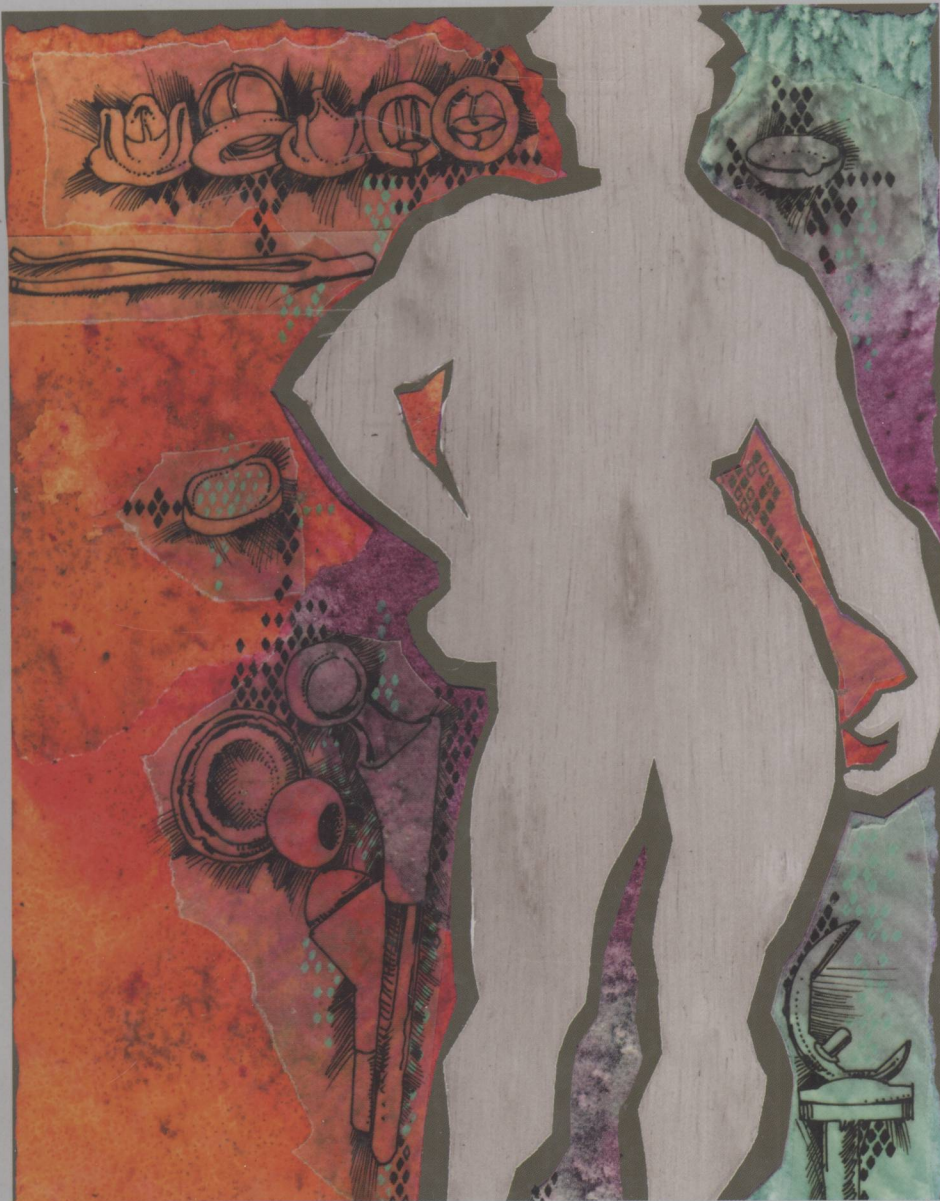


Pearson Prentice Hall Bioengineering

# BIOMATERIALS

The Intersection of Biology  
and Materials Science



J. S. Temenoff | A. G. Mikos

R318.08  
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# Biomaterials

## The Intersection of Biology and Materials Science

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E2008001239



Upper Saddle River, New Jersey 07458

Library of Congress Cataloging-in-Publication Data on file.

Editorial Director, Computer Science, Engineering, and Advanced Mathematics: *Marcia J. Horton*  
Senior Editor: *Holly Stark*  
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Pearson Prentice Hall  
Pearson Education, Inc.  
Upper Saddle River, New Jersey 07458

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Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

ISBN 0-13-009710-1  
978-0-13-009710-1

Pearson Education LTD., *London*  
Pearson Education Australia Pty, Limited, *Sydney*  
Pearson Education Singapore, Pte. Ltd  
Pearson Education North Asia Ltd., *Hong Kong*  
Pearson Education Canada, Ltd., *Toronto*  
Pearson Education de Mexico, S.A. de C.V.  
Pearson Education Japan, *Tokyo*  
Pearson Education Malaysia, Pte. Ltd.  
Pearson Education, Inc., *Upper Saddle River, New Jersey*

# Dedications

To my mother, who encouraged me to ask “Why?”  
and my father, who encouraged me to ask “How?”

