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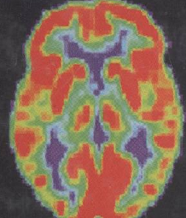
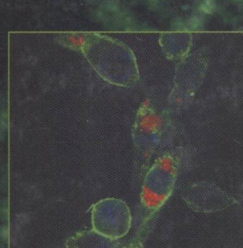
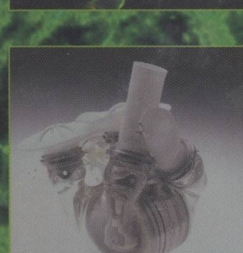
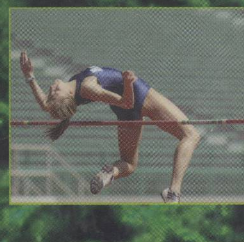


BIOMEDICAL ENGINEERING





Bridging Medicine and Technology



W. MARK SALTZMAN

BIOMEDICAL ENGINEERING

Bridging Medicine and Technology

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BIOMEDICAL ENGINEERING

Bridging Medicine and Technology

This is an ideal text for an introduction to biomedical engineering. The book presents the basic science knowledge used by biomedical engineers at a level accessible to all students 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. This introduction to bioengineering assembles foundational resources from molecular and cellular biology and physiology and relates them 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. 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.

W. Mark Saltzman is the Goizueta Foundation Professor of Chemical and Biomedical Engineering at Yale University. His research interests include materials for controlled drug delivery, drug delivery to the brain, and tissue engineering. He has taught at Johns Hopkins University and Cornell University and, after joining the Yale faculty in 2002, was named the first Chair of the Department of Biomedical Engineering.

Professor Saltzman has published more than 150 research papers, 3 authored books, and 2 edited books, and he is an inventor on more than 10 patents. His many honors and awards include a Camille and Henry Dreyfus Foundation Teacher-Scholar Award (1990), the Allan C. Davis Medal as Maryland's Outstanding Young Engineer (1995), the Controlled Release Society Young Investigator Award (1996), Fellow of the American Institute of Biological and Medical Engineers (1997), the Professional Progress in Engineering Award from Iowa State University (2000), Britton Chance Distinguished Lecturer in Engineering and Medicine at the University of Pennsylvania (2000), and Distinguished Lecturer of the Biomedical Engineering Society (2004).

CAMBRIDGE TEXTS IN BIOMEDICAL ENGINEERING

The *Cambridge Texts in Biomedical Engineering* series provides a forum for high-quality, accessible 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, but not limited to, biomechanics, physiology, biomedical instrumentation, imaging, signals and systems, cell engineering, and bioinformatics. The series blends theory and practice and is aimed primarily at biomedical engineering students, but it is suitable for broader courses in engineering, life science, and medicine.

To Zach and Alex

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

Preface

The field of biomedical engineering has expanded markedly in the past ten 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 field in which they would like to specialize. Each chosen specialty has a specific set of course requirements and is 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 fields of specialization and current research.

As a general introduction to the field, 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. 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 20 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 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 following table.

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

Acknowledgments

I have many people to thank, for encouragement and direct participation. It is a long list, and undoubtedly incomplete. For the past seven years, I have been immersed in a milieu rich in inspiration, creation, and succor. So I profited from brushes and asides, from long conversations and wisdom overheard.

I thank the Whitaker Foundation for their generous financial support, 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 over the past decade.

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. 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 gave one of the chapters a careful reading and provided thoughtful edits and suggestions, which made each chapter better, more readable. I thank Ian Suydam (Chapter 2), Kim Woodrow (Chapter 3), Michael Caplan (Chapter 5), Michelle Kelly (Chapter 7), Peter Aronson (Chapter 9), Deepak Vashishith (Chapter 10), and Themis Kyriakides (Chapter 15).

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, Walter Boron, Emile Boulpaep, and Peter Aronson can be felt in Chapters 5, 7, 8, and 9, 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. 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—and her never-say-no generosity—this text would still be in binders.

I thank Caroline, for letting me be me, as she is she. It is a marvel, isn't it, this unexpected shower, rescuing a late summer afternoon? Thanks, Caroline, for sharing it with 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

Contents

PART 3. BIOMEDICAL ENGINEERING