IC1

The Neurodynamics of Simple Decisions: Drift-Diffusion Equations As Models for Single Brains, and for Group Behaviors

I will describe how simple stochastic differential equations can model evidence accumulation and decision making, sketching their derivation from biophysically-detailed models of spiking neurons, and relating them to the sequential probability ratio test from statistical decision theory. This connection yields a speed-accuracy tradeoff that optimizes rewards in a simple two-alternative perceptual decision task. I will compare the resulting model predictions with human behavior and advance explanations for failures to optimize. Finally, I will show how drift-diffusion models can be extended to describe choices in a social gambling task in which players receive limited information regarding other group members' choices and rewards. The talk will draw on joint work with Fuat Balci, Rafal Bogacz, Jonathan Cohen, Philip Eckhoff, Deborah Prentice, Andrea Nedic, Patrick Simen, Damon Tomlin, KongFatt Wong-Lin and Miriam Zacksenhouse Research supported by NIMH and AFOSR.

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IC2

Using Optimization Models in Public Forest Management

Mathematical programming models have been used in public forest management for forty years. Through the 1970's–80's, linear programming models used for scheduling timber harvests were most common. The past two decades have seen an explosion of growth in breadth and depth in this field. A wide range of natural resource problems are now being addressed with more sophisticated optimization techniques. These applications often function like "cottage industries" as funding opportunities and technical expertise remain spotty. While national investments continue on mixed-integer linear applications aimed at large-scale problems such as reducing wildfire suppression costs, increasing success on smaller problems could continue to generate demand for optimization methods.

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IC3

Stirring Tails of Evolution

One of the most fundamental issues in biology is the nature of evolutionary transitions from single cell organisms to multicellular ones. Not surprisingly for microscopic life in a fluid environment, many of the processes involved are related to transport and locomotion, for efficient exchange of chemical species with the environment is one of the most basic features of life. This is particularly so in the case of flagellated eukaryotes such as green algae, whose members serve as model organisms for the study of transitions to multicellularity. In this talk I will summarize recent theoretical and experimental work addressing a number of interrelated aspects of evolutionary transitions in the Volvocine green algae, which range from unicellular *Chlamydomonas* to *Volvox*, with thousands of cells. Phenomena to be discussed include allometry of nutrient uptake, phenotypic plasticity, flagellar synchronization, hydrodynamic bound states, and the dynamics of adaptive phototaxis.

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IC4

Mechanics of Cell Migration

Animal cells crawl on surfaces using the lamellipod – flat dynamic network of actin polymers enveloped by the cell membrane. Recent experiments showed that the cell geometry is correlated with speed and with actin dynamics. I will present mathematical models of actin network self-organization and viscoelastic flow explaining these observations. According to this model, a force balance between membrane tension, pushing actin network and centripetal myosin-powered contraction of this network can explain the cell shape and motility. In addition, I will discuss Darci flow of cytoplasm and its role in the cell movements.

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IC5

How to Model a Virus Infection

I will discuss the art of modeling the kinetics of viral infections within a single host. I will show how modeling can give insight into the underlying biology of the virus and hosts response to infection. I will draw on examples from HIV and hepatitis C virus (HCV) infection and treatment. I will end with a discussion of recent data collected from HCV infected patients that call into question some of the premises we have built into our models for the10 years. I will also discuss the need for new generations of models that are in some cases need to be multiscale, spatial, age-structured or stochastic

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IC6

Discrete Dynamic Modeling of Signal Transduction Networks

Modeling the dynamics of complex biological systems is challenging even when well-established biochemical frameworks are applicable. In the case of regulatory and signaling systems that include heterogeneous components and interactions, and/or are sparsely documented in terms of quantitative information, modeling is often thought impossible. This talk will argue for the usefulness of a discrete dynamic framework in incorporating qualitative interaction information into a predictive model. I will present examples of predictive discrete dynamic models of plant drought signaling, interactions between bacteria and a mammalian immune system, and survival signaling in cytotoxic T cells. All models are based on a reconstruction of the network of interactions among several dozen components and on qualitative interaction and activity information. The models make predictions regarding the key nodes

whose (in)activity is necessary for reaching a desired outcome, such as stomatal opening, the clearance of the bacteria, or apoptosis of T cells. Several of these predictions were validated experimentally. The success of the models indicate that network-based discrete dynamic modeling is a promising framework that allows system-level analysis and predictions that would not be feasible using traditional methods.

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IC7

Mathematics and Brain: Filling Some of the Blanks Between Biochemistry and Bioimaging

Understanding the functioning of the brain remains one of the big challenges of modern science. Functional imaging methodologies provide various windows to the cerebral activity, and mathematics has a central role in the development and improvement of the different modalities, from modeling of the noise to addressing the severe ill-posedness of some of the methods, in addition to providing means to incorporate additional, complementary information in the imaging algorithms. Different imaging modalities measure different aspects of brain activity. Some modalities are sensitive to electromagnetic neuronal activity, some measure metabolic activity while others are measure changes in cerebral blood flow. In order to understand the interconnections among them, and ultimately what we can infer about brain activity, it is necessary to have a mathematical model that combines these different aspects. This talk will address challenges related to functional imaging modalities, outlining algorithms designed to cope with the ill-posedness of the underlying problems, and outline an ongoing modeling effort aiming to understand the connection between neuronal activity, metabolism and hemodynamics in living brain.

Daniela Calvetti
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IC8

Targets to Populations to Individuals

Pharmaceutical clinical studies have a high failure rate due to complexity and a limited ability to predict outcomes earlier in the R&D process. Large scale models of human physiology have been built to predict the performance of pharmaceutical targets and compounds before clinical studies have been performed. These models encompass both target physiology as well as clinical measures, enabling the quantitative analysis of targets and compounds on clinical outcomes. Populations of virtual patients are developed to be consistent with existing clinical data sets, then simulated to generate population-level analyses of new therapeutics. These simulations are mined to identify biomarker panels for patient response and non-response. Examples will be provided of models, populations, and analyses along with a discussion of where this ultimately leads: personalized medicine.

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IP0

W.T. and Idalia Reid Prize in Mathematics Lecture: William T. and Idalia Reid: His Mathematics and Her Mathematical Family

The W. T. and Idelia Reid Prize in Mathematics was established in 1993 by SIAM and is funded by an endowment from the late Mrs. Idalia Reid to honor the memory of her husband Dr. W. T. Reid and his love of mathematics. Over time we often forget the people whose names are attached to the prizes that are periodically awarded for outstanding research or other contributions to our profession. Since I am the first of Professor Reid's students to be honored by this Prize, it is only fitting that I take this opportunity to review some of Dr. Reid's contributions to mathematics and Mrs. Reid's support of his mathematical colleagues and students.

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IP0

Julian Cole Prize Lecture: Mathematical Modelling of Tissue Growth

Approaches to the continuum modelling of biological tissue growth will be described, with specific emphasis on (i) novel aspects of the resulting PDE formulations that arise from the biological contexts to which they are intended to apply and (ii) the role of singular-perturbation methods in elucidating model properties. The talk will focus on recent developments in the application of multiphase continuum-mechanics descriptions, particularly in describing the growth of engineered tissue within a porous scaffold.

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IP0

AWM-SIAM Sonia Kovalevsky Lecture: Mixing It Up: Discrete and Continuous Optimal Control for Biological Models

This presentation will illustrate optimal control methods applied to several types of models, including a mixture of discrete and continuous features. The applications range from a discrete model for cardiopulmonary resuscitation to partial differential equation models for rabies in raccoons. Detailed results will be given for harvesting in a PDE fishery model that answer the question: Does a marine reserve occur when maximizing harvest yield?

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IP0

John Von Neumann Lecture - Algebra: From Linear to Non-Linear

This lecture will discuss recent applications of methods from abstract algebra in modeling and solving non-linear problems across the mathematical sciences. Techniques

that are familiar from linear algebra have natural extensions in the non-linear world of algebraic geometry, whose recent advances are now transforming our thinking about problems arising in domains such as convex optimization, statistical inference and computational molecular biology.

Bernd Sturmfels
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IP0

I.E. Block Community Lecture: The Geometry of Music

In my talk, I show how to translate the language of elementary music theory into that of contemporary geometry. It turns out that concepts such as "chord" and "chord type" are naturally represented by points in geometrical spaces known as "orbifolds." Understanding these spaces can help us to understand general constraints on musical style, as well as the inner workings of specific pieces. For example, we will see that Mozart, Chopin, and Schubert made very sophisticated use of a necklace of four-dimensional cubes representing four-note chords. The talk will be accessible to non-musicians and will exploit interactive 3D computer models that allow us to see and hear music simultaneously.

Dmitri Tymoczko
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JP1

The Dynamics of Obesity

The past two decades have seen a surge in the incidence of obesity in the developed world. Changes in body weight that can lead to obesity are known to result from imbalances between the energy derived from food and the energy expended to maintain life and perform physical work. However, quantifying this relationship has proved difficult. Here, I will show how simple concepts from dynamical systems can be used to provide a general quantitative description of how body weight will change over time. The model can then be used to answer open questions (and dispel some myths) regarding weight loss and gain and provide an explanation for the American obesity epidemic.

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MS0

Stochastic and Chance-Constrained Programming

An introduction to stochastic mathematical programming formulations will be given. Scenario-based approximations and sample-based estimations will be discussed as approaches to solving such problems. An example of a habitat restoration model that is discrete in both time and space will be presented.

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MS0

Stochasticity

Input your abstract, including TeX commands, here. The abstract should be no longer than 75 words. Only input the abstract text. Don't include title or author information here.

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MS0

Stochasticity - Part II

Input your abstract, including TeX commands, here. The abstract should be no longer than 75 words. Only input the abstract text. Don't include title or author information here.

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MS0

Optimal Control of Discrete Models

An introduction to the idea of optimal control of discrete time models will be given. The steps in formulating (choosing goal) and solving such problems will be discussed, including that the order of events in a discrete time model is crucial. An iterative forward-backward sweep method for numerical solutions of such problems will be included. An example of an epidemic model for rabies in raccoons, which is discrete in both time and space, will also be presented.

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MS1

Control Mechanism and Modeling of the Energy Metabolism

The glucose metabolism is a tight regulated system providing energy in humans. Dysfunctions of this system may lead to pathologies like obesity or diabetes. Mathematical methods are therefore established tools to simulate, control, and identify imbalances in the energy metabolism. We will present basic ideas and new research directions in physiology, mathematical modeling, control, and estimation methods.

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MS1

Impact of Environmental and Life-style Factors on Body Weight Regulation, as Assessed by a System Dynamics Model

Weight stability requires reaching a steady-state for which all the nutrients consumed are oxidized. Since the body's

fuel reserves influence the composition of the fuel mix oxidized, body composition will drift until the fuel mix oxidized matches the diet. A two-compartment (carbohydrate and fat) model shows how high dietary fat, increasing food diversity and palatability, and lower physical activity influence the expansion of the body's fat mass needed for fat oxidation to match fat intake.

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MS1

Modeling Energy Metabolism and Body Weight Change in Mice

Recently, we discovered a time-invariant curve relating body fat and fat-free masses in adult male C57BL/6 mice during weight gain and loss. Based on this discovery, we developed a mathematical model that reveals how energy expenditure and fuel selection adapt in concert with changes of food energy intake and diet composition. The model was validated by accurately predicting changes of body fat and weight under various feeding conditions in mice not used for model development.

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MS2

The Geometry of BioChemical Time

Over 25 years ago Art Winfree introduced a formalism for understanding how biological clocks can be reset. In this talk I show how a fairly simple geometry can be constructed to understand the behavior of unperturbed biological clocks. This analysis is particularly useful in determining when oscillations arise in biochemical networks, and how individual processes within these networks can regulate the oscillation's period.

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MS2

Modeling Gradient Sensing of Budding Yeast: Positive Roles for Negative Regulators

Saccharomyces cerevisiae undergo chemotrophic growth in which cells elongate in the direction of increasing pheromone concentration. We provide computational investigation of the signaling events that regulate chemotrophic growth. Our results elucidate the role of the extracellular protease Bar1 in gradient sensing. Mathematical analysis of the model for the intracellular signaling demonstrates the fine-tuned spatiotemporal dynamics through GTPase-activating proteins and the ability to generate localized oscillations in the activity of key signaling proteins.

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MS2

Harnessing Noisy Inputs: From Bistable Squid Axons to the Treatment of Infant Apneas

Abnormal neural oscillations are implicated in certain disease states, for example repetitive firing of injured axons evoking painful paresthesia and rhythmic discharges of cortical neurons in patients with epilepsy. In other clinical conditions, the pathological state manifests as a vulnerability of an oscillator to switch off, for example a prolonged pause in automatic breathing called central apnea. In this seminar I will discuss theory and experimental observations of abnormal initiation and termination of neural rhythms at the cellular, tissue and organismal levels. The findings suggest how small appropriately "tuned" noisy inputs could extinguish pathological rhythm or, conversely, could prevent dysrhythmic states. I will present experimental and clinical results on the application of these ideas to the treatment of infant apnea.

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MS2

Feedback Mechanisms in Cell Metabolism

Abstract not available at time of publication.

Michael Reed
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MS3

Title Not Available at Time of Publication

We present our recent work on modeling microbial fuel cells and the impact of various factors such as oxygen leaks and invasion of methanogens can have on these systems. The goal is to be able to quantify the potential pitfalls of these systems in order to adequately asses their commercial potential.

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MS3

Disinfection of Bacterial Biofilms and Tolerance Mechanisms

This talk will review several models of bacterial disinfection, focusing on mechanisms that provide protection to the bacteria within a biofilm. In particular, we will contrast transient protection offered by penetration limitation, differential growth rates and fluid effects with the more permanent mechanism of phenotypic variation. The aim of the talk is to discuss potential means to eliminate (hopefully in some optimal way) all bacteria within a biofilm.

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MS3

Two-Dimensional Individual-Based Model of Biofilm Growth with Continuum Eps Matrix

Biofilms are hydrated structures produced by bacteria, which adhere to a variety of surfaces in nutrient sufficient environments. Biofilms consist of bacteria enclosed in a matrix of extracellular polymeric subtracts (EPSs), which are irreversibly attached to a surface or interface. They have important consequences in a medical and industrial setting, for example, they can corrode metals, resulting a million of dollars damage, and cause infections in wound and implants.

A mathematical model of bacterial biofilm growth in two-dimensions using an Individual-Based model (IbM) is present to describe cell growth behaviour in prescribed environments. We assume that EPS is forced to move at high concentration which influence motion of bacteria and biofilm structure. Bacteria are treated as volume occupying particles that respond in various ways to the concentrations of substrates present, whereby new cellular growth requires can lead to the repositioning of neighbouring cells in order to accommodate the changes in local volume. The coupled reaction-diffusion equations for nutrient, EPS and oxygen are solved using finite-volume methods. The advantage of an IbM approach is that it can easily be extended to include multiple bacteria species with varying traits responding to multiple diffusible substrates. As an example, results are presented for a biofilm consisting of two species, which have differing tolerances to low nutrient environments.

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MS3

Effect of Biofilm Deformation on Mass Transfer and Detachment Forces

The mechanical response of the biofilm depends both on the material property of the biofilm and on the shape and morphology of biofilm-flow interface. Rheology experiments on biofilms grown under different conditions have provided differing description of the biofilm response (elastic, viscoelastic solid, viscoelastic fluid) with material parameter values varying over a wide range. In our talk, we will present the results from our simulations regarding how the detachment forces acting on the biofilm and the mass transfer to the biofilm are influenced by the different material descriptions used for the biofilm.

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MS4

Internal Degrees of Freedom in Membranes

The cell membrane is not a simple assembly of lipids and proteins. There are many internal degrees of freedom in a membrane, such as the shape of lipid molecules, the tilt direction of lipid molecules and the species of lipids and proteins in a biological membrane. Here we study two different internal degrees of freedom in membranes and their effects on the cell morphology and biological processes. Motivated by the propensity for tilt order and the common occurrence of narrow necks in the intermediate stages of biological processes such as endocytosis and vesicle trafficking, we examine how tilt order inhibits the formation of necks in the equilibrium shapes. In addition, motivated by recent experiments which showed that the mechanical properties of membranes play an important role in lipid sorting, a model is developed to study how the coupling between membrane composition and membrane bending stiffness and tension affects tubule formation in a multi-component membrane. We show that drawing a tubule from a vesicle leads to a rearrangement of composition in which the phase of higher flexibility segregates into the highly curved tubule.

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MS4

Boundary-value Problems in the Theory of Lipid Membranes

The mechanics of lipid bilayers is discussed in the context of the theory of elastic shells with fluid symmetry. New contact conditions are developed for lipid membranes interacting with curved substrates along their edges. These include the anchoring conditions familiar from liquid-crystal theory and accommodate non-uniform membranes and non-uniform adhesion between a bulk fluid or membrane and a rigid substrate. The theory is illustrated through explicit solutions and numerical simulations.

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MS4

Systematic Solvent-free Coarse-graining of Lipid Bilayers: A Success in Retaining both Computational Efficiency and Local Chemical Specificity for Mesoscopic Quantitative Simulations of Membranes

This talk will focus on systematic implicit solvent coarse-grained modeling with efforts rescuing both computational efficiency and local chemical specificity in particle-based simulations of lipid bilayers. The use of implicit solvent enables membrane simulations on large length- and time-scales at moderate computational expense. The reduced molecular friction together with a more efficient integration combine to an overall speedup of three to four orders of magnitude compared to all-atom bilayer simulations. Despite the computational speedup, much of the local chemical specificity is preserved in CG resolution.

The bonded and nonbonded interactions together with the effective cohesion mimicking the hydrophobic effect were systematically tuned by matching the structural and mechanical properties from experiments and all-atom bilayer simulations, such as saturated area per lipid, radial distribution functions, density and pressure profile across the bilayer, P2 order, etc. The CG lipid model is shown to self-assemble into a bilayer starting from a random dispersion. Its bending and stretching moduli and line tension are semi-quantitatively consistent with experiments and all-atom simulations. Simulations of POPC, DOPC and DPPC demonstrated a good parameter transferability of the CG force field from one lipid to another. Simulations at different temperatures showed the model is able to reproduce features of bilayer phase transition as well. The CG lipid model is especially useful for studies of mesoscopic membrane phenomena which nevertheless require a fair description of chemical specificity.

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MS4

Modeling Biological Membranes as Self-assembled Two-Dimensional Particle Fluids

The potentiality of two-dimensional (2D) particle-based fluid membrane models is often frustrated by the complicated multi-body inter-particle potentials needed to capture the hydrophobic interactions in the absence of explicit solvent. Here we present a one-particle-thick fluid membrane model, where each particle represents a cluster of lipid molecules. The model features an inter-particle pair potential with the interaction strength weighed by the relative particle orientations. With the anisotropic pair potential, particles can robustly self-assemble into fluid membranes with experimentally relevant properties. Despite its simple mathematical form, the model is highly tunable. Three potential parameters separately and effectively control diffusivity, bending rigidity, and spontaneous curvature of the model membrane. We demonstrate that this new model accurately predicts fluid vesicle shape transformation and naturally simulates diffusion-driven phase separation and budding with great ease. The simple mathematical form along with its comprehensive capabilities endows this model as a model system for 2D fluids.

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MS4

Adhesion of Two-component Vesicle Membranes

We study the adhesion of multi-component vesicle membrane to flat/curved substrates. By introducing a phase field function, we can distinguish the different components of the vesicle membranes, and formulate the total energy in terms of phase field function to describe the equilibrium shapes of the vesicle membranes. By numerically solving the equilibrium equations (Euler-Lagrange equations), we find a number of representative membrane shapes with a variety of parameter values. We discuss the stability of the vesicle membranes enduring the adhesion, and reveal that adhesion can promote the phase separation for the vesicle membranes.

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MS5

Using Mathematical Modeling to Understand Hepatitis C Viral (HCV) Kinetics in the Era of Direct Acting Antivirals

In the last decade mathematical models of HCV infection and treatment [(pegylated) alpha-interferon (IFN) and ribavirin] have provided insights into the dynamics of virus, host and treatment. The development of direct acting antivirals (DAA) against HCV poses new challenges along with deeper insights into HCV dynamic parameters. We will present our modeling efforts to explain various HCV kinetic profiles seen in treated patients with IFN/ribavirin/DAA taking into consideration drug pharmacokinetics and pharmacodynamics.

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MS5

HCV Viral Kinetic Modeling of Combination Treatments

In this talk, we will focus on viral kinetic modeling of interferon-based combination treatment. We describe an approach for assessing treatment efficacy of the single drugs and discuss how to test for synergism or antagonism. The model bases on an ordinary differential equation system and combines recent advances in viral kinetic modeling by including proliferation of infected cells and pharmacokinetic data of both drugs. Furthermore, an application of this model on clinical data will be sketched.

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MS5

Modeling HCV Clinical Trial Outcomes With Hy-

brid Deterministic-Stochastic Methods

We have developed a hybrid deterministic-stochastic simulation algorithm based on ODEs and the chemical master equation, both of which derive from a single set of "reactions" describing the disease and treatment. We use Monte-Carlo methods to generate cohorts of virtual patients. The simulation of treatment arms varying in dose and duration yields more realistic estimates, compared to ODEs alone, for end of treatment response (ETR), sustained virological response (SVR), and rate of relapse after treatment.

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MS5

Acute Hepatitis C Viral Kinetics in Humans: Inverse Association of Peak Viremia with Outcome

Acute hepatitis C virus (HCV) infection is associated with one of two spontaneous outcomes: resolution (clearance) or persistence, with two-thirds of untreated infections resulting in persistence. The mechanisms of clearance are poorly understood, yet they have major implications for prevention efforts since the major health effects of HCV develop in the chronic phase. We examined acutely-infected humans with acute HCV who declined treatment, finding an unexpectedly inverse association between initial level of viremia and persistence.

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MS6

Vaccinating Against HPV in a Dynamic Social Network

We develop a dynamical network model to examine the relative merits of strategies for vaccinating women against the sexually transmitted Human Papillomavirus, which can induce cervical cancer. The model community is represented as a sexual network of individuals with links dynamically created and destroyed through statistical rules based on the node characteristics. Various strategies for distributing an allotted number of doses of vaccine are tested for effectiveness in reducing the incidence of cervical cancer.

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MS6

Synchronous and Asynchronous Dynamics of Complex Neuronal Networks

A Fokker-Planck equation and its mean-field limit describe steady asynchronous and synchronously-oscillating states in neuronal networks, as well as the effects of the network architecture. For scale-free networks, the distributions of the firing rates and voltage correlations are scale free. The likelihood and temporal period of synchronous network oscillations, in which all neurons fire in unison, are captured by the Fokker-Planck description, as are differences between oscillations in all-to-all coupled and scale-free networks.

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MS6

There and Back Again: The Effect of Travel Networks on Disease Dynamics

We model motion of human populations on the large geographic scale, specifically considering population distribution and effects of an established transportation network. We distinguishes travel (with return to home) from relocation (permanent change of home)and study the effect on the dynamic social network of individuals. We focus on disease propagation along the transportation network showing how coupling between locations is affected by the various time scales (motion and disease dynamics) of the

system.

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MS6

Neuronal Network Models: The Behavior of Continuous and Discrete Stochastic Models on Different Network Topologies

We start with a current-based Integrate-and-Fire neuron model with instantaneous synaptic coupling and create equivalent Markov chain models by discretizing voltage and/or time, while keeping the mean firing rate of a single neuron constant. We connect these model neurons with real world C. Elegans neuronal network data, as well as, different random network topologies and account for excitatory neuron interactions. We investigate the interactions of the models with each network by comparing network firing rates and synchronizability.

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MS7

When are Microcircuits Well-modeled by Maximum Entropy Methods?

Recent experiments in retina and cortex have demonstrated that pairwise maximum entropy methods can approximate observed spiking patterns to a high degree of accuracy. In this talk we examine the relationship between network architecture, statistics of transmitted signals, and the order of correlation needed to explain network output in a class of simple circuits. We find that the pairwise maximum entropy fit of output spiking patterns is informative about signal statistics but not necessarily network architecture; in particular, the order of correlation cannot be used to make a common and intuitive inference about upstream projections.

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MS7

Functional Connectivity in Disassortative Scale-free Neuronal Networks

We present a study of scale-free networks of identical, conductance-based, stochastically driven, integrate-and-fire excitatory neurons. Using the mean-field approach, we show that the firing rates of neurons in scale-free networks themselves follow scale-free distribution. At the same time we show that the firing rate in such networks is strongly dependent on the degree correlation function. The analytical results are compared to the direct numerical simulations of the coupled integrate-and-fire neurons. Ultimately our analysis provides a link between the functional and anatomical connectivity of such networks.

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MS7

Coarse-grained Event Tree Analysis for Quantifying Hodgkin-Huxley Neuronal Network Dynamics

We present a method of studying the Hodgkin-Huxley (HH) neuronal network dynamics. This method is to characterize dynamic information of HH networks by using a statistical collection of spatial-temporal sequences of relevant physiological observables (such as sequences of spiking multiple neurons). This method relies on a coarse-grained projection to event trees and to the event chains that comprise these trees, and it can retain information about network dynamics that covers multiple features, swiftly and robustly. We demonstrate, through the HH neuronal networks with Poisson spike inputs, that this event tree analysis can reveal, with high reliability, information about multiple stimulus features within short realistic observation times.

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MS7

Correlation Between Spatial-frequency and Orientation-selectivity in V1 Cortex: Implications of a Network Model

We addressed how spatial frequency and orientation selectivity coexist and co-vary in Macaque primary visual cortex (V1) by simulating cortical layer 4Cα of V1 with a large-scale network model and then comparing the model's behavior with a population of cells we recorded in layer 4Cα, including the distributions of orientation and spatial frequency selectivity, the correlation between the two and others. All the results suggest that cortical inhibition provides a common mechanism for selectivity in multiple dimensions.

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MS8

Structured Juvenile Adult Models with Applica-

tion to Amphibians

We present a continuous structured juvenile-adult model which describes the dynamics of an urban amphibian population. Statistical population estimates resulting from our field data are compared to the model output using a least-squares approach. Stochastic counterparts of this deterministic model are developed and used to understand the effect of demographic stochasticity on the persistence of the population.

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MS8

Simulating Competitive Binding for HIV gp120 by Dendritic Cell Receptors

HIV gp120 binds several receptors on the surface of dendritic cells (DCs). Depending on these interactions HIV may either gain access to CD4 T cells or be degraded within DCs. To predict the outcome of these interactions we constructed a mathematical model of HIV-DC binding, analyzed the model, and show that the model reproduces several experimental observations. Based on the model we also show how HIV or DC variation may change experimental outcomes.

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MS8

Parameter Selection Methods in Inverse Problem Formulation

We discuss methods for a priori selection of parameters to be estimated in inverse problem formulations (e.g., Ordinary and Generalized Least Squares) for dynamical systems with numerous state variables and an ever larger number of parameters. We illustrate the ideas with an in-host model for HIV dynamics, which has been successfully validated with clinical data and used for prediction.

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MS8

Dynamic Models of Behavior Change in Problem Drinkers from Intensive Longitudinal Data

Advances in technology have greatly enhanced survey data collection in the behavioral sciences. Although some recent efforts have focused on how to fully exploit these rich data sets, their potential remains largely untapped. However, with most of the traditional statistical approaches it is difficult to view the observed variables as interacting, nonlinear, and mechanisms are typically not explicitly formulated. We discuss the development of dynamic system models as informed by the data, and some insights into the changes occurring in problem drinkers as they modify their behavior.

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MS9

Compact Energy Metabolism Model: Brain Controlled Energy Supply

Many mechanisms controlling the human energy metabolism still remain unidentified. We emphasize the decisive role of the brain as controller and consumer by modeling the energy metabolism in a compact dynamical system integrating energy fluxes and their control signals. As one novel characteristic, insulin is regarded as cerebral feedback signal. Hereby, our model contains the competition for energy between brain and body. The model is a step towards a systemic understanding of the energy metabolism.

