summation for Spherical Convolutions

Convolutions on the sphere are important in many aspects of the geosciences, and many unstructured numerical methods make heavy use of them. However, when discretized, these convolutions result in sums that scale as $O(N^2)$ in the number of grid points, which is challenging for scaling to large problem sizes. In this talk, I will present a fast summation technique that allows us to approximate such sums while reducing the complexity from $O(N^2)$ to $O(N \log N)$ with a spherical tree code that is suitable for a wide range of problems in the geosciences.

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MS15

Fluid Dynamics on a Rotating Sphere with Double Fourier Series and Lagrangian Advection

Vortex-based methods for a two-dimensional incompressible fluid on a rotating sphere typically require computing fluid velocity from vorticity by applying the Biot-Savart law. The discretization of the Biot-Savart integral results in an N-body problem, which, if solved by direct methods, has a computational cost that scales as $O(N^2)$, where N is the number of particles. Additionally, the discretization of this integral requires the particles to be arranged in specific ways that are impossible to maintain during the simulation beyond the initial time-step. To bypass this problem, it is common to redistribute the particles after every few time-steps, which introduces an additional cost. To reduce this computational cost, we propose a different approach where the velocity at the particles is determined at each time-step by 1) interpolating the vorticity to a fixed Eulerian grid, 2) solving a Poisson equation for the stream function on the grid, 3) computing velocity on the grid from the stream function, and 4) interpolating the velocity back to the particles. All the grid-based discretizations are done efficiently and accurately using the Double Fourier Sphere (DFS) method. We also use the DFS method for the final interpolation step and speed-up this computation using the nonuniform fast Fourier transform (NUFFT). Numerical results show that the proposed scheme is efficient, accurate, and stable and provides a promising alternative vortex-based method on the sphere.

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MS15

Adaptive Refinement with Finite Time Lyaponov Exponents in Lagrangian Numerical Methods

Finite Time Lyapunov Exponents (FTLEs) measure the maximum stretching of infinitesimal Lagrangian volumes advected by a dynamical system within a specified (finite) time horizon. These exponents are calculated from the eigenvalues of the system's Cauchy-Green strain tensor. Typically, FTLEs are used to identify the most repelling or attracting materially invariant coherent structures in fluid flow. In this study, instead of their traditional use as a flow diagnostic tool, we use FTLEs to trigger remeshing in a Lagrangian numerical method (LNM). One benefit of LNMs is that they are inherently multi-scale, i.e., they naturally cluster numerical particles in the locations requiring largest resolution such as the high-gradient regions. However, the distortion of the underlying mesh connecting these Lagrangian particles requires remeshing after a certain time. Previous implementations of LNMs have relied on heuristics to trigger remeshing in both time and space. In a Lagrangian simulation, where the trajectory of each numerical particle is known, FTLEs can be readily calculated. We use FTLE fields to both trigger remeshing and spatially redistribute numerical particles while demonstrating the enhanced numerical efficiency across different flows on a sphere. FTLE-aided simulations can be run for longer times, allowing novel vortex breakdown mechanisms on the sphere to be revealed.

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MS15

A Multiscale Numerical Method for Flow Map Approximation on the Sphere

In this talk, we will present the characteristic mapping method for flow map approximation in a spherical geometry. The method utilizes a spatiotemporal discretization of the flow map defined by a composition of short-time sub-interval flows. By leveraging this composite structure, exponentially fine scale fluid motions can be represented using only a linear increase in computational resources. We will explain how the unique resolution properties of the method result from this discretization and the preservation of a relabelling symmetry for transported quantities. Canonical numerical examples of tracer transport and barotropic flows on the sphere will be given, showcasing the ability to resolve the direct energy cascade at sub-grid scales and capture some associated inverse cascade phenomena.

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MS16

Lassa Fever and Perception of Risks in Nigeria

Lassa fever is an acute viral hemorrhagic disease caused by the Lassa virus. It is transmitted to humans through direct contact with infected *mastomys natalensis* rodents, or through food or household items contaminated with the urine or feces of infected rodents. Nigeria is an endemic country for Lassa fever, the current overall risk at the national level is considered high due to several factors including lack of awareness and education about Lassa fever. We

developed a mathematical model of Lassa fever transmission with perception of risks. We parameterize the model using Lassa fever data from 2017-2022 obtained from Nigerian Centers for Disease Prevention and Control. We carried out a sensitivity analysis and found that the perception of risks terms has a significant impact on the sensitivity analysis response function. Furthermore, disease burden decreases with increasing perception of risks.

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MS16

Unveiling the Pesticides Threat and Seasonality for Honey Bee Populations Through Mathematical Modeling

Honey bees (Apis mellifera) are vital for pollination and ecosystem stability, yet they face threats from parasitism, pesticides, and climate change. To study these impacts, we developed mathematical models to study the interactions with seasonal effects and another for pesticide exposure across different bee age stages. Our model shows that seasonality has both positive and negative effects. The timing of peak egg-laying is crucial; prolonged seasonal periods can cause colony collapse. Honey bees' exposure to the pesticide reveals a linear relationship between egg and adult bee populations, influenced by adult-to-egg mortality rates. Environmental factors, including pesticide exposure, must be included in the model. Pesticides increase adult mortality rates based on concentration, affecting peak queen egg-laying timing, baseline egg-laying rates, and adult-to-larval pollen consumption. High pesticide concentrations can lead to hive collapse. This research highlights the importance of mathematical models in understanding and managing the impacts of parasitism, pesticides, and seasonality on honey bee populations, providing critical insights for their conservation.

