CP1

A One-Dimensional Model of Blood Flow in Arteries with Friction, Convection and Unsteady Taylor Diffusion Based on the Womersley Velocity Profile

We present a one-dimensional model for blood flow in arteries, without assuming an a priori shape for the velocity profile across an artery. We combine the one-dimensional equations for conservation of mass and momentum with the Womersley model for the velocity profile. The velocity profiles produced are used to evaluate the friction, to correct the nonlinear terms and in unsteady Taylor diffusion theory. We present flow simulations for numerical and disease modeling purposes.

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CP1

Simplified Models of the Respiratory Control System.

We have developed simplified mathematical models for the control of respiration in mammals. One component consists of a model of the brainstem respiratory oscillator that incorporates regulation of frequency and amplitude of breathing in response to physiological control signals (oxygen and carbon dioxide). The neural model was coupled to simplified models of the lungs incorporating oxygen and carbon dioxide transport. The models explain some experimental observations on open- and closed-loop regulation of breathing.

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CP1

An Evolutionary Hybrid Cellular Automaton Model of Solid Tumour Growth

We propose a model of tumour growth, in which each cell is equipped with a micro-environment response network. This network determines the cellular behaviour, and is subject to mutations and subsequently Darwinian evolution. Using this approach we have investigated the impact of the tissue oxygen concentration on the growth and evolutionary dynamics of the tumour. The results show that the oxygen concentration affects both the genetic diversity and morphology of the tumour.

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CP1

Simulating Cardiac Blood-Muscle-Valve Mechanics by An Adaptive Version of the Immersed Boundary Method

Cardiac mechanics can be modeled as the interaction of a viscous incompressible fluid (the blood) and a (visco-)elastic structure (the walls and valves of the heart). The immersed boundary (IB) method is an approach to such problems. We shall present an adaptive version of the IB method and describe the application of this adaptive methodology to the three-dimensional simulation of blood flow in the heart. Computer animations of the beating heart will be shown.

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CP1

Finite Elements and Operator Splitting Method for the Numerical Simulation of Fluid Flow in Deformable Domains with Application to Blood Flow

The modeling of blood flow in human arteries involves a Fluid-Structure Interaction problem (FSI) because the region itself in which the fluid is confined changes as a consequence of the fluid motion. Several approaches are available to simulate FSI. Our goal is to explore the benefits and the applicability of a numerical algorithm based on finite elements method and operator splitting in order to avoid iterative procedures for the location of the deformable boundary.

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CP1

An Arterial Blood Pressure Model

The arterial pulse pressure waveform analysis has important clinical applications. Some approximations of the flow described by Navier-Stokes equations can be written as N-soliton solutions of a Korteweg-de Vries equation, completed by a windkessel flow. Experiments show that N = 2 or 3, leading to a model with a small number of parameters that can be useful in new diagnosis methods based on indexes of pulse pressure shape variability estimated from non-invasive measurements.

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CP1

Deformation of a Circular Rod with Twist and Bend in Fluids

The overwound or underwound double helix of DNA occurs in DNA transcription, DNA replication, and formation of DNA loops in protein-DNA interactions, which are essential in biological processes. In particular, the deformation of circular DNA molecules occurs in many prokaryotic and viral DNAs and also occurs in the mitochondria of eukaryotic cells. We consider an elastic rod in a closed circular configuration with a uniform twist that adds up to an integer number of full turns so that the triad configuration is smoothly periodic. Moreover this rod is embedded in the incompressible viscous fluid. The immersed boundary method is used to study the instability of a circular rod with twist and bend. Without twist, a closed circular rod gives an equilibrium configuration; that is, there is no net force or torque and it is stable. But with enough twist, the circular configuration becomes unstable, and the rod relaxes to a stable coiled configuration.

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CP1

The Open Nucleotide Pocket of the Profilin:actin X-Ray Structure Is Unstable and Closes in the Absence of Profilin

The open nucleotide pocket conformation of actin in the profilin:actinCaATP x-ray structure is hypothesized to be a crucial intermediate for nucleotide exchange during actin depolymerization/polymerization. The necessary modification of actin with profilin for crystallization leads to ambiguities in this interpretation. Molecular dynamics simulations of the open nucleotide pocket, profilin-free actin structure show the structure is actually unstable, and closes. Thus there is currently no thermodynamically stable structure representing the open nucleotide pocket state of actin.

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CP2

Mathematical Model of Steroidogenesis to Predict Intracellular Response to Endocrine Disrupting Compounds

Exposure to endocrine disrupting compounds (EDC) can induce adverse effects on reproduction mediated through alterations in the enzymes involved in steroidogenesis. We are developing a deterministic model of the intratesticular and intraovarian metabolic network in fish that mediates steroidogenesis. This model allows for an improved understanding of the source to outcome linkages necessary for risk assessments with EDCs. *This work was reviewed by the U.S. EPA and approved for publication but does not necessarily reflect Agency policy.*

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CP2

Combining BrdU-Labeling Experiments and Mathematical Modeling to Understand Natural Killer Cell Development and Homeostasis

Its unclear which role population dynamics play in the distribution of NK cells over different maturation stages and in shaping the receptor repertoire. Experimental data were used to test different mathematical models and to optimize population dynamical parameters. Similar studies were performed on spleen cells, in order to elucidate mature NK cell homeostasis. Results will be discussed with respect to understanding the regulation of adaptive immunity and specification of important stages in NK cell selection.

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CP2

Large Scale Statistical Parameter Estimation for the Dynamic Cardiac Metabolism During Ischemia

We propose a Bayesian methodology which integrates, via a prior distribution, constraints and prior knowledge into the parameter estimation process for a three-compartment dynamic model for the cardiac metabolism. The severely underdetermined parameter estimation problem is then solved by a combination of optimization methods and statistical sampling techniques. A study of the stability of sensitivity to serve as a basis for model reduction is also proposed.

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CP2

Germline Codon Usage As An Indicator of Immune Selection Dynamics

The genetic code defines the relationship between genotype and phenotype at the basis of all processes of evolution. Based on a network view of the genetic code, in which every codon is a node and every edge is a mutation, we studied the enclosed process of selection leading to affinity maturation of immune receptors. We found that different germline receptor DNA prime different types of change appropriate to movement in affinity landscapes of differing roughness.

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CP2

Regulation Mechanisms in the Immune System

We model interactions among effector and regulatory T cells during an immune response to two simultaneous targets to show that the system discriminates based on target behavior and not only TCR affinity. The model affirms the necessity of regulatory cells for self-tolerance, but also shows that low amounts do not hinder, but enhance strong responses by inducing T cell contraction and emigration from the lymph node, leading to rapid target elimination.

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CP2

Modeling Osteoporosis: Predicting Human Biomarker Response to Parathyroid Hormone

Parathyroid hormone (PTH) is a potent bone forming agent that is used to treat severe osteoporosis. PTH-mediated signal transduction modulates the natural bone remodeling cycle and achieves net gain in bone mass with daily dosing. A mathematical model for the human bone remodeling cycle has been developed that predicts the effects of PTH on bone remodeling and related biomarkers. Model simulations explore the effects on biomarkers of PTH dosing patterns and variability in PTH pharmacokinetics.

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CP2

Vanguard Neural Crest Cells Colonize the Gut: Mathematical and Experimental Analyses

Neural crest cells (NCC) colonize the embryonic gut. Failure of this colonization results in Hirschsprungs Disease (HD). A continuum model is developed to replicate NCC colonization and predictions are compared with experimental observations. NCC colonization is driven by vanguard proliferation. Accordingly, we examine the case where vanguard proliferation is artificially suppressed. Both experiments and modelling predict that colonization still occurs. These results explain why genes that influence NCC population size cause HD when mutated.

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CP2
Modeling Extracellular Matrix Realignment During Glioblastoma Invasion in An in Vitro Experiment

The outcome for patients with highly malignant brain tumors is extremely poor. One factor that makes GBM difficult to treat is its high invasiveness. To better understand invasion, we study a 3D assay for tumor spheroid invasion in collagen gel. Previous work indicates that invasive cells follow directed paths away from the tumor spheroid and we present a model that illustrates how the interactions between invasive cells and collagen fibrils can cause directed motility.

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CP3
Reduced Models of Networks of Electrically Coupled Neurons

Neurons in the brain are coupled both chemically (synapses) and electrically (gap junctions). In networks of chemically coupled neurons, the precise details of the voltage spikes are often unimportant. It is therefore reasonable to model voltage spike shapes either in stereotypical ways, or even not at all, as in the integrate-and-fire model. By contrast, the speed at which signals propagate through networks of electrically coupled neurons can be sensitive to the details of spike shapes. For reduced models such as integrate-and-fire models, this raises accuracy issues. We demonstrate these issues computationally, and discuss ways of resolving them.

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CP3
A Stochastic Model for Neuronal Membrane Potential and Time-Varying Inputs

We propose a stochastic model for the firing activity of a neuronal unit, that is based on a suitable exponential transformation of a continuous-time stochastic process subject to random jumps. Such a model includes the decay effect of the membrane potential in absence of stimuli, and the occurrence of various types of tyme-varying inputs. An analysis of the probability distributions of the membrane potential and of the firing times is performed.

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CP3
“Equation-Free” Modelling of Neural Systems

“Equation-free” modeling allows one to compute with the effective equations governing the macroscopic dynamics of a system even if they cannot be explicitly derived, provided that the microscopic dynamics are known. These techniques can be used to do bifurcation analysis of complex networks of neurons. We demonstrate these ideas for several types of networks, studying steady states and spatiotemporal patterns such as bumps and waves.

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CP3
Waves and Noise in Dendrites with Active Spines

Dendrites form the major components of neurons and many are equipped with excitable channels located in spines. Computationally we obtain a quasi–analytic solution which can be used to study the neural response to spatio-temporal patterns of synaptic input. We examine the robustness of the wave propagation to both space-time white and correlated noise that arise in the cable (eg electrical coupling) and spine-heads (eg stochastic gating) through weak and strong approximations.

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CP3
Neural Timing in Highly Convergent Systems

In order to study how the convergence of many variable neurons on a single target can sharpen timing information, we investigate the limit as the number of input neurons and the number of incoming spikes required to fire the target both get large with the ratio fixed. We use asymptotic forms of the density and the standard deviation near the limit to understand the behavior of octopus cells in the mammalian cochlear nucleus.

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CP3
Inverse First Passage Time Methods and Their Applications to Neuronal Modeling

We consider an Ornstein-Uhlenbeck diffusion process X_t constrained by an unknown absorbing boundary $S(t)$. We assume known the distribution of the time T when the process crosses for the first time the boundary. The aim of our study is to determine the boundary shape. Two alternative algorithms are proposed and their features are discussed. Application of these methods to a classification algorithm and to detect non-stationarity in observed data

in a neuroscience context is presented.

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CP3
Wavelet Analysis of Neurophysiological Signals

Using wavelet analysis we have studied: (a) movement-related changes in the local field potentials recorded from the subthalamic nucleus of patients with Parkinsons disease, (b) cortical control of hand movement in healthy subjects from functional MRI time series, and (c) seizure EEG in kindled epileptic rats. The mathematical framework and some results of the analysis of these neurophysiological signals will be discussed.

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CP3
Modeling Excitatory Neurotransmitter Transport Processes

Synapses in the central nervous system adapt to reflect the history of received action potentials on a molecular level, a phenomenon known as synaptic plasticity. Of recent interest is the question of "spill-over", can neurotransmitters released at one presynaptic terminal escape that cleft and eventually trigger a response in neighboring synapses? To address this question we are coordinating experiments on the transport systems responsible for mediating the uptake and sequestration of the excitatory neurotransmitter glutamate (M. Kavanaugh, UM), with the analysis of computational models.

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CP4
Virus Competition at Multiple Scales

Viruses compete and are subject to natural selection at multiple levels: within-cell, within-host and within-population (of hosts). We looked at how viruses can optimally exploit their hosts and how this behaviour may influence the most successful strategy at the between-host, or epidemiological level. I will present a fairly general way to consistently combine models of disease process and disease spread with the goal of understanding the net selection pressure on a model virus. The method is illustrated using two popular models at the within- and between-host levels.

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CP4
The Role of IL-2 in CD4 T Cell Proliferation: Insights from Modeling CFSE Data

We analyze the data on the dynamics of CFSE-labeled CD4 T cells in vitro at suboptimal concentrations of IL-2 using several mathematical models. We find that to adequately describe the data, the death rate of divided cells needs to increase with the number of divisions cells have undergone. Our results suggest that IL-2 regulates expansion of CD4 T cell by increasing dependence of cell death rate on the division number, and not by speeding up cell division.

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CP4
Influenza A Virus Infection Dynamics and its Dependence on Antibody Response

We present a mathematical model of IAV infection in an individual, explore the effect of initial viral load and perform sensitivity analysis to explore which parameters influence the onset, duration and severity of infection. Immune memory is modeled by a new variable that quantifies the antigenic distance between the virus and the existing antibodies. We find that if antibody response is low or nonexistent, chronic disease may develop.

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CP4

Ebv-Cimmsim: An Agent-Based Model of Epstein Barr Virus

Epstein Barr virus (EBV) infects more than 90% of all humans benignly for life but occasionally leads to oncogenic transformation in susceptible individuals. As EBV is a human pathogen, appropriate animal models do not exist. In this talk, I will present an agent-based model, EBV-CImmSim, which simulates both the acute and the chronic phases of EBV infection. The results of this model correspond qualitatively to data relating to the infected B-cell dynamics derived from patients presenting with acute infectious mononucleosis (AIM). Furthermore, the model suggests that EBV persistence is maintained via exit of latently infected B cells into the circulation, which acts as a reservoir for continuous reactivation of the virus. In the absence of this compartment, the infection is cleared.

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CP4

A Dynamic Model for Induced Reactivation of Latent Virus

We report on a deterministic mathematical model to describe reactivation of latent Kaposi's Sarcoma-associated Herpese Virus (KSHV) in BCBL-1 cell cultures. Model parameters are estimated from properties of uninduced cell cultures undergoing spontaneous reactivation. Additional parameters that describe chemically-induced reactivation are determined, by fitting to experimental data and standard errors are reported. This model provides good agreement with experimental data and establishes a general framework for modeling of other inducers and latent viral-cell systems.

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CP4

Continuous Model for the Rock - Scissors - Paper Game Between Bacteriocin Producing Bacteria

In this work, important aspects of bacteriocin producing bacteria and their interplay are elucidated. Various attempts to model the Resistant, Producer and Sensitive *Escherichia coli* strains in the so called RSP (Rock-Scissors-Paper) game have been made and the question arose whether there is a continuous model that admits a cyclic structure. The observations in experiments showed a cyclic dynamics of these three competing species. This paper gives a possible competitive Lotka-Volterra system model and clarifies the underlying dynamics. A continuous, spatially homogeneous competitive model, describing the interactions between these bacteria with an exact parameter set for a robust coexistence, is established. Also statistical effects will be considered. There are medical applications in eukaryotic organisms such as Malaria and infectious diseases.

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CP4

Mathematical Modeling of Hhv-6 Immune System Dynamics

We propose a mathematical model for describing the immune system response to the Human Herpesvirus-6 infection. Our research is focused on the cellular response of CD4/CD8 T-cells at infection. Starting with a simple model that can be applied to clinical data, we estimate values of important parameters. The predictions based on this beginning model, and the future work for improvement of it to a realistic model through adapting to new experimental data, will be discussed.

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CP5

Effect of Space and Stochasticity on Two Competing Plant System

The talk aims in studying the effect of space and stochasticity on two competing plant species, of which one is a superior competitor and the other, a superior disperser. The system is modeled as a spatially structured Markov process and is analyzed using systematic perturbation expansion, based on the theory of distributions to account for space and the underlying stochastic differential equations to account for stochasticity. Analytical results are compared to simulations of the underlying Markov Processes.

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CP5

The Impact of External Forcing on Invasion, Extinction and Coexistence

External forcing can have a significant impact on ecological and epidemiological systems, not only through resonance amplification and the generation of subharmonics but also in shifting the thresholds at which a species becomes extinct or invades a community. This threshold phenomenon is clearly of great importance in wildlife management and medical science. Conditions for threshold shift are determined for many species differential equation systems and their dependence on subharmonic resonance established using Lyapunov exponent analysis.

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CP5

Modeling Marine Phage Ecology

Marine phage infect bacteria, the largest biomass in the ocean, and daily destroy about 25% of the marine bacteria, playing an important role in the carbon cycle of the oceans. Still little is known about phage ecology and population dynamics. From shotgun sequencing, our mathematical models based on a Lander-Waterman algorithm explain about species diversity and abundance of marine phage. A two compartment model is developed, and parameters are fit to describe phage/bacteria dynamics. Analysis of the model gives stable and oscillatory regimes for this system that match biological experiments.

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CP5

Effects of Non-Reproductive Groups on Population Growth

We describe several population models exposed to a mild and long standing infectious disease, i.e. without significant increased natural mortality rate among infected individuals, and providing no immunity/recovery. We modify these models to include non-reproductive groups, and analyze their potential effects on the dynamics of the population. We are interested in how the non-reproductive class may curb the growth of the infected group while keeping the healthy population at acceptable levels.

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CP5

Interactions Between Dispersal, Competition and Landscape Heterogeneity

I describe and interpret results obtained from analysing a set of stochastic, spatially explicit models of population dynamics. The analytical method employed a novel mathematical technique that uses stochastic differential equations. Spatial heterogeneity is generally found to have a positive effect on populations. With regards to both patch size and dispersal scale, an intermediate level is found to be optimal, due to a conflict between minimising endogenous competition and maximising the benefits of heterogeneity.

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CP5

Modelling the Spatio-Temporal Dynamics of Multi-Species Host-Parasitoid Interactions: Aggregated Searching, Heterogeneous Patterns and Ecological Implications

A mathematical model of the spatio-temporal dynamics of a two host, two parasitoid system is presented. There is a coupling of the four species through parasitism of both hosts by one of the parasitoids. When searching for hosts, the parasitoids are observed to aggregate in response to chemical signalling cues emitted by the host plants during host feeding, a phenomenon which is widely reported. We model this aggregative parasitoid behaviour in a multi-species community using a reaction-diffusion-chemotaxis model. The spatio-temporal dynamics of our system highlight behaviour of significant interest. In addition to invasive behaviour characterised by travelling waves, we observe both quasi-chaotic dynamic heterogeneous spatio-temporal patterns and a destabilisation of the system to produce quasi-stationary heterogeneous patterns. We show that the destabilisation is due to chemotaxis. The dynamical behaviour of our system has significant ecological implications and the concepts of stability and coexistence, biological control and evolution of parasitoid searching behaviour are discussed.

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CP5

Invading Beetles in Nyc: Modeling a Contagion Process with Timing Uncertainty

We present a model of the spread of a contagious process on a network of nodes that allows the incorporation of uncertainty about the timing of events. The model is appropriate for analyzing real-world data on the spread of disease, or of an invasive species. We illustrate the model by applying it to data on the spread of the invasive Asian Longhorned Beetle among the street trees of New York City.

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CP5

Nonlinear Dynamics of a Demographically and Spatially Structured Population under Perturbation

In some situations the management objective of a nuisance population is to achieve a steady-state equilibrium significantly below the carrying capacity. Achieving such an objective through harvest may be complicated by the presence of stage and spatial structure in the target population. In such cases, optimal harvest strategies must account for differences among classes of individuals in their relative contribution to the population. We consider this heterogeneity in the dynamics of density-dependent structured populations.

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CP6

A Mechanism for Morphogen-Controlled Domain Growth

Growth is a fundamental aspect of development: it results from a tightly regulated combination of processes including cell differentiation, division and movement. Recent experimental studies have highlighted the role of a morphogen (Dpp) in controlling domain growth in the Drosophila wing. We model this phenomenon using a system of reaction-diffusion equations with advection. Analysis is carried out using a Lagrangian based approach and results show how uniform growth across the wing may be achieved.

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CP6

Data Pooling and Robust Dynamic Prediction in Predictive Fermentation Microbiology

A desirable feature of mechanistic models of bacterial population growth is that they describe the interaction between a bacterium and its micro-environment in a framework that can be calibrated under relevant experimental conditions. I present a two-phase modeling approach that permits validation the environmental dynamics prior to full model validation. In this talk, I will discuss the approach and introduce a model building and database management software that facilitates collaboration among multiple research groups via the internet.

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CP6

Hyperbolic Models for Chemosensitive Movement in Interacting Cell Systems

In the talk, we present two hyperbolic models in interacting cell systems. The first model describes chemotactic cell movement driven by a diffusive external signal while the second model in addition includes intracellular signal transduction mechanism to the cell dynamics. Macroscopic behavior in biological systems can be explained in terms of microscopic parameters of the hyperbolic models. The conditions for global existence are also investigated in terms of the properties of signal transduction network .

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CP6

Better Triple-Drug Regimen for Hiv: Evaluating

Clinically Feasible Strategies

Current HIV drug therapy, although highly effective, may cause severe side effects making adherence to the prescribed regimen difficult. We weigh the positive results of treatment, such as higher helper T-cell levels, against such negative consequences; the appropriate weights can be estimated by considering clinical determinants of when to initiate therapy. We then systematically compare clinically feasible triple-drug strategies based on expected treatment outcome, including the possibility that therapy will fail due to emergent drug resistance.

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CP6

Emergent Bursting in Small Networks of Conditional Square-wave Bursting Cells

Consider a population of neurons that are all capable of square-wave bursting when given appropriate inputs, but tuned such that some cells are silent, some are bursting, and some are tonically active. When synaptic coupling is introduced, how will the population behave? In this talk, I will discuss ways in which synaptic coupling promotes emergent bursting in the network. In particular, I will explain a mechanism that can lead to network bursting, even when none of the cells in the network burst in isolation. I will use models for conditional respiratory pacemaker cells in the pre-Botzinger complex to illustrate this mechanism.

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CP6

Reaction Diffusion and Density Dependent Chemotaxis

A system of reaction-diffusion equations with volume filling chemosensitivity is considered. Questions of existence and uniqueness ansas well as qulitative behaviour of solutions is discussed. Applications to morphogenesis and angiogenesis are outlined.

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CP6

Analyzing Morphogen Interpretation Mechanisms in the Developing Brain

The mechanism of morphogen interpretation "[Ashe HL, Briscoe J. The interpretation of morphogen gradients. Development. 2006 Feb;133(3):385-94.]" at the cellular level is important in understanding the role of morphogen gradients in cell fate specification, proliferation, and further signalling cascades. Models of morphogen interpretation mechanisms involve complex biological networks, which can be analyzed with computational tools such as logical and ODE-based methods "[THOMAS, R. and KAUFMAN, M., "Multistationarity, the basis of cell differentiation and memory. II. Logical analysis of regulatory networks in terms of feedback circuits.", Chaos 11, (2001) 180-195.]","[THOMAS, R. and KAUFMAN, M., "Multistationarity, the basis of cell differentiation and memory. I. Structural conditions of multistationarity and other nontrivial behavior.", Chaos, 11 (2001) 165-179.]". We use these tools in conjunction with experimental data to identify morphogens and interpretation mechanisms, which induce bistable behavior in the developing brain "[Monuki ES, Porter FD, Walsh CA. Patterning of the dorsal telencephalon and cerebral cortex by a roof plate-Lhx2 pathway. Neuron. 2001 Nov 20;32(4):591-604.]". We also discuss implications for biological phenomena such as robustness.

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CP6

The Role of Wnt Signaling in Colorectal Cancer: a Theoretical Study

Wnt signaling regulates gene expression in development, stem cells and colorectal cancer by controlling β-catenin levels. As β-catenin is also a primary component of adherens junctions, we developed an ODE model to investigate how transcription and adhesion interact. Some experimentalists hypothesise that the system is purely competitive, whereas others propose the presence of two forms of β-catenin. Our model allows us to discriminate between these theories on the basis of their response to specific system perturbations.

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CP7

Biological Control Through Intraguild Predation: a Case Study In

Rusty crayfish are aggressive invaders of the Great Lakes ecosystem. They interact with indigenous smallmouth bass through intraguild predation. Mature bass are predators of rusty crayfish, but predation is gape-limited, the largest crayfish escaping predation. These individuals are the most fecund and compete with juvenile bass, causing a "juvenile competitive bottleneck." We used a stage-structured model to investigate the biological control of rusty crayfish by

smallmouth bass and suggest methods for effective control.

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CP7

Stochastic Stable Population Growth in Integral Projection Models: Theory and Application

Integral projection models generalize classical matrix projection models by allowing individuals to be cross-classified by multiple attributes, discrete or continuous. We show that stochastic integral models share the qualitative properties of stochastic matrix models that are essential for applications: existence of a long-term growth rate, ergodicity of population structure, and asymptotic lognormality of total population. Case-studies demonstrate model parameterization from empirical data, and applications in situations that pose difficulties for conventional matrix models.

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CP7

Diet Selection As An Asynchronous Differential Foraging Game

An important issue addressed by Behavioural Ecology is that of the evolutionary relevancy of foraging strategies adopted by animals in quest of a patchily distributed resource, both in terms of diet selection and patch-leaving decisions under competition. Solving the corresponding asynchronous non-zero sum differential game, which involves discontinuous state feedback strategies constructed via a regular synthesis technique, requires a careful analysis of the induced discontinuities of the adjoint variables. Partial preferences arise in several fashions.

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CP7

Modelling P.HERMAPHRODITA Nematode Dispersal in Homogeneous Environments

We consider a correlated random walk in two dimensions for simulating the movement of the slug parasitic nematode *P.hermaphrodita* in order to quantify its dispersal in homogeneous environments. The correlated random walk leads to anomalous diffusion, more precisely to a fractional sub-diffusion equation. The stochastic process associated is characterized by strong memory effects on the level of the probability distribution function, i.e., unlike a Markov process, the now-state of the system depends on the entire history of its preparation.

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CP7

Effects of Genetic and Phenotypic Diversity on Predator-Prey Cycles

We examine characteristics of limit cycles in a simple predator-prey system which allows phenotypic diversity and rapid evolution in the prey species. Level of defense against predation and the community composition of the prey species determine whether the system exhibits short-duration classical predator-prey oscillations, longer "evolutionary cycles" or exists at equilibrium. Distinctive phenomena resulting from rapid prey evolution include *predator-trait* cycles in which prey density remains nearly constant while predator density and prey traits cycle.

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CP7

Modeling Wolf Movement in a Heterogeneous Environment

The effect of linear features (e.g. roads) on animal movement is not well understood. We derive an advection-diffusion model with variable coefficients for the mean transit time, which describes the expected time for a wolf to interact with environment features, including prey items. This formulation is the adjoint of the forward Kolmogorov equation. By analyzing the model under various linear feature configurations and densities, we demonstrate the effect of linear features on predator-prey interactions.

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CP7

Does Transient Spatiotemporal Chaos Apply to Ecological Systems?

A sudden, system-intrinsic collapse of spatiotemporal chaos to regular dynamics is a striking phenomenon; it was suggested as a source for species extinction. The Gray-Scott system captures fundamental ecological mechanisms like density dependent species reproduction, food competition, species decay, and dispersal. Numerical studies show that the transient time increases exponentially with medium size. The collapse process is robust to noise, but the average transient lifetime can be influenced drastically. We also find that few nonlocal connections in the network can prevent the collapse phenomenon.

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CP7

Modelling Dispersal in Highly Fragmented Landscapes

We model dispersal in highly fragmented landscapes as a correlated random walk incorporating edge-mediated behavior, and employ its diffusion approximation to derive closed expressions for various characteristics of the dispersal process, e.g. average time of an individual spending in current patch i before hitting patch j, conditional that it will hit patch j before hitting any of the other patches or dying. Our results can be used to construct individual-based simulation models of movement.

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CP8

Adaptive Control of Abnormal Rhythms in a Patch of Cardiac Tissue

Suppressing cardiac arrhythmias via implantable pacemaker devices is of obvious clinical importance. Stimuli applied by the artificial pacemaker are constrained in that they must preempt the stimuli applied by the heart's natural pacemaker cells. Using a mapping model of paced cardiac dynamics, we analyze a feedback control scheme known as extended time-delay autosynchronization (ETDAS) which operates successfully under the above constraint. We discuss optimal choice of the feedback gain and minimization of noise sensitivity.

