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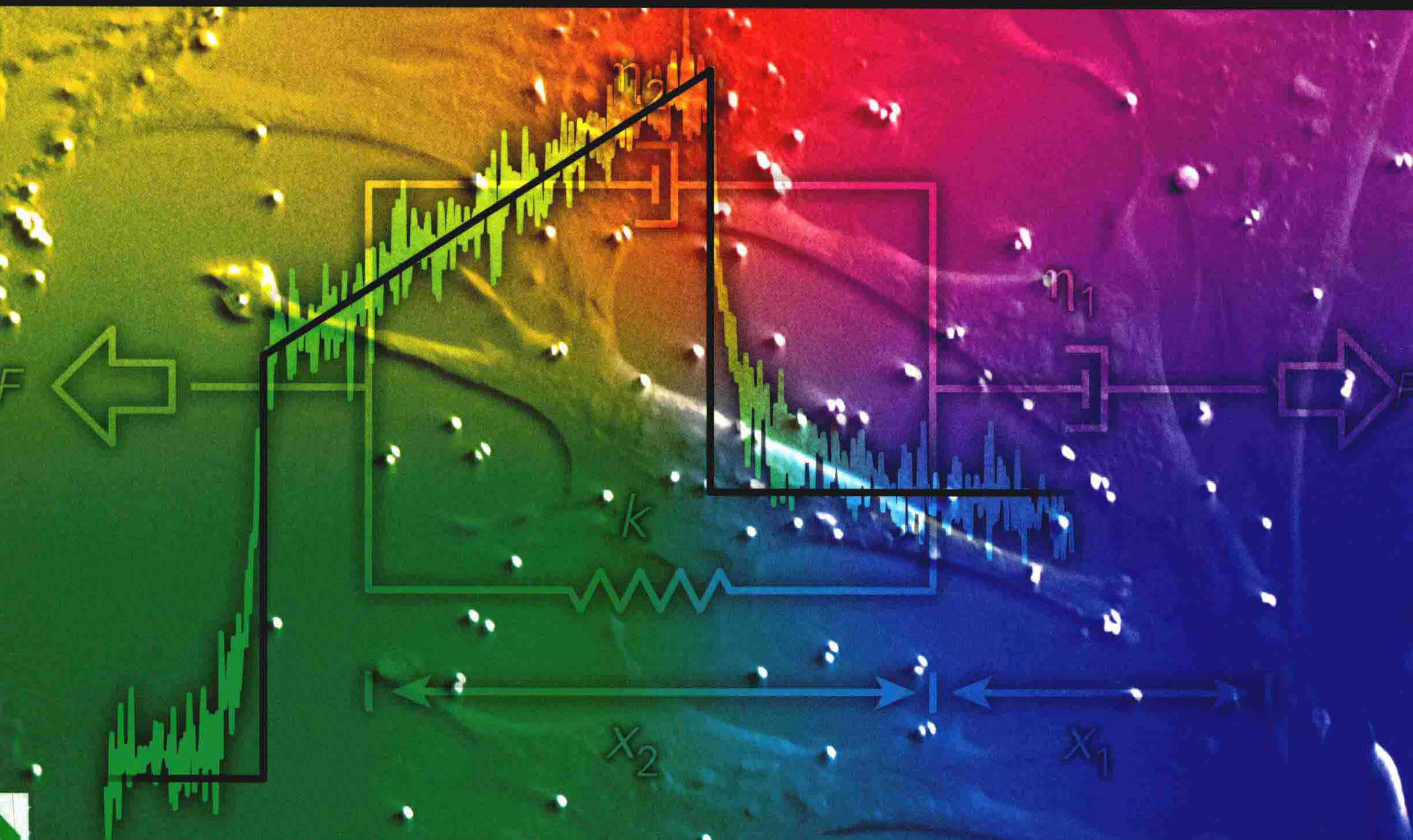
Introduction to Cell Mechanics and Mechanobiology



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Preface

In recent years, mechanical signals have become widely recognized as being critical to the proper functioning of numerous biological processes. This has led to the emergence of a new field called cellular mechanobiology, which merges cell biology with various disciplines of mechanics (including solid, fluid, statistical, computational, and experimental mechanics). Cellular mechanobiology seeks to uncover the principles by which the sensation or generation of mechanical force alters cell function. *Introduction to Cell Mechanics and Mechanobiology* presents students from a wide variety of backgrounds with the physical and mechanical principles underpinning cell and tissue behavior.

