Vijay K. Varadan, Linfeng Chen, Jining Xie

Nanomedicine

Design and Applications of Magnetic Nanomaterials, Nanosensors and Nanosystems



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NANOMEDICINE

DESIGN AND APPLICATIONS OF MAGNETIC NANOMATERIALS, NANOSENSORS AND NANOSYSTEMS

Vijay K. Varadan Linfeng Chen Jining Xie







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NANOMEDICINE

Preface

Progress in nanoscience and nanotechnology has led to the development of a new field, nanomedicine, which is generally defined as the biomedical applications of nanoscience and nanotechnology. Nanomedicine stands at the boundaries between physical, chemical, biological and medical sciences, and the advances in nanomedicine have made it possible to analyze and treat biological systems at the cell and sub-cell levels, providing revolutionary approaches for the diagnosis, prevention and treatment of some fatal diseases. For example, the *US National Cancer Institute* expects that nanoscience and nanotechnology will be harnessed for the purposes of eliminating death and suffering from cancer. Many nanomedicine approaches are already quite close to fruition, and the *US Food and Drug Administration* has started to consider the complex issues related to the approval of nanomaterials, nanodevices and nanosystems, for human betterment.

Nanomagnetism is at the forefront of nanoscience and nanotechnology, and in the field of nanomedicine, magnetic nanomaterials are among the most promising nanomaterials for clinical diagnostic and therapeutic applications. The magnetic nanomaterials used for biomedical purposes generally include zero-dimensional nanospheres, one-dimensional nanowires and nanotubes, and two-dimensional thin films. Magnetic nanoparticles, mainly including nanospheres, nanowires and nanotubes, are widely used for labeling and manipulating biomolecules, targeting drugs and genes, magnetic resonance imaging, as well as hyperthermia treatment. Magnetic thin films are often used in the development of nanosensors and nanosystems for analyzing biomolecules and diagnosing diseases.

Due to the great market potential of nanomedicine, many universities, research institutions, hospitals, commercial companies and government organizations have spent a great deal of resources in the research of magnetic nanomaterials for biomedical applications, and amazing progress has been made in this field. Some magnetic nanoparticles and nanosensors are already commercially available. Some medical applications of magnetic nanoparticles and nanosensors are under clinical trials, and encouraging results have been reported.

Despite the rapid progress in nanomedicine, we are aware of the lack of good reference books in the field of magnetic nanomaterials and their biomedical applications. Though there are excellent reviews, book chapters, and books dealing with one or several topics in this field, a book containing a comprehensive coverage of up-to-date progress in this field is not available. The research in this field requires the collaboration between researchers from different disciplines, such as physics, chemistry, materials sciences, electrical engineering, biology and medicine. However, such cross-disciplinary cooperation is not easy. For example, the languages and the tools used by materials scientists are unfamiliar to many medical experts, and vice versa. Furthermore, the ways in which physicists and biologists, or chemists and cancer researchers, think about a biomedical

xii Preface

problem may be totally different. Therefore a book, based on which the researchers with different backgrounds can communicate, is urgently needed.

Besides, due to the lack of a reference book that can provide a broad coverage and deep insight into this field, most research activities are based primarily on the information scattered throughout numerous reports and journals. Furthermore, because of the paucity of suitable textbooks, the training in this field is usually not systematic, and this is unfavorable for the further progress in this field.

This book aims to present a comprehensive treatment of this subject. It systematically discusses the synthesis techniques, the physical and chemical properties, and the working principles for biomedical applications of various types of magnetic nanomaterials. We aim to satisfy the need of a textbook for beginners and research students, and a reference book for professionals in this field. With such a book, beginners and research students can quickly obtain an overall picture of this field. Meanwhile, this book bridges the gaps between researchers from different disciplines, so that they can speak the same language, and get their ideas across to each other. The clinical doctors who are interested in this area will also find this book valuable.

