Preface

In recent years more and more colleges and universities have been introducing calculus courses specifically for students in the life sciences. This reflects a growing recognition that mathematics has become an indispensable part of any comprehensive training in the biological sciences.

Our chief goal in writing this textbook is to show students how calculus relates to biology. We motivate and illustrate the topics of calculus with examples drawn from many areas of biology, including genetics, biomechanics, medicine, pharmacology, physiology, ecology, epidemiology, and evolution, to name a few. We have paid particular attention to ensuring that all applications of the mathematics are genuine, and we provide references to the primary biological literature for many of these so that students and instructors can explore the applications in greater depth.

We strive for a style that maintains rigor without being overly formal. Although our focus is on the interface between mathematics and the life sciences, the logical structure of the book is motivated by the mathematical material. Students will come away from a course based on this book with a sound knowledge of mathematics and an understanding of the importance of mathematical arguments. Equally important, they will also come away with a clear understanding of how these mathematical concepts and techniques are central in the life sciences, just as they are in physics, chemistry, and engineering.

The book begins with a prologue entitled *Mathematics and Biology* detailing how the applications of mathematics to biology have proliferated over the past several decades and giving a preview of some of the ways in which calculus provides insight into biological phenomena.

Alternate Versions

There are two versions of this textbook. The first is entitled *Biocalculus: Calculus for the Life Sciences*; it focuses on calculus and some elements of linear algebra that are important in the life sciences. This is the second version, entitled *Biocalculus: Calculus, Probability, and Statistics for the Life Sciences*; it contains all of the content of the first version as well as three additional chapters titled *Descriptive Statistics*, *Probability*, and *Inferential Statistics* (see Content on page xviii).

Features

■ Real-World Data

We think it's important for students to see and work with real-world data in both numerical and graphical form. Accordingly, we have used data concerning biological phenomena to introduce, motivate, and illustrate the concepts of calculus. Many of the examples and exercises deal with functions defined by such numerical data or graphs. See, for example, Figure 1.1.1 (electrocardiogram), Figure 1.1.23 (malarial fever), Exercise 1.1.26 (blood alcohol concentration), Table 2 in Section 1.4 (HIV density), Table 3 in Section 1.5 (species richness in bat caves), Example 3.1.7 (growth of malarial parasites),

Exercise 3.1.42 (salmon swimming speed), Exercises 4.1.7–8 (influenza pandemic), Exercise 4.2.10 (HIV prevalence), Figure 5.1.17 (measles pathogenesis), Exercise 5.1.11 (SARS incidence), Figure 6.1.8 and Example 6.1.4 (cerebral blood flow), Table 1 and Figure 1 in Section 7.1 (yeast population), Figure 8.1.14 (antigenic cartography), Exercises 9.1.7, 9.2.48, and Examples 9.5.5 and 9.6.6 (snake reversals and stripes). And, of course, Chapters 11 and 13 are focused entirely on the analysis of biological data.

■ Graded Exercise Sets

Each exercise set is carefully graded, progressing from basic conceptual exercises and skill-development problems to more challenging problems involving applications and proofs.

■ Conceptual Exercises

One of the goals of calculus instruction is conceptual understanding, and the most important way to foster conceptual understanding is through the problems that we assign. To that end we have devised various types of problems. Some exercise sets begin with requests to explain the meanings of the basic concepts of the section. (See, for instance, the first few exercises in Sections 2.3, 2.5, 3.3, 4.1, and 8.2.) Similarly, all the review sections begin with a Concept Check and a True-False Quiz. Other exercises test conceptual understanding through graphs or tables (see Exercises 3.1.11, 5.2.41–43, 7.1.9–11, 9.1.1–2, and 9.1.26–32).

Another type of exercise uses verbal description to test conceptual understanding (see Exercises 2.5.12, 3.2.50, 4.3.47, and 5.8.29).

