# CBMS Conference: Interface of Mathematical Biology and Linear Algebra List of Posters

The poster session is held on Wednesday May 25, 16:00–18:00, in Key West Ballroom, Student Union

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Yingying Wu PhyloTransformer: A Self-supervised Discriminative Model for Mutation Prediction Based on a Multi-head Self-attention Mechanism

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Poroshat Yazdanbakhshghahyazi The Impact of Network Heterogeneity on the Spread of Infectious Diseases

Wenjing Zhang Sensitivity and Bifurcation Analysis of Tuberculosis Progression

# Abstracts of Posters

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### Modeling the Homeostatic Length of the Rod Outer Segment in Zebrafish

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Retinal photoreceptor cells, rods and cones, in the eye convert light energy into electrical signals that stimulate sight. In humans, peripherally located rods are important for night vision, while centrally located cones are responsible for daytime/color vision. Rods consist of a rod outer segment (ROS), inner segment, cell body and synaptic terminal. The ROS, consisting of stacked, discrete membranous discs, undergoes a process of continuous renewal in which newly constructed discs are added at the base (growth) and oldest discs are shed from the tip. The ROS maintains a homeostatic length by balancing growth and shedding. How this balance is controlled is unknown. If ROS homeostatic length control is lost, for example by ROS shortening, the rods can degenerate leading to blindness. We develop a model of ROS homeostatic length control, supported by experiments using data from zebrafish where ROS renewal is controlled experimentally. An ODE describes the length of ROS over time according to constant growth and ROS length-dependent shortening. Here, equilibrium analysis helps us understand the balance between growth and shortening mechanisms in maintaining homeostatic length. Also, an advection-reaction PDE describes disk addition (through a boundary condition), translocation (via advection), and shedding (reaction) in populations of ROS.

## The Idiosyncratic Polynomial of Digraphs

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The idiosyncratic polynomial of a graph G with adjacency matrix A is the characteristic polynomial of the matrix A + y(J - A - I), where I is the identity matrix and J is the all-ones matrix. It follows from a theorem of Hagos (2000) combined with an earlier result of Johnson and Newman (1980) that the idiosyncratic polynomial of a graph is reconstructible from the multiset of the idiosyncratic polynomial of its vertex-deleted subgraphs. For a digraph D with adjacency matrix A, we define its idiosyncratic polynomial as the characteristic polynomial of the matrix A + y(J - A - I) + zA. By forbidding two fixed digraphs on three vertices as induced subdigraphs, we prove that the idiosyncratic polynomial of a digraph is reconstructible from the ordered multiset of the idiosyncratic polynomial of its induced subdigraphs on three vertices. As an immediate consequence, the idiosyncratic polynomial of a tournament is reconstructible from the collection of its 3-cycles. Another consequence is that all the transitive orientations of a comparability graph have the same idiosyncratic polynomial.

## Distribution of Highly Effective Bed Nets May Not Help Eradicating Malaria in Sub-Saharan Africa: Exploring with an Evolutionary Game Theory

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Insecticide Treated bed Nets (ITN) have proven to be highly effective control measure to reduce malaria transmission. It has been discussed earlier that ITNs with high efficacy may perform better in control malaria. But, even after massive distribution of ITN, malaria persists in most of the under developing countries, compromising the long term malaria elimination goals. However, many empirical studies pointed out that usage of ITN plays an important role in its effectiveness to control malaria. Individuals ITN usage are highly driven by ITN efficacy, mosquito density due to seasonal variation, replacement period, increment in daily productivity due to ITN misuse. To explore the complex interaction of ITN usage pattern and malaria prevalence, we develop a Game-Theoretic model of ITN usage and malaria transmission. Our results show the impact of parameters like imitation rate and ITN efficacy on human behaviour are critical. The analysis indicates that higher efficacy of ITN is not always optimal to control malaria effectively, which is an important information for malaria elimination strategies.

