

# Contents

<b>Preface</b> .....	<b>vii</b>
<b>List of Contributors</b> .....	<b>xix</b>
<b>Chapter 1 Bioinspired Nanocomposites for Orthopedic Applications</b> .....	<b>1</b>
<i>Huinan Liu and Thomas J. Webster</i>	
1. Introduction .....	1
2. Basic Science of Bone .....	3
2.1. Bone Is a Nanostructured Composite .....	4
2.1.1. Organic Phase: Collagen Nanofibers and Noncollagenous Proteins .....	4
2.1.2. Inorganic Phase: Hydroxyapatite Nanocrystals .....	6
2.2. Microstructure and Macrostructure of Bone .....	6
2.3. Mechanical Properties of Bone .....	7
2.4. Bone Remodeling and Bone Cells .....	8
2.4.1. Osteoblasts .....	9
2.4.2. Osteocytes .....	11
2.4.3. Osteoclasts .....	11
3. Problems of Current Bone Substitutes .....	12
3.1. Autografts .....	12
3.2. Allografts and Xenografts .....	12
3.3. Metal and Metal Alloys .....	12
4. Bone Tissue Engineering: Promises and Challenges .....	13
4.1. Essential Requirements for Bone Scaffolds .....	15
4.1.1. Biocompatibility .....	15

4.1.2. Biodegradability .....	16
4.1.3. Mechanical Properties .....	16
4.1.4. Surface Properties .....	16
4.1.5. Osteoinductivity .....	17
4.1.6. Interconnected Three-Dimensional Structures .....	17
4.1.7. Feasible Fabrication Techniques and Sterilizability .....	18
4.2. The Choices of Materials for Bone Scaffolds .....	18
4.2.1. Biodegradable Polymers .....	19
4.2.2. Bioactive Ceramics .....	25
4.2.3. Ceramic/Polymer Biocomposites .....	26
5. Nanocomposites: Next-Generation Materials in Orthopedics .....	27
5.1. Rationale and Evidence .....	27
5.2. Fabrication Techniques of Biocomposite Scaffolds .....	30
5.2.1. Solvent-Casting/Particulate-Leaching .....	30
5.2.2. Gas-Foaming/Particulate-Leaching .....	33
5.2.3. Phase Separation and Emulsion Freeze Drying .....	36
5.2.4. Fiber Meshes/Fiber Bonding .....	39
5.2.5. Melt Molding .....	39
5.2.6. Freeze Drying and Cross-linking .....	40
5.2.7. Rapid Prototyping Techniques .....	40
5.3. Future Directions in Orthopedics .....	43
Bibliography .....	43

## **Chapter 2 Nanomaterials for Better Orthopedics ..... 53**

*Ganesan Balasundaram*

1. Introduction .....	53
2. Skeletal Complications: Osteoporosis and Bone Fracture .....	54
3. Need for Better Implantation Materials for Orthopedic Application .....	55
3.1. Cell Recognition of Implant Surfaces .....	57
3.2. Chemistry .....	59
3.3. Topography .....	60
4. A New Approach: Nanophase Orthopedic Materials .....	61
4.1. Benefits of Nanophase Bone Implant Materials .....	66

4.2. Wettability .....	67
4.3. Surface Roughness .....	68
5. Influence of Nanomaterials Functionalized with Cell Adhesive Peptides on Osteoblast Functions .....	70
6. Future Challenges .....	72
Bibliography .....	74

### **Chapter 3 Anodization: A Promising Nano-modification Technique for Titanium for Orthopedic**

#### **Applications ..... 79**

*Chang Yao and Thomas J. Webster*

1. Introduction .....	79
2. Anodization of Titanium .....	81
2.1. Basics of Anodization Process .....	81
2.2. Influences of Processing Parameters .....	82
2.3. Creation of Micron-Rough Surface .....	83
2.4. Creation of Nano-roughness .....	85
2.5. Control of Chemical Composition .....	92
3. Structure and Properties of Anodized Oxide Film .....	94
3.1. Structure .....	94
3.2. Corrosion Resistance and Adhesive Strength .....	96
3.3. Biological Properties of Anodized Titanium .....	97
3.3.1. In vitro Studies .....	97
3.3.2. Mechanisms of Increased Osteoblast Function .....	100
3.3.3. In vivo Studies .....	101
4. Future Directions .....	105
Bibliography .....	106

### **Chapter 4 Bio-inspired Carbon Nano-structures:**

#### **Orthopedic Applications ..... 111**

*Dongwoo Khang*

1. Fundamentals of Protein Adsorption and Surface Properties .....	111
1.1. Adhesion Protein .....	113
1.2. Polar and Apolar Properties of Proteins .....	113
1.3. Osteoblasts .....	115

1.4.	Carbon Nanotubes and Carbon Nanotube Composites .....	116
1.5.	Cytocompatibility of Carbon Nanotube Composites .....	118
1.6.	Analysis of Nano-surface Roughness .....	118
1.7.	Role of Nano-surface Energy .....	119
1.8.	Detecting Protein Adsorption .....	120
2.	Protein Assisted Osteoblast Adhesion on Nanophase Materials .....	121
2.1.	Osteoblast Functions on Carbon Nanotube Composite Materials .....	122
2.2.	Fibronectin Attached AFM Tip Interactions on Carbon Nanotube Composite Surfaces .....	124
2.3.	Osteoblast Functions on Micro-patterning of Carbon Nanotubes on Bio-polymers .....	126
3.	Conclusions and Summary .....	130
	Bibliography .....	130