(JST)

To Mary, Georgios, and Lydia

(AGM)

# Foreword

Biomaterials have received considerable attention over the last thirty years as a means of treating diseases and easing suffering. The focus of treatment is no longer in conventional passive devices but rather a combination of device-integrated biomaterials and the necessary therapeutic treatment. Biomaterials have found applications in approximately 8,000 various kinds of medical devices that have been used in repairing skeletal systems, returning cardiovascular functionality, replacing organs, and repairing or returning senses. Even though biomaterials have had a pronounced impact in medical treatment, a need still exists to be able to design and develop better polymer, ceramic, and metal systems along with the ability to characterize and test their properties. This book is the first in a long time to point out such need and to give students a clear picture of how to approach such subjects.

The two authors take a fresh approach to the problem. They focus on a thorough materials analysis that does not take shortcomings on mechanical properties, structure or molecular analysis, but at the same time offers a thorough presentation of biological considerations in a succinct way.

Polymeric biomaterials originated as off-the-shelf materials that clinicians were able to use in solving a problem—dialysis tubing was originally made of cellulose acetate, vascular grafts were fabricated from Dacron, and artificial hearts were molded from polyurethanes. However, these materials did not possess the chemical, physical, and biological properties necessary to prevent further complications. Thus, recent advances in synthetic techniques have allowed these properties to be imparted on biomaterials that help to alleviate the accompanying biocompatibility issues. This becomes so clear in this book!

Much consideration is given to the design of a material for a specific application. Certain properties of the material must be controlled so as to perform the necessary function and elicit the appropriate response. These properties can be tailored to the specific need by carefully controlling the structural characteristics, modifying the surface properties, and employing biomimetic characteristics in the material design. Biomimetic principles are gaining widespread acceptance in the development of biomaterials, especially for drug delivery, regenerative medicine, and nanotechnology. The use of protein moieties and protein-like components on the surface or in the bulk of synthetic materials contacting biological systems has certain advantage over traditional systems. The authors are to be congratulated for pointing this out.

This book will be a successful text because it recognizes that biomaterials are first and foremost *materials*! The authors provide a refreshing approach to the medical aspects of biomaterials. It has exceptionally lucid chapters on Cell/Materials and Protein/Materials interactions. The students will finally understand immunology when they read Chapter 12. And thrombosis, one of the most important problems of biomaterials, is simply expertly presented in Chapter 13.

This textbook is a comprehensive fundamental text that will undoubtedly become a staple in biomaterials education. It addresses the right amount of knowledge and will fill a major gap in the field of biomaterials science. Professors Temenoff and Mikos have made a great service to the field.

Nicholas A. Peppas, Sc.D.  
Fletcher S. Pratt Chair of Chemical Engineering,  
Biomedical Engineering, and Pharmacy  
University of Texas at Austin



# Preface

*Intersect*: to share a common area (*Merriam-Webster Dictionary*)

Although this book is entitled *Biomaterials: The Intersection of Biology and Materials Science*, we believe that this field has evolved over approximately the past fifty years from the intersection of multiple disparate viewpoints, including materials science, biology, engineering, and clinical, business, and regulatory perspectives. With this history, the multidisciplinary nature of biomaterials is inescapable. As educators in this field, we have taken on the particular challenge of preparing students with a broad range of backgrounds to address the complex issues associated with designing and implementing new biomedical devices.

With this in mind, we set out to write a balanced and cohesive textbook that would introduce fundamental concepts of biomaterials to undergraduate engineering majors in their second year of study or later. Given this target audience, the text assumes basic knowledge of chemistry and physics, but does not require in-depth exposure to more complex mathematical concepts such as partial differential equations, or any knowledge of cell biology or biochemistry.

After an overview of the scope of the biomaterials field, Chapter 1 reviews basic chemical principles required to understand the forces underlying the material structures introduced in Chapter 2. Chapters 3 and 4 provide more information about physical and mechanical properties of the main classes of biomaterials (metals, ceramics, and polymers). Throughout these sections, material classes are compared and contrasted to further student knowledge of how each may be optimal for different applications. After discussion of how materials are “built up” from their subunits, in Chapters 5 and 6, we turn to how these materials are “torn down” (degraded) in the body and how processing parameters affect key material properties, such as degradation and mechanical strength.

