

Contents

Preface XV

List of Contributors XIX

Part One Overview of Synthesis, Characterization, and Applications in Biomedicine 1

1	Carbon Nanomaterials: Synthetic Approaches	3
	<i>Jean-Philippe Tessonniere</i>	
1.1	Introduction	3
1.2	General Concepts on the Synthesis of Carbon (Nano-)Materials	4
1.2.1	Uncatalyzed Synthesis of Carbon (Nano-)Materials	4
1.2.2	Catalyzed Synthesis of Carbon (Nano-)Materials	5
1.3	Synthesis from Solid Precursors	6
1.3.1	Nanodiamonds	6
1.3.1.1	Turning Graphite into Diamond	7
1.3.1.2	Explosive Detonation Synthesis	7
1.3.2	Fullerenes, Nanohorns, Single- and Multi-Wall Carbon Nanotubes	9
1.4	Catalytic Chemical Vapor Deposition	10
1.4.1	Definitions	10
1.4.2	Mechanistic Aspects	12
1.4.3	Single- and Multi-Wall Carbon Nanotubes	14
1.4.3.1	Floating Catalyst CCVD	15
1.4.3.2	Immobilized Catalyst CCVD	16
1.4.4	Aligned Carbon Nanotubes	17
1.4.5	Carbon Nanotubes Synthesized from Biocompatible Catalysts	18
1.4.6	Metal- and PAH-Induced Toxicity of Carbon Nanotubes	19
1.5	Purification Techniques	20
1.6	Importance of Defects and Curvature for Further Functionalization	22
1.7	Functionalization: Creating Anchoring Points for Bioactive Molecules	23
1.7.1	Functionalization by Oxidation	24
1.7.2	Functionalization by Coupling Reactions	25

1.7.3	Noncovalent Functionalization	26
1.8	Conclusion and Outlook	26
	References	26
2	Nanocarbons: Characterization Tools	35
	<i>Dang Sheng Su</i>	
2.1	Introduction	35
2.2	Diffraction Techniques	36
2.3	Imaging	37
2.3.1	Electron Microscopy	37
2.3.1.1	Electron-Specimen Interactions	38
2.3.1.2	Scanning Electron Microscopy	39
2.3.1.3	Transmission Electron Microscopy	41
2.3.1.4	Scanning Transmission Electron Microscopy	49
2.3.2	Scanning Probe Microscopy	49
2.3.2.1	Scanning Tunneling Microscopy	49
2.3.2.2	Atomic Force Microscopy	52
2.4	Spectroscopy	53
2.4.1	Energy-Dispersive X-Ray Spectroscopy	53
2.4.2	Electron Energy-Loss Spectroscopy	55
2.4.3	X-Ray Absorption Spectroscopy	57
2.4.4	X-Ray Photoelectron Spectroscopy	58
2.4.5	Raman Spectroscopy	62
2.4.6	Infrared Spectroscopy	64
2.5	Summary	66
	References	66
3	Synthesis, Characterization, and Biomedical Applications of Graphene	69
	<i>Albert Dato, Velimir Radmilovic and Michael Frenklach</i>	
3.1	Introduction	69
3.2	Synthesis of Graphene	70
3.2.1	Chemical Exfoliation	71
3.2.2	Epitaxial Growth	71
3.2.3	Substrate-Free Gas-Phase Synthesis	72
3.2.4	Chemical Vapor Deposition	72
3.2.5	Arc Discharge of Graphite Electrodes	72
3.2.6	Liquid-Phase Production	72
3.3	Characterization of Graphene	73
3.3.1	Raman Spectroscopy	73
3.3.2	Transmission Electron Microscopy	75
3.3.3	Electron Diffraction	75
3.3.4	Electron Energy Loss Spectroscopy	76
3.3.5	Elemental Analysis	77
3.4	Biomedical Applications of Graphene	78