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MS16

Linking Models of Human Behavior, Risk Perception, Economics and Climate Change: a System Dynamics Perspective

The vast majority of climate models designed to project future global temperature trajectories ignore feedbacks between human behavioral and social system responses and the climate system. Prior research on models linking climate models to human behavior provide evidence that these linkages can significantly modify future trajectories compared to climate models based only on natural system processes. We will describe our efforts to model the interactions of climate systems and human social systems, focusing particularly on risk perception. We will describe how we model human risk perception and associated changes in attitudes as driven by the experience of climate change. We take a system dynamics approach and incorporate submodels for extreme climate events, cognition and memory processing as a balance between sensing and forgetting extreme climate events that allows for habituation, an economic growth model augmented to account for the economic impacts from a changing climate by deducting climate damages from total economic production, and associated dynamics of attitudes as affected by social norms and perceived behavioral control that determine investment in greenhouse gas abatement. These models are linked to a climate model and applied to project global temperature over this century taking account of uncertainties in model components and then compared to previous linked models that suggested there were a limited set of distinct future global temperature pathways.

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MS16

Changing Assumptions About Mosquito Habitat Availability Drive Variation in Seasonal Dengue Dynamics When Behavioral Control Is Present

Vector control for dengue can vary significantly in its effectiveness, with human behavior being a potentially important cause of that. Compliance with top-down efforts

such as spraying campaigns and bottom-up habits around aquatic habitat reduction around households are two examples of behavioral components of successful vector control. One factor that may affect bottom-up habits around aquatic habitat reduction is water storage needs, which influence the relationship between rainfall and aquatic habitat for mosquitoes. Rainfall has been associated with both more and less aquatic habitatit directly increases standing water outdoors but may lessen intentional water storage. To explore the possible consequences that this relationship may have on the effectiveness of behavioral interventions, we developed a mathematical model for the coupled dynamics of dengue virus and associated container-management behaviors. We found that the impact of container-management behaviors is largely dependent on assumptions about what drives mosquito reproduction and aquatic habitat dynamics in a given setting, and suggest this as a focus when tailoring interventions to community-specific conditions and concerns.

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MS17

Microbes and the Mushy Layer

Sea ice, which covers a significant portion of the earth's surface, is a interestingly complicated, "mushy" material consisting of a mixture of solid ice and liquid phases which are coupled by thermodynamic considerations. It also is a platform for microbial life, lots of it in fact, that uses the ice as a sort of shelter though eventually becoming part of the local food chain. A model will be presented that hypothesizes how, in turn, the resident microbial population might impact sea ice properties, brine channel structure in particular, via influence on brine osmolarity.Text may not exceed 1500 characters, including spaces for this abstract.

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MS17

Sea Ice Variability: Everything Everywhere All at Once

The Arctic sea ice cover plays a critical role in global climate change, acting as both an indicator and an amplifier of climate change. Complicating the treatment of sea ice in climate models is the large spatial variability and strong temporal evolution of the ice. There is spatial variability in the ice thickness, ice temperature, brine volume permeability, strength, albedo and transmittance. Over an annual cycle, the snow covered ice of winter is replaced by bare ice and melt ponds in summer. The annual ice evolution is influenced by variations in the timing of the onset of summer melt and fall freezeup and by ephemeral weather events, such as winter rain on snow and summer snowfalls. Results from field experiments, process studies, and climate models are presented to illustrate the full range of this variability and then to examine its impact on the state of the ice cover.

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MS17

Sharp Interface Models of Brine Inclusions

Brine inclusions play a fundamental role in sea ice, influencing permeability and albedo while providing crucial environments for krill and algae. In particular algae that are entrapped in brine inclusions release antifreeze polymers that impact the shape and structure of the brine inclusions. In particular they are known to induce a *faceted* structure on the inclusions. We propose a class of free energies for sharp interfaces that induce faceting. These break out of the traditional Canham-Helfrich approach to interfacial energy, which we show induces new mathematical challenges. We derive a class of curvature driven flows that act as gradient descents for the free energy and examine their behavior in the presence of thermal gradients typical of polar sea ice.

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MS18

Confronting structural uncertainty in aerosol effects on climate

Atmospheric aerosol has consistently been the largest source of inter-model variability in radiative forcing among climate models. Climate-relevant aerosol properties depend critically on the distribution in size, shape, and chemical composition of particle populations that evolve in time as they are transported through Earths atmosphere. However, tracking such particle-level details is computationally impractical for large-scale, long-running climate simulations. Instead, aerosol modules in large-scale atmospheric models necessarily simplify the representation of particle characteristics, leading to errors in climate-relevant aerosol properties that have not been well quantified. Here we present a framework for using particle-resolved simulations of aerosol-cloud-chemistry interactions to quantify structural errors from the numerical representation of particle population. Based on this analysis, we then show how these detailed aerosol schemes can be used to improve aerosol parameterizations in large-scale models. Through this approach, we aim to inform the development of aerosol schemes that balance model accuracy with computational efficiency, while also characterizing uncertainty from reduced representations of particle populations.

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MS18

Coupled Continuum-particle Simulations for Multiscale Simulations of Chemical Vapor Deposition

Multiscale phenomena are at the heart of many renewable energy applications, from biomass conversion processes, to electrochemistry and catalysis. Typically, these phenomena are treated separately and the coupling between the models is one sided, i.e., models and parametrizations are developed from the small-scale physics to inform the large scale physics, and passive, i.e. the simulations are performed sequentially and separately. This type of coupling has many drawbacks: parametrizations are valid for limited conditions, spatiotemporal variation of transport phenomena is neglected, and the state space may not be captured in the one-off parametrization. We address these obstacles by developing an active multiscale modeling framework that leverages software tools and infrastructures scalable on current and future DOE high-performance-computing resources. In this talk, we present the coupling of a mesh-based solver (i.e., a compressible flow solver) and a particle-based atomistic solver (i.e., kinetic Monte-Carlo). We demonstrate the coupled system by solving flow inside a chemical vapor deposition reactor for growth of a perovskite crystal. To alleviate the computational cost of the coupling to an atomistic solver, we leverage recent developments in adaptive computing to develop in-situ reduced order models of the atomistic scale physics. This approach has the additional benefit of enabling the control of uncertainty arising from the stochasticity of the atomistic solver.

