

Biomaterials Fabrication and Processing HANDBOOK

Edited by
Paul K. Chu
Xuanyong Liu



CRC Press
Taylor & Francis Group

R318
B615.2

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E2008000916



CRC Press

Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

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CRC Press is an imprint of Taylor & Francis Group, an Informa business

No claim to original U.S. Government works
Printed in the United States of America on acid-free paper
10 9 8 7 6 5 4 3 2 1

International Standard Book Number-13: 978-0-8493-7973-4 (Hardcover)

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Library of Congress Cataloging-in-Publication Data

Biomaterials fabrication and processing handbook / [edited by] Paul K. Chu and Xuanyong Liu.

p. ; cm.

"A CRC title."

Includes bibliographical references and index.

ISBN 978-0-8493-7973-4 (alk. paper)

1. Biomedical materials. 2. Biomedical engineering. I. Chu, Paul K. II. Liu, Xuanyong. III. Title.

[DNLM: 1. Biocompatible Materials. 2. Biosensing Techniques. 3. Nanotechnology--methods. 4.

Tissue Engineering--methods. QT 37 B61413 2008]

R857.M3B5696 2008

610.284--dc22

2007042613

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Preface

Biomaterials are used in the biomedical industry to replace or repair injured and nonfunctional tissues. The worldwide biomaterials market was worth over \$300 billion in 2005. This market is projected to grow at a rate of 20% per year, and a growing number of scientists and engineers are engaged in fabrication and research of biomaterials. Recognizing the ever increasing importance of biomaterials, a number of books on biomaterials were published in the past 20 years. The *Biomaterials Fabrication and Processing Handbook* is different from these published books in that it brings together the various aspects of fabrication and processing of the latest biomaterials, including tissue engineering scaffold materials, drug delivery systems, and nanobiomaterials and biosensors. Some common implant materials including hard tissue materials, blood-contacting materials, and soft tissue materials are also described in this book.

Tissue engineering involves the development of new materials or devices capable of interacting specifically with biological tissues. The key to tissue engineering is the preparation of scaffolds using materials with the appropriate composition and structure. In the drug industry, advances in drug delivery systems are very important. Controlled release can be obtained by selecting the appropriate materials to produce the drug delivery system. Attempts have been made to incorporate drug reservoirs into implantable devices for sustained and preferably controlled release. Nanotechnology also plays an important role in the biomedical and biotechnology industries and has been used in the preparation of drugs for protein delivery, tissue engineering, bones, cardiovascular biomaterials, hard tissue replacements, biosensors, and biological microelectromechanical systems (Bio-MEMS). This book covers the latest information pertaining to tissue engineering scaffold materials, drug delivery systems, and nanobiomaterials and biosensors.

The book has 21 chapters describing different types of biomaterials, and is divided into four sections, namely tissue engineering scaffold materials, drug delivery systems, nanobiomaterials and biosensors, and other biomaterials. The section on tissue engineering describes inorganic and composite bioactive scaffolds for bone tissue engineering, design, fabrication, and characterization of scaffolds via solid free-form fabrication techniques, control and monitoring of scaffold architecture for tissue engineering, rapid prototyping methods for tissue engineering applications, as well as design and fabrication principles of electrospinning of scaffolds. The section on drug delivery systems discusses nanoparticles in cancer drug delivery systems, polymeric nano/microparticles for oral delivery of proteins and peptides, nanostructured porous biomaterials for controlled drug release systems, and inorganic nanostructures for drug delivery. The section on nanobiomaterials and biosensors includes self-assembly of nanostructures as biomaterials, electrohydrodynamic processing of micro- and nanometer biological materials, fabrication and functions of biohybrid nanomaterials prepared via supramolecular approaches, polypyrrole nano- and microsensors and actuators for biomedical applications, as well as processing of biosensing materials and biosensors. The last section, which deals with other biomaterials, includes synthetic and natural degradable polymeric biomaterials, electroactive polymers as smart materials with intrinsic actuation properties such as new functionalities for biomaterials, blood-contacting surfaces, improvement of blood compatibility of biomaterials using a novel antithrombin–heparin covalent complex, surface modification of biomaterials using plasma immersion ion implantation and deposition, biomaterials for gastrointestinal medicine, repair, and reconstruction, and biomaterials for cartilage reconstruction and repair.

These chapters have been written by renowned experts in their respective fields, and this book is valuable to the biomaterials and biomedical engineering community. It is intended for a broad and diverse readership including bioengineers, materials scientists, physicians, surgeons, research students, practitioners, and researchers in materials science, bioengineering, and medicine.

Readers will be able to familiarize themselves with the latest techniques in biomaterials and processing. In addition, each chapter is accompanied by an extensive list of references for readers interested in pursuing further research.

The outstanding cooperation from contributing authors who devoted their valuable time and effort to write excellent chapters for this handbook is highly appreciated. We are also indebted to all our colleagues who have made this book a reality.

