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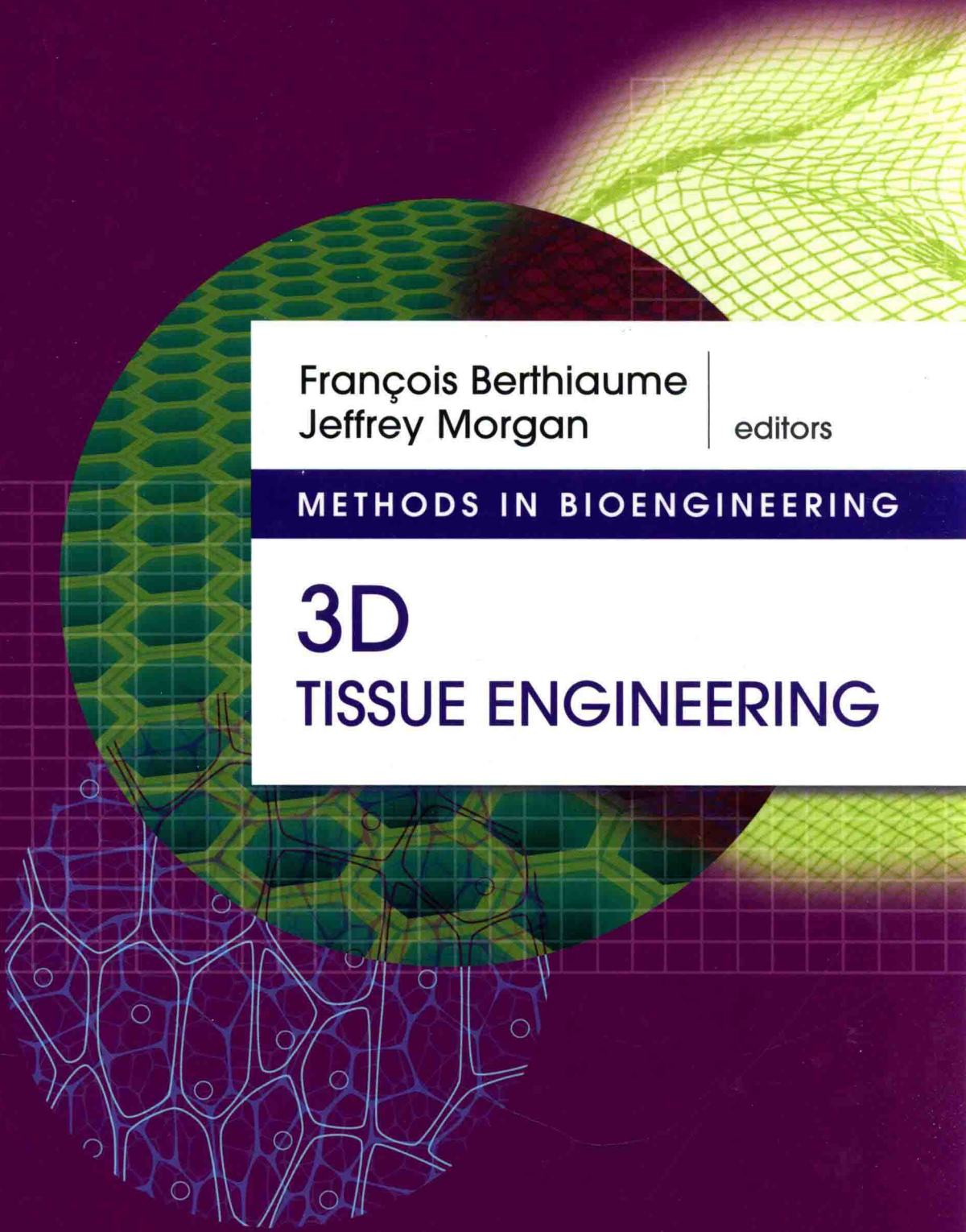

François Berthiaume
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editors

METHODS IN BIOENGINEERING

3D TISSUE ENGINEERING

Methods in Bioengineering

3D Tissue Engineering

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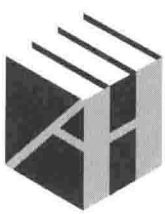