3.4.1	Biocompatible Graphene Paper	79
3.4.2	Drug Delivery	79
3.4.3	Biodevices	81
3.4.4	Imaging of Soft Materials	82
3.5	Conclusions	83
	References	83
4	Carbon Nanohorns and Their Biomedical Applications	87
	<i>Shuyun Zhu and Guobao Xu</i>	
4.1	Introduction	87
4.2	Structure and Properties	88
4.3	Functionalization	90
4.3.1	Covalent Functionalization	91
4.3.2	Noncovalent Functionalization	92
4.4	Biomedical Applications	93
4.4.1	Toxicity Assessment of SWCNHs	95
4.4.2	SWCNHs Used in Drug-Delivery Systems	95
4.4.3	SWCNHs Used in Magnetic Resonance Analysis	100
4.4.4	Biosensing Applications of SWCNHs	101
4.5	Conclusions	103
	Acknowledgments	104
	References	104
5	Bio-Inspired Magnetic Carbon Materials	111
	<i>Elby Titus, José Gracio, Duncan P. Fagg, Manjo K. Singh and Antonio C. M. Sousa</i>	
5.1	Introduction	111
5.2	Allotropic Forms of Carbon	112
5.3	Magnetism in Diamond	113
5.3.1	Biomedical Applications of Magnetic Diamond	113
5.4	Magnetism in Graphite	115
5.4.1	Biomedical Applications of Magnetic Graphite	116
5.5	Magnetism in Carbon Nanotubes/Fullerenes	117
5.5.1	Biomedical Applications of Magnetic Carbon Nanotubes/Fullerenes	120
5.6	Magnetism in Graphene	124
5.6.1	Biomedical Applications of Magnetic Graphene	125
5.7	Conclusion	126
	References	126
6	Multi-Walled Carbon Nanotubes for Drug Delivery	133
	<i>Nicole Levi-Polyachenko</i>	
6.1	Introduction	133
6.2	Gene Therapy	138
6.3	Antibacterial Therapy	140

6.4	Wound Healing	142
6.5	Chemotherapy	145
6.5.1	Hyperthermic Drug Delivery Using CNTs	146
6.5.2	Drug Transport Using CNTs	150
6.6	Summary and Future Perspectives	154
	References	155
7	Carbon Nanotube-Based Three-Dimensional Matrices for Tissue Engineering	161
	<i>Izabela Firkowska and Michael Giersig</i>	
7.1	Introduction	161
7.2	Carbon Nanotubes	162
7.3	Carbon Nanotubes for Matrix Enhancement	164
7.4	Cellular Responses to CNT-Based Matrices	166
7.5	CNT Engineering into Three-Dimensional Matrices	166
7.5.1	Vertically Aligned CNT-Based Matrices	166
7.5.2	Three-Dimensional Cavity Network of Interconnected Nanotubes	170
7.5.3	Freestanding MWNT-Based Matrix	175
7.5.3.1	Modification of the MWNT-Based Matrix Surface with Bioactive Calcium Phosphate Nanoparticles	178
7.6	Summary	180
	References	182
8	Electrochemical Biosensors Based on Carbon Nanotubes	187
	<i>Jonathan C. Claussen, Jin Shi, Alfred R. Diggs, D. Marshall Porterfield and Timothy S. Fisher</i>	
8.1	Introduction	187
8.2	CNT Properties	188
8.2.1	Mechanical	188
8.2.2	Electrical	188
8.2.3	Chemical/Electrochemical	189
8.3	Electrochemical Biosensing	190
8.4	CNT-Based Electrode Fabrication	190
8.4.1	Adsorption	190
8.4.2	Covalent Bonding	192
8.4.3	Polymer Entrapment	192
8.4.4	Aligned Arrays	195
8.4.4.1	Nanoelectrodes	197
8.4.5	Hybrid (CNT/Metal Nanoparticle) Electrodes	197
8.5	Applications	199
8.5.1	Nonenzymatic Biosensing	199
8.5.1.1	Nicotinamide Adenine Dinucleotide (NADH)	199
8.5.1.2	Homocysteine	201
8.5.1.3	Dopamine	202

8.5.1.4	Indole Acetic Acid (IAA)	202
8.5.2	Enzymatic Biosensing	203
8.5.2.1	Glucose	203
8.5.2.2	Glutamate	205
8.5.2.3	Ethanol	207
8.6	Conclusions	209
	References	210

9	Single-Walled Carbon Nanotube Biosensors	217
	<i>Jeong-O Lee and Hye-Mi So</i>	
9.1	Introduction	217
9.2	The Sensing Mechanisms of Nanotube Biosensors	218
9.3	The Immobilization of Biomolecules on SWNTs	221
9.3.1	Covalent Binding	221
9.3.2	Noncovalent Binding	222
9.3.3	Other Immobilization Methods (Metal Particles, etc.)	223
9.4	Various Receptors for Nanotube Biosensors	224
9.4.1	Aptamers	224
9.4.2	Fragment Antibodies	227
9.4.3	Enzymes and Proteins	229
9.4.4	Other Receptor Types	230
9.5	The Application of Nanotube Biosensors to Pathogen Detection	231
9.6	The Future of Nanotube Biosensors	234
	References	235
10	Environmental Impact of Fullerenes	239
	<i>Naohide Shinohara</i>	
10.1	Introduction	239
10.2	Methods Used to Prepare Fullerene Suspensions	239
10.2.1	Solubility of Fullerene	239
10.2.2	Aqueous Suspensions of Fullerenes	246
10.2.3	Toxicity of Aqueous Fullerene Suspensions as a Factor of the Dispersion Method	246
10.3	Toxicological Data Relating to Fullerenes	247
10.3.1	Toxicological Effects of C ₆₀ on Fish	247
10.3.2	Toxicological Effects of C ₆₀ on Invertebrates	250
10.3.3	Toxicological Effects of C ₆₀ on Algae	251
10.3.4	Toxicological Effects of C ₆₀ on Bacteria and Soil Microbes	251
10.3.5	Toxicological Effects of C ₆₀ on Other Organisms	254
10.4	Possible Emission Sources of C ₆₀	254
10.5	The Environmental Fate of C ₆₀	262
10.6	Fullerenes in the Environment	265
10.7	Conclusion	265
	References	266