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CP8

A Mathematical Model for the Pulsatile Secretion of Gnrh Hormone by Synchronized Gnrh Neurons

Based on recently observed autocrine effects of GnRH on its own release, we develop a mathematical model for pulsatile GnRH release in which GnRH plays the roles of a feedback regulator and a diffusible synchronizing agent. Results on both the single-cell and population models of GnRH neurons suggest that the positive and negative effects of GnRH regulation through the G-proteins is sufficient and robust in generating GnRH pulses.

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CP8

Traveling Pulses in a One-dimensional Neural Network Model with Long-range Horizontal Connections

We investigate existence and stability of traveling pulses in a one-dimensional neural network with recurrent excitation. The network model uses non-local integro-differential equations whose integral kernel represents spatial distribution of synaptic weights. The latter is decomposed into an exponential representing local connections and a set of delta functions representing long-range patchy connections. Solving for pulse solutions of the system, we determine wave-speeds relation to threshold. Stability is determined by zeroes of the associated Evans function.

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CP8

Spatially Explicit Resource Competition Modeling of Florida Plant Scrub Species

We simulated demographic consequences of resource competitive interactions for two indigenous Florida scrub species in contrasting spatial scenarios. We used data on demography, spatial distribution, and competitive interactions between *Ceratiola ericoides*, a dominant shrub and *Hypericum cumulicola*, an endemic scrub species to parameterize mathematical functions. We assessed the consequences of alternative spatial configurations on the persistence of the endemic plant as a potential management

strategy for the restoration of endangered species.

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CP8

Waves of Spreading Cortical Depression

Waves of spreading cortical depression (SD) occur in experiments on various brain structures in different animals and have been implicated in classic migraine with aura. Mechanisms that are believed to be important for SD include ion diffusion, membrane ionic currents, osmotic effects, the spatial buffer mechanism, neurotransmitter substances, gap junctions, metabolic pumps, and synaptic connections. In this talk, continuum models of SD, consisting of coupled nonlinear diffusion equations for the ion concentrations, will be described.

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CP8

Spatial Patterns Produced by Neural Field Equations

We study spatially patterned stationary solutions of an integro-differential equation introduced by Wilson and Cowan and proposed by Amari as a model of neural activity on a layer of interconnected neurons:

$$\frac{\partial u(x,t)}{\partial t} = -u(x,t) + \int_{\mathbf{R}} \omega(x-y) f(u(y,t)) dy + h.$$

In particular, we investigate the existence of N-bump stationary solutions, or solutions positive on a region that can be decomposed into a disjoint union of N finite intervals. Our focus is to extend existing results for the symmetric case, establish the linear stability of those solutions, and characterize a class of Mexican-hat coupling functions that allow N-bump solutions.

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CP8

Analysis of the Paradoxical (excitatory) Effect of Potassium Currents on Hormone Secretion

Lactotrophs are excitable cells. Electrical activity translates into calcium entry, provoking secretion of the hormone prolactin. Dopamine inhibits prolactin release by increasing potassium currents, which hyperpolarize the cells, preventing Ca entry. Surprisingly, low concentrations of dopamine can increase prolactin secretion. How can an increase in inhibitory currents strengthen hormone secretion? We show how a small increase in fast K+ currents could convert a spiking pattern into bursting and increase Ca2+ influx, increasing prolactin release.

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CP8

Stable and Metastable States in Visual Cortex

A large-scale, biophysically realistic model of turtle visual cortex is being used to study the spatiotemporal dynamics of cortical responses to visual stimuli. This presentation uses a system of linear non-autonomous ordinary differential equations to model the system. The stability of the system is then studied using the theory of Lyapunov functions for non-autonomous systems. The analysis indicates the system has a single stable fixed point and multiple metastable states.

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CP9

Coupling PDE-Based Intracellular Signaling with Membrane-Bound Monte Carlo Simulations

Microscopy evidence suggests that the spatial heterogeneity of signaling biomolecules is important in signaling pathways. Yet, most mathematical models assume a uniform distribution of signaling molecules. The work presented here couples kinetic Monte Carlo simulations, describing the spatial heterogeneity of membrane-bound ErbB receptors, with a reaction-diffusion-advection PDE system governing downstream intracellular signaling. The results show that spatial heterogeneity is important for ErbB regulation.

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CP9

Modeling and Computation of Signal Transduction of olfactory Cilia with Non-Uniform CNG and Cl(Ca) Channels Distributions

Olfactory cilia contain the known components of olfactory signal transduction, including key aspects, cyclic-nucleotide-gated (CNG) channels and Ca2+-gated Cl-

channels (Cl(Ca)). These two channels produce primary currents that are induced by signal transduction events within the cilia of olfactory receptor neuron. We use analytical and computational methods to study mathematical models of certain aspects of signal transduction in frog olfactory cilia in conjunction with known experimental results. Predictions on properties of the cilia are desired and, in particular, information on the distribution of the CNG and Cl(Ca) channels. We develop two group of mathematical models for two different experiments, one is involving interplay between CNG and Cl(Ca) channels and other one is involving the diffusion of Ca2+ into cilia and the resulting electrical activity. All models consisting of two differential equations describing Ca2+ concentration, membrane potential and some cases it is analytically solvable. Using forward problems with matching experimental data we obtain estimates of spatial distribution of Cl(Ca) channels along the length of a cilium.

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CP9
Dynamic Regulation of Interferon-Stat1 Signaling

We developed a detailed kinetic model of the Interferon-Stat1 signal transduction pathway. The model reproduces the dynamic behavior of the pathway in a quantitative manner for wildtype Stat1 and different mutant proteins. We analyzed the control exerted on interferon signaling by the individual reaction and transport steps. The numerical and analytical results show that two little understood processes, nuclear dephosphorylation and nucleo-cytoplasmic shuttling of unphosphorylated Stat1, control the amplitude and duration of Stat1 activation.

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CP9
Control of Cellular Apoptosis in Ovarian Follicles

In each ovarian cycle, only a definite number of follicles ovulate, the others degenerate through an apoptosis-mediated process. We have designed a multi-scale mathematical model where degeneration results from the hormonally-controlled confinement of follicular cells within a zone of vulnerability towards apoptosis. We study how the control operates and how to control apoptosis by considering the characteristics of the 2D-conservation law describing the age and maturity structuration of the follicular cell population.

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CP9
Multi-Scale Models for Gene Network Engineering

Armed with increasingly fast supercomputers and greater knowledge of the molecular mechanisms of gene expression, it is now practical to numerically simulate complex networks of regulated biological reactions, or gene circuits. It is also becoming feasible to calculate the free energy of noncovalent binding of regulatory proteins to specific DNA target sites. We developed a hybrid stochastic-discrete and stochastic-continuous simulation algorithm, with which we obtain an accurate time-evolution of the behavior of complex gene circuits, including a clear picture on the role of highly dilute, but significant, regulatory proteins. These regulatory proteins are responsible for the non-linear control used by biological organisms to regulate their most important processes. The network simulations provide insight, which can guide rational engineering of regulatory proteins and DNA operator sequences using molecular mechanics simulations. In this presentation we examine two important gene circuits, the bistable switch and the oscillator. We study the role of specific biomolecular interaction phenomena on the dynamics of these gene circuits. Using models that span multiple time and space scales, from atomistic, to molecular, to interaction networks we develop design principles for high quality bistable switch and oscillator circuits.

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CP9
Quasi-Equilibrium Approximation of Biochemical Reaction Networks

We consider a biochemical reaction system in which reactions between various molecular species occur on different time scales. With a graph-theoretical approach, a perturbation method and an invariant theory we eliminate fast kinetics and reduce the system on a slow time scale. Under quasi-equilibrium assumption on deterministic description of models, we explore a reduction method on a slow time scale and present conditions for a complete separation of slow and fast kinetics for the governing equation. On the stochastic description, we reduce the system on a slow time scale by utilizing a perturbation analysis on Markov processes and quasi-equilibrium approximation on fast subsystem. We make a connection between quasi-equilibrium approximation as applied to deterministic and stochastic description. We present an efficient stochastic simulation algorithm on slow time scale based on analytic results and illustrate the numerical accuracy of the approximation by simulating motivating examples.

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CP9

A Dissimilarity Parameterized Approach to the Embedding Problem in Molecularbiology

We discuss an approach to the embedding problem in structural molecular biology that treats interatomic distances (dissimilarities) as independent variables. Using distance geometry we can steer the set of dissimilarities to one corresponding to the interpoint distances of an actual configuration of atoms. Our formulation leads to a large-scale, bound constrained, nonconvex spectral optimization problem that seems less plagued by nonmeaningful local minimizers than coordinate parameterized formulations. Moreover, as we discuss, computational costs are tractable.

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CP9

Stochastic Simulation for Modeling Highly-Branched Protein-Protein Interaction Networks: Attacking Combinatorial Complexity

Automated generation of biochemical reaction networks with rule-based graphic rewriting scheme and "on-the-fly" technique have been used to model and simulate protein-protein interactions. However, complex and highly-branched networks, where number of reactions exponentially grows as higher-ordered molecular complexes being formed, still remain computationally intractable. We propose a discrete event simulation method which computes dynamics of a system without pre-generating a biochemical reaction network. This method provides a modeling and computational technique which greatly reduces the combinatorial complexity observed in most protein-protein interaction systems and present a viable way to study large molecular systems.

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CP10

Using Contact Network Models for the Spread and Control of Influenza

The threat of avian influenza and the 2004-2005 influenza vaccine supply shortage in the United States has sparked a debate about optimal vaccination strategies to reduce the burden of morbidity and mortality caused by the influenza virus. I will discuss a comparative analysis of two classes of suggested vaccination strategies: mortality-based strategies that target high risk populations and morbidity-based that target high prevalence populations. We have used the methods of contact network epidemiology to evaluate the efficacy of these strategies across a wide range of viral transmission rates and for two different age-specific mortality distributions. We have found that the optimal strategy depends critically on the viral transmission level (reproductive rate) of the virus: morbidity-based strategies outperform mortality-based strategies for moderately transmissible strains, while the reverse is true for highly transmissible strains. If time permits, I will also discuss the ramifications of mutating pathogens to the spread of disease.

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CP10

Pair-Level Approximations to the Spatio-Temporal Dynamics of Epidemics on Asymmetric Contact Networks

Existing pair approximations to the spatio-temporal dynamics of epidemics assume that the contact matrix is symmetric. There are circumstances where this is unlikely to be true for example transmission between fish farms via river networks or more generally spread by transport links. We extend the formalism to asymmetric networks and compare the results of a naive application of the symmetric model, of a partially asymmetric model, of our fully asymmetric model and of stochastic simulation.

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CP10

Evolution of Metabolic Network Functions

From the reaction content of the metabolic networks of over 200 organisms which have been retrieved from the KEGG database, we derive scenarios for networks of common ancestors as defined in the NCBI taxonomy tree. A structural analysis using the recently developed technique of network expansion allows to investigate at which stage during evolution particular network functions are discovered or lost. We further identify structural features which are responsible for the emergence of these functions.

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CP10

Comparing Evolutionary Markov Processes

Molecular evolution is often modeled as a homogeneous, positive-recurrent, irreducible Markov process. Evolution is studied using the process' infinitesimal generator, otherwise known as its "substitution matrix." Over eighty

substitution matrices have been proposed, but rigorous quantitative comparisons are lacking between them. Using composition and latent-variable analyses, we propose Hilbert-space and statistical metrics to quantify the "difference" between different substitution matrices, and by implication, different evolutionary Markov processes.

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CP10

Optimal Disease Control - the Importance of Economics and Time-Scales for Control

Using a contact-process model for the spread of crop disease over a regional scale, we examine the importance of the time-scale for control with respect to the cost of the epidemic. We analytically derive economically optimal treatment regimes using methods from control theory to show that there are significant qualitative differences between long and short-term control. We also emphasise the importance of economic constraints by deriving a critical relationship between the epidemiological and economic parameters.

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CP10

The Adaptive Dynamics of the Evolution of Host Resistance to Indirectly Transmitted Microparasites

We use adaptive dynamics and pairwise invadability plots to examine the evolutionary dynamics of host resistance to microparasitic infection transmitted indirectly via free stages. We investigate trade-offs between pathogen transmission rate and intrinsic growth rate. Adaptive dynamics distinguishes various evolutionary outcomes associated with repellors, attractors or branching points. We find criteria corresponding to these and demonstrate that a major factor deciding the evolutionary outcome is whether trade-offs are acceleratingly or deceleratingly costly.

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CP10

Simulations As a Mathematical Tool

Simulations based on a collection of physical and social action-at-a-distance forces can be used to describe interacting organisms. Examples of these will be given for both a panicking crowd and a classical biological phenomenon: niche partitioning by salamanders along a streambank-forest floor ecotone. The simulations are found to produce realistic salamander behavior, including the non-overlapping territories and interspecific niche partitioning. Furthermore, the simulations validate the functional forms used for social forces.

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CP10

On the Role of Cross-Immunity and Vaccines on the Survival of Less Fit Flu-Strains

A pathogen's route to survival involves various mechanisms including their ability to invade (host's susceptibility) and their reproductive success within an invaded host ("infectiousness"). The immunological history of an individual often plays an important role in reducing host's susceptibility or it helps the host mount a faster immunological response de facto reducing infectiousness. The cross-immunity generated by prior infections to influenza A strains from the same subtype provide a significant example. In this paper, we study the role of invasion mediated cross-immunity in a population where a precursor related strain (within the same subtype) has already become established. An uncertainty and sensitivity analysis is carried out on the ability of the invading strain to survive for given cross-immunity levels. Our findings indicate that it is possible (for relative low levels of cross-immunity) to increase the likelihood of strain coexistence even in the case when invading strains are "unfit", that is, when the basic reproductive number of the invading strain is less than one. The development of "flu" vaccines that minimally enhance herd cross-immunity levels may, by increasing genotype diversity, help facilitate the generation and survival of novel "virulent" strains, that is strains that have high levels of reproduction within the host.

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CP11

Hepatitis A: The Us and Canada As a Coupled Epidemiological System

Vaccination against Hepatitis A has been widespread in the US since 1996, and more limited in Canada, though few epidemic models of Hepatitis A have been developed. Evidence suggests correlated epidemics in the two countries. Here we analyze an epidemic model which treats the countries as coupled populations, using dynamical systems methods, in order to study the impact of vaccination in the US, and how disease dynamics in the US affect disease dynamics in Canada.

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CP11

Implications of Universal Hepatitis A Vaccination in Canada: Predictions of An Age-Structured Compartmental Model

Vaccination against Hepatitis A became widespread in the 1990s, however few transmission models have been developed. Here we develop an age-structured compartmental model to predict the impact of universal vaccination in Canada. Peculiarities of HAV transmission such as a cohort effect and travel-related incidence are addressed. The model shows that transmissibility has declined by a factor 2.8 over the past century. The model also predicts that vaccinating 4-year-olds achieves the best gains.

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CP11

Estimation and Identification of Klebsiella Pneumoniae Aggregation Dynamics

The bacterial pathogen Klebsiella pneumoniae is a cause of community- and hospital- acquired lung, urinary tract, and blood stream infections. A common contaminant of indwelling cathethers, it is theorized that a common infection pathway for this gram-negative organism is via shedding off of biofilm colonies. In an effort to better understand bacterial proliferation in the host bloodstream, we develop a size-structured PDE for the aggregation dynamics of the bacteria in an agitated suspension. We will present results of an investigation of the fragmentation properties of the viscoelastic biofilm emboli.

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CP11

Multi-Strain Disease Dynamics Due to Stochastic and Periodic Forcing

We consider the coupled-system dynamics of multi-strain diseases such as the flu, malaria and dengue fever. When the probability of reinfection to a second strain is weak, the global coupling between the strains leads to a manifold of steady endemic states. We show that the manifold is globally attracting but that stochastic noise results in motion on the manifold. We then investigate the oscillatory epidemics that result from seasonal forcing and latentcy periods.

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CP11

Maximum Likelihood Estimation in Nonlinear Dynamical Models of Hiv

The study of dynamical models of HIV, based on system of nonlinear ordinary differential equations (ODE), has considerably improved the knowledge on the pathogenesis of the infection. Complexity of those models leads to great difficulties for inference and classical sofwares for nonlinear mixed effects models cannot be used. We develop an algorithm for direct likelihood maximization adapted to the context of ODE. Based on simulated and real data, we show that it provides efficient estimations of parameters.

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CP11

Disease Modeling to Assess Outbreak Detection and Response

Bioterrorism is a serious threat that has become widely recognized since the anthrax mailings of 2001. In response, one national research activity has been the development of biosensors and networks thereof. A driving factor behind biosensor development is the potential to provide early detection of a biological attack, enabling timely treatment. This presentation introduces a disease progression and treatment model to quantify the potential benefit of early detection. To date the model has been used to assess responses to inhalation anthrax and smallpox outbreaks.

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CP11

Effects of Contact Tracing and Removal on the Spread of New Emerging Diseases

This study presents a framework for studying the effects of contact tracing, quarantine and isolation on the spread of emerging infectious diseases, using SARS outbreak data from Hong Kong as an illustration. We consider three different contact tracing functions and their effects on the diseases reproduction number, including sensitivity and uncertainty analysis. Tracing and quarantining contacts of diagnosed cases can reduce transmission greatly, but may also be cost-prohibitive on the large scale needed for eradication.

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CP11

An Sir Epidemic Model with Partial Temporary Immunity

The SIR-epidemic model considers that recovered individuals are permanently immune, while the SIS model considers recovered individuals to be immediately re-susceptible. We study the case of temporary immunity in an SIR based model with delayed coupling between the susceptible and removed classes. We perform a numerical and analytical bifurcation analysis of the resulting DDEs and describe how temporary immunity leads to recurrent outbreaks and how model parameters affect the severity and period of the outbreaks.

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CP12

Polymer Coating of Biological Surfaces

Many drug delivery systems suffer from undesirable interactions with the host immune system. It has been experimentally established that covalent attachment of suitable polymers to the surface of the drug carrier can reduce such undesirable interactions. In this talk we present and analyse mathematical and computational models of the polymer coating of biological surfaces. In particular, we apply our models to the coating of virus particles by hydrophilic polymers (such as pHPMA) which are currently used in some gene therapy systems.

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CP12

A Penalty Function Method for Distance-Constrained Molecular Dynamics Simulation

MD simulation can be used to study various dynamic properties of proteins, but a long sequence of iterations has to be carried out even for small protein motions due to the small time step (10e-15sec) required. The bonding forces are among those causing fast protein vibrations that require small time steps to integrate, but they may be replaced by a set of bond length constraints, to increase the step size and hence the simulation speed. Lagrange multiplier methods have been developed for constrained dynamics simulation. However, the multipliers have to be determined in every step to satisfy the constraints through the solution of a nonlinear system of equations. Here we propose a penalty-function method for constrained dynamics by considering the least action problem with the bond-length constraints as a constrained optimization problem and defining a quadratic penalty function for the constraints. The simulation with the penalty function method can be done by using a conventional unconstrained solver such as Verlet, only with the penalty parameter increased in an appropriate manner as the simulation proceeds. More specifically, we scale the constraints with their force constants when forming the penalty terms. The resulting force function

can then be viewed as a smooth continuation of the original force field as the penalty parameter increases. The penalty function method is easy to implement and costs less than a Lagrange multiplier method, which requires the solution of a nonlinear system of equations in every time step. We implemented the penalty function method in CHARMM and applied it to protein Bovine Pancreatic Trypsin Inhibitor (BPTI). We compared the simulation results with Verlet and Shake, and found that the penalty function method had high correlations with Shake and outperformed Verlet. In particular, the RMSD fluctuations of backbone and non-backbone atoms and the velocity auto correlations of C atoms of the protein calculated by the penalty function method agreed well with those by Shake. We describe the penalty function method and its implementation details, discuss our results and the issues to be resolved, show the advantages as well as the disadvantages of the method, and demonstrate the potential of using the method for general constrained molecular dynamics and energy minimization.

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CP12

Swelling Dynamics of Weakly Acidic Polyelectrolyte

The behavior of polyelectrolytes plays an important role in many biological processes, e.g. vesicle exocytosis. We explore a simple model of polyelectrolyte swelling, featuring flows that are driven by gradients in electro-chemical potential and that conserve volume. The mean-field potentials derive from a statistical thermodynamics model of Gibbs free energy and include pressure, electro-static potential, short-range interaction energies and entropic terms. We explore the interplay of corresponding force components during swelling.

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CP12

The Firing of an Excitable Neuron in the Presence of Stochastic Trains of Strong Synaptic Inputs

We consider a fast-slow excitable system subject to a stochastic excitatory input train, and show that under general conditions its long term behavior is captured by an irreducible Markov chain. In particular, the firing probability to each input, expected number of response failures between firings, and distribution of slow variable values between firings can be obtained analytically from the distribution of interexcitation intervals. The approach we present immediately generalizes to any pair of input trains, excitatory or inhibitory and synaptic or not, with distinct switching frequencies. We also discuss how the method can be extended to other models, such as integrate-and-fire, that feature a single variable that builds up to a threshold where an instantaneous spike and reset occur. The Markov chain analysis guarantees the existence of a limiting distribution and allows for the identification of different bifurcation events, and thus has clear advantages over direct Monte Carlo simulations. We illustrate this analysis on a model thalamocortical (TC) cell subject to two example distributions of excitatory synaptic inputs, in the cases of constant and rhythmic inhibition. The analysis shows that there is a drastic drop in the likelihood of firing just after inhibitory onset in the case of rhythmic inhibition, relative even to the case of elevated but constant inhibition. This observation provides support for a possible mechanism for the induction of motor symptoms in Parkinson's disease.

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CP12

Support Vector Regression Approach for Prediction of Relative Lipid Accessibility in Membrane Proteins

Membrane proteins constitute a significant fraction of a typical proteome and they play a number of critical functions, e.g., enabling signaling and transport through the membranes. Computational studies of membrane proteins are an important complement of (often facing serious limitations) experimental efforts in that regard. Here we present a novel protocol for prediction of relative lipid accessibility in membrane domains. The new method is based on a linear, Support Vector Regression-based model that can be used to efficiently and reliably estimate the parameters in the model from a limited number of experimentally validated examples. The new method will be available to the community through the MINNOU web server (http://minnou.cchmc.org).

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CP12

A Chemical Kinetic Model for RNA Polymerase Translocation During Transcriptional Elongation of the Nascent Rna Chain

A chemical kinetic model of the elongation dynamics of RNA polymerase along a DNA strand is introduced. Unlike previous models that attempt to explain the motion of RNA polymerase using internal strain and stresses, we propose a chemical kinetic model which governs the discrete movement of the RNA polymerase along a DNA tether, with no consideration given to elastic effects. The model's novel feature includes a 'look-ahead' feature in which nucleotides bind reversibly to the DNA prior to being incor-

porated covalently into the nascent RNA chain. Results are presented for a random DNA sequence, and also with specific DNA sequences that have been used in single-molecule experiments of the random walk of RNA polymerase along DNA. We also discuss preliminary parameter fitting results of our model to the experimental data.

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CP12

Building Molecular Surfaces Using Surface Tension Models

An important tool in the analysis of biological macromolecules is the solvent-accessible surface, a "wrapper" for the molecule which defines the boundary between the the solvent and the molecular interior. These surfaces are typically generated geometrically, through the action of a rolling probe meant to represent a single water molecule. We are exploring new, finite-element-based approaches to generate surfaces via energy minimization, under the assumption of constant solvent pressure and surface tension.

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MS1

Correlation Approaches for Extracting Process Information from Spatial Data

Small-scale spatial patterns in ecosystems (e.g. plant species distributions, epidemic patterns) are driven by environmental variation and demographic stochasticity, modified by movement and spatial interactions among species. Defining these spatial dynamics in terms of spatial correlation functions provides a natural connection to data. Here I demonstrate how, given that we know *which* spatial processes are operating, one can invert Fourier-transformed versions of correlation models to estimate the parameters of spatial processes.

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MS1

Perturbative Approach to Transient Dynamics in Spatial Ecology

The coexistance or exclusion of interacting species is of fundamental importance in ecology. If an individual's interactions extend beyond its nearest neighbours, there is a natural small parameter for developing a perturbation theory around the infinite-range, mean-field limit. This permits an asymptotically exact calculation of the contribution of space and stochasticity. I apply this to the eigenvalues describing approach to equilibrium, showing how the interaction and dispersal kernels determine the stability of spatially extended populations.

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MS1

Conditional Dispersal in Ecological Models

Traditional spatial models in ecology assume that organisms disperse randomly by simple diffusion or similar processes. In some cases, however, organisms may disperse in response to their surroundings or other organisms. McPeek and Holt introduced the term "conditional" to describe that type of dispersal. This talk will describe some models with conditional dispersal. The models are partial differential equations similar to reaction-diffusion equations, but incorporating advection or density dependent diffusion or boundary conditions.

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MS1

Spatial Stochastic Host-symbiont Models

Optimal foraging and habitat selection theories that are based on non-spatial, deterministic models predict evolution towards generalist strategies in fine-grained habitats and towards specialization in coarse-grained habitats. In addition, coevolutionary processes appear to favor extreme specialization among parasites. We introduce a spatially explicit, stochastic model that confirms the effect of habitat coarseness on specialization in the absence of coevolutionary processes. To understand the effects of coevolutionary processes, we introduce feedback between hosts and their symbionts into our spatially explicit, stochastic model. This is joint work with Nicolas Lanchier, University of Minnesota.

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MS2

The Criticality Hypothesis: How Local Cortical Networks Might Optimize Information Processing

Several models suggest that neural networks should operate near a critical point to optimize information transmission, information storage, computational power, and stability. To test this, we recorded cortical slices and cultures on 60-channel multielectrode arrays. Networks produced avalanches of neural activity whose sizes were distributed according to a power law, reminiscent of critical phenomena. Moreover, avalanches occurred in repeating patterns that could be used to store information. These data are consistent with the criticality hypothesis.

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MS2

Reverse-Correlation Techniques and Cortical Architecture

Reverse-time correlation measurements give the average orientation dynamics of individual neurons within a highly excited visual cortical neuronal network. The resulting orientation tuning curves provide specific information about the nature of cortico-cortical connections, in particular, the strength and extent of cortical inhibition. We present a set of models that uncover and explain the connection between the experimentally observed tuning curves and the relevant cortical architecture.

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MS2

Statistical Modeling of Multi-neuron Responses in Primate Retina

Neural circuits are well known to exhibit correlated spiking activity, whose origin and significance is a topic of much current interest. We show that a generalized linear model, fit using maximum likelihood, can account for the stimulus-dependence, history-dependence, and correlation structure in the spike responses of a group of nearby neurons in primate retina. We will discuss implications for the multi-neuronal coding of visual information.

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MS2

Detecting Weak Ratiometric Signals from Genetically Encoded FRET Indicators

Genetically encoded ratiometric indicators have become an important part of the neural imaging toolkit. Voltage-sensitive and calcium-sensitive indicators have been used to study neurons as well as other tissues such as the heart and liver. We present a simple, new multivariate method for teasing out small ratiometric signals from FRET- or Stokes' shift-based fluorescence data. We will present the method and show an application to sensory neurons in zebrafish.

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MS3

A Mathematical Model of Tumor Lymphangiogenesis

The lymphatic system provides a much more favorable environment for tumor invasion and metastasis than does the blood vasculature. As more specific markers for lymphangiogenesis are emerging, a modeling of this process is becoming more feasible. In this talk I shall present such a model, in terms of PDEs for the densities of lymphatic endothelial and cancer cells, concentrations of urikinase, plasminogen and extracellular matrix, and VEGF-C growth-factor. joint work with Georgios Lolas.

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MS3

Modeling the Tumor-vasculature Interaction Suggests Time-dense Antiangiogenic Schedulings

Clinical inferences can be derived from the simple ODE model of antiangiogenic therapy proposed by Hahnfeldt et al. (1999) and its generalizations. We compared constant continuous-infusion and periodic boli-based therapies, showing by analytical conditions and simulations that schedulings which guarantee the same mean drug concentration may exhibit different efficacy, with the profiles that approach the constant one being more effective. This behavior appears to depend on the functional form of the nonlinear tumor-vasculature relationship.