The book mainly consists of three parts. The introductory part (Chapters 1 and 2) gives general information about magnetic nanomaterials and their biomedical applications, and provides the physical background for understanding and exploring the biomedical applications of magnetic nanomaterials. The second part (Chapters 3 to 7) deals with various types of magnetic nanoparticles and their biomedical applications. Chapters 3 and 4 discuss the synthesis, properties and biomedical applications of magnetic nanospheres. In Chapter 5, a special type of magnetic nanoparticle and magnetosomes that naturally exist in magnetotactic bacteria are discussed. Chapters 6 and 7 discuss the synthesis, properties and biomedical applications of nanowires and nanotubes, respectively.

The third part (Chapters 8 to 10) discusses the development of biosensors, biochips, and their biomedical applications, with emphases laid on the sensing effects of magnetic thin films. Chapter 8 discusses the development of magnetic biosensors widely used in biomedical tests, mainly including magnetoresistance-based sensors, Hall-effect sensors, sensors detecting magnetic relaxations, and sensors detecting susceptibilities of ferrofluids. Chapter 9 mainly discusses the development of magnetic biochips based on the magnetic biosensors discussed in Chapter 8. Chapter 10 discusses the typical biomedical applications of magnetic biosensor and biochip technologies. In these applications, magnetic biosensors and biochips are mainly used to detect the biomolecules labeled by magnetic nanoparticles. An outlook for the biomedical applications of magnetic biosensor and biochip technologies is made at the end of this chapter.

In this book, the interdisciplinary nature of nanomedicine is emphasized. We take bits and pieces from the contributing disciplines and integrate them in ways that produce a new conceptual framework. To make the book readable, the contents of the book are systematically and logically developed from the elementary level. Each chapter presents one of the major topics in the development of functional magnetic nanomaterials and their biomedical applications, and contains a brief introduction to the basic physical and chemical principles of the topic under discussion. Therefore, each chapter is a self-contained unit, from which readers can readily obtain comprehensive information on this topic. To provide an extensive treatment of each topic, we have condensed mountains of literature into a readable account within a reasonable size. Important references have been included for the benefit of the readers who wish to pursue further their interested topics in a greater depth.

In preparing the book, we have tried to emphasize the fundamental concepts. Though a considerable amount of the contents in this book is related to experimental details and

results, we have tried to present the underlying sciences so that the readers can understand the process of applying fundamental concepts to design experiments and obtain useful results.

It should be indicated that, due to the rapid development of this field, and its interdisciplinary nature, a truly comprehensive coverage is difficult, and some important work in this field may have been missed. It is also difficult to always give proper credit to those who are the originators of new concepts and the inventors of new techniques. The summary and commentary we have written may not have grasped the essentials of the work under discussion. We hope this book does not have too many such errors, and we would appreciate it if readers could bring the errors they discover to our attention so that these can be corrected in future editions.

We would like to acknowledge the contributions made by the students and staff at the *Center of Excellence for Nano/Neuro Sensors and Systems (CENNESS)*, University of Arkansas, Fayetteville, including the contributions from Jose Abraham in Chapters 9 and 10.

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Vijay K. Varadan Linfeng Chen Jining Xie

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xvi About the Authors

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Contents

Pre	Preface			
Ab	out th	e Auth	ors	XV
1	Intr	n	1	
	1.1		is Nanoscience and Nanotechnology?	1
		1.1.1	Nanoscale: Where Physical and Biological Sciences Meet	1
		1.1.2		3
		1.1.3	87	
		1.1.4	Ji II - II - Jimiosis of I tallollatorials	8
	1.0	1.1.5	-r	9
	1.2		ets and Nanometers: Mutual Attraction	11
	1.3		al Magnetic Nanomaterials	11
		1.3.1	1 0 000	12
		1.3.2		13
		1.3.3		15
	1.4	1.3.4		16
	1.4	1.4.1	medicine and Magnetic Nanomedicine	17
		1.4.1	Inspiration from Nature	17
		1.4.2	What is Nanomedicine?	18
		1.4.3	Status of Nanomedicine	19
	1.5		Magnetic Nanomedicine	19
	1.5	1.5.1	al Biomedical Applications of Functional Magnetic Nanomaterials	20
		1.5.2	Diagnostic Applications of Magnetic Nanoparticles	20
		1.5.2	Therapeutic Applications of Magnetic Nanoparticles	22
		1.5.5	Magnetic Biosensors and Biochips Based on Magnetic Thin Films	07
		1.5.4	Trends of the Biomedical Applications of Magnetic	27
		1.5.1	Nanomaterials	20
			runomateriais	29
2	Phys	ical Ba	ckground for the Biomedical Applications of Functional	
	Mag	netic N	anomaterials	37
	2.1	Requi	rements for Biomedical Applications	37
		2.1.1	Magnetic Particles and Ferrofluids	37
		2.1.2	Biocompatibility and Chemical Stability	38

