Applied mathematics is traditionally concerned with mathematical models that arise in the physical sciences and in engineering. Such models are well established in areas of classical physics and chemistry, but are not as mature perhaps in materials science, in areas such as polymers and complex fluids. A new challenge in applied mathematics arises from the biosciences, where tremendous amounts of experimental data are currently being generated. In order to draw knowledge from these data, mathematical models need to be developed. The difficulty in developing and analyzing such models arise from the complexity of the biological processes, which flow from the molecular level to the organ level. How useful at this time are the mathematical sciences to the biosciences? In this talk I shall give you some examples from my experiences at the Mathematical Biosciences Institute.
LARRY F. ABBOTT
Volen Center for Complex Systems, Brandeis University, Waltham, MA  02454-9110

Scale-Invariant Adaptation

Neuronal responses to constant stimuli adapt so that, for example, firing rates that are high when a stimulus first appears decrease over time. Such responses are often divided into transient and sustained components, and the transition between them is modeled as an exponential decay. More careful examination, however, often reveals that adaptation is better described by a power-law function of time rather than an exponential. Because such dynamics are scale-invariant, the division of the response into transient and sustained components is ambiguous, and extracted "time constants" of adaptation depend on the duration of the experiment rather than reflecting underlying features of the dynamics. Scale-invariance has the advantage that the time scale of the adaptation matches the temporal nature of the stimuli being encountered rather than being rigidly fixed by the system. I will discuss ways of modeling and thinking about scale-invariant adaptation and examine its functional implications for sensory processing.

MARTIN GOLUBITSKY
Department of Mathematics, University of Houston, Houston, TX 77204-3008

Coupled Cell Systems: Theory and Examples

A coupled cell system is a collection of interacting dynamical systems. Coupled cell models assume that the output from each cell is important and that signals from two or more cells can be compared so that patterns of synchrony can emerge. We ask: How much of the qualitative dynamics observed in coupled cells is the result of network architecture and how much depends on the specific equations?

The ideas will be illustrated through a series of examples and three theorems. The first theorem classifies spatio-temporal symmetries of periodic solutions; the second gives necessary and sufficient conditions for synchrony in terms of network architecture; and the third shows that synchronous dynamics may itself be viewed as a coupled cell system through a quotient construction. We also show how nongeneric bifurcations with nongeneric results arise in bifurcations in coupled systems.

LEO P. KADANOFF
The James Franck Institute, The University of Chicago, 5640 South Ellis Avenue, Chicago, IL  60637

Effective Scientific Simulations

I discuss a group of computer simulations, mostly ones related to astrophysical situations. My basic question relates to the effectiveness of simulations in the generation of new scientific knowledge. Examples under consideration include studies of solar neutrino production, the early history of the universe, sonoluminescence, "cold fusion", and mechanisms for mixing in novae, supernovae, and other turbulent flows.

I point to some very successful pieces of work, and to other pieces which are quite the opposite. I argue that scientific simulations can be used either as tools for discovering new knowledge or alternatively as tools for constructing arguments about scientific or technical issues. Supported in part by the Flash Center at the University of Chicago.
**Simulating Rare Events in Lightwave Systems with Importance Sampling**

Lightwave communication systems transmit information at extremely high rates. Transmission errors are handled at slower electronic speeds, however, and thus, systems must be designed to have extremely small error rates, typically one error per 10^9 or more bits. Since overall system performance is determined by extremely rare events, the accurate modeling of such systems presents a severe mathematical and computational challenge. In this talk, recent work aimed at overcoming this difficulty will be described. In particular, the application of importance sampling (one member of a general family of variance reduction techniques) to the numerical simulation of transmission impairments induced by amplified spontaneous emission noise in soliton-based optical transmission systems will be discussed. The method allows numerical simulations to be concentrated on the noise realizations that are most likely to result in transmission errors, leading to speedups of several orders of magnitude over standard Monte Carlo methods.

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**Sound Source Location**

The problem of how an animal determines the location of a source of sound will be formulated as an inverse problem. To solve it, the ears of the animal produce the Fourier transforms of the acoustic pressure signals in the two ears. At a higher level in the brain, the difference between the phases in the two ears is formed at each frequency. Similarly the difference between the sound pressure levels at each frequency is formed. It will be explained how these interaural differences are processed to determine the direction of the source.

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**Industry-Driven Challenges in Applied Mathematics**

This talk will describe some industry-driven problems that pose interesting open questions in mathematical modelling and analysis. The topics will include:

- the dynamics of a shaped charge jet as it penetrates a target. For metal targets, it is the modelling of the elastic-plastic deformation that is crucial to the determination of the penetration depth.

- the effect of small dust particles on the flow of a cold plasma. There is an interesting analogy between the simplest continuum model for the ion velocity and the Euler equations of inviscid fluid dynamics.