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MS9

A Model of Mitochondrial ATP and Free Radical Production

Beta-cell mitochondria play a central role in glucose-stimulated insulin secretion (GSIS). Based on current data, we present a model of mitochondrial respiration, ATP synthesis, and free radical production in response to nutrient exposure. The model is consistent with a number of experimental observations. Mechanisms hypothesized to inhibit GSIS are tested and strategies for increasing GSIS while decreasing oxidative stress are suggested. The model is useful in predicting the insulin secretion rate and quantifying beta-cell function.

This work was supported by the Intramural Research Program, NIDDK, NIH.

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MS9

A Simple Mathematical Model for Weight Change

A differential equation model of weight change based on the energy balance equation is paired to an algebraic relationship between fat free mass and fat mass derived from a large nationally representative sample of recently released data collected by the Centers for Disease Control. We validate the model's ability to predict individual participants' weight change by comparing model estimates of final weight data from two recent underfeeding studies and one overfeeding study. Mean absolute error and standard deviation between model predictions and observed measurements of final weight is less than 1.8 ± 1.3 kg for the underfeeding studies and 2.5 ± 1.6 kg for the overfeeding study. Comparison of the model predictions to other one dimensional models of weight change shows improvement in mean absolute error, standard deviation of mean absolute error, and group mean predictions. The maximum absolute individual error decreased by approximately 60% substantiating reliability in individual weight change predictions. The model provides a viable method for estimating individual weight change as a result of changes in intake and determining individual dietary adherence during weight change studies.

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MS10

Evolution's Choice: Speed vs. Robustness in Feed-forward Biochemical Reaction Networks

Substructures of many biochemical reaction networks are composed of feed-forward motifs: cycle-free directed subgraphs that are statistically more prevalent in nature than among randomly generated graphs of the same size. Given two topologically non-isomorphic motifs that accomplish the same biological function, does evolution typically prefer speed/efficiency or robustness? In this lecture, we argue for the latter, using both ODE models and real data to support our claims.

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MS10

Feedback Regulation in the Human Hypothalamic-Pituitary-Thyroid Axis: Model Development and Clinical Applications

Thyroid hormone regulation is a classic example of biological feedback control, with thyroid disorders affecting more than 300 million people worldwide. We developed a physiologically based, differential equation model of the human hypothalamic-pituitary-thyroid axis, in order to address several clinical applications. The model is broken into two major components: the thyroid and brain submodels, each quantified from clinical data. We combined these two submodels to form a complete closed loop model, which we validated using additional independent clinical data. Using the closed-loop model, we address several applications in replacement thyroid hormone bioequivalence (equivalence between different brands/preparations), circadian rhythms, and thyroid cancer.

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MS10

The Motile Behavior of Flagellated Bacteria and its Utilization in Microscale Actuation

This talk is motivated by an effort to harness the motility of flagellated bacteria to actuate microscale structures. Flagellated bacteria such as *E. coli* exhibit random walk like behavior that originates in their cellular response to chemical stimuli. Bacteria cells are also known to respond to other stimuli, such as UV radiation and electromagnetic field. In this talk, we present mathematical models for the behavior of single cells under the stimuli, and the dynamics of the actuated microstructure, and show how motion control can potentially be achieved.

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MS10

Myogenic Response of Renal Afferent Arteriole

We developed a mathematical model of an afferent arteriole, to be used as an essential component in models of integrated renal hemodynamic regulation. The model incorporates the ionic transports, cell-membrane potential, smooth muscle cell contraction, and the mechanics of a thick-walled cylinder. Also, myogenic response is incorporated, based on the hypothesis that the dependence of calcium-channel openings on voltage is shifted by changes

in muscle stress, such that vessel diameter decreases with increasing pressure and vice versa.

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MS11

An Exclusion Principle for Biofilm Models

Due to spatial structure, biofilm community ecology differs in important ways from ecologies of well-mixed microbial systems such as those present in chemostats. Here we consider a widely used class of 1D biofilm models and shown via an exclusion principle resulting from competition for space that these models lead to restrictions on ecological structure. As a result it will be argued that downward mobility is necessary at least in models and possibly in actuality.

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MS11

Some Observations on the Wanner-Gujer-Kissel Model with Zero-Order Reaction Kinetics

We consider the mixed-species biofilm model of Wanner, Gujer and Kissel for zero order kinetics. This model can be solved almost explicitly, except for a scalar equation in one variable. This theory leads to a condition on the structure of the growth matrix describing the system. We will illustrate that numerical computations for the full model show that the zero-order case often provides good approximations for steady states in thin biofilms.

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MS11

Bacteriophage and Bacteria in a Flow Reactor

The Levin-Stewart model of bacteriophage predation of bacteria in a chemostat is modified for a flow reactor in which bacteria are motile, phage diffuse, and advection brings fresh nutrient and removes medium, cells and phage. A fixed latent period for phage results in a system of delayed reaction-diffusion equations with non-local nonlinearities. Basic reproductive numbers are obtained for bacteria and for phage which are analogous to ones obtained for the chemostat. Persistence and extinction results are obtained for both bacteria and phage. Simulations show interesting behavior of the model equations.

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MS11

On the Well-Posedness of a Mathematical Model of Quorum-Sensing in Patchy Biofilm Communities

Quorum-sensing is a mechanism of cell communication to coordinate behavior in groups. Recently, a model describing the effect of quorum sensing in a growing bacterial biofilm community was introduced. It consists of four density-dependent diffusion-reaction equations and combines a deterministic non-linear diffusion-reaction biofilm model with a model of quorum sensing for suspended populations. We will show the existence and uniqueness of solutions of this model.

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MS12

Phase Field Modeling of the Dynamics of Multicomponent Vesicles

We develop a thermodynamically consistent phase-field model to simulate the dynamics of multicomponent vesicles. The model accounts for bending stiffness, spontaneous curvature, excess (surface) energy and a line tension between the coexisting surface phases. Our approach is similar to that recently used by Wang and Du with a key difference. Here, we concentrate on the dynamic evolution and solve the surface mass conservation equation explicitly; this equation was not considered by Wang and Du. The resulting fourth-order, strongly coupled system of nonlinear, nonlocal equations are solved numerically using an adaptive finite element numerical method. Although the system is valid for three-dimensions, we limit our studies here to two-dimensions where the vesicle is a curve. Differences between the spontaneous curvatures and the bending rigidities of the surface phases are found numerically to lead to the formation of buds, asymmetric vesicle shapes and vesicle fission even in two-dimensions. In addition, simulations of configurations far- from-equilibrium indicate that phase separation via spinodal decomposition and coarsening not only affect the vesicle shape but also that the vesicle shape affects the phase separation dynamics, especially the coarsening and may lead to lower energy states than might be achieved by evolving initially phase-separated configurations. This is joint work with Axel Voigt and Andreas Ratz.

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MS12

Instability of a Non-Conducting Lipid Membrane Triggered by a Dc Electric Pulse

The stability of a lipid bilayer membrane subjected to a

DC electric pulse is investigated. The thin lipid membrane is impermeable to ions and thus acts as a capacitor. The model consists of conservation of current, which obeys Ohm's law, and the Stokes equations to describe fluid motion. Small amplitude perturbations of a planar membrane are considered. These results are relevant to understanding the physical mechanisms of electroporation of biomembranes.

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MS12

Surface Finite Elements for Biomembranes with Phase Separation

We consider vesicles formed by lipid bilayers with intramembrane phase interfaces. A gradient flow dynamics to compute equilibrium shapes has been defined coupling a geometric evolution law for the membrane hypersurface to a surface Allen-Cahn equation for the interfaces. The discretization is based on H^1 conforming quadratic isoparametric surface finite elements and a semi-implicit time discretization. Issues are the sharp interface limit, grid regularity, adaptive mesh refinement, and the influence of various physical parameters.

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MS12

Simulations of Multicomponent Vesicle Membranes and Actomyosin Driven Cell Oscillations

Cell membranes can have very complex components. And the shape of cell membranes can be determined by a lot of effects, such as the elastic bending energy, osmotic pressure, surface tension, etc. The most important issue maybe the insider structure of the cell. In this talk, we will analysis the dynamics of the actin filaments and myosin II and how they change the cell shapes. Some preliminary simulations will be presented as well.

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MS13

The Impact of Hepatitis C intra-cellular Viral Evolution on Treatment Response

Current in-vivo anti-viral therapy models consider only cell infection dynamics, disregarding the intra-cellular replication. Viral decline with non-resistant virus or permanent rebound is then observed. However, other patterns are observed during direct anti-viral therapy against HCV. We developed a model that includes intra-cellular and cell-infection levels (ICCI model) implemented as simple ODE equations, a non-mean-field deterministic model and a stochastic simulation. These approaches yield important implications for understand the clinical course of DAV-C therapy.

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MS13

Modeling HCV Drug Resistance: The Role of Replication Space

Approximately 170 million people worldwide are infected with hepatitis C virus (HCV). Current standard therapy leads to sustained viral elimination in only about 50% of patients treated. Telaprevir, a novel HCV protease inhibitor, has demonstrated substantial antiviral activity in patients with chronic HCV infection. However, drug-resistant variants emerge at frequencies of 5 to 20% of the total virus population as early as the second day after treatment initiation. Here, using probabilistic and viral dynamic models, we show that such rapid emergence of drug resistance is expected. We calculate that all possible single and double mutant viruses preexist before treatment, and that one additional mutation is expected to arise during therapy. Examining data from a clinical trial of telaprevir therapy for HCV infection in detail, we show that our model fits the observed dynamics of both drug-sensitive and -resistant viruses, and argue that combination therapy of direct antivirals will require drug combinations that have a genetic barrier of four or more mutations.

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MS13

Capturing Additional Information from HCV Trial Data

Capturing the viral kinetics of HCV drug therapy has happily been made more difficult by new, efficacious treatments. The biphasic decline of viral load is often partially hidden because of a rapid viral decline below level of quantitation. We use a new approximation of a standard set of viral load differential equations to analyze data from a protease inhibitor phase Ib monotherapy clinical trial. The new approximation yields additional information about the

viral decline - infected cell clearance rates - without additional data.

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MS13

Viral Dynamic Modeling Approaches to Support Clinical Development

A viral dynamic model in response to a triple combination regimen of telaprevir, peginterferon, and ribavirin has been developed. The model accounted for evolutionary dynamics of Hepatitis-C virus (HCV) quasispecies. The model was trained using HCV RNA dynamics data from Phase 2 treatment-naïve studies. The model was validated by demonstrating comparable SVR rates between observed and predictions in subsequent studies. Details of the methods will be discussed, including the use of Jacobian software to overcome limitations in NONMEM and Matlab. Applications of the model to support clinical development will be discussed.

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MS14

Extracting Non-linear Integrate-and-fire Models From Experimental Data using Dynamic I-V Curves

The dynamic I-V curve method extracts the response properties of a neuron while it is subject to a fluctuating stimulus that mimics in vivo-like fluctuating synaptic drive. The projection of the resulting history-dependent trans-membrane current onto a one-dimensional current-voltage relation provides the basis for a tractable nonlinear integrate-and-fire model. An attractive feature of the method is that it can be used in spike-triggered mode to quantify the patterns of post-spike refractoriness seen in different classes of cortical neurons. We apply here this method to generate reduced models of cortical layer-5 pyramidal cells and interneurons. The resulting low-dimensional neuron models—of the refractory exponential integrate-and-fire type—provide highly accurate predictions for spike times, demonstrating the potential of the dynamic I-V method for the construction of tractable models and rapid experimental classification of cortical neurons.

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MS14

Overview of Neuronal Dynamics and Computation

Mechanistically, a neuron subject to a time-varying input can be modeled as a non-autonomous dynamical system. From an information-theoretic perspective, a neuron's response can be thought of as encoding the input, and models of that encoding can be built with statistical tools. I will provide a brief introduction to modeling in both frameworks and present an example where we can analytically derive a coding model—the linear-nonlinear-Poisson model—from a simple dynamical model of the nonlinear integrate-and-fire type. In doing so, we gain insight into how dynamics determine coding.

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MS14

How do Neurons Integrate Information? Clues from Optimal Signal Processing Theory

Drift-diffusion (DD) and leaky competing accumulator (LCA) models have been used to model evidence accumulation in simple perceptual decisions for over 40 years. Indeed, the former is a continuum limit of the the sequential probability ratio test, which is optimal in that it delivers a decision of guaranteed accuracy in the shortest possible time. More recently intracellular recordings in primates have located brain areas in which neural firing rates rise like DD sample paths, and biophysically-based spiking neuron models have been constructed, simulated, and in some cases reduced to nonlinear LCA and DD models. I will describe a recent reduction, using mean field theory, of an integrate-and-fire network with adjustable synaptic gains modeling neuromodulation, show that the reduced model captures key aspects of the full system's behavior, explain how its rich phase plane and bifurcation structures suggest that the DD picture is perhaps too simple, and point out a number of shortcomings and open problems. The larger picture to which this work contributes will be sketched in a plenary talk at the same conference. This is joint work with Philip Eckhoff and KongFatt Wong-Lin.

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MS14

Information Representation in Correlated Spike Trains

Negative-feedback processes are ubiquitous in neural systems. One common type of process is a spike-triggered

adaptation current. Adaptation currents can introduce temporal correlations in the spike train, where a longer interspike interval (ISI) between spikes is more likely followed by a shorter ISI and vice versa, a pattern that is common in biological neurons. We derive and analyze a probabilistically independent decomposition of adaptation-mediated correlated spike trains. Further, a mutual information calculation shows that the decomposition can be a complete representation of the stimulus information. Our decomposition suggests a biologically plausible way that adaptation states of neurons can represent, communicate, and decode the high levels of information contained in their temporal spike pattern sequences.

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MS15

Modeling and Simulation of Dynamical Evolution in Complex Bio-Fluids

Biomaterials, or more precisely complex bio-fluids are made up of a host of soft/ deformable macromolecules and therefore they are bona fide soft matter or complex fluids. In these materials there exist a number of interfaces between different components or same component of different densities. A complex fluid model based on solid thermo and hydrodynamical principle would be instrumental in resolving the intricate dynamical interaction among the constituents. In this talk, I will discuss a phase field model based on kinetic theories to describe the multicomponent complex biofluids. I will give a few examples like biofilms, biofabrication using cell printing technology, etc. to illustrate the usefulness of these models. Various improvements to resolve dynamics at finer scales will be discussed as well.

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MS15

Stable Finite Difference, Adaptive Nonlinear Multigrid Simulation of a Diffuse-Interface Model For Tumor Growth

I begin by presenting a diffuse interface model for tumor growth that incorporates aspects of the tumor microenvironment, such as the availability of nutrient and oxygen and the stiffness of the host tissue. In the asymptotic limit as the diffuse interface thickness goes to zero, well know sharp interface models are obtained that treat tumor growth as a free boundary problem. I then compare the tumor model to a simplified model, known as the Cahn-Hilliard-Hele-Shaw (CHHS) equation, which is amenable to numerical and PDE analysis. I show how a good numerical scheme for the CHHS equation can be made to work well for the much more complicated tumor model. In particular, for both the full tumor model and the CHHS equation, I will demonstrate a stable, adaptive nonlinear-multigrid, finite-difference framework for solving the equations efficiently in 2 and 3D.

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MS15

Adaptive Mesh Refinement for Modeling the Electrical Wave Propagation in the Heart

In mathematical biology of the heart, the electrical cardiac dynamics can be modeled by a system of singularly perturbed reaction-diffusion equations, coupled with a set of stiff ordinary differential equations. The modeling with standard numerical methods on uniform grids is still extremely expensive nowadays. In this talk, I will present a space and time adaptive mesh refinement algorithm for the modeling. Numerical simulations will be presented demonstrating the performance of the algorithm.

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MS15

Computational Analysis of Tiktaalik Roseae Pectoral Fin Development

Recently scientists have found a missing link between fishes and walking land creatures by discovering fossils of the Tiktaalik roseae, which was a kind of "large shallow water fish" living on the earth about 375 million years ago. The pectoral fins of Tiktaalik reveal that development of the distal skeleton of modern animals was underway before the origin of tetrapods (Shubin et al., 2006). In this paper, we developed a moving grid discontinuous Galerkin finite element model to study the newly discovered Tiktaalik pectoral fin. Via systematic numerical simulations, we show that our computational model can give good prediction on the structure of the Tiktaalik pectoral fin. Parameter studies show two of important factors of the computational model for accurately predicting the Tiktaalik fin pattern formation. This is a joint work with J. Zhu, S.A. Newman and M.S. Alber.

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MS16

Optimizing the Phase-resetting Curve for Maximum Reliability of Spiking to Broadband Signals

The Phase Resetting Curve (PRC) describes the response of a neural oscillator to small perturbations in membrane potential. Its usefulness for predicting the dynamics of weakly coupled deterministic networks has been well characterized. However, inputs to real neurons may be more accurately described as barrages of synaptic noise. Effective connectivity between cells may thus arise in the form of correlations between noisy input streams. In this context, we use variational techniques to explore the influence of PRC shape on measures of correlated activity among otherwise uncoupled noise-driven neural oscillators.

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MS16

Synchronization of Periodically Driven Noisy Inte-

grate and Fire Neurons

How do noisy individual neurons respond to rhythmic drive from a surrounding population? Simple models such as Lapicque's leaky integrate-and-fire (LIF) neuron may help understand synchronization in neural populations. Keener et al classified the possible behaviors of a deterministic LIF driven by sinusoidal input. Tuckwell and others investigated the noisy LIF with constant input in terms of the first passage times of an Ornstein-Uhlenbeck stochastic process (OUP). We will discuss synchronization of the OUP subjected to periodic forcing, and the existence of an invariant measure for the firing times relative to the phase of a periodic stimulus.

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MS16

Avalanches in a Stochastic Model of Spiking Neurons

Neuronal avalanches are a form of spontaneous activity observed in cortical slice and other types of nervous tissue. They are characterized by irregular population bursts, where the burst size obeys a power law distribution. We present a model of neuronal avalanches based on stochastic single neurons connected in a excitatory and inhibitory network. We show that these avalanches are due to the network having functionally feedforward dynamics in the presence of noise.

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MS16

Mechanisms of Simple Perceptual Decision Making Processes

Perceptual decision-making, an omnipresent component of everyday life, plays a pivotal role in cognitive tasks. In this presentation, I will talk about mechanisms underlying simple two-option perceptual decision-making processes by studying a biologically realistic reduced two-variable model and phenomenological drift-diffusion models.

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MS17

Optimal Control of the Spread of Malaria Super-Infectivity

Malaria is a life-threatening disease caused by parasites of the species *plasmodium*, that are transmitted to people through the bites of infected mosquitoes. *Plasmodium falciparum* and *Plasmodium vivax* are the two most common species, *Plasmodium falciparum* is the most deadly. *Plasmodium falciparum* malaria is still a major cause of mortality and morbidity in the tropical and subtropical areas of the globe. In the 2009 Malaria World Report, the statistics showed that Half of the worlds population is at risk of malaria, with an estimated 243 million cases that led to about 863 000 deaths in 2008, a slight drop from the 2006 statistics. This drop can be attributed to a number of improved policies, including increases in international funding, research, the use of insectide treated bednets and artemisinin-based combination therapy, and a revival of support for indoor residential insectide spraying. Despite this slight drop, there are still challenges that may lead to significant increase in the malaria burden. These include the global financial slow down and the changing climatic conditions, both of which affects the endemic malaria regions. In this talk, a deterministic model for malaria transmission will be presented. This system of differential equations incorporates the re-infection of symptomatic individuals, a phenomenon known as superinfection. Qualitative analysis of the model reveals the presence of backward bifurcation a phenomenon where stable disease free equilibrium co-exists with a stable endemic equilibrium when the associated reproduction threshold is less than unity. Optimal control theory is then applied to the model to study the time dependent treatment efforts to minimize the infected while keeping the implementation cost at a minimum.

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MS17

Discrete Time Optimal Control of Species Augmentation

Species augmentation is a method of reducing species loss via augmenting declining/threatened populations with individuals from captive-bred or stable, wild populations. We developed a diffference equation model and optimal control formulation for discrete time augmentation of a general declining population. We show numerical results for scenarios of diffferent illustrative parameter sets.

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MS17

Optimal Control Applied to Native-Invasive Population Dynamics via a PDE Model

We present a model for population interactions between a native and an invasive species using a system of parabolic partial differential equations (PDEs), where the effect of disturbance in the system (such as flooding) is modeled as a control variable in the growth terms. The motivating example is cottonwood-salt cedar competition, with flooding being detrimental at low and high levels and being advantageous at medium levels, which led us to consider quadratic growth functions of the control. The goal is to maximize the native species while minimizing the cost of implementing the control. A new existence result for an optimal control with these quadratic growth functions is given. Numerical examples are given for various parameter values. The results provide suggestions for managing

the disturbance regime when invasive species are present.

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MS17

Optimal Treatment Strategies of Tuberculosis in South Korea

We have constructed a tuberculosis (TB) model in South Korea using the SEIR model with the time-dependent parameters. South Korea ranked the highest TB incidence among members of the Organization for Economic Cooperation and Development (OECD) in 2004. The observed data from the Korea Center for Disease Control and Prevention (KCDC) shows a certain rise of the incidence people after 2001 yr because of increasing foreign workers with active-TB and starting the operation of the Korean Tuberculosis Surveillance System. The least-square curve fitting have been used for beat fitting the parameters in our model to the observed data. In this work, we also propose the optimal treatment strategies of TB model in South Korea using optimal control theory based on our TB model from 2001 yr to 2008 yr. A behavior changing control, a latent treatment control and an infectious treatment control are considered. We propose the optimal treatment strategies of TB in South Korea for the short period (2010 yr - 2020 yr) and the long period (2010 yr - 2050 yr), in order to minimize the numbers of incidence and infectious individuals.

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MS18

Self-Organizing Mechanical Systems That Shape Embryos and Organs

The early stages of developing embryos are marked by dramatic movements, large deformations, and tissue remodeling. Large-scale movements that sculpt the embryo are ultimately driven by coordinated movement of the actomyosin cytoskeleton. Our group has developed methods to observe actomyosin contractions, the forces they generate, and their role in maintaining the mechanical resistance to deformation in living tissues. We use these tools to explore the biomechanical rules and principles that coordinate self-organization during morphogenesis.

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MS18

Symmetry and Stability Properties of Confined Microtubule Cytoskeletons

The aster of microtubules radiating from the centrosome is the central structural feature in many cell types. Analysis of static equilibria of confined asters of microtubules possessing flexural rigidity will be presented, with a special attention paid to the question of stability of central symmetry. The strongly nonlinear behavior of the confined aster has implications for design and interpretation of experiments aimed at elucidating the mechanics of centrosome positioning in real cells.

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MS18

Mechanics of Electromotile Cells and Membranes

Prestin is a recently discovered membrane protein that makes cells electromotile, i.e., changing their dimensions in response to changes in the transmembrane potential. Prestin is uniquely fast, and it responds to AC potential changes up to tens of kHz. The core of prestin-associated electromechanical coupling is protein conformational change and electric charge transfer. We propose a model of charge transfer by prestin under high-frequency electric fields and develop novel constitutive relations for membranes containing prestin.

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MS18

Self-assembly of the Contractile Ring: Kinetics of Formation and Instability Regimes

We study a stochastic aggregation model for the assembly of the contractile ring from a band of myosin nodes during fission yeast mitosis. Bands of nodes condense into rings when the range of node interactions exceeds the band width. Wide bands are unstable to clump formation due to Poisson density fluctuations. We calculate node kinetics and times for ring vs. clump formation and test them with simulations. These results suggest clump formation mechanisms in mutants.

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MS19

Stability and Bifurcations in an Epidemic Model with Temporary Immunity

In this talk I will present the derivation of an epidemic model with distributed time delay that describes the dynamics of infectious diseases with varying immunity. I will show that solutions of the model are always positive, and the model has at most two steady states: disease-free and endemic. It is proved that the disease-free equilibrium is locally and globally asymptotically stable. When an endemic equilibrium exists, it is possible to analytically prove its local and global stability using Lyapunov functionals. Bifurcation analysis is performed using DDE-BIFTOOL and traceDDE to investigate different dynamical regimes in the model using numerical continuation for different values of system parameters and different integral kernels. In the case of a constant period of temporary immunity, numerical simulations are performed to illustrate how the dynamics changes depending on the duration of immunity.

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MS19

Mutually Delay-coupled Oscillators in Multi-strain and Spatial Disease Dynamics

We consider oscillations resulting from delayed-global coupling between strains of a multi-strain disease, and delayed-local coupling in a spatially spreading disease. Delayed global coupling leads to oscillations that may be be synchronous or asynchronous, which will have consequences on field measurements of the disease prevalence. In the case of delayed-local coupling neighboring oscillators can either excite or inhibit oscillations at a specific spatial point. Analytical and numerical results describe the conditions for and the characteristics of the oscillatory solutions.

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MS19

A Criterion for Local Stability of Delayed Ordinary Differential Equations

A criterion for local stability based on the coefficients of the characteristic equation is presented, then it is applied to a few systems of delayed ordinary differential equations taken from several applications including one on malaria transmission, to show that although it is a method that is not difficult to evaluate, it can be used to obtain useful information about stability.

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MS19

A SIRC Model with Delay for Influenza A (H1N1)

We propose a SIRC model with delay to describe the recent influenza A(H1N1) outbreak in the state of Yucatán, Mexico. A time delay is introduced to model the incubation period of the virus. Local stability analysis of the proposed model is carried out.

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MS20

Modeling Dormancy in Biofilms and Planktonic Cultures

We present models of dormancy in a planktonic culture and in bio?lm, and examine the relative advantage of short dormancy versus long dor- mancy times in each case.

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MS20

Measuring and Modeling the Oxygen Profile in a Nitrifying Moving Bed Biofilm Reactor

The Moving Bed Biofilm Reactor is well-established for wastewater treatment where bacteria grow as a biofilm on the protective surfaces of suspended carriers. Since oxygen is crucial for nitrification, we measured the oxygen profile in situ with microelectrodes and simulated it by implementing a classical 1D-model with an added CSTR equation. This way, we could also estimate the erosion parameter λ as a function of the flow velocity of the influent water.

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MS20

Title Not Available at Time of Publication

Abstract not available at time of publication.

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MS20

Statistical Handling of Experimental Data from Bacterial Aggregates

Suspended bacterial aggregates represent an intermediate lifestyle between planktonic and biofilm existence that is believed to be important in survival and dissemination of bacterial communities. As with biofilms, the fate of these structures is strongly influenced by complicated intercellular adhesiveness and extrinsically imposed hydrodynamic forces. Experimentally dissecting these effects is a challenge made more difficult by the measurement systems involved (e.g., particle sizing apparatus), the tendency to large within-group experimental variability, and a lack of statistical tools of comparable elegance to the mathematical models typically invoked. In this presentation I will discuss some recent work from our lab to develop tools for drawing inferences about the sometimes pathologic data sets produced in this experimental field.

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MS21

Synaptic Depression Permits Co-existent Activity Patterns in Inhibitory Neuronal Networks

We consider a two-cell inhibitory neuronal network where the synapses display short-term synaptic depression. Our results show that synaptic depression expands the number of possible stable activity patterns the network can support and allows for co-existence of different stable patterns. Specifically, we show that the network is able to support different types of n-m anti-phase firing patterns, where one neuron fires n spikes followed by the other neuron firing m spikes. When maximal synaptic conductances are identical, n-n anti-phase firing patterns are obtained and there are conductance intervals over which different pairs of these solutions co-exist. The multitude of n-m anti-phase patterns and their co-existence are not found when the synapses are non-depressing. We apply geometric singular perturbation methods to derive necessary conditions for the existence and co-existence of different anti-phase solutions. Implications of these co-existent activity patterns for the function of central pattern generating networks will be discussed.

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MS21

Coherent Oscillations in Firing Rate Models with Adaptation

Interactions in spatially-extended, neural network firing rate models are mediated through nonlocal spatial interactions arising from synaptic coupling. Though adaptation is a local process intrinsic to the neurons themselves, we describe the effects of adaptation on generating and modulating spatially coherent oscillations in a variety of classes of neural network models that are driven by an input inhomogeneity.

