An Introduction to Mathematical Modeling in Physiology, Cell Biology, and Immunology

American Mathematical Society Short Course
January 8–9, 2001
New Orleans, Louisiana

James Sneyd
Editor
AMS SHORT COURSE LECTURE NOTES
Introductory Survey Lectures
published as a subseries of
Proceedings of Symposia in Applied Mathematics
Proceedings of Symposia in Applied Mathematics

Volume 59

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p. cm. — (Proceedings of symposia in applied mathematics, ISSN 0160-7634 ; v. 59. AMS short course lecture notes)
Includes bibliographical references and index.
ISBN 0-8218-2816-9 (alk. paper)

Library of Congress Cataloging-in-Publication Data
p. cm. — (Proceedings of symposia in applied mathematics, ISSN 0160-7634 ; v. 59. AMS short course lecture notes)
Includes bibliographical references and index.
ISBN 0-8218-2816-9 (alk. paper)

2000 Mathematics Subject Classification. Primary 92C05, 92C20, 92C30, 92C37; Secondary 92D10, 92D30.

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Introduction

In the past few years there has been such a tremendous explosion of interest in mathematical biology that one could claim, without undue exaggeration, that biology is now one of the principal sources of mathematical applications. Spurred on in large part by advances in computing power, biological applications have reached deep into almost every traditional area of mathematics, and research in the generic field of mathematical biology is now so broad and vast that it has itself splintered into a multitude of separate sub-disciplines.

However, although mathematical biology has tremendous vitality and energy, there are still substantial barriers to any mathematician wishing to enter the field. Firstly, research in mathematical biology is done along very different lines than is most other mathematical research, as it is judged entirely on the quality of the science, not on the complexity or elegance of the mathematics involved. This requires not only a rather different mindset from the mathematician, but also from that mathematician’s colleagues, who may be sitting on review or promotion committees. Secondly, it requires a substantial investment in time to learn the biological vocabulary and facts, and to establish collaborations with experimentalists. The personal skills necessary to work with a group of experimentalists, each with their own agenda and opinions, are not always those fostered by a degree in mathematics.

Breaking down these barriers is to the benefit of all mathematicians, as the close involvement of mathematics in the biological sciences greatly enriches both disciplines. In addition (to raise more mercenary points) such interdisciplinary efforts tend to be highly regarded by funding agencies and academic administrations.

The goal of this volume is to present a selected number of topics in mathematical biology to a mathematical audience. It aims to show how research in the field is done, what kind of mathematics is used, how one might best enter the field, what the outstanding questions are, as well as a brief historical survey of each topic so as to put current research into perspective. Because mathematical biology is such a huge field, ranging from studies of individual molecules such as DNA, to the study of entire populations, it is simply not possible to provide an overview of the entire field in a single volume. Thus, this volume consists of a series of talks covering a relatively restricted range of topics, with greater coverage of one topic, that of excitable cell physiology.

Electrically excitable cells form the basis of all neuronal activity and muscular contraction, and for this reason they have been a subject of intense investigation for well over a hundred years. Fortunately, because of the electrical nature of the cellular activity, it is possible to make experimental measurements with high
accuracy and reproducibility, a fact that makes them ideal for mathematical investigation. Thus, it is in the study of electrically excitable cells that mathematics and physiology have traditionally had their closest links.

The opening chapter of this volume provides an introduction to the mathematics of electrically excitable cells. It discusses the basic theories of the action potential, including the Hodgkin-Huxley equations and the Morris-Lecar model. It provides the first glimpse of the complex types of oscillations found in various neurons, and of the complexities to be expected when individual neurons are connected to one another by synapses.

In the second chapter we delve into the visual system in more depth. This, again, involves the study of neurons, but this time in a different context from the previous chapter, and with a more specific physiological focus. This chapter discusses basic theories of edge detection, receptive fields, light adaptation, and orientation detection, including an overview of the structure of the visual system.

Muscle cells are a particular kind of electrically excitable cell, one designed to convert an electrical signal to a force. Thus their physiology is similar in many respects to that of other excitable cells, but the context is very different, and the mathematics has a different flavour. An understanding of the electrical properties of cardiac muscle is crucial for our understanding of what causes the heart to fail, an occurrence which kills millions of people every year. In the third chapter we discuss how we may use mathematics to study and understand cardiac arrhythmias.

The fourth chapter appears to digress somewhat from this overall theme of excitability, discussing as it does the dynamics of calcium inside cells which are, in general, not electrically excitable. This divergence, however, is less great than it might appear at first, as intracellular calcium homeostasis depends on the phenomenon of calcium excitability, as opposed to electrical excitability. The mathematical equations are similar to those of electrical excitability, but, once again, the context and physiology are quite different. The study of calcium dynamics is one of the most recent of the topics discussed in this volume, being only about eleven or twelve years old. It is a fine example of how new physiological observations can be understood, at least in part, by appealing to a more general mathematical theory that was developed in a different physiological context.

With those four chapters we leave the overview of the modelling of excitable cells, and their applications to physiological problems, and move on to a wider range of topics. From a very long list of possible topics we have chosen to discuss two that represent highly important areas of mathematical biology, areas in which there are already many mathematicians working.

The first topic, human genetics, involves modelling on a level rather more macroscopic than that of an individual cell, being concerned instead with the genetic properties of entire populations. In addition, the mathematics used is of a different kind, with much more of a probability flavour. The particular topic presented, that of modeling the dynamics of genetic diseases in isolated populations, is an example of how analytical and numerical approaches can be combined to study large real-world data sets.

Finally, we discuss some models in immunology, particularly models of the HIV virus. For obvious reasons there is a tremendous amount of experimental and theoretical work being performed in this area. Our chapter highlights the (often overlooked) fact that very simple mathematical models can be used to great effect. As we show, even the simplest of mathematical models, when combined
with experimental data, can be used to obtain results that, in hindsight, should have been obvious, but, without the model, rarely are.

Despite the breadth of this volume, the vast majority of mathematical biology remains unaddressed here. Our aim is merely to show how, in the few areas considered here, mathematics has played an important role in the study of a biological problem. In many respects, biology is the new frontier for applied mathematicians. We hope that the demonstration of how mathematics can be usefully used in biology will encourage yet more mathematicians to join our ranks.

James Sneyd
University of Auckland
New Zealand
August 2002
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