

2023 Shanks Workshop on Advances in Mathematical and Theoretical Biology

Plenary Abstracts:

Modeling the Growth, Invasion and Competition of Aedes Mosquitoes

Shigui Ruan (University of Miami)

The Aedes mosquitoes, in particular *Aedes aegypti* and *Aedes albopictus*, are the primary vectors that transmit several arboviral diseases, including chikungunya fever, dengue fever, yellow fever, and Zika. Recently, the world has been experiencing a series of major outbreaks of these vector-borne diseases (for example, the 2016 Zika outbreak in Florida, etc.). In order to study the transmission dynamics of these vector-borne diseases, it is very important and necessary to understand the population dynamics, current distributions and movements of Aedes mosquitoes for successful surveillance and control programs. In this talk, we will introduce some of our recent studies on modeling the population dynamics of Aedes mosquitoes, the invasion of *Aedes albopictus* mosquitoes, and the competition between *Aedes aegypti* and *Aedes Albopictus* mosquitoes in Florida. In particular, we propose a competition model with road-field diffusion in which the invasive population not only disperses in the interior of the spatial domain but also moves faster on the boundary of the domain. Both strong-weak and weak-weak competitions are discussed. It is shown that the asymptotic spreading speed of the wave fronts is increasing only if the road diffusion rate is greater than the field diffusion rate. Numerical simulations are presented to illustrate our analytical results and to explain the current estimated distributions of these two mosquito species in Florida.

Neurodegenerative diseases: nice collaboration stories between biologists and mathematician leading to a better understanding of prion and Alzheimer's diseases

Laurent Pujon-Menjouet (Université Claude Bernard Lyon 1)

Through the past two decades, a great collaboration started between biologist and mathematicians to understand the complex dynamics of neurodegenerative diseases. During this presentation, we will dive into a short overview of the prion and Alzheimer's disease models and show how mathematics have been helping to bring light to some unexplained observations. We will deal with size structured differential equations with polymerization and fragmentation terms (of Smoluchowski type), some hybrid models (continuous in time, discrete in size, of Becker-

Döring type). Finally we will add some diffusion terms to describe the spread of the disease in the brain, and the effect of stress and inflammatory processes.

Behaviour change and control and mitigation strategies for epidemic outbreaks

Jorge Velasco-Hernandez (Instituto de Matemáticas)

We describe some of the models we have published on the control and mitigation of infectious diseases. Public health policies implemented to control or mitigate a disease require both knowledge of the state of the epidemic (incidence, prevalence, hospitalizations, deaths) and its impact on the local, regional and national economy. This implies that decisions must be made taking into account these factors which, by nature, have a significant degree of uncertainty. The models we will review exemplify how this problem is addressed from different perspectives and assumptions.

Diffusive Models for the Spread of Infectious Disease

William Fitzgibbon (University of Houston)

Description of epidemics dates back to antiquity. The first person to attempt to quantify these events was by John Gaunt in the late 17th Century. The mathematical modeling of epidemics began the work of Bernoulli about 100 years later. The Compartmental SIR models (and their variants) of the outbreak and spread of infectious disease that are commonly in use today emerged from the work Harris, Ross, Kermack and McKendrick in the early twentieth century. Disease diffusion occurs when disease spreads across a geographic region. The idea of using a diffusion mechanism to describe the spatial spread of a disease is relatively recent. Bailey introduced a 2x2 cross diffusion model in the 1950's. Our discussion will begin with the more analytically tractable model,

$$\begin{aligned}(\partial S)/\partial t &= d(\partial^2 S)/\partial x^2 - \sigma SI \\ \partial I/\partial t &= d(\partial^2 I)/\partial x^2 + \sigma SI - \lambda I.\end{aligned}$$

Independently G. Webb and V. Capasso established the classical well-posedness of this system and described the long-term dynamics of the system. In addition to the fact that diffusive SIR models have subsequently been the subject of numerous studies they also serve as an important prototype of quasi-positive, mass - controlled reaction diffusion system. To this day distributed parameter systems incorporating the key features of SIR kinetics are of active interest. Our purpose shall be tracing the development of the theory and application of epidemiological models with a high degree of spatial heterogeneity that evolved from the work of Capasso and Webb.

Multi-Scale Models of Infectious Disease Dynamics and Validating with Data

Hayriye Gulbudak (University of Louisiana at Lafayette)

The bidirectional feedback induced through population and individual-level infectious disease and host immune dynamics requires development of innovative multi-scale models. In this talk, I will introduce structured nonlinear partial differential equation models linking immunology and epidemiology, along with novel stability analysis and computational tools for simulating ODE-PDE hybrid systems to understand the nonlinear dynamics and apply them to biological data. Applying the modeling framework to dengue virus, we first demonstrate how intermediate levels of antibodies enhance infection severity within a host, and scale up to population wide antibody level distributions evolving through multiple infections by distinct strains and waning immunity. Then, to test the theoretical results, we fit primary and secondary dengue infection data to provide evidence of antibody dependent enhancement. These results have critical implications for optimal vaccination policy, and the modeling framework is currently being applied to examine the emergence of COVID-19 variants.