Paul K. Chu
Xuanyong Liu

Editors



Paul K. Chu is a professor (chair) of materials engineering at the City University of Hong Kong. He received a BS in mathematics from The Ohio State University in 1977 and an MS and a PhD in chemistry from Cornell University in 1979 and 1982, respectively. Professor Chu's research activities are quite diverse, encompassing plasma surface engineering and various types of materials and nanotechnology. He has published over 550 journal papers and has been granted eight U.S. and three Chinese patents. He is a fellow of the IEEE, AVS, and HKIE, senior editor of *IEEE Transactions on Plasma Science*, associate editor of *International Journal of Plasma Science and Engineering*, and a member of the editorial board of *Materials Science & Engineering: Reports*, *Surface and Interface Engineering*, and *Biomolecular Engineering*. He is a member of the Plasma-Based Ion

Implantation and Deposition International Committee, Ion Implantation Technology International Committee, and IEEE Plasma Science and Application Executive Committee.



Xuanyong Liu is an associate professor of materials engineering at the Shanghai Institute of Ceramics, Chinese Academy of Sciences (SICCAS), and a professor at Hunan University. He received a BS and an MS in materials science and engineering from Hunan University in 1996 and 1999, respectively, and a PhD in materials science and engineering from SICCAS in 2002. His doctoral dissertation was awarded the National Excellent Doctoral Dissertation of People's Republic of China in 2004. Professor Liu's primary research focus is on surface modification of biomaterials. He has founded the Surface Engineering of Biomaterials Group in SICCAS and has published over 70 journal papers, including 14 papers on biomaterials.

Contributors

Arti Ahluwalia

Interdepartmental Research Center
“E. Piaggio” and Department
of Chemical Engineering
University of Pisa
Pisa, Italy

Hua Ai

National Engineering Research Center
for Biomaterials
Sichuan University
Chengdu, China

Katsuhiko Ariga

WPI Center for Materials Nanoarchitectonics
National Institute for Materials Science
Tsukuba, Japan

Halil Murat Aydin

Institute for Science and Technology
in Medicine
Keele University
Staffordshire, U.K.

Pierre Olivier Bagnaninchi

Institute for Science and Technology
in Medicine
Keele University
Staffordshire, U.K.

Yevgeny Berdichevsky

Electrical and Computer Engineering
Department
University of California
San Diego, California, U.S.A.

Leslie Roy Berry

Henderson Research Centre
Hamilton, Ontario, Canada

Aldo R. Boccaccini

Department of Materials
Imperial College
London, U.K.

Oana Bretcanu

Department of Materials
Imperial College
London, U.K.

Federico Carpi

Interdepartmental Research Centre
“E. Piaggio”
University of Pisa
Pisa, Italy

Anthony Kam Chuen Chan

Henderson Research Centre
Hamilton, Ontario, Canada

Qi-Zhi Chen

Department of Materials
Imperial College
London, U.K.

Paul K. Chu

Department of Physics and Materials
Science
City University of Hong Kong
Hong Kong, China

Robert Lewis Clark

Center for Biologically Inspired Materials
and Material Systems
Pratt School of Engineering
Duke University
Durham, North Carolina, U.S.A.

Cassilda Cunha-Reis

Institute for Science and Technology
in Medicine
Keele University
Staffordshire, U.K.

Richard M. Day

Department of Medicine
University College
London, U.K.

Danilo De Rossi

Interdepartmental Research Centre "E. Piaggio"
University of Pisa
Pisa, Italy

Sanjukta Deb

Department of Biomaterials
Dental Institute, King's College
London, U.K.

Andrew K. Ekaputra

Graduate Program in Bioengineering
National University of Singapore
Singapore

Mirosława El Fray

Division of Biomaterials and Microbiological
Technologies
Szczecin University of Technology Polymer
Institute
Szczecin, Poland

Yujiang Fan

National Engineering Research Center
for Biomaterials
Sichuan University
Chengdu, China

Ricky K.Y. Fu

Department of Physics and Materials Science
City University of Hong Kong
Hong Kong, China

Zhongwei Gu

National Engineering Research Center
for Biomaterials
Sichuan University
Chengdu, China

Dietmar W. Hutmacher

Division of Regenerative Medicine
Institute of Health and Biomedical
Innovation
Queensland University of Technology
Brisbane, Australia

So Yeon Kim

Division of Engineering Education
College of Engineering
Chungnam National University
Daejeon, South Korea

Menno L.W. Knetsch

Centre for Biomaterials Research
University of Maastricht
Maastricht, The Netherlands

Krzysztof J. Kurzydłowski

Division of Materials Design
Faculty of Materials Science and Engineering
Warsaw University of Technology
Warsaw, Poland

Young Moo Lee

School of Chemical Engineering
Hanyang University
Seoul, South Korea

Jifan Li

Hitachi Chemical Research Center
Irvine, California, U.S.A.

Yang Yang Li

Hitachi Chemical Research Center
Irvine, California, U.S.A.
and
Department of Physics and Materials Science
City University of Hong Kong
Hong Kong, China

Xuanyong Liu

Shanghai Institute of Ceramics
Chinese Academy of Sciences
Shanghai, China
and
Department of Physics and Materials Science
City University of Hong Kong
Hong Kong, China

Yanyan Liu

Shanghai Institute of Ceramics
Chinese Academy of Sciences
Shanghai, China
and
Laboratory of Special Functional Materials
Henan University
Kaifeng, China

Yu-Hwa Lo

Electrical and Computer Engineering
Department
University of California
San Diego, California, U.S.A.