11	Computational Tools for the Biomedical Application of Carbon Nanomaterials	271
	<i>Leela Rakesh</i>	
11.1	Introduction	271
11.2	Simulation Methods	278
11.2.1	Background	278
11.2.2	Molecular Modeling	280
11.3	Results and Discussions	281
11.3.1	Branched PEGylated DPCC Functionalized PTX Physical Loading on SWNTs	287
11.3.2	Interaction of Irinotecan-co-br-PEG-DPCC-unco-SWNT and with ssDNA (Adenine-Thymine (AT))	292
11.3.3	Interaction of Nanotube with 20-Base Pair Guanine–Thymine -ssDNA in the Presence of Calcitriol	296
11.4	Future Perspectives	298
11.5	Executive Summary	300
	Acknowledgments	301
	References	301
	Part Two Overview of Applications in Cancer	307
12	Carbon Nanotubes for Cancer Therapy	309
	<i>William H. Gmeiner</i>	
12.1	Introduction	309
12.1.1	Limitations of Current Therapy Options	309
12.1.2	Developing Nanomaterials for Cancer Treatment	310
12.1.3	CNTs: Physical Properties, Manufacture, and Chemical Modifications	311
12.2	Hyperthermia for Cancer Treatment	312
12.2.1	Current Ablative Technologies	315
12.2.2	Use of CNTs for Hyperthermia Treatment	316
12.3	CNTs for Drug Delivery	320
12.3.1	Localization of CNTs to Malignant Tissues	321
12.3.2	Drug Delivery Using CNTs	322
12.4	Imaging Using CNTs	323
12.5	CNT-Related Toxicity	324
12.6	Summary and Future Perspective	325
	Acknowledgments	326
	Abbreviations	326
	References	327
13	Cancer Treatment with Carbon Nanotubes, Using Thermal Ablation or Association with Anticancer Agents	333
	<i>Roger G. Harrison, Luís F. F. Neves, Whitney M. Prickett and David Luu</i>	
13.1	Introduction	333

13.2	Use of Nanotubes as Heated Particles	334
13.3	Use of Anticancer Agents Associated with Nanotubes	338
13.4	Summary	343
13.5	Future Perspective	344
	Acknowledgments	345
	References	345
14	Carbon Nanotubes for Targeted Cancer Therapy	349
	<i>Reema Zeineldin</i>	
14.1	Introduction	349
14.2	Cancer	350
14.3	Conventional Cancer Chemotherapy versus Nanocarrier-Mediated Drug Delivery	352
14.3.1	Challenges with Chemical Compounds as Therapeutic Agents	352
14.3.2	Advantages of Nanocarriers as Drug-Delivery Vehicles	352
14.4	Carbon Nanotubes as Drug-Delivery Vehicles	353
14.5	Cellular Uptake of CNTs	354
14.6	Functionalization of CNTs with Polyethylene Glycol	355
14.7	Targeting of Cancers	357
14.7.1	Passive Targeting	357
14.7.2	Active Targeting	358
14.7.3	Trafficking of Targeted Drug-Delivery Vehicles	358
14.8	Targeted Cancer Therapy Employing CNTs and a Critique of Current Studies	359
14.8.1	erbB Family Members	360
14.8.2	Folate Receptor α	363
14.8.3	Biotin Receptor	365
14.8.4	Integrins	366
14.8.5	Markers for Lymphomas or Leukemias	367
14.8.6	Disialoganglioside (GD2)	368
14.9	Summary and Future Perspective	368
	Acknowledgments	371
	References	371
15	Application of Carbon Nanotubes to Brain Tumor Therapy	381
	<i>Dongchang Zhao and Behnam Badie</i>	
15.1	Introduction	381
15.2	The Current Challenge of Brain Tumor Therapy	382
15.2.1	Current Status of Clinical Practice in Brain Tumor Therapy	382
15.2.2	The Progress of Investigational Therapies for Brain Tumors	382
15.2.2.1	Targeted Molecular Therapy	382
15.2.2.2	Anti-Angiogenic Therapy	383
15.2.2.3	Immunotherapy	383
15.2.2.4	Gene Therapy	384
15.3	The Characteristics of CNTs for Biological Applications	385
15.3.1	Single-Walled and Multi-Walled Carbon Nanotubes	385