Computational methods for inferring tumor evolution and heterogeneity

Jasmine Foo (University of Minnesota-Twin Cities)

Tumors are typically comprised of heterogeneous cell populations exhibiting diverse phenotypes. This heterogeneity, which is correlated with tumor aggressiveness and treatment-failure, confounds current drug screening efforts to identify effective candidate therapies for individual tumors. In the first part of the talk I will present a modeling-driven statistical framework that enables the deconvolution of tumor samples into individual subcomponents exhibiting differential drug-response, using standard bulk drug-screen measurements. In the second part of the talk I will present some efforts towards obtaining insights about tumor evolution from standard genomic data. In particular, we analyze the site frequency spectrum (SFS), a population summary statistic of genomic data, for exponentially growing tumor populations, and we demonstrate how these results can in principle be used to gain insights into tumor evolutionary parameters.

Session 1 Abstracts:

Modeling COVID-19 dynamics: From within-host to between-host

Libin Rong (University of Florida)

The infection by SARS-CoV-2 has caused the COVID-19 pandemic. Although a large number of modeling studies have shed light on the transmission dynamics of COVID-19 at the population level, the within-host viral dynamics of SARS-CoV-2 infection have been inadequately investigated. In this talk, I will present models based on different assumptions to study the within-host virus dynamics of SARS-CoV-2 infection and compare them with the viral load data in infected patients and non-human primates collected from different countries. The infection in some individuals undergoes several distinct stages including a plateau phase in which the viral load does not decline or even rebounds after a minor decline from the peak. This may explain the hyperinflammatory responses and high transmissibility of COVID-19. The adaptive immune response may play a critical role in the recovery from infection, whereas a late and slow initiation of seroconversion may lead to viral persistence. I will also introduce a multi-scale model that links the within-host and between-host dynamics. The work may improve our understanding of the epidemiological triad of pathogen, host, and environment for COVID-19.

The Heterogeneous Severity of COVID-19 in African Countries: A Modeling Approach

Xueying (Snow) Wang (Washington State University)

The COVID-19 pandemic has had a considerable impact on global health and economics. The impact in African countries has not been investigated thoroughly via fitting epidemic models to the reported COVID-19 deaths. We downloaded the data for the 12 most-affected countries with the highest cumulative COVID-19 deaths to estimate the time-varying basic reproductive number $R_0(t)$ and infection attack rate. We develop a simple epidemic model and fitted it to reported COVID-19 deaths in 12 African countries using iterated filtering and allowing a flexible transmission rate. We observe high heterogeneity in the case-fatality rate across the countries, which may be due to different reporting or testing efforts. South Africa, Tunisia, and Libya were most affected, exhibiting a relatively higher $R_0(t)$ and infection attack rate. Thus, to effectively control the spread of COVID-19 epidemics in Africa, there is a need to consider other mitigation strategies (such as improvements in socioeconomic well-being, healthcare systems, the water supply, and awareness campaigns).

The impact of Travel Frequency on Infectious Disease Dynamics for Multi-Patch Models

Seoyun Choe (University of Central Florida)

After the beginning of the COVID-19 pandemic around the world, travel restriction policies internationally and domestically have been important issues. In mathematical epidemiology, there are several modelings about the impact of varying residence times or travel restrictions, such as lockdowns on the infectious disease dynamics in a heterogeneous environment. We set two kinds of multi-patch models: Lagrangian and Euler models. For the Euler model, we explored how the travel frequency (restriction) affects the pattern of disease dynamics for a multi-patch model. For the Lagrangian model, we proved that the basic reproduction number is monotonically decreasing with respect to the travel restriction factor. Also, we derived the final size relation by using the weighted geometric mean. Numerical simulations illustrate that the final size of the outbreak depends on the travel restriction measure as well as the transmissibility. Moreover, we investigated patch-specific optimal treatment strategies.

Session 2 Abstracts:

Study of prion dissemination in brain tissue : A synthetic approach

Basile Fornara (INRAe)

Prion diseases, or Transmissible Spongiform Encephalopathies (TSE), are neurodegenerative disorders caused by the accumulation of misfolded conformers (PrP^{Sc}) of the host-encoded cellular prion protein (PrP^C). Throughout the infection, the PrP^{Sc} seeds disseminate in the central nervous system and convert PrP^C by changing their conformation leading to the formation of extracellular pathogenic insoluble aggregates.

Our current understanding of prion dissemination mechanisms fails to explain the phenotypical differences from one prion strain to another such as incubation times or lesion profiles. To tackle this issue, we developed an *in silico* model of prion dissemination based on stochastic reaction-diffusion processes solved with the Gillespie Algorithm. Using this novel approach, we undergo a parametric study of the model to explain the tendency of strains to target specific brain areas.

We brought to light new dissemination pathways as well as key parameters influencing the selection of assemblies and affected tissues. This will hopefully lead to a better understanding of the mechanisms behind prion dissemination and in turn shine a new light on neurodegenerative disorders which involve protein misfolding.

Machine Learning of Collective Behaviors from Observation

Ming Zhong (Illinois Institute of Technology)

Collective Behaviors (aka Self Organization) occurs naturally in bird flocking, cell aggregation, ant raiding, locust swarm, etc. It is challenging and intriguing to understand self organization from the mathematical point of view. We offer a statistical/machine learning approach to explain collective behaviors from observation data; moreover, our learning approach can aid in validating and improving the modeling of collective behaviors.

We develop a learning framework to derive physically meaningful and physical dynamical systems to explain collective behaviors from observation [1]. We then investigate the steady state properties of our learned estimators [2]. We also extend the learning approach for dynamical models constrained on Riemannian manifolds [3]. We further improve our learning capability to infer interaction variables as well as interaction kernels [4]. We even study the effectiveness of our learning method on the NASA Jet Propulsion Laboratory's modern Ephemerides [5]. Upon careful inspection of our model, we discover that it even captures portion of the general relativity effects. A complete learning theory on second-order systems is presented [6], as well as two new models on emergence of social hierarchy [7] and concurrent emergence of flocking and synchronization [8].