■ Projects

One way of involving students and making them active learners is to have them work (perhaps in groups) on extended projects that give a feeling of substantial accomplishment when completed. We have provided 24 projects in *Biocalculus: Calculus for the Life Sciences* and an additional four in *Biocalculus: Calculus, Probability, and Statistics for the Life Sciences*. *Drug Resistance in Malaria* (page 78), for example, asks students to construct a recursion for the frequency of the gene that causes resistance to an antimalarial drug. The project *Flapping and Gliding* (page 297) asks how birds can minimize power and energy by flapping their wings versus gliding. In *The Tragedy of the Commons: An Introduction to Game Theory* (page 298), two companies are exploiting the same fish population and students determine optimal fishing efforts. The project *Disease Progression and Immunity* (page 394) is a nice application of areas between curves. *DNA Supercoiling* (page 783) uses ideas from probability theory to predict how DNA is coiled and compacted into cells. We think that, even when projects are not assigned, students might well be intrigued by them when they come across them between sections.

■ Case Studies

We also provide two case studies: (1) *Kill Curves and Antibiotic Effectiveness* and (2) *Hosts, Parasites, and Time-Travel*. These are extended real-world applications from the primary literature that are more involved than the projects and that tie together multiple mathematical ideas throughout the book. An introduction to each case study is provided at the beginning of the book (page xli), and then each case study recurs in various chapters as the student learns additional mathematical techniques. The case studies can be used at the beginning of a course as motivation for learning the mathematics, and they can then be returned to throughout the course as they recur in the textbook. Alternatively,

a case study may be assigned at the end of a course so students can work through all components of the case study in its entirety once all of the mathematical ideas are in place. Case studies might also be assigned to students as term projects. Additional case studies will be posted on the website www.stewartcalculus.com as they become available.

■ Biology Background

Although we give the biological background for each of the applications throughout the textbook, it is sometimes useful to have additional information about how the biological phenomenon was translated into the language of mathematics. In order to maintain a clear and logical flow of the mathematical ideas in the text, we have therefore included such information, along with animations, further references, and downloadable data on the website www.stewartcalculus.com. Applications for which such additional information is available are marked with the icon BB in the text.

■ Technology

The availability of technology makes it more important to clearly understand the concepts that underlie the images on the screen. But, when properly used, graphing calculators and computers are powerful tools for discovering and understanding those concepts. (See the section *Calculators, Computers, and Other Graphing Devices* on page xxvi for a discussion of these and other computing devices.) These textbooks can be used either with or without technology and we use two special symbols to indicate clearly when a particular type of machine is required. The icon indicates an exercise that definitely requires the use of such technology, but that is not to say that it can't be used on the other exercises as well. The symbol CAS is reserved for problems in which the full resources of a computer algebra system (like Maple, Mathematica, or the TI-89/92) are required. But technology doesn't make pencil and paper obsolete. Hand calculation and sketches are often preferable to technology for illustrating and reinforcing some concepts. Both instructors and students need to develop the ability to decide where the hand or the machine is appropriate.

■ Tools for Enriching Calculus (TEC)

TEC is a companion to the text and is intended to enrich and complement its contents. (It is now accessible in Enhanced WebAssign and CengageBrain.com. Selected Visuals and Modules are available at www.stewartcalculus.com.) Developed in collaboration with Harvey Keynes, Dan Clegg, and Hubert Hohn, TEC uses a discovery and exploratory approach. In sections of the book where technology is particularly appropriate, marginal icons TEC direct students to TEC Visuals and Modules that provide a laboratory environment in which they can explore the topic in different ways and at different levels. **Visuals are animations of figures in text; Modules are more elaborate activities and include exercises**. Instructors can choose to become involved at several different levels, ranging from simply encouraging students to use the Visuals and Modules for independent exploration, to assigning specific exercises from those included with each Module, to creating additional exercises, labs, and projects that make use of the Visuals and Modules.

