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Introduction

Mathematical biology is, broadly speaking, the use of mathematics to study how biological objects do what they do. And what they do is characterized by change. If nothing is changing it is not alive. For any living organism, dormant seeds notwithstanding, there is always something that is changing. Something is being created and something is being destroyed. And when a living organism dies, it does not stop changing quite yet, but the change is characterized by degradation, as complex molecules and structures that required energy and specialized information to construct, degrade and deteriorate.

What this means is that life must be thought of as a *process* and to understand what is happening, one must think about how to describe processes and things that are changing. That is why to begin the study of how to use mathematics to study biology, it makes sense to talk about change, that is, objects or collections of objects that vary in time and are created or destroyed and to study these using dynamical descriptions. The natural mathematical language for this is the language of differential and/or difference equations where the natural independent variable is time. Indeed, there are a number of excellent books that introduce their readers to mathematical biology using the language of time varying dynamical systems. There is a lot of insight that can be gained from these studies of dynamical descriptions of biological processes. (For example, [**2**][**3**][**8**][**11**][**15**][**16**][**18**][**50**].)

However, this perspective is limited when it comes to understanding most real biological situations, because biological objects are essentially *never* homogeneously distributed in space, or well-mixed, even in a test tube or on a Petrie dish, let alone inside the human body or on a mountain slope. In fact, it is a primary feature of biological objects that there are spatial differences and correspondingly movement of objects from one place to another. So, whether one is studying the spread of an infectious disease or an invasive species, or the movement of an electrical signal along a nerve axon, it is crucially important to include the effects of spatial differences.

The ultimate goal of this book, then, is to use mathematics to begin to tell the story of how biological objects do what they do, such as communicate, make structures, make measurements and decisions, search for food, etc., all things necessary for survival. But this story can be told using mathematics only if certain mathematical tools are understood. The first of these tools is mathematical modeling, i.e., the ability to turn a verbal description of some process into quantifiable terms and equations that can be studied. Back in the day, when I was still a student, we called these word problems. Second, because we are dealing with processes that evolve in both space and time, we use multivariable dynamical systems. Consequently, a subplot of this story is the study of partial differential equations, primarily diffusion reaction equations. So part of what is hoped for this text is that it will expand your mathematical toolbox to include multivariable differential equations, i.e., partial differential equations and their approximations.

There are two broad areas of biology that are discussed here, namely population level and cellular level, i.e., physiology. Biology at the population level is relatively easy to discuss because it does not require an extensive biological background to understand the issues involved. Many of the issues involved are part of our everyday experience, or at least our internet newsfeed reading. For this reason population level modeling is a popular entry point for mathematical biology modeling. However, the models that are used tend to be highly qualitative and difficult to use to make specific quantitative predictions or observations. Cell biology and physiology, on the other hand, require more biological background, but have the advantage that the mechanisms involved are much more readily quantifiable and testable, lending themselves to more specific and detailed predictions and observations. In my experience, very few mathematics students have had an introduction to cell biology, and so processes at the cellular level are less familiar to them. My hope is that these topics are presented in a way that a person with only a modest background of biology can understand. (Or, consult Wikipedia or [**35**] when my introductions here are lacking.) It is useful, but not absolutely necessary, to have studied more introductory mathematical biology material.

This book is intended for an advanced undergraduate audience, with no previous background in partial differential equations, although beginning graduate students should also find this useful. Prerequisites for this exploration include multivariable calculus, ordinary differential equations and basic aspects of probability theory and stochastic processes. However, to make sure that we are all on the same page, Chapter one is devoted to a quick review or introduction of these topics. So, in Chapter one, you will find summaries of the mathematical background that is needed from multivariable calculus, from ordinary differential equations, and from probability theory, stochastic processes and stochastic simulations, because these are used a lot.

Since understanding the solutions of partial differential equations is generally rather difficult, and analytical approaches are quite limited, numerical simulation is a must. Consequently, this material is presented from a heavily computational perspective, using Matlab to compute solutions and to make plots. So, in the Appendix A you will find a primer for Matlab and a list of all of the Matlab codes that were used for the simulations and to make the plots. All of these codes are available for download at

`http://www.math.utah.edu/~keener/books/Ugrad_PDE/matlab_codes/`

The hope is that these codes can be readily used and easily modified for Exercises and projects, and that this will facilitate the process of hands-on learning to understand this material.

The content of the book is organized pedagogically around mathematical material, starting simply and adding mathematical complexity as we proceed. We start with basic diffusion processes, then move to diffusion with reaction, then to advection with reaction, then advection with diffusion, and finally combinations of all three advection, diffusion and reaction. However, all of the equations studied here are derived with specific biological processes in mind. Specifically, the first ten chapters of this text each introduce new mathematical ideas or techniques, while chapters 11 through 14 do not introduce any new mathematics but use what has been described earlier to study interesting and important biological processes.