[1]: Lu, Zhong, Tang, Maggioni, Nonparametric inference of interaction laws in systems of agents from trajectory data, PNAS, 2019.

[2]: Zhong, Miller, Maggioni, Data-driven discovery of emergent behaviors in collective dynamics, Physica D, 2020.

[3]: Maggioni, Miller, Qiu, Zhong, Learning Interaction Kernels for Agent Systems on Riemannian Manifolds, PMLR, 2021.

[4]: Feng, Maggioni, Martin, Zhong, Learning Interaction Variables and Kernels from Observations of Agent-Based Systems, IFAC-PapersOnLine, 2022.

[5]: Zhong, Miller, Maggioni, Machine Learning for Discovering Effective Interaction Kernels between Celestial Bodies from Ephemerides, under revision, 2023.

[6]: Miller, Tang, Zhong, Maggioni, Learning Theory for Inferring Interaction Kernels in Second-Order Interacting Agent Systems, under revision, 2023.

[7]: Greene, Tadmor, Zhong, The Emergence of Social Hierarchy in Collective Motion of Living Matters, submitted, 2023.

[8]: Gerew, Zhong, Swarmalators that Flock and Sync, in preparation, 2023.

Utilizing Stochastic Fluctuations to Disambiguate Density-Dependent Mechanisms

Linh Huynh (University of Utah)

Density dependence is important in the ecology and evolution of microbial and cancer cells. Typically, we can only measure net growth rates, but the underlying density-dependent mechanisms that give rise to the observed dynamics can manifest in birth processes, death processes, or both. Therefore, we utilize the mean and variance of cell number fluctuations to separately identify birth and death rates from time series that follow stochastic birth-death processes with logistic growth. Our nonparametric method provides a novel perspective on stochastic parameter identifiability, which we validate by analyzing the accuracy in terms of the discretization bin size. We apply our method to the scenario where a homogeneous cell population goes through three stages: (1) grows naturally to its carrying capacity, (2) is treated with a drug that reduces its carrying capacity, and (3) overcomes the drug effect to restore its original carrying capacity. In each stage, we disambiguate whether the dynamics occur through the birth process, death process, or some combination of the two, which contributes to understanding drug resistance mechanisms.

Session 3 Abstracts:

An Undergraduate Text in Mathematical Epidemiology

Meredith Greer (Bates College)

This will be the first presentation of an in-progress text for a semester-long undergraduate course in mathematical epidemiology. Topics relate primarily to compartmental models using differential equations. The course assumes just one semester of calculus as a prerequisite, with an alternate pathway through the topics if linear algebra is also a prerequisite. Students taking the course work in groups, communicate verbally and in writing, perform data analysis, apply mathematics meaningfully to real-world issues, contemplate career options, and analyze differential equations, mainly (but not only) using qualitative methods. Course goals track closely with the Mathematical Association of America's most recent curriculum guide for undergraduate mathematics majors. The course could serve as the culmination of a math major, but even better, it can be taken early, to spur student interest in differential equations, linear algebra, numerical analysis, mathematical modeling, and more. The text includes uses of compartmental models that extend far beyond epidemics, so that students see a wider range of uses for this style of modeling.

The influence of Glenn Webb on mathematical finance: Chaos for the Nobel Prize winning Black-Merton-Scholes semigroup on stock options, and a novel Feynman-Kac formula for zero coupon bonds

Jerome Goldstein (University of Memphis)

Glenn Webb and coauthors showed that seemingly simple linear PDE are sometimes governed by (Co) semigroups that are chaotic. This inspired our (H. Emamirad, G. Goldstein, J. Goldstein) chaos result for the BMS equation which led to their 1997 Nobel Prize in Economics. The ideas involved in the proof are quite complicated and involve lots of new tools, including continuous curves of eigenvalues in the upper half complex plane and special weighted norms. The BMS equation has the form $du/dt=P(A)u$, where P is a quadratic polynomial in $A=x d/dx$. The linear Cox-Ingersoll-Ross semigroup for bonds involves noncommuting operators. Again, special weighted spaces are needed, and a novel Feynman-Kac formula and its limit, not involving integrals, gives the solution in a very complicated way. This result is due to G. Goldstein, J. Goldstein, the late R. M. Mininni, and S. Romanelli.

Reminiscing about a Project that Started at Vanderbilt University

Joanna Wares (University of Richmond)

From 2008 – 2011, I was a postdoc at Vanderbilt and Glenn Webb was my mentor. During this time, I taught Vanderbilt's Mathematical Biology course. In that course, I had students create their own mathematical models. One student, Joseph Crivelli, extended Dingli's oncolytic virus model for his project. Joe and I continued working on this project for many years after this course, bringing in new collaborators, and spawning a small field in the cancer modeling community. In this talk, I will reminisce about the origin of this project and describe what happened after I left Vanderbilt.

Session 4 Abstracts:

Analysis of an SIR Model Subject to Intermittent Treatment

Jeffrey Morgan (University of Houston)

We study the long-term behavior of a partially dissipative SIR model with constant susceptible growth that can result in unbounded growth of infectives in the absence of treatment. We show that intermittent long-term treatment can lead to bounds on the infectives, and that in the absence of constant growth for susceptibles, intermittent treatment causes the susceptibles to converge to a positive function, and the infectives to converge to 0.