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MS21

Waves, Bumps, and Binocular Rivalry in Neural Fields with Synaptic Depression

We study the dynamics of spatially extended neural fields with synaptic depression. For a continuous firing rate function, we show the network supports self-sustained oscillations, target waves, and spiral waves. In the high gain limit, we study the stability of stationary bump solutions. Due to discontinuities in the depression variable, we must use a piecewise smooth stability analysis and find the form of spectral equation depends on the sign of the perturbation. Finally, we formulate a competitive neural model in terms of multiple hypercolumns driven by visual stimuli, where switching is induced by a slow synaptic depression. Standing bump solutions in the model can lose stability through a Hopf bifurcation as input is reduced, leading to binocular rivalry type solutions.

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MS21

Bayesian Sampling in Perceptual Bistability

When an observer views a stimulus that allows two distinct interpretations, only one interpretation is perceived at any given time, and perception switches between the two in a stochastic manner. Well-known examples of this phenomenon, called perceptual bistability, are the Necker cube and the face-vase illusion. I will show experimental results that strongly suggest that the dynamics of perceptual bistability arises from a sampling process of an underlying probability distribution over the causes of the stimulus. Next, I will describe diffusion models embedded in double-well potentials, known to perform Langevin Monte-Carlo sampling, that generate the observed behaviors. The generality of this model will be illustrated with rate-based models and more biophysically realistic spiking neurons endowed with attractor dynamics.

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MS22

Dynamics of Motor Proteins in the Divided-Pathway Model

We investigated theoretically molecular motors that follow the so-called divided-pathway model using master-equation approach. The biochemical pathway for this model consists

of combination of sequential and parallel-chain segments. Recent single-molecule experiments indicate that myosins-V motor proteins most probably follow this model. The model is solved explicitly by mapping it into the parallel-chain model for which exact soluions already exist. Analysis of dynamic properties for this model indicates that even small changes in the biochemical pathways have a strong effect on dynamics of motor proteins.

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MS22

On Coarse-Grained Random Walk Models for Brownian Motors

We compute the large-scale transport properties of the basic flashing ratchet mathematical model for (Brownian) molecular motors and consider whether the underlying continuous-space, continuous-time Markovian model can be coarse-grained as a discrete-state, continuous-time Markovian random walk model. We provide a theoretical framework for the conditions under which Markovianity emerges in the discretized model and two mechanisms by which the discretized model incurs non-Markovian aspects.

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MS22

Competitive and Cooperative Dynamics of a Molecular Motor Pair

We introduce a system of stochastic differential equations describing the dynamics of multiple kinesin or dynein-type molecular motors that are tethered to a single cargo. We coarse-grain the stepping of the motors while observing the experimentally established relationship between applied forces and the resulting mean speed of the motors. Via stochastic averaging we study qualitative aspects of the motor-cargo complex as it depends on the number of motors in the system.

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MS22

Mathematical Structure of Stochastic Differential Equations and its Implication on Molecular Motor Dynamics

Theoretical studies of nonequilibrium systems are impeded by lacking general framework. In this work we first showed that a transformation introduced by Ao recently (J. Phys. A **37**, L25 (2004)) is related to previous works of Graham (Z. Physik B **26**, 397 (1977)) and Eyink *et al.* (J. Stat. Phys. **83**, 385 (1996)), which can also be viewed as generalization of the Helmholtz's theorem in vector calculus. We then showed that systems described by ordinary stochastic differential equations with white noises can be mapped to thermostated Hamiltonian systems. A steady-state of a dissipative system corresponds to the equilibrium state of the corresponding Hamiltonian system. This results provides a solid theoretical ground for corresponding studies on nonequilibrium dynamics, especially on nonequilibrium steady state. Many results of thermodynamic equilibrium systems can be directly applied to nonequilibrium steady states. We discussed several implications of the present work, especially on motor dynamics.

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MS23

Modeling Interferon-alpha Mediated Inhibition Kinetics of Hepatitis C Virus (HCV) RNA: In Vitro and In Vivo

Understanding of alpha-interferon (IFN) mode of action(s) against HCV infection was mainly derived from modeling serum HCV-RNA kinetics in treated patients. The viral kinetics within cells in-vivo is not known. With the recent development of cell-culture systems, modeling intracellular HCV-RNA kinetics during treatment is feasible. Our recent experimental data and modeling efforts will be presented. This is joint work with Drs. Susan Uprichard and Alan Perelson, among others.

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MS23

Modeling Hepatitis Delta Infection

Hepatitis Delta Virus (HDV) is a satellite of Hepatitis B Virus (HBV), and can only reproduce in hepatocytes which are simultaneously infected with HBV. Patients chronically infected with both HBV and HDV are more likely to experience liver failure, hepatocellular carcinoma, and cirrhosis than those infected with HBV alone. We develop a model of HBV-HDV infection to explore the roles of the two infections, their interactions, and the immune response in patient outcomes.

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MS23

Regulatory T Cells and HIV

Since our early success with modeling the Human Immunodeficiency Virus (HIV), I have been actively exploring ways to substantially improve modeling, through the use of model selection, identifiability, observability and sen-

sitivity and its application to infectious diseases and Diabetes. Scientific research is at the beginning of an era where mathematical modeling, if done correctly, will lead to important discoveries about the pathogenesis of disease. While my collaborators and I have been successful defining the kinetic rates and disease parameters using mathematical models for HIV and Hepatitis B virus (HBV), significant further advancement will require a new way of thinking about modeling. It is not sufficient to generate increasingly complex, heavily parameterized models without essential experimental data or any real mathematical proof that the proposed model is the "best" one for the system. Hence, my group is pioneering the application of theories associated with model selection, identifiability, observability, controllability, and sensitivity. All of these tools are crucial to advance the quantitative understanding of human disease pathogenesis and our currently being applied to study the dynamics of HIV during primary infection. Recently experimental work on regulatory T cells, a CD4 subset of T cells, has been implicated as a possible mechanism for controlling viral dynamics during primary infection and latency. Other work has suggested that these cells are highly vulnerable to HIV infection and may in fact, aid in the viral production. With all the varieties of interdependent cells that regulate and protect the body during infection, mathematical modeling is key to providing a road map to understanding the immune system's response to infection.

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MS23

Viral Dynamics 2010: New Models and Challenges

I will provide an overview of recent modeling work on acute HIV infection stimulated by new experimental findings. I will discuss new deterministic models that incorporate time-varying infectivity parameters, and stochastic models that allow one to account for delays from time of infection to the time of appearance of detectable viremia, and which can be used to distinguish between continuous and burst viral production.

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MS23

Innate Immune Responses to RSV Infection

Respiratory syncytial virus is a seasonal upper respiratory tract infection in humans. It is believed that the innate immune response plays an important role control of infection, but the precise form of this immune response is incompletely understood. Here, I'll present the results of a model-based analysis of recent tissue-culture experiments on RSV infection and discussion the resulting inferences regarding viral dynamics.

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MS24

Efficient Integration Factor Time Discretization of Discontinuous Galerkin Methods on Unstructured Meshes

Discontinuous Galerkin (DG) methods are a class of popular high order accuracy finite element methods for numerically solving various partial differential equations (PDEs). In this paper, we combine the integrating factor (an efficient and robust time discretization technique) with a DG spatial discretization and develop a high order implicit integrating factor DG (IIF-DG) method for solving reaction-diffusion systems on two dimensional (2D) unstructured meshes. We apply the Krylov subspace approximations to eficiently evaluate the product of the matrix exponential with vectors. Numerical examples are shown to demonstrate the accuracy, efficiency and robustness of the method.

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MS24

Spatial Dynamics of Stem Cells and Multi-stage Cell Lineages in Tissue Stratification

In developing and self-renewing tissues, differentiated cell types are typically specified through the actions of multistage cell lineages. Typically, as the tissue reaches a tightly controlled steady-state size, the cells at different lineage stages also assume distinct spatial locations within the tissue. In this talk, I will present modeling and simulations which explores several plausible strategies that can be utilized to create stratification during development or regeneration of olfactory epithelium (OE) in mouse.

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MS24

Surface Phase Separation and Morphological Transition of a Biomembrane

Experiments show membranes with multiple lipid components separate into coexisting phases with distinct compositions. It is suggested that bending and line tension give

rise to a variety of morphologies. Here, we present a model to study the relaxation dynamics of a membrane in fluid. The model is capable of describing the nonlinear coupling among flow, membrane morphology and phase evolutions. Numerical results show that surface tension variation and flow introduce nontrivial motion and membrane morphologies.

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MS24

Mathematical Modeling and Computational Studies of Cancer Stem Cells

Cancer stem cells (SCs) drive tumor growth, and apparently effective therapeutic agents very often fail to cure cancer patients. Cancer SCs are becoming recognized as a necessary target for effective anticancer therapy, and the task now is to control or eliminate cancer SC population. In this talk, we will discuss mathematical models to study the dynamical changes in cell populations in tissues that are characteristic of cancer development. We shall discuss how secreted feedback factors with symmetrical/asymmetrical cancer SC division in tumors may be applied to control the various cell populations in colonic tissues during colorectal cancer (CRC) development.

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MS25

How the Shape of the PRC Determines the Degree of Stochastic Synchronization

A pair of uncoupled general oscillators receiving partially correlated Poisson inputs can undergo stochastic synchronization (SS). I will present some recent results on the relationship between the shape of the phase-resetting curve (PRC) and the degree of SS between the oscillators obtained using perturbation methods. A closed-form expression describing the relation between the shape of the PRC and the probability density function(PDF) of the phase difference between the oscillators will be used to compare the degree of SS in oscillators with differently shaped PRCs. Applying these general results to specific models of neuronal oscillators, I will describe the dependence of SS on the membership of the PRC (type I or type II) and the dependence of SS on input correlation for two specific neuronal models (Integrate-and-fire and the Wang-Buzsaki hippocampal interneuron model).

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MS25

Mechanisms of Very Fast Oscillations in Networks of Axons Coupled by Gap Junctions

Gap junctions are associated with very fast oscillations (VFOs, $>$ 80 Hz) in the neocortex and hippocampus. We show how an axonal plexus (a network of axons connected by gap junctions) can exhibit (1) noisy activity, (2) stochastically-driven VFOs, or (3) re-entrant VFOs depending on the somatic voltage (V_S) and gap junction conductance (g_{gj}). We discuss applications of this analysis for VFOs in gamma oscillations, slow-wave sleep, and seizure initiation.

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MS25

Synchrony in Stochastic Pulse-coupled Neuronal Network Models

We investigate the interplay between fluctuations, which de-synchronize, and synaptic coupling through network connections, which synchronize model networks of integrate-and-fire neurons. By calculating the probability to remain synchronized, we explore the significance of the local network topology and of more physiological additions to the model on its ability to maintain synchrony. We calculate the random time between synchronous events in terms of a first-passage-time problem for a single neuron.

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MS25

Synchronization in Networks of Electrically Coupled Neurons

We investigate how synchrony is generated in networks of electrically coupled integrate-and-fire neurons subject to noisy and heterogeneous inputs. Using the Fokker-Planck formalism, we find that synchrony can appear via a Hopf bifurcation from the asynchronous state to an oscillatory state. If the transmission of action potentials via the electrical synapses is effectively excitatory, the Hopf bifurcation is supercritical, while effectively inhibitory transmission due to pronounced hyperpolarization leads to a subcritical bifurcation.

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MS26

Multi-scale Modeling of Cell Division and Feedbacks in Cellular Differentiation

Given an intracellular network with positive feedback, how does a growing cell population obtain a bimodal distribution (related to a high and a low expression state)?
We show that cell division and the subsequent partition of intracellular products can destabilize the high state. We present some example mechanisms that can produce robust bimodal distributions: heterogeneous cell division and death, stochastic and asymmetric partition of intracellular products.

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MS26

Imaging and Mathematical Analysis of HIV Gag Trafficking in Cells

Progeny virion assembly of human immunodeficiency virus (HIV) involves thousands of viral encoded Gag protein in the infected cell. The molecular and cellular mechanisms underlying this highly regulated process remain largely elusive. We here describe a recombinant lentivirus that was engineered to infect a wide spectrum of mammalian cells via VSV-G envelop pseduotyping. The recombinant lentivirus also encodes HIV Gag fused with GFP, allowing us to examine Gag transport dynamics in the infected cell. In HEK 293T cells, diffused Gag-GFP was observed as early as 10 hours post infection and remained so throughout the experiment period up to 72 hours post infection. In addition, bright Gag-GFP puncta appeared around 24 hours post infection and they demonstrated transportation trajectories with significantly varied velocities and directionalities. Similar Gag distribution and transportation dynamics were also observed in Cos-7 cells. These different distribution patterns might reflect HIV Gag proteins at different stages of the virion assembly process. Based on these observations, we also proposed mathematical models to simulate Gag assembly process. Our computational analysis demonstrated that Gag diffusion alone is not sufficient to medicate virion production and active Gag transport is likely required. This is consistent with our imaging observation that some Gag-GFP particles migrate at velocities much greater than random diffusion. Taken together, we suggest that multiple Gag kinetics contributes to virion assembly; and combinational imaging and mathematical analysis would help shed new lights on better understanding the process. This is a joint work with Liangqun Huang, James Liu, Judy Mufti, and Roberto Munoz-Alicea at Colorado State University.

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MS26

Stoichiometry Quantification of Structural Components in Nanoparticles by Photobleaching: Simple Math Analysis and Single Molecule Appraches

In nanobiotechnology, building blocks or modules can either be isolated as a functional units from living cells or viruses (the "Top down" approach) or via bimolecular assembly from recombinant and synthetic components (the "Bottom up" approach). Both approaches require knowledge of the stoichiometry of the biological structures, which frequently occur as multimers, that is, the morphological complex is composed of multiple copies of one or more macromolecule subunits. This presentation will address following methods to quantify the stoichiometry. 1)by binomial distribution using the mixture of mutant and wild type components; 2) by concentration dependent slopes of log/log plot curves; 3) by finding the common multiples of each modules; 4) by single molecule imaging applying the photobleaching technology.

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MS26

A Critical Quantity for Noise Attenuation in Biological Systems

Feedback modules, which appear ubiquitously in biological regulations, are often subject to disturbances from the input, leading to fluctuations in the output. We have identified a critical quantity: the signed activation time that dictates the noise attenuation capability in feedback systems. Our findings suggest that the inverse relationship between the noise amplification rate and the signed activation time could be a general principle for many biological systems regardless of specific regulations or feedback loops.

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MS27

A Stochastic Programming Approach to Forest Management with Natural Disturbances

Decision-making in timber harvesting and mature forest core area management has been addressed by numerous of deterministic models. This research presents a multistage full recourse stochastic programming model that aims to improve the reliability of forest management decisions by considering the potential impact of random fire disturbances. Timber revenue and mature forest core areas are our two major management objectives. Fire is assumed to influence both forest conditions and available management actions. A sample average approximation approach is used to solve the problems. Order statistics are used to formulate reliability constraints. The size of our model grows fast when the sample size or the number of stages is increased. Model outputs demonstrate the impacts of random fire events on forest management decisions and the potential challenges regarding computation time and memory requirement for a multistage full recourse model.

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MS27

Optimization of a Delayed-Differential Model of the Immune Response

In this talk we will present techniques for the analysis and optimization of a mathematical model of the immune response to to tumor antigen. The model consists of a system of delay differential equations, and is calibrated to experimental data from murine experiments performed specifically for the purpose of the development of the mathematical model. The goal of the model is to suggest dose and scheduling protocols that would maximize the cellular immune response. There is not a definitive answer to what constitutes the "best" response: is it the maximum peak response, the long-term levels, or the functionality of the immune cells? We therefore compare the results from several optimization techniques, with a few different objective functions.

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MS27

Optimal Control of a Model for Cholera

Although many mechanisms of the spread of cholera have been understood for about two hundred years, our understanding of the role of the aquatic reservoir and of the role of humans of different ages in spreading disease continues to evolve. We compare two models for a cholera epidemic: one which considers disease dynamics on a time scale of hours and days, and is appropriate for short-term interventions, and a second, appropriate for long-term strategies, which considers the dynamics on a larger time scale. With the latter model, we target optimal control measures with those that can reasonably be considered in a poor region that has some infrastructure to support long-term intervention. While tragedies such as the recent cholera deaths in Zimbabwe cannot be avoided in areas with crises of government, we consider what mitigation strategies can target the most essential causes for the spread of cholera with the smallest possible financial cost to the affected regions.

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MS27

An Efficient and Robust Numerical Algorithm for Estimating Parameters in Turing Systems

We present a new algorithm for estimating parameters in reaction-diffusion systems that display pattern formation via the mechanism of diffusion-driven instability. A Modified Discrete Optimal Control Algorithm (MDOCA) is illustrated with the Schnakenberg and Gierer-Meinhardt reaction-diffusion systems using PDE constrained optimization techniques. The MDOCA algorithm is a modification of a standard variable-step gradient algorithm that yields a huge saving in computational cost. The results of numerical experiments demonstrate that the algorithm accurately estimated key parameters associated with stationary target functions generated from the models themselves. Furthermore, the robustness of the algorithm was verified by performing experiments with target functions perturbed with various levels of additive noise. The MDOCA algorithm could have important applications in the mathematical modeling of realistic Turing systems when experimental data are available.

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MS28

Cytoplasmic Streaming and the Physics of the Vacuolar Membrane

While cytoplasmic streaming was described first in 1774 by Bonaventura Corti, its role in cellular physiology is still rather mysterious. In this talk I will describe a combination of experimental and theoretical work aimed at solving this mystery. Cytoplasmic streaming also interacts very strongly with the tonoplast, the lipid membrane that encloses the vacuole, raising a whole host of fascinating issues in the hydrodynamics of membranes that will be outlined.

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MS28

Flow of Cytoplasm in Moving Cell

Fluid dynamics are implicated in cell motility because of the hydrodynamic forces they induce and because of their influence on transport of motile machinery components. I will present a mathematical model of the Darcy flow of cytoplasm squeezed through cytoskeleton by hydrostatic pressure generated at the rear of the cell by myosin contraction. Numerical solutions of the model equations predict that fluid flow is directed forward. The model predictions

compare well with experiments.

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MS28

A Computational Model of Bleb Formation

Blebbing occurs when the cytoskeleton detaches from the cell membrane, resulting in the pressure-driven flow of cytosol towards the area of detachment and the local expansion of the cell membrane. We present a dynamic computational model of the cell that includes mechanics of and the interactions between the intracelluar fluid, the actin cortex, and the cell membrane. The model is used to investigate the role of myosin-generated cortical tension in bleb formation.

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MS28

Ethology and Rheology of Amoeba

Ethological experiments on Physarum polycephalum, a kind of true slime mold, have indicated that the unicellular organisms possess ability of information processing, e.g., maze-solving, memorizing of period of repeated stimulations. Mathematical models have shown that the intelligent behaviors are closely related to protoplasm flow in Physarum polycephalum. In this talk, I will discuss several topics of the slime mold intelligence, paying attention to rheological aspects of the intelligent behaviors.

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MS29

Dynamics of Distribtutions of Bacterial Emboli in Flow

We consider a model for the dynamics of bacterial aggregates in a hydrodynamic system, such as for example bacteria in the blood stream. We model a size-structured population based on the Smoluchowski coagulation equations, a nonlinear transport PDE. We discuss evidence that a widely used post-fragmentation distribution is incorrect as well as properties of growth leading to self-similar solutions to the equations.

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MS29

Thin-Film Modelling of Bacterial Biofilms

The application of thin-film approaches to describing the growth and spreading of, and cell-cell communication within, a bacterial biofilm will be outlined.

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MS29

Social Evolution Theory and Biofilms

Darwin's theory of natural selection suggests that individuals will strive to selfishly increase their reproductive success. However, cooperation, where individuals perform apparently costly actions to benefit others, is observed at all levels of biological organization. Bacteria form elaborate biofilms that suggest strong cooperation yet, are as individual organisms, they are subjected to natural selection. What prevents evolutionary exploitation from harming the entire biofilm? I analyze this problem under the lens of 'social evolution theory' using simulation and experiments to show bacteria can solve the conflict between individual and social interests.

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MS29

Mathematical Model of Biofilm Induced Calcite Precipitation

We consider the following biomineralization problem. Urea hydrolysis catalyzed by biofilm increases the pH value and produces carbonate ions. In the presence of calcium ions, calcite ($CaCO_3$) will precipitate and form crystal once its saturation index exceeds certain critical value. We present a mathematical model including the important chemical, physical and biological processes (Ureolysis and pH value change, advection, diffusion and crystal precipitation, biofilm growth and deformation) involved in the problem. Some computation results and discussion will also be given.

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MS30

Mixed-mode-oscillations in a Network of Inhibitory Cells with Adaptation

Small amplitude oscillations followed by large excursions during periodic cycles were observed in electrophysiological recordings of spiny cells in entorhinal cortex and in central pattern generators for respiratory rhythms. More recently, these *mixed-mode-oscillations* (MMOs) were also found in realistic conductance-based models. We report now the existence of MMOs in a simple rate model of mutual inhibitory neuronal populations with adaptation. Interestingly, there is no autocatalytic process in the model and the network components are not intrinsic oscillators. In fact, the MMOs result from the interaction of coupling and local feedback. We identify the mechanism responsible for the formation of MMOs, and discuss their potential functional role.

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MS30

The Role of Adaptation in Recurrent Networks of ON and OFF Cells and their Processing of Input

We investigate the role of adaptation in a neural field model, composed of ON and OFF cells, with delayed recurrent connections. As external spatio-temporal inputs drive the network, ON cells perceive inputs directly, while the OFF cells receive an inverted image of the original signals. Via global and delayed inhibitory connections, these signals may cause the system to enter states of sustained oscillatory activity via an Andronov-Hopf bifurcation. We first review the mechanism by which static inputs cause oscillatory responses. We then perform a bifurcation analysis of our model incorporating neural adaptation. We further show how the oscillatory response threshold is altered by the incorporation of adaptation, which makes oscillations less prevalent. We support these results with numerical experiments, and discuss their implications for electrosensation and other sensory modalities.

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MS30

The Dynamical Modeling of Mental Disorders

Brain imaging experiments have showed that the various brain functions are represented by different activity patterns. Such patterns are continuously changing in time and, in fact, it is a movie that can be considered as a sequence of metastable mental states. Each mental state is a result of the interaction of emotional, cognitive and perceptional coordinated brain modes. We build the dynamical model of mental activity that describe such interactions. For the creation of the mode, we have used some general rules or principles i.e. modes competition for the energy and informational recourses, stability to the noise and in the same time the sensitivity to the informative messages, and transitivity of the brain dynamics. The model demonstrates a spectrum of qualitatively different activity depending on the value of the small number of control parameters. It is possible, based on this, to characterize quantitatively the different normal and pathological mental dynamics. In particular, we showed that dynamic images of the different anxiety disorders i.e. panic disorder and obsessive-compulsive disorder have represented by different dynamical images and different numbers, like Kolmogorov-Sinai entropy.

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MS30

Multi-phase Respiratory Rhythms

The respiratory central pattern generator in the mammalian brainstem can produce a variety of rhythmic activity patterns, depending on environmental conditions and metabolic demands. These activity patterns are multi-phasic, featuring rapid switches between phases in which different populations of neurons are active. I will present results from a minimal computational model for a 5-population network suggesting possible mechanisms through which experimentally observed rhythms emerge under perturbations such as low oxygen or high carbon dioxide. This work will emphasize mechanisms for switching between phases and the importance of changes in which populations control particular phase transitions.

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MS31

A Multiscale Strategy for Molecular Motors

The kinesin molecular motor family takes a single 8 nanometer step forward for each ATP hydrolyzed except in rare cases. Recent experiments have demonstrated mulitiple steps including frequent back steps may be possible if the necklinker connecting the heads of the kinesin are extended. This talk will present a detailed intra-step model of kinesin stepping which allows for multiple steps and show that asymptotic quantities can be caclulated using a combination of limit theorems for semi-Markov processes and matrix analytic techniques for Markov chains.

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MS31

Some Aspects of Molecular and Effective Diffusion

We study the effective potential and effective diffusion of molecular motors. A molecular motor is driven by switching among a set of potentials, one for each chemical state. An effective potential function can be defined to mimic the average driving force as a function of motor position. An effective diffusion coefficient can also be defined based on the long time variance of motor position. We are going to discuss the issue of to what extent the local time stochastic behavior of motor position can also be captured in this approach.

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MS31

Learning from Microtubule Curvature

Recent experiments in living epithelial cells suggest that molecular motors are primarily responsible for the observed dynamical bending deformations of microtubules. In vitro microtubule gliding assays are ideal model systems to study such motor mediated interactions. Using coarse-grained Langevin simulations of gliding assays, we study the fundamental mechanisms of bending and transport in these systems. We also demonstrate how curvature distributions can be used as a successful tool to characterize the observed deformations.

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MS31

The Influence of the Look-ahead Model on Error-correcting Mechanisms During Transcription

In this talk we study the error rate of RNA synthesis in the look-ahead model for transcription elongation. The model's central assumption is the existence of a *window of activity* in which ribonucleoside triphosphates (rNTPs) bind reversibly to the template DNA strand before being hydrolyzed and linked covalently to the nascent RNA chain. An unknown, but important, integer parameter of this model is the window size w. Using mathematical analysis and computer simulation, we study the rate at which transcriptional errors occur as a function of w. We find dramatic reduction in the error rate of transcription as w increases, especially for small values of w.

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MS32

Influenza Dynamics Influenced by Medication Strategies and Vaccination

Patients at risk for complications of influenza are commonly treated with antiviral medications, which however also could be used to control outbreaks. The adamantanes and neuraminidase inhibitors are active against influenza A, but avian influenza (H5N1) is resistant to oseltamivir and swine influenza (H1N1) to the adamantanes (but see postscript). To explore influenza medication strategies (pre-exposure or prophylaxis, post-exposure/pre-symptom onset, and treatment at successive clinical stages) that may affect evolution of resistance (select for resistant strains within or facilitate their spread between hosts), we elaborated a published transmission model and chose parameters from the literature. Then we derived the reproduction numbers of sensitive and resistant strains, peak and final sizes, and time to peak. We demonstrate that the influenza dynamics depends critically on a modified control reproduction number (different from the traditional control reproduction number). Finally, we made these results accessible via user-friendly Mathematica notebooks.

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MS32

Selection for Resistance to Oseltamivir in Seasonal and Pandemic H1N1 Influenza.

In 2009, a novel reassortant strain of H1N1 influenza A emerged as a lineage distinct from seasonal H1N1. The primary treatment for pandemic H1N1 is the antiviral drug oseltamivir. Although many seasonal H1N1 strains around the world are resistant to oseltamivir, initially, pandemic H1N1 strains have been susceptible to oseltamivir. Using phylogenetic analysis of neuraminidase sequences, we show that both seasonal and pandemic lineages of H1N1 are evolving to selective pressure for resistance to oseltamivir.

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MS32

Adaptive Immune Response to IAV Infection

In this talk, I will introduce mathematical models which embrace major portions of the body's immune reaction to influenza type A, with implications for treatment and vaccine designs. One of our main motivations of developing our model was that real world experiments simply cannot be executed fast enough to investigate many complex facets of viral infection. We developed a two-compartment model that quantifies the interplay between viral replication and adaptive immunity. Our model accurately replicated previously published experiments including i) a set of viral and immune cell temporal kinetics, ii) the role of CD4 help for antibody persistence and iii) the consequences of immune depletion experiments. The model analysis showed that lung resident CD8 T cells can be potentially as effective for viral clearance as neutralizing antibodies when present at the time of challenge. The model predicts drugs to limit viral infection and/or production must be administered within 2 days of infection, with a benefit of combination therapy when administered early. Our simulation showed that when B cell response depends on cellular immune cell priming, regulation of antigen presentation has greater influence on the kinetics of viral clearance than the efficiency of virus neutralization or cellular cytotoxic-

ity. Alternatively, when B cell activation s directly induced by virus, the rate of viral production is the most critical parameter for controlling duration of disease. Take together, we demonstrated the possibility of the use of mathematical model to examine explicit biological scenarios and generate experimentally testable hypotheses.

