

CONTENTS

Contributors, xiii

Preface, xxi

How to Use this Book, xxiii

Biomaterials Science: An Evolving, Multidisciplinary Endeavor, xxv

Buddy D. Ratner, Allan S. Hoffman, Frederick J. Schoen, and Jack E. Lemons

History of Biomaterials, xli

Buddy D. Ratner

PART ONE

Materials Science and Engineering

SECTION I.1 Properties of Materials

I.1.1 Introduction: Properties of Materials: The Palette of the Biomaterials Engineer, 5

Jack E. Lemons

I.1.2 The Nature of Matter and Materials, 6

Buddy D. Ratner

I.1.3 Bulk Properties of Materials, 9

Christopher Viney

I.1.4 Finite Element Analysis in Biomechanics, 21

Michael Sacks, Antonio D'Amore, and Christopher Hobson

I.1.5 Surface Properties and Surface Characterization of Biomaterials, 34

Buddy D. Ratner

I.1.6 Role of Water in Biomaterials, 55

Buddy D. Ratner

SECTION I.2 Classes of Materials used in Medicine

I.2.1 Introduction: The Diversity and Versatility of Biomaterials, 63

Allan S. Hoffman

I.2.2 Polymers: Basic Principles, 64

Daniel E. Heath and Stuart L. Cooper

A. Polyurethanes, 79

Daniel E. Heath and Stuart L. Cooper

B. Silicones, 82

André Colas and Jim Curtis

C. Fluorinated Biomaterials, 92

Fang Liu and David W. Grainger

D. Acrylics, 103

Joe Antonucci and Sabine Dickens

- I.2.3 Metals: Basic Principles, 111**
John B. Brunski
- A. Titanium and Nitinol (NiTi), 120**
Abhay Pandit, Josep Planell, and Melba Navarro
 - B. Stainless Steels, 124**
Phillip J. Andersen
- I.2.4 Ceramics, Glasses, and Glass-Ceramics: Basic Principles, 128**
Larry L. Hench and Serena M. Best
- A. Natural and Synthetic Hydroxyapatites, 151**
Adele L. Boskey
 - B. Alumina, 162**
Ketul C. Papat and Tejal A. Desai
- I.2.5 Hydrogels, 166**
Nicholas A. Peppas and Allan S. Hoffman
- I.2.6 Degradable and Resorbable Biomaterials, 179**
Matthew Treiser, Sascha Abramson, Robert Langer, and Joachim Kohn
- I.2.7 Engineered Natural Materials, 195**
Glenn D. Prestwich and Sarah Atzet
- I.2.8 Pyrolytic Carbon For Long-Term Medical Implants, 209**
Robert B. More, Axel D. Haubold, and Jack C. Bokros
- I.2.9 Composites, 223**
Claudio Migliaresi
- I.2.10 Non-fouling Surfaces, 241**
Buddy D. Ratner and Allan S. Hoffman
- I.2.11 Applications of “Smart Polymers” as Biomaterials, 247**
Allan S. Hoffman
- I.2.12 Physicochemical Surface Modification of Materials Used in Medicine, 259**
Buddy D. Ratner and Allan S. Hoffman
- I.2.13 Surface Patterning, 276**
Ryan T. Hill and Ashutosh Chilkoti
- I.2.14 Medical Fibers and Biotextiles, 301**
Martin W. King and Sangwon Chung
- I.2.15 Textured and Porous Materials, 321**
Heidi E. Koschwanetz and William M. Reichert
- I.2.16 Electrospinning Fundamentals and Applications, 332**
Robert Akins and John Rabolt
- I.2.17 Surface-Immobilized Biomolecules, 339**
Allan S. Hoffman and Jeffrey A. Hubbell
- I.2.18 Biomimetic Materials, 349**
Drew Elizabeth Glaser and Christopher Viney
- I.2.19 Microparticles and Nanoparticles, 360**
Shalu Suri, Gang Ruan, Jessica Winter, Christine E. Schmidt

PART TWO Biology and Medicine

SECTION II.1 Some Background Concepts

- II.1.1 Introduction: Biology and Medicine – Key Concepts in the Use of Biomaterials in Surgery and Medical Devices, 393**
Buddy D. Ratner
- II.1.2 Adsorbed Proteins on Biomaterials, 394**
Thomas A. Horbett
- II.1.3 Cells and Surfaces *in vitro*, 408**
S. Adam Hacking and Ali Khademhosseini
- II.1.4 Cell Function and Response to Injury, 427**
Richard N. Mitchell and Frederick J. Schoen
- II.1.5 Tissues, the Extracellular Matrix, and Cell–Biomaterial Interactions, 452**
Frederick J. Schoen and Richard N. Mitchell
- II.1.6 Effects of Mechanical Forces on Cells and Tissues (The Liquid–Cell Interface), 474**
Daniel E. Conway, Suzanne G. Eskin, and Larry V. McIntire
- II.1.7 Stem Cells: Key Concepts, 487**
Richard L. Carpenedo and Todd C. McDevitt