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MS18

Enhanced Sea Ice Mechanics with the Material Point Method

Sea ice plays an important role in the global climate by reflecting solar radiation and influencing ocean circulation. To accurately simulate the complex interactions between sea ice, atmosphere, and ocean in the coupled system, a sea ice model must be able to capture large seasonal changes in ice cover as well as complex deformation due to atmospheric winds and ocean currents. Lagrangian particle methods have certain advantages over Eulerian grid-based methods for sea ice modeling due to their ability to naturally handle advection, maintain a sharp ice edge, and capture large deformations. In this talk we describe a new sea ice model being implemented within the MPAS-Seaice framework in the Energy Exascale Earth System Model (E3SM). The model is based on the Material-Point-Method (MPM), which couples Lagrangian particles with an efficient mesh-based solution of the equations of motion. To implement this method within MPAS, the MPM algorithm has been adapted to a spherical Voronoi mesh and modified to include a high-order mapping from particles to grid. We will describe the implementation of the MPAS-Seaice-MPM algorithm, show that components of the algorithm converge as expected, and demonstrate performance on standard sea ice test cases.

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MS18

Discrete-element and Material-point Method-based Solvers for Sustainable Technologies

We present the use of discrete element method (DEM) and material point method (MPM) in three relevant green technology applications that include biomass feedstock handling, lithium-ion battery manufacturing, and high-pressure reverse osmosis. Our open-source DEM and MPM solvers are developed using performance portable grid and particle management library, AMReX, thus enabling superior performance on NVIDIA and AMD GPUs with ¿ 100 million particles. Our DEM solver resolves the motion of individual particles in a granular system and includes a bonded sphere method for modeling non-spherical particles along with Hertzian and liquid bridge-based contact models. We simulate highly variable biomass feedstock flows in large-scale hoppers for biofuel production and electrode calendering in battery manufacturing using DEM. Our simulations predict flow blockage in large scale biomass hoppers and electrode microstructure variations, thus providing valuable information for biofuel and battery manufacturers, respectively. The second half of the talk will be on MPM and its application towards pore resolved simulations of reverse osmosis membranes under compressive loads. We present a validation study of our MPM simulations with membrane microscopy imaging thus providing useful insights on membrane stability under high pressure conditions. We also present a spectral stability analysis of using linear hat, quadratic and cubic spline basis in MPM indicating regions of numerical stability.

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MS19

Extended Vortex Methods for the Shallow Water Equations

Vortex methods are high-order accurate Lagrangian numerical methods for fluid dynamics problems. As a Lagrangian scheme, their solutions naturally adapt to the flow as it evolves and can therefore represent a dynamically evolving range of scales in multiscale simulations. Traditionally, vortex methods are applied to incompressible fluid dynamics models. In this work, we discuss their extension to the shallow water equations, which may have nonzero velocity divergence, to provide the opportunity to study wave-vortex interactions in a Lagrangian context. An adaptive refinement and remeshing capabilities are introduced and the scheme is demonstrated using examples related to global atmospheric and oceanic circulations.

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MS19

Adaptive Nonhydrostatic-Hydrostatic Hybridizable Discontinuous Galerkin Ocean Solver

Numerical modeling of ocean physics is essential for multiple applications. However, the large range of scales and interactions involved in ocean dynamics make numerical modeling challenging and expensive. While many regional ocean models resort to a hydrostatic (HS) approximation that reduces the computational burden, a challenge is to capture ocean phenomena involving complex dynamics over a wider range of scales and processes, from regional to small scales (thousands of kilometers to meters). Resolving local dynamics such as nonlinear internal waves, subduction, and overturning require expensive non-hydrostatic (NHS) ocean models. We start from a hybridizable discontinuous Galerkin (HDG) finite element NHS ocean solver well suited for multidynamics systems. We present a new adaptive algorithm to decompose a domain into NHS and HS dynamics subdomains and reduce the cost associated with the NHS pressure solution step. These subdomains are adapted based on numerical NHS estimators, such that NHS dynamics is used only where needed. We investigate different numerical approaches to ensure stability with respect to fast free-surface gravity waves and our adaptive model scheme. The costs and accuracy of the adaptive solver are analysed with simulations of strongly stratified, oscillatory flow over seamounts. Realistic NHS-HS simulations of Rayleigh-Taylor instability-driven subduction events are carried out by nesting MSEAS operational data-assimilative HS ocean modeling system.

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MS19

Constrained Interpolation with Radial Basis Functions on the Sphere

Radial basis functions (RBFs) are a powerful tool for constructing high-order accurate interpolants of scattered data in arbitrary dimension and on manifolds. We present a method of constructing RBF interpolants using constraints to ensure that properties such as, e.g., integral conservation or local bounds, are preserved. We defined a constrained quadratic minimization problem that combines possibly non-linear constraints with RBF interpolation. We demonstrate the method for applications of scattered data interpolation on the sphere.

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MS19

A Geometric Multigrid Method for Unstructured Discretizations on the Sphere

A new meshfree geometric multigrid (MGM) method is presented for solving linear systems that arise from discretizing elliptic PDEs on unstructured grids on the sphere. The method uses a Poisson disk sampling-type technique for coarsening the vertices of an unstructured grid or the nodes of a point cloud, and new meshfree restriction/interpolation operators based on polyharmonic splines for transferring information between the coarsened levels. These components are then combined with standard smoothing and operator coarsening methods in a V-cycle iteration. We demonstrate the applicability of the method as a solver and preconditioner for several problems discretized with finite volume, discontinuous Galerkin, and radial basis function finite differences. We also perform a side-by-side comparison to algebraic multigrid (AMG) methods for solving the same systems.

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MS20

The Implications of Covariate Climate Risks and Strategic Decision-Making for Cooperative Risk

Management

Several governments have tested formal index-based insurance to build climate resilience among smallholder farmers. Yet, adoption of such programs has generated concerns that insurance may crowd out long-established informal risk transfer arrangements. Understanding this phenomenon requires new analytic approaches that capture dynamics of human social behaviour when facing risky events. Here, we develop a modelling framework, based on evolutionary game theory and empirical data from Nepal and Ethiopia, to demonstrate that insurance may introduce a new social dilemma in farmer risk management strategies. We find that while socially optimal risk management is achieved when all farmers pursue a combination of formal and informal risk transfer, a community of self-interested agents is unable to maintain this coexistence under rising climate risks. We find that a combination of pro-social preferences - namely, moderate altruism and solidarity - helps farmers overcome these concerns and achieve the social optimum. Among other benefits, behavioural interventions that cue such preferences can reduce farmer expected losses by 26.5 percent and save approximately 5 percent of community agricultural income under climate risk levels likely to emerge in the coming decades.

