Contents

Preface XV
List of Contributors XIX

Part One Metal Oxide Nanomaterials 1

1 The Biomimetic Synthesis of Metal Oxide Nanomaterials 3
Leila F. Deravi, Joshua D. Swartz and David W. Wright
1.1 Introduction 3
1.2 Metal Oxides in Nature 4
1.2.1 Components of Biomineralization 5
1.2.2 Biomineralization Optimization 6
1.3 Biomimetic Synthesis of Metal Oxide Nanomaterials 7
1.4 Constrained Biomineralization 8
1.4.1 Bacterial Synthesis of Metal Oxide Nanomaterials 8
1.4.2 Synthesis of Protein-Functionalized Ferromagnetic Co₃O₄ Nanocrystals 9
1.4.3 Room-Temperature Synthesis of Barium Titanate 10
1.4.4 Biomimetic Synthesis of Magnetite 11
1.4.4.1 Biomimetic Synthesis of Iron Oxide 11
1.4.5 Metal Oxide Synthesis within a Protein Cage—Ferritin 14
1.4.5.1 Mineralization of Non-Natural Metal Oxides Using Ferritin 14
1.4.6 Viral Templates for Metal Oxide Synthesis 15
1.4.7 Hydrolysis of Metal Oxides Using Peptide Nanorings as Templates 16
1.4.7.1 Enzymatic Peptide Nanoassembly of Crystalline Ga₂O₃ 17
1.4.7.2 Synthesis of Ferroelectric BT Nanoparticles Using Peptide Nanorings 18
1.4.8 Synthesis of ZnO from Templated Butterfly Wings 19
1.4.9 Ionic Liquid-Assisted Co₃O₄ Synthesis 20
1.4.10 Conclusions 21
1.5 Mediated Mineralization 21
Contents

1.5.1 The Three-Tier Architecture of Nacreous Layers 22
1.5.2 Echinoderms 23
1.5.2.1 Biomimetic Synthesis of Metal Oxides Using Echinoderms as Inspiration 24
1.5.3 Diatoms 28
1.5.3.1 Biological Synthesis of Silica Nanoparticles 30
1.5.3.2 Biomimetic Synthesis of Silica Nanoparticles 31
1.5.3.3 Other Biomimetic Templates 45
1.5.3.4 Non-natural Metal Oxide Synthesis Using Biomimetic Peptides 47
1.5.4 Conclusions 48
1.6 Future Perspectives: Processing Metal Oxide Nanomaterials 48
References 50

2 Synthesis of Symmetric and Asymmetric Nanosilica for Materials, Optical and Medical Applications 55
Yongquan Qu, Jennifer Lien and Ting Guo
2.1 Introduction 55
2.2 Synthesis of Nanosilica 59
2.2.1 Symmetric Nanosilica 59
2.2.1.1 Catalytic Methods 63
2.2.1.2 Noncatalytic Growth 65
2.2.2 Asymmetric Silica Nanomaterials 68
2.2.2.1 Catalytic Growth 68
2.2.2.2 Noncatalytic Growth 69
2.3 Characterization 70
2.4 Applications of Symmetric and Asymmetric Nanosilica 72
2.4.1 Symmetric Nanosilica 73
2.4.1.1 Silica Nanomaterials as Drug Delivery Vehicles 73
2.4.1.2 Silica Nanomaterials as a Catalyst Host and Sensors 76
2.4.1.3 Silica Nanomaterials as Optical Materials 76
2.4.1.4 Nanosilica in Other Applications 77
2.4.2 Asymmetric Nanosilica 78
2.5 Conclusions 78
Acknowledgments 78
References 78

3 One-Dimensional Silica Structures and Their Applications to the Biological Sciences 83
Daniel Choi, David McIlroy, James Nagler, Eric Aston, Patrick Hrdlicka,
Kurt Gustin, Rod Hill, Deborah Stenkamp and Joshua Branen
3.1 Introduction 83
3.2 Synthesis of Silica Nanowires and Nanosprings 84
3.2.1 Catalyst Preparation and Application 85
3.2.2 Methods for VLS Synthesis of Nanowires 86
3.2.2.1 Flow Reaction Formation of Nanowires 86
3.2.3 Laser Ablation of Nanowires 87
3.2.4 Chemical Vapor Deposition and Plasma-Enhanced Chemical Vapor Deposition of Nanowires 88
3.3 Functionalization of Silica 1-D Silica Nanomaterials 90
3.4 Toxicology Studies on 1-D Silica Nanomaterials 94
3.4.1 Intracellular Targeted Delivery 94
3.4.2 A Typical Cellular Targeting Strategy Using 1-D NS-Based Nanostructures 94
3.4.2.1 In Vitro Toxicity of 1-D Nanostructures 97
3.4.2.2 In Vivo Toxicity of 1-D Nanostructures 99
3.5 Biological Applications of 1-D Silica Nanomaterials 101
3.5.1 Biodetection 101
References 103