15.3.2	Functionalization of CNTs	385
15.3.2.1	Covalent Surface Modification	385
15.3.2.2	Noncovalent Surface Modification	386
15.3.3	CNT Delivery System	386
15.3.3.1	Delivery of Antibodies and Peptides	387
15.3.3.2	Delivery of siRNA	387
15.3.3.3	Delivery of DNA Molecules	387
15.3.3.4	Delivery of CpG	388
15.3.3.5	Delivery of Vaccines	388
15.3.3.6	Delivery of Chemical Drugs	388
15.4	Strategies of Application of CNTs to Brain Tumor Therapy	389
15.4.1	CNTs Targeting Brain Tumor-Macrophages	389
15.4.1.1	Internalization of CNTs by BV2 Microglia Cells <i>in vitro</i>	389
15.4.1.2	Preferential Uptake of CNTs by Macrophages in a Glioma Model	390
15.4.1.3	Phosphatidylserine-Coated CNTs Targeting Microglia/ Macrophages	391
15.4.2	CNTs Targeting Tumor Cells and Preliminary Efforts Towards <i>In Vivo</i> Cancer Therapy	392
15.4.2.1	CNTs Actively Targeting Tumor Cells	392
15.4.2.2	CNTs Passively Targeting Tumor Cells	392
15.4.2.3	CNTs Thermal Effects on Tumor Cells	393
15.5	Toxicity Issues of CNTs in Brain Tumor Therapy	394
15.6	Conclusions and Future Directions	395
	Acknowledgments	395
	References	395
16	Carbon Nanotubes in Cancer Therapy, including Boron Neutron Capture Therapy (BNCT)	403
	<i>Amartya Chakrabarti, Hiren Patel, John Price, John A. Maguire and Narayan S. Hosmane</i>	
16.1	Introduction	403
16.2	Carbon Nanotubes in the Treatment of Cancer	403
16.2.1	Drug Delivery	404
16.2.2	Imaging and Probing	406
16.2.3	Photothermal and Photoacoustic Therapy	407
16.3	BNCT and Its Development through Nanotechnology	409
16.3.1	BNCT: A Brief Overview	409
16.3.2	Liposomes	411
16.3.3	Dendritic Macromolecules	411
16.3.4	Magnetic Nanoparticles	413
16.4	The Role of Carbon Nanotubes in BNCT	413
16.5	Summary and Future Outlook	415
	References	415

17	Fullerenes in Photodynamic Therapy	419
	<i>Sulbha K. Sharma, Ying-Ying Huang, Paweł Mroz, Tim Wharton, Long Y. Chiang and Michael R. Hamblin</i>	
17.1	Introduction	419
17.2	Photodynamic Therapy	420
17.2.1	Traditional Photosensitizers	421
17.2.2	Photophysics and Photochemistry in PDT	422
17.2.3	Anticancer Mechanism of PDT	424
17.2.3.1	Cellular Effects	424
17.2.3.2	<i>In Vivo</i> Effects	425
17.2.4	Antimicrobial Mechanism of PDT	425
17.3	Fullerenes as Photosensitizers	425
17.3.1	Photophysics of Fullerenes	426
17.3.2	Photochemistry of Fullerenes	427
17.3.3	Interactions of Fullerenes with DNA	429
17.3.4	Drug-Delivery Strategies for Fullerenes	430
17.3.5	Strategies to Overcome the Unfavorable Spectral Absorption of Fullerenes	432
17.3.5.1	Covalent Attachment of Light-Harvesting Antennae to Fullerenes	433
17.3.5.2	Two-Photon PDT	434
17.4	Anticancer Effects of Fullerenes	436
17.4.1	<i>In Vitro</i> PDT with Fullerenes	436
17.4.2	<i>In Vivo</i> PDT with Fullerenes	438
17.5	Fullerenes for Antimicrobial Photoinactivation	439
17.5.1	Photoinactivation of Viruses	439
17.5.2	Photoinactivation of Bacteria and Other Pathogens	440
17.6	Summary and Future Perspectives	441
	Acknowledgments	442
	References	442

Index 449