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MS20

The Dynamics of Social Mobilization and Climate Activism

The formation of activist groups– including those inspired by the climate crisis– can spark social movements, coalitions, and revolutions. The creation of such groups can be influenced by social ties, network structure, ideology and culture, and the institutional environment. Yet, the relative importance of these factors, the mechanisms through which individuals develop or lose their commitment to a cause, and the channels through which likeminded individuals find each other and establish social connections are not thoroughly understood. In this work, we develop a theory that begins to explain two phenomena: 1) how a potential activist's conviction co-evolves with their social network, and 2) how "socially mobilizable activist networks" tend to arise or disappear based on the distribution of potential activists and overall environment. We illustrate this theory by modifying the adaptive voter model with a conviction variable, which represents the strength with which an individual holds on to their beliefs and the comfort of holding on to them in their network, encapsulating the co-evolutionary dynamics of networks and attitudes. We apply this framework to climate activism and the social aspects of it. As is expected from empirical evidence, we find that activists are systematically discouraged by exposure to disengaged individuals. However, some situations with increased interaction payoffs and strong homophily preferences favor the formation of activist networks.

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MS20

Collective Behavior, Epidemic Dynamics, and Ecosystem Stability

Ecosystems are defined by networks of interactions among organisms and with their environments. Species interactions, including competition and parasitism, play well-studied roles in ecosystem diversity and stability. However, intraspecific behavioral interactions may also scale up to affect ecosystem dynamics. An important instance of this is collective behavior, where individual responses to the states and fates of neighbors cause emergent group behaviors. Collective behavior is widely distributed across taxa and ecosystems, from biofilms to cities, and impacts the way many populations consume resources, experience risk, and reproduce. However collective behavior is rarely included in ecological models. I will present data-driven analyses which indicate the potential for collective behavior to play a key role in ecosystem stability and diversity, through emergent social-ecological feedback in consumer-resource systems. I will describe related work on seasonal infectious disease epidemics in cities, where collective human mobility patterns in urban centers may incubate critical chains of transmission outside of the peak season, creating systematic differences among cities in how their transmission patterns are shaped by climate. I will also discuss how the emergent properties of cities can be leveraged to create "immune systems which offer novel prospects for forecasting and control of seasonal epidemics and pandemic threats.

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MS20

Spatial Social Dilemmas Promote Diversity

Cooperative interactions between species are the foundation of all mutualistic associations. Compared to within species interactions, the problem of cooperation is exacerbated because acts of cooperation bestow benefits not just to another individual but to a member of another species. To achieve mutual benefits, inter-species coordination is required, which increases the threat of exploitation by defectors. Here we show that in the spatial prisoners dilemma surprisingly rich dynamics emerge with distinct dynamical domains separated by critical phase transitions. Most importantly, cooperative behaviour not only persists, but may result in intriguing, spontaneous symmetry breaking. Evolution may favour asymmetric states that effectively separate species into cooperative producers and defecting consumers. Surprisingly, the asymmetry becomes more pronounced under more benign conditions for cooperation.

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MS23

Infusing Multivariable Calculus with Social, Climate, and Sustainability Problems

Math literacy and skills are just one part of an education essential to providing young people with the background necessary to tackle the world's most challenging issues. While math classes typically involve classic problems from physics, engineering, and biology, it is more recent that we begin to see problems that involve social issues, climate issues, and other large and complex problems facing society. I will describe a project and lens through which we infused a multivariable calculus curriculum with application across climate science, ecology, oceanography, but also gerrymandering, the economics of carbon taxation, and misinformation. We will share how we simplified complex problems into simple frameworks that could pique student interest, and remain accessible to first year students. We also shared the stories of the climate scientists involved in developing the problems, to create role models for beginning students who have yet to choose a major or life path.

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MS23

The Myraid Ways in which Mathematics is Relevant to Climate

Over the past fifteen years, the Mathematics and Climate Research Network has developed ideas and techniques for addressing scientific problems in climate science. We have come to understand and appreciate the fundamental ways in which mathematics is highly relevant to climate through work on dynamical systems in reduced-order models to sea ice mechanics and desertification. On the data side, we have developed novel schemes for assimilating data into large models. I will discuss what we have learned interspersed with some of my own experiences in injecting mathematics into the curriculum at UNC-CH.

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MS23

Hot Planet, Hot Topic: Integrating Climate Science into Undergraduate Mathematics Courses

Climate change is the key global issue of our time. Our students have a strong interest in seeing how the mathematics they are learning in the classroom can be applied to understand this important problem. Topics from climate science can also be used to motivate further study in mathematics. In this talk I will present examples from some of my undergraduate mathematics courses, ranging from the Keeling curve in Calc 1 to energy balance models in an upper-level math modeling course. One of the appealing features of climate-themed examples is the broad range of mathematics employed (e.g., calculus, differential equations, dynamical systems, statistics). I will also discuss some topics and activities (including a field trip!) from an undergraduate seminar on math and climate that I was fortunate to teach a few years ago.

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MS23

Breakout Session: Brainstorm Climate Problems for Your Course of Interest

This breakout session offers minisymposium attendees an opportunity to generate applied math problems that bring specific climate phenomena into their chosen course in the undergraduate mathematics curriculum. Participants may work with supplied data and models, or go in their own direction. We will facilitate working groups through guided and interactive problem formulation. Each group will share their ideas at the end of the session.

