Preface

Research in the life sciences benefits from advances in instrumentation and data acquisition—advances that have precipitated a veritable 'data deluge', for instance in high-throughput screening. This data deluge seems to have prompted a rapprochement between biology and mathematics, across the great divide that has traditionally been perceived to separate these disciplines. This book is for those who are bridging this gap, acquainting mathematicians with research problems in the biological sciences and explaining to biologists what they should and should not expect mathematics to contribute to these problems. The aim of this book is, on the one hand, to show mathematicians how they can bring mathematical techniques to bear on real-life problems, and, on the other hand, to give biologists the opportunity to become *conversant* with mathematical modelling techniques, sufficiently so as to be able to work in a multidisciplinary team with mathematicians.

This book is based on an undergraduate-level course for biology students, an undergraduate-level course taught to mathematics students, as well as postgraduate-level modules for mixed groups consisting of both biology and mathematics graduates. While each of these groups presents particular difficulties and the challenge of teaching an interdisciplinary subject to any one of these groups cannot be underestimated, the experience of teaching such diverse groups brings out the fact that bright, open-minded young people from diverse disciplines have a great deal in common, far more than the much-vaunted gulf between the life sciences and mathematics might suggest.

The topics covered range from enzymes to ecosystems, with an emphasis on modelling techniques that have proved to be useful in a variety of contexts. Much emphasis in this book is placed on model formulation, i.e. the translation of biological knowledge into mathematical equations, model interpretation, which is the translation back from mathematical expressions to biological statements, and model evaluation, the critical assessment of model structure in view of scientific needs and available data. These are skills which both the life scientist and the mathematician on a multidisciplinary team must master, and for which neither unidisciplinary curriculum tends to prepare them. There is less emphasis on detailed biological knowledge (this is not an introduction to general biology) or mathematical techniques.[1]

My credentials for writing this book are simple: I have published over 30 papers at the interface of the life sciences and mathematics (with an educational background in both fields) and I have been involved in

[1] Accordingly, topics such as Lipschitz continuity, Dulac–Poincaré–Bendixson criteria, Jordan normal forms and Lyapunov functions are not extensively covered. The focus of this book is on *modelling techniques* applied to the life sciences.

teaching mathematical biology on either side of the great divide as well as on the bridge across it, in the multidisciplinary doctoral training centres at Warwick University.[2] True, mathematics and biology employ distinct research methodologies and require different mind sets, but this does not mean that mathematics cannot become one of the many useful tools of biological research, much as chemistry, engineering, and physics have contributed to modern biology. Let us hope that the great divide will be viewed by future natural scientists as a quaint and needless impediment to progress. Perhaps this book will, in some small way, help the aspiring young scientists of today become the multidisciplinarians of tomorrow.

[2]Biologist readers may thus be reassured that this is a maths book written by someone who knows how they look at things. Still, there is no such thing as 'mathematics for biologists' (notwithstanding the plethora of books with titles along these lines, which tend to pander to the biologist's averred *dysmathematica* by simply omitting 'difficult' material). For better or for worse, there is just mathematics, which is the same for dummies and geniuses alike.

Organization of this book Figure 1 shows how this book is organized. Chapters 1 and 2 constitute part I, a minimal course for the novice: an example-driven tour of basic ideas and principles that arise in many modelling contexts. Chapter 1 addresses the raison-d'être of a mathematical approach to biology and discusses what we mean by the key terms 'model' and 'biological system'. Chapter 2 reviews, through a series of case studies, some of the most frequently used modelling techniques.

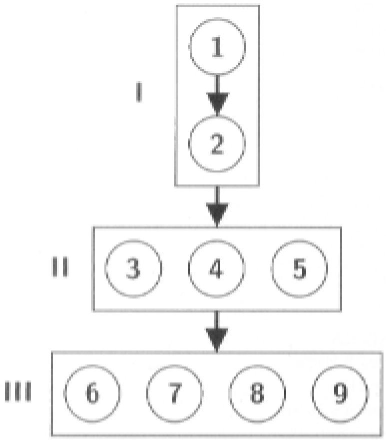

Fig. 1 Modular organization of this book.

Part II consists of Chapters 3, 4, and 5, which treat various aspects of modelling methodology: working with ordinary differential equations, confronting models with data (measurements, parameter estimation and statistics), and the principles and practice of model building. Part I together with the three methodological chapters of part II comprise a core course.

Chapters 6, 7, 8, and 9 introduce a range of modelling applications in the life and health sciences: growth and nutrition of individuals and mathematical ecology, infection and immunity, physiology, and stochastic processes. The chapters in part III (6–9) are arranged in ascending order of mathematical sophistication. These chapters can be read independently from one another following any selection from part II; chapters in part II (3–5) can be read independently from one another, following part I (1–2).