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MS3

A New Cancer Drug Regimen Based on the Interplay Between Tumor Growth and Angiogenesis - Prediction of a Mathematical Model

We mathematically modeled the interplay between key biological, pathological and pharmacological processes underlying drug-patient interactions, from the molecular level to that of the whole organism. Simulating a large number of treatment options, we showed that unlike the recommended regimen, applying large doses every three weeks, the optimal treatment schedule for common anticancer drugs, such as docetaxel and doxorubicin, is one of relatively small doses, the dosing interval being one week.

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MS3

Stochastic Geometrical Methods for the Statistical Analysis of Tumor-induced Angiogenesis

Tumor-induced angiogenesis may be modelled as a birth-and-growth stochastic process, which is composed of branching and subsequent growth of vessel networks. The growth of vessels (and possibly the inhibition of growth, via drugs) is coupled with interacting underlying fields, so that the geometric structure of vessels becomes spatially heterogeneous. Here we provide methods of statistical analysis for the estimation of geometric densities that characterize the morphology of a real system.

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MS4

Parameter Estimation in PBPK Models

A physiologically based pharmacokinetic (PBPK) model for TCDD was used as the framework for models of TCDD, PCB126, PeCDF, and a mixture of these three chemicals. A goal was to assess how a model developed specifically for TCDD would serve as a general Ah receptor model for individual dioxin-like chemicals as well as a mixture of dioxin-like chemicals. I'll discuss the mixture model and efforts on variance estimates for the model parameters and predictions.

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MS4

Development of an Air-Tissue Computational Fluid Dynamics Model to Describe Extraction of Hydrogen Sulfide in Rat Nasal Passages

Rats exposed to hydrogen sulfide (H_2S) develop olfactory neuronal loss (ONL). A computational fluid dynamics model was developed to simulate H_2S uptake in the rat nasal cavity. Wall mass flux was governed by H_2S reaction kinetics in nasal tissue with kinetic parameters estimated from a pharmacokinetic model. Regions with predicted high H_2S flux were associated with sites that develop ONL, indicating that airflow patterns play an important role in the distribution of H_2S-induced lesions.

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MS4

One of the Applications of Physiologically Based Pharmacokinetic Modeling: Interpretation of Biomonitoring Data

Physiologically based pharmacokinetic (PBPK) modeling has been applied broadly for a wide variety of compounds to describe the relationship between external and internal measures of exposure. As a measure of internal exposure, biomonitoring data reveal the presence of chemicals in human populations. To interpret the health implications of such data, however, requires knowledge of dosimetry that can be provided by PBPK modeling.

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MS4

Modeling Sensory Irritation Response in Rats

A model describing the decrease in respiration from inhaled gases that irritate nasal cavity nerves in rats is presented. The model is optimized to describe respiratory response data and evaluated through sensitivity analysis. The model predicts data well and reasonably describes the physiological system of sensory irritant response. (This abstract does not reflect EPA policy.)

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MS5

Some Lessons in Math and Biology Education

I summarize experiences from a project that coupled math and biology undergraduates in field and laboratory research projects. This encouraged the students to jointly develop hypotheses and appropriate experimental systems to address them, in conjunction with development of mathematical models. I'll also present educational survey results of attendees at the 2005 SMB/ESMTB meeting. The survey allows differences to be determined based upon education background of the respondent, their gender and country of origin.

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MS5

CoMBiNe- A Computational and Mathematical Biology Network

I will present an overview of a new project supported by the Shodor Education Foundation to help make integrating mathematics, computation, and biology in the classroom easier. We are developing an electronic resource in coordination with the National Science Digital Library through the Shodor Foundation's CSERD website for easy access to basic introduction, interactive activities, laboratory ideas, and references of mathematical and computational topics in biology. The project will make use of existing materials and provide a searchable, indexed interface to help faculty make the discovery and integration of those materials routine and seamless.

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MS5

Computational Science Education and Research for Undergraduate Biology Majors

From ecology to spread of disease to metabolism, biology offers a wealth of interesting applications for undergraduates in computational science. Moreover, with a foundation in mathematics and computer science, biology majors can perform meaningful interdisciplinary research in internships, graduate school, and post-graduate positions. This talk covers some of the applications, materials, and opportunities that have evolved through Wofford College's Emphasis in Computational Science.

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MS5

Creating a Mathematical Biology Course for Biology Majors

In spite of the surge in applications of mathematics in biology, biology majors often take only the minimum number of mathematics courses. We discuss efforts to create a mathematical biology course targeted at biology majors with minimal prerequisites (1 semester of calculus). Course emphasis is in the modeling process, particularly as it relates to the scientific method. Communication and interpretation is stressed, thereby giving this course a novel aspect to mathematics majors as well. Higher level mathematics are introduced in a way that might motivate biology students to take further mathematics courses.

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MS6

Functional Analysis of Biochemical Signaling Pathways Mediating the Acute Inflammatory Response

Acute inflammation in the skin is mediated by IL-1 signaling. We have used CellDesigner software to develop a detailed, visual representation of this signaling. Functional modules are abstracted from the visual representation. Quantitative description of the modules and their key interactions allows essential behaviors of the IL 1 pathway to be captured while omitting many of the molecule-to-molecule interactions depicted in the visual model. (This presentation does not necessarily reflect policies of the U.S.EPA.)

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MS6

The Challenge of in Vivo Experiments in Support of Systems Biology Models

Systems biology models have specific biologically-based structures and parameters. After structure is decided, a large number of diverse parameters must be determined for a model to accurately predict behavior. Theoretically, parameters from intact organisms are more appropriate than parameters from cell lines. Estimation of parameters using an intact in vivo system can bring a wide variety of challenges. Examples of various types of model parameters and their estimation using in vivo methods will be discussed.

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MS6

Statistical Issues in the Development of Systems Biology Models

Abstract not available at press time.

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MS6

Application of Functional Genomics Technologies to Understand the Topology of Signaling Networks

Over the past decade, the focus on genomic sequencing and gene discovery has provided a virtual parts list that comprise the molecular machinery of the cell. Today, the focus has shifted towards obtaining a broader understanding of gene function and how the various genes are contextually organized into signaling modules. In this presentation, we will discuss the application of high-coverage functional genomic screens together with bioinformatic tools for dissecting cell signaling modules.

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MS7

Modeling and Computation of Signal Transduction in Olfactory Cilia with Non-Uniform CNG and Cl(Ca) Channels Distributions

Signal transduction in olfactory cilia is produced primarily by the cyclic-nucleotide-gated (CNG) and Ca2+-gated Cl (Cl(Ca)) ion channels.We use analytical and computational methods to study mathematical models in conjunction with known experimental results. We develop differential equation models for two different experiments, one involves the interplay between CNG and Cl(Ca) channels and the other, the diffusion of Ca2+ into cilia and resulting electrical activity. The Ca2+ concentration and membrane potential are simulated in our study. We obtain predictions on the distribution of the Cl(Ca) ion channels and placement of the channel types in order to optimize the electrical signal.

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MS7

Methods to Estimate Distributed Parameters in Neuronal Cable Theory Models

Spatially distributed ionic channel densities in a nerve cell determine the type of excitable responses of the cell. These densities are typically represented by constant parameters, but it is known that channels are non-uniformly distributed. We will discuss two numerical approaches to identifying a non-constant conductance, one being a marching method based on overspecified boundary data, the other a pde-constrained optimization method. These will be applied to linear and nonlinear cable models.

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MS7

Channel Localization Via Calcium Imaging

Calcium, the most important of the second messengers, locally modulates the excitability of nerve and muscle. We exploit the ability to monitor cytosolic calcium, throughout intact cells, with sub-millisecond temporal resolution and sub-micron spatial resolution in the construction of a map of channel density. In the process we pose and solve two inverse problems: (1) Infer from the change in cytosolic calcium Fluorescence the associated membrane calcium current in space and time, and (2) Infer from the calcium current the nonuniform distribution of all participating channels.

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MS7

Ion Channel Distributions in Olfactory Neurons: Asymptotic Analysis

Transduction of an odor into an electrical signal to the brain involves the activation of cyclic-nucleotide-gated (CNG) channels in olfactory cilia. An inverse problem is presented which uses experimental measurements of electrical activity to determine the distribution of CNG channels along the cilium. The model, which consists of two nonlinear partial differential equations, is studied using perturbation techniques. A one-dimensional computer minimization and special delay iteration are used with the perturbation formulas to obtain solutions in the cases of simulated and experimental data.

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MS7

Identification of Ion Channel Distributions in Olfactory

Recent discoveries are revealing that cilia, which are small hairlike cellular projections, play a fundamental role in many diseases. In our lab we have focused on olfactory cilia and the determination of the distributions of their various ion channel types. Transduction of an odorant molecule into an electrical signal begins in these olfactory cilia. Our research findings suggest that the profile of their channel distributions is quite different than the shapes previously considered. This diversity of shapes appears to have a significant impact on the strength of the transmitted signal. Although fully experimental procedures (immunocytochemistry) appear to be feasible for some (but currently not all) of the channel types they are very difficult and have not been successful to date. As an alternative, we have formed sets of data which measure the current response due to specific ion channels during the diffusion of a ligand into a cilium. This data, in conjunction with the computational solution of an inverse problem arising in our mathematical model of this ciliary diffusion process, has led to estimates of ion channel distributions. These inverse problems are argueably more difficult than, but related to, a well-studied (though apparently not well-understood) class of such inverse problems. In this talk we provide an overview of our work on this problem and its context. We also formulate a particular integral equation problem that arises in the solution of the inverse problem and describe some theoretical and computational results.

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MS8

Some Spatial Aspects of Control and Management in Disease Ecology

Recent approaches on spatial spread of wildlife diseases and infestations provide assessments of control methods. Little work has been done to determine optimal spatio-temporal controls, allowing choice of objective functions for economic costs of control and associated disease costs. We describe case studies using a mixture of analytic and computational methods to derive optimal spatial controls. Linking these methods to geographic information systems provides managers and epidemiologists with efficient tools to manage disease spread.

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MS8

Host Extinction Dynamics in Epidemiology Models

We present a SI model formulated through birth and death processes. This model reveals and corrects errors in similar exisitng models. Complete mathematical investigation of this simple model shows that the host extinction dynamics can happen and the outcomes may depend on the initial conditions. We also present some extensions of this model to structured SI models, including delay differential equation SI models. We show that host extinction dynamics is ubiquitous to many well formulated epidemiology models.

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MS8

Evolutionary Suicide by Hypertumor: a Novel Hypothesis for the Cause of Necrosis in Malignant Neoplasia.

Tumor necrosis is a common feature of malignancy. Recent mathematical models suggest that necrosis may be caused by hypertumors—tumors growing on a tumor. Hypertumors arise when a cell strain trades away the ability to secrete tumor angiogenesis factors to gain growth potential. What results is an area of tissue characterized by aggressive histology and hypoxia, ultimately causing the definitive ecological collapse of necrosis. Here I elucidate conditions under which natural selection favors the hypertumor.

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MS8

Introduction to Disease Ecology with a Case Study

Rabies, the most important viral zoonotic disease worldwide, has been undergoing epidemic expansion along the eastern seaboard of the United States since the mid-1970s following an accidental introduction of rabid raccoons from a source of endemic infection in the southeastern US. Using data submitted from US States to the Centers for Disease Control and Prevention, we have constructed stochastic simulations of the spatial dynamics of rabies as it has spread into new geographic region. The simulation was constructed as an interaction network with nodes of the network defined by township and county centroids. Interaction strengths along specific connections were sensitive to local geographic conditions and parameterized against reported data on the time and spatial location of detected rabid animals. The parameterized model has proven to be a valuable model for strategic planning for disease emergence and to direct the development of spatial control strategies.

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MS8

Case Study of Disease Ecology: Avian Flu

Avian Influenza or bird flu has recently been the subject of much media attention and public interest. Opinions on its potential to spawn a global pandemic range from the alarmist to the cautiously skeptical. In this talk deterministic models are presented for both the temporal trajectories of the bird flu both in avian as well as human populations. Of particular interest is the propensity of an infection of an avian population to induce a human pandemic.

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MS9

New Multiscale Approaches for Examining the Structure and Dynamics of Membrane Bound Proteins

Some new approaches for simulating membrane bound proteins in lipid bilayers will be presented. Specifically, some aspects of Multiscale Coupling will be elaborated on, where atomistic-level simulations of membrane bound proteins (such as the influenza A virus M2 proton channel) are directly coupled to corresponding field theory-based meso-

scopic bilayer/viscous solvent simulations. The protein is observed to couple to the long-wavelength stress fields arising at the mesoscopic level, and small structural changes are indicated.

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MS9

Boundary Layer Analysis of the Shape of Two-phase Lipid Vesicles

We present approximate analytical solutions of the shape equations of giant unilameller vesicles with fluid phase coexistence using a boundary layer calculation. We show that the boundary layer calculation agrees well with the numerical solution for a variety of parameter values. We demonstrate, using the best fit parameter values of our earlier work, that the shape obtained from the boundary layer calculation matches well with the experimental shapes. The approximate calculation eliminates the laborious and time consuming iterative task of manually tuning parameters to obtain a suitable numerical shape. It also facilitates the determination and influence on shape of material parameters associated with the resistance to changes in mean and Gaussian curvature and with any distributed or localized spontaneous curvature.

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MS9

Forces and Geometry in 3-D Membrane Mechanics

Abstract not available at press time.

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MS9

Simulation of Multicomponent Vesicle Membranes and Membranes with Open Edges

We will present numerical algorithms to simulate the recent experimental observations of multicomponent vesicle membranes based on a variational phase field approach. The approach can also be used to simulate membranes with free edges. The effectiveness of our simulation approach will be demonstrated.

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MS9

Adaptive Algorithms for the Simulation of Vesicle Membranes

Abstract not available at press time.

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MS10

Individualized Response-guided Monitoring of Cancer Therapy: A Simulation-based Approach

Abstract not available at press time.

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MS10

From
Tissue Sample to Cancer Prognosis: Data Quantification and Application for Protein Biomarkers

Abstract not available at press time.

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MS10

Insights from Data Driven Modeling and Model Driven Drug Design

Abstract not available at press time.

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MS11

Numerical Analysis of a Degenerate Biofilm Model

Recently, a doubly degenerated diffusion-reaction modelling framework was proposed that is able to describe the formation of spatially heterogeneous biofilm morphologies, such as cluster-and-channel or "mushroom" biofilm architectures. In this presentation we review the basics of the model, its application to mixed culture biofilms, and discuss numerical strategies how to solve it.

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MS11
Thin-film Modelling of Biofilm Growth

Abstract not available at press time.

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MS11
Biofilms and the Plasmid Maintenance Question

Abstract not available at press time.

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MS11
Drug Delivery in Bacterial Biofilms

A continuum modelling approach is used to describe biofilm growth based on fluid dynamics and conservation laws. The modelling considers the role of nutrient and bacterial cell-cell signalling, both important factors in the normal development of biofilms. The model is extended to investigate the effects of an externally applied anti-biotic treatments (that directly kill bacteria) and cell-signalling targeting drugs. A number of key results are established based on asymptotic and numeric analysis of the model.

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MS12
The Effect of Luminal Depletion on the Dynamics of Ca-regulated Ca Channels

We analyze how the dynamics of depletion and refilling of a restricted volume of endoplasmic reticulum associated with an intracellular Ca-regulated Ca channel influences it's stochastic gating and equilibrium properties. We emphasize numerical solutions of advection-reaction equations describing probability densities representing cytosolic [Ca] and lumenal [Ca] conditioned on the channel's state. Extensions of this approach can give insight into the effect of luminal depletion on the characteristics of Ca puffs and sparks.

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MS12
Analysis of the Effect of Residual Calcium on the Gating of Calcium-regulated Calcium Channels

We study the effect of 'residual calcium' on the stochastic gating of several inositol-4,5-triphosphate receptor models coupled to a differential equation describing a dynamic calcium domain. Using Monte-Carlo simulations, numerical solution of a system of Fokker-Planck-type equations and analytical methods, we show how the equilibrium open probability of such models depends on the time constant for calcium domain formation and collapse compared to the characteristic time scale for calcium channel gating.

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MS12
Calcium Waves as a Signal for Late Long Term Potentiation

As a coincidence of synaptic stimulation and back propagating action potentials, the initiation of calcium waves in dendrites of hippocampal pyramidal cells has been shown experimentally. It is also known that calcium is a critical second messenger for gene regulation within the nucleus. We construct and analyze a model which incorporates an appropriate spatial mechanism of calcium signaling to account for protein production leading to synaptic strengthening indicative of late long term potentiation.

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MS12
A Model of the Roles of Essential Kinases in the Induction and Expression of Late Long-Term Potentiation

The induction of late long-term potentiation (L-LTP) relies on several key second messengers and kinases. We developed a model representing synaptic actions of protein kinase A, MAP kinase, and CaM kinase II, and activation of transcription by CaM kinase IV and MAP kinase. The model simulates electrical and chemical L-LTP, inhibitor effects, and synaptic tagging. Supralinear stimulus-response relationships are essential to translate brief stimuli into long-lasting synaptic strengthening. The model suggests experimental tests and clarifies relationships of hippocampal L-LTP with synaptic strengthening in other organisms.

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MS13
Mathematical Modeling of Cancer Virotherapy

Cancer therapy with replicating viruses may have various outcomes which can be best understood by mathematical modeling. We propose a model which includes most salient features of virotherapy: kinetics of untreated tumor, infec-

tion of tumor cells, replication of viruses, elimination of infected tumor cells and effects of immune response on virus by cytotoxic T-cells. The model is validated by available data on virotherapy for multiple myeloma in SCID mice. Relevant equilibrium points are evaluated, and by using simulations we analyze the influence of model parameters on the outcome of the therapy. We also propose a model for virotherapy enhanced by radiation. Viruses engineered to express thyroid sodium iodide symporter make infected cells targets for radioactive idodide. The effects of radiation upon administration of radioactive iodide may lead to elimination of tumor cells, when virotherapy alone is not sufficient. We evaluate various therapeutic scenarios and discuss therapy optimization.

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MS13

A Model for Antimitotic Chemotherapy: The Importance of the Proliferation Ratio

A model for antimitotic chemotherapy is presented which suggests the limits of such therapy and explores the efficacy of different therapy regimes. The proliferation ratio and so the tumor age on therapy commencement will be shown to be a key factor in these efficacies.

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MS13

Modeling Gompertzian Tumor Growth through Cell Dynamics

A model for Gompertzian tumor growth based on cell dynamics and cell quiescence is presented. The model predicts that tumors of the same carrying capacity may have significantly different proliferation profiles which depend on quiescent cell death rate. The model is applied to specific examples of multiple myeloma, parathyroid and testicular tumors.

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MS13

Optimizing Topotecan Therapy in Pediatric Neuroblastoma

Topotecan (TPT) has activity in a dose/schedule dependent manner against neuroblastoma. Mathematical models are described that incorporate the growth of neuroblastoma along with the antitumor and toxic effects of TPT. In addition, optimal control methods are used to aid in designing effective treatment strategies. The goal of this analysis is to combine the various known pharmacokinetic and pharmacodynamic results of TPT in a formal mathematical framework to design more effective treatment approaches in pediatric neuroblastoma.

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MS14

Mechanics Explains the Structures of Coiled Polymers in Bacteria

Abstract not available at press time.

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MS14

A Stochastic Immersed Boundary Method Incorporating Fluctuations : Toward Modeling Cell Micromechanics

The mechanics of many cellular systems involve elastic structures which interact with a fluid, for example the outer cell membrane deforms during protrusions generated during motility and cell organelles such as the Golgi Apparatus and Mitochondria involve membranes which deform and bud vesicular and tubular structures during biological processes. Modeling, analyzing, and simulating the mechanics of such systems presents many mathematical challenges. The immersed boundary method is one modeling approach for such systems, and has been applied to many macroscopic biological problems, such as blood flow in the heart and lift generation in insect flight. At the length scales of cells and cell organelles, thermal fluctuations also become significant and must be taken into account. In this talk we discuss an extension of the immersed boundary method framework which incorporates thermal fluctuations through appropriate stochastic forcing terms in the fluid equations. This gives a system of stiff SPDE's for which standard numerical approaches perform poorly. We discuss a novel stochastic numerical method which exploits stochastic calculus to handle stiff features of the equations. We further show how this numerical method can be applied in practice to model the basic microscopic mechanics of polymers, polymer knots, membrane sheets, and vesicles. We also discuss preliminary work on modeling the dynamics of cell organelle structures.

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MS14

T-Cell Receptor Signaling Model Predicts Multiple Activation Levels and Switching Mechanisms

A properly functioning immune system requires ligand-appropriate T-cell responses. Theoretically, T-cell responses (viral, self, and partial) to antigens are biologically controlled by two parameters: receptor to peptide ratio (μ) and specific peptide affinity (κ). An experimentally-verified mass-action ODE model describing this signaling process is derived with minimal rate constant fitting. Simulations varying μ) and κ suggest existence of multiple quasi-stable states corresponding with appropriate immune re-

sponses, implying possible switching mechanisms controlling T-cell receptor activation.

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MS14

Finding Gene Regulatory Sites: Protein Localization

Abstract not available at press time.

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MS14

Stochasticity in Gene Regulatory Networks and Cell Signaling Pathways

First a model of a synthetic gene regulatory networks will be presented. This stochastic model quantitatively captured the means and distributions of the expression from this modular system and accurately predict the in vivo behavior of an expanded network that included positive feedback. The model also revealed the counterintuitive prediction that noise in protein expression levels can increase upon arrest of cell division, which was confirmed experimentally. Then a stochastic model of the biochemical steps that regulate activation of the MAPK in yeast signaling pathway will be used to demonstrate the use of equation free method to quickly compute the steady state distribution of activated MAPK.

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MS15

Modeling Chemotaxis in Escherichia coli: From Single Receptors to Strongly-coupled Clusters

The chemotaxis network in E. coli is remarkable for its sensitivity to small relative changes in the concentrations of multiple chemical signals. We present a model for signal integration by mixed clusters of interacting two-state chemoreceptors. Our model results compare favorably to the results obtained by Sourjik and Berg using in vivo fluorescence resonance energy transfer (FRET). Importantly, we identify two distinct regimes of behavior, depending on the relative energies of the two states of the receptors. In regime I, coupling of receptors leads to high sensitivity, while in regime II, coupling of receptors leads to high cooperativity, i.e. high Hill coefficient. For homogeneous receptors, we predict an observable transition between regime I and regime II with increasing receptor methylation or amidation. Furthermore, we address the question of adaptation within our model.

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MS15

From Signal Transduction to Spatial Pattern Formation in E. coli

Appropriate responses to signals in the environment are essential for the survival of any organism, and thus sophisticated means of detecting external signals, transducing them into internal signals, and altering behavioral patterns appropriately have evolved. Many organisms use a random-walk search strategy to search for food when the signals are spatially uniform, and bias movement appropriately when a suitable change in signal is detected. The collective behavior of bacterial populations provides an example of how cell-level decision-making translates into population-level behavior, and illustrates the mathematical problem of incorporating individual-level behavior into population-level models. In this talk we focus on the flagellated bacterium *E. coli*, for which a great deal is known about signal detection, transduction and cell-level swimming behavior. We review the biological background on individual and population-level processes and discuss the velocity-jump approach used for describing population-level behavior based on individual-level intracellular processes. We also show how aspects of the signal transduction and response enter into the macroscopic equations, and discuss computational issues that arise in the bacterial pattern formation problem.

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MS15

Diversity in Bacterial Chemotaxis

The chemotaxis pathways in Escherichia coliand Bacillus subtilisboth regulate the same task, namely excitation and adaptation to environmental signals. Both pathways employ orthologous genes that genetically complement between the two species (i.e. can function in the heterologous host). Yet how these orthologs contribute to network function in each organism is different due to differences in the pathway topologies. Bacterial chemotaxis, therefore, provides an excellent system for studying the structure and evolution of biological networks using comparative analysis. We present mathematical models for the pathways regulating chemotaxis in E. coli and B. subtilis. By analyzing the two models, we identify a common regulatory

strategy in both organisms. These results demonstrate the limitations of pathway inferences based solely on protein homology and indicate the need for a theoretical metric to analyze functionally similar pathways. We then demonstrate how comparative analysis can be used to reconstruct pathways in species with limited experimental data such as Helicobacter pylori, illustrating the power of comparative network analysis as a tool for analyzing, dissecting, and reconstructing complex biological networks.

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MS15

Modelling Bacterial Chemotaxis: From Molecular Interaction to Cellular Behavior

I will first review some of the recent progress made in modelling various aspects of the bacterial chemotaxis pathway. I will then focus on describing our works on understanding molecular level cooperativity, which is responsible for large signal amplification sustained in a wide dynamic range in bacterial chemotaxis.

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MS16

Epidemiological Approaches in the Study of Social Dynamics: Drinking Dynamics at US colleges

Abstract not available at press time.

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MS16

Estimating the Reproductive Number and the Effect of Hypothetical Interventions for the Spanish Flu Pandemic in Geneva, Switzerland

Recurrent outbreaks of the avian H5N1 influenza virus in several regions of the world pose a global pandemic threat. I will present an analysis of historical hospital notification data of the 1918 influenza pandemic in Geneva, Switzerland. We estimated the number of secondary cases generated by a primary case during its period of infectiousness during the first two waves of infection. We then used these estimates to evaluate the single and combined effect of reductions in the overall influenza transmission rate via effective isolation strategies in hospitals or via reductions in the susceptibility of the general population through, for example, increasing hygiene and protective measures (e.g., increase hand washing, use of face masks), prophylactic antiviral use, and vaccination. Some model parameters are estimated by fitting an epidemic model to the data and others are obtained from published literature. We estimated the reproductive number for the spring wave $R_1 + 1.49$ (95 % CI: $1.45 - 1.53$) and the fall wave $R_2 = 3.75$ (95 % CI: $3.57 - 3.93$). We found that the implementation of single-component interventions is unlikely to achieve containment while control through their combined effect is feasible.

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MS16

Comparing Rubella Vaccination Strategies in China - Modeling and Simulation

Computer simulations of a deterministic model are used to predict the effect of the changing age distribution in China on the dynamics of rubella epidemiology and the incidence of congenital rubella syndrome (CRS). In comparing rubella vaccination strategies for China using simulations, our results predict some severe consequences of the current policy and suggest better alternatives for reducing and eliminating the incidence of CRS.

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MS16

Disease Emergence in Multi-host, Multi-patch Epidemic Models

Most pathogens are capable of infecting multiple hosts. These multiple hosts provide many avenues for the disease to emerge. In this investigation, we formulate and analyze multi-host and multi-patch epidemic models and determine conditions under which the disease can emerge. In particular, SIS and SIR epidemic models are formulated for a pathogen that can infect n different hosts. The basic reproduction number is computed and shown to increase with n, the number of hosts that can be infected. The SIS model for two hosts is studied in detail. Necessary and sufficient conditions are derived for the global stability of an endemic equilibrium. Numerical examples illustrate the dynamics of the two- and three-host epidemic models. The models have applications to hantavirus in rodents and other zoonotic diseases with multiple hosts.

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MS16

Could Low-efficacy Malaria Vaccines Increase Secondary Infections in Endemic Areas?

Recent breakthroughs in malaria vaccines have given new hope that a safe, effective malaria vaccine may be found. The following epidemiological question is addressed: could the introduction of a low or medium efficacy malaria vaccine lead to an increase in the number of secondary infections and what characteristics of such a vaccine will have the greatest effect on the outcome? A mathematical model is developed for a malaria vaccine that is given once prior to infection which accounts for separate malaria infection events. There is a threshold depending on the relative transmission probability, the recovery rate and the acquired immunity rate. If the recovery rate decreases, then there will always be fewer secondary infections. However, if the recovery rate increases, then there is a "shoulder" within which the number of secondary infections will decrease. Beyond this, the number of secondary infections will increase unless the transmission probability is sufficiently lowered. This effect is lessened as the acquired immunity rate increases. If the transmission probability is not sufficiently lowered, then vaccinated individuals will always cause more secondary infections than unprotected individuals. For low efficacy vaccines, this will be correlated to an increase in the overall severity of the disease in endemic areas.