Bunichiro Nakajima

Hitachi Chemical Research Center
Irvine, California, U.S.A.

S. Sajeesh

Division of Biosurface Technology
Sree Chitra Tirunal Institute for Medical
Sciences and Technology
Thiruvananthapuram, India

Chandra P. Sharma

Division of Biosurface Technology
Sree Chitra Tirunal Institute for Medical
Sciences and Technology
Thiruvananthapuram, India

Wojciech Swieszkowski

Division of Materials Design
Faculty of Materials Science and Engineering
Warsaw University of Technology
Warsaw, Poland

Giovanni Vozzi

Interdepartmental Research Center "E. Piaggio"
and Department of Chemical Engineering
University of Pisa
Pisa, Italy

Maria Ann Woodruff

Division of Regenerative Medicine
Institute of Health and Biomedical Innovation
Queensland University of Technology
Brisbane, Australia

Yiquan Wu

Center for Biologically Inspired Materials
and Material Systems
Pratt School of Engineering
Duke University
Durham, North Carolina, U.S.A.

Ying Yang

Institute for Science and Technology
in Medicine
School of Medicine
Keele University
Staffordshire, U.K.

Yu Yang

Shanghai Institute of Ceramics
Chinese Academy of Sciences
Shanghai, China

Yingchun Zhu

Shanghai Institute of Ceramics
Chinese Academy of Sciences
Shanghai, China

Ying-Jie Zhu

State Key Laboratory of High
Performance Ceramics
and Superfine Microstructures
Shanghai Institute of Ceramics
Chinese Academy of Sciences
Shanghai, China

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Part I

Tissue Engineering Scaffold Materials

1 Inorganic and Composite Bioactive Scaffolds for Bone Tissue Engineering

Qi-Zhi Chen, Oana Bretcanu, and Aldo R. Boccaccini

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1.1 INTRODUCTION

Being a modern discipline, tissue engineering encounters various challenges, such as the development of suitable scaffolds that temporarily provide mechanical support to cells at an early stage of implantation until the cells are able to produce their own extracellular matrix (ECM) [1]. Numerous biomaterials and techniques to produce three-dimensional (3-D) tissue-engineering scaffolds have been considered; biomaterials include polymers, ceramics, and their composites, as discussed in the literature [1–3]. In this chapter, we present an up-to-date summary of the fabrication technologies for tissue-engineering scaffolds, including the choice of suitable materials and related fabrication techniques, with a focus on the development of synthetic scaffolds based on bioceramics, glasses, and their composites combined with biopolymers for bone regeneration. Being one of the most promising technologies, the replication method for the production of highly porous, biodegradable, and mechanically competent Bioglass®-derived glass-ceramic scaffolds is highlighted. The enhancement of scaffold properties and functions by surface modification is also discussed, and examples of novel approaches are given.

1.2 DESIGN OF 3-D SCAFFOLDS

In an organ, cells and their ECM are organized into 3-D tissues. Therefore, in tissue engineering a highly porous 3-D matrix (i.e., scaffold) is necessary to accommodate cells and to guide their growth and tissue regeneration in 3-D structures. This is particularly relevant in the field of bone tissue engineering and regeneration, bone being a highly hierarchical 3-D composite structure. Moreover, the structure of bone tissue varies with its location in the body. So the selection of configurations as well as appropriate biomaterials depends on the anatomic site for regeneration, the mechanical loads present at the site, and the desired rate of incorporation. Ideally, the scaffold should be porous enough to support cell penetration, tissue ingrowth, rapid vascular invasion, and nutrient delivery. Moreover, the matrix should be designed to guide the formation of new bones in anatomically relevant shapes, and its degradation kinetics should be such that the biodegradable scaffold retains its physical (e.g., mechanical) properties for at least 6 months (for *in vitro* and *in vivo* tissue regeneration) [1,3]. Important scaffold design parameters are summarized in Table 1.1.

The design of highly porous scaffolds involves a critical issue related to their mechanical properties and structural integrity, which are time dependent. For example, it has been reported that the compressive strength of hydroxyapatite scaffolds increases from ~10 to ~30 MPa because of tissue ingrowth *in vivo* [5]. This finding leads to a conclusion that it might not be necessary to have a starting scaffold with a mechanical strength equal to that of a bone, because cultured cells on the scaffold *in vitro* will create a biocomposite and increase the strength of the scaffold significantly.

Another factor that affects scaffold design is the need for vascularization and angiogenesis in the constructs [6]. *In vitro* engineering approaches face the problem of critical thickness while regenerating tissue in the absence of true vascularization: mass transportation into tissue is difficult beyond a thin peripheral layer of a tissue construct even if artificial means are used to supply nutrients and oxygen [7]. Diffusion barriers that are present *in vitro* are most likely to become more