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MS24

Existence and Uniqueness Analysis of An Atmosphere-Ocean Surface Exchange Algorithm with Applications to Global Climate Models

The atmosphere and ocean interact through the exchange of surface fluxes which, in global climate models, are derived from a system of nonlinear equations. These equations may be cast as a dynamical system whose equilibria are solutions of the nonlinear equations. From this perspective, we analyze the existence and uniqueness of these equilibria and demonstrate that under certain conditions, the surface fluxes described by the atmosphere-ocean surface flux equations are not well-defined in the sense that the equation set does not have a solution. We discuss various regularization techniques to ensure existence and uniqueness of the surface fluxes and numerically demonstrate their robustness. This work was performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under Contract DE-AC52-07NA27344. LLNL-ABS-857846-DRAFT.

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MS24

An Overview of Thermodynamically Consistent Coupling for Geophysical Fluid Dynamics

Earth system models consist of a number of components such as ocean, atmosphere, land and ice models; which must be coupled together to form a complete model. Additionally, within a component there might be a variety of subcomponents that are similarly coupled together. A key example is the coupling between the dynamical core (reversible adiabatic dynamics) and physics parameterizations in an atmospheric model. Ideally these couplings are thermodynamically consistent: they obey the laws of thermodynamics, including conservation of energy and generation of entropy. Unfortunately, most existing coupling strategies are not, and require the use of ad-hoc fixers to restore properties. In this talk we will discuss a strategy for thermodynamically consistent coupling based on the use of thermodynamic potentials and geometric mechanics formulations (such as variational, Hamiltonian and metriplectic).

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MS24

Complex Ice-Ocean Dynamical Modes in Simulated Polar Oceans Using Flux Couplers

In early climate models, sea ice equations were often integrated and coupled within ocean or atmospheric codes. As fully coupled models progressed, software used to exchange mass, energy, and state evolved to improve conservation across the simulated Earth system of atmosphere, land, ocean, and sea ice components. Sea ice was modularized as its own individual component, bringing advantages in the development of community codes with complex polar column physics and biogeochemistry, and in computationally efficient approximations of sea ice rheology. Most advanced Earth system models now treat sea ice as a separate entity from other components. But something was also lost in that evolution: Inherent in coupled sea ice ocean dynamics is the fact that sea ice mechanics is part of the oceans barotropic mode. Sea ice thermodynamics are often coupled at frequencies set by the timestep of radiation schemes in atmospheric models, at the expense of coupling sea ice dynamics at highly infrequent timesteps relative to an ocean models barotropic integration. This can create instabilities in the ice-ocean solution, allowing artificial chaotic modes in the simulated ice-ocean boundary layer. I describe different types of instabilities that can emerge and focus on one in particular associated with time-lagged inertial oscillations. Finally, I present a solution to this problem, affecting the architecture of future Earth system models.

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MS24

Overcoming Challenges in Evaluating Numerical Process Coupling in Global Atmosphere Simulation

The E3SM atmosphere model (EAM) consists of modular components that are each responsible for a different subset of processes. The atmospheric state is primarily advanced in time by combining the results of each component independently updating a state given to it. While the model equations and discretization approaches used to update the state are thoroughly documented for some components, other components lack sufficient detail to perform rigorous theoretical analysis of the coupling methods. Furthermore, some components provide numerous runtime options that modify the model equations, the discretization, or both. To overcome these issues, this work leverages an error analysis framework that distinguishes process splitting error from other discretization errors. By assuming exact time integration within each component, the framework successfully reasons why a change in the aerosol processes coupling method resulted in significantly improved EAM aerosol dust lifetime simulation. The combination of empirical evidence and mathematical underpinnings motivated the adoption of the change in E3SM. The framework also attributes error terms to decisions made in constructing fractional steps methods, allowing domain scientists to quickly develop new coupling approaches catered to their accuracy, stability, and/or computation needs. The error analysis framework and its applications thus far will be presented. Prepared by LLNL under Contract DE-AC52-07NA27344. LLNL-ABS-857956.

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MS25

Punctuated Evolution of SARS-CoV-2: Probing the Impacts of Biological and Behavioral Host Heterogeneity

Why has SARS-CoV-2 exhibited a pattern of punctuated evolution, characterized by rapid bursts of genetic diversity? Multiple possible explanations for the observed saltational evolution have been offered, ranging from purely biological factors (such as prolonged infection and accelerated evolution within immunocompromised hosts) to more behavioral aspects (e.g. "cryptic" evolution in isolated and largely un-sequenced populations). In this talk, I will employ a combination of large-scale genomic analysis, simple branching process models and more elaborate individual-based models to probe different explanations for the saltational evolutionary pattern of SARS-CoV-2. More generally, I will highlight how behavior, such as mobility patterns and public health responses (in the form of e.g. viral sequencing patterns), can affect the observed genetic diversity of a virus. To this end, I will (if time permits) discuss a few different mathematical notions of viral (genomic) diversity, including some recently introduced diversity measures.

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MS25

Opinion Dynamics: Mechanisms for Multiple Epidemic Waves

Polling on a variety of topics clearly shows that opinions can shift on a relatively fast timescale in the absence of any regulations. These intrinsic opinion dynamics can interact with disease dynamics to significantly change epidemic outcomes such as final size or number of waves. In particular, the number of epidemic waves, and the relative size of these waves, appears to have a complex relationship with the opinion dynamics. For example, the relative rate of opinion and disease dynamics, the type of influence different groups exert on each other, and the entities that have an influence all play a role. In this talk, we will explore, through a series of ODE models, the relationship between opinion dynamics and multi-wave behaviour.

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MS27

Exact Nonlinear State Estimation: Theory and Ensemble Approximations

The majority of data assimilation (DA) methods in the geosciences are based on Gaussian assumptions. While these assumptions facilitate efficient algorithms, they cause analysis biases and subsequent forecast degradations. Nonparametric, particle-based DA algorithms have superior accuracy, but their application to high-dimensional models still poses operational challenges. This talk will introduce a new nonlinear estimation theory which attempts to bridge the existing gap in DA methodology. Specifically, a Conjugate Transform Filter (CTF) will be derived and shown to generalize the celebrated Kalman filter to arbitrarily non-Gaussian distributions. The new filter has several desirable properties, such as its ability to preserve statistical relationships in the prior state and its convergence to highly accurate observations. An ensemble approximation of the new theory (ECTF) will be also presented and validated through idealized statistical experiments depicting common challenges in Earth system models. Results from these experiments indicate that the greatest benefits from ECTF occur when observation errors are small relative to the forecast uncertainty and when state variables exhibit strong nonlinear dependencies. A more complete summary of all findings can be found on https://arxiv.org/abs/2310.10976.

