PREFACE

This book is based on the course in mathematical biology that I have given for many years at the Graduate School of Medical Sciences of Cornell University. The course was designed to develop in the graduate biology student an awareness of and familiarity with some mathematical techniques and methods which have been applied to biology. The need for such a course has arisen because biological information has become more quantitative, and the quantitative approach to biology has concomitantly grown in importance. The mathematics required for the text is a course in elementary calculus.

Biology deals with phenomena that are intrinsically more complex and more difficult to investigate than those normally studied in the "hard" sciences such as physics. Consequently, it is more susceptible to the introduction of hypotheses whose correctness cannot be adequately tested. Furthermore, mathematical models of biological systems, with their inherent propensity for simplification and idealization, are sometimes so speculative that they have only the merest pretense of being accountable to biological observations. In the past, this lack of accountability on the part of such speculative models has been a disservice to "mathematical biology," and has caused biologists to view this subject with a healthy skepticism. Here I use the term "mathematical biology" in a restricted sense that excludes biostatistics, the latter discipline having its own accepted and distinct role in the history of biology.

Nevertheless, there is a body of mathematical ideas and models that is so closely intertwined with biological observations, it has a more or less established place in the literature of modern biology. These diverse mathematical contributions to biology compose what may perhaps be called "classical" mathematical biology. It is upon the literature of these contributions that this book is largely based.

Often, these mathematical contributions have been presented to the biology student in a fragmented fashion. Consequently students of biology

learn to use mathematical formulas and techniques whose theoretical justification is hazy in the minds of many of them. Furthermore, nowhere is there to be found a presentation of this body of knowledge in a single volume. This book aims at remedying, at least partially, these defects.

I have made no attempt to be encyclopedic. Rather, the plan of the work has been to select five areas of mathematical biology and present them in a unified fashion, the unifying thread being the underlying mathematical structure. The classification scheme of the text is mixed: The first three subjects, cell growth, enzymatic reactions, and physiological tracers, are biological. The last two subjects, biological fluid dynamics and diffusion, are biophysical. The sequence in which these subjects are presented is so designed that the mathematical subject matter appears in increasing order of difficulty. Mathematically, the subject matter essentially follows a course in elementary differential equations, although linear algebra and graph theory are also touched upon. However the book is not designed to be and is very far from being a textbook in mathematics.

I trust I do not have to apologize for all the mathematical topics in biology which have been excluded. It seemed more sensible from the very beginning to proceed in depth in a few areas, rather than to treat a broader set of topics, at the cost of being more superficial or mathematically repetitive. Some topics were excluded because they did not satisfy the constraint on selection imposed by the underlying mathematical structure. And inevitably, my own particular interests (those of a mathematical physicist who came late to biology) and those of the Graduate School of Medical Sciences of Cornell University have exerted their influence in shaping this book. In any case, it is well to keep in mind that these notes are meant to be an introductory textbook only.

Every subject has its own particular jargon or vocabulary consisting of words having a technical meaning known only to the specialists in that subject. Biology and mathematics are no exceptions to this rule. It is a common experience that a lack of understanding of these special words is the greatest obstacle to reading and understanding the technical literature in a new subject. Since these notes are designed to remove the aura of mystery that surrounds the mathematical approach to biological data, I have made an effort to alert the reader to the usage of this mathematical jargon. This is accomplished, first, by bold facing all words that have a special technical meaning, and second, by providing some explanatory comment as to usage or meaning.

It is my hope that this book can also be useful to mathematically sophisticated students such as those with backgrounds in mathematics, physics, and engineering, who have little knowledge of biology but are nevertheless interested in the quantitative approach to it. Therefore, I have taken pains

to treat the technical jargon of biology in the same manner that I have treated the technical jargon of mathematics. The resulting explanatory biological comments will, of course, be superfluous to the student of biology, who I hope will be as tolerant of this practice as the mathematically sophisticated student will be of the mathematical comments.

The sections marked with an asterisk are more mathematically difficult to follow than the others. It is worthwhile to read through Section 2.2*, which is concerned with the early time behavior of enzymatic reactions, even if the mathematical discussion, which is in any case sketchy, is slighted. However, Sections 3.11* and 5.12* can be conveniently skipped, as I have often done in classroom practice, without any loss of continuity. They contain a more advanced mathematical discussion of material that has been previously presented.

It has been my teaching experience that students find some refresher lectures on calculus useful at the beginning of the course. I have also given supplementary lectures on the elements of linear algebra, as needed. These lectures form the substance of the mathematical appendices.

Problems that are more difficult to solve than others are also marked with an asterisk. These problems are intended for mathematically sophisticated students only. In general, the problems tend to be difficult to solve. Partially, this is an unavoidable consequence of my having made many of the problems relate to biological research investigations reported in the literature. However, the problems are generously provided with hints, and I urge the reader to try them, even if he finds he gets "stuck" at some point and cannot proceed further. If he will then, and only then, consult the solutions provided at the end of the book, he will surely have learned something from the attempt, as the experience of my students seems to bear out.

I wish to take this opportunity to thank my colleagues and students who, wittingly or not, have aided my biological education. In particular, my colleagues M. Earl Balis, Rudy H. Haschemeyer and Merry M. Sherman deserve special mention for their assistance while this book was in preparation. I am deeply grateful to my good friend and colleague Joseph B. Keller who read the entire manuscript and made numerous useful suggestions. Finally, I am grateful to my wife Shirley for her help and encouragement.

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