

## Contents

<b>Foreword</b>	<i>xv</i>
<b>Preface</b>	<i>xvii</i>
<b>Acknowledgments</b>	<i>xix</i>
<b>1</b>	<b>General Introduction and Background of Photofunctional Nanomaterials in Biomedical Applications</b> 1
	<i>Chunxia Li and Jun Lin</i>
1.1	Introduction to Nanomaterials 1
1.1.1	Surface and Interfacial Effects 1
1.1.2	Small Size Effect 2
1.1.3	Quantum Size Effect 2
1.1.4	Macroscopic Quantum Tunneling Effects 2
1.2	Introduction and Classification of Photofunctional Nanomaterials 3
1.2.1	Capture of Photons 3
1.2.2	Absorption and Conversion of Photons 4
1.2.3	Physical-chemical Processes at the Surface Interface 5
1.3	Introduction to Nanobiomedicine 6
1.3.1	Nano-drug Delivery Systems 6
1.3.2	Nano-imaging Technology 6
1.3.3	Nano-diagnostic Technologies 6
1.3.4	Nanotherapeutic Technology 8
1.3.5	Nano-biosensors 8
1.3.6	Tissue Engineering 8
1.4	Classification of Photofunctional Nanomaterials 9
1.4.1	Fluorescent Nanomaterials 9
1.4.1.1	Quantum Dots 10
1.4.1.2	Silicon-Based Fluorescent Nanomaterials 12
1.4.1.3	Rare Earth Luminescent Nanomaterials 13
1.4.1.4	Organic Fluorescent Nanomaterials 18
1.4.2	Photothermal Nanomaterials 20
1.4.2.1	Metallic Photothermal Nanomaterials 20
1.4.2.2	Semiconductor Photothermal Nanomaterials 22
1.4.2.3	Organic Photothermal Nanomaterials 22

1.4.2.4	Carbon-Based Photothermal Nanomaterials	24
1.4.2.5	Certain Two-Dimensional (2D) Nanomaterials	26
1.4.2.6	Biomass Photothermal Nanomaterials	27
1.4.3	Photodynamic Nanomaterials	29
1.4.3.1	Photosensitizer-Loaded Nanomaterials	29
1.4.3.2	Nanomaterials with Intrinsic Photodynamic Effects	32
1.4.3.3	Energy Conversion Nanomaterials for Photosensitizers	33
1.4.4	Photoelectrochemical Nanomaterials	38
1.4.4.1	Photocurrent Signal Generation Mechanism	39
1.4.4.2	Core Elements of Photoelectrochemical Biosensors	40
1.4.4.3	Types of Photoelectrochemical Biosensors	41
1.4.5	Photoacoustic Nanomaterials	45
1.4.5.1	Introduction to Photoacoustic Imaging	46
1.4.5.2	Selection of Photoacoustic Contrast Agents	46
1.5	Conclusion	55
	References	55
<b>2</b>	<b>Mechanism in Rare-Earth-Doped Luminescence Nanomaterials</b>	<b>77</b>
	<i>Yulei Chang</i>	
2.1	Introduction	77
2.2	Composition of RE-Doped Luminescence Nanomaterials: Substrate (Host), Activator, and Sensitizer	77
2.3	Mechanism of RE-Doped Luminescence Nanomaterials	79
2.3.1	Luminescence: Downshifting, Upconversion, and Downconversion	79
2.3.1.1	Downshifting Luminescence	79
2.3.1.2	Upconversion Luminescence (UCL)	81
2.3.1.3	Downconversion/Quantum Cutting (QC)	83
2.3.2	Nonradiative Transition: Energy Transfer and Migration	83
2.3.2.1	Energy Transfer (ET)	83
2.3.2.2	Energy Migration (EM)	84
2.4	Luminescence Modulation	85
2.4.1	Crystal Field (CF) Regulation	85
2.4.2	Surface Defects Passivation	87
2.4.3	ET Regulation	89
2.4.3.1	Multicolor Tuning (MCT) of UCL	89
2.4.3.2	Energy Transfer–Triggered Novel Upconversion Excitation	90
2.4.4	Cross-Relaxation (CR) Regulation	90
2.4.4.1	Alleviating Concentration Quenching (CQ) for Highly Doped UCNPs	91
2.4.4.2	NIR Downshifting Modulation by CR	92
2.4.5	Phonon-Assisted Energy Transfer (PAET)	93
2.4.6	Dye Sensitization	95
2.4.6.1	Dye-Sensitized Core Nanoparticles	95
2.4.6.2	Dye-Sensitized Core–Shell Nanoparticles	96