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MS27

Machine Learning of Model Errors in Dynamical Systems

The development of data-informed predictive models for dynamical systems is of widespread interest in many disciplines. We present a unifying framework for blending mechanistic and machine-learning approaches to identify dynamical systems from noisily and partially observed data. We compare pure data-driven learning with hybrid models which incorporate imperfect domain knowledge. Our formulation is agnostic to the chosen machine learning model, is presented in both continuous and discrete-time settings, and is compatible both with model errors that exhibit substantial memory and errors that are memoryless. We will present formulations and experiments to examine data-driven point-wise and distributional estimates of differential equations in these settings. We will conclude with recent work towards capturing uncertainties in the identified model errors.

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MS27

Consistent Spectral Approximation of Koopman Operators: Applications to Climate Dynamics

Koopman operators and transfer operators transform nonlinear dynamics in phase space to linear dynamics on vector spaces of functions, enabling the use of spectral techniques without modeling constraints such as linearity. The extraction of approximate Koopman eigenfunctions (and the associated eigenfrequencies) from an unknown system is nontrivial, particularly if the system has mixed or continuous spectrum. We discuss a spectrally-accurate approach to approximate the Koopman operator from data via a compactification of the resolvent of the Koopman generator. We then discuss implementations of this technique to a range of systems including Lorenz 63 and the tropical atmosphere, where we can identify nonlinear interactions between the annual cycle and the Quasi-Biennial Oscillation.

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MS28

Climate Models Without Calculus

Simple ideas combining conservation of energy with data can be the basis of conceptual climate models that can illustrate climate processes and can even make crude predictions. Some examples will be discussed.

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MS28

Breakout Session: Brainstorm Strategies for Implementing Climate in the Classroom

This breakout session offers minisymposium attendees an opportunity to reflect on and discuss how they might incorporate climate applications in their own mathematics classroom. We will discuss challenges that may arise–for example, fitting applications into a course schedule, draw-

ing on students scientific backgrounds, and addressing climate anxiety–and brainstorm strategies for working with these challenges.

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MS28

Climate-related Math Classroom Examples, Ideas, and Issues

My objectives for this talk are as follows: 1) provide tangible examples of introducing climate into the math classroom; 2) provide ideas on how to produce your own materials; and 3) discuss some potential issues regarding incorporating climate into the math classroom.

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MS28

Integrating Climate Change into Natural Science Seminar Courses

This talk underscores the critical need to infuse climate change content into a natural science seminar course with a focus on applied mathematics. As we confront the escalating challenges of climate change, this interdisciplinary approach aims to equip the next generation with the knowledge and skills essential for understanding, communicating, and addressing complex environmental issues. The course emphasizes the timely and imperative nature of this integration, providing a holistic educational experience that prepares students to contribute meaningfully to the global effort in combating climate change.

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MS29

Conservative Transport of Entropy and Moisture on the Charney-Phillips Grid

Local conservation of energy and mass (including that of moisture) are increasingly important properties for atmospheric models. A standard modelling choice to achieve this is to use conservative transport schemes, which couple the transport of entropy and moisture variables to the transport of the density field. If entropy and moisture variables actually satisfy the advective form of the transport equation, then it is also important that the transport of these variables should also be consistent, in the sense that a constant field will be preserved. It is also vital that the transport of moisture variables maintains the positivity of these fields. However, some models (including the Met Offices new LFRic-Atmosphere model) use a Charney-Phillips grid: staggering entropy and moisture variables from the density. This is motivated by the good gravity wave dispersion properties of this staggering, but it makes achieving conservation properties more challenging! This talk presents a framework for how these properties can be achieved simultaneously in the Met Offices LFRic-Atmosphere model, including in flows with large Courant numbers.

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MS29

Analyzing the Stability of Surface Coupling Methods in Earth System Models Using a Simple Boundary Layer Model

This study is motivated by instabilities arising from explicitly coupled surface momentum fluxes between the atmosphere and land in the Energy Exascale Earth System Model and Community Earth System Model. In these models, the near-surface wind is not only affected by surface fluxes and vertical diffusion, but also by resolved-scale dynamics and the Coriolis effect. The discretization of each model is complicated, since the vertical grid is not uniform, and different processes are sequentially split and do not always use the same time step or horizontal grid. We can analyze an atmospheric column using a simplified boundary layer model, linearized about the steady state wind profile. Taking a single atmospheric time step using a given coupling method can be viewed as solving an initial boundary problem for which there is an exact analytic solution. Using this solution, we can evaluate the coupled system using a given coupling method and coupling frequency, without assuming a specific spatial or temporal discretization for the atmosphere model. The method is considered stable for our purposes if the resulting system has a stable fixed point corresponding to the true steady state of our simple model. This allows us to write simple conditions for the maximum step size usable by certain surface coupling methods. Furthermore, details about the atmosphere model discretization (e.g. the vertical grid) can be used to refine estimates of the maximum stable coupling step size.