## Algebraic and Combinatorial Approaches for Counting Cycles Arising in Population Biology

#### Brian Chau University of Alberta bchau1@ualberta.ca

The literature contains many algebraic and combinatorial approaches for deriving the net reproduction number and generalized target reproduction numbers from digraphs and associated matrices. These numbers describe the growth or decline of a population and are often used for population management analysis when used as a measure of the effort needed to control a population. They may also provide some biological insight in some forms. The Cycle Union approach by Lewis et al. (2019) does not provide a biologically intuitive form of these numbers but does have the benefit of being a computationally simple approach. It requires finding, categorizing, and counting the permutations of disjoint cycles, or cycles unions. Finding and categorizing all cycle unions is a simple, but tedious task prone to errors without a proper counting strategy. We developed cycle union counting patterns for Leslie Matrices, Lefkovitch Matrices, Sub-Diagonal Lower Triangle Transition Matrices, and Lower Triangle Transition Matrices to serve as a foundation for future work. Presented are counting patterns targeting individual arcs and the closed-form summations of the cycle unions.

#### **Reference:**

M.A. Lewis, Z. Shuai, P. van den Driessche (2019). A general theory for target reproduction numbers with applications to ecology and epidemiology. *Journal of Mathematical Biology*, 78:2317–2339.

# The General Non-Stationary Anderson Parabolic Model with Correlated White Noise

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We study the non-stationary Anderson parabolic problem on the lattice  $Z^d$ , i.e., the equation

$$\begin{split} &\frac{\partial u}{\partial t} = \kappa L u(t,x) + \xi(t,x) u(t,x) \\ &u(0,x) = 1, (t,x) \in [0,\infty) \times Z^d \end{split}$$

Here L is non-local Laplacian,  $\xi(t, x), t \ge 0, x \in Z^d$  is the family of the correlated white noises and  $\kappa \ge 0$  is the diffusion coefficient. We devoted to existence-uniqueness theorems for this model in the weighted Hilbert space  $L^2(Z^d)$  and Feynman-Kac representation u(t, x). The moments equations of u(t, x) are derived and studied using the spectral analysis of the corresponding Schrödinger operators with special class of the positive definite potentials. The analysis reveals several bifurcations depending on the properties of the kernel of L and the correlation function in the potential.

## The Impact of the Travel Restriction on the Infectious Disease Dynamics in Multi-Patch Models

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In the ongoing COVID-19 pandemic around the world, governments might pose various travel restriction policies internationally as well as domestically. There are several to model the impact of varying residence times or travel restrictions such as lockdown on the infectious disease dynamics in a heterogeneous environment. We derived the basic reproduction number and proved that it is monotonically decreasing with respect to the travel restriction factor. Numerical simulations illustrate that the final size of the outbreak depends on the travel restriction measure as well as the transmissibility. Moreover, we investigate patch-specific optimal treatment strategies.

## To Eat or Not to Eat? A Lesson Learnt from Modelling Listeriosis of RTE Food Products

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Cross contamination that results in food-borne disease outbreaks remains a major problem in processed foods globally. In this paper, a mathematical model that takes into consideration cross contamination of Listeria monocytogenes from a food processing plant environment is formulated using a system of ordinary differential equations. The model has three equilibria: the disease-free equilibrium, Listeria-free equilibrium, and endemic equilibrium points. A contamination threshold ( $\mathcal{R}_f$ ) is determined. Analysis of the model shows that the disease-free equilibrium point is locally stable for  $\mathcal{R}_f < 1$  while the Listeria-free and endemic equilibria are locally stable for  $\mathcal{R}_f > 1$  The time-dependent sensitivity analysis is performed using Latin hypercube sampling to determine model input parameters that significantly affect the severity of the listeriosis. Numerical simulations are carried out, and the results are discussed. The results show that a reduction in the number of contaminated workers and removal of contaminated food products are essential in eliminating the disease in the human population and vice versa. The results have significant public health implications in the management and containment of any listeriosis disease outbreak.