SECTION II.2 Host Reaction to Biomaterials and Their Evaluation

- II.2.1 Introduction: Biological Responses to Biomaterials, 499**
Frederick J. Schoen
- II.2.2 Inflammation, Wound Healing, and the Foreign-Body Response, 503**
James M. Anderson
- II.2.3 Innate and Adaptive Immunity: The Immune Response to Foreign Materials, 512**
Richard N. Mitchell
- II.2.4 The Complement System, 533**
Richard J. Johnson
- II.2.5 Systemic Toxicity and Hypersensitivity, 545**
Arne Hensten and Nils Jacobsen
- II.2.6 Blood Coagulation and Blood–Materials Interactions, 551**
Stephen R. Hanson and Erik I. Tucker
- II.2.7 Tumors Associated with Biomaterials and Implants, 558**
Frederick J. Schoen
- II.2.8 Biofilms, Biomaterials, and Device-Related Infections, 565**
Paul Stoodley, Luanne Hall-Stoodley, Bill Costerton, Patrick DeMeo, Mark Shirtliff, Ellen Gawalt, and Sandeep Kathju

SECTION II.3 Biological Testing of Biomaterials

- II.3.1 How Well Will It Work? Introduction to Testing Biomaterials, 587**
Buddy D. Ratner
- II.3.2 The Concept and Assessment of Biocompatibility, 588**
Buddy D. Ratner and Frederick J. Schoen
- II.3.3 In Vitro Assessment of Cell and Tissue Compatibility, 593**
Michael F. Wolf, Kelly P. Coleman, and Gregory M. Lewerenz
- II.3.4 In Vivo Assessment of Tissue Compatibility, 609**
James M. Anderson and Frederick J. Schoen
- II.3.5 Evaluation of Blood–Materials Interactions, 617**
Buddy D. Ratner and Thomas A. Horbett
- II.3.6 Animal Surgery and Care of Animals, 635**
David Lee-Parritz
- II.3.7 Large Animal Models in Cardiac and Vascular Biomaterials Research and Assessment, 653**
Richard W. Bianco, Karen R. Wasiluk, Jessica M. Voight, Matthew T. Lahti, Andrew L. Rivard, and Robert P. Gallegos
- II.3.8 Microscopy for Biomaterials Science, 677**
Kip D. Hauch and Buddy D. Ratner

SECTION II.4 Degradation of Materials in the Biological Environment

- II.4.1 Introduction: The Body Fights Back – Degradation of Materials in the Biological Environment, 695**
Buddy D. Ratner
- II.4.2 Chemical and Biochemical Degradation of Polymers Intended to be Biostable, 696**
Arthur J. Coury
- II.4.3 The Biodegradation of Biodegradable Polymeric Biomaterials, 716**
Chien-Chi Lin and Kristi S. Anseth
- II.4.4 Degradative Effects of the Biological Environment on Metals and Ceramics, 728**
David F. Williams and Rachel L. Williams
- II.4.5 Pathological Calcification of Biomaterials, 739**
Frederick J. Schoen and Robert J. Levy

SECTION II.5 Applications of Biomaterials

- II.5.1 Introduction: Applications of Biomaterials, 757**
Frederick J. Schoen and Jack E. Lemons
- II.5.2 Nonthrombogenic Materials and Strategies: Case Study, 758**
Michael V. Sefton
- II.5.3 Introduction to Cardiovascular Medical Devices, 760**
Frederick J. Schoen
 - A. Substitute Heart Valves, 761**
Frederick J. Schoen and Robert F. Padera, Jr.
 - B. Endovascular Stents, Vascular Grafts, and Stent Grafts, 771**
Frederick J. Schoen and Robert F. Padera, Jr.