vi Contents

		2.1.3	Magnetic Properties	39
		2.1.4	Physical Properties	39
	2.2	Funda	mentals of Nanomagnetism	39
		2.2.1	Basic Concepts of Nanomagnetism	40
		2.2.2	Superparamagnetism	48
		2.2.3	Nanoparticle Assemblies	50
		2.2.4	Colloidal Magnetic Nanoparticles	50
		2.2.5	Heating Mechanisms for Hyperthermia	54
	2.3	Magn	etic Relaxation of Ferrofluids	55
		2.3.1	Debye Theory	56
		2.3.2	Magnetic Relaxations of Magnetic Fluids	56
		2.3.3	Ferromagnetic Resonances	58
		2.3.4	Characterization of the Electromagnetic Responses of Ferrofluids	60
	2.4	Magn	etorheology of Ferrofluids	69
		2.4.1	Effects of Magnetic Field on Ferrofluid Viscosity	69
		2.4.2	Rheometers for the Study of Magnetorheology Fluids	71
	2.5	Manip	pulation of Magnetic Particles in Fluids	72
		2.5.1	Magnetic Nanoparticles and Microparticles	73
		2.5.2	Forces on Magnetic Particles by Magnetic Fields	74
		2.5.3	Mechanism of Magnetic Manipulation	75
	2.6		ctions Between Biological Nanomaterials and Functionalized	
		Magn	etic Nanoparticles	76
		2.6.1	e	77
			Targeting to Cell Receptors	78
			Targeted Cell Uptake	79
		2.6.4	Interactions Between Magnetic Nanoparticles and Cell	
			Membranes	80
3	Mag	netic N	Janoparticles	85
	3.1	Introd	luction	85
	3.2		s of Nanomagnetics	85
		3.2.1		85
		3.2.2		86
		3.2.3		86
	3.3	Synth	nesis Techniques	87
		3.3.1	Chemical Methods	88
		3.3.2	Biological Methods	90
	3.4	Synth	esis of Magnetic Nanoparticles	91
		3.4.1	Synthesis of Magnetic Monometallic Nanoparticles	91
		3.4.2	Synthesis of Magnetic Alloy Nanoparticles	95
		3.4.3	Synthesis of Magnetic Oxide Nanoparticles	98
		3.4.4	Synthesis of Magnetic Core-shell Nanoparticles	108
	3.5	Bio-ir	nspired Magnetic Nanoparticles	113
	3.6	Funct	ionalization of Magnetic Nanoparticles	116
		3.6.1	Functionalized with Organic Molecules	116
		3.6.2	Functionalized with Biological Entities	122
	3.7	Future	e Prospects	126