4 Approaches to the Biofunctionalization of Spherical Silica Nanomaterials 109
Michihiro Nakamura
4.1 Introduction 109
4.2 Silica Nanoparticles 112
4.2.1 Inorganic Silica Nanoparticles 113
4.2.2 Organosilica Nanoparticles 114
4.2.2.1 Organically Modified Silane Nanoparticles (ORMOSIL Nanoparticles) 114
4.2.2.2 Functional Organosilica Nanoparticles 115
4.2.2.3 Multisilicate Nanoparticles 119
4.3 Biofunctionalization of Silica Nanoparticles 122
4.3.1 Surface Biofunctionalization 123
4.3.1.1 Surface Biofunctionalization of Inorganic Silica Nanoparticles 123
4.3.1.2 Surface Biofunctionalization of Organosilica Nanoparticles 126
4.3.2 Internal Biofunctionalization 133
4.3.2.1 An Overview 133
4.3.2.2 Preparation of Fluorescent Silica Nanoparticles 134
4.4 Applications 144
4.4.1 Advantages of Biofunctionalized Silica Nanoparticles 145
4.4.2 Applications in Medical Diagnosis 146
4.4.2.1 Genes 146
4.4.2.2 Detection of Proteins 147
4.4.2.3 Detection of Microbes 147
4.4.2.4 Multiplexed Assays 148
4.4.3 Imaging 148
4.4.4 Applications in Medical Therapy 151
4.4.4.1 Drug Delivery 151
4.4.4.2 Gene Delivery 152
4.4.4.3 Photodynamic Therapy 153
4.5 Summary and Future Perspectives 153
References 154
5 Mesoporous Cage-Like Silica Monoliths for Optical Sensing of Pollutant Ions 163

Sherif A. El-Safty, Kohmei Halada and Hirohisa Yamada

5.1 Introduction 163
5.1.1 Basic Concept of Optical Nanosensor Schemes 164
5.1.2 Toxicity and Deleterious Effects of the Metal Ions 166
5.1.2.1 Toxicity of Cadmium Ions 166
5.1.2.2 Toxicity of Antimony Ions 167
5.1.2.3 Toxicity of Mercury Ions 167
5.1.2.4 Toxicity of Lead Ions 167
5.2 General Sensing Techniques for Metal Ions 168
5.3 General Designs of Optical Nanosensors Based on Mesoporous Silica Carriers 169
5.3.1 Optical Nanosensor of Cage HOM-TPPS Sink for Hg(II) Ions 170
5.3.2 Optical Nanosensor of Cage HOM-PR Sink for Sb(III) Ions 172
5.3.3 Optical Nanosensor of Cage HOM-TMPyP Sink for Cd(II) Ions 173
5.3.4 Optical Nanosensor of Cage HOM-DZ Sink for Pb(II) Ions 175
5.4 Optical Sensing Assays of Metal Ions Using Nanosensors 178
5.5 One-Step and Simple Ion-Sensing Procedures 180
5.6 The Calibration Graphs and Analytical Parameters of Nanosensors 183
5.7 The Advantages of Nanosensor Designs 185
5.7.1 Retention of Uniformity of Nanosensor Cage-Like Sinks 185
5.7.2 Rapid Time-Response of Metal Ion-Sensing Systems 187
5.7.3 Stability of the Monolithic Nanosensors 189
5.7.4 Reversibility of the Metal Ion-Sensing Systems 190
5.7.5 Optically Selective Nanosensors for Trace-Level Toxic Ions 192
5.8 Conclusions and Outlook 194
References 195