The specific content of the book is as follows: As already described, Chapter one contains an introduction/review of the three main tools that are used extensively in this book. These are multivariable calculus, the qualitative theory of ordinary differential equations (especially phase plane analysis) and stochastic processes and their simulation. Chapter two introduces the main tool of mathematical modeling, namely, counting, or more formally, conservation laws and how to write equations that keep track of things. In Chapters 3, 4, and 5, we describe diffusion, derivations of diffusion equations, simulation of diffusion processes, and solution techniques for equations describing diffusion. In Chapter 6, we begin to include what happens when there are chemical reactions as well as diffusion, focussing on Fisher's equation for the spread of a growing, but limited population. Here we include discussion of populations whose dynamics are similar to those of Fishers's equation, including sustainability on an animal preserve, spatial spread of an epidemic, glucose consumption by bacteria in a Petrie dish, the spread of rabies in foxes in England, and the role of myoglobin in enhancing the delivery of oxygen to muscle tissue. Then, in Chapter 7, we introduce the bistable equation, with four examples of dynamics (spread of spruce budworm in northeastern forests, spread of *wolbachia* infection in mosquitoes, spread of the electrical action potential in nerve axons, and spread of calcium release in frog eggs following fertilization) whose mathematical description is that of the bistable equation. This chapter illustrates my long-held belief in the importance of transferable principles. That is, it is often the case as illustrated here that processes transpire according to the same principles and therefore their mathematical descriptions have common features that can inform each other even though the vocabulary describing the details is vastly different. Chapter 8 provides a study of the bistable equation, and examples of propagation of signals via travelling waves, as well as causes for propagation failure. Some of these are spatial inhomogeneities in the medium, including damage to neurons from traumatic brain injury, or effects from the discrete nature of the medium, such as in cardiac tissue or calcium release sites in muscle cells. Chapter 9 introduces advection-reaction equations and the important technique of the method of characteristics. Some of the problems included here include the dynamics of age-structured epidemics, dynamics of red blood cell production, the counter-current mechanism for delivery of oxygen to muscle tissue, and protein-mediated friction and the contraction of muscle fibers. Included also is a discussion of Burgers' equation, but from a perspective and with an application (formation of gels) different than that found in most introductory books on partial differential equations. Finally, Chapter 10 introduces diffusion-advection equations, including a discussion of the Ornstein-Uhlenbeck process.

No new mathematical ideas are introduced in the remaining chapters, as these are dedicated to the description of interesting processes which we are now fully prepared to study. These include chemotaxis, i.e., the bacterial search for food (Chapter 11), pattern formation including the famous Turing mechanism, formation of tiger bush stripes in semi-arid climates, and cell polarization (Chapter 12), dispersal-renewal processes and the spread of invasive species (Chapter 13), and collective behavior of organisms, including quorum sensing by bacteria, and swarming of flying birds or insects or swimming fish (Chapter 14).

As with any new topic of study, it is important to do exercises. Here I have tried to provide a gamut of exercises, from fairly routine, to more challenging. However, many of the exercises involve simulation and for these the Matlab codes presented with the main text can be modified to carry out the requested computation. Some, but not nearly all, of the answers to exercises are provided at the end of this book (in Appendix C), in order to help students know if they are getting the right answer. However, instructors who are working through this material for the first time may want a little more guidance. For those of you in this situation, a fairly extensive solution manual is available from the AMS after appropriate verification of your status.

As you can see from the above description, the mathematical focus of this book is diffusion reaction equations. However, this constitutes only the most basic introduction to this topic and does not explore its more theoretical aspects. Consequently, for those who are interested in pursuing the more theoretical aspects of this subject matter, I recommend books such as [**7**][**9**][**19**][**26**][**58**][**65**]. A book with a similar philosophy to study biological processes using partial differential equations, but at a more advanced level, is [**49**].

The material described here is drawn from a course in Mathematical Biology that I and my colleagues have taught at the University of Utah for many years. I owe a debt of gratitude to colleagues Fred Adler, Alla Borisyuk, Aaron Fogelson, and Sean Lawley, from whom I have taken course notes and homework exercises used in the development of this text. I am also very appreciative of the hard work of Alex Beams and Amanda Alexander who did the Herculean task of reading this text and making numerous invaluable suggestions. Thanks to all of you.

As with any work such as this, there are bound to be errors that have not yet been found. As you work through this text and exercises, please let me know those that you find, and I will post an updated list of these on my website.

And now that this project is finished, hopefully I will have more time for poisson processing.

Jim Keener

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