Oscillations in epidemic models: the role of infection and recovery times

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Traditional epidemic models consider that individual processes occur at constant rates. That is, an infected individual has a constant probability per unit time of recovering from infection after contagion. This assumption certainly fails for almost all infectious diseases, in which the infection time usually follows a probability distribution more or less spread around a mean value. We show a general treatment for an SIRS model in which both the infected and the immune phases admit such a description. The general behavior of the system shows transitions between endemic and oscillating situations that could be relevant in many real scenarios. The interaction with the other main source of oscillations, seasonality, will also be discussed.

Can activation of latently infected cells reduce the size of the HIV reservoir?

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While antiretroviral drugs can drive HIV to undetectably low levels in the blood, eradication is hindered by the persistence of long-lived, latently infected memory CD4 T cells. Immune activation therapy aims to eliminate this latent reservoir by reactivating these memory cells, exposing them to removal by the immune system and the cytotoxic effects of active infection. In this paper we develop a mathematical model that investigates the use of immune activation strategies while limiting virus and latent class rebound. Our model considers infection of two memory classes, central and transitional CD4 T cells and the role that general immune activation therapy has on their elimination. Further, we incorporate ways to control viral rebound by blocking activated cell proliferation through anti proliferation therapy. Using the model we provide insight into the control of latent infection and subsequently into the long term control of HIV infection.

Optimal vaccine procurement strategy for smallpox epidemic

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In this study, epidemiological modeling is used to develop optimal order policy for vaccine requirements for an anticipated epidemic or pandemic attack. Based on a compartmental model for the dispersion of smallpox virus, we consider vaccination as the main control policy in addition to hospitalization and quarantine. Solution to a set of ordinary differential equations is used to estimate the need for vaccines for two different population sizes. Assuming zero initial stock level for smallpox vaccines, we propose a minimum cost vaccine procurement strategy by determining optimal order quantity and order timing to stop the dispersion of epidemic as early as possible. Dynamic programming is used to solve the single commodity inventory model under deterministic time varying demand rate.

The stability analysis and impact of predator mortality rate on age-structured models

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This paper analyzes the effects of an age-structured prey-predator system where the prey has two stages, juvenile and adult. Three different models are used to evaluate the benefits of this structure with regards to predator mortality rate and stability of the system. We assessed how various parameters for prey growth rate and death rate affected each model and we determined necessary conditions for stability in all cases. The focus of this paper is to find the conditions necessary to ensure asymptotic stability of the equilibrium point where both the predator and prey can co-exist. More specifically, we demonstrate how the importance of predator mortality rate changes in each system.
Dynamics of evolution in two-patch ecological models

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In most habitat selection models in theoretical ecology, one assumes that organisms tend to move towards areas that locally maximize organisms' fitness. It remains unclear, though, in the presence of realistic constraints such as errors in habitat assessment and various costs, which general movement strategies might actually result in higher fitness and thus be termed adaptive. We study a single-species, two-patch habitat selection model and compute, analytically, a set of optimal information-use strategies. These strategies use both fitness-based and habitat-based information. We demonstrate that these strategies are evolutionarily stable and convergent by applying tools from adaptive dynamics and basic linear stability theory. Furthermore, we show that in the presence of certain types of costs, an organism can maximize its fitness by ignoring information about fitness in favor of acting upon more proximate habitat cues.

 Mathematical model for mutation acquisition in tumorigenesis

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Most tissues consist of three classes of cells: stem cells, transit-amplifying progenitor cells, and differentiated cells. Many tumors also have a hierarchical organization, with the bulk of the tumor composed of relatively differentiated short-lived cells with a limited replicative potential. Tumors are thought to be maintained by a small subpopulation of cancer stem cells (CSC), which have the capacity to proliferate indefinitely, and drive tumor growth. It is unclear whether CSCs originate from stem cells or from de-differentiated mature cells. We consider a hybrid stochastic deterministic model of mutation acquisition in stem cells and their progeny. We study the effects of competition between cells both at the stem cell level (in a stochastic model) and the progenitor level (in an age structured PDE model), as well as the effects of de-differentiation of progenitor cells to stem-cell like state. We give estimates on the necessary division and mutation rates to maintain a stable cohort of mutant transit-amplifying cells due to progenitor mutations alone. However, to obtain unlimited growth, de-differentiation from progenitor to stem cell state is essential. Interestingly, effects of de-differentiation only become important once homeostasis, which limits the number of cells in the stem cell pool, is lost.

