Biomedical Engineering

The second edition of this popular introductory undergraduate textbook uses theory, examples, applications, and a problem-solving approach to convey the impact of biomedical engineering. Updates throughout the book highlight the important advances made over recent years, including iPS cells, microRNA, nanomedicine, imaging technology, biosensors, and drug delivery systems, giving students a modern description of the various subfields of biomedical engineering.

Highlight features:

- All of the molecular biology, cellular biology, and human physiology background that students need to understand the context in which biomedical engineers' work is provided.
- Mathematical treatments are boxed for students who wish to apply them to engineering analysis.
- An expanded set of profiles in biomedical engineering showcase the broad range of career paths open to students who make biomedical engineering their calling.
- Over 200 quantitative and qualitative exercises, many new to this edition, are included at the end of chapters to consolidate learning.

W. Mark Saltzman is the Goizueta Professor of Chemical and Biomedical Engineering at Yale University, and was the founding Chair of the Yale Department of Biomedical Engineering. He has taught numerous courses on topics in biomedical engineering in the last three decades, and has been widely recognised for his excellence in research and teaching. He is a Fellow of the American Institute for Medical and Biological Engineering, and a Fellow of the Biomedical Engineering Society. He is also the recipient of the 2014 Mines Medal and has been elected to the Institute of Medicine of the National Academies.

"This book sets a gold standard for textbooks in biomedical engineering. It is beautifully and clearly written, and explains all aspects, old and very new, of biomedical engineering in ways that are both exciting to the reader as well as easy to understand."

Robert Langer, Massachusetts Institute of Technology

"This textbook is a wonderful summary of the field of biomedical engineering—a must have for any faculty member teaching an introductory BME course! As usual, Professor Saltzman has provided rich context and broad examples; he does an excellent job of weaving in valuable scenarios that are realistic, yet interesting—a great tool for engaging students! There are many creative and useful features to the text: the figures and illustrations provide much value to understanding the material, the problem sets offer both conceptual and quantitative review of the material, and the "Key Concepts and Definitions" and "Useful Links" sections at the end of each chapter are very practical for a student new to the field of BME. Of particular note, the "Profiles in BME" vignettes for each chapter add a personal touch and serve to connect students to role models who are real people (with real stories) making an impact on the world."

Christine E. Schmidt, University of Florida

"This is an excellent book that covers the fundamentals of a broad array of specific fields within biomedical engineering. This textbook will certainly be adopted by many introductory biomedical engineering courses due to its meaningful organization, clear writing, illuminative figures, and variety of problems for students to work through. Its breadth and scope will stimulate all readers. Once again, Mark Saltzman has accomplished a major achievement by providing such a comprehensive text for students and educators alike."

Melissa Krebs, Colorado School of Mines

"This is a truly exceptional textbook. It is completely up-to-date and comprehensive, yet it is so readable that you can dip in at any page and find something that grabs you. It is designed for undergraduate students, and is a tremendous resource for course development—but equally, it is one of those essential bookshelf books, the one you will turn to when you need 'to brush up on your biology', or 'get your head straight on the engineering stuff'. A must for anyone interested in the very far-reaching field of biomedical engineering."

Quentin Pankhurst, University College London

CAMBRIDGE TEXTS IN BIOMEDICAL ENGINEERING

Cambridge Texts in Biomedical Engineering provide a forum for high-quality textbooks targeted at undergraduate and graduate courses in biomedical engineering. It covers a broad range of biomedical engineering topics from introductory texts to advanced topics, including biomechanics, physiology, biomedical instrumentation, imaging, signals and systems, cell engineering, and bioinformatics, as well as other relevant subjects, with a blending of theory and practice. While aiming primarily at biomedical engineering students, this series is also suitable for courses in broader disciplines in engineering, the life sciences and medicine.

Biomedical Engineering

Bridging Medicine and Technology

W. Mark Saltzman
Yale University

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To Noa and Zach and Alex

There is no luckier, happier father on earth than I.

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Preface

The field of biomedical engineering has expanded markedly in the past 15 years. This growth is supported by advances in biological science, which have created new opportunities for development of tools for diagnosis of and therapy for human disease. This book is designed as a textbook for an introductory course in biomedical engineering. The text was written to be accessible for most entering college students. In short, the book presents some of the basic science knowledge used by biomedical engineers and illustrates the first steps in applying this knowledge to solve problems in human medicine.