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MS32

Ensemble Modeling of in-host Response to IAV Infection and Treatment Strategies

Ensemble models of biological systems provide probabilistic predictions of the dynamics that approximate the variability of response among individuals. We present an ensemble model of the human immune response to influenza A virus infection, consisting of an ODE system with probability distribution on parameters reflecting the goodness of fit to empirical data. This model is used to compute probabilistic estimates on the trajectories of the immune response, duration of disease, maximum tissue damage, likelihood of rebound of disease and superspreaders. It is found that the strength, duration and time of initiation of antiviral treatment have significant effects on treatment benefits and on possible adverse effects.

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MS33

GPU Algorithms for Integrative Multicellular Biological Modeling

Graphical processing units (GPU) have attracted interest due to their ability to greatly speedup certain types of calculations, but writing efficient scalable programs is not a trivial task; there are numerous technical issues that must be considered to achieve optimal performance. We demonstrate how using GPUs expands the possibility of developing more integrative multicellular biological models while decreasing the computational cost to simulate those models. In the process, we discuss various programmatic issues and provide a set of design guidelines for GPU programming that are instructive to avoid common pitfalls as well as to extract performance from the GPU architecture.

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MS33

Computational Analysis of Spatial Dynamics in Cell Signaling

The proper growth, development, and survival of an organism require extensive and accurate communication among the cells of the organism. Hence, cells sense and react to a wide variety of stimuli, which convey information such as nutrients, harmful insults, and the state of neighboring cells. In this talk, we will present our recent results on spatial dynamics of cell polarization (a single cell system) and developmental patterning (multi-cellular systems).

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MS33

Numerical Simulation of Cahn-Hilliard-Hele-Shaw Equations

Unconditionally energy stable and solvable schemes for the Cahn-Hilliard-Hele-Shaw (CHHS) equation are presented in the talk. This equation arises in models for spinodal decomposition of a binary fluid in a Hele-Shaw cell, tumor growth and cell sorting, and two phase flows in porous media. A convex splitting technique for this specialized conserved gradient flow is utilized, which gives a non-increasing energy. Some numerical simulation results are also presented in the talk.

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MS33

Positive Preserving High Order Well Balanced Discontinuous Galerkin Methods for the Shallow Water Equations

Shallow water equations with a non-flat bottom topography have been widely used to model flows in rivers and coastal areas. An important difficulty arising in the simulations is the appearance of dry areas, and standard numerical methods may fail in the presence of these areas. These equations also have steady state solutions in which the flux gradients are nonzero but exactly balanced by the source term. In this presentation we propose a recently developed high order discontinuous Galerkin (DG) method which can preserve the steady state exactly, and at the same time is positivity preserving. A rigorous proof will show that this DG method keeps the water height non-negative, without destroying the mass-conservation. Some numerical tests are performed to verify the positivity, well balanced property, high order accuracy, and good resolution for smooth and discontinuous solutions.

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MS34

Temporal and Spatial Correlations in Neural Networks: Avalanches and Maximum Entropy

Recent work has shown that activity in living neural networks can propagate in the form of avalanches whose sizes follow a power law distribution. In seemingly unrelated work, maximum entropy models have been shown to ac-

count for spatial correlations in neural networks. Could these two different ways of viewing neural network activity be related to each other? Here, we will explore whether or not including temporal correlations in maximum entropy models will lead to neuronal avalanches.

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MS34

Cortical Correlations are Modulated by Feedforward Sensory Afference

Correlated variability of neural activity is modulated during numerous cognitive processes. Nevertheless, how specific neural circuits shape correlated variability is poorly understood. Feedforward inhibitory circuits are widespread throughout the central nervous system and determine spike time precision of trial averaged activity as well as receptive field structure. We examine the variable activity of pairs of nearby excitatory and inhibitory cells in Layer 2/3 somatosensory cortex, key elements in this core cortical disynaptic feedforward inhibitory circuit. A global synaptic field positively correlates these cells types during spontaneous activity, while sensory stimulation decorrelates their spiking activity. A minimal computational model of a feedforward inhibitory circuit explains this sensory-evoked decorrelation through a threshold nonlinearity, regulating inhibitory firing, which shifts the balance of correlating synaptic fluctuations and anticorrelating inhibition during spontaneous and evoked responses. Sensory evoked network decorrelation by feedforward inhibition shows a key influence of cortical circuitry for population based coding schemes.

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MS34

Parametrizing Network Properties by Second-order Statistics

One possible avenue toward understanding basic features of networks is to develop parametrized classes of networks and explore their properties. We present a set of second-order statistics that represent deviations from random networks and capture interactions among edges. We build ensembles of neurons parametrized by those statistics to explore their effect on frequencies of higher-order network motifs. We outline how to add neuronal dynamics onto the nodes in order to study the behavior of neuronal networks with these connectivity statistics.

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MS34

Maximally Informative Input/output Functions in Biological Networks

Many organisms rely on complex biological networks both within and between cells to process information about their environments. As such, performance of these networks can be quantified using the tools of information theory. Biological networks often involve large numbers of nodes and encode multiple inputs. This makes it difficult to compute the optimal output of even individual nodes with respect to multidimensional inputs. However, progress can be made with two biologically realistic simplifications. The first simplification takes advantage of the fact that in many cases, the nodes of both neural and gene regulatory networks can be described as binary variables, being either 'on' or 'off'. The second simplification is to consider only sigmoidal-like input/output functions with sharp transitions termed "decision boundaries" because they divide the input space into on/off regions. Note that this second simplification does not imply that each node is driven by one particular linear combination of inputs. In fact, previous work has determined that optimal decision boundaries in the case of independent nodes (neurons) are curved when inputs have large, non-Gaussian fluctuations, as is typical of the natural sensory environment. Curved decision boundaries in turn indicate that multiple stimulus dimensions affect responses of a single node, in agreement with recent findings for neurons throughout the visual pathway, as well as at some stages of auditory and somatosensory pathways. Here we extend this approach to networks of interacting neurons and find the optimal set of decision boundaries. We find that for relatively simple input stimuli, such as Gaussian stimuli, the optimal network strategy is to have each neuron/gene operate independently. However, for a distribution approximating those of natural environments, the optimal strategy is to have the nodes of the network couple. Importantly, we find that the strength of coupling should increase with noise in neural responses, providing a mechanism of error-correction. This approach has three practical applications that may be useful for future experimental studies. First and foremost, it suggests ways of inferring interaction strengths with unmeasured parts of the network based solely on the properties of input/output functions for measured network nodes. Second, in the situation where input/output functions are known for at least a pair of nodes, it yields a criterion for determining whether the effective interaction between these nodes will require higher-order interactions with nodes other than the two under consideration. Finally, in the situation where the effective pairwise interactions are sufficient, as has been recently demonstrated for neurons in the retina, protein sequences, and some gene regulatory networks, this approach provides a way to find the maximally informative pairwise interactions, which can then be compared with experimental measurements.

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MS35

Growth Detection: A Novel Role for CD4+ T cells

Effective regulation and appropriate activation of the immune system is traditionally understood in terms of pattern recognition mechanisms, route of infection effects and dosage-dependent responses. Recently, several experiments have suggested that antigen kinetics may play a role in immune system decision-making as well. The mechanisms underlying this mode of immune system regulation, however, are poorly understood. We develop a mathematical model that takes into account the kinetics and signaling interactions that have been reported between Th1, Th2, Th17 and iTreg cells. We investigate the conditions under which the network of interacting antigen-specific CD4+ T cells is capable of accurately and robustly classifying pathogens based on their relative rates of population growth.

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MS35

The Antiviral Response in Dendritic Cells is Controlled by a Choreographed Cascade of Transcription Factors

The basic design principles of eukaryotic cells are poorly understood. Specific changes in cell state associated with global gene expression changes typically depend on integration of multiple stimuli. Whether such a gene program emerges from a parallel or convergent pathway architecture is unknown. We investigated the transcriptional network mediating the antiviral program of the human dendritic cell, a master regulator of immune responses. The antiviral state results from activation of viral pattern sensors as well as from autocrine and paracrine signaling. To deduce causality and coherence of transcriptional events responsible for this state, we developed and validated by experiment a new approach integrating genome-wide expression kinetics and time-dependent promotor analysis. Most individual genes are targeted by multiple factors, indicating robustness against virus-encoded immune evasion gens. We find a stepwise multi-factor cascading control mechanism drives the response, where the majority of gene regulatory events are orchestrated by a single convergent network.

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MS35

Optimal Modulation of Viral CTL Epitope Repertoire

Following cell entry, viruses can be detected by Cytotoxic T Lymphocytes. These Cytotoxic T Lymphocytes can induce host cell apoptosis and following it the destruction of the infecting virus. Viral detection is mediated by viral protein epitopes. Thus, viruses with fewer epitopes have a higher survival probability and are selected through evolution. However, mutations have a fitness cost and on evolutionary periods, viruses maintain some epitopes. The number of epitopes in each viral protein is a balance between the selective advantage of having less epitopes and the cost of mutations. Here we present a bioinformatic analysis of the number of epitopes in various viral proteins and an optimization framework to explain these numbers. We show, using a genomic analysis and a theoretical optimization framework, that a critical factor affecting the number of presented epitopes is the expression stage in the viral life cycle of the gene coding for the protein. The early expression of epitopes can lead to the destruction of the host cell, before budding can take place, and thus to the destruction of the virus. A lower number of epitopes is expected in early proteins even if the late proteins have a much higher copy number.

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MS35

Agent Based Model of Virus Infection in Human Cells

Abstract not available at time of publication.

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MS36

Mechanics of Fins, Krill, and Pollen Grains

We describe recent studies of three different systems in biomechanics. First, we consider how pollen grains of angiosperm flowers survive the process of dehydrating and rehydrating by simple geometrical and mechanical properties of the pollen wall. Second, we optimize a fin ray–the supporting structure in flexible fish fins–for stiffness. Third, we use a drag coefficient model of swimming krill to show that metachronal or syncopated propulsor dynamics are optimal for maximizing thrust and efficiency.

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MS36

Characterizing the Mechanism(s) Behind Lateral Platelet Motion Using a Lattice Boltzmann-Immersed Boundary Method

Platelets play an essential role in blood clotting by adhering to damaged vessel walls and releasing chemicals. Under arterial flow conditions, platelets have an enhanced concentration near vessel walls that depends on the fluid dynamics of blood as a heterogeneous medium. We use a lattice Boltzmann-Immersed Boundary method to solve the flow dynamics of red cells and platelets in a periodic vessel with no-slip boundary conditions. Our results indicate that the effective diffusion of platelets due to red blood cells may be 1000 fold larger than Brownian motion and that platelet diffusion is highly non-uniform across the vessel diameter.

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MS36

Hydrodynamic Behavior of Helical Flagella by the Immersed Boundary Method

Flagellar bundling is an important aspect of locomotion in bacteria such as *Escherichia coli*. To study the hydrodynamic behavior of helical flagella, we present a computational model that is based on the geometry of the bacterial flagellar filament at the micron scale. We consider two model flagella, each of which has a rotary motor at its base with the rotation rate of the motor set at 100Hz. Bundling occurs when both flagella are left-handed helices turning counterclockwise (when viewed from the non-motor end of the flagellum looking back towards the motor) or when both flagella are right-handed helices turning clockwise. Helical flagella of the other combinations of handedness and rotation direction do not bundle.

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MS36

Aerodynamics of Insect Flight with Bristled Wings

A common feature among the smallest flying insects is the bristled structure of their wings. In general, the smaller the insect (and the lower the Re), the larger the wing surface area occupied by bristles. Possible roles of this structure include the reduction of forces required to fling the wings apart and increased stability during parachuting. In this presentation, we use immersed boundary methods to explore the aerodynamic advantages gained by the bristled structure.

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MS37

Hyperbaric Oxygen Therapy vs De-oxygenation Therapy in Wound Healing

A mathematical model of epidermal wound healing is presented. We compare the therapeutic use of oxygen under pressure known as hyperbaric oxygen therapy to that of removing oxygen from the wound region which we will call de-oxygenation. The model is express as a system of reaction-diffusion equations capturing oxygen availability, capillaries regeneration and growth factor production. We present numerical results for both normal and chronic wounds for the model in one dimension.

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MS37

Wound Healing and the Biomechanics of Cell Motility

Some stages of wound healing involve cell proliferation and cell motility. We have developed a biomechanical model for cell motility which emphasizes the role of contraction and peeling. We couple cell motion to the mechanics of collagen to give an account of matrix deformation along with cell motion, as in the case of fibroblasts.

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MS37

An ODE Model of Collagen Accumulation During Wound Healing

Wound healing is achieved through the production of collagen by fibroblast cells. In this differential equation model we investigate the competing actions of fibroblast cells and inflammatory cells on collagen accumulation. The healing time course prediction and collagen accumulation are confirmed with experimental data. The model can replicate non healing wounds as well and will be used to investigate the impact of circulating systemic hormones on wound and patient outcomes.

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MS37

Mathematical Models for Foreign Body Reactions

in 2D

The foreign body reactions are commonly referred to the network of immune and inflammatory reactions of human or animal bodies to foreign objects placed in tissues. They are basic biological processes, and are also highly relevant to bioengineering applications in implants, as fibrotic tissue formations surrounding medical implants have been found to substantially reduce the effectiveness of devices. Despite of intensive research on determining the mechanisms governing such complex responses, few mechanistic mathematical tools have been developed to study such foreign body reactions. This study focuses on kinetics-based predictive models in order to analyze outcomes of multiple interactive complex reactions of various cells/proteins and biochemical processes and to understand transient behavior during the entire period (up to several months). Computational models based on continuum and multi-scale methods were constructed to investigate the time dynamics as well as spatial variation of foreign body reaction kinetics. Several numerical examples will be discussed.

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MS38

Computational Modeling of Extracorporeal Shock Wave Therapy

Extracorporeal Shock Wave Therapy (ESWT) is a non-invasive treatment for bone fractures that fail to heal, necrotic wounds and strained tendons. ESWT is similar to lithotripsy, a non-surgical treatment for kidney stones. In this treatment a shock wave is generated in water and then focused using an acoustic lens or reflector so the energy of the wave is concentrated in a small region. This technique has been used since the 1980's, but the underlying biological mechanisms are not well understood. In this thesis we have computationally investigated shock wave propagation in ESWT by solving a Lagrangian form of the Isentropic Euler equations in the fluid and linear elasticity in the bone using high-resolution finite volume methods. We have also incorporated tissue-like materials into the model through variation of the parameters in the Tait equation of state. This work differs from prior modeling of ESWT in that we are solving a full three-dimensional system of equations so we can handle complex bone geometries, and our formulation of the equations enables us to consider shear stresses generated within the bone. In this talk I will give a brief overview of shock wave therapy, and prior modeling efforts. Then I'll discuss the set of equations we use to model the wave propagation and show some results validating this approach. I will show results from three-dimensional calculations that provide insight as to how doctors might optimize shock wave therapy for nonunions and heterotopic ossifications.

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MS38

Top Down, Bottom Up, or Cohort Dominated? Explaining Clear Water Phase Dynamics in Temperate Lakes

We pose two mathematical models for spring clear-water phase dynamics (CWP) in temperate lakes. One specifically addresses food web interactions between grazers and algal prey, with the food quality of the algal prey varying over the course of the season according to a simulated temperature-driven algal succession. The second model assumes that cycles in the clear-water phase may be explained by one or more cohorts of zooplankton passing from juvenile through breeding adult stage. Statistical correlations between ice-out time, spring bloom, and CWP onset suggest that CWP start is governed largely by temperature. We suggest that the end of the CWP may arise due to some combination of fish predation (top down) and/or starvation (bottom up) as the algal succession under grazing pressure tends toward large colonial greens or toxic cyanobacteria.

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MS38

Locust Swarms: Discrete Models, Homogenization, and Variational Minimization

We build an individual-based model for locust swarms incorporating social interactions, gravity, wind, and the boundary formed by the ground. For some parameters, the model produces a rolling "bubble" with grounded locusts, airborne locusts, and an unpopulated center, similar to actual locust swarms. To further understand this structure, we formulate a one-dimensional continuum problem describing a vertical slice. Using variational methods, we find exact solutions which agree closely with simulations of the discrete problem.

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MS38

Modeling the Impacts of Climatic Conditions on Streamflow in a Salmon-Bearing Rangeland Watershed: Asotin Creek, Washington

Asotin Creek, a tributary to the Snake River and draining about 325 square miles, is a salmon-bearing stream in the Columbia River Basin. With its headwaters originating in the Blue Mountains, the watershed varies in elevation from 6,200 ft to 800 ft. The watershed receives a mean annual precipitation of 23 inches, ranging from more than 45 inches in higher elevations to 12 inches in the lower elevations. Minimum streamflow and stream temperature are among the crucial factors affecting salmon survival. To assess the influence of climatic conditions on streamflow, we applied the Water Erosion Prediction Project (WEPP) model on the Asotin Creek Watershed. The WEPP model is a process-based, continuous-simulation, water erosion model built on the fundamentals of hydrology, plant science, hydraulics, and erosion mechanics. Climate inputs are the major drive of the model simulation. In this study, we used three methods (basin-average, Thiessen polygon, inverse-distance) to process climatic data from several weather stations, including the USDA NRCS SNOTEL and NOAA stations. The results showed that WEPP-simulated streamflows using climate data from the inverse-distance method were most agreeable with field-measured values.

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MS39

Simulation and System Identification Technique for Arterial System

The central role of arterial hemodynamics in atherosclerosis is different from that in hypertension, which imposes different modeling requirements to capture the disease state. An enhanced immersed boundary method is developed for atherosclerosis studies to accurately simulate the detailed blood flow inside complex elastic arterial segments. For hypertension studies, novel system identification techniques are subsequently applied to extract compact passive models of arterial segments, which are interconnected to efficiently simulate a large arterial network for pressure and averaged flow.

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MS39

Some Advances in Computational Electrocardiology

The electrical activation of the heart is the biological process that generates the contraction of the cardiac muscle, pumping the blood to the whole body. In physiological conditions, the pacemaker cells of the sinoatrial node generate an action potential, that is a sudden variation of the cell transmembrane potential $u = ui - ue$, namely the difference between the intracellular potential ui and the extracellular one ue. Following preferential conduction pathways, the electrical stimulus propagates throughout the heart wall and causes the contraction of the heart chambers. Due to this coupling between the electrophysiology and the mechanical behaviour, when some anomalies occur in the action potential propagation, the proper function of the heart pump can be affected. The action potential propagation can be mathematically described by coupling a model for the ionic currents, owing through the membrane of a single cell, with a macroscopical model that describes the propagation of the electrical signal in the cardiac tissue. Such model can be derived from a homogenization of the electrostatic laws for the potential in the intracellular and extracellular space. One of the most accurate model available in literature is the Bidomain model, a degenerate, quasi-linear, parabolic system, consisting of two non-linear partial differential equations for the intracellular and extracellular potential. Due to the degenerate nature of the problem, its discretization leads to an ill-conditioned linear system and, as a consequence, its numerical resolution is very expensive. The models that describe ionic currents in cardiac cells in general consist of stiff systems of ordinary differential equations. The intrinsic complexity of the coupled problem requires ad hoc numerical methods. The aim of this talk is to describe some numerical techniques to solve these equations. In particular we consider the Bidomain equations coupled with the Luo-Rudy model that describes the ionic dynamics for a ventricular cell. We present a time-adaptive exponential scheme [2], explicitly devised to solve Luo-Rudy like models, and we introduce a model-based block-triangular preconditioner [1] for the solution of the Bidomain system. We also introduce a model adaptive procedure, based on a domain decomposition approach [4], where a simplified model (called Monodomain) is solved in regions of the computational domain where the high accuracy of the Bidomain is not needed [3].

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MS39

A Generalization of the Classical Approach for

Handling Closure in 1D Models of the Arterial System.

Classical 1D blood flow equations are obtained by making a series of approximations to the cross sectionally averaged Navier-Stokes equations. Closure is attained by assuming either a uniform or parabolic velocity profile. The resulting equations are limited in their ability to model even fully developed pulsatile flow. Here, the approach to resolving closure is generalized. The resulting 1D equations provide a significantly better match to the Navier-Stokes equations in relevant benchmark problems. This approach has been extended to non-Newtonian models.

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MS39

Three-Dimensional (3D) Computational Fluid Dynamics (CFD) Simulations of Ozone Uptake in the Respiratory Tract

Ozone (O_3), the major component of photochemical smog, causes a reproducible heterogeneous pattern of lung injury. We hypothesize that the spatial distribution of injury mirrors an analogous distribution of O_3 dose delivered to different tissue sites in the respiratory tract. The use of 3D CFD in idealized and anatomically accurate airway geometries to predict local O_3 uptake and to investigate the effects of respiratory flow rate and airway structure on O_3 uptake will be described.

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MS40

Opportunities at MBI

This talk will survey opportunities for research positions at MBI (postdoctoral fellows, early career visitors, long term visitors, and participants), describe the major programs that are being planned at the institute for the next two years, and advertise the opportunities for members of the mathematical sciences and biosciences communities to propose programs (from a couple of days to yearlong) at MBI.

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MS40

Research and Education Opportunities at NIMBioS

The unique features of our research and education programs at the National Institute for Mathematical and Biological Synthesis will be presented. The nature of working groups, our main research activities, will be discussed. The difference between working groups and workshops will be explained. Our education and outreach activities including students at all levels will be introduced.

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MS40

At the Intersection of Math and Evolutionary science: Integrating Across Disciplines, Methods, Theories, and Data at NESCent

NESCent, The National Evolutionary Synthesis Center, is a collaborative effort of Duke University, University of North Carolina at Chapel Hill and North Carolina State University and is sponsored by NSF. Our mission is to facilitate broadly synthetic research to address fundamental questions in evolutionary science. Synthetic research takes many forms but includes integrating novel data sets and models to address important problems within a discipline, developing new analytical approaches and tools, and combining methods and perspectives from multiple disciplines to answer and even create new fundamental scientific questions. I will present our past and ongoing activities at NESCent linking mathematics and evolutionary science that allowed for advancements in evolutionary science and discuss initiatives and opportunities for the future.

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MS40

Extending Majority Consensus Trees to Represent Wandering Taxa

Biologists commonly use the majority consensus tree to visually summarize Bayesian posterior distributions on evolutionary tree shape. This summary combines full splits that individually have strong support into a single topology that may have multifurcations. In order to reveal hidden structure in tree distributions, we extend the majority consensus to represent supported partial splits (of only some leaf taxa) by introducing a new tree structure in which each branch may have a range of attachment locations.

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MS41

Large-Scale Epidemic Simulations: Enabling Decision Support Through Supercomputing

Agent-based modeling provides epidemiologist with the means to understand how infectious disease can spread through a population. Through the use of a highly detailed, heterogeneous representation of a population, ABMs allow researchers and decision makers to simulate the effect of mitigation strategies at a level not attainable by much less computationally demanding compartment models. This detail comes at the price of greatly increasing the computational cost of simulation. With advances in high-performance parallel computing, methods that were once prohibitively expensive have become quite commonplace in the toolkits of groups that study a variety of diseases. In this presentation, advances in supercomputing and agent-based modeling will be discussed, and examples of how

they have been brought to bear in helping understand preparedness for the H1N1 pandemic.

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MS41

Adaptive Vaccination Strategies to Mitigate Pandemic Influenza: Mexico as a Case Study

We explore vaccination strategies against pandemic influenza in Mexico using an age-structured transmission model calibrated against local epidemiological data from the Spring 2009 A(H1N1) pandemic. In the context of limited vaccine supplies, we evaluate age-targeted allocation strategies that either prioritize youngest children and persons over 65 years of age, as for seasonal influenza, or adaptively prioritize age groups based on the age patterns of hospitalization and death monitored in real-time during the early stages of the pandemic. Overall the adaptive vaccination strategy outperformed the seasonal influenza vaccination allocation strategy for a wide range of disease and vaccine coverage parameters. This modeling approach could inform policies for Mexico and other countries with similar demographic features and vaccine resources issues, with regard to the mitigation of the S-OIV pandemic. We also discuss logistical issues associated with the implementation of adaptive vaccination strategies in the context of past and future influenza pandemics.

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MS41

Models of Antibody Responses Following Virus Infection

During the course of an individual's viral infection, the virus population may consist of a distribution of different variants produced by mutation and selection. Consequently, the immune system attempts to build a response that is broad enough to handle the diversity of virus strains present. We design novel mathematical models of virus-antibody interaction and focus on the roles of competition and cross-reactivity among neutralizing antibodies, viral evolution and the role of non-neutralizing antibodies.

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MS41

Modeling the Killer T Cells Immunodominance in Influenza Infection

Antigen-specific killer T cells (CD8+ cells) play an important role in virus clearance. The aim of this talk is to introduce and analyze mathematical models of the dynamics of killer T cells and the differential expansion of antigen-specific CD8+ cell, called immunodominance, in the influenza infection. Understanding qualitative impact of killer T cells is very important for the design of T-cell-based vaccines that promote early virus clearance. The systematical analysis of these model systems show that the behaviors of the models are similar for high killer T cells density generating reasonable dynamics. Our models try to shed some light on possible explanations of the some aspect immunodominance in influenza infection by studying the effect of the epitope of the antigen presented on the surface of the infected cells and the effect of Interferon-γ

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MS42

Interactions of Noisy Oscillators

It is well known that coupling in a population can lower the variability of the entire network; the collective activity is more regular. In this talk, we show that coupling can regularize the individual as well. Specifically, we show that even coupling to a noisier system can reduce the noise. We illustrate this analytically with both coupled Ornstein-Uhlenbeck systems and coupled oscillators. In some cases, noise reduction is a nonmonotonic function of the coupling strength.

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MS42

Stochastic Dynamics of Local and Global Calcium Responses in Cardiac Myocytes

We present a realistic but minimal model of cardiac excitation-contraction coupling that accurately represents the stochastic dynamics of heterogeneous local Ca signals in a population of diadic subspaces and junctional SR depletion domains. Starting from a probability density description we derive a moment closure reduction that is nearly 10,000-times more computationally ef?cient than corresponding Monte Carlo simulations. The model is applied to study alternating SR Ca release under periodical stimulation by depolarizing voltage pulses.

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MS42

Influence of Cellular Substructure on Gene Expression and Regulation

We will give an overview of our recent work investigating the influence of incorporating cellular substructure into stochastic reaction-diffusion models of gene regulation and expression. Extensions to the reaction-diffusion master equation that incorporate effects due to the chromatin fiber matrix are introduced. These new mathematical models are then used to study the role of nuclear substructure on the motion of individual proteins and mRNAs within nuclei. We show for certain distributions of binding sites that volume exclusion due to chromatin may reduce the time needed for a regulatory protein to locate a binding site.

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MS43

Large Fluctuations and Optimal Paths in the Master Equation Approach to Stochastic Neurodynamics

We consider a master equation formulation of stochastic neurodynamics involving a recurrent network of synaptically coupled homogeneous neuronal populations each consisting of N identical neurons. The state of the network is specified by the fraction of active or spiking neurons in each population, and transition rates are chosen so that in the thermodynamic or mean-field limit we recover standard rate-based models. Using a WKB approximation of solutions to the neural master equation, we show how the effects of large fluctuations can be analyzed in terms of an effective Hamiltonian dynamical system. Under a Gaussian approximation, this reduces to a Langevin description of the network dynamics.

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MS43

Effective Rate Equations for Pulse Coupled Neural Networks

Neural network rate equations do not include information about phase relationships. Using an approach developed for the Kuramoto model of coupled oscillators, we analyze a pulse coupled system of quadratic integrate-and-fire neurons. We develop a density representation of the network dynamics which captures the finite size fluctuations. This representation includes the density of phase information and the activity via coupled equations. We describe how disorder in the network affects the stability of asynchronous firing states.

