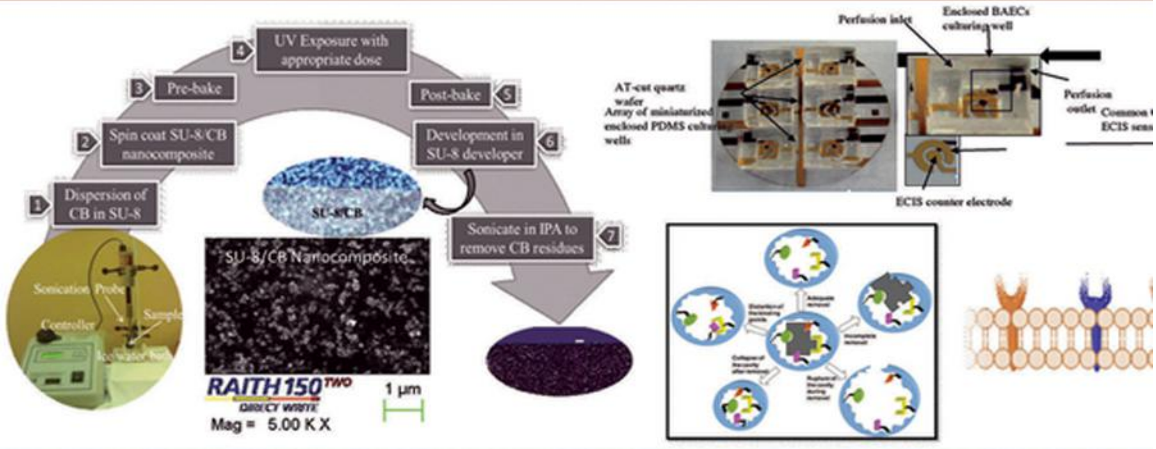
Advance Materials Series

ADVANCED BIOMATERIALS AND BIODEVICES



Edited By

Ashutosh Tiwari and Anis N. Nordin

Scrivener Publishing

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Advanced Biomaterials and Biodevices

Scrivener Publishing
100 Cummings Center, Suite 541J
Beverly, MA 01915-6106

Advanced Materials Series

The Advanced Materials Series provides recent advancements of the fascinating field of advanced materials science and technology, particularly in the area of structure, synthesis and processing, characterization, advanced-state properties, and applications. The volumes will cover theoretical and experimental approaches of molecular device materials, biomimetic materials, hybrid-type composite materials, functionalized polymers, superamolecular systems, information- and energy-transfer materials, biobased and biodegradable or environmental friendly materials. Each volume will be devoted to one broad subject and the multidisciplinary aspects will be drawn out in full.

Series Editor: Dr. Ashutosh Tiwari
Biosensors and Bioelectronics Centre
Linköping University
SE-581 83 Linköping
Sweden
E-mail: ashutosh.tiwari@liu.se

Managing Editors:
Swapneel Despande and Sudheesh K. Shukla

Publishers at Scrivener
Martin Scrivener(martin@scrivenerpublishing.com)
Phillip Carmical (pcarmical@scrivenerpublishing.com)

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Cover design by Russell Richardson

Library of Congress Cataloging-in-Publication Data:

ISBN 978-1-118-77363-5

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

Contents

Preface

Biomaterials are the most rapidly emerging field of biodevices. The design and development of biomaterials play a significant role in the diagnosis, treatment and prevention of diseases. Recently a variety of scaffolds/carriers have been evaluated for tissue regeneration, drug delivery, sensing and imaging. Liposomes and microspheres have been developed for sustained delivery and several anti-cancer drugs have been successfully formulated using biomaterials. Targeting of drugs to certain physiological sites has emerged as a promising tool for treatment, as it improves drug efficiency and requires reduced drug dosage. Using biodevices to target drugs may improve therapeutic success through limiting adverse drug effects, which results in better patient compliance and medication adherence. When used with highly selective and sensitive biomaterials, cutting-edge biodevices can allow the rapid and accurate diagnosis of diseases; creating a platform for research and development, especially in the field of treatment for prognosis and detection of diseases in the early stage. The emphasis of this book is the emerging area of biomaterials and biodevices that incorporate therapeutic agents, molecular targeting and diagnostic imaging capabilities.