Biomedical engineering now encompasses a range of fields of specialization including bioinstrumentation, bioimaging, biomechanics, biomaterials, and biomolecular engineering. Most undergraduate students majoring in biomedical engineering are faced with a decision, early in their program of study, regarding the subfield in which they would like to specialize. Each subfield has a set of course requirements, which can be supplemented by wise selection of elective and supporting coursework. Also, many young students of biomedical engineering use independent research projects as a source of inspiration and preparation but have difficulty identifying research areas that are right for them. Therefore, a second goal of this book is to link knowledge of basic science and engineering to current research, and the accompanying opportunities to create new medical products, in each subfield.

As a general introduction, this textbook assembles foundational resources from molecular and cellular biology and physiology and relates this science to various subspecialties of biomedical engineering. The first two parts of the book present basic information in molecular/cellular biology and human physiology; quantitative concepts are stressed in these sections. Comprehension of these basic life science principles provides the context in which biomedical engineers interact and innovate. The third part of the book introduces the subspecialties in biomedical engineering and emphasizes – through examples and profiles of people in the field – the types of problems biomedical engineers solve. Organization of the chapters into these three major parts allows course instructors and students to customize their usage of some or all of the chapters depending on the background of the students and the availability of other course offerings in the curriculum.

WHICH STUDENTS PROFIT FROM THIS BOOK?

A significant number of students come to college with a clear idea of pursuing a career in biomedical engineering. Of course, these students benefit tremendously from a rigorous overview of the field, ideally provided in their first year. Most of these students leave the course even more certain about their choice of career. Many of them jump right into independent study or research projects: This overview of the diverse applications of biomedical engineering provides them with the information that they need to select research projects—or future courses—that will move them in the right direction.

I have also found this material to be interesting to engineering students who are trying to decide which of the engineering degree programs is right for them. The material in this textbook might also be used to introduce undeclared or undecided engineering majors to the field of biomedical engineering. Students enter college with varying degrees of competence in science and math. Some do not know what biomedical engineering encompasses and whether they have the adequate secondary education training to succeed. Exposure to the topics presented here may inspire some of these students to further their studies in biomedical engineering.

Also, I encourage instructors to make their course accessible to students who are not likely to become engineering majors; biomedical technology is increasingly important to the life of all educated citizens. I have taught courses in this subject to freshmen at three different universities over the past 25 years; students with a variety of intended majors always enroll in the course (mathematics, history, economics, English, fine arts, and anthropology majors have participated in the past few years). In fact, it is these students who appear to be most changed by the experience.

TO THE INSTRUCTOR

Teachers of courses directed to early undergraduates in biomedical engineering struggle against competing forces: The diverse backgrounds of the students pull you to start from first principles, and the rapid progress of the field pushes you to cover more and more topics. To address this, I have presented more material than I am capable of covering in a one-semester course for freshmen students. In a typical 13-week semester, I find that only 12–13 of the 16 chapters can be covered comfortably. Assuming that this will be true for your situation as well, I recommend that you assess the level of experience of your students and decide which chapters are most valuable in creating a coherent and satisfying course. Many students arrive at college with a sophisticated understanding of cellular and molecular biology; therefore, I do not cover Part 1 (Chapters 2–5) in detail. Condensing this early material allows me to include almost all of the other chapters. Part 1 is still available to the student, of course, and most of them profit from reading these chapters, as they need as the course progresses, even if the

Modular approaches to teaching an introductory course in biomedical engineering using this text

Week of the course	Comprehensive approach	Applications emphasis	Physiology emphasis	Cellular engineering emphasis
1	Chap. 1 and 2	Chap. 1	Chap. 1	Chap. 1
2	Chap. 3 and 4	Chap. 2–5 (selected)	Chap. 2–4 (selected)	Chap. 2 and 3
3	Chap. 5	Chap. 10	Chap. 5	Chap. 4
4	Chap. 7	Chap. 10 and 11	Chap. 6	Chap. 5
5	Chap. 8	Chap. 11	Chap. 7	Chap. 6–9 (selected)
6	Chap. 9	Chap. 12	Chap. 8	Chap. 10
7	Midterm review	Midterm review	Midterm review	Midterm review
8	Chap. 10	Chap. 2–5 (selected)	Chap. 9	Chap. 11
9	Chap. 11	Chap. 13	Chap. 10	Chap. 12
10	Chap. 12	Chap. 14	Chap. 11 and 12	Chap. 13
11	Chap. 13 and 14	Chap. 15	Chap. 13	Chap. 14
12	Chap. 15	Chap. 16	Chap. 14	Chap. 15
13	Chap. 16	Chap. 16	Chap. 15	Chap. 16

details are not covered in lecture. In courses that emphasize biomedical engineering, and not the biological sciences, the instructor might want to cover only Part 3 of the book and use the previous parts as reference material.

