# Numerical and Statistical Methods for Bioengineering

This is the first MATLAB-based numerical methods textbook for bioengineers that uniquely integrates modeling concepts with statistical analysis, while maintaining a focus on enabling the user to report the error or uncertainty in their result. Between traditional numerical method topics of linear modeling concepts, non-linear root finding, and numerical integration, chapters on hypothesis testing, data regression, and probability are interweaved. A unique feature of the book is the inclusion of examples from clinical trials and bioinformatics, which are not found in other numerical methods textbooks for engineers. With a wealth of biomedical engineering examples, case studies on topical biomedical research, and the inclusion of end of chapter problems, this is a perfect core text for a one-semester undergraduate course.

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# Numerical and Statistical Methods for Bioengineering

## Applications in MATLAB

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# Preface

Biomedical engineering programs have exploded in popularity and number over the past 20 years. In many programs, the fundamentals of engineering science are taught from textbooks borrowed from other, more traditional, engineering fields: statics, transport phenomena, circuits. Other courses in the biomedical engineering curriculum are so multidisciplinary (think of tissue engineering, Introduction to BME) that this approach does not apply; fortunately, excellent new textbooks have recently emerged on these topics. On the surface, numerical and statistical methods would seem to fall into this first category, and likely explains why biomedical engineers have not yet contributed textbooks on this subject. I mean … math is math, right? Well, not exactly.

There exist some unique aspects of biomedical engineering relevant to numerical analysis. Graduate research in biomedical engineering is more often *hypothesis driven*, compared to research in other engineering disciplines. Similarly, biomedical engineers in industry design, test, and produce medical devices, instruments, and drugs, and thus must concern themselves with human clinical trials and gaining approval from regulatory agencies such as the US Food & Drug Administration. As a result, statistics and hypothesis testing play a bigger role in biomedical engineering and must be taught at the curricular level. This increased emphasis on statistical analysis is reflected in special "program criteria" established for biomedical engineering degree programs by the Accreditation Board for Engineering and Technology (ABET) in the USA.

There are many general textbooks on numerical methods available for undergraduate and graduate students in engineering; some of these use MATLAB as the teaching platform. A good undergraduate text along these lines is *Numerical Methods with Matlab* by G. Recktenwald, and a good graduate-level reference on numerical methods is the well-known *Numerical Recipes* by W. H. Press *et al.* These texts do a good job of covering topics such as programming basics, nonlinear root finding, systems of linear equations, least-squares curve fitting, and numerical integration, but tend not to devote much space to statistics and hypothesis testing. Certainly, topics such as genomic data and design of clinical trails are not covered. But beyond the basic numerical algorithms that may be common to engineering and the physical sciences, one thing an instructor learns is that *biomedical engineering students want to work on biomedical problems*! This requires a biomedical engineering instructor to supplement a general numerical methods textbook with a gathering of relevant lecture examples, homework, and exam problems, a labor-intensive task to be sure and one that may leave students confused and unsatisfied with their textbook investment. This book is designed to fill an unmet need, by providing a complete numerical and statistical methods textbook, tailored to the unique requirements of the modern BME curriculum and implemented in MATLAB, which is inundated with examples drawn from across the spectrum of biomedical science.

This book is designed to serve as the primary textbook for a one-semester course in numerical and statistical methods for biomedical engineering students. The level of the book is appropriate for sophomore year through first year of graduate studies, depending on the pace of the course and the number of advanced, optional topics that are covered. A course based on this book, together with later opportunities for implementation in a laboratory course or senior design project, is intended to fulfil the statistics and hypothesis testing requirements of the program criteria established by ABET, and served this purpose at the University of Rochester. The material within this book formed the basis for the required junior-level course "Biomedical computation," offered at the University of Rochester from 2002 to 2008. As of Fall 2009, an accelerated version of the "Biomedical computation" course is now offered at the masters level at Cornell University. It is recommended that students have previously taken calculus and an introductory programming course; a semester of linear algebra is helpful but not required. It is our hope that this book will also serve as a valuable reference for bioengineering practitioners and other researchers working in quantitative branches of the life sciences such as biophysics and physiology.

## Format

As with most textbooks, the chapters have been organized so that concepts are progressively built upon as the reader advances from one chapter to the next. Chapters 1 and 2 develop basic concepts, such as types of errors, linear algebra concepts, linear problems, and linear regression, that are referred to in later chapters. Chapters 3 (Probability and statistics) and 5 (Nonlinear root-finding techniques) draw upon the material covered in Chapters 1 and 2. Chapter 4 (Hypothesis testing) exclusively draws upon the material covered in Chapter 3, and can be covered at any point after Chapter 3 (Sections 3.1 to 3.5) is completed. The material on linear regression error in Chapter 3 should precede the coverage of Chapter 8 (Nonlinear model regression and optimization). The following chapter order is strongly recommended to provide a seamless transition from one topic to the next:

Chapter 1 → Chapter 2 → Chapter 3 → Chapter 5 → Chapter 6 → Chapter 8.

Chapter 4 can be covered at any time once the first three chapters are completed, while Chapter 7 can be covered at any time after working through Chapters 1, 2, 3, and 5. Chapter 9 covers an elective topic that can be taken up at any time during a course of study.

The examples provided in each chapter are of two types: Examples and Boxes. The problems presented in the Examples are more straightforward and the equations simpler. Examples either illustrate concepts already introduced in earlier sections or are used to present new concepts. They are relatively quick to work through compared to the Boxes since little additional background information is needed to understand the example problems. The Boxes discuss biomedical research, clinical, or industrial problems and include an explanation of relevant biology or engineering concepts to present the nature of the problem. In a majority of the Boxes, the equations to be solved numerically are derived from first principles to provide a more complete understanding of the problem. The problems covered in Boxes can be more challenging and require more involvement by the reader. While the Examples are critical in mastering the text material, the choice of which boxed problems to focus on is left to the instructor or reader.

As a recurring theme of this book, we illustrate the implementation of numerical methods through programming with the technical software package MATLAB. Previous experience with MATLAB is not necessary to follow and understand this book, although some prior programming knowledge is recommended. The best way to learn how to program in a new language is to jump right into coding when a need presents itself. Sophistication of the code is increased gradually in successive chapters. New commands and programming concepts are introduced on a need-to-know basis. Readers who are unfamiliar with MATLAB should first study Appendix A, Introduction to MATLAB, to orient themselves with the MATLAB programming environment and to learn the basic commands and programming terminology. Examples and Boxed problems are accompanied by the MATLAB code containing the numerical algorithm to solve the numerical or statistical problem. The MATLAB programs presented throughout the book illustrate code writing practice. We show two ways to use MATLAB as a tool for solving numerical problems: (1) by developing a program (m-file) that contains the numerical algorithm, and (2) using built-in functions supplied by MATLAB to solve a problem numerically. While self-written numerical algorithms coded in MATLAB are instructive for teaching, MATLAB built-in functions that compute the numerical solution can be more efficient and robust for use in practice. The reader is taught to integrate MATLAB functions into their written code to solve a specific problem (e.g. the backslash operator).

The book has its own website hosted by Cambridge University Press at www.cambridge.org/kingmody. All of the m-files and numerical data sets within this book can be found at this website, along with additional MATLAB programs relevant to the topics and problems covered in the text.

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If readers wish to suggest additional topics or comments, please write to us. We welcome all comments and criticisms as this book (and the field of biomedical engineering) continue to evolve.