Analysis of the basic reproduction number of reaction-diffusion epidemic models

Yixiang Wu (Middle Tennessee State University)

The basic reproduction number R_0 serves as a threshold parameter of many epidemic models for disease extinction or spread. We investigate R_0 for spatial reaction-diffusion partial differential equations epidemic models. We define R_0 as the spectral radius of a product of a local basic reproduction number R , and strongly positive compact linear operators with spectral radii one. This definition of R , viewed as a multiplication operator, is motivated by the definition of basic reproduction numbers for ordinary differential equations epidemic models. We investigate the relation of R_0 and R . This is a joint work with Pierre Magal and Glenn Webb.

An Immuno-Epidemiological Model of the Foot-and-Mouth Disease in South African Buffalo

Summer Atkins (Louisiana State University)

Foot-and-mouth disease (FMD) is a highly contagious disease of cloven-hoofed animals. Although not deadly, FMD can cause major delays in meat and dairy production. An interesting component regarding the study of FMD is that the foot-and-mouth disease virus (FMDV) can persist in some host populations (reservoirs) for long periods of time, causing the pathogens to reemerge in susceptible populations. In this talk we present a novel immuno-epidemiological model of FMDV in South-African buffalo. Buffalo can undergo two phases of the disease, the acute stage and the carrier stage. In our model we split the infectious population into these two phases so that we can dynamically capture the immunological characteristics of both stages of the disease and to better understand the carrier's role in transmission. Mathematical analysis is performed on the model. Additionally, we use sensitivity analysis to observe the impact that immunological parameters have on the basic reproduction number.

Session 5 Abstracts:

Kinetic Monte Carlo Simulations of Multicellular Aggregate Self-Assembly in Biofabrication

Yi Sun (University of South Carolina)

We present a three-dimensional lattice model to study self-assembly and fusion of multicellular aggregate systems by using kinetic Monte Carlo (KMC) simulations. This model is developed to describe and predict the time evolution of postprinting morphological structure formation during

tissue or organ maturation in a novel biofabrication process or technology known as bioprinting. Here we implement the model with an efficient KMC algorithm to simulate the making of a set of tissues/organs in several designer's geometries like a ring, a sheet and a tube, which can involve a large number of cells. We also study the process of cell sorting/migration within the cellular aggregates formed by multiple types of cells with different adhesivities.

On modeling malaria dynamics with seasonal factor

Chidozie Williams Chukwu (Wake Forest University)

In this talk, we discuss a malaria model with a seasonal factor and apply optimal control variables in insecticide, prevention and treatment. The malaria model without seasonal factor has two equilibria; the disease-free equilibrium and the endemic equilibrium. The existence and local stability of the equilibria depend on the basic reproduction number. We further analyze the parameters' sensitivity to determine which are the most influential in the model. Then, the malaria model, by considering a seasonal factor, is presented. The simulation results indicate that the seasonal factor tends to be more influential on the dynamics of the infected mosquitoes and the human population in the region with a hot climate. Furthermore, the existence of the optimal control variable in the malaria model with seasonal factors is determined through the Pontryagin Maximum Principle. Numerical simulation of the model with the optimal control shows that providing controls in the form of insecticide, prevention, and treatment simultaneously are effective in reducing the number of the exposed and infectious in the human population and also the infectious mosquito population.

Role of IL-23 neutralization in psoriasis – insights from a mechanistic PK/PD model and meta-analysis of clinical data

Georgi Kapitanov (Applied BioMath)

Blocking of IL-23 has shown a profound effect on patient outcomes in psoriasis. The current IL-23 binding monoclonal antibodies show differences in dosing regimens, pharmacokinetics, affinity for the target, and efficacy outcomes in the clinic. The goal of the current work is to use a mechanistic pharmacokinetics/pharmacodynamics mathematical model to estimate projected free IL-23 neutralization for the different therapeutic molecules and connect it to clinical efficacy outcomes. The meta-analysis indicates a sigmoid-like relationship and suggests that the best current anti-IL23 antibodies are close to saturating the efficacy that can be achieved by this pathway in psoriasis.

Session 6 Abstracts:

An approach to model the bird migration and the transmission dynamics of bird flu among migration birds

Rongsong Liu (University of Wyoming)

An approach to modelling bird migration is proposed, in which there is a region where birds do not move but spend time breeding. Birds leave this breeding region and enter a migration flyway which is effectively a one-way corridor starting and ending at the breeding location. Mathematically, the flyway is a curve parametrised by arc-length. Flight speed depends on position along the flyway, to take account of factors such as wind and the pausing of birds at various locations for wintering or stopovers. Per-capita mortality along the flyway is both position and age-dependent, allowing for increased risks at stopover locations due to predation, and increased risks to immature birds. We also model indirect transmission, via contact with viruses, of avian influenza in migratory and nonmigratory birds, taking into account age structure. Sufficient conditions are obtained for the local stability of the disease-free equilibrium (for a species without migration) and for the disease-free periodic solution (for a migratory species).

Eco-evolutionary dynamics of virus and immune response network

Cameron Browne (University of Louisiana at Lafayette)

Population dynamics and evolutionary genetics underlie the structure of ecosystems. We analyze a resource-prey-predator differential equation network model to characterize the emergence of distinct stable equilibria and persistence of different diverse collections of virus and immune populations. Using binary sequences to code viral strain resistance to immune responses, we prove that bifurcations are determined and simplified by a certain evolutionary genetics measure of nonlinearity in the map from viral sequences to fitness landscape. The results generalize to decipher stability, structure and invasion of ecological networks based on an algebra of binary sequences encoding resistance/fitness trade-offs.