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MS16

Mathematical Models of Tuberculosis Re-infections and Multiple Strains

The reemerge of tuberculosis (TB), the TB co-infections with HIV and the fast growing of multiple-drug resistant tuberculosis (MDR-TB) have brought new challenges for controlling and eliminating this old disease. In this talk, the transmission dynamics of tuberculosis is studied by a mathematical model that incorporates re-infections and multiple strains. The model presents several distinct bifurcations and multiple stable nontrivial steady states for both the basic reproductive number less than one and greater than one. It shows that a single tipping point cannot totally determine the transmission dynamics and the full picture of the dynamics are determined not only by parameters but also by the initial data. It also shows that MDR-TB can survival independent of drug-sensitive TB.

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MS17

Oscillation Mechanism of Intracellular Calcium Dynamics

Abstract not available at press time.

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MS17

Calcium Signaling Differentiation in the Maturing Xenopus oocyte: A Modeling Approach

The calcium signaling apparatus undergoes significant changes during oocyte maturation. Brief, local simulation through caged IP3 or calcium gives rise to sweaping and long-lasting intracellular Ca2+ elevations in the mature egg, while the reponse in the occyte is local and short. To the contrary, Ca2+ puffs, spatially and temporally limited release events through single clusters of release channels, are shorter in the mature egg. We use mathematical modeling in conjunction with experimental analysis (Klaled Machaca, U of Arkansas, Med. Sciences) to identify changes in the Ca2+ signaling machinery during oocyte maturation consistent with the experimental findings. We hypothesize that incraesed IP3 affinity of the IP3 receptors in the mature egg causes the long-lasting Ca2+ elevation in the mature egg. We further hypothesize that clustering of release channel clusters to larger superclusters gives rise to the shortening of the Ca2+ puffs in the mature egg.

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MS17

Messages Diffuse Faster than Messengers

Abstract not available at press time.

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MS17

Stochastic Gating of Instantaneously Coupled Calcium-regulated Calcium Channels

Although there is consensus that calcium puffs and sparks arise from the cooperative action of multiple intracellular calcium channels, the precise relationship between single-channel kinetics and the collective phenomena of stochastic calcium excitability is not well understood. Here we present and analyze several stochastic automata network models of calcium release sites that include calcium activation, calcium inactivation, or both.

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MS18

Beads in Mucus, Generalized Langevin Equations, and State Space Models

Abstract not available at press time.

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MS18

Cholera Population Dynamics - Inference for Par-

tially Observed Systems

A population model for cholera in Bangladesh is investigated as a case study in inferring infectious disease dynamics from data. Inference for nonlinear state space models can be a challenging step in developing stochastic dynamical models appropriate for infectious diseases. This motivates the introduction of a new method for likelihood based inference, which we call MAPLE (Maximum A Posterori Limit Likelihood Estimation). The MAPLE algorithm computes a maximum likelihood estimator as the limit of an average of Bayesian posterior mean estimators. The new methodology has computational advantages and a theoretical justification.

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MS18
Stochastic Challenges in Single-molecule Biophysics

Recent advances in nanotechnology allow scientists for the first time to follow a biological process on a single molecule basis. These advances also raise many challenging stochastic inference and modeling problems. First, by zooming in on single molecules, recent single-molecule experiments revealed that many classical models derived from oversimplified assumptions are no longer valid. Second, the stochastic nature of the experimental data and the presence of latent processes much complicate the inference. In this talk we will use the modeling of subdiffusion phenomenon in protein conformational fluctuations and the modeling of enzyme reaction pathways to illustrate the stochastic challenges in single-molecule biophysics.

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MS18
Multiscale Approximations to Reaction Networks

A reaction network is a chemical system involving multiple reactions and chemical species. Stochastic models of such networks treat the system as a continuous time Markov chain on the number of molecules of each species with reactions as possible transitions of the chain. In many cases of biological interest some of the chemical species in the network are present in much greater abundance than others and reaction rate constants can vary over several orders of magnitude. We consider approaches to approximation of such models that take the multiscale nature of the system into account. Our primary example is a model of a cell's viral infection for which we apply a combination of averaging and law of large number arguments to show that the "slow" component of the model can be approximated by a deterministic equation and to characterize the asymptotic distribution of the "fast" components. The main goal is to illustrate techniques that can be used to reduce the dimensionality of much more complex models.

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MS19
Mathematical Models of Cancer

In this talk we will present an overview of recent developments in the mathematical modelling of cancer growth. We will focus specifically on partial differential equation and discrete models of tumour-induced angiogenesis (including blood flow and drug delivery) and cancer cell invasion of tissue (the role of the urokinase plasminogen activation system). Mathematical and clinical/therapeutic implications of the model results will be discussed.

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MS19
Evolutionary Models of Carcinogenesis

Abstract not available at press time.

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MS19
Mathematics-driven Experimental Oncology

Abstract not available at press time.

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MS19
Mathematical Modeling in Clinical Oncology

Abstract not available at press time.

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MS20
Title not available at press time

Abstract not available at press time.

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MS20
New Approaches to Studying Stochastic Chemical Kinetics in Biochemical Reaction Networks

We used various analytic and numerical methods to elucidate complex dynamics in stochastic signal transduction. We demonstrate that the commonly used linear noise approximation to solving the chemical master equation fails when the number of proteins becomes too low. Consequently, we developed a new analytical approximation to

the solution of the master equation, based on the generating function approach, which works in a much wider range of protein number fluctuations. We show that in a linear signaling pathway, a reaction rate at a node could be tuned so the node acts either as a noise amplifier or as a noise filter. For more complex cascades, we mapped the the stochastic chemical kinetics master equation into a quantum field theoretical problem, which we solved using the variational principle.

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MS20

The Role of Population Dynamics in Phenotypic Variability

A population of genetically identical cells is known to exhibit a substantial phenotypic variability. This variability originates from both intrinsic and extrinsic sources. We concentrate on the role of population dynamics as an unavoidable source of variations. A clonal population is modeled as an ensemble of nearly identical genetic circuits whose dynamics is altered by the growth and division of cells. The predictions of theoretical analysis is compared with experimental measurements at the single-cell level.

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MS20

Control of Cell Cycle Entry by a Bistable Myc/Rb/E2F Switch

The entry of mammalian cell cycle is associated with a distinct time point, the restriction point (R-point), at which cells are committed to proliferation. Removal of growth factors before the R-point rejects cells back to the quiescence. Removal of growth factors after the R-point, however, does not prevent completion of the cell cycle. Despite its importance in maintaining normal cell physiology, the molecular nature of the R-point remains elusive due to lack of integrated understanding of the underlying regulatory network. Here we combined mathematical modeling with detailed experimentation in a mammalian cell culture system to gain insight into the R-point control. Our results suggest that the Myc-Rb-E2F pathway functions as a bistable switch that separates quiescence and proliferation. Once turned-on, as characterized by activation of E2F, the switch can trigger S-phase in a digital all-or-none manner. Furthermore, E2F activation is dependant on both the duration and the level of input growth stimuli. Correspondingly, the cell cycle entry is governed by a restriction curve (R-curve), at which each point represents the minimum duration required for growth stimuli at a given level to activate E2F expression. Genetic and biochemical modifications of the R-curve may contribute to development of cancer and terminal quiescence.

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MS21

Introduce Undergrad Research Presentations 3 and 4

Abstract not available at press time.

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MS21

Introduce 2 Undergrad Research Presentations 5 and 6

Abstract not available at press time.

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MS21

Introduce 2 Undergrad Research Presentations 1 and 2

Abstract not available at press time.

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MS22

Validation and Applications of a Non-linear One-dimensional Model of Pulse

We present a non-linear 1D model of blood pressure and velocity pulse wave propagation in the larger arteries to understand the performance of the system in healthy conditions and how anatomic variations and cardiovascular pathologies, such as atherosclerosis, affect the pattern of pulse waves. We validate our 1D model by comparison against a well-defined laboratory model with 35 arteries. Our numerical model is able to capture the main wave propagation features measured in the experiment.

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MS22

Sensitivity Analysis and Parameter Estimation for

a Model of the Cardiovascular

Abstract not available at press time.

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MS22

Sensitivity Analysis and Parameter Estimation for a Model of the Cardiovascular

Abstract not available at press time.

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MS22

Autonomic and Vascular Regulation in Aging

Human aging is associated with changes in the autonomic control that may affect interactions among multiple organ systems. Regulatory changes in the cardiovascular and cerebrovascular systems may have broad impact on cerebral perfusion and adaptation to activities of daily living, namely to the orthostatic stress. Genetic, environmental and behavioral risk factors, however, may have additive nonlinear effects on systemic regulation that may accelerate aging process and functional decline.

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MS22

Blood Flow Changes Caused by Respiratory Mechanical Effects

Changing pressure in the trunk due to respiration alters pressure for arteries and veins in the chest and stomach region in humans. This talk presents 1D models of the cardiovascular system and the respiratory pump. These models serve as tools for understanding the physiology and allow variations from normal resting conditions to exercise. We show how to evaluate physiological conditions in response to CPR. Results raised a spectrum of problems that require clarification related to the role of pumps, the differences between flows and pressures, and the function of valves.

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MS23

A Hybrid Model of Tumour Invasion: Evolution and the Microenvironment

The importance of tumour cell/microenvironment iterations is currently of great interest to the biological community. In particular, both the immediate microenvironment (cell-cell or cell-matrix interactions) and the extended microenvironment (e.g. vascular bed) are thought to play crucial roles in both tumour progression and suppression. In this talk we present a hybrid discrete/continuum mathematical model which describes the invasion of host tissue by tumour cells and examines how mutations in cell phenotypic attributes (e.g. P53 mutation, cell-cell adhesion, invasiveness) affect both tumour morpholgy and genetic makeup. In the model, we focus on four key variables implicated in the invasion process, namely, tumour cells, host tissue (extracellular matrix, ECM), matrix-degradative enzymes (MDE) associated with the tumour cells and oxygen supplied by the angiogenic network. In particular we will discuss the evolutionary implications of tumours growth in either harsh/mild microenvironmental conditions.

Sandy Anderson
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MS23

Mathematical Modeling of Cellular Signaling: Lipid Signaling Kinetics

Our goal is the construction of a comprehensive mathematical model for the uridine 5-diphosphate signaling pathway in the macrophage, a type of white blood cell. The mathematical model currently includes a system of nonlinear ODEs that describe the major pathway components, with an emphasis on the production and degradation of diacylglycerol, a cellular second messenger molecule which plays an important role in initiating various changes in cell behavior. Modeling techniques, challenges, and computational simulations will be presented. (Joint work with H. Alex Brown, Jeffrey Forrester, Mark Byrne and other members of the Brown lab.)

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MS23

Nonlinear Simulation of Tumor Growth

In this talk, I will focus on recent efforts to study solid tumor progression. Here we focus on a continuum-scale description and pose the problem in terms of conservation laws for nutrients, chemical factors and tumor cell populations. We develop a multiscale mixture model that accounts for cell-to-cell adhesion. We analyze the equations and develop accurate, adaptive numerical schemes. We relate the model to more classical single-phase models and we demonstrate the predictive capability of the model through comparisons with experimental studies of tumor growth. We then discuss extensions to include the effect of residual stress.

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MS23

Drug Delivery to Solid Tumors

Physiological transport barriers limit the distribution of systemically administered chemotherapeutics in solid tumors. Intratumoral delivery is a promising technique that can improve the efficacy of existing chemotherapeutics by

circumventing physiological barriers. I will present a continuum reaction diffusion model of intratumoral delivery of paclitaxel loaded microspheres and illustrate how simulations augmented by analytical approximations can help to elucidate the impact of cell pharmacokinetics, tumor morphology, microsphere release kinetics and spatial distribution on intratumoral drug distribution.

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MS24
Wavelets in Medical Sciences-Case Studies

Abstract not available at press time.

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MS24
Multifractal Analysis of Pollution of Delhi and Bombay

Abstract not available at press time.

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MS24
New Fractal Methods for Time Series Analysis

Abstract not available at press time.

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MS24
Multifractal Analysis of ECG

Abstract not available at press time.

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MS25
Air-Mucus Transport in the Lung

Abstract not available at press time.

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MS25
Exact and Asymptotic Hydrodynamics Solutions for Low Reynolds Number Spinning Rods

Abstract not available at press time.

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MS25
Bio Fluids Experiments: Nanoscale-Macro Scale

Abstract not available at press time.

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MS25
Nanoscale Biological Manipulation

Abstract not available at press time.

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MS26
A Novel Algorithm for MALDI-TOF MS Data Preprocessing Using Wavelets

Mass Spectrometry, especially matrix assisted laser desorption/ionization (MALDI) time of flight (TOF), is emerging as a leading technique in the proteomics revolution. It can be used to find disease-related protein patterns in mixtures of proteins derived from easily obtained samples. In this paper, a novel algorithm for MALDI-TOF MS data preprocessing is developed. A MatLab implementation shows the preprocessing steps consecutively including step-interval unification, adaptive stationary discrete wavelet denoising, baseline correction using splines, normalization, and peak detection, a newly designed peak alignment method using clustering techniques.

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MS26
Incorporating Covariates in Survival Analysis Using Artificial Neural Networks

In survival analysis, the Cox proportional hazards model is widely used to incorporate covariates. However, it has strong assumptions and requires knowledge of all covariates under consideration at every failure time. We consider time-dependent covariates and propose a method based on artificial neural networks. This method relaxes the assumptions and allows us to perform inference using the observed covariates values. We illustrate its use through simulations and apply it to a study of lung cancer.

Yali Liu
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MS26
Simulation of Solid Tumor Growth

We develop and check the accuracy a mathematical model for solid tumor growth. The model uses a set of partial differential equations describing the spatio-temperal changes in cell concentrations based on reaction-diffusion dynamics and the law of mass conservation. Unlike existing models, this model takes into account higher dimensions and arbitrary geometries, and incorporates random mitotic rate and nutrient supply. Furthermore, the model incorporate the dependence of cell proliferation rate on the growth inhibiting factors secreted by necrotic cells. The model is solved using B-spline collocation method. The results are compared with the published experimental data. The biological and clinical implications are discussed.

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MS26
Stochastic and State Space Models of Carcinogenesis

In this lecture, I will summarize the most recent development of cancer biology from the past 5-10 years. By articulating these biological studies, I will then propose some stochastic and state space models for carcinogenesis. I will develop stochastic differential equations for the state variables. Using these stochastic equations as the stochastic system model, I will then propose some state space models with the stochastic observation model being based on cancer incidence data available from SEER or other studies. A general Bayesian procedure using multi-level Gibbs sampling and predictive inferences to estimate the parameters and to predict the state variables will be developed. The models and the methods are illustrated by using the British physician data and some environmental data.

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MS27
Modelling Multi-stage Breast Cancer Development, Treatment and Recurrence

Models of the step-wise development of cancer help in the understanding of how the disease develops and lead to more efficient treatment strategies that prevent local recurrence. In breast cancer, about 10-30 percent of patients develop a recurrent tumour within a few years of the primary treatment. We present a model of the multi-stage development of breast tumours with respect to clonal breast formation, examine radiation treatment strategies, and discuss the risks of local recurrence.

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MS27
Derivation of the Tumor Control Probability (TCP) for Radiation Treatment

The Tumour Control Probability (TCP) is used as an indicator of the effectiveness of radiation treatment of cancer. Standard TCP models do not include the cell cycle of cancer cells. In my talk, I will derive a cell cycle cancer growth model from physical principles. This model can be extended to a nonlinear birth-death process, which then gives an explicit formula for the TCP. This TCP formula is an extension of the model of Zaider and Minerbo (joint work with A. Dawson). This talk related to G. de Vries' talk in the Minisymposium on "Mathematical Models of Interactions in Biological Rythms".

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MS27
Anti Bcl-2 Therapy Inhibits Tumoral Angiogenesis

Recent experiments show that vascular endothelial growth factor (VEGF) is the crucial mediator of downstream events that ultimately lead to enhanced endothelial cell survival and increased vascular density within many tumours. The newly discovered pathway involves upregulation of the anti-apoptotic protein Bcl-2, which in turn leads to increased production of interleukin-8 (IL-8). The VEGF - Bcl-2 - IL-8 pathway suggests new targets for the development of anti-angiogenic strategies. In this talk, I present and validate a mathematical model designed to predict the effect of the therapeutic blockage of VEGF, IL-8, and Bcl-2 at different stages of tumour progression.

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MS27
Metamodeling the Tumor-immune System Interaction

Tumoral dynamics and antitumor immunotherapies are likely to be influenced by the modalities of interaction between tumor cells and immune system effectors, and by the inter-effectors interactions. In the framework of the theory of competing populations, we study here the influence of the proliferation response of effectors to tumor burden, and of cooperation and/or competition between immune system effectors, by means of a meta-modeling approach.

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MS28

Resolving the Bursting Mechanisms in a Two-compartment Pyloric Dilator Cell Model

The role of electrical coupling between neurons with widely different intrinsic properties is not well understood. We systematically reduce a multi-compartment conductance-based model of electrically coupled neurons in the crustacean pyloric network that exhibits multi-stable modes of oscillation. We determine the low-dimensional organizing structure behind its multi-stability in a "critical regime" of the dynamics, and thus study the dependence of the systems selection of network oscillation on initial conditions and parameters such as the electrical coupling strength.

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MS28

Multistability of Half-center Bursting in a Two-cell Inhibitory Network with T-currents Analyzed via a Poincare Return Map

We explore the dynamics of a network of two type-I model neurons endowed with T-currents and coupled by reciprocal inhibition. The post-inhibitory rebound due to the T-current deinactivation allows the network to maintain a stable antiphase (half-center) periodic bursting, whereby a burst in one cell causes a rebound burst in the partner cell. We show that the existence and stability of bursting solutions is captured by a 1D Poincare return map, and find that multiple bursting states with different numbers of spikes per burst can be co-stable for a range of parameter values.

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MS28

The Role of Feedback to Descending Projection Neurons in Rhythmic Motor Pattern Generation

Pattern-generating networks are generally studied assuming feed-forward architecture from descending projection neurons that initiate, terminate or modify the network output. Yet, in all complex systems, feedback to descending inputs is pervasive and mostly not understood. We model the interaction between the gastric mill motor network and two identified descending projection neurons in the crab. Using reduced mathematical models, we demonstrate that rhythmic feedback to descending neurons moves the locus of pattern-generation from a half-center oscillator to an excitation-feedback circuit.

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MS28

Exploring a Mammalian Locomotor CPG Network via Analysis of Reduced Subnetworks

We examine a detailed conductance-based model of a neuronal network in the neonatal rodent spinal cord that serves as a central pattern generator for coordinated locomotion. The size of the full model precludes detailed analysis; symmetry and functionality considerations are used to isolate reduced subnetworks that are building blocks or schematics of the full network. The phase-response and synchronization properties of the subnetworks illuminate the corresponding properties of the larger system.

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MS29

Structural Monotonicity of Chemical Reaction Networks

New results linking the structural and dynamical properties of certain chemical reaction networks will be presented. The key idea is to find appropriate coordinates in which the system is monotone, so that convergence results can be applied to prove that solutions converge. An important feature of our results is that they are independent of the precise form of the reaction kinetics. For instance, we do not require that they are of mass action type. The main tools used in the proofs come from graph theory and dynamical systems theory. This is joint work with David Angeli (University of Firenze) and Eduardo Sontag (Rutgers

University).

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MS29

Convex and Toric Geometry for the Dynamics of Reaction Networks

The stability problem of complex reaction networks with nonlinear kinetics can be addressed by reformulation in convex coordinates and by using the properties of certain algebraic structures defined on the reaction monomials. The procedure is exemplified using a Hopf bifurcation, showing which features in a network can give rise to chemical oscillations.

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MS29

Graph-theoretic Approach to Oscillations in Biochemical Networks with Multiple Delays

In chemical modeling, delays represent subsystems of unknown intermediates and delay system models capture the essential properties of a chemical mechanism when only a few details are available. We use a bipartite graph to represent the chemical mechanism, and show that if certain subgraphs are present in the graph then the corresponding delay model can admit oscillations for some values of the system's parameters. Our subgraph condition for oscillations generalizes the condition of a negative (feedback) cycle which is usually used in the biochemical literature.

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MS29

What is the Origin of Cell Diversity?

Complexity of interactive gene regulation is considered to be responsible for generating diversity of distinct cell types in developmental process. I studied diversity of cell types by analyzing the number of steady states (or attractors) of gene activity using network models. The results were contrary to the previous arguments. Neither gene number nor connectivity between genes increases number of steady states. Number of loops in gene regulation rather increases number of steady states.

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MS30

Dynamics of Polymer Veils

This project focuses on the formation and dynamics of patterns created by the interaction between swimming bacteria, thin polymeric gels, and fluid motion. Here motile marine bacteria chemotactically aggregate to a layer over marine sediment and begin producing polymer which eventually forms a loose hydrogel. Bacteria are transiently attached to this gel by stalks. Bacteria attached to the veil rotate their flagella, which produces a small fluid flow that draws nutrient rich water across the veil. Meanwhile bacteria continuously detach and re-attach from the veil. Detached bacteria actively swim and are also advected by the fluid flow, coupling the bacterial concentration to the fluid flow. The bacteria tend to attach at the boundary between regions of relatively high and low polymer concentration evidently because of fluid effects. This aggregation is reinforced by the evolving fluid dynamics which tends to push bacteria away from voids and towards the edges. Visual observation of the veil shows regular hexagonal arrays or rolls depending on the experimental parameters. We describe the pattern formation that occurs in this system using both analytic and numerical techniques. Boundary Integral Methods will be used to simulate the fluid flow that is generated by attached bacteria; a reaction-diffusion-advection model will be formulated to describe the translocation of and nutrient consumption by the attached and detached bacteria and the nutrient concentration. We will also use gel mechanics to explore the effects of viscoelastic properties of the veil. These systems will be coupled together to create a full model for pattern formation in systems of sulfur-oxidizing bacteria.

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MS30

Flow Through Flowing Structures: A Mulitphase Model of True Slime Mold

The true slime mold physarum polycephalum is a single cell organism reaching up to meters in size. The cytoplasm shows periodic shuttle streaming through a network of tublar structures reaching velocities up to 1 mm/s. The motion is driven by the periodic contraction of an actin-myosin gel and is necessary to transmit chemical signals and organize structures over large distances. We present a mechanochemical mulitfluid model of the sol/gel that describes the initiation of streaming.

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MS30

Transport Along A Contracting Tube

In addition to passing kidney stones, the peristaltic contractions of the ureter also propel urine toward the bladder in boluses. Thus, flow in CDs is very different from flow in a pipe with fixed diameter, because the linear velocity of the boluses is determined, not by urine flow rates, but by the velocity of the peristaltic waves, whereas the lengths of the boluses, and thus the contact time with the CD epithelium, vary with urine flow rates. We model solute and fluid transport along an actively contracting tube as an immersed boundary problem, in axisymmetric cylindrical coordinates. The model equations embody the principal of

mass conservation of solute and water, and represent single-barrier transport processes. Model solutions are computed using a second-order immersed interface-type method. The model can be used to assess the effective tubular transport properties of the CD undergoing peristalsis.

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MS30

The Endothelial Glycocalyx: Flow, Permeability, and Stress

Fluid mechanical forces from blood are transmitted across the membrane of endothelial cells via the glycocalyx, a dense matrix of membrane-bound macromolecules whose structure is not well understood. Using mathematical models we explore the effect of matrix permeability on flow through the matrix and the resulting fluid stresses exerted on the matrix. We also use physical models to measure flow as a function of the size and spatial distribution of 'macromolecules'.

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MS31

The UBM Program at NJIT

The Undergraduate Biology and Mathematics Training Program seeks to train undergraduates at the interface of biology and mathematics through a combination of curricular activities and research project based activities. In this talk, we will provide an overview of our program describing student cohort activities in the Spring, Summer and Fall semesters. We will also describe the two main research projects conducted by the 2005 cohort of students. One project involved quantifying the formation of plant borders, the other focused on determining the location of gap junctions in neuronal networks.

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MS31

The UBM Program at Truman State

At Truman, faculty and undergraduates in the biology and the mathematical sciences are engaged in multi-semester collaborative interdisciplinary research experiences. The outcomes of this NSF UBM supported program include fostering sustained cross-disciplinary collaborative relationships between faculty and preparing our undergraduates to work in an interdisciplinary fashion. These ends are achieved through research activities and a year-long program of seminars and workshops. Preliminary assessment data will be used to illuminate successes

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MS31

Interdisciplinary Training for Undergraduates in Biological and Mathematical Sciences at Arizona State University

The UBM program at ASU intimately combines new cross-disciplinary courses and summer research programs. The former are constructed to allow maximal participation among undergraduate cadres, and facilitate life science majors to achieve a minor in mathematics, and, likewise, mathematics majors to enrich their education with a minor in bioscience. Research projects span modeling of ecological and evolutionary processes through the lens of stoichiometric constraints, bio-economics, chemostat theory, and modeling of visual perception. The program's holistic approach in mathematical biology training can also vertically integrate all the relevant components in the ASU education system. The program has already trained 17 students.

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MS31

REUs on DEEP Problems

In the past few years, I have the privilege to mentor over a dozen research experiences for undergraduates (REUs)

on problems concerning the dynamics of ecology and evolutionary processes (DEEP). These research experiences have varied in mathematical content (ranging from proving theorems to empirically testing predictions in mesocosms), group size (ranging from one student in isolation to three students as part of a larger REU program), duration (from one month to two years), final outcomes and degree of interdisciplinary involvement. In this talk, I will give an overview of these experiences and share stories of success, failure, and unexpected surprises.

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MS32

Adaptive Multiscale Stochastic Simulation of Biochemical Systems

Biochemical systems are inherently multiscale and stochastic. In microscopic systems formed by living cells, the small numbers of reactant molecules can result in dynamical behavior that is discrete and stochastic rather than continuous and deterministic. An analysis tool that respects these dynamical characteristics is the stochastic simulation algorithm (SSA), a numerical simulation procedure that is essentially exact for chemical systems that are spatially homogeneous or well stirred. Despite recent improvements, as a procedure that simulates every reaction event, the SSA is necessarily inefficient for most realistic problems. There are two main reasons for this, both arising from the multiscale nature of the underlying problem: (1) stiffness, i.e. the presence of multiple timescales, the fastest of which are stable; and (2) the need to include in the simulation both species that are present in relatively small quantities and should be modeled by a discrete stochastic process, and species that are present in larger quantities and are more efficiently modeled by a deterministic differential equation (or at some scale in between). Discrete stochastic simulation algorithms that can efficiently solve the multiscale problem are highly desired. This talk will introduce our recent work in multiscale stochastic simulation methods for biochemical systems.

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MS32

STOCHKIT: Software Tools for Discrete Stochastic and Multiscale Simulation of Biochemical Systems

Traditional ordinary differential equation-based approaches to simulation of chemical reacting systems fail to capture the randomness inherent in such systems at scales common in intracellular biochemical processes. We present StochKit, an efficient, extensible stochastic simulation framework that aims to make stochastic simulation accessible to practicing biologists and chemists, while remaining open to extension via new stochastic and multiscale algorithms.

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MS32

Moment Approach for Computing Discrete-stochastic Biological Systems

It has now been demonstrated that the behavior of low molecular number reaction systems encountered in biological settings frequently requires a discrete-stochastic description via the chemical master equation (CME). However, solving this differential-difference equation for the probability distributions of most biochemical systems typically presents substantial computational challenges. We consider an alternative, but equivalent representation of CME probability in terms of its factorial moments. This *f*-moment approach results in a formulation, which exhibits significant advantages for computing certain CME system properties.

