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Mathematical Biology
An Introduction with Maple and Matlab

Second Edition

Springer

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Preface

Biology is a source of fascination for most scientists, whether their training is in the life sciences or not. In particular, there is a special satisfaction in discovering an understanding of biology in the context of another science like mathematics. Fortunately there are plenty of interesting problems (and fun) in biology, and virtually all scientific disciplines have become the richer for it. For example, two major journals, *Mathematical Biosciences* and *Journal of Mathematical Biology*, have tripled in size since their inceptions 20–25 years ago.

More recently, the advent of genomics has spawned whole new fields of study in the biosciences, fields such as proteomics, comparative genomics, genomic medicine, pharmacogenomics, and structural genomics among them. These new disciplines are as much mathematical as biological.

The various sciences have a great deal to give to one another, but there are still too many fences separating them. In writing this book we have adopted the philosophy that mathematical biology is not merely the intrusion of one science into another, but that it has a unity of its own, in which both biology and mathematics should be equal, complete, and flow smoothly into and out of one another. There is a timeliness in calculating a protocol for administering a drug. Likewise, the significance of bones being "sinks" for lead accumulation while bonemeal is being sold as a dietary calcium supplement adds new meaning to mathematics as a *life science*. The dynamics of a compartmentalized system are classical; applications to biology can be novel. Exponential and logistic population growths are standard studies; the delay in the increase of AIDS cases behind the increase in the HIV-positive population is provocative.

With these ideas in mind we decided that our book would have to possess several important features. For example, it would have to be *understandable to students of either biology or mathematics*, the latter referring to any science students who normally take more than two years of calculus, i.e., majors in mathematics, physics, chemistry, and engineering.

A prime objective of this text is to introduce students of mathematics to the interesting mathematical problems and future challenges in biology.

No prior study of biology would be necessary.

Mathematics students rarely take biology as part of their degree programs, but our experience has been that very rapid progress is possible once a foundation has been laid. Thus the *coverage of biology would be extensive*, considerably more than actually needed to put the mathematics of the book into context. This would permit mathematics students to have much greater latitude in subsequent studies, especially in the "what-if" applications of a computer algebra system. It would also help to satisfy the intense intellectual interest that mathematics students have in the life sciences, as has been manifested in our classes.

Genomics is proving that mathematics is as much a part of biology as it is of physics. We urge biology students to equip themselves with two years' study of mathematics that includes calculus with linear algebra, differential equations, and some discrete mathematics. For the student with one year's study of calculus with linear algebra, we can say that our exposition of mathematics beyond that level is complete and self-contained. Thus we offer a focused expansion of your mathematical knowledge. Our biology students have had no problems with this approach.

We have divided the book into three parts:

Part I: Cells, Signals, Growth, and Populations;
Part II: Systems and Diseases;
Part III: Genomics.

One reason for this is that the mathematics of genomics is more abstract and advanced. *Moreover, an objective of this text is to introduce both biology and mathematics students to the new field of algebraic statistics*.

To help ease the burden of coping with the mathematics of the book we offer a chapter, Mathtools, dedicated as a refresher or an introduction to the mathematics needed for Parts I and II. At the same time, this chapter serves as a tutorial for the two computer systems, MAPLE and MATLAB that we use to accompany the mathematical derivations. All the computer syntax for the remainder of the text is illustrated here. In order to make this more useful, we construct a "code index," preceding the usual term index, that shows on which page of the text various code techniques are used.

Every chapter should have "mathematical laboratory biology experiments."

This is another important goal of the text. It is the computer algebra system that makes the mathematics accessible to nonmathematicians. More than that, powerful mathematical software essentially allows for interactive experimentation with biological models. These systems incorporate hundreds of mathematical techniques and algorithms and perform all the laborious and time-consuming calculations in seconds.

Once a biological system has been modeled, one can then perform "biology" experiments on the model using the computer algebra system. Often these are

experiments that could not be done easily on the real system, such as ascertaining the long-term effects of lead ingestion or the effect of reduced sodium conductance to an action potential. Of course one should always be aware that the real biology is the final arbiter of any such experiment. This hands-on approach provides a rich source of information through the use of "what-if" input and thus allows students to grasp important biological and mathematical concepts in a way that is not possible otherwise.

A note about these exercises/experiments. We start out at the beginning in Chapter 2 with very simple and basic computer algebra commands and progress to more elaborate ones later in the book. By means of line-by-line comments we encourage the student to learn how to master the software and use it as a powerful tool. In this spirit, we also provide a "code index" as mentioned above. Even so, this book is not about programming. At the end of each modeling section, we may ask that the student perform computational experiments on the mathematical models developed in the section. The computer syntax provided there can be downloaded and used for this purpose. The websites are

www.springer.com/978-0-387-70983-3,
www.math.gatech.edu/˜herod,
www.math.gatech.edu/˜shenk.

At other times, we ask the student to construct, investigate, and report on a model similar to or an extension of one in the section. Generally, we provide the necessary computer code. It might seem that it is only necessary to download the code from our webpage and press the return key a few times. But in fact, the science is in observing and interpreting the computed results, and in going beyond that by posing questions about the phenomenon that may or may not be answerable by the model.

Most importantly, the biology and mathematics would be integrated.

Each chapter deals with a major topic, such as lead poisoning, and we begin by presenting a thorough foundation of fundamental biology. This leads into a discussion of a related mathematical concept and its elucidation with the computer algebra system. Thus for each major topic, the biology and the mathematics are combined into an integrated whole.

To summarize, we hope that mathematics students will look at this book as a way to learn enough biology to make good models and that biology students will see it as an opportunity to understand the dynamics of a biological system. For both these students and their engineering classmates, perhaps this book can present a new perspective for a life's work.

In teaching the material ourselves, we usually spend a week (three class periods) per chapter. On the first day we discuss the biology of the chapter, and on the second we talk about the mathematics and derivations. The third day is "lab" day, in which the students attempt the assigned exercises/experiments. This may be performed in an actual computer laboratory where help with MAPLE or MATLAB is available. Also, students can break up into small groups and work together; preferably the group

memberships should change every week. Some of the derivations in the text are involved. We include them for completeness and for the interested student. The one day we spend in class on the derivations is tailored to the level of mathematical depth we think is appropriate.

Acknowledgments

We are deeply indebted to Professor Edward Yeargers for allowing us to use the biology material he wrote for our earlier book, *An Introduction to the Mathematics of Biology*. Now in retirement but still the consumate teacher, Professor Yeargers wished us well in this new endeavor and expressed satisfaction that his pedagogical influence might reach a new generation of students.

We also wish to thank Ann Kostant, who communicated to us the greatest enthusiasm and encouragement for a major expansion of our earlier work to incorporate topics in the new and burgeoning field of genomics. And we would like to thank John Spiegelman for his monumental effort and high-quality results at preparing the tables and figures and reformatting the computer codes. Of course, since we reviewed the syntax carefully before going to press, any errors therein are ours alone.

Finally, we give a special thanks to our students, who show an abiding interest in the material and ask insightful and thought-provoking questions. Some of them keep in touch after having entered and established themselves in a career in this or some related field. Ultimately, it is for them that our effort is sustained.

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Contents