- high-frequency asymptotics in the aircraft industry. One problem is that of how to incorporate localised diffraction effects into ray theory algorithms; another is that of the acoustic field generated by aircraft accelerating through sonic speed which still poses some interesting focusing problems.
JONATHAN BELL  
Department of Mathematics and Statistics, University of Maryland, Baltimore County, 1000 Hilltop Circle, Baltimore, MD 21250  
Waves of Excitation in Neural Field Models  
The neocortex is a distinctly layered, densely packed, neural structure. Thus, to consider large-scale patterns and dynamic activity, it has been reasonable to model the layers as continuum fields of excitable cells. With the increasing use of multiple electrode recordings and fMRI imaging studies, traveling waves of activity have become more important objects of study. I will discuss some recent work in existence, shape, and stability of waves of excitation in simplified neural field models. Here the neural connections are locally excitatory, distally inhibitory, and there is a single threshold for cells to achieve firing. I will then discuss ongoing work dealing with two-level firing rates, and self-organizing neural fields with neural plasticity.

ANDREW BELMONTE  
W.G. Pritchard Laboratories, Department of Mathematics, Pennsylvania State University, University Park, PA 16802  
Impact of a Solid into a Viscoelastic Micellar Fluid  
We present an experimental study of the impact of a solid sphere on the free surface of a viscoelastic worm-like micellar fluid. Spheres of various sizes and densities are dropped from different heights above the fluid surface, below which transient oscillations are observed. It is well known that entry of a solid into a Newtonian fluid is characterized by the Froude number; our measurements of sphere penetration scale with the ratio of kinetic energy to the elastic modulus of the fluid. The cavity formed by the sphere also undergoes transitions from a smooth to fractured surface texture, dependent on both the Deborah number and the ratio of gravitational force to elasticity. Analogies between this system and impact in granular materials will also be discussed.

ANDREA BERTOZZI  
Department of Mathematics, University of California at Los Angeles, 405 Hilgard Avenue, Los Angeles, CA 90095-1555  
Shocks in Driven Liquid Films  
Driven contact line problems in thin liquid films are an active area of research. The mathematical theory of shock waves has recently been shown to play an important role in our understanding of basic properties of the contact line motion. I will present the theory for two recently studied experimental systems: (1) Thermally driven films counterbalanced by gravity are described by a scalar conservation with a non-convex flux. Such systems are known to produce “undercompressive shocks” in which characteristics emerge from the shock on one side. (2) A related problem is that of particle laden flow driven by gravity. The differential settling rate of the particles with respect to the fluid results in the formation of double shock fronts which are solutions of a system of two conservation laws for the motion of the species. Comparison between theory and experiment will be discussed, along with open mathematical problems directly related to the experiments.
RICHARD BERTRAM

Department of Mathematics and Institute of Molecular Biophysics, Florida State University, Tallahassee, FL 32306

Modeling Network Interactions Between the Hypothalamus and Pituitary

The pituitary is the primary hormone-releasing gland. It contains a number of different cell types, including lactotrophs, gonadotrophs, thyrotrophs, melanotrophs, somatotrophs, and corticotrophs. These cells secrete different hormones, and each hormone has numerous cell targets in the brain and elsewhere in the body. The timing of hormone release is crucial to its function, and is controlled by the hypothalamus. This brain region is composed of nuclei that influence the pituitary cells in a variety of ways. As one might expect for a highly regulated system, there is two-way feedback between the pituitary and the hypothalamus. We will discuss our current effort to understand the network interactions involved in the regulated secretion of the hormone prolactin from pituitary lactotrophs. During the first ten days of pregnancy in rats, this hormone is secreted in a rhythmic fashion, consisting of two pulses per day. These pulses have functional significance, since pregnancy is aborted if the prolactin secretory pattern is suppressed. The model we have developed consists of coupled nonlinear delay differential equations. Model variables represent the gross activity level of neurons in two nuclei of the hypothalamus, a population of interneurons, and pituitary lactotrophs. This model is currently being used to design experiments in collaborating laboratories.

LORA BILLINGS

Department of Mathematical Sciences, Montclair State University, Upper Montclair, NJ 07043

Chaotic Desynchronization of Multi-Strain Diseases

As we become more sophisticated in our resources to fight disease, pathogens become more resilient in their means to survive. Multi-strain viruses now exhibit antibody-dependent enhancement (ADE), in which infection with a single serotype is asymptomatic, but infection with a second serotype leads to serious illness accompanied by greater infectivity. This talk will present a multi-strain model with ADE based on the dynamics of dengue in Thailand. We study the general dynamics and bifurcation structure of the system. For sufficiently small ADE, the number of infectives of each serotype synchronizes, with outbreaks occurring in phase. However, when the ADE increases past a threshold, the system becomes chaotic, and infectives of each serotype desynchronize. A thorough understanding of the dynamics is the best way to prescribe appropriate defensive measures without unintended consequences.