 Further analysis on high order singularities of LKE model

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In this paper, a novel two-dimensional Lotka-Volterra type model that incorporates chemical heterogeneity of the grazer-producer system is further studied. Given the differential property of the digestion rate function, we verified the type of high order equilibriums in this model and discuss the possible number of inner equilibriums in the model. A sufficient condition to support the existence of the limit cycle in the system was also given using Hopf bifurcation theory.

 Hierarchal inductive process modeling and analysis

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Understanding the Phytoplankton dynamic in the Ross Sea Polynya may yield useful knowledge in the search for solving the worlds rising carbon dioxide levels. Modeling such dynamics is a very lengthy and tedious process that can be helped with the use of computational tools like HIPM. This system relies on knowledge that is already available, in the shape of time series data and process library, to construct and then evaluate these models. In this research models were ranked by sum of squared error, from lowest to highest. The lowest being the best t model. Some of the questions that arise from the use of HIPM are about the amount and value of the time series provided to the software, from which we formulated two hypotheses. Will having more time series better the output of the system? Will time series for different variables provide different quality of output? Through 31 experiments and mathematical analysis, we began to answer these questions. The computational result showed us that our first hypothesis does not always hold true, which is thought to be because of the way the fit is measured. On the other hand the mathematical analysis showed us many variations, over all the experiments, in the zooplankton equation structure which can be indication that the process library needs to be better defined and that the system needs to take into consideration not only
Phaeocystis antarctica phytoplankton species but also diatoms. This thesis provides the start to an answer for this hypothesis but further research is still needed.

The importance of stochasticity and safety nets in breaking disease-induced poverty traps

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Deterministic and stochastic models are applied to investigate feedback between infectious diseases and poverty. It is shown that economic development in deterministic models requires significant external changes to the initial conditions, or a change in the parametric structure of the system. Therefore, vicious cycles of disease and poverty (disease-induced poverty traps) arising from deterministic models lead to more limited policy options. In contrast, it is demonstrated that there is always some probability that a population will escape or fall into a poverty trap in stochastic models. A “safety net”, defined as an externally enforced minimum level of health or economic condition can guarantee ultimate escape from the poverty trap, even when it is set within the basin of attraction of the poverty trap or implemented only as an economic or health care intervention. Based on the analysis of the stochastic model, the following two economic and public health intervention questions are answered: (i) Is it more effective to provide health care or income/income generating resources to enable populations to escape from poverty traps? (ii) How long will it take a population that is caught in a poverty trap to become developed when the initial conditions are reinforced by safety nets?

A note on age-character-dependent model in population dynamics

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We consider a linear time continuous age and character dependent model of 1-sex population such that our character variable is body weight at birth or future body weight with age factor. We use a priori estimate and contraction mapping principle to establish existence of a weak solution.

State and parameter estimation for nonlinear models

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We present and compare efficient methods for estimating variables and parameters of systems of ordinary differential equations by adapting the model output to an observed time series from the (physical) process described by the model. In particular, optimization based methods are considered where the optimization method exploits the particular structure of the relevant cost function [1]. We apply these data assimilation methods to (chaotic) time series generated by different types of dynamical systems, including low and high dimensional chaos, delay systems, and biological cell models.[1] J. Schumann-Bischoff and U. Parlitz, State and parameter estimation using unconstrained optimization, Phys. Rev. E 84, 056214 (2011)

Mathematical model for mutation acquisition in tumorigenesis

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Transmissible spongiform encephalopathies, or prion diseases, are a group of fatal neurodegenerative disorders of humans and animals. The pathogenic process is typically associated with conformational conversion of a cellular protein, called prion or PrP\textsubscript{C}, to a misfolded isoform, called PrP\textsubscript{Sc}. The “protein-only” model asserts that this rogue PrP\textsubscript{Sc} represents the infectious prion agent, self-propagating by binding to PrP\textsubscript{C} and inducing its conversion to the abnormal PrP\textsubscript{Sc}. This scenario was quantitatively described as a nucleation-dependent amyloid polymerization. However, inconsistent results follow from this theory in comparison to in vitro polymerization experiments. Indeed although the dynamics of polymerization resemble a simple nucleus-dependent fibrillogenesis, neither the initial concentration dependence nor off-pathway hypothesis fit with completely experimental results. In order to reconcile the experimental results with the nucleus dependent polymerization, we have postulated the existence of an on-pathway step that takes place before nucleation. Here we show that micelles were formed leading to an amyloid competent isoform of the prion protein (i.e. PrP\textsuperscript{*}) necessary to engage the nucleation and then amyloid polymerization. To analyse the consequences of this proposition, we developed a quantitative model with an explicit description of the
microscopic processes, and we compared to experimental data with the predicted results. A detailed analysis of the lag phase under several conditions has been done to validate a micelle on-pathway as an explanation of amyloid dynamic. We recall here the original theoretical model and some of the main results, we show then the inconsistencies with the experiment results. We propose the new model taking the new biological assumptions of prion formation into account and compare it to experimental data. The model consists of systems of non linear differential and partial differential equations describing polymerization and fragmentation of polymers.