<u>Contents</u> vii

4	Bio	medical Applications of Magnetic Nanoparticles	129				
	4.1	4.1 Introduction					
	4.2	Diagnostic Applications	129 132				
		4.2.1 Enhancement of Magnetic Resonance Imaging	132				
		4.2.2 Magnetic Labeling	136				
		4.2.3 Spatially Resolved Magnetorelaxometry	139				
		4.2.4 Magnetic Separation and Purification	141				
		4.2.5 Biological Assay System	144				
		4.2.6 Biosensors	147				
	4.3	Therapeutic Applications	152				
		4.3.1 Drug and Gene Target Delivery	152				
		4.3.2 Hyperthermia Treatment	159				
		4.3.3 Eye Surgery	164				
		4.3.4 Antitumor Effects	166				
	4.4	Physiological Aspects	168				
	4.5	Toxic Effects	169				
5	Mag	gnetosomes and their Biomedical Applications	175				
	5.1	Introduction	175				
		5.1.1 Magnetotactic Bacteria and Magnetosomes	175				
		5.1.2 Basic Properties of Magnetosomes	177				
		5.1.3 Magnetotaxis and Magneto-aerotaxis	180				
	5.2	Magnetosome Formation	182				
		5.2.1 Biochemistry and Gene Expression	182				
		5.2.2 Formation Procedure	183				
		5.2.3 Cell Biology of Magnetosomes (Komeili 2007)	185				
	5.3	Cultivation of Magnetotactic Bacteria	187				
		5.3.1 Mass Cultivation of Magnetotactic Bacteria	188				
		5.3.2 Continuous Cultivation of Magnetotactic Bacteria	189				
	5.4	Characterization of Magnetosomes	191				
		5.4.1 Biochemical Characterization	191				
		5.4.2 Microstructure Characterization	192				
		5.4.3 Magnetization Characterization	195				
		5.4.4 Susceptibility Characterization	199				
		5.4.5 Trajectory Characterization	200				
	5.5	Biomedical Applications of Magnetosomes	201				
		5.5.1 Applications of Magnetic Cells	202				
		5.5.2 Applications of Isolated Magnetosome Particles	205				
6	Mag	netic Nanowires and their Biomedical Applications	215				
	6.1	Introduction	215				
		6.1.1 Arrayed and Dispersed Nanowires	216				
		6.1.2 Single-segment, Multi-segment and Multi-layer Nanowires	216				
		6.1.3 Other Nanowire Structures	217				
	6.2	Magnetism of Magnetic Nanowires	219				
		6.2.1 Shape Anisotropy	219				

viii Contents

		6.2.2	Switching in Single-domain Particles (Sun et al. 2005)	222
		6.2.3	Magnetization Hysteresis Loops	224
		6.2.4	Multiple-segment Nanowires	229
	6.3	Templ	ate-based Synthesis of Magnetic Nanowires	229
		6.3.1	Fabrication of Nanoporous Templates	230
		6.3.2	Electrochemical Deposition	232
		6.3.3	Electroprecipitation	237
		6.3.4	Self-assembly of Nanowires	238
	6.4	Chara	cterization of Magnetic Nanowires	240
		6.4.1	Electrical Properties	240
			Magnetization Properties	243
		6.4.3		247
	6.5		ionalization of Magnetic Nanowires	250
		6.5.1	Chemical Functionalization	250
		6.5.2	Biological Functionalization	251
		6.5.3	Assembly by Surface Chemistry	253
	6.6	_	etic Nanowires in Suspension	254
		6.6.1	Responses of Magnetic Nanowires in Suspension	254
		6.6.2	Magnetic Trapping of Nanowires	255
		6.6.3	·	256 258
	6.7	6.6.4		259
	0.7	6.7.1	edical Applications of Magnetic Nanowires Confinement of Magnetic Nanoparticles	260
		6.7.1		262
		6.7.3	Suspended Biosensing System (Tok <i>et al.</i> 2006)	266
		6.7.4		267
		6.7.5	Hybrid Devices	268
		0.7.0	njona Bernets	
7	Mag	netic N	anotubes and their Biomedical Applications	273
	7.1	Introd	luction	273
	7.2		etism of Nanotubes	274
	7.3		functionality of Magnetic Nanotubes	278
			Inner and Outer Surfaces of Nanotubes	278
		7.3.2	Magnetic Encapsulated Nanotubes	279
	7.4	Synth	esis and Characterization of Magnetic Nanotubes	279
		7.4.1	Single Element Magnetic Nanotubes	280
		7.4.2	Magnetic Oxide Nanotubes	284
		7.4.3	Alloyed Magnetic Nanotubes	292
		7.4.4	Doped Magnetic Nanotubes	296
		7.4.5	Hybrid Magnetic Nanotubes	306
	7.5		edical Applications of Magnetic Nanotubes	312
		7.5.1	Bioseparation	312
		7.5.2	Cell Manipulation	314
		7.5.3	Drug and Gene Delivery	315
		7.5.4	Neuronal Applications	319
		7.5.5	Magnetic Force Microscope	323