VICTORIA BOOTH

Department of Mathematics, University of Michigan, Ann Arbor, MI 48109-1109

Mean Theta Phase of Model CA1 Pyramidal Cell Firing Changes with Location of Synaptic Stimuli

In recordings from rat hippocampal CA1 place cells during learning and subsequent sleep episodes, Poe et al. (2000) observed changes in place cell activity during reactivation of cell firing in REM sleep. Specifically, the mean phase of place cell firing in relation to the theta rhythm membrane oscillation reversed during REM reactivation over the course of several days as the animal became familiar with the environment. Cells with place fields in an initially novel environment switched from firing near the theta rhythm peaks to firing near the theta troughs during REM while maintaining their theta peak activity during waking exploration. In a computational modeling study, we investigated neural mechanisms underlying this experience-dependent theta phase reversal by incorporating the differential in the phase of the theta rhythm drive at the two excitatory afferent pathways to CA1 and testing model CA1 cell responses to inputs at these two paths. We will discuss simulation results that show that firing in response to proximal (Schaffer collateral) synaptic
input occurs preferentially near the peaks of the theta membrane oscillation while firing in response to distal dendritic (temporo-ammonic) synaptic input occurs near the theta troughs. These results support the hypothesis that the gradual shift to theta trough firing would result from a growing potentiation of synapses in the direct, temporo-ammonic pathway while initially-potentiated Schaffer collateral synapses are depotentiated.

JARED BRONSKI
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The Periodic Modulational Instability

We consider the stability of standing wave solutions to the nonlinear Schrödinger (NLS) equation, $i\psi_t = \psi_{xx} + V(x)\psi \pm |\psi|^2 \psi$, where the potential $V(x)$ has period 1 and the standing wave solution is either periodic ($\psi(x+1,t) = \psi(x,t)$) or antiperiodic ($\psi(x+1,t) = -\psi(x,t)$). We study the Floquet spectrum of the non-self-adjoint operator governing stability. We use the Hamiltonian structure of the problem, together with some symmetries, to derive a sufficient condition for the existence of a modulational instability. In particular, we show that the stability of plane waves of the integrable NLS equation ($V=0$) is unusual, in that one typically has a modulational instability in the defocusing as well as the focusing cases. This is joint work with Zoi Rapti.

JAVIER CABRERA
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Statistical Analysis of Data from Comparative DNA Microarray Experiments

DNA microarray technology has enabled researchers in functional genomics to monitor gene expression profiles for thousands of genes at a time.

Most microarray experiments are comparative in nature. For example, suppose that we want to know which genes are expressed differently in two or more types of cells (e.g., a cancer cell and a normal cell). DNA microarray experiments will measure the expression levels of large sets of genes across the different types of cells. By comparing these expression levels, we will know which genes are differentially expressed in the two types of cells.

While these data are often analyzed via a series of t tests, it has been observed that, if the sample size per group is small (as it often is), the dependence between the t test statistic and the pooled standard error estimate leads to an excessively high false positive rate for low variance genes and an excessively high false negative rate for high variance genes. Idiosyncratic features of the data exacerbate the problem: the data are longer tailed than a Gaussian, the variability of a gene depends on its expression level, and the genes are co-dependent in clumps. We propose a model, which posits minimal distributional assumptions, and a conditional t suite of tests, which produces a critical envelope instead of a critical value, to analyze such data. The model is also generalized to statistical methods for multiple comparisons. This research was done jointly with Dhammika Amaratunga, J&J PRD.

RUSSELL CAFLISCH
Department of Mathematics, University of California Los Angeles, 405 Hilgard Avenue, Los Angeles, CA 90095-1555

Singularities in Incompressible Fluid Dynamics

Singularities can occur in incompressible fluid flow due to amplification of vorticity along a fluid interface and possibly in the interior of the flow. This talk will discuss results on singularity formation for a variety of different fluid flows and the physical significance of these results.
Electromagnetic Inverse Scattering for a Buried Object

We are concerned with the problem of determining the shape of an obstacle embedded in a known inhomogeneous background from a knowledge of the scattered electric and magnetic fields measured on a given surface.

Our contribution is to present a method for solving this problem that
1. avoids the need for any a priori knowledge of the physical properties of the scattering object.
2. avoids the need to compute the Green’s function for the background media.

The method is a combination of the linear sampling method with the gap reciprocity functional. Like the linear sampling method, our method is based on the characterization of the boundary of the scattering object by the solution of a linear integral equation that is set up independently of the physical properties of the object. But, since we are making use of both the (measured) electric and magnetic fields as our data, we can avoid the need to know the Green’s function of the background media.