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MS43

Correlation Shaping in Spiking Neural Networks

Correlated activity between pairs of neural outputs is a central theme in brain dynamics. There is mounting experimental evidence that the degree of correlation is influences by, for example, stimulus structure, attentional bias, and neural pathologies to name a few. Using a linear response approach we present specific circuit mechanisms that promote a *shaping* of pairwise correlations in spiking neuron models. Our framework matches spiking data recorded from rodent somatosensoy cortex and brainstem of weakly electric fish.

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MS43

Impact of Coherent Behavior on Information in Neuronal Networks.

Correlated activity in neural tissue strongly impacts the information carried by populations of neurons. It is therefore important to understand how correlated activity is generated and propagated. I will give a mechanistic description of both processes in terms of a simple integrate-and-fire model without assuming that the inputs are Gaussian processes. This allows for a more detailed examination of the interplay between excitation and inhibition. I will also discuss the impact of correlations on the information carried in the neural activity.

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MS44

Analysis of Transient Dynamics Motivated by a Mathematical Model of the Inflammatory Response

The goal of this talk is to describe the analysis of a specific aspect of transient dynamics not covered by previous theory. The question addressed is whether one component of a perturbed solution to a system of differential equations can overtake the corresponding component of a reference solution as both converge to a stable node at the origin, given that the perturbed solution was initially farther away and that both solutions are nonnegative for all time.

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MS44

Ecological and Evolutionary Dynamics of Ecosys-

tems and Bifurcation Analysis

In ecosystem models parameters that describe physiological process such as growth, reproduction and mortality are taken constant. Due to mutations these parameters change. The evolutionary dynamics can be studied by calculation of transcritical bifurcations of equilibria or limit cycles of a system consisting of the competing resident and mutant population. Also the evolution of the body size of a population when seasonality variates temporally at a geological time scale of 20,000-400,000 years (Milankovitch-cycles) is studied.

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MS44

After-depolarization and Excitability in Pyramidal Neurons

Pyramidal neurons are excitable cells in the hippocampus. They exhibit so-called after-depolarization (ADP), which is is a positive deflection of the membrane potential that takes place after a spike generated by a short depolarizing current injection. Recent results suggest that ADP is an essential feature that appears to organize the excitability of the pyramidal neuron. We use the relation between time scales of the kinetics of the ion channels and model reduction techniques, along with a bifurcation analysis to study this transient phenomenon.

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MS44

Overlapped Bifurcation Diagrams for Analysis of Nested Fast-Slow Systems

We discuss a model for electrical activity, calcium oscillations, and metabolic oscillations in insulin-secreting pancreatic beta-cells that can be decomposed into a relatively fast electrical-calcium oscillator (EO) and a slow metabolic oscillator (MO). We show how overlapping one-parameter bifurcation diagrams of the two systems can account for the diverse behaviors of the combined system and how resetting by electrical stimuli can expose the relative contributions of the EO and MO to various patterns.

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MS45

Accelerated DNA Repair by Charge Transport: Stochastic Analysis and Deterministic Models

A Charge Transport (CT) mechanism has been proposed in several papers (for example see Yavin et al. PNAS 102 3546 (2005)) to explain the colocalization of Base Excision Repair enzymes to lesions on DNA. The CT mechanism relies on redox reactions of iron-sulfur cofactors on the enzyme. Electrons are released by recently adsorbed enzymes and travel along the DNA. The electrons can scatter back to the enzyme to destabilize it and knock it off the strand, or they can be absorbed by nearby lesions and guanine radicals. I will first present a stochastic description for the electron dynamics in a discrete model of CT-mediated enzyme kinetics. By calculating the enzyme adsorption/desorption probabilities, I develop an implicit electron Monte Carlo scheme and use it to simulate the build-up of enzyme density along a DNA strand. Then, I will present a Partial Differential Equation (PDE) model for CT-mediated enzyme binding, desorption and redistribution. The model incorporates the effect of finite enzyme copy number, enzyme diffusion along DNA and a mean field description of electron dynamics. By computing the flux of enzymes into a lesion, the search time for an enzyme to find a lesion can be estimated. The results show that the CT mechanism can significantly accelerate the search of repair enzymes.

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MS45

Cooperative Cargo Transport by One or Two Teams of Molecular Motors

We use stochastic models to study cooperative transport by teams of molecular motors. We find that run lengths increase strongly with motor number, in agreement with experimental data. Furthermore we show that a tug-of-war between two motor teams is sufficient for fast bidirectional movements due to an instability based on force-dependent unbinding of motors from filaments. Our model also illuminates the role of regulatory proteins and allows to rationalize counterintuitive motor parameters.

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MS45

Random Intermittent Search and the Tug-of-war Model of Motor-driven Transport

We formulate a "tug-of-war' model of microtubule cargo transport by multiple molecular motors as an intermittent random search for a hidden target along a one-dimensional track. Performing a quasi-steady state (QSS) reduction of the associated differential Chapman-Kolmogorov equation, we calculate the mean first passage time (MFPT) for finding the target, and show that there exists an optimal

level of adenosine triphosphate (ATP) concentration that minimizes the MFPT. This suggests that ATP concentration could act as a control signal for optimizing the search process.

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MS45

Intercellular Communication in the Immune System: Networks or Chance

Functional Cellular Communication in the Immune System... Cellular Networking Dendritic Cells(DC) are the primary immune sentinels within the body, serving to harvest and process antigen from pathogens and other sources for subsequent presentation to the effector cells of the immune system. Using high speed 3 dimensional multicolor imaging tools we have previously shown that these cells are connected by a network of fine tubules. These tubules are able to conduct a calcium flux between cells leading to large scale activation of the DCs. An intriguing extension of these observations is the possibility that these tubules could serve to transfer antigen between cells leading to effective amplification of the immune response over short distances. Using a combination of high speed multidimensional imaging and these new probes we have convincingly demonstrated that protein may be transferred from cell to cell via the previously defined tubules, and be taken up into antigen processing compartments. This mechanism of communication is limited by the length of the tubules. The possibility of long distance communication has also been considered. The cells seem to act as separate neworked clusters Collectively, these investigations which required the use of a combination of cutting edge probes and imaging technologies show that the ability of DCs to share molecular information may represent an important and newly discovered process in generating and effecting an appropriate immune response.

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MS46

Correlating Theoretical Solutions with Real-world Practice in Mathematical Modeling of Wound Healing Therapies

Wound healing involves complex interactions of multiple cell types and molecular mediators. Abnormalities in this system due to diabetes and other diseases result in poor healing. We are using population-based sets of ordinary differential equations to analyze cell migration, cell mitosis and cell death, and using rates of production and decay to capture changes in growth factors, matrix components and other molecular mediators. We are comparing predictions from this model with clinical trial and empiric data for advanced therapies.

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MS46

Mathematical Modeling of Diabetic Wound Closure – A Multidisciplinary Approach

Human skin wounds are a major public health issue and economic problem in the US and beyond, and so far modeling has generally concentrated on wound healing in healthy patients. We now look at wound healing in Db/Db mice as a model for diabetic wound healing. Using experimental results for wound closure over time, i.e., wound contraction over time plus skin growth (epithelialization) over time, for both nondiabetic and diabetic mice, we will discuss the healing of diabetic wounds and the extent of the applicability of a mechanochemical model for wound contraction previously developed for nondiabetic wounds. A mechanochemical model includes partial differential equations describing the mechanical forces on the wound tissue as well as the conservation of chemicals/variables playing major roles in the wound healing.

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MS46

A Multidisciplinary Approach to Modeling Wound Healing

The impact of non-healing wounds on the US economy is estimated at $20 billion/annum in direct costs. Current research efforts have failed to deliver effective therapies for patients with chronic wounds. This mini-symposium seeks to present an overview of the clinical issues involved in non-healing wounds (Liu), then three differing approaches to mathematical modeling of non-healing wounds. First, a mechanochemical model of diabetic wound healing in mice will be presented (Lin), followed by a study relating an ODE model of cell dynamics to real-world practice in wound healing (Ko and Li), and concluding with a PDE formulation of ischemic wound healing in a porcine model (Xue).

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MS46

A Mathematical Model of Ischemic Cutaneous Wounds

Chronic wounds represent a major public health problem affecting 6.5 million people in the United States. Ischemia, primarily caused by peripheral artery diseases, represents a major complicating factor in cutaneous wound healing. In this talk, we present a mathematical model of ischemic dermal wounds. The model consists of a coupled system of partial differential equations in the partially healed region, with the wound boundary as a free boundary. The extracellular matrix (ECM) is assumed to be viscoelastic, and the free boundary moves with the velocity of the ECM at the boundary. The model equations involve the concentration of oxygen, PDGF and VEGF, the densities of macrophages,

fibroblasts, capillary tips and sprouts, and the density and velocity of the ECM. Simulations of the model demonstrate how ischemic conditions may limit macrophage recruitment to the wound-site and impair wound closure. The results are in general agreement with experimental findings.

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MS47

I Love my ODE, but Sometimes Loving means Letting Go: Design Considerations in Building in Silico Equivalents of Common Experimental Assays

Experimentation in vitro is a vital part of the process by which the clinical and epidemiological characteristics of a particular influenza virus strain, for example, are determined. We detail the considerations which must be made in designing appropriate theoretical/mathematical models of these experiments and show how modeling can increase the information output of such experiments. Starting from a traditional system of ordinary differential equations (ODEs), common to infectious disease modeling, we broaden the approach by introducing more complex models, applicable to more general experimental geometries and assumptions about the biological properties of viruses, cells and their interaction. We apply the new model to experimental plaque growth of two influenza strains, one resistant to the antiviral olseltamivir, and extract the values of key infection parameters specific to each strain. This characterization reveals important information about the effect of the resistance-conferring mutation and facilitates an understanding the strain's future fitness and virulence.

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MS47

Mathematical Modeling of the Control of a Tick-borne Disease

Ticks have very unique life histories that create epidemics that differ from other vector-borne diseases. Our tick-borne disease model is designed for the lone star tick (*Amblyomma americanum*) and the spread of human monocytic ehrlichiosis (*Ehrlichia chaffeensis*). Optimal control techniques are employed to assess the potential for reducing the percent of ticks infected. This study explores the relationship between the mathematical structure of the optimal control and the resulting predicted optimal interventions.

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MS47

Epidemiological Impact of a Herpes Simplex Virus Type 2 Vaccine for Young Females

Genital herpes is one of the most incident and prevalent sexually transmitted infections in the world. Currently, a candidate vaccine against HSV-2, the main cause of genital herpes, is in clinical trials, however, it seems that vaccine efficacy is limited only to women who are HSV-1 and HSV-2 negative. If this vaccine, or a future one, is approved to be administered to the population, it is imperative that an effective vaccination program be determined. We have developed a mathematical model to describe the dynamics of HSV-2 disease in a population, including a vaccination strategy targeting 13 year old girls. The vaccination program is similar to one that is already in place for HPV. We delineate the population by age, sex and sexual behaviour. Results show that this vaccination program is effective in reducing HSV-2 prevalence, however, this highly depends on the proportion of girls vaccinated, the age of sexual maturation, and the immunogenecity of the vaccine (whether it prevents infection or disease). Eradication is very hard to achieve.

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MS47

Modeling Immune Dynamics of Equine Infectious Anemia Virus

Use of mathematical modeling became a very important tool in various interdisciplinary problems in general, and in biology in particular. Broad range of complex biological phenomena can be efficiently simulated using computational mathematics, while biological experiments either very costly, extremely time consuming or simply impossible. The main goal of this project is to develop an efficient and accurate mathematical model of an Equine Infectious Anemia Virus (EIAV). The lentivirus subgroup that contains EIAV also includes human immunodeficiency virus (HIV). The similarities between these two viruses are making the study of EIAV is very important to the research on HIV. The developed model consists of the system of ordinary differential equations and based on existing HIV models. However, unlike majority of HIV models EIAV model includes the Humoral Immune Response (HIR) in addition to cytotoxic T-lymphocyte (CTL) response. Results of numerical experiments for different parameters and comparison of HIR and CTL responses will be presented.

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MS48

Evolution of Strategies for Rhinovirus Immune Ma-

nipulation

Rhinoviruses are cleared by the host immune system after causing minimal cell death and often without inducing long-term immune memory. This mystery has tremendous implications for the population dynamics, diversity, and evolution of these viruses. By binding receptors on antigen-presenting cells and inhibiting their function, rhinoviruses redirect a systemic adaptive immune response into a localized innate response. We use a compartmentalized, ordinary differential equation model to understand the dynamics of rhinovirus immune manipulation.

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MS48

Effects of HIV-1 Latency and Reactivation on Antiviral Therapy

In patients receiving anti-retroviral therapy, memory T cells latently infected with HIV remain at an extremely low but apparently stable levels over long periods of time, balancing cell proliferation with viral reactivation and subsequent cell death. Therapies designed to remove cells by reactivating the virus may simultaneously trigger infected cell proliferation. We present deterministic and stochastic mathematical models that describe the long-term dynamics of latently infected cells to identify the break-even point for therapy.

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MS48

A Delay Differential Equation Model for the Cell-cycle Specificity of Vesicular Stomatitis Virus Efficacy

A mathematical model of cancer treatment with vesicular stomatitis virus (VSV), an oncolytic virus which selectively kills a wide range of human tumor cell types, is developed and analyzed. VSV can infect cells during all phases of the cell cycle except during the resting phase. Since the interphase of the cell cycle has a minimum biological time course, a system of delay differential equations is used to model the cell cycle-specific nature of VSV treatment.

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MS48

Antiviral Intervention During an Influenza Pandemic Driven by Individual Versus Population Interest

To evaluate optimal coverage of antiviral drugs during pandemic influenza for both the individual and the population, we developed an epidemiological game-theoretic model of influenza transmission. We parameterize the model with survey data on actual perceptions regarding influenza and antiviral drugs. We find that the demand for antiviral drugs driven by self-interest would likely be far lower than that which would maximize overall utility for the population, if individuals made decisions based on their beliefs.

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MS49

The Maximal Compartment Size in Chemical Reaction-diffusion Networks

I will discuss how to discretize space for the stochastic model of chemical reaction-diffusion networks. The system is modeled using a continuous time Markov jump process with diffusion as a jump to the neighboring compartment. The maximal compartment size for spatial discretization is suggested in the stochastic model, and the conditions for the exponential convergence to the uniform solution in the corresponding deterministic model approximate the maximal compartment size from the stochastic model well.

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MS49

Applications of Random Walks to Biological Data Clustering

The need to interpret and extract possible inferences from high-dimensional datasets has led over the past decades to the development of dimensionality reduction and data clustering techniques. In this talk, we present a novel fuzzy

spectral clustering algorithm that combines seamlessly the strengths of existing spectral approaches to clustering with various desirable properties of fuzzy methods. We discuss examples of genetic expression datasets for which the developed methodology outperforms other frequently used algorithms.

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MS49

Sustained Oscillations in a Gene Regulatory Network

At the heart of gene expression mechanisms are two basic processes: transcription of DNA to mRNA, and translation of mRNA to proteins. We will analyze two models where the protein concentration inhibits the transcription mechanism. This negative feedback leads to oscillations that are observed in simulations, and can be explained by analysis of the small-number stochastic system but are not predicted by mass-action ODE approximations.

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MS49

Stochastic Analysis of Pattern Formation in Drosophila

A small number of BMP molecules are involved in the dorsal pattern formation process of Drosophila, which could lead to large stochastic fluctuations. However, type IV collagen involved in the transport system of BMP and SBP produced by the positive feedback can attenuate noise. In this talk, we show how type IV collagen and SBP affect the evolution of noise numerically and analytically.

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MS50

Size Distribution of Pancreatic Islets

Cross-sectional information of tissue morphology can be used to deduce the dynamics of tissue growth. Here we study size distributions of pancreatic islets, mainly consisted of beta cells. The exact functional form of the islet-size distributions has not been determined due to technical limitations, although several skew distributions such as lognormal, Weibull, inverse Gaussian, and gamma distributions have been proposed. Recently we have established a novel method to scan entire three-dimensional islets in an intact pancreas using trangenic mice in which beta cells are specifically tagged with a fluorescent protein (Kilimnik et al., Am. J. Physiol. Endocrinol. Metab. 297:1331-1338, 2009). Bayesian model comparison applied to this data leads to the conclusion that islet-size distribution is a lognormal distribution. In addition, it has been reported that every beta cell has an equal potential for proliferation. Therefore, we introduce a simple islet-growth model to connect the lognormal size distribution and the characteristic beta-cell proliferation. Furthermore, we will discuss accelerated islet growth under a tumor condition (insulinoma), and islet fission.

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MS50

Parameter Estimation in a Model Predicting Heart Rate during Head-up Tilt

The main role of the cardiovascular system is to maintain adequate oxygenation of all tissue; it does so by maintaining blood flow and pressure at a fairly constant level. To do so a number of quantities are regulated when the system is exposed to stress. One of the main regulatory systems is the baroreflex system, which regulate heart rate, cardiac contractility, and vessel tone in response to changes in arterial blood pressure. In this study we analyze regulation of heart rate in response to changes in blood pressure observed during head-up tilt. To do so we apply a nonlinear delay differential equations model predicting dynamics of heart rate, via submodels that estimate sympathetic and parasympathetic outflow, which vary in response to changes in blood pressure. The objective of this study is to determine what subset of model parameters can be predicted reliably given the model combined with data. To understand the parameter space for this model we apply sensitivity analysis, subset selection based on singular value decomposition, and analysis of parameter correlations. We show that estimating only a subset of model parameters will allow us to predict measured heart rate data.

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MS50

Parameter Estimation in Physiology Revisited

Parameter estimation in physiology is an important and challenging problem. Different areas in physiology need different approaches since the purpose of the parameter estimation plays a role. For example, the goal may be to develop methods for clinical diagnostics and decision support in real time treatment of patients. If observables of the individual collaborating mechanisms do not exist the physiological system is not practically identifiable and parameter estimation is a generic problem. In addition clinical data are often corrupted by noise and furthermore a traditional maximum-likelihood approach resulting in a weighted least square problem may run into problems due to the complexity of the optimization landscape with lots of local minima. Thus strategies have to be developed to circumvent such problems, e.g. incorporation of sensitivity analysis, correlation analysis, subset selection analysis etc. A major issue in these methods is uniqueness. The considerations and methods will be illustrated by an example taken from diabetes.

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MS50

Discovering Waves of Adipose Tissue Growth

n mammals, calories ingested in excess of those used are stored primarily as fat in adipose tissue; consistent ingestion of excess calories requires an enlargement of the adipose tissue mass. Thus, a dysfunction in adipose tissue growth may be a key factor in insulin resistance due to imbalanced fat storage and disrupted insulin action. Adipose tissue growth requires the recruitment and then the development of adipose precursor cells, but little is known about these processes in vivo. In this study, adipose cell-size probability distributions were measured in two Zucker fa/fa rats over a period of 151 and 163 days, from four weeks of age, using micro-biopsies to obtain subcutaneous (inguinal) fat tissue from the animals. These longitudinal probability distributions were analyzed using Bayesian model comparison to assess the probability of periodic phenomena. Adipose tissue growth in this strain of rat exhibits a striking temporal periodicity of approximately 55 days. A simple model is proposed for the periodicity, with PPAR signaling driven by a deficit in lipid uptake capacity leading to the periodic recruitment of new adipocytes. This model predicts that the observed period will be diet- dependent.

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MS51

Multiscale Model of Venous Thrombus Formation

Multiscale model is used for studying the role of Factor VII (FVII) in venous thrombus formation. A detailed submodel of the tissue factor (TF) pathway of blood coagulation is introduced within the framework to provide a detailed description of coagulation cascade. It is shown that low levels of FVII in blood result in a significant delay in thrombin production demonstrating that FVII plays an active role in promoting thrombus development at an early stage. In addition, a new subcellular element method for simulating cellular components in blood will be presented.

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MS51

Lattice Kinetic Monte Carlo Simulations of Aggregating Systems in Complex Flow Fields

Aggregation of cellular species in flow is generally described with continuum population balance equations (PBE). Aggregation kernels are generally impossible to derive for the complex flows in realistic applications where a direct simulation approach may be required. We compare the lattice kinetic Monte Carlo method to well-known solutions of PBE with respect to aggregation kernels and lattice discretization. The method is extended to arbitrary flows, sticking coefficients, open systems, and platelet aggregation.

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MS51

A Spatial-Temporal Model of Blood Coagulation and Platelet Deposition Under Flow

In the event of a vascular injury, a blood clot will form to prevent bleeding. This response involves two intertwined processes: platelet aggregation and coagulation. Activated platelets are critical to coagulation in that they provide localized reactive surfaces on which many of the coagulation reactions occur. The final product from the coagulation cascade directly couples the coagulation system to platelet aggregation by acting as a strong activator of platelets and cleaving blood-borne fibrinogen into fibrin which then forms a mesh to help stabilize platelet aggregates. Together, the fibrin mesh and the platelet aggregates comprise a blood clot, which in some cases, can grow to occlusive diameters. Transport of coagulation proteins to and from the vicinity of the injury is controlled largely by the dynamics of the blood flow. It is crucial to learn how blood flow affects the growth of clots, and how the growing masses, in turn, feed back and affect the fluid motion. In this talk, I will describe our spatial-temporal model of platelet deposition and blood coagulation under flow that includes detailed descriptions of the coagulation biochemistry, chemical activation and deposition of blood platelets, as well as the two-way interaction between the fluid dynamics and the growing platelet mass. I also discuss applications of our model to specific blood pathologies.

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MS51

Spatial Distribution and Thresholds Control the Outcome of Autocatalytic Blood Coagulation - Numerical Models and Microfluidic Experiments

Spatially-resolved simulations of blood coagulation can predict interesting behavior of this complex system. We used rate equations to describe the kinetics of clotting factors and inhibitors, coupled with simple diffusion or Navier-Stokes flow. In agreement with microfluidic experiments, we found that localized surface "patches" of tissue factor could initiate simulated coagulation only when larger than a threshold diameter or sufficiently confined. Patches of simulated bacterial proteases, activating thrombin and factor X, exhibited similar spatial behavior.

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MS52

Dynamics of Commonly Driven Elliptic Bursters

Intrinsically bursting neurons arise in many contexts. The governing equations usually have multiple timescales, giving rise to solutions that can have complex responses to perturbations. In this talk, I will present a study of a populations of elliptic bursters driven by a common input. In particular, we will investigate the effects of the driving signal's attributes (strength, periodicity, etc) on the synchronization and desynchronization of the population. I will present a reduction of the resulting dynamics to a simple discrete (random) dynamical system and study its behavior analytically and numerically. Possible applications to therapeutic methods based on electrical stimulation will be discussed.

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MS52

Controlling Populations of Neurons

We present an event-based feedback control method with a fixed stimulus magnitude constraint for randomizing the asymptotic phase of oscillatory neurons by time-optimally driving the neuron's state to its phaseless set, a point at which its phase is undefined and is extremely sensitive to background noise. When applied to a network of globally coupled neurons that are firing in synchrony, the applied control signal desynchronizes the population in a demand-controlled way.

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MS52

Circuit Properties that Influence Oscillatory Activity in Auditory Cortex

In many cortices, interactions between excitatory and inhibitory neurons generate network gamma oscillations. Through network model simulations, we show that experimentally recorded neural connection patterns and the synaptic properties of excitatory-inhibitory microcircuits permit the spatial extent of network inputs to modulate the magnitude of gamma oscillations. These findings suggest a novel mechanism by which oscillatory activity in the auditory cortex can be modulated by adjusting the spatial distribution of afferent input.

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MS52

Network Adaptation Through Neurogenesis: Pattern Separation in Olfaction

The network of the olfactory bulb is observed to enhance differences between activation patterns representing highly similar odors. Their complexity suggests that adaptation is important for this network. We show that recurrent, but not feedforward networks can adapt to this task effectively based on simultaneous correlations between input channels. Even in adult animals the olfactory bulb is persistently being rewired through neurogenesis and activity-dependent cell death. We show that this provides an effective adaptation mechanism.

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MS53

Modeling the Electrophysiology of the Suprachiasmatic Nucleus

Neurons in the suprachiasmatic nucleus (SCN) of the hy-

pothalamus are thought to communicate time of day information through circadian variation of their firing frequency, with low rates during the night and higher rates during the day. We study the electrical activity of the SCN through simulations of a detailed model of the ionic currents within SCN neurons, and find surprising behaviors at both the cellular and network levels.

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MS53

Modeling the Circadian Clock: From Molecular Mechanism to Physiological Disorders

Circadian rhythms originate from intertwined feedback processes in genetic regulatory networks. Based on experimental data, computational models of increasing complexity have been proposed for the molecular mechanism of these rhythms in mammals. Theoretical results pertain not only to the molecular bases of circadian rhythms but also to physiological disorders linked to perturbations of the human circadian clock such as sleep phase disorders, mood or bipolar disorders, jet lag, chronic jet lag and shift work.

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MS53

Modeling the Precision of Circadian Oscillators

Circadian clocks control behavioral and physiological rhythms in mammals, while showing remarkable precision for weeks. We combine modeling with quantitative analysis of luminescence data to study the quality factor (Q) of autonomous circadian oscillators. Modeling molecular noise predicts that precision decreases with reduced transcription, which is verified experimentally. We present approximations for Q that hold in different regimes, to assess precision in common circadian oscillator models and identify parameters that control this key property.

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MS53

From Bioluminescence Recordings to Entrainment Properties: Quantifying the Circadian Clock

We have analyzed bioluminescence time-series of circadian clock proteins in mouse cells. We extracted observationally well-defined parameters assuming two simple mathematical models: one describing a damped oscillator driven by noise, and one describing a self-sustained noisy oscillator. Both models describe the data well. However, the models predict distinctly different responses to entrainment signals, and we have begun to compare results of entrainment experiments to the predictions of our single-cell data analysis.

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MS54

Agent-based Dynamic Knowledge Representation of Inflammation: Insights for Interventions and Control

Inflammation is a critical and complex biological process for the maintenance of organism integrity. It is a highly conserved and robust system; however, because of these properties disease states resulting from disordered inflammation are very resistant to reductionist attempts at control. Agent-based modeling is a simulation method that can dynamically integrate the multiplicity of known mechanisms of inflammation. Examination of inflammation ABMs can provide vital insight into viable control strategies suitable for translational research.

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MS54

A Computational Model of the Spread of Inflammation Between Organs During Multiple Organ Failure

During an inflammatory response the interplay between the blood and tissue immune components is essential to recovery. This systemic response compromises organ function and can lead to multiple organ failure. We have developed an ODE model, which captures the blood and tissue dynamics within an inflamed organ. We then linked multiple tissue units together creating a multi-organ system and explored the spread of inflammation between organs and the onset of multiple organ failure.

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MS54

Identifying the Rules of Engagement Enabling Leukocyte Rolling and Adhesion using a Synthetic Model

We have constructed a synthetic in silico model for use as an experimental system for testing the plausibility of mechanistic hypotheses of how molecular components may interact to cause leukocyte behaviors during rolling, activation, and adhesion to endothelial surfaces. Here we will present

how the model was used to explore the hypothesized role of LFA-1 clustering events on the leukocyte membrane in mediating leukocyte adhesion during inflammation

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MS54

Probabilistic Approaches to Inverse Problems in Physiology, with Applications to Intensive Care Medicine

The inverse problem of parameter and state estimation from available observations for mechanistic mathematical models of physiological processes is one of the most challenging steps in moving from theory to application. This talk will, using practical examples, present an overview of established as well as recently developed numerical approaches that approximate full posterior distributions on joint parameter and state space, potentially enabling meaningful inference even in challenging situations where traditional point estimators encounter difficulties.

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MS55

Stochastic Models for Spread of Viral Infection Within and Between Hosts

New stochastic models for spread of viral infection within a host and between hosts are formulated and discussed. The dynamics of continuous-time Markov chain and stochastic differential equation models are compared with the dynamics of the corresponding ordinary differential equation models. The stochastic models provide new insights into the process of viral establishment, distinct from the deterministic model. Applications to spread of hantavirus in rodents and humans are discussed.