Contents

ix

8	Ma	gnetic Biosensors	329			
	8.1	Introduction				
		8.1.1 Biosensors and Magnetic Biosensors	329 329			
		8.1.2 Magnetic Biosensing Schemes	330			
		8.1.3 Magnetic Properties of a Magnetic Bead	332			
		8.1.4 Typical Types of Magnetic Biosensors	335			
		8.1.5 Sensor Sensitivity and Dynamic Range	338			
	8.2	Magnetoresistance-based Sensors	339			
		8.2.1 Giant Magnetoresistance Sensor	339			
		8.2.2 Anisotropic Magnetoresistance Sensor	343			
		8.2.3 Spin Valve Sensor	346			
		8.2.4 Magnetic Tunnel Junction Sensor	349			
	8.3	Hall Effect Sensors	351			
		8.3.1 Silicon Hall Effect Sensor	351			
		8.3.2 Planar Hall Effect Sensor	353			
		8.3.3 Extraordinary Hall Effect Sensor	356			
		8.3.4 Quantum Well Hall Effect Sensor	358			
	8.4	Other Sensors Detecting Stray Magnetic Fields	362			
		8.4.1 Giant Magnetoimpedance Sensor	362			
		8.4.2 Frequency Mixing Method	364			
	0.5	8.4.3 Superconducting Quantum Interference Detectors	366			
	8.5	Sensors Detecting Magnetic Relaxations	370			
		8.5.1 SQUID MRX	370			
	0.6	8.5.2 Fluxgate MRX	373			
	8.6	Sensors Detecting Ferrofluid Susceptibility	375			
		8.6.1 Theoretical Background	375			
		8.6.2 Slit Toroid Method	376			
		8.6.3 Coil Methods	376			
		8.6.4 PPMS Method	382			
9	Magnetic Biochips: Basic Principles					
	9.1	Introduction	387			
		9.1.1 Sensor Arrays and Integrated Biochips	387			
		9.1.2 Manipulation of Biomolecules	393			
		9.1.3 Detection of Biomolecules	393			
	9.2	Biochips Based on Giant Magnetoresistance Sensors	401			
	9.3	Biochips Based on Spin Valve Sensors	402			
	9.4	Biochips Based on Magnetic Tunnel Junctions	408			
	9.5	Fully Integrated Biochips	413 417			
10	Bion	nedical Applications of Magnetic Biosensors and Biochips	421			
	7					
	10.2 10.3					
		January Diochips				
	10.4	435				

x			Contents

10.5	Study of the Interactions Between Biomolecules	439		
10.6	Detection of Biological Warfare Agents	441		
10.7	Environmental Monitoring and Cleanup	446		
10.8	Outlook	449		
Apper	ndix-Units for Magnetic Properties	455		
Index		457		
maex	index 43			

Introduction

1.1 What is Nanoscience and Nanotechnology?

In the lexicology of science and technology, the prefix 'nano' refers to one-billionth of a unit. For example, one nanometer (nm) is one billionth (10⁻⁹) of a meter. The nanometer scale is the natural spatial context for molecules and their interactions. Nanoscience and nanotechnology deal with the objects at the nanometer scale (National Science and Technology Council 1999a). The properties and functions of objects at the nanometer scale are significantly different from those at a larger scale. Generally speaking, nanoscience investigates the properties of materials at atomic, molecular and macromolecular scales, while nanotechnologies deal with the design, production and application of devices and systems by controlling their shapes and sizes at the nanometer scale (Royal Society and Royal Academy of Engineering 2004).