Some examples of approaches for arranging the chapters into semester-long courses that emphasize different aspects of biomedical engineering are presented in the preceding table.

WHAT IS NEW IN THE SECOND EDITION

The second edition builds on the strengths of the first edition, but adds new material that will be helpful to students and instructors. Each chapter has been updated, with new text added to highlight important advances in biomedical engineering since the first edition appeared in 2009. The second edition includes new information reflecting recent advances in biological science (such as iPS cells and microRNA), as well as advances in engineering and technology (such as nanomedicine, biosensors, imaging technology, and drug delivery systems). Each chapter has also been revised to improve readability. More qualitative and quantitative practice material—in the form of Questions and Problems—has been added to each chapter. Overall, there are 20% more Questions and Problems in the second edition. Finally, the popular Profiles in BME sections have been updated and expanded, with new profiles describing additional biomedical engineers, representing a broad range of career paths and diverse interests.

Acknowledgments

I have many people to thank, for encouragement and direct participation. It is a long list, and undoubtedly incomplete. For the past 12 years, I have been immersed in a milieu rich in creativity and industriousness. So I profited from brushes and asides, from long conversations and wisdom overheard. I thank my colleagues and friends at Yale University for providing intellectual stimulation, personal support, and inspiration.

I thank the Whitaker Foundation for their generous financial support of the first edition, which made it possible for me to transform notes and notions into text. I am particularly grateful to Jack Linehan, who has been a steady source of inspiration and advice to me. I thank Kyle Vanderlick, Dean of the School of Engineering and Applied Sciences at Yale, for creating the space I needed to complete this second edition.

I thank Peter Gordon of Cambridge University Press, who has been the most stalwart supporter of this project. Peter is everything one could hope for in an editor: He is wise, generous with praise, and direct (yet kind) with criticism. Thankfully, he is also patient. I thank Michelle Carey for her brilliant support, which was even more substantial in the preparation of this second edition. What a pleasure, to be an author for Cambridge University Press.

I thank Veronique Tran for her help in the inception of this project, her critical assistance in overall organization of the book, and her work on early versions of Chapters 2, 6, and 11. It was Veronique who urged this project forward at the start, and it would not have happened without her effort and enthusiasm. I thank Lawrence Staib, who co-authored Chapter 12 and shaped it into one of my favorite chapters in the book. I thank Rachael Sirianni, who continues to amaze me with the breadth of her talents: Rachael's photography enhances every chapter.

I burdened generous friends; each of them read part of the manuscript carefully and provided thoughtful edits and suggestions, making each chapter better, more readable. I thank Ian Suydam (Chapter 2), Kim Woodrow (Chapter 3), Michael Caplan (Chapter 5), Parwiz Abrahimi (Chapter 6), Michelle Kelly (Chapter 7), Peter Aronson (Chapter 9), Deepak Vashishith (Chapter 10), Themis Kyriakides (Chapter 15), and Kathryn Miller-Jensen (Chapter 16).

I am grateful to my co-instructors in Physiological Systems (BENG 350) at Yale, who have been exceptional colleagues and patient, enthusiastic teachers of physiology. The influence of Michael Caplan, Elizabeth Holt, Walter Boron, Emile Boulpaep, Peter Aronson, and Stuart Campbell can be felt in Chapters 5, 6, 7, 8, 9, and 10, respectively. I have profited from their examples as teachers.

