

Contents

CHAPTER 1

Colloidal Quantum Dots: Synthesis, Photophysical Properties, and Biofunctionalization Strategies

1.1	Introduction	1
1.2	Chemistry and Physics of Semiconductor Quantum Dots	2
1.2.1	Basic Physical Properties of Semiconductor Quantum Dots	2
1.2.2	Synthesis, Characterization, and Capping Strategies	4
1.3	Strategies for Surface-Functionalization and Conjugation to Biomolecules	13
1.3.1	Water-Solubilization Strategies	13
1.3.2	Methods for Conjugating QDs with Biomolecular Receptors	18
1.4	Concluding Remarks and Future Outlook	19
	Acknowledgments	20
	References	21

CHAPTER 2

Colloidal Chemical Synthesis of Organic-Dispersible Uniform Magnetic Nanoparticles

2.1	Magnetism of Nanoparticles	27
2.2	Transition Metal Nanoparticles	30
2.2.1	Cobalt Nanoparticles	30
2.2.2	Iron and Nickel Nanoparticles	32
2.3	Metal Alloy Nanoparticles	33
2.3.1	FePt Nanoparticles	33
2.3.2	Other Metal Alloy Nanoparticles	34
2.4	Metal Oxide Nanoparticles	35
2.4.1	Monometallic Oxide Nanoparticles	35
2.4.2	Bimetallic Ferrite Nanoparticles	38
2.5	Representative Synthetic Procedures for Magnetic Nanoparticles	39
2.5.1	Iron Nanoparticles	39
2.5.2	Iron Oxide Nanoparticles	40
	References	41

CHAPTER 3

Peptide-Functionalized Quantum Dots for Live Diagnostic Imaging and Therapeutic Applications

3.1	Introduction	45
-----	--------------	----

3.2	Phytochelatin Peptides: The All-in-One Solubilization/ Functionalization Approach	47
3.3	Colloidal and Photophysical Properties of Peptide-Coated Qdots	50
3.4	Live Cell Dynamic Imaging	52
	3.4.1 Single-Particle Tracking of Cell-Surface Membrane Receptors	52
	3.4.2 Peptide-Mediated Intracellular Delivery and Targeting of Qdots	54
3.5	Live Animal Imaging	55
	3.5.1 Near-Infrared Deep-Tissue Dual-Modality Imaging	56
	3.5.2 In Vivo Targeting of Tumor Vasculature	57
3.6	Beyond Diagnostic Imaging: Sensing and Therapeutic Applications	59
	3.6.1 Cleavable Peptides for Proteases Activity	59
	3.6.2 Photodynamic Therapy	61
3.7	Conclusion and Perspectives	63
	Acknowledgments	64
	References	64

CHAPTER 4

	Resonance Energy Transfer-Based Sensing Using Quantum Dot Bioconjugates	71
4.1	Introduction and Background	71
4.2	Unique Attributes of Quantum Dots As FRET Donors	73
	4.2.1 Improving the Spectral Overlap by Tuning QD Emission	73
	4.2.2 Significant Reduction of Direct Excitation of the Acceptor	74
	4.2.3 Increase FRET Efficiency by Arraying Multiple Acceptors around a Single QD	74
	4.2.4 Achieving Multiplex FRET Configurations with One Excitation Source	76
	4.2.5 Multiphoton FRET Configurations	77
4.3	FRET-Based Biosensing with Quantum Dots	79
	4.3.1 Competitive Sensing Using QD-Protein Conjugates	79
	4.3.2 Sensing Enzymatic Activity Using QD-Peptide and QD-Oligonucleotide Substrates	82
	4.3.3 Detection of Hybridization Using QD-Nucleic Acid Conjugates	85
	4.3.4 pH and Ion Sensing	88
4.4	Quantum Dots As Sensitizers for Photodynamic Therapy	91
4.5	Special Sensing Configurations	93
4.6	Conclusions and Outlook	96
	Acknowledgments	97
	References	97

CHAPTER 5

	Use of Luminescent Quantum Dots to Image and Initiate Biological Functions	101
5.1	Introduction	101
5.2	Multivalency Allows Multifunctionality	103
5.3	Stimuli-Responsive Polymers and Qds As Tools for Imaging	109
5.4	Conclusions	110
	Acknowledgments	111

References	111
------------	-----

CHAPTER 6

Single Particle Investigation of Biological Processes Using QD-Bioconjugates	115
6.1 Introduction	115
6.2 Physical Properties of Single QDs	116
6.3 In Vitro Detection of Biomolecular Interactions Using Single QD Fluorescence	116
6.3.1 Detection of Biomolecules Using Multicolor Colocalization of QD Probes	117
6.3.2 Colocalization Studies Using Streptavidin-Coupled QD-Dye Pairs	119
6.3.3 Fluorescence Energy Transfer from Single QD to Organic Fluorophores	119
6.4 In Vitro and In Vivo Tracking of Protein Using Single QDs	124
6.4.1 In Vitro Detection of Kinesin and Myosin Motor Movement	124
6.4.2 Tracking of Protein Receptors in Live Cells	126
6.5 Conclusion	129
Acknowledgments	129
References	130