- 2.4.7 Combined Excitation Regulation 97
  - 2.4.7.1 ESA 97
  - 2.4.7.2 STED 98
- 2.4.8 External Field Modulation 98
  - 2.4.8.1 Magnetic Field Modulation 98
  - 2.4.8.2 Electric Field Modulation 100
  - 2.4.8.3 Plasma Resonance Enhancement 104
- References 105
  
- 3 Upconversion and NIR-II Luminescence Modulation of Rare-Earth Composites Using Material Informatics 117**  
*Wenjing Li and Ruichan Lv*
- 3.1 Introduction 117
- 3.2 Typical Processes of Upconversion Luminescence 118
  - 3.2.1 Excited State Absorption 118
  - 3.2.2 Photon Avalanche 119
  - 3.2.3 Energy Transfer 119
  - 3.2.4 Cross-Relaxation 120
  - 3.2.5 Cooperative Upconversion 120
  - 3.2.6 Second Harmonic Generation 121
- 3.3 Synthesis Methods of Upconversion Nanoparticles 121
  - 3.3.1 Thermal Decomposition Methods 121
  - 3.3.2 Hydrothermal/Solvothermal Method 122
  - 3.3.3 Co-precipitation Method 123
  - 3.3.4 Sol–Gel Method 123
  - 3.3.5 Other Methods 124
- 3.4 Material Informatics in UCL 126
  - 3.4.1 Genetic Algorithm 126
  - 3.4.2 Particle Swarm Optimization 127
  - 3.4.3 Simulated Annealing 127
  - 3.4.4 Other Methods 128
- 3.5 Cancer Therapy Based on UCNPs 130
  - 3.5.1 Photodynamic Therapy 131
  - 3.5.2 Photothermal Therapy 131
  - 3.5.3 Photo-Immunotherapy 133
  - 3.5.4 Photo-Gene Therapy 135
- 3.6 Conclusion and Perspective 136
- References 137
  
- 4 Composites Based on Lanthanide-Doped Upconversion Nanomaterials and Metal–Organic Frameworks: Fabrication and Bioapplications 147**  
*Ze Yuan and Xiaoji Xie*
- 4.1 Introduction 147
- 4.2 Fabrications of Composites 148

- 4.2.1 In Situ Encapsulation 148
- 4.2.2 Partial Embedment 155
- 4.2.3 Interfacial Attachment 157
- 4.3 Bioapplications 159
  - 4.3.1 Therapy 159
  - 4.3.2 Bioimaging 169
  - 4.3.3 Biosensing 170
- 4.4 Conclusion and Perspectives 172
- References 173

## 5 Lanthanide-Doped Nanomaterials for Luminescence

### Biosensing and Biodetection 181

*Zhijie Ju, Peng Zhao, and Renren Deng*

- 5.1 Introduction 181
- 5.2 Basics of Optical Bioprobe and Lanthanide-Doped Nanoparticles 181
  - 5.2.1 Design Considerations for Bioprobe Development 181
  - 5.2.2 Characteristics of Lanthanide-Doped Nanoparticles 182
  - 5.2.3 NIR Biological Windows 186
  - 5.2.4 Energy Transfer: A Key Factor in Biodetection 187
- 5.3 Synthesis and Functionalization of Lanthanide-Doped Nanocrystals 189
  - 5.3.1 Design and Synthesis of Core-Shell Structured Nanocrystals 189
    - 5.3.1.1 Design of Upconversion Nanoparticles (UCNPs) 190
    - 5.3.1.2 Design of Downshifting Nanoparticles (DSNPs) 191
  - 5.3.2 Functionalization of Lanthanide-Doped Nanoparticles (LnNPs) 192
    - 5.3.2.1 Amphiphilic Polymer Absorption 192
    - 5.3.2.2 Ligand Removal 192
    - 5.3.2.3 Ligand Exchange 192
    - 5.3.2.4 Surface Silanization 193
- 5.4 Applications of Luminescence Biosensing and Biodetection 193
  - 5.4.1 Temperature Sensing 193
  - 5.4.2 pH Sensing 196
  - 5.4.3 Detection of Biomolecules 198
  - 5.4.4 Detection of Small Molecules and Ions 202
- 5.5 Integrated Devices for Point-of-Care Testing 208
- 5.6 Summary 211
- References 212

