



Table of Contents

Preface

Summary Article

Individual Contributions

Statistics as the information science

Statistical issues for databases, the internet, and experimental data

Mathematics in image processing, computer graphics, and computer vision

Future challenges in analysis

Getting inspiration from electrical engineering and computer graphics to develop interesting new mathematics

Research opportunities in nonlinear partial differential equations

Risk assessment for the solutions of partial differential equations

Discrete mathematics for information technology

Random matrix theory, quantum physics, and analytic number theory

Mathematics in materials science

Mathematical biology: analysis at multiple scales

Number Theory and its Connections to Geometry and Analysis

Revealing hidden values: inverse problems in science and industry

Complex stochastic models for perception and inference

Model theory and tame mathematics

Beyond flatland: the future of space

Mathematical Biology: Analysis at Multiple Scales

N. KOPELL, G. OSTER AND S. LEVIN

The three topics discussed below reflect three levels of organization in which mathematics can play a significant role and in which it is already having an important impact. The first deals with scales so small that there is no distinction between physics and chemistry. The second deals with systems-level neurobiology and cardiology, with issues that concern multi-cellular tissues. The final one concerns ecology and the environment, in which the interactions are among populations of organisms and their environmental context. All of the fields share some common issues: they deal with extremely complicated phenomena, in which descriptions that are as detailed as current knowledge allows are not conceptually or computationally tractable. Thus, the mathematical issues include the development of algorithms for faster computation, but they also include the very large challenges of finding smaller descriptions that capture the essential features of the systems in question, and working to scale up the insights to more complicated situations. This requires analysis as well as computation.

1. MOLECULAR MOTORS

Cells move, and within every cell is an immensely complicated network of moving parts: organelles, vesicles, filaments forming and dissolving, all in ceaseless motion, apparently chaotic, but exquisitely coordinated. All these movements are driven by molecular motors, and so their proper regulation and functioning is as vital to the functioning of a cell as is DNA. Indeed, the replication and transcription of DNA itself is orchestrated by molecular motors. These molecular engines are proteins that are specialized to generate mechanical forces. Examples include the "walking motors" myosin, dynein, and kinesin; rotary motors such as the bacterial flagellar motor and DNA helicase; and the actin polymerization motor that drives the propulsion of many bacterial pathogens. Walker and Boyer won the 1996 Nobel prize for the elucidation of the structure and biochemistry of the rotary motor ATP synthase.

The study of molecular motors, in all their variety, is one of the "hot" fields in cell biology. This is because recent technical advances have made it possible to make chemical and mechanical measurements on single molecules, rather than moles of molecules. This has given birth to a new field of inquiry: single molecule mechanochemistry. Accompanying these developments is renewed interest in mathematical modeling of single molecule biophysics and biochemistry. This in turn has led to advances in stochastic modeling techniques and numerical algorithms. The goal of these models is to provide a unified picture of the operating principles of these molecular machines: their coordinated mechanics and chemistry. The mechanics of single molecules can be modeled at several levels of organization. The most complete depiction involves molecular dynamics simulations using Langevin equations to represent each atom in the protein. This requires great computational effort, and is limited to time spans of a few picoseconds, far too short to capture the mechanical motions relevant to their function. Therefore, the most productive approach to modeling single molecule mechanochemistry has been to take a more "mesoscopic" viewpoint and describe the motions of single proteins using stochastic differential equations describing a few collective coordinates. These mechanical models must be coupled to the biochemistry. For such systems, numerical schemes have been developed that are both efficient and that guarantee that physical constraints such as detailed balance are obeyed.

All studies to date have tried to represent protein motions by a few geometrical coordinates. A major obstacle to more detailed modeling that takes into account

and time

Mathematics in
molecular biology
and medicine

The year 2000 in
geometry and
topology

Computations and
numerical
simulations

Numbers, insights
and pictures: using
mathematics and
computing to
understand
mathematical
models

List of Contributors
with Affiliations

more internal variables and protein structure is the need to integrate multidimensional stochastic equations. For example, a protein with but three internal geometrical coordinates and four kinetic states requires solution of hundreds of simultaneous equations, depending on the resolution required to compare with experiments. Of course, faster computers help, but better computational algorithms as well as clever new approaches to stochastic modeling of collective behaviors are necessary.

2. EXCITABLE MEDIA IN NEUROBIOLOGY AND CARDIOLOGY

One of the most important current scientific problems is to understand how the brain functions; in this challenge, there is almost unbounded opportunity for contributions from mathematics. Electrical activity in the nervous system, muscles and the heart are governed by related equations that describe how voltage changes across the cell membrane. The set of equations describing this activity in the nervous system are the so-called Hodgkin-Huxley equations, for which Hodgkin and Huxley received the Nobel prize half a century ago. These are actually a class of equations with some common properties, and serve as a mathematical framework in much the same way as the Navier-Stokes equations do in fluid mechanics. The full equations are highly nonlinear partial differential equations; by ignoring the effects of the spatial extent of individual neurons, they can be treated as ordinary differential equations.