- C. Other Cardiovascular Devices, 784**
Robert F. Padera, Jr. and Frederick J. Schoen
- D. Implantable Cardiac Assist Devices and IABPs, 799**
Marc A. Simon, Harvey S. Borovetz, William R. Wagner
- II.5.4 Artificial Cells, 811**
Thomas Ming Swi Chang
- II.5.5 Extracorporeal Artificial Organs, 827**
Alastair Campbell Ritchie
- II.5.6 Orthopedic Applications, 841**
Nadim James Hallab and Joshua James Jacobs
- II.5.7 Dental Implantation, 882**
Jack E. Lemons and Carl E. Misch
- II.5.8 Adhesives and Sealants, 889**
David Christopher Watts
- II.5.9 Ophthalmologic Applications: Introduction, 905**
Roger Steinert and Rakhi Jain
 - A. Biomaterials: Contact Lenses, 909**
Jean Jacob
 - B. Intraocular Lens Implants: A Scientific Perspective, 917**
Anil S. Patel
 - C. Corneal Inlays and Onlays, 930**
Crystal Cunanan
 - D. Ophthalmologic Applications: Glaucoma Drains and Implants, 940**
Crystal Cunanan
 - E. The Development of a Retinal Prosthesis: A Significant Biomaterials Challenge, 946**
Mark S. Humayun, Adrian P. Rowley, John J. Whalen III, James D. Weiland, and Armand R. Tanguay, Jr.
- II.5.10 Bioelectrodes, 957**
Ramakrishna Venugopalan and Ray Ideker
- II.5.11 Cochlear Prostheses, 967**
Francis A. Spelman
- II.5.12 The Role of Biomaterials in Stimulating Bioelectrodes, 981**
P. Hunter Peckham, D. Michael Ackermann, Jr., and Christa W. Moss
- II.5.13 Medical Biosensors, 996**
Lisa LaFleur and Paul Yager
- II.5.14 Burn Dressings and Skin Substitutes, 1006**
Douglas L. Helm, Britlyn D. Orgill, Rei Ogawa, and Dennis P. Orgill
- II.5.15 Sutures, 1010**
M. Scott Taylor and Shalaby W. Shalaby
- II.5.16 Drug Delivery Systems, 1024**
Allan S. Hoffman, Editor
 - A. Introduction, 1024**
Allan S. Hoffman
 - B. Injected Nanocarriers, 1027**
Allan S. Hoffman, Wayne R. Gombotz, and Suzie H. Pun, Editors

- B.1. Introduction, 1027**
Allan S. Hoffman
- B.2. PEGylation of Drugs and Nanocarriers, 1028**
Allan S. Hoffman and Suzie H. Pun
- B.3. Targeting, 1028**
Patrick S. Stayton, Bilal Ghosn, and John T. Wilson
- B.4. Polymer–Drug Conjugates, 1036**
Suzie H. Pun and Allan S. Hoffman
- B.5. Liposomes, 1039**
Wayne R. Gombotz
- B.6. Polymeric Micelles, 1041**
Wayne R. Gombotz and Allan S. Hoffman
- B.7. Dendrimers, 1045**
Wayne R. Gombotz
- B.8. Nucleic Acid Delivery, 1047**
Suzie H. Pun and Allan S. Hoffman
- B.9. Polymeric and Albuminated Drug Nanoparticles, 1054**
Wayne R. Gombotz
- C. Injected Depot DDS, 1055**
Wayne R. Gombotz and Allan S. Hoffman
- D. Implants and Inserts, 1062**
Lothar W. Kleiner and Jeremy C. Wright
- E. Smart DDS, 1071**
Allan S. Hoffman
- F. Transdermal DDS, 1073**
Gary Cleary
- G. Oral Drug Delivery, 1083**
Clive G. Wilson
- II.5.17 Diagnostic Applications of Biomaterials, 1087**
Gonzalo Domingo, Kenneth R. Hawkins, Roger B. Peck, and Bernhard H. Weigl
- II.5.18 Medical Applications of Silicones, 1106**
Jim Curtis and André Colas
- SECTION II.6 Applications of Biomaterials in Functional Tissue Engineering**
 - II.6.1 Introduction: Rebuilding Humans using Biology and Biomaterials, 1119**
Frederick J. Schoen
 - II.6.2 Overview of Tissue Engineering Concepts and Applications, 1122**
Debanjan Sarkar, Weian Zhao, Sebastian Schaefer, James A. Ankrum, Grace S. L. Teo, Maria Nunes Pereira, Lino Ferreira, and Jeffrey M. Karp
 - II.6.3 Tissue Engineering Scaffolds, 1138**
Milind Singh, F. Kurtis Kasper, and Antonios G. Mikos
 - II.6.4 Cell Sources for Tissue Engineering: Mesenchymal Stem Cells, 1159**
Arnold I. Caplan
 - II.6.5 Micromechanical Design Criteria for Tissue Engineering Biomaterials, 1165**
Kaustabh Ghosh, Charles K. Thodeti and Donald E. Ingber