## Understanding Non-Equilibrium Steady States

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Physical systems are characterized by their response to perturbations. The Fluctuation Dissipation Theorem predicts the behavior of systems in equilibrium. Can an expression be derived using methods from quantum field theory to describe the vertex response to a perturbation, and is the Fluctuation Dissipation Theorem modified as a result of these perturbations. Using Berezin integration and properties of determinants we derive said expression. The derivation yields the same result as the less rigorous methods. We learn the Fluctuation Dissipation Theorem has an equilibrium-like response to a vertex perturbation making the Fluctuation Dissipation theorem a bad indicator of whether a system is in equilibrium or out of equilibrium.

# Long-Time Behavior for ODE and Finite Volume Approaches for Studying Multilevel Selection in Evolutionary Game Theory

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In many biological systems, natural selection acts simultaneously on multiple levels of organization. This scenario typically presents an evolutionary conflict between the incentive of individuals to cheat and the collective incentive to establish cooperation within a group. One approach for studying the dynamics of multilevel selection is to consider a hyperbolic PDE model of a group-structured population, in which members within a single group compete with each other for individual-level replication; while the group also competes against other groups for group-level replication. In this poster, we will explore the derivation and analysis of a finite volume discretization for this PDE. By considering an associate linear system of ODEs to the nonlinear discretized system, we can use the Perron-Frobenius theorem to show that the finite volume approximation admits a unique, globally stable steady state distribution. Using techniques from numerical analysis, we can further show that this steady state to the discretized system converges to a steady state density of the original PDE model in the limit of infinite grid size. As the PDE has an infinitely family of steady state densities, the convergence of the numerical states to a particular steady state of the PDE model may serve as principle for selecting among the steady states in terms of achievability under the long-time behavior for the underlying finite population model from which the PDE is derived.

# Mathematical Analysis of an HIV/AIDS Epidemic Model

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A mathematical model is a powerful tool for interpreting and analyzing the dynamics of diseases. Here, we present a non-linear mathematical model which investigates the spread and control of HIV in different populations. The present study fitted the model, which exhibits two equilibrium points such as the disease-free equilibrium and the endemic equilibrium points. The global stability of these equilibrium points is also carefully investigated. The model is analyzed by using the rudimentary reproduction number  $R_0$ .

#### Asymptotic Analysis of a Nonlinear Oscillator with Damping

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We consider the following second order evolution equation modelling a nonlinear oscillator with damping

$$u''(t) + \gamma u'(t) + Au(t) = f(t) \tag{SEE}$$

Where f(t) is a maximal monotone and  $\alpha$ -inverse strongly monotone operator in a real Hilbert space H. With suitable assumptions on  $\gamma$  and f(t) we show that the zero set of A is nonempty, if and only if (SEE) has a bounded solution and in this case we provide approximation results for elements of the zero set of A by proving weak and strong convergence theorems for solutions to (SEE) showing that the limit belongs to the zero set of A. As a discrete version of (SEE), we consider the following second order difference equation

$$u_{n+1} - u_n - a_n(u_n - u_{n-1}) + \lambda_n A u_{n+1} = f(t),$$

where f(t) is assumed to be only maximal monotone (possibly multivalued). By using the results in [11], we prove ergodic, weak and strong convergence theorems for the sequence  $u_n$ , and show that the limit is the asymptotic center of  $u_n$  and belongs to the zero set of A. This again shows that the zero set of A is nonempty if and only if  $u_n$  is bounded. Also these results solve an open problem raised in [2], namely the study of the convergence results for the inexact inertial proximal algorithm. Our paper is motivated by the previous results in [611] and significantly improves upon the results of H. Attouch and P. E. Maing [3], and F. Alvarez and H. Attouch [2].

