
Applications of Dynamical Systems in Biology

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BELAL ABUELNASR, University of Waterloo

Effects of Diabetes on Renal Calcium Homeostasis

We present a model of the nephron tubule, accounting for renal epithelial solute reabsorption. This renal epithelial transport model was employed to investigate a variety of conditions and illnesses that significantly impact renal function, such as diabetes. This model was recently improved and currently accounts for 17 solutes, including calcium. We employ this model to study diabetes with a focus on diabetic renal calcium homeostasis. In particular, we investigate seemingly contradicting experimental findings in regard to renal calcium transport in diabetes. We also use the model to investigate the effects of diabetic treatments on calcium homeostasis.

SUE ANN CAMPBELL, University of Waterloo

Distributed Time Delay and Synchronization in a Neural Mass Model

We consider a neural field model for a brain network which is a network of Wilson-Cowan nodes with homeostatic adjustment of the inhibitory coupling strength and time delayed, excitatory coupling. Without time delay, the system has been shown to exhibit rich dynamics including oscillations, mixed-mode oscillations, and chaos. We show how synchronization of the nodes depends on both the connectivity structure of the network and the attributes of the distribution of time delays in the connections between nodes. We show that Hopf bifurcations induced by the excitatory coupling, the connectivity structure and the delay lead to different patterns of phase-locked oscillations, either synchronized or desynchronized. Finally, we study how the mean and variance of the distribution affect the results.

ERIC CYTRYNBAUM, University of British Columbia

Spatiotemporal patterning in reptile tooth replacement

For over a century, the development and replacement of reptile teeth has been of interest in comparative anatomy and evolutionary biology due to the prevalence of teeth in the fossil record and, more recently, for understanding spatiotemporal patterning in developmental biology as well as the fundamentals of tooth replacement for a clinical context. In collaboration with the Richman Lab (UBC Dentistry), we are using the Leopard Gecko as a model organism to understand the mechanisms underlying the regular and long-lasting spatiotemporal patterns of tooth replacement seen in many polyphyodonts. I will describe the data and our implementation and analysis of several mechanisms that have been proposed in the past to explain the observations. Finding shortcomings in these models, I will describe a new model consisting of phase oscillators coupled by a diffusing inhibitor which does better at explaining the data.

QI DENG, York University

Uncovering the impact of infection routes on within-host MPXV dynamics: insights from a mathematical modeling study

The unprecedented mpox outbreak in non-endemic regions during 2022-2023, which has seen a recent resurgence in late 2023-2024, poses a significant public health threat. Despite its global spread, the viral dynamics of mpox infection and the specific characteristics driving these outbreaks remain insufficiently explored. We propose mathematical models to examine the interactions between host immune responses and the virus across three distinct infection routes (intravenous, intradermal, and intrarectal). The models are calibrated using viral load data from macaques infected through each of these three infection routes. Subsequently, we calculate the infectiousness of each infected macaque, finding that the proportion of presymptomatic infectiousness is highest in those infected via sexual contact, followed by skin-to-skin contact. These observations demonstrate that close contact during sexual activity is a significant route of viral transmission, with presymptomatic spread playing a crucial role in the 2022-2023 multi-country outbreak and potentially also in the 2023-2024 multi-source outbreak. Leveraging

model predictions and infectiousness data, we assess the impact of antiviral drugs on interventions against mpox infection. The results suggest that early administration of antiviral drugs can reduce peak viral loads, even in individuals with compromised immunity.

NICOLAS DOYON, Laval University

Using the Finite Element method to solve the Poisson Nernst-Planck equations in neural structures

Systems of ordinary differential equation are often used in models of computational neuroscience. While this is appropriate when the spatial dimension is neglected or when the geometry is greatly simplified, this formalism is not well suited to describe complex spatial structures in which case one has to rely on systems of partial differential equations.

In neural structures, the concentration of ionic species and the electric potential evolve in an intertwined manner according to the Poisson-Nernst-Planck system of equations. Solving this system provides the evolution of the distribution of the electric field and ionic concentrations without having to rely on oversimplifying assumptions. However, solving these equations poses many methodological challenges as there is a trade-off between computational cost and accuracy.

Except for very simple geometries, the spatial domain has to be divided into a mesh or a grid on which an approximate solutions can be computed. However, to best way to do this is unclear as many numerical approaches are available. We apply the finite element method with second order elements to two typical structures: a single node of Ranvier and a dendritic spine. We show that this improves the quality of the solution when compared to simpler approaches and that the solutions can be computed at a reasonable numerical cost.

KATHARINE FAULKNER, University of British Columbia

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.

KELSEY GASIOR, University of Notre Dame

The Impact of Dynamical System Nondimensionalization on Sensitivity Analysis when Modeling the Epithelial Mesenchymal Transition

The epithelial mesenchymal transition (EMT) is a process that allows carcinoma cells to lose their adhesivity and migrate away from a tumor. Further, cells can maintain this invasiveness after they leave their original microenvironment, suggesting that there is an underlying bistable switch. We developed a mathematical model that examined the relationships between E-cadherin and Slug and their responses to tumor-level factors, such as cell-cell contact and TGF- β . Phenomenological model behavior was derived from biological experiments and, ultimately, this model showed how cells at different positions within a tumor can use exogenous factors to undergo EMT. However, the nonlinear dynamics and estimated model parameters make it challenging to analyze and understand what parameters contribute to the observed E-cadherin and Slug changes. Thus, we turn to sensitivity analysis. This work seeks to understand the true impact of commonly used mathematical techniques on dynamical systems, such as nondimensionalization, on sensitivity analysis results. The global sensitivity analysis Latin Hypercube Sampling (LHS) and Partial Rank Correlation Coefficient (PRCC) was used on the original E-cadherin-Slug model, as well as seven different possible nondimensionalized versions. By comparing these eight different iterations against each other, this work shows that the issues from performing sensitivity analysis following nondimensionalization are two-fold: (1) nondimensionalization can obscure or exclude important parameters from in-depth analysis and (2) how a model is nondimensionalized can, potentially, change analysis results. Ultimately, this work cautions against using model nondimensionalization prior to sensitivity analysis if the subsequent results are meant to guide future experiments.