The book is comprised of 15 chapters in total and has been divided into two major categories: "Cutting-edge Biomaterials" and "Innovative Biodevices." The first section, "Cutting-edge Biomaterials," focuses on state-of-the-art biomaterials such as nanostructures, smart polymers and nanoshells which can be used for medical applications. The first chapter, "Frontiers for Bulk Nanostructured Metals in Biomedical Applications," illustrates the use of severe plastic deformation technique (SPD) to enhance the properties of nanostructured metals. This technique has been highly successful in augmenting the biomedical and mechanical properties of metals such as titanium, magnesium, cobalt and stainless steel. The second chapter, "Stimuli-responsive Materials Used as Medical Devices in Loading and Releasing of Drugs," describes the potential of different polymers for use in controlled drug release. The main objective of using stimuli-responsive materials is to improve the performance of medical devices.

However, the use of these materials is still in its infancy, as they are still prone to infections, inflammation and biofilm formation on their surface. Chapter three, “Recent Advances with Liposomes as Drug Carriers,” is a very interesting and comprehensive chapter which explains the use of artificially prepared bilayered phospholipid vesicles as a tool for drug delivery. Significant advancements in the last couple of decades have improved the efficiency of liposomes as a drug carrier and solved numerous problems related to their use. Among these are improvements in terms of the selectivity of drug carriers using engineered peptides, the use of dual-ligand combinations to reduce non-specific interactions with healthy tissues and also lowering ligand concentration using high-affinity ligands.

The chapter on “Fabrication, Properties of Nanoshells with Controllable Surface Charge and Its Applications,” describes the methods used to synthesize and assemble monodispersed core-shell nanoparticles. These methods are useful for improving adsorption of CNT for ultrasensitive detection using surface-enhanced Raman scattering. The chapter, “Advanced Healthcare Materials: Chitosan,” provides a review of chitin and chitosan as renewable healthcare biopolymers for biomedical applications such as wound healing or tissue regeneration, drug delivery and antimicrobial studies. The next chapter, “Chitosan and Low Molecular Weight Chitosan: Biological and Biomedical Applications,” also describes chitosan’s immunological and antioxidant properties, as well as its use for the treatment of tumors and viruses. The chapter, “Anticipating Behavior of Advanced Materials in Healthcare,” provides a general overview on the key aspects which need to be considered when developing advanced materials for healthcare applications.

Having advanced biomaterials is pointless if they cannot be used efficiently to reach targeted users. The reader is presented with a different point of view in the next section of the book, “Innovative Biodevices,” which explains how biodevices operate and how they can be used for biomedical applications. The first chapter in this section, “Label-Free Biochips,” illustrates a variety of miniature biodevices which can be used to measure different biomarkers for diseases. Unlike traditional optical imaging, the use of mini, dye-free sensors has the advantage of requiring less medical samples and providing noise-free measurement results. The next chapter, “Polymer MEMS Sensors,” illustrates another set of microelectromechanical systems (MEMS) sensors that are based on cantilevers. These miniature cantilevers can convert biological signals into different electrical signals (current, resistance and voltage).

The next chapters move away from describing devices to illustrating state-of-the-art techniques to improve them. “Assembly of Polymers/Metal Nanoparticles and Their Applications as Medical Devices,” demonstrates the use of polymer-coated metal nanoparticles in medical devices. Polymer-metal nanoparticles are favored due to their low toxicity and antibacterial and antiviral properties. The MEMS technologies often employ the top-down approach to build their devices. An emerging bottom-up technique uses nanostructures to form building blocks for the devices. The chapter, "Combination of Molecular Imprinting and Nanotechnology: Beginning of a New Horizon," explains this new concept and its advantages such as enzyme-like and antibody-like properties, small physical size, solubility, flexibility and recognition site accessibility. The next chapter, "Prussian Blue and Analogues: Biosensing Applications in Health Care," educates the readers on why Prussian blue, a transitional metal, has recently become very popular in biosensing applications. The chapter, "Efficiency of Biosensors as New Generation of Analytical Approaches for the Biochemical Diagnostics of Diseases," evaluates different types of biosensors (electrochemical, optical) in terms of their cost effectiveness, selectivity and sensitivity. "Nanoparticles: Scope in Drug Delivery," illustrates the use of nanoparticles (solid lipid, polymeric, liposomes, mesoporous silica) for drug-targeting to improve the efficiency of drug delivery in humans. Better drug efficacy is especially important in hazardous diseases such as cancer, which still uses toxic drugs for treatment. While having numerous advantages such as reduced dosage frequencies, versatile administration methods and better disease management, it is still too soon to know the long-term effects of these nanoparticles on humans and the environment. The final chapter, "Smart Polypeptide Nanocarriers for Malignancy Therapeutics," reviews the recent advances in stimuli-responsive polypeptide nanocarriers for malignancy therapeutics.