## 6 Rare Earth Luminescent Nanomaterials for Gene Delivery 219

*Jiajun Li and Tao Zhang*

- 6.1 Introduction 219
- 6.2 UCNPs Nanovectors 221
- 6.3 Surface Modification 221
  - 6.3.1 Silica 221
  - 6.3.2 Cationic Polymers 223

- 6.4 Increasing Endosomal Escape 224
- 6.5 Controlling Delivery Strategy 225
  - 6.5.1 Photodegradable Polymers 226
  - 6.5.2 Changes in Carrier Surface Charge 226
  - 6.5.3 Photoisomerization 228
  - 6.5.4 Microenvironments Stimulation 228
    - 6.5.4.1 Reactive Oxygen Species (ROS) 228
    - 6.5.4.2 Matrixmetallo Proteinases (MMPs) 229
  - 6.5.5 Light Cage 230
  - 6.5.6 Orthogonal Control 231
  - 6.5.7 Release Monitoring 233
- 6.6 Gene Therapy and Syndication 234
  - 6.6.1 Phototherapy 234
  - 6.6.2 Chemotherapy 235
- 6.7 Other Lanthanide-Based Nanovectors 236
- 6.8 Perspective 238
- References 239
  
- 7 Biosafety of Rare-Earth-Doped Nanomaterials 247**  
*Yang Li and Guanying Chen*
  - 7.1 Internalization of UCNPs into Cells 247
  - 7.2 Distribution of UCNPs 249
  - 7.3 Excretion Behavior of UCNPs 252
  - 7.4 The Toxic Effect of Cell Incubated with UCNPs 253
  - 7.5 Toxic Effect of UCNPs In Vivo 256
  - 7.6 Conclusions and Prospects 258
  - References 259
  
- 8 Design and Construction of Photosensitizers for Photodynamic Therapy of Tumor 269**  
*Ruohao Zhang, Jing Feng, Yifei Zhou, Jitong Gong, and Hongjie Zhang*
  - 8.1 Introduction 269
  - 8.2 Small Molecule Photosensitizers 273
    - 8.2.1 Porphyrins 273
    - 8.2.2 Phthalocyanines 275
    - 8.2.3 BODIPYs 277
    - 8.2.4 Indocyanine Dyes 278
    - 8.2.5 AIEgens 278
  - 8.3 Metal Complexes 279
    - 8.3.1 Ru(II) Complexes 279
    - 8.3.2 Ir(III) Complexes 280
    - 8.3.3 MOFs 282
    - 8.3.4 COFs 282
    - 8.3.5 HOFs 284
  - 8.4 Inorganic Photosensitizers 284

- 8.4.1 Carbon-Based Photosensitizers 284
- 8.4.2 Silicon-Based Photosensitizers 285
- 8.4.3 Simple Substance Photosensitizers 286
- 8.4.4 Metal Oxides-Based Photosensitizers 288
- 8.4.5 Lanthanide Upconversion Nanoparticles-Based PSs 290
- 8.5 Conclusions and Perspectives 292
- References 293

## 9 Persistent Luminescent Materials for Optical Information

### Storage Applications 305

*Cunjian Lin, Yixi Zhuang, and Rong-Jun Xie*

- 9.1 Introduction 305
- 9.2 Luminescent Mechanism of Persistent Luminescent Materials with Deep Traps 307
- 9.3 Persistent Luminescent Materials with Deep Traps 308
  - 9.3.1 Halides or Oxyhalides 309
  - 9.3.2 Sulfides 318
  - 9.3.3 Oxides 320
    - 9.3.3.1 Monobasic Cation Oxide 320
    - 9.3.3.2 Silicate/Germanate/Stannate 321
    - 9.3.3.3 Aluminate/Gallate 323
    - 9.3.3.4 Titanate/Zirconate 326
    - 9.3.3.5 Oxide Glass 327
  - 9.3.4 Nitride or Oxynitrides 327
- 9.4 Outlooks 331
- References 332