This textbook arose from a cell mechanics course at Stanford University first offered by two of us in 2005. Over several iterations, we taught from a set of course notes and chapter excerpts—having found no textbook to cover the necessary breadth of topics. Our colleagues had similar experiences teaching with the same adhoc approach, which convinced us of the need for a comprehensive instructional tool in this area. Another reason we felt compelled to write this text is that cell mechanics provides an excellent substrate to introduce many types of mechanics (solid, fluid, statistical, experimental, and even computational). These topics are traditionally covered in separate courses with applications largely focused on engineering structures. As authors, we have varied backgrounds, but share a common fondness for the insights mechanical engineering brings to cell biology.

Introduction to Cell Mechanics and Mechanobiology is intended for advanced undergraduates and early graduate students in biological engineering and biomedical engineering, including those not necessarily in a biomechanics track. We do not assume an extensive knowledge in any area of biology or mechanics. We do assume that students have a mathematics background common to all areas of engineering and quantitative science, meaning exposure to calculus, ordinary differential equations, and linear algebra.

The field of cell mechanics encompasses advanced concepts, such as large deformation mechanics and nonlinear mechanics. We do not expect our audience to have a strong background in the advanced mathematics of continuum mechanics. Our intent is to avoid graduate-level mathematics wherever possible. In our approach, the treatment of tensor mathematics—central to large deformation mechanics (common in cell mechanics)—poses unique difficulties. To show simplified mathematical derivations measuring mechanical parameters in the context of living cells, we present tensors "by analogy" as matrices, rather than introducing them in a fully rigorous fashion. For example, we skip index notation entirely. Admittedly, this approach may be less satisfying to mechanicians, which we also consider ourselves. However, we hope that the advantages of this approach will outweigh our oversimplifications.

The book is grouped into two parts: (I) Principles and (II) Practices. We have written the chapters to allow instructors flexibility in presentation, depending on the level of students and the length of the course. After introducing cell mechanics as a framework in Chapter 1, we provide a review of cell biology in Chapter 2. The next four chapters establish the necessary concepts in mechanics with enough depth that the student attains a basic competency and appreciation for each topic. Chapter 3 covers solid mechanics—including rigid and deformable bodies as well as a short overview of large-deformation mechanics. Fluid mechanics (Chapter 4) is important for cell mechanics not only in cytoplasmic flow, but also as a physical signal that regulates cell mechanobiological behavior. Chapter 5 dives into statistical mechanics, with descriptions of energy, entropy, and random walks, common themes for understanding the aggregate behavior of systems composed of many objects. In Chapter 6, we describe experimental methods, an area that is always changing, but is essential in demonstrating how theory may be reconciled with actual experiments. These fundamentals in Part I are followed by cell mechanics proper in Part II. Chapters 7–9 begin with a discussion of an aspect of cell biology followed by analysis of the mechanics. We undertake polymer mechanics in Chapter 7 from a continuum and a statistical viewpoint and examine situations in which both need to be considered simultaneously. These tools are applied to individual cytoskeletal polymers as well as to other polymers such as DNA. Polymer networks are presented in Chapter 8, with a focus on the role of the cytoskeleton in regulating physical properties, such as red blood cell shape and limitations on cell protrusion lengths. Chapter 9 examines the bilayer membrane, from both the perspective of matter floating around within it (diffusion) as well as a mechanical perspective of bending and stretching. The last two chapters address mechanobiology. Chapter 10 is focused on cellular force generation and the related processes of adhesion and migration. Chapter 11 discusses the process of mechanosensing or mechanotransduction and intracellular signaling. These last chapters do not have as much rigorous mechanical engineering mathematics, but are an integral part of cell biomechanics.