#### Modeling and Analysis of Social Contagion in Overweight and Obesity Epidemic

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Overweight and obesity have become a global epidemic due to the increasing unhealthy eating habits and sedentary lifestyles. Even though many intervention programs have been introduced, a mathematical approach to analyze the growing obesity epidemic is still crucial to plan and estimate the effectiveness of obesity intervention and prevention programs. By treating excess weight gain as a disease transmitted by social influence, we propose a compartment model to predict the incidence of excess weight gain. Mathematical analysis shows that the system has at most two endemic equilibrium points ( $E^*$ ) and the disease-free equilibrium point  $E_0$ . Applying the compound matrix method for the local stability, we prove that  $E_0$  is locally asymptotically stable if the basic reproduction number  $R_0 < 1$ ., i.e., the obesity can be eliminated when  $R_0 < 1$ . Furthermore, a closed-form formula for the occurrence of backward bifurcation is provided. In this scenario, a complete disease eradication cannot be expected if and only if  $R_0 < 1$ . By applying fluctuation lemma, we prove the global stability of  $E_0$  and provide a parameter condition to eradicate the overweight and obesity epidemic. For the proposed model, we considered that the parameter  $\sigma$ , rate of relative hazard of weight regain is greater than unity. Due to biological reasons, the parameter  $\sigma$ can also be less than or unity. To discuss the global stability of  $E_0$  for  $0 < \sigma \leq 1$ , we construct a Lyapunov function by applying a matrix-theoretic method that uses the Perron eigenvector. Hence,  $R_0 = 1$  is a sharp threshold for the disease elimination for  $0 < \sigma \leq 1$ . By the compound matrix method for the local stability, the unique non-trivial equilibrium  $(E^*)$  shows asymptotic stability when  $R_0 > 1$  under some parameter conditions. Moreover, in the presence of bi-stability, obtaining global dynamics are complicated due to the non-existence of compact absorbing sets. By applying the geometric approach using a compound matrix method, we discuss the global dynamics of the disease when  $R_0 > 1$ . The dynamics are examined of the overweight population through a numerical bifurcation analysis. Analytical and numerical analysis show that the proposed model is sufficient to show the complex epidemic patterns of the obesity epidemic, such as backward bifurcation and bi-stability.

## Fixed Point for a Contraction Type Mapping on a Complete Metric Space

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Having presented a new version of Kannan mapping theorem by changing the delta in Graghty definition on a complete metric space, we generalize some theorems and an example. After that, we present some results on Boyd-Wong theorem.

## Human Papillomvirus Vaccination Strategy: Modeling and Implications

#### <u>Shasha Gao</u> University of Florida shashagao@ufl.edu

Vaccination is effective in preventing human papillomavirus (HPV) infection. It is imperative to investigate who should be vaccinated and what the best vaccine distribution strategy is. We use a dynamic model to assess HPV vaccination strategies in a heterosexual population combined with gay, bisexual, and other men who have sex with men (MSM). The basic reproduction numbers for heterosexual females, heterosexual males and MSM as well as their average for the total population are obtained. We also derive a threshold parameter, based on basic reproduction numbers, for model analysis. From the analysis and numerical investigations, we have several conclusions.

(1) To eliminate HPV infection, the priority of vaccination should be given to MSM, especially in countries that have already achieved high coverage in females. The heterosexual population gets great benefit but MSM only get minor benefit from vaccinating heterosexual females or males.

(2) The best vaccination strategy is to vaccinate MSM firstly as many as possible, then heterosexual females, lastly heterosexual males.

(3) Given a fixed vaccination coverage of MSM, distributing the remaining vaccines to only heterosexual females or males leads to a similar prevalence in the total population. This prevalence is lower than that when vaccines are distributed to both genders. The evener the distribution, the higher the prevalence in the total population. This study provides information that may help policymakers formulate guidelines for vaccine distribution to reduce HPV prevalence.

## Dynamics of a Two-Strain Cholera Model with Environmental Component

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Cholera can survive, proliferate, and compete in the aquatic environment, necessary factors to consider when modeling its long-term dynamics. We combine and extend previously studied SIRP (infectious disease models incorporating pathogen environmental concentration) and multi-strains models to consider the strain diversity of cholera and more accurately analyze its transmission dynamics and long-term behavior (e.g. coexistence versus competitive exclusion). We focus on distinct serotypes, strains which differ only in cross-immunity after host infection. This model extends the single-strain model to a two-strain SIRP cholera model, considering two distinct serotypes of the bacteria, Ogawa and Inaba. Via typical deterministic modelling techniques, we derive and analyze disease-free, boundary, and coexistence equilibria for the model. Population persistence methods allow us to determine long-term behavior of the strains when our basic reproduction number is greater than one.