■ Enhanced WebAssign

Technology is having an impact on the way homework is assigned to students, particularly in large classes. The use of online homework is growing and its appeal depends on ease of use, grading precision, and reliability. We have been working with the calculus

community and WebAssign to develop a robust online homework system. Up to 50% of the exercises in each section are assignable as online homework, including free response, multiple choice, and multi-part formats.

The system also includes *Active Examples,* in which students are guided in step-by-step tutorials through text examples, with links to the textbook and to video solutions. The system features a customizable *YouBook*, a *Show My Work* feature, *Just in Time* review of precalculus prerequisites, an *Assignment Editor,* and an *Answer Evaluator* that accepts mathematically equivalent answers and allows for homework grading in much the same way that an instructor grades.

■ Website

The site www.stewartcalculus.com includes the following.

- Algebra Review
- Lies My Calculator and Computer Told Me
- History of Mathematics, with links to the better historical websites
- Additional Topics (complete with exercise sets): Approximate Integration: The Trapezoidal Rule and Simpson's Rule, First-Order Linear Differential Equations, Second-Order Linear Differential Equations, Double Integrals, Infinite Series, and Fourier Series
- Archived Problems (drill exercises and their solutions)
- Challenge Problems
- Links, for particular topics, to outside Web resources
- Selected Tools for Enriching Calculus (TEC) Modules and Visuals
- Case Studies
- Biology Background material, denoted by the icon BB in the text
- Data sets

Content

Diagnostic Tests The books begin with four diagnostic tests, in Basic Algebra, Analytic Geometry, Functions, and Trigonometry.

Prologue This is an essay entitled *Mathematics and Biology*. It details how the applications of mathematics to biology have proliferated over the past several decades and highlights some of the applications that will appear throughout the book.

Case Studies The case studies are introduced here so that they can be used as motivation for learning the mathematics. Each case study then recurs at the ends of various chapters throughout the book.

1 Functions and Sequences The first three sections are a review of functions from precalculus, but in the context of biological applications. Sections 1.4 and 1.5 review exponential and logarithmic functions; the latter section includes semilog and log-log plots because of their importance in the life sciences. The final section introduces sequences at a much earlier stage than in most calculus books. Emphasis is placed on recursive sequences, that is, difference equations, allowing us to discuss discrete-time models in the biological sciences.

2 Limits We begin with limits of sequences as a follow-up to their introduction in Section 1.6. We feel that the basic idea of a limit is best understood in the context of sequences. Then it makes sense to follow with the limit of a function at infinity, which we present in the setting of the Monod growth function. Then we consider limits of functions at finite numbers, first geometrically and numerically, then algebraically. (The precise definition is given in Appendix D.) Continuity is illustrated by population harvesting and collapse.

3 Derivatives Derivatives are introduced in the context of rate of change of blood alcohol concentration and tangent lines. All the basic functions, including the exponential and logarithmic functions, are differentiated here. When derivatives are computed in applied settings, students are asked to explain their meanings.

4 Applications of Derivatives The basic facts concerning extreme values and shapes of curves are deduced using the Mean Value Theorem as the starting point. In the section on l'Hospital's Rule we use it to compare rates of growth of functions. Among the applications of optimization, we investigate foraging by bumblebees and aquatic birds. The Stability Criterion for Recursive Sequences is justified intuitively and a proof based on the Mean Value Theorem is given in Appendix E.

5 Integrals The definite integral is motivated by the area problem, the distance problem, and the measles pathogenesis problem. (The area under the pathogenesis curve up to the time symptoms occur is equal to the total amount of infection needed to develop symptoms.) Emphasis is placed on explaining the meanings of integrals in various contexts and on estimating their values from graphs and tables. There is no separate chapter on techniques of integration, but substitution and parts are covered here, as well as the simplest cases of partial fractions.

6 Applications of Integrals The Kety-Schmidt method for measuring cerebral blood flow is presented as an application of areas between curves. Other applications include the average value of a fish population, blood flow in arteries, the cardiac output of the heart, and the volume of a liver.