Chapters 7 and 8 are both the physical and intellectual centers of this text as they represent contact between the materials science and the biological concepts in the book. Topics covered in these chapters include surface modification techniques and their effects on protein adsorption. Chapter 9 relates how cells react to these adsorbed proteins in general, before leading into a discussion of particular cell responses (acute inflammation and wound healing) in Chapters 10 and 11. No depiction of biological response to implanted materials would be complete without a discussion of immune response and hypersensitivity (Chapter 12), thrombosis (Chapter 13) and infection, tumorigenesis, and pathologic calcification (Chapter 14).

To maintain a balanced discussion, the fourteen chapters in this book were purposefully divided into seven chapters on materials science, and seven chapters on the biological response. Continuing the spirit of “intersection,” characterization methods and regulatory issues were not written as insular sections, but rather included throughout book as appropriate.

The twenty-first century will surely present even greater challenges to the biomaterialist in integrating ever more complex biological knowledge into the design of improved materials. We believe that exploration of overlap between these disparate fields is essential and hope that this book provides a first step for many future biomaterialists in discovering vital intersections of their own.

# Acknowledgments

The development and production of a textbook such as this is an ambitious undertaking that requires the contributions of a myriad of talented and dedicated individuals. Accordingly, we would like to acknowledge the several individuals and institutions whose assistance and perseverance made the completion of this text possible. Two individuals were indispensable in the preparation of this work. Kurt Kasper, Ph.D. (Rice University) provided summaries for each of the chapters, authored the example problems that occur throughout the text, contributed to writing select sections of the text, and worked diligently in editing the various drafts of this book. Mark Sweigart, Ph.D. (Rice University) wrote the end-of-chapter problems, industriously assembled all of the figures for this textbook, formatted all of the equations, and patiently edited the text for stylistic consistency. Elizabeth Christensen, Ph.D. (Rice University) and Michael Hacker, Ph.D. (Rice University) contributed select figures and kindly compiled literature reports that were integrated into the material in this text. Additionally, we thank the entire biomaterials faculty at Georgia Tech and Emory University for their feedback during the preparation of the text, particularly Julia Babensee, Ph.D. and Andrés García, Ph.D., who contributed to the end-of-chapter problems.

Further, we are indebted to the various pioneers in biomaterials research who thoroughly reviewed the first draft of this book. Specifically, we extend our deep appreciation to James M. Anderson, M.D., Ph.D. (Case Western Reserve University), Joel D. Bumgardner, Ph.D. (University of Memphis), Arnold I. Caplan, Ph.D. (Case Western Reserve University), M. Cindy Farach-Carson, Ph.D. (University of Delaware), Paul S. Engel, Ph.D. (Rice University), John A. Jansen, D.D.S., Ph.D. (Radboud University Nijmegen Medical Center), Robert Langer, Sc.D. (Massachusetts Institute of Technology), Nicholas A. Peppas, Sc.D. (University of Texas at Austin), Alan J. Russell, Ph.D. (University of Pittsburgh), and Frederick J. Schoen, M.D., Ph.D. (Brigham and Women's Hospital) for their meticulous reviews and constructive comments.

We would also like to acknowledge several individuals who played vital roles in the evaluation and development of the text. Particularly, we thank Valeria Milam, Ph.D. (Georgia Tech) for helping to test this book in the classroom and for providing valuable alterations to the various drafts of the text. We also thank Larry McIntire, Ph.D. and Robert Nerem, Ph.D. for their comments on this book, as well as for providing a dynamic and supportive environment in which to test this text. We appreciate the teaching assistants and students in the Georgia Tech Introduction to Biomaterials classes (BMED 4823/MSE 4803 and BMED/MSE 4751) in the Spring and Fall Semesters of 2006 and the Spring Semester of 2007 for their patience during the classroom testing of this textbook. We also thank Simon Young, D.D.S. (Rice University) and the graduate students in the laboratory of Johnna Temenoff, Ph.D. at Georgia Tech/Emory University (namely, Kelly Brink, Derek Doroski, Jeremy Lim, and Peter Yang) for their perseverance and diligence in helping edit the final drafts of this book.

We extend also our gratitude to several other individuals who were essential in attending to the details surrounding the production of this book. Carol D. Lofton (Rice University) worked tirelessly to secure the copyright permissions needed for



publication. Also, the staff in the Coulter Department of Biomedical Engineering at Georgia Tech/Emory University kindly assisted in the preparations of the various drafts of the text and in obtaining the required copyright permissions. Finally, we acknowledge the artistic talent of Karen Ku, who drew the inspirational art work appearing on the cover of this book.

J. S. TEMENOFF  
A. G. MIKOS

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