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MT1

Differentiable Programming in Julia with Enzyme

See tutorial details

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MT1

Differentiable Programming in Julia with Enzyme

See tutorial details

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See tutorial details

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MT2

Differentiable Earth System Models in Julia

See tutorial details

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MT2

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PP1

Analysis of Seasonal Land Surface Temperature (lst)

During few last years, climate change including global warming which is attributed to human activities and also its long-term adverse effects on the planets functions have been identified as the most challenging discussion topics which have arisen many concerns and efforts to find the possible solutions. Since the warmth arising from Earths landscapes affects the worlds weather and climate patterns, we decided to study the changes in the Land Surface Temperature (LST) patterns in different seasons through nonlinear methods. Here, we particularly want to estimate the non-integer dimension and fractal structure of the land surface temperature. For this study, the (LST) data has been obtained during the daytime by the Moderate Resolution Imaging Spectroradiometer (MODIS) on NASAs Terra satellite. Depending on what time of the year data has been collected, temperatures change in different ranges. Since equatorial regions remain warm, and Antarctica and Greenland remain cold, and also because altitude affects temperature, we selected Riley County in the U.S. state of Kansas, which does not belong to any of this type locations and we are interested to observe the seasonal changes in temperature in this county. The results of the present study show that the Land Surface Temperature (LST) belongs to the class of fractal process with non-integer dimension.

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PP1

Application of Discrete Wavelet Transform (dwt) in Studying Drought Severity in Contiguous Usa

Drought has been defined as a moisture deficit which adversely affects environmental, economical and social aspects of life on the planet. North America similar to many parts of the world has a little ability to predict the exact time drought will happen next. However, looking at historical climate data can help to better recognition and forecasting of drought. In this study, for the first time in climate studies, we explore the possibility that the Drought Monitor database belongs to class of fractal process which can be characterized using a single scaling exponent. The Drought Monitor map identifies areas of drought and labels them by intensity: D0 abnormally dry, D1 moderate drought, D2 severe drought, D3 extreme drought, and D4 exceptional drought. The vibration analysis using power spectral densities (PSD) method has been carried out to discover whether some type of power-law scaling exists for various statistical moments at different scales of this database. We perform multi-fractal analysis to estimate the multi-fractal spectrum of each group. We apply Higuchi algorithm to find the fractal complexity of each group and then compare them for different time intervals. Our findings reveal that we have a narrow range of exponents for D0-D3 and a wide range of exponent for D4. Therefore, D4 belongs to class of multi-fractal process for which a large number of scaling exponents are required to characterize the scaling structure, however, D0-D3 are mono-fractal.

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PP1

Physics Informed Neural Network for Solving the Shallow Water Equations on Grids of Arbitrary Geometry

Many physical phenomena exhibit wave behavior, including fluids, acoustics, and electromagnetics. When simulating wave behavior, the most common difficulty is wave reflections that lead to numerical oscillations, especially on grids with complex geometries. In this research, we investigated if a neural network can accurately model wave behavior when extensive reflections are involved. If proven true, such a neural network would be useful, as neural networks are amongst the fastest techniques for solving mathematical models. We trained a neural network to simulate the shallow water equations on a grid where the right boundary is fitted to a 5pt, 8pt, or 11pt spline. The simulation scenario called for a wave to be given an initial velocity in the right direction, causing it to impinge upon and then re-

flect off of the right boundary. To add more complexity, we allowed the initial wave location to be a random point on the grid. Our training methodology involved both supervised learning with sample data points and unsupervised learning with the residuals of the shallow water equations acting as a loss function. Over five experiments, the neural network learned to model wave reflection with a mean squared error of 9.7797E-06 for the simplest scenario and 1.6595E-05 for the most complex scenario. We have proven that a neural network is capable of learning wave behavior with reflections, with applications in computational acoustics to the modeling detonation wave reflection.

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PP1

Most Probable Transition Path to An Ice-Free State in a Model for Arctic Energy Balance

Given the impending disappearance of Arctic sea ice and its implications for the global climate system, understanding how the Arctic transitions to an ice-free state may be useful for predicting and mitigating potential changes to the Arctic system. We consider a stochastic Arctic energy balance model with periodic forcing and a piecewise-smooth drift, where the periodic state may transition from a stable perennially ice-covered state to a stable perennially ice-free state as a rare event. We calculate the most probable transition path from the ice-covered to the ice-free state as the minimizer of the Friedlin-Wentzell rate functional, with a correction term necessary for the minimizer to cross the switches in the system. We compare this path with equivalent ones generated using the gradient flow of the smoothed system and Monte Carlo simulations. This provides an initial case study of the theoretical most probable transition path in a physical piecewise-smooth model.

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PP1

Neural Operator Based Flooding Simulation of Arbitrarily Built Environments

Flooding has become a worrisome consequence of climate change. Coastal flooding is expected to increase due to rising sea levels, affecting communities and seaside habitats. Flash flooding is also a concern due to extreme precipitation events. In early 2023, atmospheric river storms dropped 32 trillion gallons of water on California. In one county, this rainfall caused a levee to burst, leaving a town underwater. Due to these detrimental consequences, it is crucial to have fast and accurate flood simulation software. Unfortunately, such software are usually quite slow. For example, SWASH, a popular program for simulating coastal flooding, requires 40 hours to run one realistic scenario. In this research, we have created a set of Fourier Neural Operators (FNOs) that can predict flooding on a 1024 x 1024 simulation grid with an inference time of only 7 seconds. We achieved such an FNO after training it on hundreds of simulation scenarios, each utilizing a different arbitrarily drawn grid. Because FNOs learn in infinite dimensions, they can simulate flooding on geometries completely outside of their original training dataset. In effect, a user can draw a town with arbitrary buildings, streets, cars, and other geometries, and the FNOs should still be able to make an accurate prediction. Indeed, we validated our FNOs at three different time steps and found that the FNO was able to correctly predict the wet and dry state of any grid cell with an average accuracy of 99.47%.