DONGLIN HAN, University of Alberta

Retrospective estimation of proportion of total infections of COVID-19 during the first wave in Alberta

Mathematical modeling has been extensively used during the COVID-19 pandemic to project the spatial and temporal trend of the transmission and spread of the infection. However, earlier model projections were overestimated due to factors such as limited data and understanding of the virus at the beginning of the pandemic, rapidly evolving situations, and changes in human behavior. After almost three years of the pandemic, with all the medical knowledge we have gained of the SARS-Cov-2 virus and its variants, information on the public health measures that were implemented, and the epidemiological and public health data on the pandemic that are available, can we use mathematical models to retrospectively estimate the proportion of a population that were infected during a COVID-19 wave? Our study aimed to give an affirmative answer to this question, by demonstrating how simple mathematical models of COVID-19 of SIR type can be used to produce estimations of the proportion of infected population during the first COVID-19 wave in the Province of Alberta, Canada, during March-May of 2020. We analyzed daily new COVID-19 case and testing data during the period from March 5 - June 1, 2020 from Alberta Health and incorporated information on changes in public health measures related to COVID-19, such as social gathering restrictions, school closures, testing policies, quarantine and isolation, and contact tracing, to ensure accurate reflection in our model. Our modeling approach was also adapted to provide dependable long-term model projections for subsequent COVID-19 waves.

MERLIN PELZ, University of Minnesota, Twin Cities

Synchronized Memory-Dependent Intracellular Oscillations in Compartmental-Reaction Diffusion Systems

The Kuramoto model has been used in the last decades to gain insight into the behaviour of coupled discrete oscillators, as it is simple enough to be analyzed and exhibits a breadth of possible behaviours, such as synchronization, oscillation quenching, and chaos. However, the question arises how one can derive precise coupling terms between spatially localized oscillators that interact through a time-dependent diffusion field. We focus on a compartmental-reaction diffusion system with nonlinear intracellular kinetics of two species inside each small and well-separated cell with reactive boundary conditions. For the case of one-bulk diffusing species in \mathbb{R}^2 , we derive a new memory-dependent integro-ODE system that characterizes how intracellular oscillations in the collection of cells are coupled through the PDE bulk-diffusion field. By using a fast numerical approach relying on the “sum-of-exponentials” method to derive a time-marching scheme for this nonlocal system, diffusion induced synchrony (in-phase, anti-phase, mixed-mode etc.) is examined for various spatial arrangements of cells. This theoretical modelling framework, relevant when spatially localized nonlinear oscillators are coupled through a PDE diffusion field, is distinct from the traditional Kuramoto paradigm for studying oscillator synchronization on networks or graphs. It opens up new avenues for characterizing synchronization phenomena associated with various discrete oscillatory systems in the sciences, such as quorum-sensing behaviour. (This is joint work with Michael J. Ward.)

SPANDAN SENGUPTA, University of Toronto

Using a Population Rate Model of the CA1 Hippocampus to examine cell-type specific contributions to theta-gamma coupled rhythms

The rodent hippocampus is an extensively studied brain region expressing well-defined rhythmic activities with functional and behavioural correlates. The co-expression of theta (3-12 Hz) and gamma (20-100 Hz) rhythms may represent a general coding scheme and particular changes in these coupled rhythms occur in disease states.

We develop a population rate model of the CA1 hippocampus that combines excitatory pyramidal cells and three distinct inhibitory cell types (bistratified cells, PV-expressing and CCK-expressing basket cells), that were found to be essential for theta-gamma coupled rhythms. We use a combination of theoretical and numerical analyses to examine specific contributions by cell types and subcircuits.

We find CCK-expressing basket cells initiate coupled rhythms and regularise theta; PV-expressing basket cells enhance both theta and gamma rhythms; pyramidal and bistratified cells govern the generation of theta rhythms, and PV-expressing basket and pyramidal cells play dominant roles in controlling theta frequencies. We use these insights to predict a two-stage process by which theta-gamma coupled oscillations may arise in generalisable circuit motifs of excitatory and inhibitory cell types.

ADAM STINCHCOMBE, University of Toronto

A mathematical model for the role of dopamine-D2 self-regulation in the production of ultradian rhythms

Ultradian behavioural rhythms are highly-flexible oscillations in goal-directed behaviour with periods shorter than a day. They remain mysterious in both their biochemical mechanisms and their functional significance, but are generally believed to be a reflection of neural dynamics. We propose that D2 autoreceptor-dependent dopamine self-regulation in the midbrain-striatal synapses gives rise to ultradian rhythmicity. We express this hypothesis in an ordinary differential equation based mathematical model in a dual-negative feedback-loop structure. Numerical integration and bifurcation analysis shows that the oscillations have a flexible and parameter-sensitive period in agreement with experimental observation. The model also demonstrates the masking-entraining effects of circadian (approximately 24 hour) regulation on ultradian rhythms and the rapid-resetting effect of transient excitation. This reveals the crucial role of circadian-ultradian interaction in consolidating behavioural activity and coordinating the motivation to engage in recurring, albeit not highly predictable events, such as social interactions.