Numerical examples will be presented showing the performance of our method. This research is joint work with Houssem Haddar and M’Barek Fares from INRIA, Paris.

Semiparametric Maximum Likelihood Estimation Exploiting Gene-Environment Independence in Case-Control Studies

We consider the problem of maximum-likelihood estimation in case-control studies of gene-environment associations with disease when genetic and environmental exposures can be assumed to be independent in the underlying population. Traditional logistic regression analysis may not be efficient in this setting. We study the semiparametric maximum likelihood estimators of logistic regression parameters that exploit the gene-environment independence assumption and leave the distribution of the environmental exposures to be nonparametric. We use a profile-likelihood technique to derive a simple algorithm for obtaining the estimator and study the asymptotic theory. The results are extended to situations where genetic and environmental factors are independent, conditional on some other factors. Simulation studies investigate small sample properties. The method is illustrated using data from a case-control study designed to investigate the interplay of BRCA1/2 mutations and oral contraceptive use in the aetiology of ovarian cancer.

Flapping Flight as a Bifurcation in Frequency Reynolds Number

We describe observations of swimming by a swimming mollusc which suggest that the small wings used by it in “forward flight” become effective for forward motion only above a critical Reynolds number based upon flapping frequency. Models for this bifurcation are developed. We also describe experiments and computations carried out in the Courant Applied Mathematics Laboratory, involving a freely flapping blade, which elaborate the nature of the bifurcation. A new experiment utilizing a small passive flapper in an oscillating airflow suggests a similar bifurcation to hovering flight.
Zheng, Wise, and Cristini, Bulletin of Mathematical Biology (2005) developed a multiscale, two-dimensional tumor simulator with the capability of showing tumoral lesion progression through the stages of diffusion-limited dormancy, neo-vascularization (angiogenesis) and consequent rapid growth and tissue invasion. In this paper, we extend their simulator to describe delivery of chemotherapeutic drugs to a highly perfused tumoral lesion and the tumor cells' response to the therapy. We perform 2-D simulations based on a rigorous parameter estimation that demonstrate fundamental convective and diffusive transport limitations in delivering anticancer drug into tumors, whether this delivery is via free drug administration (e.g., intravenous drip), or via 100 nm nanoparticles injected into the bloodstream, and releasing the drug that then diffuses into the tumoral tissue, or via smaller 1-10 nm nanoparticles that are capable of diffusing directly and targeting the individual tumor cell. Even in a best-case scenario involving: constant ("smart") drug release from the nanoparticles; a homogenous tumor of one cell type, which is drug-sensitive and does not develop resistance; targeted nanoparticle delivery, with resulting low host tissue toxicity; and for model parameters calibrated to ensure sufficient drug or nanoparticle blood concentration to rapidly kill all cells in vitro; our analysis shows that fundamental transport limitations are severe and that drug levels inside the tumor are far less than in vitro, leaving large parts of the tumor with inadequate drug concentration. A comparison of cell death rates predicted by our simulations reveals that the in vivo rate of tumor shrinkage is several orders of magnitude less than in vitro for equal chemotherapeutic carrier concentrations in the blood serum and in vitro, and after some shrinkage the tumor may achieve a new mass equilibrium far above detectable levels. We also demonstrate that adjuvant anti-angiogenic therapy "normalizing" the vasculature may ameliorate transport limitations, although leading to unwanted tumor fragmentation. Finally, our results suggest that small nanoparticles equipped with active transport mechanisms (e.g., chemotaxis) would overcome the predicted limitations and result in improved tumor response. This study is published in Sinek, Frieboes, Zheng, and Cristini, Biomedical Microdevices (2004).

Modeling of, and the resultant predictions and comparison with experiment for, flow of worm-like micellar solutions is presented. Worm-like micelles are self-assembling very long cylindrical structures composed of amphiphilic surfactant molecules. The resultant flexible structures can entangle and thus behave much like polymers in solution, but in addition they break and reform; thus, they are referred to as 'living polymers'. The microstructure affects the macroscopic flow properties and vice versa. Both a “bead-spring” model (valid for dilute solutions) and a network model (valid for concentrated solutions) are discussed. Through a mesoscale bead-spring description a coupled stress/density model for the flow of micellar solutions is presented. The coupled nonlinear partial differential equation macroscale model comes from a mesoscale derivation which systematically includes finite extent of the bead-spring and slippage/tumbling of the bead-spring. The non-affine motion is related to micellar break-up. Numerical results for cylindrical Taylor-Couette flow are presented. The stress/strain-rate curve exhibits a plateau as observed in experiments, and as well shear banding is predicted both in velocity gradients and in the alignment/orientation of the bead-springs. Future work involving extensional flows and network models is discussed. Joint work with Gareth McKinley (MIT) and Lou Rossi and Paula Vasquez (University of Delaware). This work was supported by an NSF-DMS grant.