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MS32

Stochastic Modeling of the Eukaryotic Cell Cycle

Events of the eukaryotic cell cycle (DNA synthesis, mitosis and cell division) are regulated by a complicated network of interacting protein kinases, phosphatases, transcription factors and proteases. Deterministic models (nonlinear ODEs) have proved very useful in accounting for average properties of populations of growing-dividing cells, for understanding how the control system works in normal cells (and why it fails when certain genes are mutated), and for predicting counterintuitive outcomes of novel experiments. But deterministic models are insufficient to deal with a growing body of experimental results on the variability of the cell cycle control system within single cells. To account for such variability will require a careful accounting of all sources of stochastic fluctuations in the control system, including molecular noise at the level of gene expression, protein synthesis and degradation, protein-protein interactions, and random events in the division process and the distribution of molecular components to the two daughter cells. I will present some preliminary results on my research group's attempts, to date, to convert phenomenological deterministic ODE models into elementary reaction mechanisms suitable for exact stochastic simulations.

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MS33

Mathematical Analysis of Effector Caspase Amplification in the Death Receptor Network in Single-cells

A proposed mechanism of ligand-induced single-cell rapid all-or-none death is positive feedback in the apoptotic network. However, this hypothesis is not supported experimentally in HeLa cells. Apoptosis is described by an experimentally verified, mass-action ODE model, which indicates that in single HeLa cells, the mitochondrial death pathway is responsible for rapid, all-or-none apoptosis. As a corollary of Singular Perturbation model reduction, a threshold parameter is identified that when crossed, ini-

tiates fast, all-or-none mitochondrial cell death.

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MS33

Monotonicity and the Stability of Biochemical Systems

We use the concept of monotone dynamical systems to study certain biochemical networks and predict their long time behavior. We show that under certain qualitative and quantitative conditions, the systems in question present global attractivity towards one or several equilibria. Crucially, the system itself is not necessarily required to be monotone in some important cases. Some results can be generalized to systems with delays or reaction terms.

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MS33

Rule-based Modeling of Biochemical Networks

The modular structure of signaling proteins gives rise to complex networks that are challenging to model. The conventional approach to specifying these networks is error-prone and fraught with hidden assumptions that are difficult to justify. As an alternative, we have developed a modeling language that allows a rule-based description of signaling biochemistry based on protein modularity. We discuss various approaches to simulating rule-based models and the insights that can be gained about the underlying biology.

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MS33

Signal Transduction at Point-blank Range: Brownian Dynamics Simulations of Receptor-mediated Ras/PI 3-kinase Crosstalk

We have developed an efficient Brownian dynamics model for stochastic simulation and computational analysis of signal transduction reactions on cell membranes. For a relatively simple system, the collision coupling mechanism, the simulations are in quantitative agreement with continuum theory. We have used this validated approach to study the spatial interplay and crosstalk between two receptor-mediated signal transduction pathways, involving activation of Ras and phosphoinositide (PI) 3-kinase, at the single molecule level.

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MS34

A Model of the Epithelial-Mesenchymal Transition (EMT) Regulatory Network

EMT, a fundamental process governing embryonic development in multicellular organisms, has recently been implicated in the early stages of cancer metastasis. During this transition, epithelial cells lose adhesive properties and acquire a motile mesenchymal phenotype. EMT is directly correlated with the downregulation of E-cadherin, a protein involved in adherens junctions holding epithelial cells together. Several oncogenic pathways are now known to induce E-cadherin downregulation. We will present a model EMT regulatory network involving the TGF-beta, Ras and Wnt signaling pathways. Our computer simulations demonstrate how a reduction in E-cadherin levels correlate with the induction of EMT and, in parallel, how the mesenchymal marker, vimentin, is upregulated.

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MS34

A Mathematical Model of the G2 to M Transition

A mathematical model of the cell cycle transion from G2 phase into Mitosis has been developed. The purpose of this model is to ascertain (in collaboration with experimentalists) the biochemical mechanisms involved in the DNA damage G2 checkpoint response and to model the effect of disruption of checkpoint response pathways on cellular

outcomes.

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MS34

Cellular Identity, Microenvironment, and Genomic Integrity

In development, a balance between cellular proliferation, differentiation, and death emerges in collective genetic response to naturally varied intrinsic and extrinsic factors. Highthroughput efforts to "interrogate" systems have led to putative causal relationships, on a molecular level; i.e., databases of pathways of interacting gene products. Of note, it seems that cell-type and experimental-preparation specificity is of paramount importance. I will present work on top-down modelling that addresses genomic integrity, microenvironment, and lineage commitment during neurogenesis.

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MS34

A Mathematical Model of Haemopoiesis as Exemplified by CD34 Cell Mobilization into the Peripheral Blood

We propose to simulate the kinetics of haemopoietic cells, including CD34+cells, with a mathematical model consisting of nonlinear, coupled, ordinary differential equations. This minimal model mimics the known kinetics of haemopoietic progenitor cells in the bone marrow and the CD34+ cells, white blood cells, and platelets from the peripheral blood in the presence of the granulocyte colony-stimulating factor. Perturbations within this system, subjected to granulocyte colony-stimulating factor treatment and apheresis of peripheral blood progenitor cells (CD34+ cells) in healthy individuals, are reproduced. With this model, we make predictions for reducing the length of time with neutropenia after high-dose chemotherapy. Results based on this model indicate that myelosuppressive treatment combined with infusion of CD34+ peripheral blood progenitor cells provides a faster recovery of the haemopoietic system than does treatment with the granulocyte colony-stimulating factor alone. Additionally, this model predicts that infusion of white blood cells and platelets can relieve the symptoms of neutropenia and thrombocytopenia, respectively, without drastically hindering the haemopoietic recovery period after high-dose chemotherapy.

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MS35

Systems Approaches to Understanding Robustness and Performance in Circadian Rhythm

The regulatory architecture responsible for robust maintenance of 24 hour cycles is analyzed as a control system. Circadian rhythms possess the ability to entrain their internal phase to that of the environment. This ability relies on the phase response of circadian gene regulation to dfferent environmental cues, of which light is the most obvious and important. Dynamic analysis of oscillatory systems necessitate the development of methods specific for these systems' attributes, such as the period and phase. Investigation of the phase behavior of Drosophila circadian rhythm gives experimentally testable predictions for the control mechanisms of circadian phase and period responses.

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MS35

Incorporating Mechanisms for Fatigue into a Cognitive Architecture

This research uses outputs from mathematical models that characterize how circadian rhythms and sleep-wake homeostasis influence overall human cognitive functioning. The mathematical models are used to represent fatigue by driving parameter changes in a cognitive architecture, which uses a common set of mechanisms to produce psychologically valid performance predictions across a range of tasks. With mechanisms to represent fatigue, quantitative, a priori predictions can be made about the impact of sleep loss in particular tasks.

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MS35

Frontiers in Modeling Circadian Rhythms, its Inputs and Outputs

Complementary experimental and modeling efforts have allowed determination of key features of the human circadian system and its effects on performance. Limit cycle oscillators are used model the 2-dimensional state circadian system. Current efforts include incorporating the effect of wavelength of light and non-photic effects on the input pathway, and circadian control of melatonin rhythms. The use of analysis and modeling of data to understand the physiology will be discussed.

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MS35

Modeling Individual Differences

Reducing or displacing sleep consistently leads to neurobehavioral impairment, although the magnitude of impairment varies considerably among individuals. Sleep-dependent changes in neurobehavioral performance across time of day and over days have been captured in biomathematical models. However, these models do not deal with inter-individual differences. Novel approaches to biomathematical prediction of performance in the face of inter-individual differences, and the physiologic implications thereof, will be discussed.

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MS36

Can We Discern Cause-and-effect in Polycystic Ovarian Syndrome (PCOS) and Diabetes?

Soon after PCOS was defined as Amenorrhea associated with bilateral polycystic ovaries, obesity (up to 50%) and androgen excess (up to 80+ %) were recognized as common features. Hormonal studies confirmed both excess androgen (ovarian and adrenal) and insulin resistance (IR) and/or type 2 diabetes (up to 80+ %). Since effective therapies treat either IR or androgen excess, a positive feedback mechanism involving insulin and androgen signaling must be central to the causal pathway in PCOS.

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MS36

BK Channel Diversity: Consequences for Cellular Excitability

BK channels are expressed in many tissues throughout the body, where they play diverse roles in the control of cellular excitability. This diversity arises from different cellular contexts, as well as alternative splice variants, accessory subunits, and modulation by circulating steroids on multiple time scales. To capture the diversity and its consequences, we model whole cell excitability using stochastic simulation of a BK channel gating model.

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MS36

Glucose Sensing by Combined Metabolic and Ionic Oscillations in Pancreatic Islets

Pancreatic beta-cells secrete insulin to maintain blood glucose within a narrow range. We have proposed that secretion is mediated by a combination of fast electrical and slow metabolic oscillations. The fast and slow oscillations both follow the typical pattern of relaxation oscillators - off, oscillating, saturated - but may differ in the thresholds for the transitions. The nine resulting combinations account for most of the oscillatory patterns observed, including pure fast and pure slow.

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MS36

Improving Clinical Outcomes Through Data Mining

With the advent of electronic medical records, opportunities are emerging to apply advance mathematical modeling and data mining methods to improve the quality of healthcare. Practice management software is being developed to suggest the most favorable treatment plans to physicians given the complex array of diagnostic information available. Medical arenas with fee-for-services or where competition for patients is acute (eg. assisted reproduction) are particularly interested in modeling approaches to improve results and revenue.

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MS37

Odor Identity and Concentration Coding in a Model Olfactory System

Using realistic computational model of the locust olfactory system we studied its response properties for different odor concentrations. A dimension reduction analysis revealed that projection neurons activities for different odors diverged quickly in the response space while the activities corresponding to different concentrations of a particular odor evolved along neighboring trajectories. Both the identity and the concentration of odors, therefore, can be encoded in the spatiotemporal firing patterns of projection neurons activity.

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MS37

Dynamic Clustering in a Model of the Insect's Antennal Lobe

Abstract not available at press time.

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MS37

Neural Dynamics in the Antennal Lobe: Sensory Coding and Memory Traces in an Insects Brain

I will present a detailed analysis of the neural dynamics in the antennal lobe of the honeybee, as recorded with calcium-imaging. The analysis yields three important results: 1) the neural dynamics possess odor specific-attractors; 2) the perceptron provides a realistic model for odor recognition and odor discrimination; 3) the spontaneous activity of this network contains memory traces that are stored following the Hebbian learning rule, and they

can be retrieved through a principal component analysis.

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MS37

Encoding a Temporally Structured Sensory Stimulus with a Temporally Structured Neural Representation

Can the temporal structure of a stimulus interfere with the spatio-temporal structure of the neural representation? We investigated this in the locust olfactory system. When odors were presented in trains of nearly overlapping pulses, responses of first-order interneurons changed reliably and often greatly with pulse position, as responses to one pulse interfered with subsequent responses. However, ensemble based spatio-temporal coding could disambiguate these patterns, providing an invariant response to the stimulus in second-order interneurons.

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MS38

Effect of Antibiotic on Heterogeneous Bacterial Populations

We consider a mathematical model of two microbial strains competing for a common nutrient while exposed to periodic dosing of an antibiotic or growth inhibitor. One strain is assumed to be more resistant to the drug but slower growing than its competitor. The focus of our work is on obtaining sufficient conditions for successful drug treatment, i.e., eradication of the bacteria, and on finding conditions implying persistence of one or more of the strains. This amounts to a stability analysis of the periodic solutions of the model.

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MS38

Competition for Multiple Resources

We discuss a standard chemostat model of three species competing for three essential resources. We show that the model can have at least two limit cycles, or an unstable limit cycle. The results suggest that this standard model can exhibit both equilibrium dynamics and non-equilibrium dynamics for a given set of parameter values. (Joint work with Hal L. Smith and Steven M. Baer)

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MS38

Stoichiometric Model that Links Cellular Machinery with Global Nutrient Ratios

Redfield ratios are one of the largest-scale patterns found in the Biosphere. First identified by Harvard oceanographer Alfred Redfield in 1930s, the pattern refers to the remarkable similarity of carbon(C) : Nitrogen (N) : Phosphorus (P) ratios in open ocean and phytoplankton. In particular, Redfield ratios state that for every P atom there are about 16 N atoms in both oceanic water and phytoplankton. Due to the importance of Redfield ratio to biogeochemical cycles, carbon balance and, hence, global climate, numerous attempts have been made to explain it. Here, we derive Redfield ratios by linking molecular processes on cell level with competition among species and global nutrient feedbacks. First, we show that N:P=16 can stem from fundamental molecular constants such as N content in amino acids, and N and P content in nucleotides to manifest itself in a biochemically optimal RNA:Protein ratio. Next, we incorporate this biochemical optimum into the ODE model of competition between phytoplankton species to show how the pattern found on molecular scale can propagate itself to global Redfield ratio. The necessary condition for this to happen is nutrient feedbacks that indeed exist in oceans.

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MS38

A Resource-based Model of Microbial Quiescence

The implications of microbial quiescence are analyzed through a model that involves "wake-up" and "sleep" rates for cell transition between a quiescent and an active state. These rates depend on resource levels, turning on and off at thresholds which may not coincide. The population is either washed out or a single "survival" steady state exists. Proportional nutrient enrichment is used to analytically and numerically explore the steady state bifurcating from the washout state.

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MS39

Mechanisms of Chromosome Segregation in Bud-

ding Yeast

We have used quantitative fluorescence microscopy to count the number of proteins that comprise the microtubule binding site at the kinetochore. These measurements represent the minimal molecular requirements for assembling one kinetochore-MT attachment. We propose that the core centromere nucleosome (120 bp wrapped around a Cse4 containing nucleosome) and flanking chromatin adopts a cruciform configuration in metaphase. This establishes the geometry for the microtubule attachment site.

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MS39

Modeling Polymer Dynamics in Bacterial Cell Division

In order to correctly divide into two daughter cells, E. coli uses a remarkable dynamic process whereby it alternately assembles and disassembles a linear polymer at each of its ends which suppresses the formation of the division ring everywhere but at the midpoint of the cell. By modeling this process, we replicate much of the experimentally observed behaviour and thereby generate a set of mechanistic constraints and experimentally testable quantitative predictions.

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MS39

FtsZ Self-Assembly Dynamics and Bacterial Cell Division

FtsZ, a bacterial tubulin homolog, forms a ring that constricts to divide the cell. The ring is constructed from single-stranded protofilaments, which have been visualized by EM in vitro. Protofilaments are turning over very rapidly, with a half time of 8 sec both in vitro and in vivo. The protofilaments transit from a straight to a curved conformation, and we propose that this is the basis for the constriction force.

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MS39

Modeling the Stochastic Mechanics of the Budding Yeast Mitotic Spindle

Proper segregation of chromosomes is one of the most fundamental cellular processes. The physical movement and separation that occurs during each round of division in eukaryotes is mediated largely by microtubules in a complex known as the mitotic spindle. We have developed stochastic models for microtubule assembly that describe the physical and chemical forces that influence the dynamics. We have focussed our modeling efforts on budding yeast, because it has the simplest mitotic spindle and therefore is likely the most tractable.

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MS40

Modeling Shear Wave Propagation in Biotissue: An Internal Variable Approach to Dissipation

In this presentation, we examine the propagation of disturbances consisting primarily of shear waves through biotissue. We develop a model based on specific physical geometries in polar coordinates, using the well known equations of motion and a set of constitutive equations based on the internal variable method outlined in [H.T Banks, J.H. Barnes, A.Eberhardt, H.Tran, and S.Wynne,Modeling and computation of propagating waves from coronary stenoses, *Computational and Applied Mathematics*,Vol 21, N.3, 2002]. Computational results first for a viscoelastic homogeneous medium are presented and compared to previous findings. We then consider a more complex geometry by introducing heterogeneities into the medium. The resulting simulations are discussed.

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MS40

Multiphasic Models for Chondron Deformation under Micropipette Aspiration

The chondron of articular cartilage consists of a cell and its encapsulating pericellular matrix (PCM). Previous application of a single phase layered elastic contact solution for micropipette aspiration demonstrated a considerable decrease in apparent PCM stiffness of isolated human chondrons with osteoarthritis. We extend this layered elastic solution by treating the chondron as a multiphasic (solid-fluid, or solid-fluid-ion) material to quantify the relative contributions of collagen and proteoglycan fixed charge density to apparent PCM stiffness.

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MS40

Modeling Auricular Chondrocytes for Lining of Vascular Stents

Stents are tube-like meshes used in the treatment of coronary artery diseases. They serve to prop the diseased arteries open and to secure normal blood flow. Although stents have revolutionized the treatement of coronary artery diseases, there are various clinical complications in patient follow-ups.The major one is re-stenosis or re-narrowing of coronary arteries which might lead to a heart attack. Restenosis is largely related to the development of scar tissue

(neo-intimal hyperplasia) that occurs within an artery after it has been treated with a foreign device with poor biocompatibility. To improve the biocompatibility of stents, a team of cardiologists around Dr. Rosenstrauch at the Texas Heart Institute is investigating the use of genetically engineered auricular chondrocytes for lining a stent. Stents lined with geneticaly engineered chondrocytes might lower the re-stenosis reates and provide a long-lasting biocompatible prothesis. The speaker will talk about a mathematical model describing the growth of auricular chondrocytes on a stent in the novel environment: exposed to controlled flow conditions for enhanced growth.

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MS40

Modeling Scanning Microphotolysis to Measure Molecular Diffusion in Articular Cartilage

Diffusion is the primary mode of transport of solutes through articular cartilage. We developed a mathematical model of scanning microphotolysis (SCAMP) to measure macromolecular diffusion in subcellular-size volumes of cartilage. SCAMP is a rapid, single-line photobleaching procedure that accounts for out-of-plane bleaching at high magnification. Data was analyzed by best-fit comparison to simulations generated using alternating direction implicit discretization of the diffusion-reaction equation in conjunction with the 3-D bleaching (excitation) and point-spread (detection) profiles.

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MS40

Biphasic Modeling and Optimization of Mouse Cartilage in Compression for Material Property Determinations

Cartilage mechanical properties are important measures of tissue function. Mouse models of cartilage degeneration are important for studying a role for genetic background in this process. A micro-indentation testing system was used to determine the compressive and biphasic mechanical properties of cartilage in the small joints of the mouse. A nonlinear optimization program employing a genetic algorithm for parameter estimation, combined with a biphasic finite element model of the micro-indentation test, was developed to obtain the biphasic, compressive material properties of articular cartilage.

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MS41

How and Why Cells Make Networks within the Pituitary Gland

Pituitary cells that secrete growth hormone (GH) are distributed according to a 3D-network. The architecture of this network is robust across lifespan and displays modularity correlated with pituitary GH content and body growth. Importantly, this anatomical network supports functional connectivity revealed by spatially stereotyped motifs of cell synchronization after stimulation by GH-releasing hormone. This type of network may be a critical determinant for coordinated secretory pulses by the pituitary gland and other endocrine tissues.

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MS41

A Model for the Switch Between the Pulse and Surge Pattern of GnRH Secretion

We propose a mathematical model allowing for the alternating pulse and surge pattern of GnRH (Gonadotropin Releasing Hormone) secretion. The model is based on the coupling between two FitzHugh-Nagumo systems running on different time scales. The analysis of the slow/fast dynamics allows to explain different secretion patterns (slow oscillations, fast oscillations and periodical surge). Specifications on the parameter values are derived from physiological knowledge in terms of amplitude, frequency and plateau length of oscillations.

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MS41

An Electrophysiological Approach to Gathering Data Needed to Model the Gonadotropin-releasing Hormone Neural Network

Gonadotropin-releasing hormone (GnRH) secreting neurons form the final common pathway for the central regulation of fertility. This is accomplished by releasing GnRH in a frequency-modulated pattern to code downstream reproductive activity. We use electrophysiological approaches to understand how individual GnRH neurons initiate, maintain and terminate action potential firing, how these cells coordinate activity to produce distinct hormone pulses and how this activity is modulated by homeostatic and non-homeostatic feedback.

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MS41
Catastrophe Theory Model of Hyperthyroidism

Abstract not available at press time.

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MS42
Progress in Sleep Studies and Modeling

Recent studies at the molecular, cellular, and systems level offer several candidate mechanisms by which sleep states may enhance learning, thereby serving an important cognitive function. We will outline the scope of these hypothesized effects and some approaches to modeling them. We will also describe efforts to understand the dynamics of sleep-wake cyclicity, focusing on modeling and quantitative analysis, especially dynamical systems and stochastic modeling approaches.

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MS42
Modeling Learning and Forgetting in REM Sleep

In a computational modeling study, we investigate the reversal of hippocampal cell activity in REM sleep from a firing pattern that promotes synaptic strengthening (or learning) to a pattern more consistent with synaptic weakening (or forgetting) during the course of memory consolidation. Numerical simulations using a biophysically accurate neuron model support our hypothesis that changes in the relative strengths or efficacies of the two synaptic pathways targeting hippocampal cells cause this reversal.

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MS42
Network Dynamics and Mechanisms of Transition in the Mouse Sleep-Wake Network

Behavioral states (wake, NREM sleep, and REM sleep) and transitions between them are regulated by a network of neurons in the brainstem and hypothalamus. We model network dynamics with a system of coupled Morris-Lecar-type relaxation oscillators. The fast-slow nature of the equations captures network behavior on multiple time scales. We study mechanisms of transition in reduced models obtained using combinations of fast-slow and dominant scale techniques. We also discuss canard-like behavior in the equations.

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MS42
The Function of Sleep for Learning and Memory

Experimental recordings show that hippocampal cells fire in the same manner during REM sleep as during waking learning, supporting a strengthening of LTP, the building block for learning. Once the memory is consolidated, reactivation firing during REM reverses in a manner that supports depotentiation, or weakening of those hippocampal synapses encoding the memory. This finding is consistent with the idea that the hippocampus is an assembly warehouse rather than permanent repository of complex associative memories.

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MS43
Support-vector Regression Approach for Prediction of Relative Lipid Accessibility in Membrane Proteins

Computational prediction of relative solvent accessibility for amino acid residues in soluble proteins plays an important role in folding simulations, protein structure prediction and functional annotations. Here, we present a novel protocol for prediction of relative lipid accessibility in membrane domains. The new method is based on a linear, Support Vector Regression-based model that can be used to efficiently and reliably estimate the parameters in the model from a limited number of experimentally validated examples. The new method will be available to the community through the MINNOU web server (http://minnou.cchmc.org).

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MS43
A Prototype of the Human-virus Interactome Resource

The large amounts of information generated by research in systems biology makes it necessary for biologists to employ literature mining tools in their work. We describe the prototype of a digital library containing interactions between human and viral proteins, which provides virologists

a tool to rapidly identify protein interactions responsible for infection. The data is obtained by text mining the literature and searching proteomic databases, and needs to be updated frequently.

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MS43

A Two-level Architecture for Proteomic Networks

We describe an approach to clustering protein-protein interaction networks in order to identify functional modules. Our algorithm accounts for the small-world nature of the network by dissecting the protein interaction network into a global subnetwork of hub proteins (connected to several clusters), and a local network consisting of cluster proteins.

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MS43

Peptide Mass Fingerprinting Via Machine Learning: New Algorithms and Applications

Peptide Mass Fingerprinting is a process by which the identity of a protein is determined by measuring the masses of its tryptic peptides (its fingerprint) via mass spectrometry. The process requires a database search, whereby the experimentally determined spectrum is compared against theoretical spectra, which requires an appropriate metric. We propose new algorithms to design metrics to increase the specificity and sensitivity of the process. Early computational results are promising.

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MS44

A Stochastic Model of the Tubuloglomerular Feedback Mechanism in a Rat Nephron

Experimental studies have demonstrated the presence of self-sustained oscillations in proximal tubular pressure in the nephrons of rats. The oscillations are regular in normotensive Sprague-Dawley rats, and highly irregular in spontaneously hypertensive rats. A dynamic model of the renal autoregulation has been extended to include a stochastic differential equations model of one of the main parameters that determines feedback gain. The model reproduces fluctuations and irregularities in both period and amplitude that the former deterministic models failed to describe. This approach assumes that the gain exhibits spontaneous erratic variations, which can be explained by a variety of influences, which change over time (blood pressure, hormone levels etc). Estimation of key parameters of the model reveals important differences in the autoregulation mechanisms between the two strains of rats. This insight was achieved by directly modeling the dynamic features of the feedback gain, normally modeled with a constant that is not capable of capturing time variations.

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MS44

Theoretical Effects of Convection and Epithelial NO Production on NO Distribution in the Renal Medullary Microcirculation

The objective of this study is to develop a three-dimensional mathematical model of nitric oxide (NO) transport in the renal medulla in order to investigate how NO affects blood distribution in the medulla. Using a one-unit model, that is, a single vasa recta embedded in interstitium and surrounded by nephron loops, we have found that convection (i.e., blood flow per se) has negligible effects on NO concentration in pericytes, i.e., the smooth muscle-like cells that impart contractile properties to descending vasa recta (DVR). However, the shear stress-mediated ef-

fects of blood flow on NO generation rates, and therefore on NO concentrations, are predicted to be significant. We are expanding the model to include all vessels and tubular segments based on one vascular bundle and surrounding tubules, to examine whether the heterogeneous structure of the medulla and the tubular production of NO result in NO concentration differences between short and long vasa recta, respectively, thereby affecting blood flow distribution between the outer medullary vascular bundles and the peripheral capillaries.

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MS44

Dynamics in Coupled Nephrons may Contribute to Irregular Flow Oscillations in Spontaneously Hypertensive Rats

We used a bifurcation analysis of a mathematical model of two nephrons, coupled through their tubuloglomerular feedback (TGF) systems, to investigate the role of coupling in the emergence of irregular tubular flow oscillations in spontaneously hypertensive rats (SHR). We analyzed a characteristic equation for a model of coupled nephrons having NaCl backleak; that characteristic equation revealed a number of parameter regions having the potential for differing stable dynamic states. Numerical simulations using the full model equations exhibit a number of differing dynamic behaviors in these regions. Some behaviors show marked irregularity and exhibit a degree of spectral complexity that is consistent with physiologic experiments in SHR.

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MS44

Estimation of Parameters for Maximum Urine Concentrating Capability in a Mathematical Model of the Rat Inner Medulla

A nonlinear optimization technique was used to estimate parameter sets that maximize the ratio of the urine osmolality to the total NaCl active transport rate in a mathematical model of the urine concentrating mechanism. The parameters were allowed to vary within ranges suggested by physiologic experiments. A set of parameters that yielded results close to reported experimental values was identified. Research supported by NIH grants DK-42091 and S06GM08102, and NSF grant DMS-0340654.

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MS44

Nephron Initiated Interactions in a Renal Vascular Network

Blood flow to single nephrons is governed by two nonlinear regulators that operate in each nephron, and by nonlinear interactions between the two. One mechanism, tubuloglomerular feedback (TGF), senses NaCl concentration in tubular fluid, and the other senses intravascular pressure. Both mechanisms are nonlinear, and each generates a characteristic limit cycle oscillation. The two oscillations interact in each nephron. In addition, TGF initiates a signal that is propagated retrograde down the nephron's afferent arteriole, and the excitation spreads to adjacent nephrons, inducing synchronization of the TGF oscillations. Approximately 20 nephrons derive their blood supplies from a single cortical radial artery, and all are within range of signal propagation from each of the others. We have modeled this interaction, and have also included juxtamedullary nephrons, whose longer length produces TGF oscillations with longer periods than those of the cortical nephrons. There are two initial conclusions: 1) increasing coupling strength increases the amplitude of the TGF oscillation in individual nephrons, and 2) although the activity of the longer nephrons can influence even the most distant cortical nephrons, the entire nephron ensemble does not become fully synchronized at a single frequency at any level of coupling strength. The cortical nephrons can become syncrhonized at a single frequency even at fairly low coupling strength, and the juxtamedullary nephrons can become synchronized at high coupling strength, and the two groups show evidence of interaction, but a single frequency is not achieved. Supported by NIH Grant EB003508.

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MS44

A Mathematical Model of Distal Convoluted Tubule (DCT): Determinants of Potassium Secretion

This simulation of rat DCT includes luminal and peritubular cell membrane transporters responsible for Na reabsorption in exchange for K secretion. Early tubule conditions are conducive to maximal K fluxes, while late conditions require K transport against an electrochemical gradient; the model identifies the transporters that optimize K secretion under each condition. Tubule inlet volume flow and Na concentration both enhance K secretion; the model tubule identifies the relative importance of each factor.