Biology is one of the most active fundamental sciences, and it is also a science that is the most visible to the public. The need for improvement in medicine for the treatment of disease or, in a general sense, for the amelioration, correction and prevention of dysfunction in health, will never disappear (Whitesides and Wong 2006). The combination of biology and medicine, generally referred to as 'biomedicine', represents a most exciting blend of science and technology. The nanoscale provides a junction for biomedicine and materials science and technology. This book discusses the developments in nanoscience and nanotechnology and their applications in biomedicine.

1.1.1 Nanoscale: Where Physical and Biological Sciences Meet

As indicated in Figure 1.1, nanoscale is generally defined as the range from the size of atoms up to 100 nanometers, and a nanomaterial is usually defined as a material whose smallest dimension is less than 100 nanometers (Yih and Wei 2005). In a general sense, nanomaterials include all the structures, devices and systems at nanoscale. In some cases the size limit of a nanomaterial can be extended up to 1000 nm, and the essential point is that a nanomaterial exhibits unique properties that are quite different from those at a larger scale.

In Figure 1.1, a lot of biological entities are within the range of nanoscale, such as proteins, antibodies, viruses and bacteria, and they are usually called biological nanomaterials. The special functions and properties of biological nanomaterials provide much inspiration for the design of non-biological nanomaterials; meanwhile, due to their suitable sizes, non-biological nanomaterials can be used to access or manipulate biological nanomaterials (Yih and Wei 2005). Nanomaterials with sizes smaller than 50 nm can get

2 Introduction

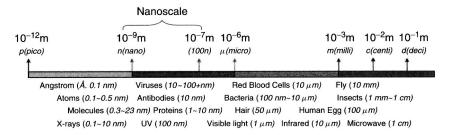


Figure 1.1 Nanoscale and typical materials whose dimension ranges are comparable to nanoscale. (Yih and Wei 2005)

inside most cells without difficulty. When nanomaterials with sizes smaller than 20 nm travel around the circulatory system of the body, they can move out of blood vessels. Therefore, after special treatments, nanomaterials are widely used as targeted drug delivery vehicles, which carry chemotherapeutic agents or therapeutic genes into the desired malignant cells while saving healthy cells. It should be noted that, in most of the technical literatures, nanomaterials are usually referred as non-biological nanomaterials, though biological entities and biological techniques have been widely used in the design and synthesis of non-biological nanomaterials.

The biological and physical sciences share a common interest in nanoscale, and the integration of biology and materials at the nanoscale has the potential to revolutionize many fields of science and technology. A vigorous trade across the borders of these areas exists in the development of new materials and tools, and the investigation of new phenomena. The advances in physical sciences offer materials useful in cell and molecular biology, and provide tools for characterizing cells and sub-cellular components; meanwhile the progress in biology provides a window for researchers to understand the most sophisticated functional nanostructures that have ever existed (Whitesides 2003).

1.1.2 Nanoscience

Nanoscience investigates those objects whose smallest dimensions range from several nanometers up to 100 nanometers (Royal Society and Royal Academy of Engineering 2004; Poole and Ownes 2003). As nanoscale may be the final engineering scale people have yet to master, nanoscience is regarded as a launch pad to a new technological era by many scientists and engineers (National Science and Technology Council 1999a).

Due mainly to the following two reasons, nanomaterials exhibit properties that are quite different from those of materials at large scales (Royal Society and Royal Academy of Engineering 2004; National Science and Technology Council 1999b). First, the surface areas of nanomaterials are much larger than those of the materials with the same mass but in a larger form. A larger surface area usually results in more reactive chemical properties, and also affects the mechanical or electrical properties of the materials. Second, nanomaterials are the natural home of quantum effects. At the nanoscale, quantum effects dominate the behaviors of a material, affecting its optical, electrical and magnetic properties.

1.1.2.1 Quantum Effect

To study the properties of the objects in the normal-sized realm, such as cars and houses, it is not usually necessary to use quantum mechanics, which is used by scientists to describe the properties of materials at the atom and electron levels. However, researchers