- II.6.6 Bioreactors for Tissue Engineering, 1178**
Nina Tandon, Elisa Cimetta, Sarindr Bhumiratana, Amandine Godier-Furnemont, Robert Maidhof, and Gordana Vunjak-Novakovic
- II.6.7 Bone Tissue Engineering, 1194**
Justin L. Brown, Sangamesh G. Kumbhar, and Cato T. Laurencin
- II.6.8 Cartilage and Ligament Tissue Engineering: Biomaterials, Cellular Interactions, and Regenerative Strategies, 1214**
Catherine K. Kuo, Wan-Ju Li, and Rocky S. Tuan
- II.6.9 Blood Vessel Tissue Engineering, 1237**
Stacey C. Schutte and Robert M. Nerem
- II.6.10 Heart Valve Tissue Engineering, 1246**
Frederick J. Schoen and Simon P. Hoerstrup
- II.6.11 Cardiac Muscle Tissue Engineering, 1262**
Amandine Godier-Furnemont and Gordana Vunjak-Novakovic
- II.6.12 Tissue-engineered Skin Substitutes, 1276**
J. N. Mansbridge
- II.6.13 Esophageal and Gastrointestinal Tissue Engineering, 1288**
Buddy D. Ratner
- II.6.14 Neuronal Tissue Engineering, 1291**
Isaac P. Clements, Jennifer M. Munson, and Ravi V. Bellamkonda
- II.6.15 Immunoisolation, 1306**
Roshni S. Rainbow and Michael J. Lysaght
- II.6.16 Tissue Engineering with Decellularized Tissues, 1316**
Stephen F. Badylak, Bryan N. Brown, and Thomas W. Gilbert

PART THREE

Practical Aspects of Biomaterials

SECTION III.1 Implants, Devices, and Biomaterials: Special Considerations

- III.1.1 Introduction: Implants, Devices, and Biomaterials: Special Considerations, 1337**
Frederick J. Schoen
- III.1.2 Sterilization of Implants and Devices, 1339**
Byron Lambert and Jeffrey Martin
- III.1.3 Correlation, Materials Properties, Statistics and Biomaterials Science, 1354**
Buddy D. Ratner
- III.1.4 Device Failure Mode Analysis, 1361**
Frederick J. Schoen and Allan S. Hoffman
- III.1.5 Implant Retrieval and Evaluation, 1368**
James M. Anderson, Frederick J. Schoen, Stanley A. Brown, and Katharine Merrit

SECTION III.2 Voluntary Standards, Regulatory Compliance, and Non-Technical Issues

- III.2.1 Introduction: Voluntary Standards, Regulatory Compliance, and Other Non-technical Issues, 1387**
Frederick J. Schoen and Jack E. Lemons

- III.2.2 Commercialization: What it Takes to get a Product to Market, 1389**
Joshua Tolkoﬀ and Richard Anders
- III.2.3 Voluntary Consensus Standards, 1399**
Jack E. Lemons
- III.2.4 Regulatory Overview for Medical Products using Biomaterials, 1405**
Elaine Duncan
- III.2.5 Principles of Reimbursement for Medical Devices, 1413**
Fred Cahn
- III.2.6 Corporate Considerations on Biomaterials and Medical Devices: Case Studies in Regulation and Reimbursement, 1418**
Gail D. Baura
- III.2.7 Ethical Issues in Biomaterials and Medical Devices, 1425**
Taufiek Rajab, Andrew L. Rivard, Karen R. Wasiluk, Robert P. Gallegos, and Richard W. Bianco
- III.2.8 Legal Aspects of Biomaterials, 1431**
Jay P. Mayesh and Angela R. Vicari
- III.2.9 Clinical Trials for Medical Devices, 1443**
Gary L. Grunkemeier, Ruyun Jin, Lian Wang, and Albert Starr
- III.2.10 Entrepreneurship in Biomaterials, 1459**
Robert Langer, Jason Fuller, and Mark Levin
- III.2.11 Postmarket Considerations in Biomaterials and Medical Devices, 1472**
David W. Feigal, Jr.

Appendices

- Appendix A: Properties of Biological Fluids, 1479**
Steven M. Slack
- Appendix B: Properties of Soft Materials, 1483**
M. Cristina L. Martins
- Appendix C: Chemical Compositions of Metals Used for Implants, 1485**
Jack E. Lemons
- Appendix D: The Biomaterials Literature, 1486**
Buddy D. Ratner
- Appendix E: Chapter II.5.2 — Nonthrombogenic Treatments and Strategies, 1488**
Michael V. Sefton, Cynthia H. Gemmell, and Maud B. Gorbet
- Appendix F: Chapter II.5.16 — Drug Delivery Systems: H, Mucosal Drug Delivery, 1510**
Ying Lu and Kinam Park
- Appendix G: Chapter II.5.16 — Drug Delivery Systems: I, Smart Hydrogels as *In Vivo* Drug Delivery Systems, 1518**
Sungwon Kim and Kinam Park
- Index, 1525**