A number of people contributed essential administrative and research support—tracking down papers and facts, producing figures, proofreading, and creating and solving homework problems. For their work on the first edition, I thank Tiffanee Green, Michael Henry, Kofi Buaku Atsina, Florence Kwo, and Salvador Joel Nunez Gastelum. Two special people did this and much more: Audrey Lin and Jennifer Saucier-Sawyer proofread, edited, pursued figures (and permissions for figures), and managed to keep binders, drafts, and sticky notes organized. More than this, they smiled at every obstacle, accommodated every idea, and remained positive as I missed deadlines. Without Audrey's expert help in the final push on the first edition—and her never-say-no generosity—this text would still be in binders. For the second edition, I thank Anthony Bianchi, Julie Chang, and Elias Quijano. Anthony and Julie persevered through the final flurry of edits and proofreading, with good spirits and exceptional attention to detail. This new edition would not have been possible without Elias's continuous help over the past two years. I am so impressed with Elias, who teaches me something new about patience, generosity, common sense, and biomedical engineering each day.

Something remarkable happened between the first and second edition. I got married! Thank you, Christina, for being my partner and friend and for inspiring me to shine, in your eyes. Your quiet strength and boundless spirit are constant sources of inspiration to me.

Abbreviations and Acronyms

3D-	three-dimensional
3DCRT	three-dimensional conformal radiation therapy
Ab	antibody
ADA	adenosine deaminase deficiency
ADH	anti-diuretic hormone
ADP	adenosine diphosphate
AIDS	acquired immune deficiency syndrome
AML	acute myeloid leukemia
APC	antigen presenting cell
ATP	adenosine-5′-triphosphate
AV	atrioventricular
BBB	blood–brain barrier
BCG	bacillus Calmette–Guérin
BME	biomedical engineering
BMR	basal metabolic rate
BSA	bovine serum albumin
CABG	coronary artery bypass graft
CLL	chronic lymphocytic leukemia
CT	computed tomography
DAG	diacylglycerol
DNA	deoxyribonucleic acid
EBRT	external beam radiation therapy
ECF	extracellular fluid
ECG	electrocardiography, electrocardiogram
ECM	extracellular matrix
EGF	epidermal growth factor
EGFR	epidermal growth factor receptor
EVAc	poly(ethylene-co-vinyl acetate)
FBR	foreign body response
FDA	U.S. Food and Drug Administration
fMRI	functional magnetic resonance imaging
GFR	glomerular filtration rate
GFP	green fluorescent protein

HIV	human immunodeficiency virus
HPV	human papillomavirus
HSC	hematopoietic stem cells
HUVEC	human umbilical vein endothelial cells
ICAM	intercellular adhesion molecule
Ig	immunoglobulin
IL-2	interleukin 2
IMRT	intensity-modulated radiation therapy
IR	infrared
IRS	insulin receptor substrate
ISF	interstitial fluid
LDL	low-density lipoprotein
mAbs	monoclonal antibodies
MHC	major histocompatibility complex
MRI	magnetic resonance imaging
MW	molecular weight
NHL	non-Hodgkin's lymphoma
NMR	nuclear magnetic resonance
PAH	para-aminohippuric acid
PAN	polyacrylonitrile
PCR	polymerase chain reaction
PDMS	polydimethylsiloxane
PE	polyethylene
PEG	poly(ethylene glycol)
PET	positron emission tomography *or* poly(ethylene terephthalate)
PEU	polyurethane
pHEMA	poly(2-hydroxymethacrylate)
PIP3	phosphatidylinositol 3,4,5-trisphosphate
PKB	protein kinase B
PLGA	poly(lactide-co-glycolide)
pMMA	poly(methyl methacrylate)
PP	polypropylene
PS	polystyrene
PSA	prostate specific antigen
PSu	polysulphone
PTFE	poly(tetrafluoroethylene)
PVC	poly(vinyl chloride)
PVP	poly(vinyl pyrrolidone)
RBC	red blood cell

RF	radio frequency
RGD	three peptide sequence of arginine (R), glycine (G), and aspartic acid (D)
RNA	ribonucleic acid
RPF	renal plasma flow
rRNA	ribosomal RNA
RSV	respiratory syncytial virus
RTK	receptor tyrosine kinase
SA	sinoatrial
SARS	Severe Acute Respiratory Syndrome
SGOT	serum glutamic oxaloacetic transaminase
siRNA	small interfering RNA
sMRI	structural magnetic resonance imaging
SPECT	single photon emission computed tomography
TIL	tumor-infiltrating lymphocytes
tRNA	transfer RNA
UV-VIS	ultraviolet-visible spectroscopy
VEGF	vascular endothelial cell growth factor
WBC	white blood cells
WHO	World Health Organization