6 Nanoscale Bioactive Silicate Glasses in Biomedical Applications 203

Tobias J. Brunner, Wendelin J. Stark and Aldo R. Boccaccini

6.1 Introduction 203
6.2 Fabrication of Nanoscale Bioactive Glass Particles and Fibers 204
6.2.1 Liquid-Phase Synthesis Method (Sol–Gel Technique) 204
6.2.2 Gas-Phase Synthesis Method (Flame Spray Synthesis) 207
6.3 Applications of Nanoscale Bioactive Glasses 208
6.3.1 Conventional Bioactive Glasses 208
6.3.2 Advantages of Nanometric Bioactive Glasses 209
6.3.3 Applications in Dentistry 210
6.3.3.1 Remineralization 211
6.3.3.2 Antimicrobial Effects 212
6.3.4 Applications in Tissue Engineering 213
6.4 Summary and Future Perspective 216
References 216
7 Toxicity of Spherical and Anisotropic Nanosilica 221
Yuhui Jin, Samuel Lohstreter and Julia Xiaojun Zhao
7.1 Introduction 221
7.2 Synthesis of Amorphous Silica Nanoparticles 223
7.3 Invasion Pathways of Silica Nanomaterials into Living Systems 225
7.3.1 Exposure via the Respiratory Tract 225
7.3.2 Exposure via the Gastrointestinal Tract 228
7.3.3 Skin Contact 229
7.3.4 A Brief Summary 230
7.4 Mechanism of Nanomaterials-Induced Toxicity 230
7.4.1 Photoactive Nanomaterials-Induced Toxicity 231
7.4.2 Toxicity of Silica Nanoparticles 231
7.4.2.1 In Vitro Studies of Silica Nanomaterials-Induced Toxicity 231
7.4.2.2 In Vivo Studies of Silica Nanomaterials-Induced Toxicity 232
7.4.2.3 Mechanism of Silica Nanomaterials-Induced Toxicity 233
7.5 Effects of Silica Nanomaterial Properties on Toxicity 233
7.5.1 Effect of Silica Nanomaterial Size 234
7.5.2 Effect of Silica Nanomaterial Shape 235
7.5.3 Effects of Silica Nanomaterial Surface Properties 236
7.5.4 Effect of Dopants 236
7.5.5 Effects of Dose and Interaction Time 237
7.6 Toxicity of Silica Nanomaterials: A Summary 237
7.7 Perspectives on Silica Nanomaterials 238
Acknowledgments 238
References 239

8 Zirconia Nanomaterials: Synthesis and Biomedical Application 245
Georg Garnweitner
8.1 Introduction 245
8.2 Synthesis of Zirconia Nanomaterials 246
8.2.1 Historical Overview 246
8.2.2 Solvent-Based Synthesis of Zirconia Nanoparticles 248
8.2.2.1 Hydrothermal Synthesis Strategies 249
8.2.2.2 Precipitation Techniques 251
8.2.2.3 The Pechini Method 252
8.2.2.4 Combustion Synthesis/Auto-Ignition 253
8.2.2.5 Sol–Gel Methods 254
8.2.2.6 Nonaqueous/Nonhydrolytic Sol–Gel Technique 255
8.2.3 Gas-Phase Synthesis of Zirconia Nanoparticles 256
8.2.4 Top-Down Methods to Zirconia Nanoparticles 258
8.2.5 Synthesis of Zirconia Nanorods and Nanowires 259
8.3 Biomedical Applications of Zirconia Nanomaterials 263
8.3.1 Nanostructured Zirconia-Based Bioceramics 263
8.3.1.1 Joint Replacements 265
8.3.1.2 Dental Implants 267
10.3.4 Overall Trends Observed in DPD Simulations 345
10.4 The Next Steps, and Future Opportunities 346
10.5 Summary and Outlook 348
Acknowledgments 349
References 350