7 Differential Equations Modeling is the theme that unifies this introductory treatment of differential equations. The chapter begins by constructing a model for yeast population size as a way to motivate the formulation of differential equations. We then show how phase plots allow us to gain considerable qualitative information about the behavior of differential equations; phase plots also provide a simple introduction to bifurcation theory. Examples range from cancer progression to individual growth, to ecology, to anesthesiology. Direction fields and Euler's method are then studied before separable equations are solved explicitly, so that qualitative, numerical, and analytical approaches are given equal consideration. The final two sections of this chapter explore systems of two differential equations. This brief introduction is given here because it allows students to see some applications of systems of differential equations without requiring any additional mathematical preparation. A more complete treatment is then given in Chapter 10.

8 Vectors and Matrix Models We start by introducing higher-dimensional coordinate systems and their applications in the life sciences including antigenic cartography and genome expression profiles. Vectors are then introduced, along with the dot product, and these are shown to provide insight ranging from influenza epidemiology, to cardiology, to vaccine escape, to the discovery of new biological compounds. They also provide some of the tools necessary for the treatment of multivariable calculus in Chapter 9. The remainder of this chapter is then devoted to the application of further ideas from linear algebra to biology. A brief introduction to matrix algebra is followed by a section where these ideas are used to model many different biological phenomena with the aid of matrix diagrams. The final three sections are devoted to the mathematical analysis of

such models. This includes a treatment of eigenvalues and eigenvectors, which will also be needed as preparation for Chapter 10, and a treatment of the long-term behavior of matrix models using Perron-Frobenius Theory.

9 Multivariable Calculus Partial derivatives are introduced by looking at a specific column in a table of values of the heat index (perceived air temperature) as a function of the actual temperature and the relative humidity. Applications include body mass index, infectious disease control, lizard energy expenditure, and removal of urea from the blood in dialysis. If there isn't time to cover the entire chapter, then it would make sense to cover just sections 9.1 and 9.2 (preceded by 8.1) and perhaps 9.6. But if Section 9.5 is covered, then Sections 8.2 and 8.3 are prerequisites.

10 Systems of Linear Differential Equations Again modeling is the theme that unifies this chapter. Systems of linear differential equations enjoy very wide application in the life sciences and they also form the basis for the study of systems of nonlinear differential equations. To aid in visualization we focus on two-dimensional systems, and we begin with a qualitative exploration of the different sorts of behaviors that are possible in the context of population dynamics and radioimmunotherapy. The general solution to two-dimensional systems is then derived with the use of eigenvalues and eigenvectors. The third section then illustrates these results with four extended applications involving metapopulations, the immune system, gene regulation, and the transport of environmental pollutants. The chapter ends with a section that shows how the ideas from systems of linear differential equations can be used to understand local stability properties of equilibria in systems of nonlinear differential equations. To cover this chapter students will first need sections 8.1–8.4 and 8.6–8.7.

11 Descriptive Statistics Statistical analyses are central in most areas of biology. The basic ideas of descriptive statistics are presented here, including types of variables, measures of central tendency and spread, and graphical descriptions of data. Single variables are treated first, followed by an examination of the descriptive statistics for relationships between variables, including the calculus behind the least-square fit for scatter plots. A brief introduction to inferential statistics and its relationship to descriptive statistics is also given, including a discussion of causation in statistical analyses.

12 Probability Probability theory represents an important area of mathematics in the life sciences and it also forms the foundation for the study of inferential statistics. Basic principles of counting and their application are introduced first, and these are then used to motivate an intuitive definition of probability. This definition is then generalized to the axiomatic definition of probability in an accessible way that highlights the meanings of the axioms in a biological context. Conditional probability is then introduced with important applications to disease testing, handedness, color blindness, genetic disorders, and gender. The final two sections introduce discrete and continuous random variables and illustrate how these arise naturally in many biological contexts, from disease outbreaks to DNA supercoiling. They also demonstrate how the concepts of differentiation and integration are central components of probability theory.