CHAPTER 7

Assessment of the Issues Related to the Toxicity of Quantum Dots	133
7.1 Introduction	133
7.2 General Considerations	134
7.2.1 Routes of Exposure	134
7.2.2 Mechanisms of Cellular Internalization of QDs	135
7.2.3 Detection of QD-Induced Cytotoxicity	136
7.3 Mechanisms of Quantum Dots Cytotoxicity	138
7.3.1 Release of Toxic Metal Ions	138
7.3.2 Effects of Capping Materials on Cytotoxicity	140
7.3.3 Effects of QD Size on Cytotoxicity	141
7.3.4 Effects of Reactive Oxygen Species on Cytotoxicity	142
7.3.5 Effects of QDs on Genomic DNA	147
7.4 Bioaccumulation and Clearance of QDs	150
7.5 Outlook	153
Acknowledgments	154
References	154

CHAPTER 8

Chemical and Biological Sensing Based on Gold Nanoparticles	161
8.1 Introduction	161
8.2 Synthesis of Gold Nanoparticles	162
8.3 Physical Properties of Gold Nanoparticles	164
8.4 Colorimetric Sensing	165
8.4.1 Colorimetric Detection of Metal Ions and Anions	166

8.4.2	Colorimetric Detection of Biomaterials	167
8.5	Fluorescence Sensing	170
8.6	Electrical and Electrochemical Sensing	172
8.7	Surface Enhanced Raman Scattering-Based Sensing	179
8.8	Gold Nanoparticle-Amplified SPR Sensing	180
8.9	Quartz Crystal Microbalance-Based Sensing	181
8.10	Gold Nanoparticle-Based Bio-Barcode Assay	182
8.11	Concluding Remarks	183
	Acknowledgments	185
	References	185
CHAPTER 9		
	Plasmon-Resonant Gold Nanorods: Photophysical Properties Applied Toward Biological Imaging and Therapy	197
9.1	Introduction	197
9.2	Synthesis	198
9.3	Optical Properties	200
9.3.1	Absorption	200
9.3.2	Plasmon-Resonant Scattering	202
9.3.3	Linear Photoluminescence	202
9.3.4	Nonlinear Optical Properties	203
9.3.5	Other Optical Properties	205
9.4	Surface Chemistry and Biocompatibility	206
9.4.1	Bioconjugation Methods	206
9.4.2	Cytotoxicity and Nonspecific Cell Uptake	208
9.5	Biological Applications of Gold Nanorods	209
9.5.1	Contrast Agents for Imaging	209
9.5.2	Photothermal Therapy	213
9.5.3	Ex Vivo Bioanalytical Applications	215
9.6	Outlook	217
	References	218
CHAPTER 10		
	Magnetic Nanoparticles in Biomedical Applications	235
10.1	Introduction	235
10.2	Nanoscale Magnetic Properties	235
10.3	Magnetic Resonance Imaging (MRI) Contrast Agent	237
10.4	Magnetic Separation	241
10.5	Magnetic Drug Delivery	245
10.6	Conclusions	247
	References	247
CHAPTER 11		
	Magnetic Nanoparticles-Assisted Cellular MR Imaging and Their Biomedical Applications	251
11.1	Introduction	251

11.2	Characterization of MRI Contrast Agents or Magnetic Nanoparticles Used in Cell Labeling for CMRI	252
11.2.1	Paramagnetic Agents	252
11.2.2	Superparamagnetic Agents	253
11.3	Methods for Labeling Cells with Magnetic Nanoparticles for CMRI	255
11.3.1	Endocytosis of Contrast Agents	256
11.3.2	Modified Nanoparticles for Cell Labeling	257
11.3.3	Transfection Agent Mediated Cell Labeling	260
11.3.4	Other Methods of Cell Labeling	260
11.4	Methods to Monitor the Functional Status of Labeled Cells or Toxicity Following Labeling	261
11.4.1	Determination of Cell Viability	262
11.4.2	Determination of Cell Function	263
11.4.3	Determination of Cell Differentiation Capacity	263
11.5	MRI Techniques to Detect Cells Labeled with Superparamagnetic Iron Oxides	263
11.6	Animal Studies That Have Utilized CMRI	265
11.6.1	Stem Cell Tracking	265
11.6.2	Intracranial Tumor Studies	265
11.6.3	Tumor Angiogenesis	266
11.6.4	Stroke and Trauma Models	268
11.6.5	Myocardial Infarction and Vascular Models	269
11.6.6	Models of Multiple Sclerosis	272
11.7	Translation to the Clinic	273
11.7.1	Human Studies	273
11.7.2	Regulatory Issues	274
	References	276
	About the Editors	289
	List of Contributors	290
	Index	293