MATHEMATICAL MODELING OF THYROID DISORDERS AND DIABETES

Boya Yang (University of Florida)

Endocrine disorders are complex diseases threatening global health with high incidences. Diabetes is the leading endocrine disease affecting socio-economic development and has multiple pathogenic pathways. Hyperglycemia, or elevated blood glucose, is an aftereffect of uncontrolled diabetes, damaging many of the human body's functions over time. Thyroid disease

is the second most frequent endocrine disorder in medical practice following diabetes. Endocrine axes are the intricate physiological regulatory systems connecting with each other and other body systems (e.g., the digestive system). Hormonal diseases have an important impact on glucose control and can exacerbate the progression of diabetes. Medications. Mathematical modeling and computer simulations provide a quantitative approach to investigating disease progression and treatment, which can promote precise medicine and improve prognosis. Few mathematical models have been proposed to investigate the long-course evolution of type 2 diabetes owing to the inherent difficulty in capturing the complexity of diabetes. A limited number of mathematical models have been proposed to study the abnormality in the thyroid gland, hindering the optimal treatment of thyroid disorders. Moreover, a model quantitatively investigating the comorbidity of thyroid diseases and diabetes is desired to facilitate the treatment where a robust control of multiple hormone secretions is needed.

In this talk, I will present the modeling frameworks we have established for the study of the progression of type 2 diabetes, thyroid disorders, and hyperthyroidism-induced diabetes. The feasibility for healthcare professionals to apply these models in predicting the variations of relevant physiological indexes and choosing optimal dosage regimens for treating thyroid disorders and hyperthyroid-induced diabetes will be demonstrated. This study may encourage precise interventions to prevent the corresponding diseases and facilitate individualized patient treatment.

Session 7 Abstracts:

Instantaneous Blowup and Nonexistence of Positive Solutions on \mathbb{R}^N and H^1

Gisèle Goldstein (University of Houston)

The parabolic partial differential equation

$$\frac{\partial u}{\partial t} = \Delta u + \frac{c}{|x|^2} u$$

(1)

For $x \in \mathbb{R}^N, t > 0$ has remarkable scaling and other properties. It was the first example of instantaneous blowup. For

$$c \leq C(N) = \left(\frac{N-2}{2}\right)^2,$$

(1) has many positive solutions, but for $c > C(N)$, (1) has no nonnegative solutions other than zero. Moreover, suppose $c > C(N)$ and $u(x, 0) = f(x) \geq 0$, where f is not 0 a.e. and f is a good initial condition (when $c = 0$). Replace $V(x) = \frac{c}{|x|^2}$ by

$$V_n(x) = \min\{V(x), cn^2\}.$$

Then $\{V_n\}$ is an increasing sequence of bounded functions, and let $u_n(x, t)$ be the corresponding positive solution of

$$\frac{\partial u}{\partial t} = \Delta u + V_n u.$$

Then

$$u_n(x, t) \rightarrow +\infty \text{ as } n \rightarrow \infty$$

for all $x \in \mathbb{R}^N, t > 0$. This result is due to P. Baras and J. Goldstein (1984) and was the first example of instantaneous blowup.

The same result holds when \mathbb{R}^N is replaced by the Heisenberg group \mathbb{H}^N . The underlying space is topologically \mathbb{R}^{2N+1} , but the corresponding Laplacian is the sum of $2N$ squares of vector fields, not $2N + 1$ vector fields; thus, the Heisenberg Laplacian is not uniformly elliptic. Nevertheless, with the appropriate potential for the Heisenberg group, instantaneous blowup still holds. The difficult proof is based on extending DeGiorgi-Nash-Moser theory from \mathbb{R}^N to \mathbb{H}^N : This result appeared in 2022 in the *Annali della Scuola Normale Superiore di Pisa*. The authors are Gisèle and Jerry Goldstein, Alessia Kogoi, Abdelaziz Rhandi and Cristian Tacelli.

Related results for the modified Ornstein-Uhlenbeck equation and some non-linear equations (such as fast diffusion and the p-Laplace equation) with potentials will also be presented.

Automatic segmentation of multielectrode array

John Jurkiewicz (University of Wisconsin-Milwaukee)

A new multi-electrode array-based application for the long-term recording of action potentials from electrogenic cells makes possible exciting cardiac electrophysiology studies in health and disease. With hundreds of simultaneous electrode recordings being acquired over a period of days, the main challenge becomes achieving reliable signal identification and quantification. We introduce an algorithm capable of automatically extracting regions of high-quality action potentials from terabyte size experimental results and to map the trains of action potentials into a low-dimensional feature space for analysis. Our algorithm finds regions of acceptable action potentials in large data sets of electrophysiological readings. Our work contributes towards a non-invasive approach for cardiomyocyte functional maturation, as well as developmental, pathological and pharmacological studies. As the human-derived cardiac model tissue has the genetic makeup of its donor, a powerful tool for individual drug toxicity screening emerges.