Suggested courses Part I by itself is suitable for a 10- to 15-lecture core course for life scientists at either undergraduate or postgraduate level with little mathematical background. The mathematics can be treated mostly intuitively, or occasionally as an advanced apparatus that produces certain results without us needing to peek inside the black box. For a longer course (15 to 25 lectures), lectures on material from part I can be interspersed with the easier material from part II. This format has been taught with considerable success to Year 2 undergraduates in the biological sciences. A similar combination of material from parts I and II, with a greater emphasis on the more advanced material from part II, has been taught with great success as a 15-lecture course to Year 2 undergraduates in the mathematical and physical sciences. A longer course for Year 2 or Year 3 mathematics students combines this material with a selection of material from part III.

Learning objectives for multidisciplinary teaching The following learning objectives would typically be covered in a brief module for mathematicians, whereas for biologists, a brief module would only cover the first four or five of these:

- translate a simple biological problem into a mathematical model;
- give a biological interpretation for simple systems of ODEs and their behaviour;
- distinguish dimensions from units, and determine the dimensions of quantities;
- non-dimensionalize a model;
- assign the correct scale of measurement to data;
- formulate an informed opinion on the status of modelling in modern science;
- apply the methods of Bernoulli and separation of variables in solving ODEs;
- solve small linear systems of ODEs with constant coefficients.

Multidisciplinary[3] courses at the postgraduate level are increasingly seen as a way forward to deliver a generation of scientists that can 'toggle' between the mindsets of biology and mathematics. The challenge of such courses is to teach to an audience of students who arrive with very different backgrounds across the natural and mathematical sciences.[4] A solution which has proved to be successful in practice is to combine part I with selected material from part II assigned on an individual basis to the students based on their immediate learning priority (e.g. mathematics graduates are assigned Chapter 4, on data and statistics, whereas biology graduates are assigned parts of Chapter 3 on differential equations), augmented with group work in which students with different expertise help one another working through primary research publications in mathematical biology. Material from part III has been taught as part of a 'quantitative biology' module at the multidisciplinary Master's level.

[3]Also known as *interdisciplinary*, *cross-disciplinary*, and *discipline-hopping* courses.

[4]A book that crosses boundaries between disciplines cannot avoid using jargon from various fields, from analytical philosophy to analytical chemistry. Thus the reader will encounter unfamiliar terms, even if he or she is already an expert in some of the topics discussed here. An early reviewer indignantly (and erroneously) protested that I had frivolously coined unwelcome neologisms, in scathing terms that I found rather unpleasant. Therefore I stress again that all terms of art in this text are quite current in one field of human enquiry or another.

Prerequisites My preferred way of learning mathematics is to work through an interesting scientific problem and locate and study relevant material from maths textbooks as I go along. It is therefore natural that I have written this book following an example-driven approach. However, experience has shown that there are also those who feel more comfortable having mastered the requisite maths first before turning to applications. Such students may wish to work through Appendix A *before* embarking on this book. Whereas this appendix is self-contained, absolute beginners are likely to find it too terse and are encouraged to consult additional textbooks listed at the end of Appendix A. My advice to the life scientist is not to worry too much about the maths and simply try to follow the argument[5] and let the interesting biology serve as a motivation to learn the mathematics. One learns far more being stuck on a single problem for a long time than one does studying other people's worked solutions, which is why this book does not contain any.

[5]Roger Penrose—no slouch when it comes to maths—confesses that on first reading he *simply skips* any formulæ that seem hard to understand.

Self-study This book is also intended to serve as a starting point for investigators (at the postgraduate level and beyond) who wish to know more about mathematical biology, coming either from a life sciences or a mathematical sciences background. A key priority for such investigators is to maximize the knowledge or insight gained from the investment of time. The modular approach of the book should be helpful in this respect; the life scientist can initially focus on part I and refer to part II as needed, whereas the mathematician can take any of the chapters in part III as a quick introduction to the various fields covered.

As an aid to self-study, numerous marginal exercises[6] have been included. The most committed reader will work each of those, whereas the more hurried reader should at least glance at them (since they often contain more detailed hints about the derivation of the results in the main text) and the reader who is most pressed for time can simply skip them on first reading. Marginal notes[7] are also provided to furnish background information, historical sidelights, or further explanation.

A note concerning technical terminology: a term of art related to modelling is set in **bold type** when it first appears. These will either be mathematics-related terms or life sciences terms that are essential to a mechanistic understanding of the problem at hand. Additional life sciences jargon is set *slanted* to indicate that the context in which it appears explains or defines the term concerned.

[6] Indicated by this logogram: . The marginal exercises correspond to classroom breaks where the students are asked to work the exercise, either at their desks or at the black board.

[7] Marginal notes are occasionally used to make the reader aware of terminology that, while not central to the present text, will aid him or her in quickly locating further information on the internet.

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