Biomaterials Fabrication and Processing HANDBOOK

Edited by
Paul K. Chu
Xuanyong Liu

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HANDBOOK

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
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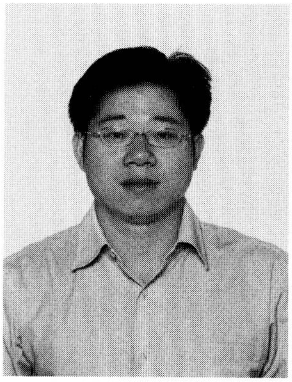
Editors

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.

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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