Antimicrobial De-escalation in Intensive Care Units: Implications on Clinical Trial Design Provided by Mathematical Models

Xi Huo (University of Miami)

Antimicrobial de-escalation refers to reducing the spectrum of antibiotics used in treating bacterial infections. This strategy is widely recommended in many antimicrobial stewardship programs and is believed to reduce patients' exposure to broad-spectrum antibiotics and prevent resistance. However, the ecological benefits of de-escalation have not been universally observed in clinical studies. In this talk, I will present the computer simulations we conducted to assess the ecological effects of de-escalation on the resistance prevalence of *Pseudomonas aeruginosa* - a frequent pathogen causing nosocomial infections. Synthetic data produced by the models are then used to estimate the sample size and study period needed to observe the predicted effects in clinical trials. Our results show that de-escalation can reduce colonization and infections caused by bacterial strains resistant to the empiric antibiotic, limit the use of broad-spectrum antibiotics, and avoid inappropriate empiric therapies. Further, we show that de-escalation could reduce the overall superinfection incidence, and this benefit becomes more evident under good compliance with hand hygiene protocols among health care workers. Finally, we find that any clinical study aiming to observe the essential effects of de-escalation should involve at least ten arms and last for four years - a size never attained in prior studies. This study explains the controversial findings of de-escalation in previous clinical studies and illustrates how mathematical models can inform outcome expectations and guide the design of clinical studies.

Session 8 Abstracts:

A discrete time stage structured model for host parasitoid interaction with pest control

Jenita Jahangir (University of Louisiana at Lafayette)

We propose a discrete-time host-parasitoid model with stage structure in both species. For this model, we establish conditions for the existence and global stability of the extinction and parasitoid-free equilibria as well as conditions for the existence and uniqueness of an interior equilibrium. We study the model numerically to examine how pesticide spraying may interact with natural enemies (parasitoids) to control the pest (host) species. We then extend the model to an impulsive difference system that incorporates both periodic pesticide spraying and augmentation of the natural enemies to suppress the pest population. For this system we determine when the pest-eradication periodic solution is globally attracting. We also examine how varying the control measures (pesticide concentration, natural enemy augmentation, and the frequency of applications) may lead to different pest outbreak or persistence outcomes when eradication does not occur.

Bistability in models of Hepatitis B virus dynamics

Nazia Afrin (University of Louisiana at Lafayette)

HBV is a major global health concern with 1.5 million newly infected cases each year. It's an infection of the liver caused by the Hepatitis B virus. In this preliminary study, we formulate and analyze a within-host model that describes the progression of acute HBV in liver cells (hepatocytes). We derive the basic reproduction number R_0 and investigate the stability of the equilibria via threshold analysis. Analytical and numerical results show that the model exhibits complex bifurcation dynamics such as backward bifurcation. Finally, we discuss the epidemiological implications of bistable dynamics.

Session 9 Abstracts:

Population Persistence in Stream Networks: Growth Rate and Biomass

Tung Nguyen (Texas A&M University)

We consider the logistic metapopulation model over a stream network and use the population growth rate and the total biomass (of the positive equilibrium) as measures for population persistence. Our objective is to find distributions of resources that maximize these persistence measures. We begin our study by considering stream networks consisting of three nodes and prove that the strategy to maximize the total biomass is to concentrate all the resources in the most upstream locations. In contrast, when the diffusion rates are sufficiently small, the population growth rate is maximized when all resources are concentrated in one of the most downstream locations. These two main results are generalized to stream networks with any number of patches.

Integrating wastewater-based epidemiology and mechanistic models: Implications for public health and variant emergence

Samantha Brozak (Arizona State University)

Wastewater-based epidemiology (WBE) is an emerging tool for community disease surveillance. WBE has become prominent during the COVID-19 pandemic as a near-real time, cost-effective method for surveillance without delays associated with clinical data. Community transmission

and variant emergence may be monitored through quantifying and sequencing viral particles shed via stool by infected individuals. We connect a standard epidemic SEIR model to the dynamics of viral RNA in the sewer shed. Using data from the greater Boston area from October 2020 to January 2021, we show that this model captures the temporal fluctuations of viral particles, but prevalences peaks earlier and higher than reported. We also show how WBE and the SEIR model can be extended to improve our understanding of the circulation of multiple strains of a disease, specifically COVID-19.

Forecasting the effect of PREP on HIV propagation with a system of difference-differential equations with delays

Gregoire Ranson (York university)

HIV/AIDS epidemic is still worldwide active with no existing definitive cure. Based on the WHO recommendations stated in 2014, a treatment, called Pre-Exposure Prophylaxis (PrEP) has been used globally, and in particular in France since 2016 to prevent from HIV infection. In this paper, we propose a new compartmental epidemiological model with a particular focus on the limited protection time offered by this new treatment. We describe the PrEP compartment with an age-structured hyperbolic equation and introduce a differential equation on the parameter that governs the PrEP starting process. This leads to a nonlinear difference differential system with discrete delay. After a local stability analysis, we characterize the global behaviors of the linear and non-linear cases. Finally, we illustrate the solutions with numerical simulations based on data of the French male homosexual population. We show that the choice of a logistic time-dynamics combined with our Hill function-like model leads to a perfect data fit. These results enable us to forecast the evolution of the HIV epidemics in France if the populations keep using PrEP.

Session 10 Abstracts:

Optimal Impulse Control of a Late-Season Model of a West Nile Virus Epidemic

Rachel Leander (Middle Tennessee State University)

This presentation concerns a late-season model of a West Nile virus epidemic that includes transmission between bird hosts and mosquito vectors, mosquito life stages, and pesticide dynamics. Our model describes three mosquito life stages; eggs, larvae, and adults, and three pesticides; two types of larvicide and one adulticide. The basic reproduction number for the model epidemic is analyzed in the absence of control, and impulsive optimal control problems are constructed. Objective functions are designed to balance the cost of the insecticide

application schedule with the benefit of (1) vector control: reducing the number of mosquitoes or (2) disease control: reducing the disease burden. The resulting impulsive optimal control problems are then reformulated as nonlinear optimization problems in order to derive necessary conditions for the characterization of optimal controls. Numerical simulations are used to address three questions: How does the control and its impact on the system vary with the objective type? Is it beneficial to optimize the treatment timing? How does the control and its impact on the population vary with the type of pesticide used?