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MS55

The Impact of Spatial Heterogeneity in the Transmission of Dengue on the Synchrony of Incidence

Dengue is a mosquito-borne virus that exhibits multiannual cycles, mediated by cycling of immunity to the four antigenically distinct serotypes. Cycles in the central high population density area of Thailand have been ahead in phase of the northern and southern parts of the country. We present evidence of large variability in basic reproductive numbers across Thailand. Stochastic meta-population models that incorporate spatial heterogeneity show multiannual dynamics qualitatively similar to those exhibited by the data.

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MS55

Evolving Towards the Optimal Path to Epidemic Extinction

In large, finite populations which support an infectious disease, rare events due to stochastic fluctuations can induce epidemic extinction. The process of extinction proceeds along an optimal path which maximizes the probability of extinction in the large population limit. We show the optimal path also possesses a maximal sensitivity to initial conditions. As a result, the optimal path emerges naturally from the dynamics and may be explicitly constructed using finite-time Lyapunov exponents. Our theory is general, and is applied to several stochastic epidemiological models.

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MS55

Epidemic Extinction in Adaptive Networks with Random Pulsed Vaccination

We study epidemic spread in an adaptive social network with avoidance behavior. Random pulsed vaccination is included with a Poisson distributed schedule. We examine the rate of epidemic extinction as a function of vaccine parameters, both numerically and through analysis of a stochastic mean field formulation for a finite population. Social adaptation and vaccination together lead to orders of magnitude reduction in the epidemic lifetime.

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MS56

Stiffness in Multiscale Stochastic Simulation of Bio-

chemical Systems

Typical multiscale biochemical models contain fast-scale and slow-scale reactions, where "fast" reactions fire much more frequently than "slow" ones. This feature often causes stiffness in discrete stochastic simulation methods such as Gillespie's algorithm and tau-leaping methods leading to inefficient simulation. This talk proposes a new strategy to automatically detect stiffness and identify species that cause stiffness. Stiffness reduction methods are also discussed. Numerical results on a heat shock protein regulation model demonstrate the efficiency and accuracy of the proposed method for multiscale biochemical systems.

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MS56

Model Reduction for Chemical Reaction Networks: It's a Subtle Business!

Deterministic (ODE) models of chemically reacting systems routinely make use of approximations such as Michaelis-Menten to reduce both complexity and stiffness. We address the question of when can such a model reduction be accomplished accurately and with a significant gain in simulation efficiency, in the context of stochastic chemical kinetics.

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MS56

Sensitivity Estimation for Stochastic Biochemical Systems

Parametric sensitivity analysis is particularly challenging for discrete stochastic representations of biochemical networks as typically large number of Montecarlo simulations are required. We describe two methods based on the random time change representation of jump processes that provide for an efficient way to compute sensitivities. One approach is via path wise finite differences and the other is via a direct computation of a suitably regularized path wise derivative.

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MS57

Coevolution in Diverse Protein Families

Coevolving amino acid (AA) residues within protein sequences that originate from a common ancestor are important for its function. A novel graph construct was used to identify coevolving residues from pairs of AA positions in aligned, evolutionarily related sequences. Position pairs having high mutual information with many other pairs were computed. Using subsets of more closely related sequences, recent evolutionary traits of coevolving positions were uncovered. Differences in recent evolutionary signature were matched to receptor-ligand recognition traits unique to subsets.

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MS57

Probabilistic Graphical Models for Integrating Sequence and Structure Information

I will discuss the use of undirected probabilistic graphical models, also known as Markov Random Fields (MRF), for modeling multivariate probability distributions over protein sequence and/or structure. Many challenges in Structural Biology can be posed, and solved as inference problems on MRFs, including: structure prediction, free energy calculations, protein design, and the elucidation of the mechanisms that govern allosteric regulation. The presentation will first cover basic issues of representation, inference, and learning, and then review some recent applications of MRFs. No prior background in MRFs is assumed.

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MS57

Detecting Conserved Function of Evolutionarily Diverged Noncoding Elements

Gene regulatory elements consist of modules of specific sequence motifs with large stretches of inactive DNA separating them. We propose an alignment model contemplating evolutionary divergence in inactive DNA with preservation of active sites. With this approach, we were able to restore ancestral identity of 1640 human and zebrafish regulatory elements separated by 400 million years of evolution. This constitutes the first genome-wide computational method designed to reconstruct ancestral identity of vertebrate regulatory networks.

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MS57

Deciphering Gene Functions via Entromics

Entromics explains the physics of genome evolution and changes via mutation. It is a new theory with a two-law axiomatic basis: 1st. quantifies the thermodynamics of incorporating DNA-segments into a genome. 2nd. describes

the energy of chromosome assembly. Mathematically, Entromics uses homomorphisms of Eulerian graphs representing DNA and graph-distance derived partition functions. The maximal entropy principle results in a Planck distribution of incorporation energies in the genome, discovering new homologies in genomic function encodings.

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MS58

Exploring Models of Chemotherapy Scheduling

Numerous influential studies exploring the design of chemotherapy scheduling protocols have emerged with the development of mathematical oncology, including the investigations of Goldie, Coldman, Norton and Simon. We further scrutinise the classical models of chemotherapy protocol design to ascertain their robustness to the inclusion of additional tumour and treatment biology, in particular cell cycle phase specificity, pharmacokinetics and toxicity constraints; we also briefly explore the applicability of these modelling frameworks in the palliative setting.

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MS58

Role of Microenvironment in Breast Cancer Invasion: A Multiscale Model

Fibroblasts and myofibroblasts near the tumor microenvironment are important players in tumor growth and metastasis because of their unique ability to coordinate events which increase tumor cell proliferation and invasion to stroma, especially in breast cancer. It has been experimentally shown that fibroblasts play an important role in promoting breast cancer progression. We will present a mathematical model in order to better understand this complex interaction between stroma and transformed epithelial cells near a breast duct.

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MS58

The Evolutionary Impact of Androgen Levels on Prostate Cancer and Treatments in a Multi-scale Mathematical Model

High androgen levels may increase abnormal cell proliferation while low levels of androgen are suspected to induce selective pressure for abnormal cells. We model the evolution of a heterogeneous prostate cell population and find that low androgen environments select more strongly for elevated AR expression than do normal environments. Our results suggest that a low androgen environment may delay progression to a malignant phenotype, but result in a more dangerous cancer should one arise.

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MS58

Microenvironmental and Cell-specific Factors in Tumor Initiation

Epithelial tissues form highly organized barriers between different body compartments and require tight coordination between different cell life processes to ensure their integrity. In contrast, the disruption of epithelial architecture is thought to be involved in the emergence of cancers and in the initiation of its invasion. We address questions of when the initiated cell begins to show altered behavior and what events lead to tissue deformations and tumors. We present a computational model that investigates cell intrinsic sensitivity to extrinsic cues and predicts the disruptive effects of altered cell-microenvironment interactions. The obtained computational results are compared to in vitro experiments and in vivo samples.

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MS59

Modelling Cell-extracellular Matrix Interactions with a Force Based Model

In this talk I will discuss a force model of cell-extracellular interactions. The extracellular matrix is modeled as a network of springs and the cells interact with the extracellular network at defined points in the network. The model is used to simulate fibroblast populated collagen lattices and other systems related to wound healing. A more phenomenological model of cell-extracellular matrix will also be discussed.

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MS59

Using Mathematical Modeling to Assess the Efficacy of Oxygen for Problem Wounds: The Use of Hyperbaric or Topical Oxygen Therapies

We extend a previously developed mathematical model (Schugart et al., 2008) for acute wound healing to investigate the application of hyperbaric and topical oxygen therapies to treat wounds. In this talk, I will present the model, a sensitivity analysis of the model, and simulation results for treating the wound with hyperbaric and topical oxygen therapies.

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MS59

A Mathematical Model for Wound Closure, Angiogenesis and Wound Contraction

Cutaneous wound healing is a complicated process involving processes like coagulation, signalling from platelets, wound contraction, angiogenesis and wound closure. In this study, we present a model for cutaneous wound healing that couples mathematical models for these subprocesses. The model consists of a set of diffusion-reaction equations and visco-elastic equations. Finite-element solutions, model implications, as well as mathematical analysis are presented. Some of these ideas can be applied to tumor growth.

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MS59

Individual and Collective Cancer Cell Migration in 3D: The Role of Matrix Properties and Cell Density

Until now, our approach to study migration has been focused largely on cells on two-dimensional substrates that are far from in vivo. In order to address this critical deficiency, we have developed computational tools to study single and collective cell motion in native like 3D environments. Our results, which show very good agreement with experiments, suggest an intricate balance between matrix structure, mechanics and cell signaling in regulating speed and directionality during invasion and migration.

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MS60

Mathematical Models of Fibrinolysis: A Multiscale Approach

We study fibrinolysis (the degradation of fibrin by plasmin) using a multi-scale model intended to answer the following question: Why do coarse clots composed of thick fibers lyse more quickly than fine clots composed of thin fibers, despite the fact that individual thin fibers lyse more quickly than individual thick fibers? We use stochastic methods to model lytic processes on scales ranging from individual fiber cross section to whole clot.

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MS60

Patient Specific Models of Platelet Signaling in Response to Combinatorial Agonists

To understand how human platelets integrate diverse signals encountered during thrombosis, a high throughput assay measured intracellular calcium responses to pairwise combinations of 6 major agonists: ADP, convulxin, SFLLRN, AYPGKF, and PGE2. The calcium responses to single agonists at 0.1, 1, 10 x EC50 and 135 pairwise combinations trained a neural network (NN) model to predict the entire 6-dimensional platelet response space. These compact NN representations will be useful in multi-scale modeling of thrombosis.

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MS60

Modeling of Fibrin Polymerization and Branching

The blood clotting enzyme thrombin converts fibrinogen molecules into fibrin monomers which polymerize to form a fibrous three dimensional gel. The concentration of thrombin affects the architecture of this gel. We propose a mechanism by which fibrin branching can occur and show that this mechanism can lead to dependence of the gel's structure on the rate at which monomer is supplied, in a manner that mirrors experimental results. The origin of this dependence is explained.

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MS60

Contributions of Branching Points to Fibrin Network Strength and Stability

Blood clots are primarily composed of a network of branched fibrin fibers. These fibrin networks stabilize the primary platelets and enable blood clots to withstand the blood flow during wound healing at sites of vascular injury. The structure of the network is believed to be an essential component to its function. In the present study, a three-dimensional mechanical model of a fibrin network was developed to determine the detailed relationship be-

tween the network structure and its mechanical properties. We compare the mechanical responses of the network for two distinct structures; high branching vs. low branching based on image analysis of in situ fibrin network data.

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MS61

Synchrony of Noisy Neural Oscillators with Multiplicative Noise

Neural systems are generally stochastic, exhibiting asynchronous behavior in the absence of stimuli. We study the stability of the asynchronous state of noisy oscillators where the noise is multiplicative for physiological realism, in contrast to previous studies with additive noise. This presents analytical difficulties that are overcome with a novel method where we linearize around an asymptotic steady state assuming weak noise and weak coupling. Critical parameters are analytically derived for a variety of systems.

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MS61

Synchronization of Coupled Limit Cycles

Abstract not available at time of publication.

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MS61

The Transfer of Correlations by Integrate-and-fire Models with Point Process Inputs

Correlations between the spiking activity of neurons impact dynamical behavior and population coding in neuronal networks. A fundamental problem in the study of correlations is that of correlation transfer: given that two neurons receive correlated inputs, what is the correlation between their outputs? Recent studies have addressed this question by modeling subthreshold activity as a continuous diffusion process. Such models are obtained in the limit of a large number of inputs with infinitesimal postsynaptic response amplitudes, and may not fully capture the statistical properties the neurons' responses. I will talk about recent work on the problem of correlation transfer using models with finite postsynaptic potentials, where input spike trains are modeled as point processes. This approach yields intuitive insights into the mechanisms behind correlation transfer in drift and fluctuation dominated regimes, and allows us to model neuronal mechanisms such as synaptic noise and recurrent coupling in a natural way. Moreover, excitatory and inhibitory inputs can be treated separately. We find that the effects of synaptic noise and excitatory–to–inhibitory correlations, which are often ignored when inputs are modeled as Gaussian noise, can greatly reduce output correlations.

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MS61

Influence of Correlations in Large Networks

Abstract not available at time of publication.

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MS61

Reliability and Frequency Control in a Computational Model of the Locus Coeruleus Network

We consider electrically coupled ensembles of Hodgkin-Huxley type systems modeling LC network. In the presence of noise the network exhibits spontaneous firing. Surprisingly, the firing rate is a nonmontone function of the coupling strength. We study the dependence of the rate of firing on the strength of coupling as well as on network connectivity and noise intensity. Furthermore, we investigate network responses to spatially and temporally patterned input. The results of this study elucidate the mechanisms controlling transition from tonic to phasic firing in the LC network.

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MS62

Modeling the Neuronal Interaction Between the SCN and Sleep-wake Regulatory Systems

Recent experimental advances have identified both feedforward and feedback components involved in neuronal interactions between the suprachiasmatic nucleus (SCN) and sleep-wake regulatory systems. However, many details of these mechanisms remain unclear. Using a novel network modeling framework, we investigated interactions among primary brainstem and hypothalamic nuclei involved in rat sleep-wake regulation. We analyze the dynamic influences of the circadian pacemaker on sleep-wake patterning and the feedback effects of transitions in behavioral state on SCN activity.

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MS62

Mathematical Modeling of Human Circadian Rhythms and Performance

We have developed a mathematical model of the effects of light and non-photic cues on the human circadian pacemaker's phase and amplitude. The outputs of this model are used as inputs along with sleep-wake schedule and lighting exposure to a second model that predicts performance and alertness. These models have "real-world" applications for the prediction of times of poor performance and alertness in night-work, shift-work, extended duty or jet-lag schedules. Current work is focused on refining the models to make individual-based predictions based on demographic data.

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MS62

Dynamics of Sleep/wake Homeostatic Degradation and Circadian Modulation of Cognitive Performance

Several mathematical models have been developed to predict cognitive performance for a variety of wake/sleep scenarios. These models utilize the interaction of two biological processes: sleep/wake homeostasis and circadian rhythmicity, and are shown to generalize to a broad class of models formulated as coupled nonhomogeneous first-order ordinary differential equations. We investigate the dynamic properties of this model class: states of equilibrium, stability and bifurcation properties. New data are being utilized to refine the nonhomogeneity of the circadian rhythm independently and in interaction with the sleep/wake homeostat.

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MS62

Using Physiologically-based Modeling to Determine the Mechanisms Underlying

Modeling interactions between the suprachiasmatic nucleus and nuclei in the brainstem and hypothalamus provides insights into the sleep/wake and circadian functioning of the whole organism. We show that a physiologically-based model of this system can be used to identify potential physiological mechanisms that underlie inter-individual differences in chronotype, and the generation of spontaneous internal desynchrony behavior. In each case, the model fits well when compared directly with experimental data.

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MS63

Modeling the Interplay of the Inflammatory Response and Probiotic Treatment in Necrotizing Enterocolitis

Necrotizing enterocolitis (NEC) is a severe disease of preterm infants characterized by increased intestinal permeability and an exaggerated inflammatory response. A mathematical model is used to analyze the protective mechanisms of probiotics, which are beneficial bacteria species shown to be an effective treatment for NEC. While treatment with probiotics restores a stable health state in many cases, the model also predicts conditions under which this therapy may contribute to an increased inflammatory response.

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MS63

Predicting Clinical Outcomes Using Detailed Physiological Models

Many clinicians believe outcomes for severe sepsis patients depend critically on events during the early days of treatment. We test this hypothesis with experiments on a detailed mathematical model of physiology, representing pa-

tient health as trajectories in an uncertain clinical state space where observations are very limited. We discuss the creation of realistic in-silico patients, and analyze how certainty in outcome prediction depends on the duration of early observation and richness of measurements collected.

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MS63

Treating Severe Infections with Blood Purification

Severe infections are frequently accompanied by shutdown of organ systems and death, with many patients requiring intensive medical support. The degree of sickness is determined not only by severity of infection, but also by the severity of the body's immune response. mathematical models may impact our understanding of this disease and guide therapeutic intervention. We present a case study of the usefulness of systems engineering disease process, where the clinical effectiveness of the adsorption of blood cytokines by an extracorporeal filter, when viewed from a modeling perspective, allows data synthesis and leads to new mechanistic hypotheses generation.

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MS63

A System Identification Approach for Modeling Host-Pathogen Interaction and Intervention Design

A general data driven approach for modeling host-pathogen interaction based on time course experimental data will be presented. The approach can utilize simultaneously data at hierarchy of levels including, genomic, proteomic, cellular and physiological levels. It provides a multiscale dynamical mechanistic model that integrates across these scales. Intervention design is discussed in a control theory setting. Application to modeling Influenza A and Francisella Tularensis will be shown.

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MS64

Plug-and-Play Inference for Stochastic Dynamical Systems

An increasingly fruitful approach to ecological inference queries time-series data using stochastic dynamical systems (AKA state-space models, partially-observed Markov processes). Rigorous inference using such models has traditionally been extremely challenging. Furthermore, most existing methods place severe restrictions on the form of the models that can be entertained. *Plug-and-play* methods, by contrast, require only simulation and are thus free of such restrictions. These methods accelerate scientific progress by allowing one to entertain and compare multiple competing hypotheses. I will point out several of these methods and describe one, Iterated Filtering, in some detail, using ecological examples to show that one can use it to ask and answer questions previously unaddressable. Along the way, I will introduce a software package, pomp, that implements a number of plug-and-play methods and is a platform upon which other algorithms can be easily implemented.

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MS64

Stochastic Spatio-Temporal Models Confronted with Experimental Data: Extinction, Invasion, and Climate Change

Prediction in ecology must take into account considerable uncertainties that are generated by stochastic and nonlinear processes. We derive mechanistic stochastic models at the population level by scaling up from stochastic processes at the level of individuals. By fitting these stochastic models to experimental data from a model laboratory system, we show that accurate prediction of extinction, invasive spread, and response to climate change depends critically on factors contributing to stochasticity.

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MS64

Spatial Patterns in Stage-Structured Populations with Density Dependent Dispersal: An Application to Tribolium

Spatial segregation among life cycle stages has been observed in many stage-structured species, both in homo-

geneous and heterogeneous environments. We investigate density dependent dispersal of life cycle stages as a mechanism responsible for this separation by using stage-structured, integrodifference equation models that incorporate density dependent dispersal kernels. We construct a spatial model to describe the population dynamics of the flour beetle species Tribolium brevicornis and use it to assess density dependent dispersal mechanisms that are able to explain spatial formations observed in this species.

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MS64

Invasion Speeds of Structured Populations in Random Environments

We live in a time where climate models predict future increases in environmental variability and biological invasions are becoming increasingly frequent. A key to developing effective responses to biological invasions in increasingly variable environments will be estimates of their rates of spatial spread and the associated uncertainty of these estimates. Using stochastic, stage-structured, integrodifference equation models, invasion speeds are shown to be asymptotically normally distributed with a variance that decreases in time. These methods are applied to a simple juvenile-adult model with stochastic variation in reproduction and an illustrative example with published data for the perennial herb, Calathea ovandensis. These examples buttressed by additional analysis reveal that increased variability in vital rates simultaneously slow down invasions yet generate greater uncertainty about rates of spatial spread. Moreover, while temporal autocorrelations in vital rates inflate variability in invasion speeds, the effect of these autocorrelations on the average invasion speed can be positive or negative depending on life history traits and how well vital rates "remember" the past.

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MS65

Error Analysis of Tau-leap Methods

While exact simulation methods exist for discrete-stochastic models of biochemical reaction networks, they are oftentimes too inefficient for use because the number of computations scales linearly with the number of reaction events; thus, approximate algorithms are used. Stochastically modeled reaction networks often have "natural scales' and it is crucial that these be accounted for when developing and analyzing approximation methods. We have recently demonstrated this fact by showing that a midpoint type algorithm thought to be no more accurate than an Euler type method is in fact an order of magnitude more accurate in a certain scaling–something previously observed only through examples. I will describe the analysis performed and show why we reach fundamentally different conclusions than previous analyses.

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MS65

Analysis of Tau-leaping Scheme and Some Applications in Mathematical Biology

The tau-leaping algorithm is proposed by D.T. Gillespie in 2001 for accelerating the simulation for chemical reaction systems. It is faster than the traditional stochastic simulation algorithm (SSA), which is an exact simulation algorithm. In this lecture, I will overview some recent mathematical results on tau-leaping done by our group, which include the analysis, construction of the new algorithm, and some applications in mathematical biology.

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MS65

Numerical Methods for Stochastic Bio-Chemical Reacting Networks with Multiple Time Scales

Multiscale and stochastic approaches play a crucial role in faithfully capturing the dynamical features and making insightful predictions of cellular reacting systems involving gene expression. Despite their accuracy, the standard stochastic simulation algorithms are necessarily inefficient for most of the realistic problems with a multiscale nature characterized by multiple time scales induced by widely disparate reactions rates. In this talk, I will discuss some recent progress on using asymptotic techniques for probability theory to simplify the complex networks and help to design efficient numerical schemes.

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MS66

Spatial Characterization of Coronary Artery Pathologies using Optical Coherence Tomography

Optical coherence tomography gives spatial resolution of artery pathologies ¿10x that of intravascular ultrasound (IVUS). Pathologies correlate with hemodynamic indices such as wall shear stress (WSS) often quantified with computational fluid dynamics (CFD). Prior techniques for spatial model reconstruction oriented IVUS images onto a transducer path estimated from bi-plane angiography as a parameterized curve, then applied rotations using differential methods (e.g. discrete Frenet) that may risk errors at higher orders. We aimed to utilize the superior resolution of OCT combined with computed tomography (CT) and graph theory to create patient-specific models of the left circumflex artery (LCX) with thrombus during pre- and post-stent phases, from which WSS will be quantified using CFD. OCT images acquired and segmented with the LightLab®system were processed with MATLAB to define 3D lumen segments. A centerline created automatically from CT data using ITK-Snap and VMTK open source software is used with landmarks from CT to orthogonally

pre-register the OCT segments. The unknown path of the OCT transducer is determined using Djikstra's algorithm with a k-level graph of mesh points at each pre-registered segment. Final registration onto the transducer path applies rotations independent of local derivatives such that segment centroids align with the centerline. Final segments are lofted as a solid model in Simvascular (wiki.simtk.org). This robust methodology generates LCX geometries with precise 3D locations of pathologies and will improve future assessment of WSS indices.

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MS66

Imaging of Mechanical Properties in Normal and Aneurysmal Abdominal Aortas In Vivo

Arterial stiffening is associated with increased cardiovascular mortality. In this paper, two different ultrasound-based methods used for mapping the mechanical properties of the aorta in vivo will be presented: 1) the novel pulse wave imaging (PWI) method for visualization of the pulse wave during propagation and for calculation of the underlying wall mechanical properties; and 2) mapping of the stress-strain relationship and identifying the moduli of the different wall constituents using the wall strain and luminal pressure waveforms.

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MS66

A Visco-elastic Model of Arterial Wall Dynamics from Direct In-vivo Measurement of Pressure and Wall Motion

Large arteries act as conduits of blood to the circulation, and their function affects hemodynamics near the heart. Characterizing conduit artery wall motion requires a model that accounts for its non-linear, visco-elastic, behavior. We present such a model, and fit it to pressure and wall-motion data measured in-vivo in rodents. We also discuss challenges associated with using the model to infer new biology relevant to the treatment of cardiovascular diseases.

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MS66

Modeling and Model Analysis of Nonlinear Viscoelasticity of Ovine Arteries

A better understanding of the biomechanical properties of the arterial wall can aid in the improvement of graft design and implementation. In this study we focus on developing a constitutive relationship describing the dynamic response of changes in cross-sectional vessel area induced by time-varying arterial blood pressure. We used inverse mathematical modeling on a 4-parameter Kelvin (linear) viscoelastic model and a 5&6-parameter nonlinear viscoelastic models and tested them on in-vitro data from male Merino sheep. Parameter estimation, sensitivity and statistical analysis approaches were used to investigate and describe the viscoelastic vascular wall properties allowing us to compare models and choose the most adequate one that enabled parameter estimation within physiological ranges.

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MS67

What Fire is in Mine Ears?

The cochlea of the inner ear is a biological transducer with an astounding constellation of performance characteristics, including sensitivity to sub-atomic displacements with microsecond mechanical response times; wideband operation spanning three orders-of-magnitude in frequency; and an input dynamic range of 120 dB, corresponding to a million-million-fold change in signal energy. All of this is achieved by self-maintaining biological tissue, most of which is salty water. Analysis of mechanical data demonstrates that the cochlea boosts its performance by acting as a wideband, hydromechanical laser amplifier. A by-product of the laser-like amplification within the cochlea is the spontaneous generation of sound by the ear.

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MS67

Transient and Stationary Responses in a Nonlinear Model of Cochlear Mechanics

Mechanics of mammalian cochleae are evidently nonlinear, but how nonlinear? A recent publication suggested that cochlear nonlinearity is not instantaneous because cochlear responses to Gaussian noise are observed to be quasi-linear even at high intensity. In contrast, our cochlear model with instantaneous nonlinearity produces quasi-linear responses in time-domain simulations. The model also produces realistic distortion-product emissions. Implications of these model results should promote better understanding of cochlear mechanics and hair-cell dynamics.

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MS67
Modeling the Nonlinear Dynamics of the Cochlea

A linear active model of the cochlea (with a 3D representation of the fluid and structure and feedback from outer hair cell somatic motility) has been developed previously to approximate the response of the cochlea to acoustic input. A nonlinear formulation of the model (with an efficient alternating frequency/time method) is implemented here to predict the stationary response of the basilar membrane to single-tone (gain and harmonic distortion) and two-tone inputs (distortion products).

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MS67
A Ratchet Mechanism for Low-Frequency Mammalian Hearing

The sensitivity and frequency selectivity of hearing result from tuned amplification by an active process in the mechanoreceptive hair cells. The nature of the active process in the mammalian cochlea is intensely debated, for outer hair cells exhibit two forms of mechanical activity, active hair-bundle motility and membrane-based electromotility. Here we show theoretically that active hair-bundle motility and electromotility can together implement an efficient mechanism for amplification that functions like a ratchet: sound-evoked forces acting on the basilar membrane are transmitted to the hair bundles while electromotility decouples the active hair-bundle forces from the basilar membrane. Through a combination of analytical and computational techniques we demonstrate that the ratchet mechanism can naturally account for a variety of unexplained experimental observations from low-frequency hearing.

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MS68
Multiscale Analysis of Cardiac Rhythm Disturbances in Genetically Altered Substrate

While harmful cardiac gene mutations render the heart at high risk for the incidence of life threatening arrhythmias, the fatal event takes a long time to develop because it needs an adequate triggering event. The nature of this event and the associated mechanism of arrhythmia are poorly understood. Based on large scale simulations we characterize wave dynamics in a realistic model of the cardiac ventricles, and determine excitation conditions for the initiation of abnormal rhythm. We further suggest that the site of initiation of the abnormal rhythm could be predicted for specific patient conditions.

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MS68
Efficient Stochastic Simulation of Cardiac Excitation-Contraction Coupling

Cardiac excitation-contraction (EC) coupling are the series of events from electrical excitation of the heart through calcium dynamics to contraction. Previous studies have show that certain characteristics of EC coupling require stochastic simulation as they depend upon the stochastic recruitment of different calcium release units of the heart. However, stochastic simulations typically use Monte Carlo Methods that can be computationally expensive. We present efficient methods that allow the solution of this problem.

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MS68
Extremely Fast Numerical Algorithms Implemented on Graphics Processing Units

Modern Graphical Processor Units (GPU) offer a unique computing platform. Although there unique multiprocessor architecture was developed for the video and gaming industry, there are many physics based applications that can make use of their tremendous power. Over the past eight years we have developed redeveloped a number of numerical algorithms to run on GPUs. In this talk we will describe the use of GPU's in modeling electrical activity of the heart. Our GPU implementation is roughly 20 times faster than standard best in class 4 core workstation implementations of our existing cardiac simulation model.