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MS45

Modeling Influenza Vaccination Using Minority

Games

Seasonal epidemics of influenza remain a major global health concern and a pandemic of influenza is expected imminently. One of the national health objectives of the United States is to increase the influenza vaccination coverage in order to prevent or substantially reduce influenza epidemics. Vaccination is voluntary and the vaccine is effective for one season only; thus an individual needs to decide every year whether to vaccinate or not. Generally, individuals are selfish as their sole interest is to avoid getting infected, preferably without having to vaccinate. Here we address the question of whether selfish individuals can adapt their vaccination behavior to prevent severe influenza epidemics or whether public health programs are necessary. Inspired by Minority Games, we construct an individual-level model and we analyze the adaptive dynamics of vaccination behavior for influenza in a population of non-communicating selfish individuals. We find that most of the time influenza epidemics cannot be prevented by vaccination, and occasionally severe epidemics occur even without the introduction of pandemic strains.

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MS45

Game Theory and the Developing World

The principles of social justice and health as a human right in the developing world have been advocated as the main justification for health assistance from rich to poor countries. While we do not disagree with this, we argue that a strategy that emphasizes the shared benefit to rich and poor countries would facilitate this process. We propose that the accomplishment of these challenging tasks should be viewed from the perspective of game theory, where the interests of the parties (in this case rich and poor countries) overlap. As the world becomes increasingly integrated with globalization, economic development in resource-poor countries will increase the opportunities for richer countries to profit from investment in the developing world. Global health has political and international security implications for the developed world, as well.

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MS45

Modeling Social Conflicts of Public Health

Public health strategies that are optimal for the community are not necessarily optimal for the individual. For example, if most of the community is vaccinated, it can be best for an individual to refuse vaccination. This way they receive the benefits of reduced disease prevalence while avoiding anticipated adverse effects of the vaccine. Such conflicts can undermine public health programs, and their mathematical analysis involves an interesting application of game theory.

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MS45

Controlling Influenza Epidemics via Public Health Vaccination Incentives

Using a Minority Game model that describes the adaptive dynamics of vaccination coverage for influenza in a population of non-communicating selfish individuals, we ask if certain public health incentives could be used to help prevent influenza epidemics. Specifically, we evaluate the potential effects of the two following incentives: 1) If the head of the family pays to get vaccinated then their family gets vaccinated for free; 2) If an individual pays to get vaccinated then that individual will get free vaccinations for a certain number of successive years. Vaccinating families would increase: the average prevalence, the variability in prevalence and the frequency of epidemics. However, we show that certain public health incentives that offer free vaccination could ameliorate influenza epidemics. We show that it is possible to construct public health incentives that help the vaccination coverage to remain very close to the critical vaccination coverage with only small variability. We discuss public health implications.

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MS46

Walking on Water

We present the results of a combined experimental and theoretical investigation of the hydrodynamics of water-walking creatures. We enumerate the many styles of hydrodynamic propulsion at the free surface, and the resulting distinctions form the basis of a dynamic classification of all water-walkers. We consider creatures spanning a broad range of scales, from millimetric insects reliant on surface tension, to tail-walking dolphins. Accompanying adventures in biorobotics are described.

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MS46

The Role of Bristled Wings in Tiny Insect Flight

The smallest flying insects often use 'clap and fling' to augment lift forces generated during flight. There is, however, an aerodynamic cost for this behavior. For low Reynolds number flight, very large drag forces are generated during clap and fling. Another feature common to most tiny flying insects is wing ciliation. Using a porous media version of the immersed boundary method, the effect of wing ciliation (i.e. wing bristles) on flight aerodynamics will be explored.

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MS46

Computational Simulation of Metachronal Waves in Cilia

A simulation of the formation of metachronal waves in carpets of pulmonary cilia is presented. The cilia move in a two-layer fluid model. The fluid layer adjacent to the cilia base is purely viscous while the tips of the cilia move through a viscoelastic fluid. An overlapping fixed-moving grid formulation is employed to capture the effect of the cilia on the surrounding fluid. The 9+2 internal microtubule structure of an individual cilium is modeled using large-deflection, curved, finite-element beams. Realistic models of the forces exerted by dynein molecules are extracted from measurements of observed cilia shapes. The possibility of formation of metachronal waves under different assumptions of boundary conditions is investigated and shown to be dependent on the surrounding geometry.

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MS46

A Model of Force Generation in Motile Cells

Directed migration of amoeboid cells is involved in processes such as embryonic development, wound healing, and the metastasis of cancer. Migration entails force generation within cells, and understanding how this force generation is controlled in space and time to produce cellular motility is a major challenge. I present a continuum model of cell motility in which the active deformation of the cell results from spatially-controlled remodeling of the cytoskeleton, and force is transmitted to the substrate via controlled adhesion sites. The passive cellular response is viscoelastic. Finite element simulations of this model reproduce cell traction patterns that are observed experimentally.

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MS47

Mechanistic Temperature Compensation of the Circadian Clock

One of the key features of the molecular mechanism underlying the circadian clock is its ability to robustly compensate for changes in temperature over a range of 10 C or more, a feature that isnt typical of models of the clock mechanism. Here we discuss alternate ways of achieving robust temperature compensation and explore the idea that evolution has optimized the interaction of several feedback loops to produce an oscillator whose period is tightly regulated.

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MS47

Controlling the Period of Intracellular Clocks

The basic function of circadian (24-hour) clocks within cells is to provide 24-hour timing of biological events. The period of the clocks is affected by genetic mutations, but is remarkably robust to changes in temperature. Several mathematical models and techniques will be presented to determine the period of cellular circadian clocks. These mathematical theories of period regulations will be validated against experimental data.

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MS47

Modeling Circadian Rhythms: Deterministic and Stochastic Approaches

In most organisms the detailed molecular mechanism of the circadian clock involves interlocked positive and negative feedback loops. We studied deterministic models of increasing complexity for the occurrence of autonomous circadian oscillations, for their entrainment by light-dark cycles, and their phase shifting by light pulses. Stochastic versions of these models indicate that the robustness of circadian rhythms with respect to molecular noise is affected upon entrainment by light-dark cycles, by the cooperativity in repression, the proximity from a bifurcation point, the rate of association of the inhibitory protein to the promoter of the clock gene, and the coupling between oscillating cells.

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MS47

System Biology Reveals an Opposite Role for Tau in Circadian Rhythms

Circadian rhythms are stable 24 hour physiologic cycles regulated by negative feedback loops. The tau mutation in casein kinase I (CKI?tau) causes a four hour shorting of rhythms and a decrease of kinase activity in vitro. It is difficult to reconcile this loss of function with the current model of circadian clock function. The Forger-Peskin model, a detailed quantitative model of the mammalian circadian clock, predicts the opposite, that CKI?tau must be a gain of function mutation. We have verified this counterintuitive modeling prediction and find that CKI?tau produces a gain of function in cells These findings experimentally validate the systems biology approach and provide a remarkable example of how a specific mutation can be both a loss and a gain of function depending on the substrate.

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MS48

Problem-Based Learning: A Way to Motivate Undergraduates at the Math/Bio Interface

Mathematics and statistics are essential to properly describe dynamical phenomena, to construct experimental plans, and to predict general rules in the life sciences. With this in mind, I teach a course in France taken by more than 800 students annually. Students are divided into small groups and special interactive exercises are built to introduce them to the modeling process. I will present some of the activities we have developed and how students motivation has increased significantly.

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MS48

The State of Mathematical Biology Training in the UK

With researchers across the world showing a growing interest in the education of mathematical biologists, in this talk I examine and compare the training offered by institutions across the UK. In particular, I will discuss the mathematical biology education at the undergraduate and postgraduate level in both mathematics and biology departments. I will look at the final career destination of these students and investigate how the training prepares students for a career in mathematical biology research.

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MS48

Computational Tools for a Two-Course Calculus Sequence for Biology Majors

The Department of Mathematics at Benedictine University has begun to offer a rigorous two-semester calculus sequence for biology students. Two important course goals are the integration of mathematical and biological reasoning through the understanding of biological models and the development of skills to use appropriate computational software to analyze and solve biological problems. We discuss how and why we use Excel, Derive, Berkeley Madonna, and MATLAB to achieve these goals.

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MS48

BIO SIGMAA

A new special interest group in the MAA. This talk will discuss the new SIGMAA, its direction, and a few upcoming inaugural events. We will also have an open discussion on how the new SIGMAA can work with SMB to promote and support mathematical and computational biology.

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MS49

Mitigating Immunodominance in Multi-Epitope Tumor Vaccines by Polytopic Vaccination

The refractory nature of cancer to many standard therapies has led to substantial efforts to achieve immune control. We describe a theory that elucidates the mechanism by which polytopic, or multi-site, vaccination mitigates immunodominance in therapeutic T-cell vaccines for cancer. By inducing a T-cell response to each cancer-associated epitope in a distinct lymph node, vaccine efficacy is increased and immunodominance is reduced. Our approach captures the dynamic characteristics between the T-cell receptors and tumor.

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MS49

Prediction of Treatment Outcome for Laser Surgery of Prostate Cancer

Temperature is usually used as the control variable in laser therapy, it is however not an effective measure of treatment outcomes. We proposed models that predict cell damage and heat shock protein in the prostate tumor to characterize effectiveness of the treatment and likelihood of cancer recurrence. These models can optimize the therapy outcome by mitigating tumor recurrence and resistance to follow-up chemotherapy and radiation therapy due to HSP expression and insufficient injury.

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MS49

Protein Wrapping as a Selectivity Switch in the Pharmacological Oncokinome

Kinases are central targets for drug-based treatments of cancer. Progress in drug development faces challenges due to undesirable cross-reactivity and difficulties in modulating selectivity. We present a structure-based predictor of cross reactivity and validate it against affinity fingerprinting of the kinases and our own drug re-design geared at sharpening the inhibitory impact. The predictor compares patterns of packing defects and introduces a packing distance between kinases shown to be equivalent to the pharmacological distance.

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MS49

Mathematical Modeling of Angiogenesis in Cancer Research

Angiogenesis is critical for tumor growth. To understand mechanisms of angiogenesis, we have developed a mathematical model to simulate two-dimensional angiogenesis in the cornea, a commonly used tissue for testing efficacies of angiogenic and antiangiogenic agents. One of the advantages of the model is that results from numerical simulations can be compared directly with experimental data. Specifically, the dose responses to bFGF, an angiogenic factor, predicted by the model are consistent with experimental observations.

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MS50

Randomized Approximation Algorithms for Set Multicover Problems with Applications to Reverse Engineering of Protein and Gene Networks

In this paper we investigate the computational complexities of a combinatorial problem that arises in the reverse engineering of protein and gene networks. Our contributions are as follows:

- We abstract a combinatorial version of the problem and observe that this is "equivalent" to the set multicover problem when the "coverage" factor k is a function of the number of elements n of the universe. An important special case for our application is the case in which $k = n - 1$.
- We observe that the standard greedy algorithm produces an approximation ratio of $\Omega(\log n)$ even if k is "large", i.e., $k = n - c$ for some constant $c > 0$.
- Let $1 < a < n$ denotes the maximum number of elements in any given set in our set multicover problem. Then, we show that a non-trivial analysis of a simple randomized polynomial-time approximation algorithm for this problem yields an expected approximation ratio $E[r(a, k)]$ that is an increasing function of a/k. The behavior of $E[r(a, k)]$ is "roughly" as follows: it is about $\ln(a/k)$ when a/k is at least about $e^2 \approx 7.39$, and for smaller values of a/k it decreases towards 1 as a linear function of $\sqrt{a/k}$ with $\lim_{a/k \to 0} E[r(a, k)] = 1$. Our randomized algorithm is a cascade of a deterministic and a randomized rounding step parameterized by a quantity β followed by a greedy solution for the remaining problem. We also comment about the impossibility of a significantly faster convergence of $E[r(a, k)]$ towards 1 for any randomized approximation algorithm.

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MS50

Identifying Functional Constraints on the Quantitative Evolutionary Design of a Metabolic Circuit

We address the following questions for the well-characterized coupled redox cycles of NADPH and glutathione in human erythrocytes. Suppose that network topology and kinetic mechanisms are conserved, that mutations can alter the values of any enzyme kinetic parameter over broad ranges, but only circuits that fulfill the performance specifications of the wild type are selected. Do the selected circuits share a well-defined design? What specific functional requirements evolutionarily constrain the values of each parameter?

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MS50

The Apparent First-order Kinetics of the Substrate Disappearance in Enzyme Digestion: A Theoretical Investigation

We theoretically investigate the kinetics for protein digestion by mathematically formulating rate equations for two proposed mechanisms namely the one by one and zipper mechanisms. Our analysis shows that the kinetics of digestion follows apparent first-order kinetics irrespective of the mechanism for low initial substrate concentration with respect to the initial enzyme concentration. Also our results suggest new experimental protocol that could reveal information on the mechanism of digestion.

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MS50

On the Distinguishability of Growth Factor Trafficking Kinetics

We analyze a model of EGF receptor trafficking under steady state sorting conditions and derive uniformly valid analytical approximations for constitutively trafficking receptors. Interestingly, these approximations take on the same functional form under a wide range of conditions that includes the extremes of perfectly stable and unstable endosomal complexes. This illustrates that it is possible to fit experimental data to a model that assumes a stable endosomal complex even when this premise is invalid.

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MS51

The Emerging Role of Modeling and Simulation at All Stages of Drug Development

Recent estimates by FDA have projected that of all new

drugs initially tested in human subjects, only 8 percent eventually make it to the bedside. The primary cause of drug failure in the clinic is the selection of an inappropriate dose and schedule. Modeling mathematically describes what the body does to administered drug (Pharmacokinetics) and what the drug does to the body (Pharmacodynamics) to guide and provide rational/quantitative basis for dose regimen selection throughout drug development.

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MS51

Case Studies of Innovative Problem Solving in Therapeutic Protein Development

Therapeutic proteins (MW ¿1000 Da), have unique pharmacokinetic (PK) and pharmacodynamic (PD) properties compared to small molecules. Different approaches currently being applied for the optimization of dosing in clinical development of therapeutic proteins include, (i) mechanistic PK/PD modeling to predict drug effects; (ii) nonlinear mixed effect modeling to assess variability and identify covariate effect on drug disposition; and (iii) using Monte Carlo simulation to guide strategic decision making on fixed dosing-vs.-weight-based dosing for monoclonal antibodies.

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MS51

Quantitative Structure-Pharmacokinetic Relationships (QSPKR) using Bayesian Neural Networks

Where the number of molecular descriptors is typically greater than the number of tested compounds, Bayesian neural networks may provide predicted time-series data that allow for PK modeling, data characterization, and primary parameter estimation, without the significant limitations that accompany most other methods of in silico modeling. Such capabilities hold the promise of reducing the failure rate of compounds in development, while providing key insights into the molecular, physiological, and pharmacological factors controlling drug dose-exposure-response relationships.

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MS51

Improving Clinical Trial Designs using Clinical Trial Simulation (CTS)

The failure of a clinical trial to provide successful outcomes is a significant problem in drug development because failed trials must be repeated at a considerable expense to a company. Using simulation-based design optimization (SBDO) methods, information gained from Clinical Trial Simulation (CTS) is expanded to not only identify the best design but also the robustness of the design. Thus, more than one design is proposed that will provide a successful trial outcome.

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MS52

Interaction of Biological rhythms : Its Relevance, by Means of Examples, for Physiology

Abstract not available at press time.

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MS52

Chronotherapy Strategies in Cancer: It's About Time

Cancer chemotherapy causes major cytotoxic stress on normal tissues. Chronotherapy takes advantage of the existence of optimal treatment times; fast renewing tissues, both normal and tumoral, display a circadian rhythmicity in drug susceptibility. With a cell cycle model, we devise the best strategies for colorectal cancer treatment, taking into account toxicity on the hematopoietic system. We show how the best schedule depends on the interplay between the cell cycle kinetics, the circadian amplitude of drug susceptibility and the treatment itself.

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MS52

Effect of Noise on Cardiac Arrhythmias Associated with Long-QT Syndrome

Early afterdepolarizations (EADs) can induce cardiac arrhythmias. In a mathematical model of ventricular cells, we show that fluctuations generated by additive Gaussian white current noise or the stochastic opening and closing of ionic channels influence the genesis of EADs. Prolonged repolarization was simulated by partially blocking a potassium current (IKs). The stochastic fluctuations induced EADs with patterns that depend on the noise amplitude. The relevance to arrhythmias in patients with Long-QT syndrome will be discussed.

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MS52

Interactions of the Cell Cycle and Radiation Treatment of Cancer

The determination of cancer treatment schedules with radiotherapy is highly dependent on mathematical models of proliferation and the effect of radiation on cells. Although much is known about the cell cycle, few models used in the study of radiotherapy take the cell cycle into account. We construct a model describing the dynamics of proliferating cells (highly sensitive to radiotherapy) and resting cells (less sensitive to radiotherapy), and examine the significance of the cell cycle and its regulation on the effectiveness of radiotherapy. We find that the subpopulation of resting cells may contribute to failure in radiotherapy. This presentation relates to the talk given by T. Hillen in the minisymposium "Mathematical Modeling of Cancer Treatment".

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MS53

Finding the Center - How to Solve Simple Geometry Problems at the Cellular Scale

Fragments of fish pigment cells can form and center aggregates of pigment granules by dynein-motor-driven transport along a self-organized radial array of microtubules (MTs). I will present a quantitative model that describes pigment aggregation, MT-aster self-organization and the subsequent centering of both structures. I will present analysis and simulations of a set of partial integro-differential equations describing the coupled granule-MT interaction that successfully explains much of the observed beahviour and sheds light on role of polymer dynamics and polymer-motor interactions in cytoskeletal organization.

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MS53

A Divergent Mechanism of Spatial Gradient Sensing Revealed through Quantitative Imaging and Modeling

Directed migration of eukaryotic cells often relies on their ability to distinguish receptor-mediated signaling at different subcellular locations, a phenomenon known as spatial sensing. We have analyzed, using mathematical models and live-cell imaging experiments, the sensitivity of platelet-derived growth factor (PDGF) gradient sensing in fibroblasts. We demonstrate that PDGF detection is governed by mechanisms that are fundamentally distinct from those characterized in other chemotactic cells, with implications for fibroblast chemotaxis during wound invasion.

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MS53

Intracellular Gradients and Microtubule Chemotaxis

Microtubules are linear filaments of the intracellular cytoskeleton that serve to organize cytoplasmic components. A major question in understanding cytoplasmic organization is how the self-assembly of microtubules is controlled spatially and temporally. We have found that intracellular chemical gradients could potentially play a significant role in microtubule organization and would be affected by the size and shape of the cell itself.

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MS53

Dynamics of Cell Adhesion: Mass-action Kinetics in the Presence of Long-range Interactions

A model is presented that explains why focal adhesions in stationary or slowly moving cells tend to concentrate at cell periphery in high curvature regions. According to the theory, adhesions move in the direction opposite to contractile forces exerted on them by stress fibers. This translocation to the periphery occurs by treadmilling with the speed proportional to the diffusion coefficient of integrins, the key surface receptors mediating adhesion assembly.

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MS54

Biocalculus in the Community College: Transfer, Workforce, and Continuing Education

A majority of students who successfully complete undergraduate life science degrees fulfill their math requirements at community colleges. To fully implement the national reforms called for in recent reports, two-year colleges must be included. In this talk, a successful biocalculus course developed for the community college population will be detailed. The course audience includes those going directly into industry, those transferring to baccalaureate programs, and those already in research working to obtain a quantitative

perspective.

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MS54
Biocalculus: Reflecting the Needs of the Students

There are three basic paths to teaching calculus to students of biology. The first is the course that emphasizes the standard calculus topics and minimizes the special background and interests of the students. The second is the course that emphasizes those aspects of calculus that mathematicians have found useful when doing biomathematics. The third is the course that emphasizes the needs of the students and minimizes some standard topics usually found in a calculus course. Here, the third path is described through examples and test material developed over 25 years at Marquette University. In general, spreadsheets replace algebra, and data is the primary object of study, instead of function and equation. This approach allows the development of all standard results while also providing a clear path to courses in statistics.

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MS54
Calculus and Beyond

Calculus is an important tool for the biological sciences, and the development of targeted textbooks is a key ingredient to motivating freshmen biology majors and demonstrate to them the importance of acquiring the means to express biological processes in a formal and precise language. Beyond calculus, modeling, stochastic processes, and statistical tools are important quantitative skills every biology student must acquire. This talk will present efforts in this direction by the author.

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MS54
Biocalculus and Beyond: Getting Biology Majors at William and Mary Hooked on Mathematics and Reeling Them In

Like many campuses throughout the United States, William and Mary has bought hook, line, and sinker into building curricular bridges between mathematics and biology. As part of this initiative, I developed a two semester calculus sequence for the life sciences whose goals include substitutability for the regular calculus sequence and introducing biology majors to the excitement of modeling. I will share some of my harrowing tales of trying to navigate between this interdisciplinary Sylla and Charybdis and my successes and failures of enticing students into higher level mathematics courses. These higher level courses, in addition to the regular mathematical fare, include several at the interface of mathematics and biology. I will compare and contrast my experiences in teaching two of these courses, a sophomore introduction to mathematical biology and a junior/senior co-taught seminar on metapopulation ecology, that differ drastically in size, structure, and content.

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MS55
The Evolution of Defence Portfolios in Integro-difference Models of

Some organisms maintain a battery of defensive strategies against their exploiters, while others fail to employ a defence that seems obvious. We investigate the evolution of defence portfolios in a discrete-time model with a mutation kernel, resulting in a system of integro-difference equations. We introduce the concept of strategy-blocking, where one strategy prevents the appearance of another that would be adaptive in its absence, and discuss why reed warblers reject cuckoo eggs but not cuckoo chicks.

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MS55
Adaptive Speciation: Theory and Evolutionary Experiments

Understanding the origin of diversity is a fundamental problem in biology. According to traditional evolutionary theory, the process of diversification is a by-product of geographical separation. However, I will show that diversification as an adaptive response to biological interactions is also a plausible evolutionary process. I will describe models for evolutionary branching based on the mathematical framework of adaptive dynamics as well as ongoing efforts to test our theory in evolving *Escherichia coli* populations.

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MS55
The Evolution of Microbial Diversity in Spatially Homogeneous Environments Containing a Single Resource

According to the competitive exclusion principle a simple habitat, defined to be a spatially homogeneous environment that contains a single resource, can only ever support one competitor. Contrary to this theoretical prediction a number of laboratory experiments of microbial evolution have found that diversity can evolve in simple habitats. Using a system of non-local PDEs we test a hypothesis that biochemical trade-offs of microbial metabolism play an important role in the evolution of microbial diversity

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MS55
Evolution of Developmental Timing – Warming

Climate and Phenological Change

Cold blooded organisms develop nonlinearly with respect to temperatures; with seasonal swings tend synchronizing developmental timing and conveying higher fitness. Persistence of species depends on whether adaptation of phenology can track rates of climate change. Our approach couples existing models of phenology and quantitative genetic theory to predict how phenological parameters may evolve. Evolutionary trajectories are characterized by rapid changes to create synchrony, followed by gradual adaptation to parameters with marginal dynamic properties.

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MS56

Gates and Oscillators: A Network Model of the Mammalian Circadian Clock

The mammalian circadian clock, in the suprachiasmatic nucleus has at least two anatomically and functionally distinct cellular constituents. Some cells respond rapidly upon receipt of direct retinal input but are not electrically rhythmic while others have endogenous molecular oscillations, but do not immediately respond to photic input. Using these two phenotypes, we have modeled maintenance of phase coherence among autonomous cellular oscillators, showing that a common mechanism can account for both free-running rhythms and entrainment.

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MS56

Synchrony Among Daily Oscillators in the Brain

Specific brain areas act as circadian pacemakers required for daily rhythms in behavior and physiology. In vivo and in vitro, multiple circadian oscillators synchronize to each other to sustain near 24-h rhythms. Using long-duration recording methods, we have begun to study signals required for coordinated activity. We find that a neuropeptide (vasoactive intestinal polypeptide) plays a critical role in entrainment among neurons within one pacemaker, the suprachiasmatic nucleus, which regulates daily rhythms in locomotion.

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MS56

Design Principles for Phase Splitting Behavior of Coupled Cellular Oscillators

Hamsters housed in constant light exhibit a phenomenon known as splitting, in which an animal's single daily bout of locomotor activity dissociates into two components that are about 12hr apart. Recent data show that this phenomenon is due to reorganization of the cellular oscillators in the SCN with its right and left halves oscillating in antiphase. To better understand the splitting, we have applied mathematical reasoning to infer the essential design principles of this phenomenon

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MS56

Suprachiasmatic Nucleus: A Primer for Mathematicians

The suprachiasmatic nucleus (SCN) in the anterior hypothalamus is a paired nucleus straddling the midline and composed of 16,000 heterogeneous, densely-packed neurons. A wealth of data indicates that it is the site of the master circadian clock in mammals. Now we need to understand how multiple single-cell circadian oscillators within the SCN synchronize to each other and the environmental light schedule to create an integrated tissue pacemaker with coherent molecular and electrical rhythmicity

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MS57

Cyton Theory: A Framework for Evaluating the Cellular Calculus of Signal Integration

How receptor-mediated signals are integrated simultaneously by lymphocytes to control rates of both growth and death is a complex problem. We are developing a model of the lymphocyte built on an internal mechanical unit called the cyton and show how it can explain and resolve signal integration problems using a cellular calculus. The development of a numerical solver allows the interplay between proliferation and survival to be extracted from CFSE and BrDU incorporation data.

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MS57

The Impact of Affinity on Proliferation and Death in the Immune Response

High affinity B-lymphocytes are critical for protection from extracellular pathogens, such as bacteria and parasites. To understand the basis for positive selection of these cells, we have investigated transgenic mice expressing B cell receptors of varying affinity. Proliferation and death rates are estimated through a model-based analysis of time-series labeling data (e.g., BrdU and Casp). These methods have enabled us to elucidate how B cell fate is governed by its ability to bind antigen.

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MS57

Elucidating Lymphocyte Development Using BrdU Labeling

Immune responses involve many cell types, including B, T and NK lymphocytes expressing a diversity of receptors for foreign antigens and self-molecules. The dynamics of immune cell repertoires, in particular their development, are highly complex and non-linear. Understanding the population dynamics which underlie lymphocyte development is essential for elucidating the causes of various immune dysfunctions and cancers. The results of our studies combining combine modeling with BrdU data to address this issue will be reported.

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MS57

Quantifying Cell Turnover Using CFSE Data

The CFSE dilution assay is used to estimate the parameters determining cell division and death in vitro/in vivo. For homogeneous cell populations, we consider the "Smith-Martin" model of cell turnover and analyze different techniques for estimating its parameters. The CFSE data alone allows to estimate only the duration of the division phase, and in some cases the average division time can be determined using Gett-Hodgkin method. Additional measurements are required to estimate all model parameters.

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MS58

Optimum Scheduling of Countermeasures

The use of mathematical models to automatically generate optimal circadian adjustment schedules (CAS) includes computational challenges. CAS are necessary for individuals working night shifts or traveling rapidly across time zones. CAS are used by NASA to help shuttle crew adapt to shifts in the sleep wake cycle. An iterative technique developed to design CAS will be presented and compared to other methods, including model based predictive control and the calculus of variation.

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MS58

The Use of Biomathematical Models Within Operational Fatigue Risk Management Systems

Biomathematical models of work-related fatigue are becoming widely used in industrial, emergency response, and military operations. The inputs available for modeling vary in these different settings, as does the information required by managers and commanders for decision-making. In addition, biomathematical models are being rapidly integrated into broader systems of operational risk management. The practical components, considerations and complexities of different fatigue risk management systems will be detailed.

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MS58

Applications of a Fatigue Model for Predicting and Managing the Consequences of Fatigue in the Transportation Industry

Abstract not available at press time.

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MS58

Identifying Two-process Performance Models using Limited Data

Abstract not available at press time.

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MS59

Stocastic Modeling of Experiments on Virus-stimulated Interferon Beta Induction in Single Human Dendritic Cells

Abstract not available at press time.