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Methods in Bioengineering

3D Tissue Engineering

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Preface

The emerging field of tissue engineering has great promise for the replacement and repair of tissues and organs that have been lost or compromised by disease or trauma. In fact, the first wave of new medical therapies based on the principles and methods of tissue engineering is currently available. Other tissue engineering therapies are under active clinical evaluation and still more are energetically under investigation in labs throughout the world. Far from being a mature and static field, the fundamental methods of tissue engineering are in an extraordinary creative phase of refinement, improvement, and innovation. These methods are tackling ever-increasing problems in the medical application of tissue engineering and will form the underpinnings of future medical therapies.

Concordant with this activity is a growing recognition that conventional in vitro cell culture (the growth of a single thin layer of living cells on flat rigid plastic dishes) does not adequately replicate the biological function and complexity found in vivo. Missing are cell-to-cell interactions, cell-to-matrix interactions, biomechanical effects, and the influence of the limitations of diffusion, to name just a few. Tissue engineering is offering new methods for the culture of cells in 3D, and these systems more accurately replicate the complex microenvironments and phenotypes found in vivo. In addition to being adopted as fundamental tools for basic science studies, such 3D cell culture systems are being used to reduce the cost and use of animals in research and are being used for toxicology testing and drug discovery.

In this volume of the Artech House Methods in Bioengineering Series, detailed protocols are provided for a wide spectrum of complementary tissue engineering methods. Covered in this volume are methods for the fabrication of scaffolds from synthetic polymers, peptides that self-assemble, and the quantitative methods to characterize the mechanical and chemical properties of these scaffolds. Scaffold fabrication and design have been an important part of the field of tissue engineering, and this field is advancing beyond the first generation of scaffolds. Methods are provided for the derivation of these scaffolds to increase their functionality via enhanced cell attachment or the ability to act as drug delivery systems for small molecules and bioactive peptides. Also covered are the formation of various forms of hydrogels and their functionalizations and characterizations. Such hydrogels offer new possibilities for the transplantation and encapsulation of cells. A method is provided for the scaffold-free self-assembly of 3D multicellular microtissues that maximize cell-to-cell interactions. These 3D microtissues can be

formed in the shape of spheroids, toroids, and honeycombs, which open up new possibilities. Another method covers the use of chip-based design for making bioreactors of cells. Other methods are also covered that use these materials (scaffolds, hydrogels, and cells) as building blocks to create even larger structures with complex shapes using layer-by-layer deposition or macromolding approaches. In total, this is an impressive collection of methods for the tissue engineering toolbox that can be used singly or in combination to build complex 3D structures applicable to a variety of tissues. This book goes further by providing several chapters where these and additional tissue engineering methods are focussed on the challenges of specific tissues and organs, such as cartilage and the nervous system. Nearly all the chapters in this book provide valuable methods for the quantitative evaluation of cells and cell function via biochemical assays, immunostaining procedures, gene expression analysis, and various forms of microscopy that are often a challenge to perform in 3D cultures. In addition to detailed methods, all of the chapters are well referenced and provide guidance on anticipated results and troubleshooting, which are of value to beginners and experts alike. By providing the important details for experimental success along with the larger context, we hope that *Methods in Bioengineering: 3D Tissue Engineering* will be a source of creative innovation for the next phase in tissue engineering.

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Contents

CHAPTER

1

Chemical Modification of Porous Scaffolds Using Plasma Polymers

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Abstract

Macroporous scaffolds are of utility in many tissue-engineering applications. For a given material, surface chemical modification of the scaffold can allow control over adsorbing species from the surrounding culture media, which subsequently affects cell adhesion and function. Here we present the use of plasma polymers to introduce nitrogen-containing functionality to enhance cell adhesion in the center of a porous 3D object, while decreasing cell adhesion using a hydrophobic hexane plasma polymer at the periphery. Critically, plasma polymerization allows a gradient in chemistry to be achieved using these two polymers to counteract the tendency of cells to adhere to the periphery of a porous object.

Key terms
cell penetration
plasma polymer
porous scaffold
tissue engineering