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MS68
Ectopic Beat Formation in the Atrioventricular Node

The sinoatrial node is a complex structure with gradients in coupling, action potential gradient and response to autonomic tone. We hypothesized that shifts in the site of leading pacemaker activity caused by nervous activity can lead to ectopic beat formation. A highly detailed sinoatrial node model was inserted in a finite element model of the right atrim. Results indicate that electrotonic loading and measured gradients can account for many observed phenomena.

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MS69
Probability, Statistics and Information Theory Ap-

plied (and Misapplied) in Proteomics

The field of proteomics has been driven by advances both in instrument technology and in bioinformatics. While bioinformatics has depended upon the established reliability of the computational methods for biosequence comparison and upon the availability of large-scale annotated biosequence databases, in proteomics the application of probability and statistics appears to be encountering some pitfalls. Applications, and misapplications of probability, statistics and information theory in proteomics will be discussed, with particular emphasis on the analysis of mass-spectrometric data and on the analysis of protein modifications.

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MS69

Fitness and Genetic Load of Single Nucleotide Polymorphisms Affecting mRNA Splicing

Deleterious genetic variants can be evaluated as quantitative traits using information theory-based sequence analysis of recognition sites. To assess their effects, fitness and genetic load of SNPs are derived from changes in individual information and allele frequencies. Human SNPs that alter mRNA splicing are partitioned according to their genetic load. SNPs with high genetic loads are common in the genome and, in many instances, predicted effects are supported by gene expression studies.

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MS69

Efficiency of Molecuar Machines

Sequence logos and sequence walkers display information in DNA binding sites measured in bits. But how is information related to energy? The lower bound on joules per bit is given by the Second Law of Thermodynamics. However, measured binding sites do not reach the bound, many use only 70% of the binding energy to make selections. I present my work on explaining why this 70% efficiency appears in many molecular interactions.

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MS69

Information Theory, Statistical Physics, and Molecular Biology

In one view, the Second Law of Thermodynamics limits the information gained when a system dissipates heat. Data indicate that when some types of biomolecular reactions dissipate free energy, they yield at most about 70 percent (ln 2) of the information limit predicted by the Second Law of Thermodynamics. This talk indicates how information theoretic considerations in statistical mechanics might impose this extra energy cost on a physical system whose microstates must satisfy coding constraints.

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PP0

A Mathematical Model for Odor Discrimination

Neurons within the brain receive inputs from several hundred or several thousand other neurons. Oscillations and other patterns of neuronal activity arise throughout the central nervous system. These oscillations have been implicated in the generation of sleep rhythms, Parkinsonian tremor, sensory processing within the olfactory bulb (OB) of mammals or the antennal lobe (AL) of insects, as well as in learning and memory. Recently, Broome et al. (Neuron 2006) showed that when two odors are presented with some time gaps, there is a smooth divergence from detecting the first odor and then a smooth convergence to detecting the second odor. Fernandez et al. (J. Neurosci. 2009) showed that there is a smooth transition in the time-dependent neural representation in response to a smooth transition in the ratios of odorants. We investigate a Hodgkin-Huxley type excitatory-inhibitory neuronal networks model that reproduces several features of these experiments.

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PP0

Using a Two-Dimensional Continuum Mechanical Model to Predict Collective Cell Migration

A two-dimensional continuum mechanical model is used to simulate collective motion of the intestinal epithelial cell layer in two opposite scenarios: wound closure and cell colony expansion. Effects of the forces induced by lamellipod formation, adhesion between cells and matrix, and elastic stress in the layer are incorporated in the model. The consistency between model predictions and experimental observations indicates the utility of this model in predicting cell migration for various initial and experimental conditions.

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PP0

Rapid Reliable Results: Accurate Cardiac Simulations Without the Wait

Tissue simulations of the cardiac action potential are an essential tool for understanding mechanisms of lethal fibrillation and could find use in personalised medicine. They are computationally demanding; decreases in this demand are desirable to increase their usefulness. We present results for action potential propagation in 2D tissue using PDE time-step adaptivity based on a posteriori error estimates giving guaranteed accuracy, demonstrating a good speed-up away from the wavefront. 3D results are in preparation.

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PP0

Stochastic Estimation of Effective Diffusivity and Proliferation Rates During Wound Closure in the Intestine

Necrotizing enterocolitis is a severe inflammatory disease characterized by wounds in the intestinal wall. To more fully understand the process of wound closure in this context, a nonlinear diffusion model is compared with in vitro data to estimate the effective rates of diffusion and cell proliferation in the system. Because of inherent uncertainties, both direct optimization (simplex method) and stochastic optimization (Kalman filter) are used to obtain these rates and the uncertainty associated with them.

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PP0

Ion Concentration Dynamics and Neuronal Excitability

We develop models of individual neurons and of networks that include intra- and extra-cellular ion concentration dynamics. A reduction of the single neuron model is used to identify the bifurcation structure, leading to the identification of a novel mechanism for bursting and seizure-like events that are similar to that seen in experiments. In addition, we examine the stability of persistent states of activity and excitatory-inhibitory interplay. A possible role of cation-chloride co-transporters is also discussed.

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PP0

Effects of Spike-Driven Feedback on Neural Gain and Correlation

We study how spike-driven feedback affects gain and pairwise correlation in simple networks of LIF neurons with noisy inputs. Using both stochastic ODE simulation and linear response theory, we show feedback modulates gain and correlation in different ways over various time scales. Lastly, we show analytically that correlation modulation is strongly dependent on the time scale of the synapses involved.

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Simplified Model of Rhythm Generation in the Intact Respiratory Neural Network

Rhythm generation in the respiratory neural network is complex. Under normal conditions it involves several interacting populations of neurons but under severe conditions (for example lack of oxygen) rhythm is effectively generated by a single population. The transition between the normal and severe cases is accompanied by changes in the neural signals appearance and frequency. To help understand the underlying dynamics, a minimal phenomenological model has been developed and will be presented.

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PP0

Traveling Waves in the Spreading of Dengue Fever

Dengue fever is a multistrain mosquito-borne disease with sustained, oscillatory outbreaks over large spatial regions. An important empirical feature of the disease is subharmonic traveling waves of infection originating from a highly populated area. We present a multistrain metapopulation model that exhibits traveling waves between patches resulting from heterogeneity in contact rates. The patch with the highest contact rate leads the dynamics.

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PP0

Schnakenberg Model with Grandient for Root Hair Position

Hair cells in the roots of *Arabidopsis* in wild type produce a single hair towards the apical end. A Schnakenberg-type system is used to describe the activation of small ROP G-proteins that locate the hair site. The system is analyzed using numerical continuation and asymptotic methods. A spatial gradient of the hormone auxin is shown to be necessary and can capture the multiple hairs seen in mutants. The results shed light on the observed roles of cell length and overall auxin level in this important example of cellular morphogenesis.

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PP0

The Optimal Strategies for Tuberculosis with Exogenous Reinfection

In this work, we apply optimal control theory to the system of ordinary differential equations that describes tuberculosis (TB) with exogenous reinfection. Here, the optimal controls represent treatment or prevention. Using an objective function that is based on minimizing the infected individuals and the treatment efforts, we characterize the optimal control in the optimality system. To find the best combination of controls, the system is solved numerically for several scenarios.

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PP0

Synergy of Specifically Targeted Antiviral Therapies for Hepatitis C (STAT-C) in Combination with Standard of Care Treatments

Current therapy of chronic hepatitis C virus infection is still unsatisfactory. We studied in vitro drug interactions of STAT-C in combination with interferon and/or ribavirin. The four-parameter logistic Hill model was chosen to describe single agent dose-response activities. Model parameters were estimated using a nonlinear mixed-effects model. We assessed synergistic effects of combination therapies according to the Bliss null reference model. Overall, the approach indicates independent or slightly synergistic but no antagonistic effects.

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PP0

Modeling Sensory Input to the Lamprey Spinal Cord

We develop and evaluate a neural model of the lamprey's central pattern generator of locomotion, implemented as a chain of coupled oscillators. We simulate sensory input from edge cells, which measure the body's curvature, by forcing the chain at various positions, one at a time. By varying chain length, forcing position, and forcing connection strength in our trials, we have gained insight into how they these parameters affect entrainment range.

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PP0

Multi-Modal Optimization for Biophysical Neural Models

In addition to poorly conditioned optimization due to nonlinearities and noise, goal data may originate from different experimental scenarios with variation in underlying conditions. This can ensure that no *quantitatively* fitting solution exists. Thus, we extend multiple objective optimization for a single comparison modality (e.g., individual voltage traces) into multiple modalities. We consider "qualitative' features that help regularize the objective function for neural models, including spike shape characteristics, the frequency response curve, phase response curve, and an encoding of a desired bifurcation structure in the model. We demonstrate these methods using native support in the PyDSTool software.

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PP0

Spatial Characteristics of a Simple Stochastic Growth Model

Many physical and biological processes exhibit complex spatial distribution like bacterial growth, disease spreading, and tissue fibrosis. A simple stochastic model was developed to reproduced the diversity of patterns which is

determined by two parameters (p,D). p represents the probability of not touching an existing occupied site (8 neighbours) while increasing the density of occupied sites (D). Analysis of the model showed a non-monotonic variation of the fractal dimension and cluster fusions compared to monotonic variation of lacunarity measure with p increasing.

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PP0

In Vivo Bioimaging Analysis for Simulating Plant Growth Regulation

The mechanisms that regulate plant cells to promote growth are yet to be fully understood. Recent experiments suggest that mechanics and biochemistry signaling coupled with cell geometry interact at the cellular level to orchestrate growth and patterning in plants. The success of such experiments is greatly due to new developments in live bioimaging technologies which have enabled us to image and visualize plant cells as they change shape, divide, and grow in controlled settings in the lab. Image analysis is then necessary to transform raw images into computational models: we extract important features of cells and provide a computational description of cell geometry and tissue topology necessary to carry on developmental simulations in silico. Such models are essential in the investigation of cellular mechanotrasduction which is at the heart of computational morphodynamics.

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PP0

HIV Model Analysis, State Estimation and Optimal Control

We will present a nonlinear model for the dynamics of HIV infection, which includes multiple target cells, multiple treatment methodologies and virus specific immune response. The dynamics of the model will be studied under an optimal control based treatment schedule through applications of sensitivity equations and parameter identifiability. We then implement stochastic estimation and a Receding Horizon feedback control based treatment strategy. Finally, we will consider drug resistance and genetic level information.

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PP0

Evaluating Treatment of Hepatitis C for Hemolytic Anemia Management

The successful therapy of peg-interferon and ribavirin for Hepatitis-C is associated with the side-effect of hemolytic anemia necessitating dose reduction or therapy cessation. We formulate an ODE model which quantifies the amount of drug a body can tolerate without hemolytic anemia. Indirectly estimated parameters give the necessary increment in RBC production (due to administering of drug epoietin) to be $\geq$ 2.3 times of original RBC production rate to sustain the entire period of treatment without anemia.

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PP0

Fission-Yeast Polarity Change: Symmetry Recovery in a Dynamical System

Fission yeast recovers symmetry in a transition from monopolar to bipolar growth called new-end take off (NETO). We consider models for NETO that include (i) an autocatalytic actin filament assembly at cell tips, and (ii) dissociation self-inhibition of actin nucleators. These effects saturate as the cell elongates, and longer cells are symmetric. We present a bifurcation analysis and describe parameter dependence with a phase diagram. We suggest experiments that may distinguish between the two mechanisms.

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A Distributed Parameter Biochemical System with Delay Growth Response

This paper studies a biochemical reactor distributed pa-

rameter model with delay growth response. It has long been known that that the classical models of growth response such as Monod or Haldane models, are not able to account for the oscillations in chemostat occuring under suitable operational conditions. The need of considering a time delay in the growth response, as a source of oscillations, has been emphasized by many authors. We consider a biochemical tubular reactor with time delay, whose dynamics are described by a system of partial functional differential equations.We investigate qualitative properties of the trajectories of the system, and we prove the existence of periodic trajectories.

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PP0

A Mathematical Model for Timing the Release from Sequestration and the Resultant Brownian Migration of SeqA Clusters in E. Coli

DNA replication in Escherichia coli is initiated by DnaA binding to oriC, the replication origin. During the process of assembly of the replication factory, the DnaA is released back into the cytoplasm, where it is competent to re-initiate replication. Premature reinitiation is prevented by binding SeqA to newly formed GATC sites near the replication origin. Resolution of the resulting SeqA cluster is one aspect of timing for reinitiation. A Markov model accounting for the competition between SeqA binding and methylation for one or several GATC sites relates the timing to reaction rates, and consequently to the concentrations of SeqA and methylase. A model is proposed for segregation, the motion of the two daughter DNAs into opposite poles of the cell before septation. This entropic spring model assumes that the binding of SeqA and its subsequent clustering results in loops from both daughter nucleoids attached to the SeqA clustera at the GATC sites. As de-sequestration occurs, the cluster is divided in two, one associated with each daughter. As the loops of DNA uncoil, the two sub-clusters migrate apart due to the Brownian ratchet effect of the DNA loop.

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PP0

Adaptive Sparse Grid Method for Representations of the Free Energy Landscape of Proteins

The free energy landscape (FEL) is of importance for a quantitative understanding of the relationships between structure, dynamics, stability, and functional behavior of proteins. However, the free energy landscape of a protein is a high dimensional hyper-surface and is difficult to rationalize. Here, we describe an adaptive sparse gird method, which provides an very efficient approach for the computation of the representation of the free energy landscape of proteins.

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PP0

Towards A Realistic Epidemic Model of Swine Flu Spread: Part 1 - Inclusion of Mortality Components, Hospitalization and Quarantine of Asymptomatic Individuals

H1N1 cases were first detected in the United States in April of 2009. Since then, the CDC has reported a worldwide total of approximately 47 million cases and 9,820 deaths as of November 14, 2009. The World Health Organization declared a swine flu pandemic on June 11, 2009 by raising the pandemic alert level to Phase 6. In this paper, we present a more complete model for H1N1 spread. We construct a deterministic nonlinear multicompartmental model to illustrate the movement of H1N1 through an arbitrary size population. We then demonstrate the existence of a disease equilibrium and compute the reproductive ratio R_0 and the effective reproductive ratio R_{eff}. We compare our results to those of a previous model (Podder, 2007). We demonstrate that our extended model has peaks in each compartment that occur five days sooner than those of the Podder(2007) model and discuss the biomedical implications of this result. Comparison of the dynamics of R_0 for the two models shows that there is an non-biological bifurcation in the behavior of the Podder(2007) which does not occur in our extended model. It appears that inclusion of the additional biological/epidemiological compartments provides for a more realistic description of the epidemic spread of H1N1 in a human population. We then discuss the effect of timelag in various compartments and how that alters the dynamics for vaccination planning.

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PP0

Modeling of Viral Kinetics in Patients Chronically Infected with Hepatitis B and D

Viral kinetic models have become helpful for understanding the dynamics of viral diseases and for optimizing antiviral therapy. We developed a mechanistic viral kinetic model to analyze the dynamics of viremia in Hepatitis-B/Hepatitis-D (HBV/HDV) coinfected patients after liver transplantation. Thereby the HBV/HDV-host-interplay is modeled with a suitable non-linear differential equation system. This model is fitted to clinical data and the estimated model parameters are correlated with HBIG dosing schemes (passive immunization administered to prevent reinfection).

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PP0

Spatially-Localized Synchronous Oscillations in Synaptically-Coupled Neuronal Networks

We study the qualitative behavior of localized synchronous oscillations organized by synaptic inhibition in two spatially-extended, conductance-based neuronal network models driven by a localized constant input. Typically such equations generate complex spatiotemporal behavior, however, with strong inhibitory coupling, the response of the network is a single band of neurons firing nearly synchronous action potentials, almost periodically. We subsequently derive one and two dimensional discrete maps that qualitatively describe the behavior and bifurcations in the full model.

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Dynamics and Control of Thymocytes in Neonate Mrl+/+ Mice Exposed to Trichloroethylene (tce)

Toxicant exposure in neonates can have important consequences in the immune system development and homeostasis. Trichloroethylene (TCE) is an environmental toxicant that causes alteration in the number of immature T cells in the mouse thymus. We present a mathematical model for the maturation of thymocytes in the MRL+/+ mouse upon TCE exposure. The conditions for global stability are determined. Also, some therapeutic scenarios to revert the effects of early-life exposure to TCE are analyzed.

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PP0

Seasonal and Diurnal Wind Characteristics in Southern Sri Lanka

The characterization of the seasonal and diurnal wind takes particular importance in Southern Sri Lanka as it is at one of the extremes of the Asian land mass. In this paper, the seasonal and diurnal characteristics of the surface wind are presented for one location on the Southern coast and for another location that is 30 km interior. The monthly wind speeds are highest during July and August (9 m/s) coinciding with the passage of the Easterly low-level jet over Sri Lanka. During the remainder of the South-West monsoon, from May to September, the speed remains greater than 4 m/s. The speed during the North-East monsoon, from December to March, is also moderately high (3 m/s). During the two inter-monsoon seasons of April-May and October-November, the wind speeds are less than 2.5 m/s. The onset and withdrawal of the monsoons for 1990/91 was estimated based on the consistency of wind directions. The North-East monsoon onset in the 3rd week of November, 1990 and withdrew in the 3rd week of March, 1991. The South-West monsoon onset in the 2nd week of May and withdrew in the 3rd week of October, 1991. There is strong diurnal variability in wind velocities. Nighttime wind speeds are approximately half of the day-time high throughout the year. During the middle of the South-West monsoon, the wind directions does not show much diurnal variability. During the North-East monsoon, the wind direction changes from NNW at night to E during day-time. Similarly in the inter-monsoon months, the wind direction changes from SWW at night to S during the day. This diurnal change in wind direction is shown to be influenced by the sea breeze.

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PP0

Bursting in a Two-Compartmental Neuron Model

We study the possibility of bursting in a two-compartment model arising from the dopaminergic neuron. We found that the model can generate bursting given the difference in the time constants for variables in the two compartments. We determine conditions on heterogeneity of coupling required for bursting. We discuss how the onset of bursting can be achieved and how the number of spikes in the burst can vary. This type of bursting can also be present in neuronal networks coupled by gap junctions, which determines a broad range of applications for our results.

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PP0

Modeling the Fluid Dynamics of Feeding in the Upside Down Jellyfish, Cassiopea Sp.

This presentation focuses on describing the scaling effects in feeding of the upside down jelly?sh (Cassiopeia sp.) using computational fluid dynamics and live experiments. The immersed boundary simulates the bell of a jellyfish as an immersed, flexible boundary. A porous boundary represents the oral arms which protrude over the bell, altering the flow. The effect of the oral arms on vortex formation

and on volumetric flow rates are analyzed across a range of Reynolds numbers.

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PP0

The Dynamics of Exit from Mitosis in Budding Yeast

We have developed a deterministic ODE model for the control of Cdc14, an essential phosphatase promoting mitotic exit in yeast. The model captures the dynamics of mitotic exit in wild-type and dozens of mutant cells clarifying the roles of Esp1 and Cdc5 (Polo kinase) in mitotic exit pathways. Understanding how Polo-like kinase fits into the exit pathway is important because it is being actively pursued as a therapeutic target in the treatment of human cancer.

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PP0

Modelling of Metaliothionein Gene Network in Caenorhabditis Elegans: Mathematical Models, Predictions and Laboratory Experiments

Metallothioneins are small, cysteine-rich proteins that function in metal detoxification and homeostasis in many eukaryotes. Metallothionein gene transcription is induced via metal-responsive pathways. Here we propose and analyze some mathematical models of a gene regulatory network involving metallothionein genes in Caenorhabditis elegans. Mathematical analysis and numerical simulations of the proposed models predict certain conclusions regarding the influence of single and mixed metal ions on this network. These theoretical predictions have been verified by laboratory experiments.

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PP0

Gene Network Models Robust to Spatial Scalings and Noisy Input

Reaction-diffusion models are presented, which produce precise patterns, despite changes in the spatial domain and noisy input to the system. The equations mimic the robust pattern formation seen in early *Drosophila* development, where protein gradients scale with respect to embryo length along the anterior-posterior axis, despite variations in embryo sizes and noisy upstream gene expression. The essential properties of the model are interpreted in terms of their biologically meaningful parameters.

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PP0

Modelling Disease Spread at the US Naval Academy

We use dynamical systems and stochastic process models over the well-defined contact network that exists at the United States Naval Academy to study the spread of infectious diseases through a military barracks environment. We analyze trends and calibrate our model's parameters using data detailing class absences due to illness over the past 5 years. This data includes information on the contact network structure between midshipmen, including living arrangements in the dormitory, classes, and sports teams.

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PP0

Inclusion of Ovarian Androgens in a Model for Hormonal Regulation of the Menstrual Cycle.

A 7-hormone model of nonlinear differential equations describing the hormonal regulation of the pituitary-ovarian axis in women is presented incorporating androgen in female fertility. Expanded from Selgrade, Harris, Pasteur 2009, the new model investigates the original abnormal cycle and identifies a stable periodic solution consistent with hormone profiles of women with androgen disorders. Implications include a further understanding of the role of androgens and the simulation of external hormone therapies for infertility.

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PP0

Using Feed-Forward Networks to Infer the Activity of Feed-Back Neuronal Networks

In a network of two reciprocally inhibitory neurons, the fir-

ing time of each neuron affects the period of the other one. When these inputs are strong, an alternate method to using phase response curves is required to determine the steady state behavior. We derive a new method using two different feed-forward maps to determine existence and stability of phase-locked solutions. The method involves showing how these maps affect one another prior to composing them to find phase-locking.

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PP0

Cellular-Network and Continuum Neuronal Models for Cortical Spreading Depression

Cortical spreading depression (CSD) is a slow wave phenomenon that is associated with migraine with aura in humans. We construct and show how cellular-network and continuum neuronal models can be used to simulate the instigation and propagation of CSD waves. Our cellular-network model extends and simplifies a single neuron model proposed recently for studying the instigation of CSD. Our continuum model includes more realistic membrane ionic currents than previously used in continuum models.

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PP0

Within-Host Population Dynamics of *Mycobacterium Tuberculosis* Immunology

We consider and analyze a mathematical model for cellular immunology of Tuberculosis. From the analysis of the model, equilibria and local stabilities are determined. Among interesting dynamical behaviors of the model exist forward and backward bifurcations which raises many new challenges to effective infection control.

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PP0

Contribution of Long-Lived Productively Infected Cells in SIV Infection

The availability of potent antiviral drug and mathematical models have reveal important viral properties in HIV infection such as half-life of HIV virion, short- and long-lived productively infected cells for the last two decade. These findings really improved our understanding of HIV infection and the strategy of drug therapy. Here we are trying to understand a contribution of the long-lived cells in SIV infection by using a mathematical model and a SIV HAART model.

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PP0

Simulation of Vascular Flow Reserve in Hypertension

Human hypertension is characterized by narrowing of small blood vessels, inward remodeling. This process takes place without any change in the amount of vessel wall material. It is not known to what degree inward remodeling affects the vascular flow reserve, i.e. the ability to increase flow during increased tissue activity. We performed flow-simulations on microvascular networks of different size remodeled under varying conditions. Inward remodeling in hypertensive networks did not reduce the vascular flow reserve.

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PP0

Three-Dimensional Multispecies Nonlinear Tumor Growth: Tumor Invasion and Angiogenesis

We study 3D non-linear tumor growth by tracking multiple viable cell species populations, discrete angiogenesis vessels and individual cell movement using a hybrid continuum-discrete approach. We investigate disease progression as a function of cellular-scale parameters such as proliferation and nutrient uptake rates in both avascular and vascular regimes. We find that heterogeneity in the physiologically complex tumor microenvironment can be quanti-

tatively linked to the tumor macro-scale as a mechanism that promotes morphological instability.

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PP0

A Mathematical Model of Rift Valley Fever Virus Epidemiology: Insights into Persistence, Prevention, and Control

Rift Valley Fever Virus (RVFV) is an emergent disease of humans and ruminants vectored by mosquitoes. We develop and analyze a mathematical model of RVFV transmission described by a system of differential equations. This model is used to explore how measures of outbreak severity depend on both transmission and demographic parameters. The model is capable of generating both sustained undamped oscillations and damped oscillations to endemic equilibria. We identify conditions enabling RVFV persistence and numerically investigate methods of prevention and control. The model could be extended to address human health and economic interests.

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PP0

Approximation of Detailed Hodgkin-Huxley-Type Neuronal Models by Exponential Integrate-and-Fire Models

Using current-voltage curves and spike metrics, develop optimal strategies are developed for finding the parameters in the exponential integrate-and-fire point neuron model with adaptation current that give the best approximation to the membrane potential and firing rate dynamics of a corresponding Hodgkin-Huxley-type model. The adaptation current is modeled explicitly, but has a prescribed jump at each spike time. The results of computations using both systems give excellent agreement. Bifurcations in both models are compared.

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PP0

Rotational Model for Actin Filament Alignment by Myosin Motors

We first develop a Monte Carlo model for the alignment of actin filaments arranged in a circle. In the model, myosin motors can attach and detach randomly, and travel centripetally to rotate and align filaments. Simulations reveal an optimal velocity for maximizing alignment. We then derive two mean field models: a heuristic model that qualitatively matches, and a solution to PDE that quantitatively matches the Monte Carlo simulations. Other geometries and related problems are discussed.

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Mechanism of MDCKII Cell Polarization During Mitosis

MDCKII cells differentiated into a monolayer columnar epithelium are polarized and their polarity is quickly regained even after mitosis. Our computational model incorporating the cell surface molecular dynamics and the deformation and displacement of intercellular organelles recreates the polarization process during the mitosis and explains the involved mechanism. We can also study the roles of critical components such as diffusion, advection, microtubule growth, and displacement rate. We discuss this in terms of associated time scales

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PP0

Searching for Optimal Stimuli: Ascending a Neuron's Response Function

Many methods used to analyze neuronal response assume that neuronal activity has a fundamentally linear relationship to the stimulus. However, some neurons are strongly sensitive to multiple directions in stimulus space and so have a highly nonlinear response. It can be difficult to find optimal stimuli for these neurons. We demonstrate how successive linear approximations of their response can effectively carry out gradient ascent and move through stimulus space towards local maxima of the response.

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Balanced Synaptic Activity Modulates Spike Train Correlation

Sensory neurons have many synaptic inputs, not all of which directly transmit sensory information. Instead, some serve to modulate the neuronal response to relevant stimuli. We study how background modulatory activity shapes pairwise neuronal correlations using simulations, theory from non-equilibrium statistical mechanics, and data recorded from electrosensory pyramidal neurons in weakly electric fish. We find that changes in timescale and variability from conductance-based neuronal input lead to changes in the structure of pairwise spike correlations.

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Dynamical Properties of the Repressilator Model

The repressilator is an artificial genetic regulatory network used to mimic oscillatory behavior of more complex regulatory networks like the circadian clock. We have proven the existence of a limit cycle in the repressilator model. Oscillations arise from the existence of an absorbing torus-like region in the phase space of the model. We discuss conditions for oscillations and their properties imposed by this geometric structure.

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PP0

A Network Model of Alzheimer's Disease

We have derived a multi-scale network model to study the relationship between cholesterol and Aβ in silico to integrate with future experimental work. A pseudo-metabolic network approach has been taken to model the interactions between various signaling molecules, carrier and transport proteins, as well as other proteins that are considered pertinent to AD pathogenesis. We have also monitored the number of neurons and related synapses using a modified McCulloch-Pitts neural network.

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Time-Delayed Control of Spatio-Temporal Patterns in the Gray-Scott Model

Control of spatio-temporal chaos is an important area of research in nonlinear dynamics, with applications in chemical and biological systems. Although a lot of work has been done on the time-delayed feedback control of unstable steady states/periodic orbits, there are still many open question regarding the control of systems with spatial extent. In this presentation we will show how time-delayed feedback control can be used to control spatio-temporal chaos on an example of a cubic autocatalitic reaction described by the Gray-Scott model. Transitions to stationary spatial patterns and travelling waves will be demonstrated for different parameter regimes.