## **Chapter 5 Applications of Nanotechnology/Nanomaterials in the Nervous System ..... 135**

*Peishan Liu-Snyder*

1.	Anatomy, Physiology and Molecular Biology of the Nervous System .....	135
2.	Epidemiology, Etiology and Pathophysiologies of Neurological Disorders .....	141
2.1.	Spinal Cord Injury .....	141
2.2.	Alzheimer's Disease .....	143
2.3.	Multiple Sclerosis .....	146
3.	Current Clinical Therapies and Limitations .....	147
3.1.	Approved Treatments of SCI and Ongoing Human Clinical Trials .....	148
3.2.	Pharmacological Treatments of Alzheimer's Disease and Ongoing Human Clinical Trials .....	149
3.3.	Pharmacological Treatments of Multiple Sclerosis (MS) and Ongoing Human Clinical Trials .....	151
4.	Application of Nanotechnology on the Development of Novel Drug and Cell Delivery Systems for the Nervous System .....	153

4.1. Conventional Drug Delivery Systems and Their Limitations .....	153
4.2. Advances of Nanotechnology in Drug Delivery Systems .....	154
4.3. Nano-based Matrix for Stem Cell Delivery .....	156
4.4. Medical Imaging with Nanotechnology for Early Detection and Evaluation of Treatment .....	158
5. Applications of Nanotechnologies in Electronic Tissue Interface Devices .....	161
5.1. Cochlear Implant (Bionic Ear) .....	162
5.2. Visual Prosthesis (Bionic Eye) .....	163
5.3. Computer Brain Interface (BrainGate Technology) .....	164
5.4. Functional Electrical Stimulation (FES) .....	165
5.5. Memory and Cognitive Functions .....	166
5.6. Oscillating Field Stimulator (OFS) .....	166
6. How Can Nanotechnology Improve Performance of Electronic Tissue Interface Devices? .....	167
7. Future Directions and Considerations .....	170
Bibliography .....	171

## **Chapter 6 Vascular Nano Stents ..... 181**

*Karen M. Haberstroh*

1. Physiology of the Vascular System .....	181
1.1. Structure and Function of the Arterial System .....	181
1.2. Components of the Artery Wall .....	182
1.3. Cells of the Vascular System .....	183
1.3.1. Vascular Endothelial Cells .....	183
1.3.2. Vascular Smooth Muscle Cells .....	184
1.3.3. Vascular Fibroblasts .....	184
1.3.4. Blood Cells .....	185
2. Atherosclerosis: A Cardiovascular Disease .....	185
2.1. The Cellular Progression of Atherosclerosis .....	186
3. Treatments for Vascular Disease .....	187
3.1. Balloon Angioplasty .....	188
3.2. Vascular Stents .....	189

3.2.1. The Use of Nano-structured Biomaterials in Vascular Stent Applications .....	190
3.2.2. Problems with Current Stent Designs .....	192
3.2.3. Stent Wear Debris .....	193
4. Conclusions .....	196
Bibliography .....	196

## **Chapter 7 Nanoparticles: Determining Toxicity ..... 201**

*Ezharul Hoque Chowdhury and Toshihiro Akaike*

1. Introduction .....	201
2. Strategies for Biocompatibility Testing .....	202
2.1. Cytotoxicity .....	202
2.2. Sensitization, Irritation and Intracutaneous Reactivity .....	203
2.3. Acute Systemic Toxicity .....	203
2.4. Genotoxicity .....	204
2.5. Implantation .....	204
2.6. Hemocompatibility .....	205
2.7. Subchronic and Chronic Toxicity.....	205
2.8. Carcinogenicity .....	205
2.9. Reproductive and Developmental Toxicity .....	206
2.10. Biodegradation .....	206
2.11. Immune Responses .....	206
3. Route of Entry and Biokinetics of Nanoparticles .....	207
3.1. Respiratory Tract .....	207
3.1.1. Alveolar Macrophage-Mediated Clearance .....	208
3.1.2. Translocation across Epithelial and Endothelial Cell Layers .....	208
3.1.3. Neural Uptake and Translocation .....	209
3.2. Exposure via GI Tract and Skin .....	210
3.3. Injection Route .....	210
4. Biological Adverse Effects of Nanoparticles .....	211
4.1. Pulmonary Effects of Nanoparticles .....	211
4.1.1. Pulmonary Inflammation .....	212
4.1.2. Pulmonary Carcinogenicity .....	213
4.2. Systemic Effects of Nanoparticles .....	214

4.3. Differences in Toxicity between Nanoparticles of Different Materials .....	215
4.3.1. Particle Surface Activity .....	216
4.3.2. Particle Agglomeration/Disagglomeration .....	216
5. Conclusions .....	216
Bibliography .....	217

**Chapter 8 Nanoparticles: Effects on Human Health and the Environment ..... 221**

*Myung-Haing Cho and Jin-Kyu Lee*

1. Hopes and Concerns about Nanotechnology .....	221
2. Possible Adverse Health, Environment, and Safety Impacts .....	224
3. How to Evaluate the Toxicity of Nanoparticles? .....	226
4. Conclusions .....	231
Acknowledgements .....	232
Bibliography .....	232

**Index ..... 235**