Coauthors: Folashade Augusto, Daniel Bond, Adira Cohen, Wandu Ding, and Allis Royer

Effects of Dispersal Rates in a Two-Stage Reaction-Diffusion System

Rachidi Salako (University of Nevada Las Vegas)

The effects and evolution of dispersal in population dynamics have been widely studied from the viewpoint of reaction-advection-diffusion models. Most models assume that for any specific population, all individuals have the same dispersal behavior and experience the environment in the same way. In that case, in bounded habitats that are spatially heterogeneous but constant in time, for movement by pure diffusion, there is typically selection for slower dispersal. However, it is not always the case that individuals within a population follow movement patterns drawn from the same distribution. Within populations there may be individual variation in dispersal and in responses to environmental conditions. For example, adults and juveniles may have very different movement rates. In this talk, we will consider a reaction-diffusion system modelling the dynamics of a single population structured in two stages: adults and juveniles. We will discuss the effects of dispersal rates on the dynamics of the species and present several results on the limiting profiles of steady state solutions. In particular, necessary and sufficient conditions on the diffusion rates for the persistence of the species when one of the species doesn't move will be discussed.

Bifurcation Analysis of Critical Values for Wound Closure Outcomes in Wound Healing Experiments

Xinyue Zhao (Vanderbilt University)

In this talk, I will present a nonlinear partial differential equation containing a nonlocal advection term and a diffusion term to study wound closure outcomes in wound healing experiments. There is an extensive literature of similar models for wound healing experiments. In our work, we study the character of wound closure in these experiments in terms of the sensing radius of

cells and the force of cell-cell adhesion. We prove a bifurcation result which differentiates uniform closure of the wound from nonuniform closure of the wound, based on a critical value λ_{\star} of the force of cell-cell adhesion parameter λ . For $\lambda < \lambda_{\star}$ the steady state solution $u \equiv 1$ of the model is stable and the wound closes uniformly. For $\lambda > \lambda_{\star}$ the steady state solution $u \equiv 1$ of the model is unstable and the wound closes nonuniformly. We provide numerical simulations of the model to illustrate our results. This is a joint work with Prof. Glenn Webb.

Poster Abstracts:

A Differential Equations Model of the Impact of Medically-Assisted Treatment in Correctional Facilities on the Opioid Epidemic in Virginia

Olivia Barlow, Connor Gasgarth, Leah Ghazali, and Maniha Akram (University of Richmond)

The opioid epidemic is prevalent in countless communities throughout the United States and has yet to be mitigated. The Ordinary Differential Equations (ODE) model presented here hopes to provide insight into what changes can be made to the incarceration system, specifically in the state of Virginia, to curb the epidemic. The source of inspiration for this research was twofold. First, there is a paucity of mathematical modeling research on the severity of the opioid crisis in relation to incarceration. Second, a preliminary simple regression analysis revealed a significantly positive relationship ($p = 0.002$) between incarceration rates and opioid overdose rates in Virginia counties, using data provided by the Virginia Department of Health (VDH) and the Prison Policy Initiative (PPI). With separate compartments for individuals in medicated and non-medicated treatment, both within and outside of incarceration, this model seeks to explore the effects of offering treatment for opioid use disorder (OUD) in correctional facilities. Numerical methods are used to analyze the model with a focus on informal parameter sensitivity analysis, and the results are used to provide public policy suggestions. We found that increasing the rate of correctional facilities offering MATs would effectively lower the amount of addicted individuals in the population. In general, increasing the rate that individuals seek treatment helps reduce the total number of addicted individuals. Additionally, MAT facilities are especially important because of their much higher effectiveness compared to non-MAT facilities.

Population Dynamics in an Advective Environment

Ray Lee (Ohio State University)

In environments such as rivers and streams, species can be exposed to unidirectional drift which threatens to wash them out of the habitat. In such cases, how do the behavior of the species and the conditions at the habitat boundaries affect the ability of the species to persist?

To this end, we consider a one-dimensional reaction-diffusion equation describing single and two-species population dynamics in an advective environment, based on the modeling frameworks proposed by Lutscher, Lewis, and McCauley in 2006. There have been a number of mathematical studies related to the above question. In our work, we focus in particular on the diffusion rates of the species, and the effect of rate of loss of individuals at both the upstream and downstream boundaries.

For a single species, we prove the existence of a minimal habitat size required for persistence of the species—the so-called “critical domain size”—and provide explicit formulas in terms of model parameters. We further show that, in some cases, the critical domain size is either strictly decreasing over all diffusion rates, or monotonically increasing after first decreasing to a minimum.

We also consider competition between species differing only in their diffusion rates. For two species having large diffusion rates, we give a sufficient condition to determine whether the faster or slower diffuser wins the competition. We also note a link between these results and competition dynamics in species whose spatial niche is affected by shifting isotherms caused by climate change.

Efficient method of moments for approximating VEGF receptor models

Emmanuel Adara (University of Alabama Tuscaloosa)

The method of moments is a useful numerical technique to analyze biochemical reactions as it allows for a direct approximation of statistical measures such as the mean number of molecules. This method is more efficient in terms of time and memory compared to the chemical master equation, which is known for its high computational cost. Here, we apply the method of moments to the VEGF receptor model, which describes the role of VEGF in the regulation of blood vessel formation and growth through a series of molecular interactions between VEGF and its receptors on the surface of endothelial cells. The method's accuracy is evaluated by comparing the results with those obtained from the stochastic simulation algorithm and the chemical Langevin equation. The VEGF model is of interest because of the role of VEGF in the growth of cancer and other inflammatory diseases and the potential use of anti-VEGF therapies in the treatment of cancer.