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PP1

Mathematical and Numerical Modeling of Ocean Spray Effect on Tropical Cyclone Dynamics

Accurate forecasting of tropical cyclones (TCs) is important due to their devastating global impact. Increasing evidence shows that sea spray has a significant effect on the air-sea momentum and heat exchange within TCs emphasizing the need for its accurate modeling for improving hurricane forecasting. In this presentation, we introduce an Eulerian model of TCs spray-laden marine atmospheric boundary layer (MABL). Mathematically, the model is formulated as a boundary value problem for a system of conservation equations for mass, momentum, and thermal and turbulent kinetic energies for air and polydisperse spray. The model employs a multifluid formulation that treats air and spray droplets of different sizes as separate interacting and interpenetrating turbulent continua. Numerical and mathematical analysis of the model demonstrate that spray strongly modifies the vertical heat and momentum fluxes in the MABL affecting TC dynamics even at relatively low concentrations. Furthermore, the effect of sea spray is found to be strongly dependent on the distribution of droplet sizes. The authors acknowledge support by grants from the National Science Foundation, U.S.A. under Award No. 2302221

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PP1

Inference of Non-Newtonian Rheology Parameters in Plate-Boundary-Resolving Models of Earth's Mantle Convection

Estimating parameters in mantle flow and plate tectonics from surface observations results in an optimization problem governed by a highly nonlinear, heterogeneous, and incompressible Stokes equation. Solving this governing equation is a major challenge by itself (Our computational methods for this forward problem include adaptive mesh refinement and inexact Newton-Krylov with BFBT and multigrid preconditioning for saddle point linear systems.) Estimation of rheological parameters, for which we start with a Bayesian formulation, adds substantially to the solver challenges. To efficiently estimate parameters in the

constitutive relation, we use adjoint Stokes equations and a Newton method for the resulting PDE-constrained optimization problem. The Hessian during the Newton steps is approximated with BFGS, while a Gauss-Newton Hessian at the numerical minimum is used for quantifying uncertainties in the estimated parameters. We demonstrate successful inference on large cross-sectional models and explore how the inference can be made computationally feasible at a global scale encompassing the entire Earth.

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PP1

Advanced Bayesian Hierarchical Modeling for Robust Rainfall Estimation in Arid Saudi Regions Using Rain Gauge Data

Bayesian statistical methods have become essential in the atmospheric sciences for climate modeling, weather prediction, and evaluating weather modification techniques like cloud seeding. Accurate rainfall measurement is crucial for managing water resources in arid areas such as Saudi Arabia, where such techniques are commonly used. The Kingdom has conducted several cloud seeding projects, collecting data to analyze the efficacy of these operations. This study focuses on using rain gauge data to develop a Bayesian hierarchical model to precisely estimate seasonal and annual rainfall in the central and southwest Saudi Arabia. The model is designed to improve rainfall estimates by incorporating probabilistic analysis through Bayesian MCMC simulations. The expected outcomes include reliable rainfall estimates with standard errors, enhancing water management and contributing significantly to atmospheric sciences and weather modification practices. These estimates will also aid in assessing the impact of cloud seeding on rainfall enhancement.

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PP1

Seismic Spectral Recomposition

Spectral recomposition can be used to extract significant components from the seismic spectrum. Analysis of seismic attributes in the frequency domain for reservoir characterization, seismic attributes associated with frequencies are important to characterize stratigraphic sequences and hydrocarbon reservoirs multicomponent interpretation. The spectral recomposition is a technique to extract wave parameters as frequencies and amplitudes of the components of a seismic spectrum. Phase-shift correction of seismic reflections by means of spectral recomposition- post-critical reflection data provides useful information that allows more reliable geological characterization of the subsurface. However, the strong distortion caused by the phase shift in post-critical wavelets makes the use of post-critical reflections rather challenging. For this reason, estimating the phase shift of each wavelet of a reflection event in a data-driven manner is desirable. frequency spectrum of a wavelet can be correctly estimated, it is possible to estimate the instantaneous phase shift by estimation based on spectral recomposition of seismic data. spectral recomposition helps us visualize frequency-dependent geologic features on cross sections and time slices by extracting significant frequency components. Spectral recomposition can also indicate how frequency contents attenuate with time. Spectral recomposition splits a seismic spectrum into Ricker components.

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PP1

Drivers of Global Irrigation Expansion: The Role of Discrete Global Grid Choice

Global statistical irrigation modeling relies on geospatial data and traditionally adopts a discrete global grid based on longitude-latitude reference. However, this introduces area distortion, which may lead to biased results. We propose using the ISEA3H geodesic grid based on hexagonal cells, enabling distortion-free representation of spherical data. To understand the impact of grid choice, we employ a non-parametric statistical framework, utilizing random forest methods, to identify main drivers of historical global irrigation expansion amongst others, also using outputs from the global dynamic vegetation model LPJmL. Irrigation is crucial for food security amidst growing population, changing consumption patterns, and climate change. It significantly boosts crop yields but also alters the natural water cycle and global water resources. Understanding past irrigation expansion and its drivers is vital for global change research, resource assessment, and predicting future trends. We compare the predictive accuracy, the simulated irrigation patterns and identification of irrigation drivers between the two grid choices. Results show that using the ISEA3H grid increases the predictive accuracy by 29% compared to the longitude-latitude grid. The model identifies population density, potential productivity increase, evaporation, precipitation, and water discharge as key drivers of historical global irrigation expansion. GDP per capita also shows minimal influence.

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PP1

SIAM Convening on Climate Science, Sustainability, and Clean Energy

The SIAM Convening on Climate Science, Sustainability, and Clean Energy was a 3-day workshop held in October 2022. Participants in the workshop included domain scientists from a variety of disciplines, institutions, and companies who were charged with the identification and articulation of emerging research needs related to the workshop focus. They identified to brainstorm long-term solutions and describe the challenges, opportunities, and requirements for these plans over the next decade. This poster summarizes the outcomes of the discussions and provides information on the whitepapers that were used to generate funding recommendations to governmental agencies. This scoping workshop was funded by the U. S. National Science Foundations Critical Aspects of Sustainability program via grant DMS 2227218.

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PP1

Dynamics in a Model for Interacting Tipping Elements in the Climate System

"Tipping elements" describe large-scale components of the Earth system that may pass critical thresholds or "tipping points," after which small perturbations can cause significant long-term changes in the state of the tipping elements. Due to interactions between tipping elements, the tipping of one element can induce tipping in others, causing bifurcation cascades that can lead to irreversible changes in the climate system. To explore this phenomenon, we consider a model of coupled tipping elements with different associated time scales from Wunderling et al. (2021). We use numerical and analytical methods to study the conditions for a bifurcation cascade across various projected climate scenarios.

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