Given the diversity of topics covered in this book, it can be read both by university students and researchers from various backgrounds such as chemistry, materials science, physics, pharmacy, medical science and biomedical engineering. The interdisciplinary nature of its chapters and simple tutorial nature make it suitable as a textbook for both undergraduate and graduate students, and as a reference book for researchers seeking an overview of state-of-the-art biomaterials and devices used in biomedical applications. We hope that the chapters of this book will give its readers' valuable insight into alternative mechanisms in the field of advanced materials and innovative biodevices.

Editors
Ashutosh Tiwari, PhD, DSc
Anis Nurashikin Nordin, DSc.

Part 1

CUTTING-EDGE BIOMATERIALS

1

Frontiers for Bulk Nanostructured Metals in Biomedical Applications

T.C. Lowe[1,*] and R.Z. Valiev[2, 3]

[1]Colorado School of Mines, Golden, CO, USA
[2]Ufa State Aviation Technical University, Russia
[3]Laboratory for Mechanics of Bulk Nanomaterials, Saint Petersburg State University, Saint Petersburg, Russia

Abstract
In recent decades, the nanostructuring of metals by severe plastic deformation (SPD), aimed at enhancing their properties, has become a promising area of modern materials science and engineering. With regard to medical applications, the creation of nanostructures in metals and alloys by SPD processing can improve both mechanical and biomedical properties. This chapter describes in detail the results of the investigations relating to titanium and its alloys, cobalt-based alloys, magnesium alloys, and stainless steels, which are the most extensively used to fabricate medical implants and other articles. The examples demonstrate that nanostructured metals with advanced properties pave the way to the development of a new generation of medical devices with improved design and functionality.

Keywords: Nanostructured metals, ultrafine grains, severe plastic deformation, mechanical and biomedical properties, orthopedic implants, biomaterial, biocompatibility, titanium, Co-Cr alloys, magnesium, stainless steel

1.1 Introduction to Nanostructured Metals

1.1.1 Importance of Nanostructured Biomedical Metals

The development of advanced materials for biomedical applications continues to enable superior solutions to improve human health. While new

**Corresponding author*: lowe@mines.edu

Ashutosh Tiwari and Anis N. Nordin (eds.) Advanced Biomaterials and Biodevices, (1–52)
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engineered materials impact most product sectors, their development for biomedical applications in particular has been rapidly expanding. This is partly a result of the convergence of nanoscale science and biological science over the past decade. Nanoscience, as applied to materials, addresses the same size scales of physical phenomena that are critical in living tissues. Consequently, *Nanostructured Materials* are now being engineered at a scale that matches the size range of attributes and physiological processes associated with human cells. New nanostructured soft and hard materials are being introduced every year. As of May 2013, 1,164 patents have been issued worldwide that reference nanomaterials.

Soft material structures, such as polymers and polymer-based composites, are the most prominent class of biomedical materials. This is partly because they are similar to soft tissues that predominate in human physiology. They are readily tailored to physiological applications since their nano/micro/macro-scale internal structures and surfaces can be functionalized for specific biomedical environments. They can be made biodurable for long-time use through surgical implantation, or biodegradable for temporary functions such as aiding drug delivery.

Aside from wood and other nature-made substances, metal is the oldest class of engineered biomaterial. Gold was used by the Greeks for fractures around 200 B.C. and iron and bronzes were used in sutures as early as the 17th century [1]. Silver, gold, and platinum were used as pins and wires for fractures in the 19th century. Steel was introduced for use in bone plates and screws at the beginning of the early 20th century, and in an ever growing number of orthopedic devices in the latter half of the 20th century [1]. The metals that are most prominently used in biomedical applications today are stainless steel, titanium, and cobalt-chromium (Co-Cr) alloys. Stainless steel, invented and produced first between 1908 and 1919, was used in bone plates by 1926. Co-Cr first appeared in bone plates 10 years later. Tantalum, a refractory metal, appeared in prostheses by 1939 and has since been used as radiographic markers, vascular clips, stents, and in repair of cranial defects [2]. Titanium and its alloys appeared in bone plates and hip joints by 1947. The well-known NiTi alloy Nitinol, discovered in 1958 found its way into orthodontic applications in the 1970s and cardiovascular stents in 1991 [1, 3].

Biomedical applications have traditionally required only small volumes of metal relative to the high tonnage production volumes that are most common in the metals manufacturing industry. Consequently, the alloys used in medical applications have typically been selected from those available for high volume non-medical applications, such as aerospace. However, during the past 20 years the attention to biomedical applications of metals has continued to grow, driven in part by increasing attention to quality of life,

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