Modelling the effects of flagellar hook compliance on bacterial motility

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Individual-level models of swimming microorganisms vary in complexity from a single point singularity in the fluid to collections of hundreds of beads interconnected by elastic springs and arranged to resemble the shape of the modelled organism. We explore a model with an intermediate number of degrees of freedom for a bacterium propelled by turning a helical flagellum with a rotary motor. We use the boundary element method to accurately resolve the flow field around the cell body and flagellum, both of which are assumed to be rigid structures. Building on early models, which maintained a fixed axis of rotation of the flagellum relative to the cell body, we introduce an elastic connection between the two structures corresponding to the flagellar hook. The hook is modelled as a Kirchhoff rod and analysis of this system reveals distinct phases of swimming behaviour, with biologically relevant consequences, depending on the hook stiffness and motor frequency.

Numerical continuation of equilibria of cell population models with internal cell cycle

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Mathematical modelling of the cell cycle has been a subject of study for a few decades and J.J. Tyson and B. Nováč, as prominent leaders, have developed several widely studied models.

Our goal is to incorporate these realistic models in structured cell population ODE models to study the behaviour of the cells at population level and its dependence on the nutrient level. An equilibrium of this cell population model corresponds to a constant distribution of the mass of cells born per unit of time.

Numerically, the idea is to obtain the equilibrium as the fixed point of a map. We implement this map in our code as the output of a large collection of integrations over age for cells born with a given mass, followed by its implications for the consumption of nutrient. A found equilibrium can then be continued under parameter variation. This allows us to study the influence of natural parameters such as growth rate of the cells and the concentration of the nutrient.

I will give the results of our computations so far, starting with a model with a fairly simple choice for the cell cycle mechanism, and will give a look-out to further steps and challenges.

The randomness of gene expression

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The process by which the genetic code comes to life is a fundamentally stochastic process. In order to begin to quantify this randomness, this work models transcription using a population density approach. In the model, a single gene of interest fluctuates stochastically between an inactive state, in which transcription cannot occur, and an active state, in which discrete transcription events occur; and the individual mRNA molecules are degraded stochastically in an independent manner. The random dwell times in the inactive and active states are independent random variables drawn from any specified distributions. This problem can be reduced to a pair of integral equations for the unknown probability densities immediately after a gene switch. Previously, this sort of model with exponential dwell times has been successful in explaining experimental estimates of the distribution of random mRNA copy number within a population of isogenic cells. I will present efficient numerical methods for computing steady-state mRNA distributions, an analytic formula for the mRNA autocovariance function, and a procedure for model identification based on laboratory data.

It is hoped that these theoretical advancements will lead to a better understanding of stochastic gene expression, in theory and experimentally.
Modeling the nonlocal dispersal of invasive plant species in heterogeneous landscapes

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Mathematical models for the spread of invading organisms typically utilize population growth and dispersal dynamics in an attempt to predict an expected value of the population distribution at some point in the future. These models often ignore uncertainty in initial conditions, neglect ecological heterogeneity in the landscape, and even misrepresent the underlying stochastic growth and dispersal processes they are supposed to represent. Assuming the underlying stochastic process for the population dynamics is a contact birth process, we derive a deterministic model for the probability of species presence as a function of time and space. By abandoning any attempt to model the size or internal population dynamics of a population, our model focuses on the more realistic goal of species presence prediction resulting in an equation derived directly from the stochastic process that naturally incorporates heterogeneity in the landscape, as well as uncertainty in initial conditions.

Complex macroscopic behavior in systems of phase oscillators with adaptive coupling

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A major difficulty in the study of complex systems (e.g., neural processing and cell function) is overcoming the common disconnect between simple microscopic and complex macroscopic dynamics referred to as emergence. Utilizing recent dimension-reduction techniques for large systems of coupled phase oscillators exhibiting bistability, we analyze complex macroscopic behavior arising when the coupling is allowed to evolve slowly as a function of either macroscopic or local system properties. For example, we observe macroscopic excitability and intermittent synchrony (i.e., as observed for the classical order parameter) in a system of time-delayed Kuramoto oscillators with Hebbian and anti-Hebbian learning. We highlight the robustness of our analysis by considering systems with increasing complexity, including time-delayed oscillators with adaptive network structure and community interaction, as well as a system with bimodal frequency distribution.