Given the varied backgrounds of our students and the interdisciplinary nature of the subject, we have attempted to provide some guidance on the treatment of variables and units. At the start of the book, we present a master list of all the variables used in the text that specifies exactly what each variable is used for in a particular chapter. We have retained the "contextual" usage in each chapter, accepted within each field, to prepare students for reading the literature. Three types of boxes supplement the main text: "Advanced Material" challenges readers to think critically and problem-solve; interesting and noteworthy asides are denoted as "Nota Bene"; "Examples" provide in-depth solved calculations and explanations. Each chapter concludes with a set of Key Concepts, Problems that can be used as homework sets, and Annotated References that guide students for further study.

Online Resources

Accessible from www.garlandscience.com/cell-mechanics, Student and Instructor Resource websites provide learning and teaching tools created for *Introduction to Cell Mechanics and Mechanobiology*. The Student Resources site is open to everyone, and users have the option to register in order to use book-marking and note-taking tools. The Instructor's Resource site requires registration; access is available to instructors who have assigned the book to their course. To access the Instructor's Resource site, please contact your local sales representative or email science@garland.com. Below is an overview of the resources available for this book. Resources may be browsed by individual chapters and there is a search engine. You can also access the resources available for other Garland Science titles.

For students:

- Computer simulation modules in two formats: ready-to-run simulations that simulate the mechanical behavior of cells and tutorial MATLAB modules on simulation of cell behavior with the finite element method.
- Color versions of several figures are available, indicated by the figure legend in the text.

- A handful of animations and videos dynamically illustrate important concepts from the book.
- Solutions to selected end-of-chapter problems are available to students.

For instructors:

- In addition to color versions of several figures, all of the images from the book are available in two convenient formats: Microsoft PowerPoint® and JPEG. They have been optimized for display on a computer. Figures are searchable by figure number, figure name, or by keywords used in the figure legend from the book.
- The animations and videos that are available to students are also available on the Instructor's Resource website in two formats. The WMV-formatted movies are created for instructors who wish to use the movies in PowerPoint presentations on computers running Windows®; the QuickTime®-formatted movies are for use in PowerPoint for Apple computers or Keynote® presentations. The movies can easily be downloaded to your personal computer using the "download" button on the movie preview page.
- Solutions to selected end-of-chapter problems are available to qualified adopters.

The origin of the book is rooted in teaching from sections of outstanding books by David H. Boal, Jonathon Howard, and Howard C. Berg. We thank Roger Kamm, Vijay Pande, and Andrew Spakowitz, who taught some of us at various times and have unselfishly shared course materials and handouts and, in the case of Dr. Kamm, unpublished drafts of his own textbook. With their permission, we have incorporated their approach to some topics in Chapters 4, 5, 7, 8, and 9 and adapted several problems into sections of our book. We are grateful for their amazing willingness to share their intellectual product in the name of improving the educational experience of students around the world. We also thank reviewers Roland R. Kaunas and Peter J. Butler, who shared notes from their own courses in cell mechanics. We are profoundly appreciative of the tireless work of those who have preceded us, without whom we never could have completed this task. We thank the additional reviewers of the book, Dan Fletcher, Christian Franck, Wonmuk Hwang, Paul Janmey, Yuan Lin, Lidan You, and Diane Wagner, for their valuable insight and critiques of our drafts. We are also grateful to Summers Scholl and the editorial and production teams at Garland who took a chance on three textbook neophytes and guided us unerringly through uncharted waters. Finally we are each deeply indebted to our families, including Roberta, Jolene, VH, YYH, LHH, Joyce, Melody, Tae, and Cynthia. Without your support, patience, and understanding—as this project took us away from you on so many nights and weekends—we never could have contemplated this undertaking, much less completed it.

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Detailed Contents

PART I: PRINCIPLES