13 Inferential Statistics The final chapter addresses the important issue of how one takes information from a data set and uses it to make inferences about the population from which it was collected. We do not provide an exhaustive treatment of inferential statistics, but instead present some of its core ideas and how they relate to calculus. Sampling distributions are explained, along with confidence intervals and the logic behind hypothesis testing. The chapter concludes with a simplified treatment of the central ideas behind contingency table analysis.

Student Resources

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Enhanced WebAssign is designed to allow you to do your homework online. This proven and reliable system uses content found in this text, then enhances it to help you learn calculus more effectively. Automatically graded homework allows you to focus on your learning and get interactive study assistance outside of class. Enhanced WebAssign for *Biocalculus: Calculus, Probability, and Statistics for the Life Sciences* contains the Cengage YouBook, an interactive ebook that contains animated figures, video clips, highlighting and note-taking features, and more!

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To access additional course materials, please visit www.cengagebrain.com. At the CengageBrain.com home page, search for the ISBN of your title (from the back cover of your book) using the search box at the top of the page. This will take you to the product page where these resources can be found.

Stewart Website

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This site includes additional biological background for selected examples, exercises, and projects, including animations, further references, and downloadable data files. In addition, the site includes the following:

- Algebra Review
- Additional Topics
- Drill exercises
- Challenge Problems
- Web Links
- History of Mathematics
- Tools for Enriching Calculus (TEC)

Student Solutions Manual

ISBN: 978-1-305-11406-7

Provides completely worked-out solutions to all odd-numbered exercises in the text, giving you a chance to check your answers and ensure you took the correct steps to arrive at an answer.

A Companion to Calculus

By Dennis Ebersole, Doris Schattschneider, Alicia Sevilla, and Kay Somers

ISBN 978-0-495-01124-8

Written to improve algebra and problem-solving skills of students taking a calculus course, every chapter in this companion is keyed to a calculus topic, providing conceptual background and specific algebra techniques needed to understand and solve calculus problems related to that topic. It is designed for calculus courses that integrate the review of precalculus concepts or for individual use. Order a copy of the text or access the eBook online at www.cengagebrain.com by searching the ISBN.

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by Konrad J. Heuvers, William P. Francis, John H. Kuisti, Deborah F. Lockhart, Daniel S. Moak, and Gene M. Ortner

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- Thousands of homework problems that match your textbook's end-of-section exercises
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- *Read It* eBook pages, *Watch It* videos, *Master It* tutorials, and *Chat About It* links
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- *Personal Study Plans* (based on diagnostic quizzing) that identify chapter topics that students will need to master
- A WebAssign *Answer Evaluator* that recognizes and accepts equivalent mathematical responses in the same way an instructor grades
- A *Show My Work* feature that gives instructors the option of seeing students' detailed solutions
- Lecture videos and more!

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YouBook is an eBook that is both interactive and customizable! Containing all the content from *Biocalculus: Calculus, Probability, and Statistics for the Life Sciences, YouBook* features a text edit tool that allows instructors to modify the textbook narrative as needed. With *YouBook,* instructors can quickly reorder entire sections and chapters or hide any content they don't teach to create an eBook that perfectly matches their syllabus. Instructors can further customize the text by adding instructor-created or YouTube video links. Additional media assets include animated figures, video clips, highlighting and note-taking features, and more! *YouBook* is available within Enhanced WebAssign.

Complete Solutions Manual

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Includes worked-out solutions to all exercises and projects in the text.

Instructor Companion Website (login.cengage.com)

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- Drill exercises
- Challenge Problems
- Web Links
- History of Mathematics
- Tools for Enriching Calculus (TEC)

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Ilie Ugarcovici and his students, *DePaul University,* 2013–2014 academic year

Michael Price and his students, *University of Oregon,* 2013–2014 academic year

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JAMES STEWART

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