An SIR-type Model of Call Center Effectiveness Regarding Opioid Addiction Recovery

Liza Eubanks, Belle Tassent, and Ferah Shaikh (Rollins College)

The opioid epidemic in the United States is a complex public health emergency that, according to the CDC's U.S. Drug Overdose Death Rate Maps on age-adjusted drug overdose mortality by state, has affected West Virginia significantly more than other states.

Our project studies the drug using career by comparing assertive recovery versus passive recovery regarding an individual's own drug addiction, specifically focusing on opioid abuse. Because these categories are qualitatively defined, we use data from HELP4WV, a call center dedicated to helping West Virginians struggling with substance abuse or mental health crises. The call center is available to individuals and their loved ones to text or call 24/7, and the center helps struggling individuals access resources they need. HELP4WV reaches out to individuals 48 hours, one week, and one month after the initial call. We use follow-up call data from HELP4WV to quantify the transition rates to each path.

We construct an SIR-type model to study the effectiveness of helplines to channel individuals to an assertive recovery path by showing its effects on the long-term recovery compared to a passive recovery approach. Our model mimics the drug using career by including five compartments: susceptible, using, assertive, passive, and recovered. We use phase plane analysis, differential equations, and scientific computing to analyze the long-term effects of individuals with an assertive recovery approach on the opioid crisis.

The Extension of the SIR Model to Capture Dynamics of COVID-19 Outbreaks

Ke Tang (Vanderbilt University)

COVID-19 has exerted a great impact around the world, and the trajectory of the pandemic is vastly different across countries. While the SIR model is a widely used mathematical model in epidemiology that describes how infectious diseases spread through a population over time, it cannot account for significant factors such as varying social behaviors and the degree of social distancing when analyzing COVID-19 cases. It is thus important to quantify qualitative matters such as people's behaviors. In the paper "Social stress drives the multi-wave dynamics of COVID-19 outbreaks," the theory of general adaptation syndrome (GAS) is incorporated into a standard SIR model to demonstrate how various social behaviors (e.g. the degree of resistance a population has towards COVID-19) result in different pandemic dynamics across countries.

Throughout this paper, I will analyze the efficacy of the modified SIR model, evaluate the conclusions across 13 countries, and carry out extensions. Several other factors such as vaccine programs, asymptotic/unidentifiable infectious people, and mortality analysis will be taken into

account in addition to GAS to predict the trajectory of the pandemic and provide insights into the effectiveness of different interventions. By conducting intra-country comparisons, the paper can help understand how the change in parameters can influence the pandemic trend.

Analysis of COVID-19 Epidemic Models: Revalidating the Existing SIR Model and Exploring Future Directions

Jiayi Xu (Vanderbilt University)

The spread of epidemics poses significant challenges to public health, and mathematical models have become instrumental in understanding their dynamics and control measures. In this study, I provide an analysis of a mathematical model for epidemic dynamics that was previously studied. Specifically, I confirm the study's finding by reviewing the model, verifying its mathematical calculations, and reproducing its data. Furthermore, I address the current model's limitations and identify areas where it can be extended to improve its accuracy and make more valuable contributions to the field of epidemic modeling.

Numerical Modelling of the Diffusion-Time dependent ADC in Diffusion Weighted Imaging

Tran Tuan Khai Nguyen (Vanderbilt University)

White matter characterization is important for understanding health of the human brain. In particular, diffusion-weighted MRI (DWI) is a powerful tool in the assessment of white-matter pathophysiology non-invasively in vivo, as it is sensitive to the microstructural organization of tissue. While the apparent diffusion coefficient (ADC) measured with DWI depends upon the experimental diffusion-time, the relationship between the diffusion-time and ADC is an underexplored aspect of DWI in tissue. The overarching goal of this work is to use numerical modelling to reveal the microstructural features that underlie the diffusion-time dependent changes in the ADC in white-matter.

The aims are to [1] numerically generate realistic white-matter environment with different axon diameters, axonal heterogeneity, and axonal dispersion, and [2] examine the relationship between these axon properties and changes in apparent diffusion coefficient across diffusion time using Monte-Carlo diffusion simulations.

With the results from our work, imaging protocols will be optimized and integrated into clinical systems for a more detailed assessment of white-matter disease using ADC as a biomarker.

Age-structured compartmental model for COVID-19 using systems of ordinary differential equations

Peilun Li (Vanderbilt University)

Modeling population dynamics in epidemiology is a versatile tool that aims to predict and simulate the spread and rippling effects of a particular epidemic. Based on the framework of previous research, this paper presents a more complex compartmental, age-structured model that simulates the population dynamics of COVID-19. In specific, the model, based on observations of most of the COVID-19 cases, has 7 compartments (Susceptible, Incubation, Symptomatically Infectious, Asymptomatically Infectious, Recovered, Hospitalized, Dead), each of which is constituted by populations from 7 age groups, which are of age $[0, 9]$, $[10, 19]$, $[20, 29]$, $[30, 39]$, $[40, 59]$, $[60, 69]$, and $70+$. Furthermore, this model also considers and predicts the protective effects of social-distancing and vaccination measures on population dynamics.