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MS59

Microsimulation Modeling of Spatial Reorganization in Immunity

Abstract not available at press time.

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MS59

Modeling Immunity in the Lung to Bacterial and Viral Pathogens

Abstract not available at press time.

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MS59

: Parameter Identifiability and Statistical Inverse Problems in

Abstract not available at press time.

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MS60

Models for Directed Cell Movement in Fibre Networks

Mesenchymal motion is a form of cellular movement that occurs in three-dimensions through tissues formed from fibre networks, for example the invasion of tumor metastases through collagen networks. The movement of cells is guided by the directionality of the network and in addition, the network is degraded by proteases. I derive mathematical models for mesenchymal motion in a timely varying network tissue. The models are based on transport equations and their drift-diffusion limits. It turns out that the mean drift velocity is given by the mean orientation of the tissue and the diffusion tensor is given by the variance-covariance matrix of the tissue orientations. I will discuss relations to existing models and future applications.

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MS60

In Silico Mathematical Model of the Atherogenesis, and its Stability Analyzes

We construct a mathematical model of the early formation of an atherosclerotic lesion based on a simplification of Russell Ross paradigm. Study centres on the interplay between chemical and cellular species we employ a model of chemotaxis first given by E. F. Keller and Lee Segel and present our model as a coupled system of non-linear reaction diffusion equations. We perform numerical simulations demonstrating that our model captures certain observed features of CVD.

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MS60

Chemotaxis Models and their Application to Angiogenesis

In the current talk the author will present some recent work on chemotaxis models and their application to angiogenesis, and possibly morphogenesis.

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MS60

Modeling the Role of Environmental Cues during Angiogenesis

Angiogenesis is the growth of new capillaries and blood vessels from the existing vascular network. It is important for wound healing and is a means by which tumors become vascularized. During angiogenesis endothelial cells proliferate and migrate to form new capillaries, a process that is orchestrated by environmental cues such a growth factors. Approaches for modeling the role of environmental cues during angiogenesis will presented, along with numerical methods that preserve fundamental features (eg. mass) of the biological system.

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MS60

Traveling Wave Phenomena for System Modeling Hypertrophy and Hyperplasia in Soft Tissue

The growth of soft tissue in vivo often involves a complex interplay between various biochemical, genetic and mechanical processes. An important example of this interplay is provided by growth and remodeling of the smooth muscle cells (SMCs) within the medial layer of a large diameter human artery. Growth of SMCs is accomplished via two different processes: growth in size of individual cells (hypertrophy) and growth in the number of cells (hyperplasia). Through genetic expression, SMCs enter into distinct phases to accomplish hypertrophy and hyperplasia in which they exhibit differing mechanical (stress/strain) and transport (diffusion) processes. We describe a modeling frame for capturing these effects and discuss analytical and simulation results for an example model.

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PP1

Transmembrane Protein Structure Determination Using Solid State NMR

Nuclear Magnetic Resonance (NMR) is a technique for the study of molecular structures. Solid state NMR (ssNMR) uses orientational constraints to build an atomic model of the molecule, and has been successful in determining the structures of membrane proteins such as ion channels. We discuss mathematical problems that arise when building a model with ssNMR data. As an illustration, we build a model of the M2 transmembrane protein that is a proton channel in the Influenza A Virus.

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PP1

Compound Selection in Toxicological Studies Using Principal Component Analysis.

Several basic schemes and methods using simple statistics and Principal component analysis are used in compound selection for toxicological studies. To illustrate the method, 5 biophysical properties are used for 71 compounds relevant for hydrocarbon disposition and toxicity. A comparison between (1) a sample using the simple statistics and assessment by principal component analysis, and (2) sampling

based on uniformity in the space of the first few principal components is examined.

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PP1

Bacteria-Phage Co-Evolution As a Cause of Bacterial Diversity

Parasites are believed to play a significant role in host diversification, and there is an increasing body of experimental evidence supporting this hypothesis. In particular, experimental studies of bacterial evolution in spatially homogeneous environments have shown that the introduction of a bacterial parasite (phage) into the system significantly increases bacterial diversity. We use systems of non-local PDEs describing bacteria-phage co-evolution in order to identify ecological mechanisms that could be responsible for this increase in diversity.

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PP1

Pipath: An Algorithm For Generating α-Helical Atomic Structures From Solid-State Nmr Data

Solid-state NMR PISEMA experiments generate orientation constraints which can be used to determine a membrane protein's atomic structure. We present a new algorithm, PIPATH, that finds the most α-helical structure in agreement with the PISEMA data. PIPATH uses techniques from graph theory to find an optimal assignment and structure. The structure generated is typically quite close to the target structure and is a useful initial model for subsequent refinement

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PP1

Pipath: An Optimized Algorithm for Generating Alpha-Helical Structures from Pisema Data

Solid-state NMR PISEMA experiments generate orientation constraints which can be used to dervice a membrane protein's atomic structure. We present here a new algorithm PIPATH that finds the most α-helical structure in agreement with the PISEMA data. PIPATH uses techniques from graph theory to find an optimal assignment and structure. The structure generated is typically quite close to the target structure and is a useful initial model for subsequent refinement.

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PP1

Computational Study of Spatial Localization Effects on Signaling Cascades Dynamics

Transport phenomena and protein localization details are often left aside in the design of quantitative models of cellular signaling pathways. However, there is increasing experimental evidence showing that complex intracellular traffic

and differential spatial localization of members of a signaling cascade occur in response to many signals. Models neglecting these processes could miss significant features and lead to an incomplete understanding of the live system. In this study we used computer models to analyze how spatial localization could affect the behavior in Saccharomyces cerevisiae signaling pathways, with special emphasis put on the effects on stimuli response's dynamics. The models show that spatial localization and transport rates could play a determinant role controlling signaling response profiles.

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PP1

Extravascular Burden of Carbon Monoxide (CO) During CO Exposure and Washout

The extent of extravascular uptake of CO in CO poisoning has been debated. We developed a model of CO uptake and distribution which includes diffusion of CO from blood into tissues and binding of CO to myoglobin. After validation against data from both short and long-term human CO exposures, additional experimental studies were simulated and extravascular distributions of CO predicted. Extravascular CO levels can change independently of blood carboxyhemoglobin level, and can transiently rise during oxygen therapy.

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PP1

The High-Throughput Development of High Affinity Nucleic Acid Molecules for Targets: Complex Selex: A Mathematical Model and Computer Simulation Study

SELEX (Systematic Evolution of Ligands by EXponential) is an experimental protocol to enrich target-binding ligands from a highly complex nucleic acid library by iterative extraction and amplification of target-bound ligands. In this talk, we present mathematical model and computer algorithm for simulating SELEX experiments against complex target mixtures (the complex SELEX). We also present simulation results such as the discovery of optimal experimental conditions under which the target-binding ligands are developed in high efficiency.

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PP1

Prediction of Polyadenylation Sites of Mrna Using Support Vector Machine

Messenger RNA polyadenylation is important in cellular processes, such as mRNA stability. Many human and mouse genes have multiple polyadenylation sites (poly(A) sites) that lead to different functional transcripts. Biased alternative polyadenylation in human tissue suggests that the coordinates of similar poly(A) sites can be regulated. In this poster, the Support Vector Machine is used to predict the poly(A) sites based on the gene sequence. Our objective is to characterize the alternative polyadenylation by mathematical modeling.

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PP1

A System Equivalence Related To Dulac's Extension of Bendixson's Negative Theorem For Planar Dynamical Systems

Bendixson's Theorem [1] is useful in proving non-existence of periodic orbits for planar systems

$$\frac{dx}{dt} = F(x, y), \frac{dy}{dt} = G(x, y) \tag{1}$$

in simply connected domain D, where F, G are continuously differentiable. From the work of Dulac [2] one suspects that system (1) has periodic solutions if and only if the more general system

$$\frac{dx}{d\tau} = B(x, y)F(x, y), \frac{dy}{d\tau} = B(x, y)G(x, y) \tag{2}$$

does, which makes subcase (1) more tractable, when suitable non-zero $B(x, y)$ which are can be found. Thus, Bendixson's Theorem can be applied to system (2), where otherwise it is unfruitful in establishing non-existence of periodic solutions for system (1). The object of this note is to give a simple proof justifying this Dulac-related postulate of the equivalence of systems (1) and (2).

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PP1

Mathematical Modelling of Take-All Decline in Winter Wheat

Take-all disease of wheat is caused by the soil-borne fungus Gaeumannomyces graminis var. tritici (Ggt), which infects the roots, crown, and basal stem of plants. The highest risk of take-all occurs when wheat is planted in consecutive years. Disease severity and yield loss can be substantial in second, third, and fourth wheat crops, with the worst take-all usually occurring in the third consecutive crop. Take-all becomes less severe, and yields usually increase, with the fifth or sixth successive wheat crop. It is postulated that this occurs because of a natural increase in soil microorganisms antagonistic to the pathogen–a phenomenon known as "take-all decline," which persists only so long as wheat is grown continuously. Using mathematical modelling we test hypotheses about the mode of action of the antagonist microorganisms.

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PP1

Modeling Plasma Membrane Recruitment of Cytosolic Signaling Proteins

We visualize the stimulated translocation of cytosolic signaling proteins to the plasma membrane in live B lymphocytes with multicolor confocal fluorescence microscopy. We use previously developed image processing algorithms to systematically quantify the time course of recruitment and the spatial colocalization of signaling proteins with crosslinked receptor. We describe these events with a reaction-diffusion model and estimate relevant kinetic parameters for the translocation and the spatially localized interaction between signaling proteins and crosslinked receptor complexes.

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PP1

A Secondary Mechanism for Cardiac Excitation Propagation

It is well known that cardiac action potential propagation is possible due to intracellular coupling by gap junction channels. However, recent studies involving gap junction deficient myocytes illustrate a complicated relationship between propagation velocity and the degree of gap junctional coupling. This suggests that there might be a secondary mechanism to ensure propagation success. Here, we explore a mechanism in which propagation is supported via negative electric potentials in the narrow junctional cleft spaces between neighboring cells.

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PP1

Rapid Evolution and Predator-Prey Dynamics with Variable Costs of Defense

Predation may be a selective pressure that drives adaptation. We investigate the effects of genetic variability in predator search efficiency and anti-predator defense on the stability of a predator-prey system. In particular, we examine the impact of varied versus fixed costs of defense on population dynamics. We assume that the trade-off for investment in defense is a decrease in fecundity and that, at low prey density, defense is without cost.

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PP1

The Combined Effect of Synaptic and Cellular Resonance

We derive a mathematical theory to explain the subthreshold behavior of a resonant cell when it is stimulated by a presynaptic cell via a resonant synapse. We demonstrate how a cell combines the information contained in the frequency dependant synaptic response with its own frequency dependant behavior. Our results show that the maximal response in the postsynaptic cell occurs at a frequency located between the preferred frequencies of the synapse and cell. We show how one can tune the location of the maximal response by changing the steepness of the synaptic response - frequency profile.

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PP1

Modeling Immunological Synapse Formation and Repolarization

T cells form an immunological synapse (IS) with antigen presenting cells (APC) bearing appropriate antigenic stimuli. Experiments have shown that the IS can repolarize to another APC having a higher antigenic load. We will present FRAP experiments and extract the relevant biophysical parameters governing important processes of receptor diffusion and binding. Mechanisms of IS formation and repolarization are discussed in the context of these parameter estimates.

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PP1

A Diffusive Model of Ampa Receptor Trafficking in the Postsynaptic Membrane

AMPA receptor diffusion in the postsynaptic membrane is an essential mechanism for maintaining steady-state concentrations and affecting changes in AMPA receptor number during LTP/LTD. We propose a model of AMPA re-

ceptor trafficking that includes diffusion. We find that diffusion is critical in maintaining constituitive receptor recycling and a characteristic steady-state concentration profile. Our model provides the rate of relaxation to new steady-states set by the induction of LTP/LTD, which could be used for testing the model's validity.

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PP1

Modeling and Simulation of Circadian Rhythm of Cyanobacteria by Phosphorylation of the Proteins

We are interested in the mechanism of circadian rhythm of Cyanobacteria. We make a model by use of phosphorylation of Kai C, which is surpressed or accelerated by Kai A and Kai B. By use of it, we investigate some important properties of it theoretically.

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PP1

The Role of Gap Junctions in a Neural Field Model

Recent research has shown a high density of gap junctions in areas of the brain that experience epileptic events. Gap junctions allow direct electrical connections between neurons and cause a diffusive-type effect on neuronal voltage between surrounding cells. We extend an Amari-type neural field model by including a diffusion-like term to model gap junctions and investigate how this changes the dynamics of spatially localised solutions. Numerical work shows families of solutions are destroyed as the strength of the term modelling gap junctions increases. By placing restrictive assumptions upon the firing rate function, analytical solutions are explored.

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PP1

Ubm at Murray State University: Biomaps

The poster will provide insight into the format of the Biology and Mathematics of Population Studies (BioMaPS) program started in January 2006. The mathematics and biology students work in teams with all involved in laboratory experience and mathematical modeling studies. Research questions, schedule of the program, successes and challenges will be addressed.

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PP1

Mathematical Improbability of Using Animals As Cams for Toxicology and Medical Research

Because of differences in gene regulation, gene networks and molecular mechanisms that have been revealed by evolutionary biology and molecular biology we now understand why even two very similar complex biological systems may respond differently to the same stimuli, and hence why one such complex system (for example, inbred strains of rodents) cannot reliably predict response for a different complex system (for example, humans). Current biomedical research is studying disease and drug response at the level where known differences between complex systems become manifest, hence using nonhuman animals as causal analogical models for human disease and drug testing is a scientifically invalid paradigm. This has profound implications for using animals in toxicology testing and as models for human disease.

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PP1

Household Epidemiological Models With Clustered Resistant Individuals

The spatial structure of a population can have profound effects on the spread of epidemics. We are studying models of populations partitioned into households, where infection attempts occur both within and between households. Fixed spatially clustered resistant individuals are introduced into the population, which may actually increase the rate of spread of an epidemic, although this may then be counteracted by clustering of infectious individuals within households as well, depending on their mobility.

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PP1

Multi-Host and Multi-Patch Models of Zoonotic Diseases

Abstract not available at press time.

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PP1

Predator-Prey Equations with Prey Taxis: Discontinuous Travelling Waves

Diffusion processes have been widely used to incorporate spatial effects into predator–prey models. However, obser-

vations report that predators tend to move towards prey. Here we consider prey taxis as a primary spatial processes. Without diffusion process we show analytically that discontinuous wave solutions occur due to the singular barrier. Introduced diffusion process is shown to make these discontinuous solutions smoothly. Fractional step methods are used to demonstrate the nature of discontinuous travelling wave solutions.

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PP1

Kinetic Analysis of the Mechanism of the Cell Division Cycle in Caulobacter Crescentus

Progress in understanding cell cycle regulation in bacteria has lagged behind eukaryotes. Recently, however, the discovery of two master regulator proteins, CtrA and GcrA in Caulobacter crescentus, allows us to propose a realistic molecular mechanism for cell cycle control in this bacterium. The mechanism is cast in a quantitative model revealing the temporal dynamics of the genes and proteins regulating the cell cycle in Caulobacter wild type cells as well as in several mutants.

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PP1

A Realistic Mathematical Model of the Canine Pulmonary Veins Sleeves

Pulmonary veins (PV) are the great vessels connected between lung and left atrium and transport oxygenated blood to the heart. There are 4 pulmonary veins in human beings. At the intersection between pulmonary veins and left atrium, there is a short segment covered with striated cardiac muscle and called pulmonary vein sleeve. Due to the complex intermingled muscle bundles, pulmonary vein sleeves display characteristic electrical behavior. The cellular electrophysiological properties of pulmonary vein sleeves were reported few decades ago. However, the clinical significance of pulmonary vein was not found until recently. In patients with atrial fibrillation, it was found that ectopic foci existed in the pulmonary veins. Therefore, electrophysiological studies on pulmonary veins have drawn a lot of attention recently. For example, in the experiments of dogs and rabbits, besides the fast response type of action potential, various pacemaker-like automaticities and triggered activities, e.g., early afterdepolarizations (EAD), delayed afterdepolarizations (DAD), have been demonstrated in the pulmonary veins sleeves under physiological or pathophysiological situations (see [Hocini et al., 2002], [Ehrlich et al., 2003], [Hojo et al., 2003], [Wang et al., 2003, 2005], [Po et al., 2005], [Chen et al., 2000, 2001, 2002-a, 2002-b, 2002-c, 2003-a, 2003-b, 2003-c, 2004-a, 2004-b]). In this study, we have developed a mathematical model which fits well the experiments for the canine PV. Using this model, we have successfully reproduced the experimentally observed frequency responses, ischemia/hyperkalemia phenomena, pacemaker-like automaticities, and triggered activities of PV sleeves. Also, as in the experimental results of [Po et al., 2005], our model APD restitution curve, an important index for the breakup of reentry, was very flat, which supports the hypothesis that reentrant PV tachycardia is a potential mechanism in initiating atrial fibrillation.

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PP1

Maximizing Cell Free Ethanol Production

Ethanol production by yeast is limited by the toxic effect of ethanol on the yeast and other factors. Removing the microorganisms from the ethanol production process (cell free) has a number of advantages including greater process flexibility, more freedom to manipulate enzymes, and the ability to easily optimize the production process by altering enzyme levels. Models of the twelve enzymatic reactions involved in the production of ethanol from glucose indicate the potential to increase ethanol production.

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PP1

Multistability in a Two-Cell Inhibitory Network with Synaptic Facilitation and T-Currents

We explore the dynamics of two type-I neurons with T-like currents coupled by reciprocal inhibition.This network exhibits low-frequency tonic firing and chaotic firing states, and transitions to antiphase bursting at sufficient coupling strength, due to deinactivation of the T-currents. We show that synaptic facilitation promotes bistability between bursting and tonic activity states, and may regularize chaotic firing. In addition, we analyze the multi-stability between distinct bursting states using a one-dimensional Poincare map.

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PP1

Stochastic Modeling of Periodic Mass Antibiotic Treatments for Blinding Trachoma

We develop a stochastic mathematical model to simulate ocular chlamydial infection in communities undergoing biannual mass antibiotic treatments. Model parameters were fit using maximum likelihood estimation and data collected by our group from approximately 5000 children in Ethiopia. Simulations show infection is eliminated in more villages with each subsequent treatment. However, in villages that still harbor infection, it returns to the same, quasi-stationary distribution. Overall, local elimination is feasible; subsequent Ethiopian data confirm these results.

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PP1

Diffusion of High Energy Metabolites in Mdck Cells and Myocytes

Effective diffusion of high energy metabolites in cells is difficult to quantify. We describe mathematical models that use data for various experimental conditions (e.g., control, stress) to assess diffusion barriers and cell function requirements. We test the hypothesis that local changes modulate function without significant changes in global cytosolic concentrations of ATP, ADP and inorganic phosphate. The model is described by a diffusion equation in two space dimensions and time; namely, $\mathbf{C}' = \bigtriangledown \cdot \mathbf{D} \bigtriangledown \mathbf{C} + \mathbf{S}$, where $\mathbf{C}$, $\mathbf{D}$ and $\mathbf{S}$ are vectors of concentrations, diffusion coefficients, and sources and sinks, respectively.

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PP1

Analysis of a Simple Model of Circadian Rhythm of Arabidopsis Thaliana

We are basically interested in circadian rhythm of Arabidopsis thaliana. We consider about a simple model equation of two main components of mRNA's and its productive proteins. Under some simple conditions, it has a periodic solution. We investigate properties of the system by use of the numerical simulation and stability analysis.

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PP1

Perspectives on the Drift-Paradox Problem

Plankton are often considered passive tracers, but individual plankton behavior may dominate at smaller scales. Using a hydrodynamic model to create various flows in an idealized channel with and without rooted plants, we model plankton behavior with an individual-based model and explore the extent to which vertical migration can affect biological residence time in the channel. We gain additional insight into simulation results by studying a two-dimensional advection-diffusion equation representing the system.

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PP1

Random Networks Applied to Axon Growth

Many biological situations involve nanoscale fibers having directions and shapes that appear random. We propose and study models at the microscale (fiber growth) and at the macroscale (network scale) for the probability distribution of position and direction for curves in space. The model is applied in two space dimensions, where the direction variable is an angle. Simulations are performed to apply the theory to axonal growth, and the results are compared to data.

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PP1

A Dynamic Mechanism for Episodic Bursting

Episodic bursting is a behavior found in pancreatic beta-cells as well as in hypothalamic GnRH neurons. One mechanism that has been proposed for beta-cells is based upon oscillations in glycolysis. Here we describe an alternative method for episodic bursting based on the interaction of two activity-dependant slow variables. The dynamics of this episodic bursting mechanism can be understood though an analysis of the fast subsystem, and its modulation by one or the other slow variable.

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PP1

Confined Animal Feeding Operations As Amplifiers of Influenza

A pandemic could occur if a strain of influenza such as the H5N1 avian influenza virus evolves so that it is transmissible among humans. Domestic species such as poultry or swine could serve as local amplifiers for such a new strain of influenza. This amplification could be particularly strong if the transmission among the birds or pigs is high because they have very close contacts with each other in confined animal feeding operations (CAFOs). CAFO-workers form a bridging population between the CAFO species and the general population. In order to assess the magnitude of this amplification, we formulate and analyze a mathematical model for the transmission dynamics of a novel influenza virus with three sequentially linked populations: the CAFO species, the CAFO workers and the rest of the local population. We show that for a given percentage of CAFO workers in the community, an influenza epidemic is amplified significantly when the infectivity of the virus is low, so that the basic reproduction number in humans is just above 1.

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PP1

The Throughput of the Transitional 3 B Cell Pool Accounts for Losses Between Transitional and Mature B Cells

Our study aimed to examine the hypothesis that the transitional 3 (T3) peripheral B lymphocytes subset contains cells undergoing negative selection derived from both the emerging and mature B cells pools. To address these issues, we used mathematical models of population dynamics, and fit it to existing in vivo BrdU labeling data. We suggest that the throughput of the T3 B cells pool can account for most of the losses in B cells maturation.

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PP1

A Model for Auxin Response in Arabidopsis

Auxin is a ubiquitous plant hormone, involved during nearly all growth stages and processes. Recently reported results have elucidated the intracellular interactions that underlie observed responses to auxin. We have developed a differential equation model for auxin response in leaf cells of *Arabidopsis thaliana*. Simulation runs produce concentration profiles consistent with experimental results. The modelled cells can be coupled by auxin transport terms to allow simulations of canalization in a field of cells.

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PP1

Probability Density Approaches to Modeling Local and Global Intracellular Calcium Dynamics

Deterministic ODE models of intracellular calcium (Ca) dynamics traditionally neglect the stochastic gating of Ca channels and important aspects of local Ca signaling. Here we present a novel probability density approach to modeling Ca dynamics in cells that involves coupling ODEs for the bulk cytosolic and ER [Ca] to advection-reaction equations for the probability density of the [Ca] in cytosolic and lumenal domains associated with each channel and conditioned on channel state.

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PP1

A Model for the Actin Polymer Brownian Ratchet

Actin forms the cytoskeleton polymer allowing cells to maintain their shape and plays a role in motility. We extend models for polymer growth and decay in response to diffusion of monomers in the cytoplasm. The model includes the interaction of the cell membrane with the leading edge of polymer growth, providing a model for the Brownian Ratchet. We also discuss the distribution of actin chain length consistent with the distribution of barbed and pointed ends.

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PP1

Cancer Growth Model by Ecology with Mass Advantage, Stability and Complete Deletion Conditions Using Mass Shape Information

This cancer growth model consists of the proliferation rate λ^+ of cancer cells and with a weaker inhibition rate λ^-_{in} in a cancer mass than λ^-_{out} outside it by like immune. This means mass advantage. $\lambda^+ - \lambda^-_{in} > 1$ $\lambda^+ - \lambda^-_{out} < 1$ Results (1)A higher λ^+ gives more irregular mass shapes although λ^+ can not be easily evaluated because of other nonlinear effects. (2)The situation means the existence of stability not to make a small mass. (3)The conditions to initiate a cancer mass and its complete deletion can be calculated.

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PP1

How Deeply Memory Compression Can Be Concerned with the Knowledge Structure in Genes Like Hierarchical Neural Networks

In genes memory compression caused by the mixing of near DNA sequences through unequal crossover, gene conversion, etc. and orthogonalization through translocation and duplication can exist and speed up evolution as in the brain it is caused by Hebb rule and mutual inhibition by inhibitory cells building hierarchical knowledge structures with common characters. Here how wide range of components like not only gap genes, pair rule genes and segment polarity genes in Drosophila but also alpha helix, beta sheet, domains, motifs and modules can be concerned with memory compression is shown.

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PP1

A Spiny Branched Dendritic Tree and its Spatio-temporal Filtering Properties

The dendrites of many nerve cells are complex branching structures that receive and process thousands of synaptic inputs from other neurons. Dendritic spines can be present in large densities on the dendrites. They are equipped with excitable channels and loci for receiving excitatory synaptic input. Here we introduce a mathematical model of a branched dendritic tree based upon a generalisation of the analytically tractable Spike-Diffuse-Spike model. The active membrane dynamics of spines are modelled by an integrate-and-fire process. The spines are assumed to be discretely distributed along a passive branched dendritic structure. We obtain a quasi-analytical solution using the sum-over-paths approach formulated by Abbott et al. (Biol. Cybern., 1991, vol.66, pp. 49-60). The model supports saltatory travelling wave propagation and wave scattering amongst branched dendritic trees. It is ideally suited for the study of spatio-temporal filtering properties and neural responses to different patterns of synaptic input.

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PP1

Bursting Without a Slow Variable in a Lactotroph Model.

We describe a model of the pituitary lactotroph. Low concentration of dopamine activates an A-type K+ current. In the model this converts continuous spiking into a bursting pattern. Even though inactivation of this current is necessary for bursting it is not a slow process.

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PP1

Multiscale Modeling to Combat Colorectal Cancer

The Integrative Biology consortium brings together computer scientists, modelers and experimentalists to build a virtual tumour. We focus on colorectal cancer because of its social impact and the biological information available. The model, a hybrid cellular automaton, integrates processes at the subcellular, cellular and tissue levels. This multiscale approach enables us to investigate interactions between such processes, to combine single-level experimental data, and to test the system's overall response to different treatments.
`http://www.integrativebiology.ox.ac.uk/`

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PP1

Mathematical Modeling of Cancer Progression: Understanding the Role of the RhoC Gtpase on-off Switch in Aggressive Phenotypes of Breast Cancer

The most damaging change during cancer progression is the growth of metastases. RhoC GTPase was found to be crucial in that process in different cancers, particularly, in a highly aggressive form of breast cancer. RhoC is a molecular switch cycling between inactive (GDP-bound) and active (GTP-bound) states, tightly regulated by several regulatory proteins. We have developed a dual mathematical-experimental approach to understand this cycle and its deregulation in cancer cells in comparison with normal ones.

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PP1

Synchronization of Circadian Oscillators

Living beings adjust to the environment via synchronization of their biological clocks to external drives like the light-dark cycle and food availability patterns. Experimental entrainment patterns in activity recordings of house mice under light- and food- restriction are analyzed. Generic nonlinear entrainment behavior like phase locking, phase slipping, or free running behavior are found in this real biological circadian system. A model of coupled Van der Pol oscillators gives insight into the interaction of light- and food- entrainable biological clocks in these mice.