## 10 The Application of Ternary Quantum Dots in Tumor-Related Marker Detection, Imaging, and Therapy 343

*Ling Yang, Xiaojiao Kang, Jun Lin, and Ziyong Cheng*

- 10.1 Introduction 343
  - 10.1.1 Fundamental Properties of QDs 344
  - 10.1.2 Synthesis Methods of QDs 346
    - 10.1.2.1 Metal-Organic Synthesis Method 346
    - 10.1.2.2 Hydrophilic Synthesis Method 347
    - 10.1.2.3 Biosynthesis Method 348
  - 10.1.3 Synthesis Methods of Ternary QDs 349
    - 10.1.3.1 Hot-Injection Method 349
    - 10.1.3.2 Ion Exchange Method 350
    - 10.1.3.3 Hydrothermal Method 350
  - 10.1.4 Performance Control of QDs 351
    - 10.1.4.1 Core-Shell Structure 351
    - 10.1.4.2 Alloying 352
    - 10.1.4.3 Ioning 352
  - 10.1.5 Modification of QDs 352

- 10.1.5.1 Surfacing Ligand Molecular Exchange 352
- 10.1.5.2 Amphiphilic Organic Macromolecular Coating 353
- 10.1.6 Characterization of QDs 353
- 10.1.7 Biomedical Applications of QDs 353
  - 10.1.7.1 Biological Detection 354
  - 10.1.7.2 Cell Imaging 355
  - 10.1.7.3 Live Imaging 356
  - 10.1.7.4 Tumor Therapy 357
- 10.2 Conclusion 362
- References 363
  
- 11 Nanomaterials-Induced Pyroptosis and Immunotherapy 373**  
*Hao Chen, Binbin Ding, Jun Lin, and Ping'an Ma*
  - 11.1 Discovery and Definition of Pyroptosis 373
  - 11.2 Mechanisms of Pyroptosis 373
    - 11.2.1 Inflammasome and Pyroptosis 374
    - 11.2.2 Caspases, Gasdermins, and Pyroptosis 374
  - 11.3 Pyroptosis and Tumor Immunotherapy 376
    - 11.3.1 Ions Interference Therapy 379
    - 11.3.2 TME-Responsive Pyroptosis Therapy 386
    - 11.3.3 Demethylation-Activated Pyroptosis 386
    - 11.3.4 The Other Pyroptosis Therapies 389
  - 11.4 Summary and Outlook 392
  - References 393
  
- 12 NIR Light-Activated Conversion Nanomaterials for Photothermal/Immunotherapy 399**  
*Yaru Zhang and Zhiyao Hou*
  - 12.1 Introduction 399
  - 12.2 The Photothermal Conversion Mechanism 400
  - 12.3 Classification of Inorganic Photothermal Materials 402
    - 12.3.1 Noble Metal Nanomaterials 402
    - 12.3.2 Semiconductor Nanomaterials 406
      - 12.3.2.1 Transition Metal Oxides 406
      - 12.3.2.2 Transition Metal Chalcogenides 408
    - 12.3.3 Carbon-Based Materials 410
    - 12.3.4 Other Types of PTAs 413
  - 12.4 Mechanisms of PTT and Immunotherapy 413
    - 12.4.1 Mechanism of PTT 413
    - 12.4.2 Response of Tumor Cells to Heat Stress 414
    - 12.4.3 PTT-Induced Necrosis and Apoptosis 414
    - 12.4.4 PTT-Induced Immunogenic Cell Death 415
    - 12.4.5 The Impact of PTT on Tumor Microenvironment 416
  - 12.5 Nanomaterial-Based Photothermal/Immunotherapy 417
    - 12.5.1 PTT-Synergized ICB Therapy 417