#### Copositive Matrices, their Dual, and the Recognition Problem

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Copositivity is a generalization of positive semi-definiteness. It has applications in economics, operations research, and statistics. A symmetric matrix  $A \in M_n(\mathbb{R})$  is copositive (CoP) if for any nonnegative vector  $x \neq 0, x \in \mathbb{R}^n$ , the quadratic form  $Q(x) = x^T A x \ge 0$ . A CoP matrix is ordinary if it can be written as the the sum of a positive semidefinite (PSD) matrix and a symmetric nonnegative (sN) matrix. However, recognizing that a given CoP matrix is ordinary and determining an ordinary decomposition is an unresolved issue. Here, we discuss properties of CoP matrices and our progress on the ordinary recognition and decomposition problem.

# Absolute Triple Convoluted Norlund Summable Factor

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The indexed absolute triple convoluted Norlund summability  $|N^3, p, q, r|_k$  factor of orthogonal series has been studied for a least set of the sufficient conditions and a set of moderated results have been developed. This result is very useful as absolute summability is used for Bounded Input Bounded Output (BIBO) stability of the system. The absolute summability plays an important role in signal processing as a double digital filter in finite and infinite impulse response (FIR & IIR).

# Identifiability and Optimal Control of HIV Infection and Opioid Addiction

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On the basis of the growing association between opioid addiction and HIV infection, we develop a compartmental model to study the dynamics and optimal control of two epidemics; opioid addiction and HIV infection. We show that the disease-free-equilibrium is locally asymptotically stable when the basic reproduction number  $\mathcal{R}_0 = \max(\mathcal{R}_0^u, \mathcal{R}_0^v) \leq 1$ , here  $\mathcal{R}_0^v$  is the reproduction number of the HIV infection, and  $\mathcal{R}_0^u$  is the reproduction number of the opioid addiction. The addiction-only boundary equilibrium exists when  $\mathcal{R}_0^u \geq 1$  and it is locally asymptotically stable when the invasion number of the opioid addiction is  $\mathcal{R}_{inv}^u \leq 1$ . Similarly, the HIV-only boundary equilibrium exists when  $\mathcal{R}_0^v \geq 1$  and it is locally asymptotically stable when the invasion number of the opioid addiction is  $\mathcal{R}_{inv}^v \leq 1$ . We study structural identifiability of the parameters, estimate parameters employing yearly reported data from Central for Disease Control and Prevention (CDC), and study practical identifiability of estimated parameters. We observe the basic reproduction number  $\mathcal{R}_0$  using the parameters. Next, we introduce four distinct controls in the model for the sake of the control approach, including treatment for addictions, health care education about not sharing syringes, highly active antiretroviral therapy (HAART), and rehab treatment for opiate addicts who are HIV infected. US population using CDC data, first applying a single control in the model and observing the results, we better understand the influence of individual control.

### Using Tiers to Understand the Qualitative Behavior of Biological Interaction Networks

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Reaction networks are mainly used to model the time evolution of molecules of interacting biological and chemical species. When the abundances of the species are high, the species concentrations are modelled deterministically by a system of ordinary differential equations (ODEs). When the abundances of the species are low, the counts of species are instead modelled by a continuous time Markov chain.

Reaction networks can be associated with finite graphs, whose vertices are complexes and edges are reactions from the reaction networks. Naturally, a central question in the theory of reaction networks concerns the connections between graph properties and qualitative properties of the associated dynamical systems. In this project we show that if a reaction network possesses "strong endotacticity" (a graph property), its dynamical systems have many stability properties. In particular, the deterministic system exhibits persistence and permanence, and the stochastic system is positive recurrent and satisfies a large deviation principle (LDP) with some additional assumptions on the graph.