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PP1

Graphical Causal Reasoning Tool for Systems Biology: C-Map

Abstract available on-site at the conference. Supported by NIH Cell Migration Consortium GM64346 (KJ) and GM073180 (TE, KJ, GW)

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PP1

Reciprocity Relations Between Stokes Flows of Viscous and Viscoelastic Fluids

Linear response theory of thermal fluctuations or driven motion of tracers provides a basis for exploring viscous, elastic and compressible properties of condensed matter. Applications range from atomic physics where the methods were first developed, to recent applications in microrheology. The emphasis here is on hydrodynamics and deformations of incompressible viscoelastic materials for various geometries and driving conditions, as determined from known viscous behavior by straightforward prescriptions, called reciprocity relations. Linear response theory can be formulated to yield an explicit correspondence in the governing equations of Stokes flow between a viscous fluid and any linear viscoelastic material, valid for an arbitrary prescribed source: of force, flow, displacement or stress; local or nonlocal; steady or oscillatory. Upon specification

of the geometry and source, non-inertial and inertial viscous Stokes solutions (known as Stokes singularities) transfer to exact solutions for linear viscoelastic fluids. Reciprocity relations inform elasticity-induced contrasts in flow or displacement fields for prescribed forces or stresses; conversely, one may infer sources necessary to achieve identical responses in viscous and viscoelastic materials. Two special Stokes singularities form the basis of microrheology experiments and their interpretation: a prescribed velocity on a translating sphere and a stationary point source of force. We revisit and amplify these examples as an illustration of the reciprocity relations, focusing on measurable non-inertial and inertial features. Next, we illustrate the generality in source type and geometry of this correspondence principle by analyzing the linear response for a nonlocal, planar source of unsteady stress.

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PP1

Modeling Pattern Formation in Proteus Mirabilis Colonies

When inoculated on a hard medium, a colony of the bacterium Proteus mirabilis can form concentric ring patterns of cell density. These patterns have been described as the result of periodic colony expansion due to collective movement of swarmer cells differentiated from short-rod swimmer cells. However, recent experiments show that swimmer cells can stream inward towards the center of the colony and suggest intercellular communication between cells. We develop a new model incorporating chemotaxis of swimmers, and we present preliminary results on modeling radial spoke-like patterns.

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PP1

Dual feedback mechanisms for p53 response to DNA damage

Recent experiments indicate that p53 responds to DNA damage by series of pulses of constant amplitude and period. The mechanism and function of these pulses are not yet fully understood. We explore the pulse-generating potentials of several dual-feedback schemes (containing positive and negative feedback loops) and propose a mechanism whereby p53 pulses might coordinate cell cycle arrest and apoptosis after DNA damages.

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PP1

Pet: Parameter Estimation Toolkit

PET provides computational biologists with a graphical user interface for performing simulations and estimating parameters of mathematical models of reaction networks describing gene, protein and metabolic interactions. PET is designed 1) to manage the potentially complicated relationships between a model and simulations of a large collection of experimental observations, 2) to assist the user in manual exploration of parameter space, and 3) to provide support for automatic parameter estimation based on both global and local optimization algorithms.

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PP2

Modeling Aspects of Wound Closure: The Effects of Tgf-β and Wound Geometry

Several aspects of dermal wound healing such as the role of transforming growth factor beta (TGF-β) and the effects of wound geometry are still not completely understood. Using a diffusion equation and a linear parameter, we reproduce some of the known features of the temporal evolution of the concentration of TGF-β and predict how the concentration of TGF-β and the geometry of a wound influence the time required for healing.

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PP2

Nonequilbrium Ising Bloch Transition in Forced Nonlocally Coupled Oscillators

We study phase and amplitude models for 2:1 resonant oscillators with nonlocal coupling and show that Ising-Bloch transition is dimmed by a regime with drifting frontal oscillators causing fluctuations of propagation direction. We show that strong nonvariational effects leading to pattern formation impede the oscillators drifting and enforce transition to a Bloch front

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PP2

How Do the Basic Reproduction Ratio (R_0) and Basic Depression Ratio (D_0) Determine the Dynamics of a System with Many Host and Many Directly Transmitted Pathogen Strains?

For an individual host strain, the pathogen strain with maximum R_0 out-competes all others and survives alone with the host at a point equilibrium. For an individual pathogen strain, the host strain with minimum D_0 behaves similarly. With many host and pathogen strains how do these criteria interact and is multi-strain co-existence possible? Furthermore, can stable cycles occur? We answer these questions using a combination of algebraic and numerical studies.

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PP2

The Evolution of Parasites in Spatially Structure Host Populations: An Approximate Analytical Approach

We use approximation techniques and simulation to examine the evolution of parasites in spatially structured populations. Trade-off shapes have important implications to the evolutionary outcome and we demonstrate that there is an ES non-maximal dispersal rate. When parasite dispersal and life-history evolves, we find that transmission and virulence are maximised. We contrast the results of the approximations and simulations and highlight the problems that small selection gradients in spatially explicit populations may cause.

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PP2

Modeling Bacterial Populations Undergoing Acid Stress

Recent outbreaks of acid resistant bacterial pathogens have raised safety concerns about a wide variety of acidified food products. A model was developed to aid in understanding acid sensitivity of bacterial cells within a bacterial cell culture. Culture growth generating subpopulations of cells with varying acid resistance was simulated using Matlab software. Data from the model may be used to develop methods that ensure the safe production of a variety of acid and acidified foods.

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PP2

Synchronization and Multistability: Predictions from Phase Models

We consider a model for a network of hippocampal interneurons based on the work of Wang and Buzsaki [J. Neurosci. 16:6402-6413, 1996]. We construct a phase model representation of the network, and show that this model can give reasonably accurate quantitative information, such as the size of basins of attraction and the maximum heterogeneity permissible in the inherent frequencies of the neurons before synchrony is lost. We show that predictions of existence and stability of phase-locked solutions from the two cell network carry over to N-cell networks, either exactly or in the limit of large N.

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PP2

Using Integral Projection Models to Explore Evolution in Complex Environments: Soay Sheep As a Case Study

The selection pressures an organism experiences over its lifetime vary as a consequence of changes in its environment (both biotic and abiotic) and its own physiology. Incorporating these complexities into models is necessary in order to make accurate predictions about the life history decisions an organism makes. Using the long term individually structured Soay Sheep dataset; we show how the recently developed integral projection model may be used to develop such life history analyses.

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PP2

Phase-LikeTransition in Escaping Behaviors of Prey Flock Induced by a Predator's Attack

A prey flock escaping from a predator was investigated by using molecular dynamics (MD) simulations in a two-dimensional model. A phase-like transition was observed at a critical attack angle in the state of the flock moving in response to predator's attack. Contribution of the variables such as attack speed and angle of the predator was further discussed with regard to tactics for efficient prey capture in the prey-predator relationships.

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PP2

Determining Environmental Conditions for the Successful in-Vitro Maturation of Mammalian Oocytes

Harvesting of immature oocytes (eggs) and successful maturation in the laboratory would be a significant breakthrough in the field of assisted reproduction. Success is believed to depend on the ability to mimic the nutritional environment that pertains within the body in the ovarian follicle surrounding the oocyte, which is difficult to determine experimentally. We describe mathematical modelling using experimental data that is aimed at increasing our understanding of the in-vivo and in-vitro oocyte environments.

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PP2

Patterns on Growing Square Domains Via Mode Interactions

We consider reaction-diffusion systems on growing square domains with Neumann boundary conditions (NBC). We study transitions between two types of squares and transitions between squares and stripes using mode interactions for bifurcation problems with D_4+T^2 symmetry (*hidden symmetries*) and the symmetry constraint imposed by NBC. We obtained surprising results: the transition from squares to stripes in NBC can go through time periodic states, and there are differences between periodic boundary conditions and NBC problems.

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PP2

Biocalculus: Interdisciplinary Course Development and Validation

Benedictine University now offers a two-semester calculus sequence for majors in the biological sciences. A new textbook and lab manual for this course is currently being developed by a team of mathematicians and biologists from Benedictine University. We will discuss the content choices and how this interdisciplinary team functions. We will also present preliminary data indicating that the biocalculus students demonstrate at least the same conceptual understanding and computational skills as the traditional calculus students.

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PP2

Mathematical Models of Glucose, Insulin and Free Fatty Acid Metabolism in Juveniles Having Irregular Exercise Regimens

Hepatic glucose regulation has been notoriously difficult to study in vivo due to the liver's role in hundreds of simultaneous metabolic processes. A theoretical mathematical model is proposed examining insulin secretion, insulin sensitivity, endogenous glucose, free fatty acids and aerobic exercise in the early development of visceral adiposity. Employing deterministic, dynamic and stochastic elements, the model elucidates metabolic syndrome pathogenesis longitudinally. Model results are validated using U.S. juvenile and adult obesity and diabetes prevalence results.

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PP2

Net Reproductive Value and Graph Reduction with Applications to Control of Invasive Species

Matrix models are widely used tool for demographic analysis of age and stage structured biological populations. Dynamic properties of the model can be summarized by the net reproductive value (R_0). Here we introduce a new method to calculate and analyze R_0 directly from the life cycle graph. We show, with examples, how our method of analysis of the R_0 can be used in the design of strategies for invasive species and conservation.

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PP2

The Effect of Life-Stage Breakdown on Basins of Attraction

A stage-structured model of two competing species has been shown to exhibit multiple attractors for a variety of parameter values. Previous work has been done on computing the basins of attraction using initial conditions where only the oldest life-stage of each species is present. Here we consider the impact on these basins of attraction of splitting the initial conditions between multiple life-stages,

while keeping the total population size fixed.

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PP2

Biomechanical Modelling of Colonic Crypt Fission

Colorectal cancer is initiated by unregulated cell division in the epithelium of the small pits (crypts) that line the colon. The crypt then deforms and divides a number of times leading to a polyp or adenoma. We examine the initiation of crypt fission using a biomechanical model incorporating both intercellular forces and the forces generated by cell attachment to and movement along the basal lamina.

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PP2

Do Albatrosses Really Perform Levy Flights When Foraging?

We examine the hypothesis that wandering albatrosses (*Diomedea exulans*) undergo Lévy flights when searching for food. Lévy flights are random walks whose step lengths come from probability distributions that have infinite variance. Lévy flights have no typical scale, and so have been interpreted as comprising an efficient foraging strategy. We re-analyse the original temporal flying/floating data that were used to infer Lévy flights, and use state-space models to examine recent spatio-temporal data from satellite-tracked birds.

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PP2

A Hyperbolic Model for Animal Group Formation and Activity Patterns

The social interactions between organisms that form groups are governed by three types of forces: attraction, repulsion and alignment. I will present a nonlocal hyperbolic model that takes into consideration all these social forces to study group formation. Linear analysis and numerical simulations are used to explore the behavior of the model, and reveal a wide range of spatial patterns. These patterns can be related to the daily activities of animal groups, such as foraging and traveling.

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PP2

Towards a General Stability Theory of Population Dynamical Models

We propose a generalized model for foodchains of arbitrary length and foodwebs to study the stability properties of the equilibrium state where all species coexist. Sudden changes in the dynamics (bifurcations) can occur when parameters are varied. The main advantage of the generalized model is that its stability can be analysed without specifying the interaction functions between species. We discuss the impact of the specific shape of the functional response on the stability properties.

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PP2

Predicting Protein Production from Codon Usage Patterns: Merging Population Genetics & Protein Translation

I demonstrate how the pattern of codon usage within a gene can be used to predict protein production rates. Using a population genetics model, I formalize the relationship between the adaptation of a sequence to nonsense errors, its expression level, and its probability of fixation. I validate the approach using several hundred yeast genes. My predictions are probabilistic in nature and coincide with independently measured values.

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PP2

Effect of Spatial Inhomogeneities on the Tubuloglomerular Feedback System

We use a simple mathematical model of rat thick ascending limb (TAL) to investigate the effects of tubular nonconstant transport rate of chloride and inner radius on TGF-mediated oscillations. Mathematical models have indicated that these regular oscillations arise from a bifurcation: if feedback loop gain is sufficiently large and if the

delay in TGF signal transmission is sufficiently long, then the stable state of the system is a regular oscillation and not a time-independent steady state. In addition, experiments have shown that the TGF system in hypertensive rats may exhibit irregular oscillations. These oscillations appear to have characteristic of deterministic chaos. The mathematical model previously devised by the group has predicted that irregular oscillations may arise from coupling of nephrons with sufficiently different bifurcation parameters. As a consequence of the new mathematical results, TAL inhomogeneities may have an remarkable impact on the TGF-mediated oscillations. In particular irregular oscillations resembling those reported by experimentalists, may arise from a bifurcation, not necessarily through nephrons coupling. This research was supported in part by NIH grant DK-42091, and by National Science Foundation under Agreement No. 0112050. Co-authors: Leon Moore, Harold Layton

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PP2

Mathematical Modeling of Plastron Respiration in Ticks (Acari: Ixodidae)

Ticks are blood-feeding arthropods that are well known for their survivability. Although ticks are terrestrial organisms, they can survive extended periods of submergence under water as for example after heavy rainfall or flooding. A plastron is a physical gill consisting of a thin layer of air trapped by hydrophobic hairs or other cuticular projections. Hence a plastron is an alternate respiration system that can absorb oxygen from water. The complex spiracular plates of ticks have been postulated to serve as plastrons but until now, this has not been verified. In this study, we confirm the existence of plastron respiration in the dog tick Dermacentor variabilis. Adult dog ticks can survive submergence in water for over two weeks. Wetting the spiracular plate with alcohol, thereby debilitating any potential plastron function lowered survival to less than three days. Biomathematical studies currently in progress are modeling the efficiency of the spiracular plate as a plastron. We have developed a mathematical model to predict survivability of submerged ticks under water. This model requires determination of a suite of physical and biological parameters including volume of the air film contained within the spiracular plate, the plastron air/water interface area and the oxygen consumption and biomass of the submerged tick. It is hoped that this model can be successfully used in the future to predict underwater survivability of other species of ticks which show both interspecific and intergeneric morphological variation in spiracular plate structure. This study provides the first example of plastron respiration in the Ixodidae.

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PP2

Ecological Interference and the Persistence of Vertically Transmitted Parasites

A model that allows a virulent vertically transmitted parasite (VTP) to be maintained in a system containing a host and a horizontally transmitted parasite (HTP) is analysed. The method of persistence relies on the VTP offering the host a level of protection through reduced transmission of the HTP. The model raises questions about persistence of diseases through interactions with others, and also the stabilising effects of VTPs on dynamical systems in a biological control context.

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PP2

A Function to Predict Sleep and Wake Patterns Using Social and Circadian Factors

Recent literature suggests bio-mathematical models of work-related fatigue could be improved by accounting for social factors impacting on sleep and recovery. Currently, accuracy of existing models in operational environments is limited in certain applications. An alternate model accounting for such factors has been developed. Initial validations have been performed using operational data. Parameter stability has also been investigated using Monte Carlo simulation analysis. The development and initial validations of this model will be discussed.

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PP2

Einstein Relation Approach to Protein Folding Dynamics

We propose a protein folding simulation approach based on energy type partition and Einstein Relations for constrained movements as the important key for understanding of protein shape change dynamics. Lagrange methods ensure that the simultaneous minimization of two or more energy forms is describable in terms of the free energies, gradients or forces. Interesting point is that a structural free energy gradient exactly balances an electrical ensemble gradient leading to an infinite mobility.

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PP2

A Reduced Differential Model for Cardiac Action

Potentials

A differential model for cardiac action potentials with only ten state variables is proposed for 0D or 3D electromechanical simulations of the heart. Three variables describe the membrane potential, the main ionic currents and two others, the Na^+/Ca^{2+} exchangers and Na^+/K^+ pumps. The remaining seven variables describe the subcellular Ca^{2+} dynamics. Simulations of action potentials of pacemaker, atrial, ventricular and Purkinje fiber cells are similar to those obtained with more complex models.

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PP2

Network Environ Analysis

Network environ analysis (NEA) uses network representation of ecological systems to identify and quantify important ecosystem properties such as dominance of indirect effects, network amplification, network homogenization and network synergism. These properties provide new insights into system level behavior of ecological networks. Using NEA, objects can be studied as part of a connected system which is a fundamentally different way of investigating ecosystems. This gives a quantitative foundation to the widely held perception of the interconnectedness of nature.

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PP2

Mathematical Modeling of Tumor Spheroid Growth

Multicellular tumor spheroids are made of three layers with different mechanical properties, i.e. proliferating outer layer, quiescent middle zone, and necrotic zone. Helmlinger et al (1997)'s experiment showed that tumor growth can be regulated by stress and that mechanical properties of the outer gel, such as stiffness, can inhibit tumor growth in vitro. Using the cell-based model on the proliferating zone, continuum model on other regions, and reaction-diffusion model for nutrients on whole domain, I investigate the stress effect on tumor growth.

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PP2

Graph-theoretic Models of the Human Hsp70 ATPase Domain

In this work we represent the Human Hsp70 ATPase domain by mathematical graphs. Graphical invariants are calculated for each model generating corresponding numerical data. The graph-theoretic models coupled with data mining tools inherently combine primary sequential information, structural information and amino acid motif recognition. Previous work by the author shows that graphical invariants such as those associated with efficient computer network designs can also be indicative of protein and nucleic acid structures. These findings initiate a similar study of the HSp70 molecular chaperone.

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PP2

Does Cannibalism Stabilize a Population?

Cannibalism occurs in a variety of taxa in nature. Forms of cannibalism can include consumption of eggs by larvae or adults and predation on smaller individuals by larger ones. Sometimes cannibalism occurs without discrimination of kin. Whatever competitive advantage this confers must be visible at the population level. We consider settings in which cannibalism is beneficial to a population.

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PP2

Dynamics of a Multistage Circadian System

Tissues throughout the body exhibit circadian rhythms, forming a multi-oscillatory system whose disruption results in jet lag. Our simulations of a multistage circadian system reveal the flexibility and stability inherent in a multistage system, as well as potential pitfalls. The modeling predicts that jet lag is most severe following an eastward change of 5-8 time zones due to prolonged desynchrony of the system caused by the antidromic reentrainment of some but not all components.

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PP2
Networks of Three-Identical Coupled Systems

We consider networks of three-identical coupled systems of ODE's, where which system has at most two couplings. We show that there are 34 distinct networks of three-identical systems, at most double coupled, as opposed to only two such two-identical coupled systems of ODE's. We also show that, remarkably, transitions from a *synchonous equilibrium* that can occur are determined by the coupling structure of the network.

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PP2
Invasions, Range Limits, and Coexistence in Rivers

Spatial patterns of community composition and species replacement in rivers emerge from complex interplays of hydrological, geochemical, biological, and ecological factors. While these processes are well understood locally, a mechanistic basis for large-scale emerging patterns is lacking. We study invasion speeds, range limits, and spatially-mediated coexistence in reaction-advection-diffusion equations for two competitors in heterogeneous environments. We show that emergent patterns have plausible spatial scales, given parameter estimates for certain algae (periphyton).

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PP2
Protecting Mobile Fish: Results from Diffusion Models

Persistence of fish populations is a key goal of many marine protected areas. I introduce a PDE model of a population which has all ages of fish moving and which has a partially protected habitat. The minimum reserve size necessary for species to persist is found for a variety of parameters and boundary conditions (including periodic). These results are compared to models where only the juveniles disperse.

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PP2
Modeling Functional Consequences of Amino Acid Replacements in Proteins

A computational mutagenesis methodology based on data obtained from a multibody statistical contact potential generates both scalar residual score and vector residual profile characterizations for every single-site mutant of a protein. With a focus on mutants for which experimental activity data is available, the residual scores enable a clear elucidation of the structure-function relationship in a protein. Additionally, the residual profiles lead to accurate inferential models of mutant protein biochemical activity relative to wild type.

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PP2
A Note on Science, Mathematics, and Applied Mathematics

Science is that human activity devoted to the search for the very explanation for (i.e., for the truth about) some particular naturally occurring phenomenon. The Scientific Method is a six-stage model-building process, one which mimes the biological process by which first genetic, then neuronal, systems have been used to construct intracorporeal models for ensuring survival. We investigate whether mathematics (pure; then applied) is either necessary or sufficient for Science, but must answer negatively each question.

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PP2
Linked Selected and Neutral Loci in a Heterogeneous Environment

We analyze a system of ODEs modeling allele frequencies at two linked genomic loci, one selected and one neutral, in an environment consisting of two habitats with divergent selection. We use geometric singular perturbation theory and formal expansions to describe the dynamics and asymptotic behavior of the system. One conclusion is that marker-selected locus associations will not generally persist long enough to allow inference of dynamics and recent history at the selected locus from the state of the marker locus.

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PP2
Chemotaxis in Fluid Flows

We study the distribution of microorganisms represented as self-propelled particles, in a fluid medium. The particles are transported by the flow and, in addition, they swim in the direction of the gradient of an external (chemical) field. We show that the combined effect of chaotic mixing and chemotaxis leads to aggregation of particles on a complex manifold. We discuss the properties of the aggregates and efficiency of chemotaxis in flows with fluctuating chemical concentrations.

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PP2
Three New R's: Random Walks, Riordan Arrays, and RNA

We use an algebraic and combinatorial technique to count two classes of random walks. It is interesting that certain subsets of the walks are counted by the numbers 1,1,1,2,4,8,17,37, ... These numbers are commonly called the RNA numbers and they also count RNA secondary structures of a specified length. A bijection is constructed between the set of RNA structures of a given length and a subset of random walks of a given length and height.

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PP2
Inferring Causal Subnetworks Using Point Process Models

If one could measure simultaneously and individually the spiking activity of all neurons in a neural network, fitting a network model to the data might reveal causal connections among the neurons. However, connections from unmeasured neurons could create the illusion of causal influence among the measured neurons. We have developed a framework that addresses effects from unmeasured neurons in order to reveal causal influence among the measured neurons. The approach exploits predictions from a point process model of the relationship between neuron spikes and external variables such as a stimulus. The resulting analysis can be potentially applied to a large range of experiments where the spikes of multiple neurons are recorded simultaneously.

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PP2
On Using Wavelets for Transient Feature Selection in Odor Detection

The performance of electronic olfaction devices is highly dependent on the quality of input signals that represent the sensors response. These units collect information about the odors they are assessing using an array of 15 or more gas sensors. Consequently, these devices have a high-dimensional input feature space which makes odor classification difficult. Here a multiresolutional approximation technique called the Discrete Wavelet Transform is employed to capture only the relevant features of the sensor array dynamics. Three families of wavelets are evaluated using three statistical and neural network classifiers (K-nearest neighbor, backpropagation, and RBF neural networks) for three odor samples (bacteria , coffee and colas). The experimental results show promising classification improvements when compared to conventional steady-state classification. Thus, higher classification accuracy and speed are obtained by using transient-feature compression with Wavelet decomposition.

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PP2
A New Approache to Identify Binding Sites

We have developed a novel approach to identify protein binding sites by analyzing triangulated protein surface representation. Atom-atom interactions are derived based on interactions of neighboring surface elements using line-of-sight intersection test. Atoms are, then, converted into nodes in a edge-weighted graph. The nodes are further analyzed using a cluster algorithm. Current implementation can identify the ion binding site of calix-4-arene and the nucleotide binding site of human Ras.

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PP2
Intra-Genomic Conflict and Evolution of Gene Silencing

Using a model of early genome evolution, we investigate the hypothesis that gene silencing originally evolved as a mechanism to protect genomes from transposable elements (TEs). We show that pressure from TE replication creates weak selection in favor of TE silencers and we explore various aspects of the selective dynamics. We show that cycles of TE activity readily develop if TEs occasionally escape from silencing, due to an "arms race" between TEs and TE silencers.

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PP2

Single-Occupancy Binding In Simple Bounded and Unbounded Systems

The number of substrate molecules that can bind to the active site of an enzyme at one time is constrained. This poster presents boundary conditions corresponding to the constraint of single occupancy binding. Two simple models of substrate molecules diffusing to a single occupancy site are considered. When the diffusive time scale is much shorter than the time scale for entering the single occupancy site, the dynamics of binding are accurately described by simple approximations.

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PP2

Haart and the Epidemic of Hiv+ End Stage Renal Disease

The number of patients with HIV infection and end stage renal disease (ESRD) continues to rise. To assess the impact of antiretroviral therapy on the progression of patients with AIDS to the development of end stage renal disease, we developed a mathematical model of HIV infection in the ESRD population using available population data. The model was then used to evaluate recent data and to project the prevalence of HIV ESRD through 2020.

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PP2

Mechanistic Model of Escherichia Coli Cell Death under Acidic Conditions

By processing acidified vegetable products, e.g. pickles, there is risk of contamination by microbial pathogen such as Escherichia coli. We have developed a mechanistic mathematical model which can be used to understand the mechanism behind the killing of these deadly bacteria. Our model predicts that killing of E. coli is due to the low levels of intracellular pH. The continued development of this model will aid in enhancing safety for acidified food production.

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PP2

Reverse Correlation and Network Architecture

Reverse-time Correlation (RTC) measurements gives the average response dynamics of individual neurons within a recurrent neuronal network. The resulting RTC function provides specific information about the nature of the recurrent network connections, and in particular, the strength of inhibition. We present a set of models that uncover and explain the connection between RTC functions and network architecture.

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PP2

Distributed and Parallel Algorithms in the Life Sciences

This presentation discusses the mathematical framework to allow distributed or parallel simulation of biological systems. Both stocastic and deterministic cases are outlined. It is expected that large-scale/ high detail computational simulation of cells, tissues and organs of the human body will speed up the development of new medical devices and treatment protocols. The lung-heart system is used as an example of how distributed/parallel simulation algorithms can be successfully deployed.

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PP2

A Computational Model for Motor Pattern Switching Between Taste-Induced Ingestion and Rejection Oromotor Behaviors

We present a computational model for activity patterns similar to taste-induced ingestion (licking) and rejection (gaping) generated in the brainstem. Single-compartment, conductance-based models are used for individual neurons; cells within the network are coupled through mutual inhibition. Using geometric dynamical systems methods, we describe conditions under which a single network configuration can produce both activity patterns. The analysis predicts that prolonged inhibition of some neurons may be

an important component responsible for this switch.

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PP2

Numerical Simulation Methods for Tissue Morphogenesis

Morphogenesis is concerned with shape formations of tissues, organs and bodies and is of fundamental importance to developmental biology and tissue engineering research. To study the mechanisms of epithelial-mesenchymal tissue interactions (e.g. branching morphogenesis) in terms of geometry and mechanical force, a two-phase Newtonian fluid model is proposed and solved numerically using the immersed interface method (IIM). Jump conditions are necessary to employ the second-order accurate finite difference scheme in the immersed interface method. Interfacial jump conditions for kinematic variables (velocity and pressure) are derived for the case where the two phases may have unequal viscosity coefficients. Our results of the jump conditions match well with existing results in the literature where the viscosity coefficients are equal across the interface. I will illustrate the local Cartesian coordinates transformation techniques used in the derivations of both the jump conditions for the fluid equations and the finite difference scheme for the IIM. The interface between the two phases is chosen to be represented implicitly using zero level sets. The implementation of the two-phase fluid solver in both 2D and 3D geometry coupled with the level set method for moving interface problems is not trivial. I will show some preliminary simulation results for modeling tissue morphogenesis using our efficient numerical solver.

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PP2

When Does Spatial Structure Matter? Sir Models Between the Local and Mean Field

We extend pair-wise spatial SI models to elucidate the effects of recovery and waning immunity. We demonstrate a loss of limit cycle behaviour, and an increase in the critical transmissibility and extinction thresholds, when recover is included. We then extend the reproduction processes of hosts and infection to include proportions of global interactions. Thus, providing intermediate structures between the local and mean-field. The evolutionary dynamics of host-parasite interactions within this intermediate case is then discussed.

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PP2

A Mathematical Model of U Wave in Electrocardiogram

U wave was first observed by Einthoven and defined as the waveform occurred immediately after T wave and before P wave. With more clinic implications, U wave can be observed in various pathological conditions, such as hypokalemia, cardiac ischemia etc. Interestingly, the origin of the U wave in ECG is still not certain. Previously, we demonstrated volatile anesthetics could suppress delayed after depolarizations and triggered activity in canine ventricular preparations. Recently, we have documented that volatile anesthetics reversibly suppress U wave in clinical patients. A mathematical model of U wave will be presented.

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PP2

Computer Modeling of Perlecan Regulation on Growth Factor Binding to Vascular Surface

Certain molecules in blood circulation such as perlecan/heparan sulfate play an important role in regulating cancer growth and cardiovascular disease development, the real mechanism, however, is still under investigation. We propose a convection-diffusion-reaction model for simulating the process of perlecan regulation. An explicit-implicit splitting technique is applied to solve the coupled nonlinear system of equations, where the chemical reaction is handled by the explicit Runge-Kutta method, while the

convection-diffusion process is treated implicitly.

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