- 12.5.1.1 CTLA-4 Checkpoint 418
  - 12.5.1.2 PD-1/PD-L1 Checkpoint 420
  - 12.5.1.3 Other Immune Checkpoints 423
  - 12.5.2 PTT-Synergized Immunoadjuvant Therapy 425
  - 12.5.3 PTT-Synergized Adoptive Cellular Immunotherapy 427
  - 12.5.4 PTT-Synergized Therapeutic Cancer Vaccine 429
  - 12.6 Summary and Outlook 431
  - References 433
- 13 Near-Infrared Region-Responsive Antimicrobial Nanomaterials for the Treatment of Multidrug-Resistant Bacteria 449**  
*Manlin Qi, Shangyan Shan, Biao Dong, and Lin Wang*
- 13.1 Introduction 449
  - 13.2 The Antibacterial Mechanisms of Photofunctional Antibacterial Nanomaterials 451
  - 13.3 Photofunctional Nanomaterials and Antibacterial Activity Against MDR Bacteria 452
    - 13.3.1 Representative NIR PDT Photosensitizers 453
      - 13.3.1.1 NIR-Responsive Porphyrins 453
      - 13.3.1.2 NIR-Responsive Phthalocyanines 455
    - 13.3.2 NIR-Responsive PTT Agents 455
      - 13.3.2.1 Gold Nanoparticles and Derived Nanostructures 455
      - 13.3.2.2 Carbon Nanotubes 457
      - 13.3.2.3 Graphene Oxide 458
      - 13.3.2.4 Semiconductor Nanoparticles 458
    - 13.3.3 NIR-Responsive PDT/PTT Agents 459
      - 13.3.3.1 NIR Cyanine Dyes 459
      - 13.3.3.2 NIR QDs 461
      - 13.3.3.3 Aggregation-Induced Emission Luminogens 464
  - 13.4 Limitations and Challenges 465
    - 13.4.1 Common PDT or PTT Resistance Mechanism 465
      - 13.4.1.1 Oxidative Stress Defense 465
      - 13.4.1.2 Thermal Stress Defense 467
    - 13.4.2 MDR Bacteria Drug Resistance Mechanism 467
  - 13.5 Conclusions 468
  - References 469
- 14 Photoelectrochemical Nanomaterials for Biosensing Applications 477**  
*Qianqian Sun and Piaoping Yang*
- 14.1 Introduction 477
  - 14.2 Classification of Photoelectrochemical Materials 477
    - 14.2.1 Inorganic Photoelectrochemical Materials 479
    - 14.2.2 Organic Photoelectrochemical Materials 480
    - 14.2.3 Composite Photoelectrochemical Materials 480



- 14.3 Introduction to Biorecognition Elements 481
- 14.4 Factors Affecting the Photocurrent Signal 482
- 14.5 Signal Amplification and Bursting Strategies 484
  - 14.5.1 Photocurrent Signal Amplification Strategies 484
  - 14.5.2 Photocurrent Signal Bursting Strategies 489
- 14.6 Applications of Photoelectrochemical Biosensors 493
  - 14.6.1 Direct Photoelectrochemical Detection 493
  - 14.6.2 Photoelectrochemical Enzyme Detection 494
  - 14.6.3 Photoelectrochemical Nucleic Acid Detection 495
  - 14.6.4 Photoelectrochemical Immunoassay 497
- 14.7 Challenges and Potential Clinical Applications 498
- References 500
  
- 15 X-Ray-Induced Photodynamic Therapy for Deep-Seated Tumors 507**  
*Jinliang Liu*
  - 15.1 Introduction 507
  - 15.2 Mechanisms of Interaction Between X-Rays and Scintillation Materials 509
  - 15.3 X-Ray-Sensitive Materials 511
    - 15.3.1 Metallic Materials 511
      - 15.3.1.1 Lanthanide-based Nanophosphors 511
      - 15.3.1.2 Metal Cluster Nanomaterials 514
      - 15.3.1.3 Long-Afterglow Luminescent Nanomaterials 516
      - 15.3.1.4 Quantum Dots 518
      - 15.3.1.5 Metal–Organic Complexes 521
      - 15.3.1.6 Metal–Organic Frameworks (MOFs) 523
    - 15.3.2 Nonmetallic Materials 525
      - 15.3.2.1 Organic Materials 525
      - 15.3.2.2 Nonmetallic Inorganic Materials 526
  - 15.4 X-Ray-Activated Therapy 527
    - 15.4.1 Type I X-Ray-Excited PDT 527
    - 15.4.2 Type II X-Ray-Excited PDT 529
    - 15.4.3 Combined Type I and Type II X-Ray-Excited PDT 531
    - 15.4.4 X-Ray-Induced Generation of RNS for Dynamic Therapy 532
    - 15.4.5 Synergistic Therapy 536
  - 15.5 Conclusions and Perspectives 539
  - References 540
  
- 16 Conclusions and Perspectives 549**  
*Chunxia Li and Jun Lin*
  
- Index 551**