### The Impact of Microbial Diseases of Corals under Macroalgal Toxicity and Overfishing

#### <u>Samares Pal</u> University of Kalyani, India samaresp@gmail.com

Competition between macroalgae and corals for occupying the available space in sea bed is an important ecological process underlying coral-reef dynamics. We investigate coral-macroalgal phase shift in presence of macroalgal allelopathy and microbial infection on corals by means of an eco-epidemiological model under the assumption that the transmission of infection occurs through both contagious and non-contagious pathways. We found that the system is capable of exhibiting the existence of two stable configurations by saddle-node bifurcations.

## Statistical and Deterministic Methods for Large-Scale Dynamic Inverse Problems

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Inverse problems are ubiquitous in many fields of science such as engineering, biology, medical imaging, atmospheric science, and geophysics. Three emerging challenges on obtaining relevant solutions to large-scale and data-intensive inverse problems are ill-posedness of the problem, large dimensionality of the parameters, and the complexity of the model constraints. In this talk we discuss efficient methods for computing solutions to dynamic inverse problems, where both the quantities of interest and the forward operator may change at different time instances. We consider large-scale ill-posed problems that are made more challenging by their dynamic nature and, possibly, by the limited amount of available data per measurement step. In the first part of the talk, to remedy these difficulties, we apply efficient regularization methods that enforce simultaneous regularization in space and time (such as edge enhancement at each time instant and proximity at consecutive time instants) and achieve this with low computational cost and enhanced accuracy Pasha et al. (2021). In the remainder of the talk, we focus on designing spatial-temporal Bayesian models for estimating the parameters of linear and nonlinear dynamical inverse problems Lan et al. (2022). Numerical examples from a wide range of applications, such as tomographic reconstruction, image deblurring, and chaotic dynamical systems are used to illustrate the effectiveness of the described approaches.

#### **References:**

M. Pasha et al. (2021) Efficient edge-preserving methods for dynamic inverse problems. arXiv preprint arXiv:2107.05727.

S. Lan et al. (2022) Bayesian SpatioTemporal Modeling for Inverse Problems. In preparation.

## Dimensionality Reduction and Clustering of High-Dimensional Sparse Data with Heavy-tailed Variables and its application in gene expression data analysis

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Heavy-tailed high-dimensional data with different tail indices are common in practice, ranging from disease prediction, gene expression analysis, and risk management. Standard and existing measures of dependence do not account for the variety in tail behavior; therefore, proper measures of association with efficient estimators are required for variable selection and dimensionality reduction of heavy-tailed data.

We propose an efficient non-parametric estimator for measure of association between two heavy-tailed random variables with different tail indices and obtain its asymptotic distribution. In addition, since eigenvalues of the sample covariance matrix are not interpretable and informative when covariance matrix does not exist, we propose a new linear dimensionality reduction method as an alternative to PCA based on extended codifference. Our approach takes the tail behavior into account and returns modified eigenvalues. Finally, we provide simulation studies to compare the efficiency of linear dimensional reduction based on PCA and our novel method and apply extended codifference to clustering of single-cells based on their RNA-seq expression to identify cell types in adipose tissue.

## PhyloTransformer: A Self-supervised Discriminative Model for Mutation Prediction Based on a Multi-head Self-attention Mechanism

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Although coronaviruses have RNA proofreading functions, a large number of variants still exist as quasispecies. Identified coronaviruses might just be the tip of the iceberg, and potentially more fatal variants of concern (VOCs) may emerge over time. These VOCs may exhibit increased pathogenicity, infectivity, transmissibility, angiotensin-converting enzyme 2 (ACE2) binding affinity, and antigenicity, causing an increased threat to public health. In this article, we developed PhyloTransformer, a Transformer-based self-supervised discriminative model, which can model genetic mutations that may lead to viral reproductive advantage. We trained PhyloTransformer on 1,765.297 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) sequences to infer fitness advantages, by directly modeling the amino acid sequence mutations. PhyloTransformer utilizes advanced techniques from natural language processing, including the Fast Attention Via positive Orthogonal Random features approach (FAVOR+) and the Masked Language Model (MLM), which enable efficient and accurate intra-sequence dependency modeling over the entire RNA sequence. We measured the prediction accuracy of novel mutations and novel combinations using our method and baseline models that only take local segments as input. We found that PhyloTransformer outperformed every baseline method with statistical significance. In order to identify mutations associated with altered glycosylation that might be favored during viral evolution, we predicted the occurrence of mutations in each nucleotide of the receptor binding motif (RBM) and predicted modifications of Nglycosylation sites. We anticipate that the viral mutations predicted by PhyloTransformer may identify potential mutations of threat to guide therapeutics and vaccine design for effective targeting of future SARS-CoV-2 variants.