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PP0

Mathematical Model of Lamellipodial Dynamics During Cell Locomotion

Cell locomotion results from rapid polymerization of actin at the lamellipodia, where periodic protrusions and retractions of the leading edge are observed. We develop a mechano-chemical model to study these periodic cycles, and the effect of the different parameters on the lamellipodial dynamics. Our model demonstrated that leading edge behavior can be characterized into distinct types, including continuous protrusion, periodic protrusion-retraction cycles, and ruffling, depending on the substrate stiffness and myosin and integrin activation rates.

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PP0

A Reduced Model of a Heterogeneous Population of Bursting Neurons

We consider a heterogeneous population of bursting neurons, as used to model the pre-Bötzinger complex. Using averaging, the system can be reduced to a vector-valued differential-algebraic equation of differentiation index 1. The dynamics of this reduced system match well those of the original system. The reduced system allows one to analyse the bifurcations of the heterogeneous system, and to determine the effects of parameter heterogeneity on its dynamics.

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PP0

Effects of Waning Partial Cross-Immunity on the Maintenance of Virus Diversity

We apply a model of a diverse viral infection with multiple strains, continuous immunity, and partial cross-immunity to study how the strength and duration of the immune response control viral biodiversity. In particular, lifelong immunity, as in influenza, favors frequent serotype replacement, while shorter term immunity, as in rhinoviruses, can maintain more coexisting types. Maternal antibodies temporarily transfer immunity between generations, and we develop a novel modeling framework to consider how this intergenerational transfer effects the strength of selection for virus diversity.

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Monascin and Ankaflavin Produced by Red Mold Dioscorea Perform Potent Hypolipidemic and High Density Lipoprotein Cholesterol-Raising Effect in Hyperlipidemic Hamsters

Monascus fermented red mold dioscorea (RMD) was proven to perform greater hypolipidemic effect than red mold rice (RMR). However, more yellow pigments (monascin and ankaflavin) contents were found in RMD than in RMR. In this study, the purified monascin and ankaflavin were respectively administrated to hyperlipidemic hamster for eight weeks in order to test whether the two compounds were new hypolipidemic ingredients. In the statistic results, monascin and ankaflavin performed greater hypolipidemic and HDL-cholesterol-raising effect.

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PP0

A Computational Model of Intracellular Fluid Dynamics in Amoeboid Cells

Understanding the methods by which cells move is a fundamental problem in biology. Recent evidence has shown that the ?uid dynamics of intracellular cytoplasm can play a vital role in cell motility. Using the Immersed Boundary Method to model cortical forces, my goal is to understand how amoeboid cells coordinate cortical contractions and intracellular ?ow to generate locomotion. Specifically I investigate the interplay of waves of cortical contraction, intracellular fluid streaming, and cellular motion.

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PP0

Prediction of Influenza Hemagglutinin Binding Sites Through Dynamics Perturmation Analysis

Dynamics Perturbation Analysis (DPA) predicts protein functional sites by locating areas on a protein surface where the influence of molecular interactions on protein dynamics is large. The utility of the method has been proven but it hasn't yet been optimized. We characterize an implementation of DPA, optimize its performance, study the sensitivity of its performance to the underlying model of protein vibrations, and use the algorithm to analyze influenza proteins.

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PP0

A Fokker-Planck Neuronal Network Model to Capture Mean Firing Rate and Pair-wise Correlations in Large-scale Neuronal Networks

A Fokker-Planck neuronal network model is presented. This model can be efficiently implemented to investigate how the mean firing rate and pair-wise correlations in each population depend on certain first and second order statistical patterns of connectivity. To capture pair-wise correlations among neurons in each population, we derive the evolution equations of the joint population density $\rho(v_1, v_2, t)$ of the voltage of any pair of neurons in the population. By assuming that the input to any pair of neurons is a multivariate Poisson point process, we obtain partial differential-integral equations for each population, but closure of this system of equations requires inferring higher order statistics of activity. We simplify the framework by applying a diffusion approximation and obtain Fokker-Planck equations for each population. We prove that, under some assumptions, the coupling scheme to derive network equations can be based on only the first and second order statistics of activity and connectivity, without the need to infer higher order statistics. Also, fast numerical methods can be devised to solve this simple network model. We test the validity of our network model by comparing the numerical solutions to Monte Carlo simulations under various network configurations. Finally, we discuss the success and failure of our Fokker-Planck neuronal network model.

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Rhythmic Co-Modulation As Torus Knots: Dynamical Interaction of Theta and Gamma Oscillations in An Hippocampal Model

The nervous system produces interacting rhythms of electrical activity believed to be functionally important. We analyze the interaction of theta (4-12Hz) and gamma (30-90Hz) rhythms in a 2007 model of hippocampal oscillations. Transition among locking regimes, and the dynamics of two different mechanisms for the nesting of gamma and theta rhythms are explained by a newly defined one dimensional map that accounts for the network dynamics.

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PP0

Amplification of Asynchronous Inhibition-Mediated Synchronization by Feedback in Recurrent Networks.

Theoretical studies of synchronized oscillatory acitivity in the cortex have proposed that principal neuron synchrony can be mediated by short-latency, rapidly-decaying inhibition. However, in the olfactory bulb, the inhibitory granule cells produce long lasting, small amplitude, asynchronous and aperiodic inhibitory input and thus the narrow time window that is required to synchronize spiking does not exist. Instead, it has been suggested that correlated output of the granule cells could synchronize uncoupled mitral cells through stochastic synchronization (SS). Almost all work on SS presumes that the correlation is imposed and fixed. Building on theory that we and others have developed, we show that increased synchrony in the mitral cells could produce an increase in granule cell activity for those granule cells that share a synchronous group of mitral cells. Common granule cell input increases the input correlation to the mitral cells and hence their synchrony by providing a positive feedback loop in correlation. Thus we demonstrate the emergence and temporal evolution of input correlation in recurrent networks with feedback. We explore several theoretical models of this idea, ranging from spiking models to an analytically tractable model.

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An Algorithm for Finding Identifiable Parameter Combinations in Nonlinear ODE Models using Groebner Bases

Parameter identifiability analysis concerns finding which unknown parameters of a dynamic system ODE model can be quantified from given input/output data. If a model yields infinitely many solutions for some of the parameters, then the model is called unidentifiable. The goal becomes finding *identifiable combinations* of parameters, so that the model can be solved. We extend the differential algebra approach for analyzing identifiability and propose a method to find the "simplest" identifiable parameter combinations using Groebner Bases.

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PP0

Convergence of Growth of Subpopulations on a Grid with Migration

Several species inhabit a grid representing a geographic area. Each grid cell has its own subpopulations. The populations undergo cycles of migration and growth. Migration is governed by fixed matrices. Growth and competition parameters vary with cell. We show that under certain conditions on parameters, the array of subpopulations will converge to a fixed distribution. We give examples from simulations.

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PP0

Logical Modeling of the Differentiation of Naïve T Cells into Regulatory and Effector Cells

In this work, we have constructed a logical model for studying naïve T cell differentiation, in which elements of the signaling network are treated as Boolean variables, and interactions between elements are represented with Boolean functions. The logical model we developed reproduces several experimental observations, with respect to the level of antigen and the presence of inhibitors. The construction of this model has also suggested novel experimental avenues and identified key components requiring theoretical attention.

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Bifurcations in a System of Two Coupled FitzHugh-Nagumo Oscillators

A system of two coupled FitzHugh-Nagumo equations is investigated, with both individual oscillators being identical. The somewhat unusual coupling mechanism leads to the existence of up to five equilibrium solutions. In a natural two-dimensional parameter space, analytical results on their respective asymptotic stability will be presented, along with a numerically-guided analysis of the symmetry-influenced Hopf bifurcations occuring in this 4-dimensional phase space.

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Identification of Gene Regulation Based Upon Single Cell Measurements

The random, discrete nature of genes, RNAs, and proteins cause significant variability in single cells. Different mechanisms and reaction rates shape this variability, which can be measured using time-lapse microscopy, flow cytometry and other techniques. These measurements go beyond standard population-level observations to better constrain parameters and mechanisms of gene regulation models. To show this, we combine experimental single-cell measurements and master equation solutions to identify models for important biological systems in yeast and bacteria.

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PP0

Improving the Gauss-Newton Convergence of a Certain Position Registration Scheme

Accurate images of cardiac voltage flow are aided by precise knowledge of cardiac geometry. One low cost approach to acquiring this geometry involves inducing orthogonal linear voltage fields across the chest cavity. A electrode-bearing cathode is moved within the heart chamber, taking measurements of these fields, and the measurements are then used to reconstruct the heart geometry. This work analyzes ways to regularize the reconstruction, focusing on probe shape and the choice of orientation parameters.

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PP0

Synapses Showing a Preferred Frequency in a Reciprocally Inhibitory Neuronal Network

Recent data from our lab indicates that inhibitory synapses in a CPG network can show resonance, i.e. a maximal conductance at a preferred presynaptic frequency. We explore a network of two model neurons coupled with resonant synapses. We show that, regardless of cell type, the dynamics of each neuron can be described by a logistic map with two parameters, resulting in a bifurcation diagram characterized by a period-doubling cascade leading to chaotic dynamics.

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Single and Multiple-Spikes Traveling Wave Solu-

tions in Integrate and Fire Neural Networks

We investigate the propagation of the traveling wave fronts in a one-dimensional integrate-and-fire network of synaptically coupled neurons. For the single spike wave case, we use an integro-differential equation characterizing the evolution of the firing time as a function of spatial position to determine the relationship between the speed of the propagating wave and its acceleration. The two and multiple wave cases yields further insight on the mechanisms of stable constant-speed traveling wave solutions.

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Recruitment Waves in a Periodically Forced Bistable Array

Psychophysical and neurophysiological experiments have demonstrated that retinal cells in 1:2 phase-locking with a forcing stimulus can recruit each other to different firing cycles over time to form a traveling wave. Counterintuitively, simulations show recruitment and traveling waves even when the model appears highly symmetric. Using numerics, analysis, and asymptotics, we examine a discrete model and its continuum limit to derive a recruitment condition and explain how the traveling wave velocity depends on parameters.

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PP0

A Mathematical Model of Animal Navigation

How animals find their way whilst navigating for homing or migration has intrigued scientists for many years. Due to their ease of handling and willingness to home, the homing pigeon is an ideal candidate for study, and the recent advent of miniaturised GPS devices has made available large quantaties of high quality tracking data. We present a new mathematical model for animal navigation, which explains some interesting features of GPS-captured pigeon homing trajectories.

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PP0

Impact of Inflammation During Influenza A Virus Infection

Clinical manifestations of Influenza A Virus (IAV) infection are attributable in part to activation of the innate immune response. We developed a multiscale, autonomous ODE model of the host-virus dynamic, extending prior work. The model was calibrated to a dataset collected from test mice infected with A/PR/8/34. Cohorts were 2-4 months or 18-24 months and were infected with a non-lethal or lethal viral aliquot intranasally. Full marginal PDFs of sensitive parameters were compared between cohorts, yielding well-defined hypotheses as to how the host-virus response changes with age.

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A Computational Approach to the Investigation of Congenital Arrhythmias

We present an effort to systematically study how genetic mutations alter electrical wave dynamics thereby rendering the heart at high risk of incidence of cardiac arrhythmias. Using non-linear analysis of bioelectric data, bifurcation analysis, and large-scale simulations, we circumscribe how these mutations affect phenomena spanning several scales. We find that a premature beat occurs as a wave travels across a steep spatial gradient of protein expression with a specific orientation with respect to that gradient.

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PP0

Correlation Transfer in Parkinson's Disease

The temporal structure of inputs from the basal ganglia to the thalamus have been implicated in the symptoms of Parkinson's disease. To understand how this structure influences correlation transfer, we study a model of two thalamocortical relay neurons receiving correlated inhibitory input as well as excitatory signals. We observe that inhibitory inputs with timescales representative of parkinsonian conditions allow for a stronger transfer of correlation from input to output than do inputs found under normal conditions.

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PP0

A Dynamic Model for Disease Spread at the US

Naval Academy

We use dynamical systems to model the spread of infectious disease at the United States Naval Academy. We analyze trends and calibrate the model parameters using data detailing class absences due to illness. The model is designed as a tool to make predictions of the extent and nature of disease spread scenarios and generate recommend actions including immunization, quarantine, and isolation to best stem the spread of infectious disease.

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PP0

The Time-Course of Synchronous Neural Oscillations in Parkinson's Disease: Variability and Its Potential Network Mechanisms.

Synchronous oscillatory activity of cortical and subcortical neural circuits is believed to be relevant to the generation of symptoms of Parkinson's disease. This synchrony is not perfect and varies in time. We study the dynamics of model networks of human brain in Parkinson's disease (based on the anatomical and physiological data) to investigate the potential mechanisms of the observed variability of synchrony. The specific values of the synaptic projections in the course of the disease may be responsible for the observed variability.

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Dynamics of Protrusion and Retraction in XTC Fibroblast Lamellipodia

Cellular motility is driven by lamellipodia – thin, actin rich projections that exhibit patterns of protrusion and retraction along the mobile cell edge. We use active contours to measure the shape of Xenopus XTC fibroblasts and analyze spatiotemporal patterns of protrusion and retraction. We correlate fluctuations of the cellular edge with local actin assembly and retrograde flow, and present a coarse-grained model describing the influence of actin polymerization and mass conservation on cell shape dynamics.

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PP0

Mathematical Models of the Emergence of Hierarchy in Learning Systems

We examine different learning schemes, such as Hebbian learning, and investigate how they result in a restructuring of the "brain," in particular, into a hierarchical structure. We use graph theory tools such as, expansion, clustering and connectivity, under Principal Component Analysis, to create hierarchical regions. Then we examine how the degree of hierarchy changes during learning. We evaluate the propensity of learning algorithms for networks to migrate toward the hierarchical region in this space.

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Nonlinear Cross-Diffusion with Size Exclusion for Ion Channels

Aim of this poster is to investigate mathematical properties of a continuum model for diffusion of multiple species incorporating size exclusion effects, e. g. ions moving down a membrane channel. The system for two species leads to nonlinear cross-diffusion terms with double degeneracy, which creates signifcant novel challenges in the analysis of the system.
We study existence of solutions, asymptotics of the model and investigate the stationary system in the case of externally applied potential.

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PP0

Bistability in a Leaky-Integrate-and-Fire Model Neuronal Oscillator Coupled to a Passive Dendritic Cable

Neurons can have extensive spatial geometries, but they are often modeled as single-compartment objects that ignore the spatial anatomy of the cell. This simplification is made for mathematical tractability and computational efficiency. However, many neurons are not electrotonically compact, and single-compartment models cannot be expected to fully capture their behavior. Dendritic properties can have substantial effects on the dynamics of single neurons, as well as the activity in neuronal networks. We study the influences of general diameter passive dendrites on the dynamics of a leaky-integrate-and-fire neuronal oscillator that includes spike effects. We find that the neuron can display bistable behavior between periodic firing and quiescence. Furthermore, we identify the mechanism that causes this bistability to occur. This mechanism was previously only described in models that contain active dendritic conductances.

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PP0

Direct Numerical Simulations of Flow Instabilities

in An Idealized Total Cavopulmonary Connection

Direct numerical simulations (DNS) of flow instabilities in an idealized total cavopulmonary connection (TCPC) are conducted using the nek5000 spectral element method (SEM) code. The TCPC involves anastomosis of the inferior and superior vena cava to the left and right pulmonary arteries and represents the most common surgical solution to establish the univentricular Fontan circulation. The SEM mesh employs 1988 elements and the polynomial order is varied from 7, 9, 13, and 16 for Reynolds numbers of 600 and 950. Each simulation is conducted in parallel on up to 1024 processors. The results are analyzed to highlight unsteady vortical flow structures present in the TCPC junction even for this relatively low Reynolds number idealized flow. Mean and rms velocity statistics will be presented. Comparisons to particle imaging velocimetry (PIV) and other computational fluid dynamics (CFD) results will be presented. The effect of caval offset on flow stability and energy dissipation will also be discussed, as well as a novel device for realizing the concept of cavopulmonary support

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PP0

High-Order Large Eddy Simulation/Fictitious Domain Approach for Complex Incompressible Turbulent Flows with Applications to Hemodynamics

A high-order incompressible flow solver based on the weighted-essentially non-oscillatory (WENO) scheme for convection is coupled with a recent robust subgrid-scale (SGS) turbulence model to enable large eddy simulations (LES) of fully non-homogeneous turbulent flows. The LES model is validated for the three-dimensional lid-driven cubic cavity problem with comparisons to previously published direct numerical simulation (DNS) data. The code is here extended to be able to simulations of flows over and through complex geometries, while still retaining the simplicity of a structured Cartesian grid approach through the use of the fictitious domain approach. Numerous test cases are presented including steady flow through an idealized stenotic blood vessel, flow through a realistic carotid artery bifurcation, and flow past a model heart valve. The results highlight the ability of this code to capture complex unsteady vortical structures in relatively low Reynolds number transitional and turbulent flows important for both normal and pathological hemodynamic flows.

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PP0

Statistical Properties of the Self-Guided Dynamics Methods

Langevin dynamics simulations of proteins can provide insight into its possible conformations. However, the time scale of conformational changes makes sufficient sampling of conformation space prohibitively expensive on current computers. Previously, Wu and Brooks (2003) proposed the self-guided Langevin dynamics method to increase the rate of conformational transitions in simulations. Here we mathematically and computationally examine the statistical behavior of self-guided simulations. In particular, we study the existence and properties of equilibrium states.

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PP0

Dynamics of 3D Axisymmetric Multicomponent Vesicles in a Viscous Fluid

We develop and investigate numerically a thermodynamically consistent model of three dimensional axisymmetric multicomponent vesicles in an incompressible viscous fluid. The model is derived using an energy variation approach that accounts for different lipid surface phases, the excess energy (line energy) associated with surface phase domain boundaries, bending energy, spontaneous curvature, Gaussian bending energy, local inextensibility and fluid flow via the Stokes equations. The equations are high-order (fourth order) nonlinear and nonlocal due to incompressibility of the fluid and the local inextensibility of the vesicle membrane. To solve the equations numerically, we develop a nonstiff, pseudo-spectral boundary integral method that relies on an analysis of the equations at small scales. We present simulations of multicomponent vesicles in a quiescent and an extensional flow and investigate the effect of varying the average surface concentration of an initially unstable mixture of lipid phases. The phases then redistribute and alter the morphology of the vesicle and its dynamics. A comparison of results with experimental vesicle morphologies yields good agreement.

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PP0

Comparison of Hepatitis-C-viral Kinetic Models

Hepatitis-C-viral kinetic models have great potential as prognostic tools. We analyzed variants of such models when applied to clinical data with interferon-based standard or induction treatment. The models all include proliferation of infected cells and differ with respect to modeling the dynamics of non-infected target-cells. We compared the plausibility of predicted infected steady states and the predictions of treatment response. Interestingly, some of the models may even predict increasing viral loads during antiviral therapy.

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PP0

A Dynamical Systems Analysis of Afferent Control in a Neuro-mechanical Model of Locomotion

We consider a neuro-mechanical locomotor model consisting of a central pattern generator coupled to a mechanical limb. Activating drive establishes a rhythm, and limb feedback helps control phase switching and stabilization. Spinal cord injury simulated through termination of drive ceases the rhythm. However, increased feedback strength can restore rhythmic activity. With a reduced model, we elucidate general principles of phase/frequency control in the normal state, while deriving conditions for recovering rhythmicity in the injured state.

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PP0

The Effect of Stretch-Dependent Proliferation in a One-Dimensional Elastic Continuum Model of Enterocyte Cell Layer Migration

Nectrotizing enterocolitis is an intestinal inflammatory disease that is a major cause of death in premature infants. A recently developed mathematical model of enterocyte migration during experimental nectrotizing enterocolitis based on an assumption of elastic deformation of the cell layer is extended to incorporate stretch-dependent proliferation. Analysis and numerical results indicate that stretch-dependent proliferation does not provide an explanation of inhomogeneous boundary movement; however, sufficiently large growth results in exponential movement.

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A Fast Quadrature-Based Numerical Method for the Continuous Spectrum Biphasic Poroviscoelastic Model of Articular Cartilage

Cartilage deformation is described by the linear poroviscoelastic model, accounting for both flow-dependent and flow-independent dissipation mechanisms. Intrinsic dissipation is modeled using a constitutive relation where the solid stress depends on strain rate via a time integral with a continuous relaxation spectrum. We present an efficient method that avoids the prohibitive cost of the hereditary integral via a quadrature approximation of the relaxation function that results in a separable formulation.

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PP0

Balancing Organization and Flexibility in Foraging Dynamics

'Self-organizing' biological systems must balance network organization with response flexibility in order to successfully exploit resources in a dynamic environment. To study this balance, we investigate ant colony pheromone trail formation and foraging efficiency when food location is dynamic. Results from a self-biasing random walk model and a deterministic 'mean field' model both exhibit maximum foraging efficiency when pheromone evaporation balances trail formation with trail flexibility.

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Modeling the Effects of Tissue Architecture on Cancer Drug Penetration

In the consideration of the efficacy of cancer drug therapies, chemical susceptibility has been the primary focus. Effects of cancer tissue architecture on drug penetration have been widely overlooked. We present a computer model exploring these effects upon drug penetration into tumorous tissue using the Regularized Stokeslets method. Specifically, effects of packing density, porosity, cell size/shape, blood vessel fenestrae density, and pressure differences will be analyzed to probe the connection between drug penetration and efficacy.

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PP0

A Mathematical and Computational Model of Necrotizing Enterocolitis

Necrotizing enterocolitis (NEC) is a devastating and fatal disease that affects the gastrointestinal (GI) tract of premature infants. We have created a mathematical model to help analyze the disease. Unlike previous models that are based on ordinary differential equations, our mathematical model takes into account not only transient effects but spatial effects as well. This is accomplished by using a system of nonlinear transient partial differential equations.

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PP0

Effects of Community Structure on Epidemic Spreading on Adaptive Networks

When an epidemic spreads in a population, individuals may adaptively change the structure of the social contact network in response. Here we study the spread of epidemics on an adaptive network with community structure. Community structure is a characteristic of social networks that has been neglected in previous adaptive network models. We model the effect of heterogeneous communities on infection levels and epidemic extinction. We also show how an epidemic can alter the community structure.

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Modelling Sequence Generation in the Neocortex

Based on the principles of modular organization and recurrent connectivity we have developed a firing rate model of neocortex which incorporates the ability to learn complex sequences and form spatiotemporal patterns based on structured input. Our model incorporates synaptic adaptation, asymmetric Hebbian learning, and homeostatic regulation in order to recreate a number of putative cortical functions such as working memory, learning and reproduction of input sequences, and generation of rhythms. The sequential activity patterns exhibited by the model uncover symmetries inherent in the columnar connectivity, which may arise from regularities in afferent signals. In addition, breakdown of inhibition yields pathological dynamics which could provide insights into epilepsy and schizophrenia.

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PP0

Dendritic Morphology Contributes to Sensitivity and Robustness of a Neuron Model

Nonlinear interactions between a neuron's electrical parameters and its morphology remain largely unexplored. In models of three morphologically distinct vestibular neurons, neuronal outputs were driven by perisomatic calcium concentration, and by voltage attenuation in distal dendrites. We analyzed Hessian matrices to identify parameter combinations to which neuronal outputs were highly sensitive, and highly robust. Our method can predict precise perturbations of intrinsic properties, including morphology, sufficient to induce functional changes that underlie

neuronal plasticity.

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PP0

A Model Describing the Treatment of Lung Biofilms by Silver Carbene Complexes

Biofilms growing within the lungs of cystic fibrosis patients are the major cause of morbidity and mortality in this patient population. The goal of our investigation is to develop an effective strategy to treat lung biofilms using silver carbene complexes (SCCs). To describe the treatment of a biofilm by SCCs, we present a model composed of reaction-convection-diffusion equations for the particulate and soluble components of the biofilm. Our numerical results illustrate the efficacy of different treatment stategies.

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PP0

A Mathematical Approach for the Reconstruction of Neural Networks

Considering the abundance of recent work in the fields of network theory and neuroscience, it is no surprise that there has been extreme interest in reconstructing the topology of neural networks. Previous methods have investigated this problem experimentally with a focus on determining the topology of a single given network. In this paper we take a mathematical approach, extending the augmented sparse reconstruction method for protein networks to a system of neurons in an attempt to find a more general technique. This technique employs L^1 minimization to reconstruct a network from a set of noisy trajectories under a variety of initial conditions. Our investigation focuses on the method's performance on an experimentally documented network of neurons in the rat hippocampus. Each neuron is approximated by the FitzHugh-Nagumo model. When observing the neurons' behavior over very short time intervals immediately after initialization, the method is quite successful in its attempt to recover the structure of the given network. In light of this result, we then discuss the research that must still be done before this method can truly reconstruct general neural networks.

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Studying Bacterial Motion Using Multitarget Tracking

Video recordings of bacteria are studied in order to inform stochastic models of bacterial motion driven by chemotaxis. Large numbers of bacteria are simultaneously tracked using Bayesian techniques from multitarget tracking based on random finite set theory. These tracking methods are robust to noisy video images and the randomness of the bacteria's behaviour. Information crucial to description of bacterial motion is then extracted. Results are presented for initial tests using the species *Rhodobacter sphaeroides*.

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PP0

A Mechanical and Computational Model of Mucus Penetration in Mucociliary Transport

Mucociliary transport is a complex dynamical process that serves as defense mechanism in the lung. In this process, mucus penetration, a dynamical interaction of cilia and mucus layers with their surrounding fluid, plays important roles. Dysfunctions in mucociliary clearance will cause several lung diseases. We propose a mechanical and computational model to simulate this complex system. This model couples the time-dependent fluid dynamics and the internal force generation algorithm by ATP-induced molecular motor proteins.

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PP0

Lineages, Feedback Control and Tumor Morphol-

ogy

A multispecies diffuse-interface continuum model is used to simulate dynamics of cell lineages in solid tumors. The model consists of Cahn-Hilliard type equations for the cell species interacting through cell proliferation logic. Following biological considerations borrowed from developmental biology, a feedback system is proposed to control the cell populations in the lineages via diffusible chemical factors. The origin of tumor heterogeneity is investigated. The highly nonlinear/numerically stiff equations are solved using fully adaptive, nonlinear-multigrid schemes.

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PP0

Stability of Traveling Waves for Systems of Nonlinear Integral Recursions in Spatial Population Biology

We use spectral methods to prove a general stability theorem for traveling wave solutions to the systems of integrodifference equations arising in spatial population biology. We show that non-minimum-speed waves are exponentially asymptotically stable to small perturbations in appropriately weighted L^∞ spaces, under assumptions which apply to examples including a Laplace or Gaussian dispersal kernel a monotone (or non-monotone) growth function behaving qualitatively like the Beverton-Holt function (or Ricker function with overcompensation), and a constant probability $p \in [0, 1)$ (or $p = 0$) of remaining sedentary for a single population; as well as to a system of two populations exhibiting non-cooperation (in particular, Hassell and Comins' model) with $p = 0$ and Laplace or Gaussian dispersal kernels which can be different for the two populations.

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The Interplay Between Energetic and Structural Constraints to Community Structure

Energetic and structural constraints are regarded as two important factors underlying community structure. However, it is unclear to what degree a model community can be realized when suffering from the above constraints. We developed a model based on individual-level parameters and investigated the assembled communities from continuous and discrete species pools, respectively. Results show that the constraints in principle work together and the more rich the community is the more it suffers from energetic constraint.

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PP0

Promoter Analyses Reveal Patterns of Clustered and Spatially Organized Transcription Factor Binding Sites That Distinguish Subsets of Autophagy Genes.

The autophagy pathway is critical for homeostasis, cell survival. We hypothesize that composition, number and position of multiple TFBS are organized into distinctive clusters conserved among functionally related human autophagy gene promoter sequences. TFBS clusters identified by pattern detection and pattern matching algorithms differed among subsets of autophagy genes, suggesting differential regulation of autophagy pathway components. Functional annotation, confirmation of candidate transcription factors will allow prediction of pathways and physiological stimuli affecting autophagy gene transcription.

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