11 Porous Silicon Particles for Imaging and Therapy of Cancer 357
Rita E. Serda, Ciro Chiappini, Daniel Fine, Ennio Tasciotti and Mauro Ferrari
11.1 Introduction 357
11.2 Porous Silicon 359
11.3 Microfabrication 363
11.4 Characterization 365
11.4.1 Gravimetry 365
11.4.2 Spectroscopic Ellipsometry 366
11.4.3 X-Ray Diffraction 367
11.4.4 Nitrogen Adsorption 368
11.4.5 Sample Preparation for Electron Microscopy: Sectioning 373
11.4.5.1 Sample Preparation 375
11.5 Nanovectors for the Delivery of Therapeutics 377
11.5.1 Biocompatibility and Biodegradation 377
11.5.2 Drug Loading and Quantification of Drug Load 383
11.5.3 Nanovectors for the Delivery of Therapeutics 386
11.5.4 Towards a Multi-Stage Drug Delivery System 387
11.6 Cellular Uptake of pSi Particles 391
11.6.1 Tumor Microenvironment 391
11.6.2 Effect of Microparticle Shape on Margination 392
11.6.3 Effect of Microparticle Size on Cellular Uptake 393
11.6.4 Effect of Surface Modification on pSi Particle Uptake 396
11.6.5 Serum Opsonization Inhibits Uptake of Oxidized pSi Microparticles 397
11.7 Cancer Imaging 397
11.8 Conclusions 398
References 398

12 Spherical and Anisotropic Hydroxyapatite Nanocrystals 407
Susmita Bose, Weichang Xue, Ashis Banerjee and Amit Bandyopadhyay
12.1 Introduction 407
12.1.1 Bone Structure 407
12.1.2 Hydroxyapatite and its Crystal Structure 409
12.1.3 Synthetic HA Nanocrystals: Application to Bone Replacement and Drug/Protein Delivery 410
12.1.3.1 Bone Replacement 411
12.1.3.2 Drug Delivery 411
12.2 Synthesis of Hydroxyapatite Nanocrystals 412
12.2.1 Wet Chemical Precipitation 412
12.2.2 Sol–Gel Process  415
12.2.3 Biomimetic Synthesis  418
12.2.4 Hydrothermal Method  420
12.2.5 Mechanochemical Powder Synthesis  421
12.2.6 Solid-State Reactions  424
12.2.7 Microwave-Assisted Synthesis  424
12.2.8 Emulsion Process  425
12.2.8.1 Surfactants  425
12.2.8.2 Reverse Micelles  426
12.2.8.3 Effect of Ageing  429
12.2.8.4 Effect of Metal Ion Concentration  429
12.2.9 Other Processes  430
12.3 Characterization of Hydroxyapatite Nanocrystals  431
12.3.1 Composition and Phase Analysis  431
12.3.2 Nanoparticle Characterization for Size and Morphology  433
12.3.3 Biological Characterization  434
12.3.3.1 In Vitro Evaluation Methods: Simulated Body Fluids and Cell Culture  434
12.3.3.2 In Vivo Animal Testing  435
12.3.3.3 Toxicology of HA Nanoparticles  435
12.4 Bulk Structures Using Hydroxyapatite Nanocrystals  435
12.4.1 Microwave Sintering of Nanopowders  436
12.5 Future Trends  438
12.5.1 High-Strength HA using Nano-HA and Dopants  439
12.5.2 HA Scaffolds in Tissue Engineering  439
12.5.3 Nanoscale HA Coatings for Load-Bearing Implants  440
12.5.4 HA in Drug/Protein Delivery  440
References  441

13  Calcium Phosphate Nanoparticles in Biomineralization and Biomaterials  449
Ruikang Tang and Yurong Cai
13.1 Introduction  449
13.2 Nano-Calcium Phosphates in Hard Tissues  451
13.2.1 Bone  451
13.2.2 Tooth  452
13.2.3 Other Biological Organisms  453
13.3 Biological Formation of Calcium Phosphates  454
13.4 Characteristic Mechanical Properties  455
13.5 Stability of Nano-Calcium Phosphates  457
13.5.1 Demineralization of Biominerals  458
13.5.2 Dissolution of Pure HAP  460
13.5.3 Nanosize Effects in Biomaterials  461
13.6 Synthesis of Nano-Calcium Phosphates  462
13.6.1 Synthesis of Nano-Calcium Phosphate Particles  462
13.6.2 Biomimetic Construction using HA Nanoparticles 463
13.6.3 Nano-HA–Collagen Composites 467
13.6.4 Nano-HA Coating 468
13.7 Nano-Calcium Phosphate in Biomedical Engineering 469
13.7.1 Bone Repair 469
13.7.2 Bone-Related Cells 473
13.7.3 Enamel Repair 476
13.7.4 Other Applications 478
13.8 Summary 481
Acknowledgments 482
References 482

Index 493