One goal of the mathematical work is to understand the origin of the electrical activity in the nervous system as a consequence of the structured input to the brain and the natural dynamics of the cells and networks of cells. This information is then used to look for clues about why the dynamics is important to function. This is an enormous advance from earlier approaches, in which only the rates of neurons were thought to be important. One class of temporal patterns believed to be associated with sensory processing and cognitive states, as well as motor behavior, is the class of rhythmic patterns. Though rhythms in the nervous system have been known for almost a century, it is only recently that analysis and simulation have begun to reveal the subtlety of how cellular dynamics affect the ability of networks of neurons to create spatio-temporal patterns, and how neuromodulators can reshape or totally change these patterns. There is growing evidence that pathologies in motor or sensory patterns are associated with a wide variety of diseases, and a deeper understanding of the changes associated with the pathological dynamics can open new avenues for intervention.

Recent advances in experimental technique now allow the acquisition of data that can reveal these patterns, either in reduced preparations or in intact animals engaged in a variety of tasks. A major challenge is now to document how the spatio-temporal dynamics change in task-related contexts in different parts of the brain, and to use modeling and analysis to understand how the inputs from the senses get filtered and reshaped as they pass through many levels of processing. Dynamical systems provide an excellent framework for posing and addressing specific questions on this topic. The current framework needs to be extended to include various kinds of noise in highly nonlinear systems. Other mathematical techniques that are relevant come from probability and statistics, for example in decoding data that come from imaging techniques (fMRI, EEG, MEG); there are major questions about how to constrain the ill-posed inverse problems of decoding this data. So far, there has been essentially no work that puts together the insights from the statistical and dynamical systems approaches.

A closely related set of mathematical issues arises in the context of cardiology, since the equations governing the electrical activity of the heart muscle are very similar to the Hodgkin-Huxley equations. In this area, a central question concerns spatio-temporal patterns that are associated with potentially fatal heart fibrillation. Mathematics has been used to study how properties of the heart tissue allow the formation of these patterns, and what sorts of interventions might stop them. The mathematics includes ideas from topology as well as nonlinear partial differential equations, and the heart patterns have given rise to an active mathematical field that looks at pattern formation in chemical systems as well as biological ones.

3. ECOLOGY AND THE ENVIRONMENT

Ecology is a more mature area of mathematical biology, with a classical tradition that goes back to Volterra. Much of the early work in this area was associated with fairly simple equations that could be shown to have the kind of macroscopic dynamics one saw in the data. Currently, the field has turned to much more complex descriptions for two reasons: First, ecological research has become global, and there is a need to confront multiple scales in space and time, as well

as organizational complexity. The issues, as in neurobiology, include sorting out the relative roles of the ability to self-organize in space and time with the forcing that comes from outside the part of the system being studied. Secondly, as in the above cases, there are new tools, notably the existence of high-speed computation for doing stochastic, individual-based or microscopic simulations, from which macroscopic behavior emerges from the collective dynamics of huge numbers of individual elements. This allows many new questions to be addressed. The settings in which questions that are related to such emergent behavior are large and growing. In addition to ecological and evolutionary questions, they include the dynamics of interacting diseases, such as new and emerging pandemics, in which independent considerations at the levels of individuals, groups, cities, nations and even species must be integrated across multiple scales. The human immunological system presents similar challenges.

Mathematical tools are proving invaluable in understanding how to manage Earth's dwindling resources and to preserve the life support systems on which humanity depends. A problem of central interest is the relationship between biodiversity and ecosystem functioning, and the sustainability of the biosphere. To the extent that Earth's systems exhibit homeostasis and resiliency, those features arise from the collective behaviors of uncountable individuals. Patterns of resource use occur within a complex socio-economical context, creating a highly nonlinear dynamical system whose macroscopic features emerge from the collective selfish agendas of billions of humans. The biosphere and linked human societies represent complex adaptive systems, whose dynamics reflect the interplay between deterministic components and historical accidents. To understand how to preserve Earth's resources, we must learn how to scale from the small to the large, from the individual to the biosphere, and to simplify complex representations that incorporate a multiplicity of individual behaviors. The effort to simplify and scale is leading to advances using a variety of techniques from mathematics. These include renormalization, moment closure, Eulerian representation of Lagrangian descriptions, and the extraction of hydrodynamic limits of spatial stochastic processes.

Last Modified:
Oct 17, 2001

[Previous page](#) | [Top of this page](#) | [Next page](#)

[Policies and
Important Links](#)

| [Privacy](#)

| [FOIA](#)

| [Help](#)

| [Contact
NSF](#)

| [Contact Web
Master](#)

| [SiteMap](#)



The National Science Foundation, 4201 Wilson Boulevard, Arlington, Virginia 22230,
USA

Tel: (703) 292-5111, FIRS: (800) 877-8339 | TDD: (800) 281-8749

Last Updated:
10/17/01
[Text Only](#)