## Estimation and Simulation for Multivariate Tempered Stable Distributions

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We introduce a methodology for the simulation and parameter estimation of multivariate tempered stable distributions with an emphasis on the bivariate case. Our approach is based on an approximation due to a discretization of the spectral measure. It is then applied to two bivariate financial datasets related to exchange rates. The first is comprised of exchange rates between standard currencies, while the second is based on exchange rates related to cryptocurrencies. Our approximation results hold for a wide class of multivariate infinitely divisible distributions.

### Sensitivity and Bifurcation Analysis of Tuberculosis Progression

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Mycobacterium tuberculosis infection features various disease outcomes: clearance, latency, active disease, and latent tuberculosis infection (LTBI) reactivation. Identifying the decisive factors for disease outcomes and progression is crucial to elucidate the macrophages-tuberculosis interaction and provide insights into the apeutic strategies. To achieve this goal, we first model the disease progression as a dynamical shift among different disease outcomes, which are characterized by various steady states of bacterial concentration. The causal mechanisms of steady-state transitions can be the occurrence of transcritical and saddle-node bifurcations, which are induced by slowly changing parameters. Transcritical bifurcation, occurring when the basic reproduction number equals to one, determines whether the infection clears or spreads. Saddle-node bifurcation is the key mechanism to create and destroy steady states. Based on these two steady-state transition mechanisms, we carry out two sample-based sensitivity analyses on transcritical bifurcation conditions and saddle-node bifurcation conditions. The sensitivity analysis results suggest that the macrophage apoptosis rate is the most significant factor affecting the transition in disease outcomes. This result agrees with the discovery that the programmed cell death (apoptosis) plays a unique role in the complex microorganism-host interplay. Sensitivity analysis narrows down the parameters of interest, but cannot answer how these parameters influence the model outcomes. To do this, we employ bifurcation analvsis and numerical simulation to unfold various disease outcomes induced by the variation of macrophage apoptosis rate. Our findings support the hypothesis that the regulation mechanism of macrophage apoptosis affects the host immunity against tuberculosis infection and tuberculosis virulence. Moreover, our mathematical results suggest that new treatments and/or vaccines that regulate macrophage apoptosis with weakening bacillary viability and/or promoting adaptive immunity could have therapeutic value.

#### **Reference:**

W. Zhang, L. Ellingson, F. Frascoli, J. Heffernan (2021). An investigation of tuberculosis progression revealing the role of macrophages apoptosis via sensitivity and bifurcation analysis. *Journal of Mathematical Biology* 83(3): 1–32.

#### The Impact of Network Heterogeneity on the Spread of Infectious Diseases

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The problem of understanding how disease can spread, and subsequently lead to an outbreak (epidemic or endemic) in a heterogeneous host population, has brought the attention of both mathematicians and epidemiologists. In this poster, we revisit a multi-patch SIS model proposed by Allen et al. (2007) and derive a new expansion for the network disease growth rate. The first term in the expansion represents the average of patch disease growth rates (agreeing with the results of Allen et al.), while the second term incorporates a generalized inverse matrix, which can be regarded as a new index for network heterogeneity. Specifically, we apply this new index to illustrate the impact of hotspot arrangements on the network disease.

#### **Reference:**

L.J.S. Allen, B.M. Bolker, Y. Lou, A.L. Nevai (2007). Asymptotic profiles of the steady states for an SIS epidemic patch model. *SIAM Journal on Applied Mathematics*, 67(5):1283–1309.