Magnetic Nanoparticles in Biosensing and Medicine

Drawing together topics from a wide range of disciplines, this text provides a comprehensive insight into the fundamentals of magnetic biosensors and the applications of magnetic nanoparticles in medicine. Internationally renowned researchers showcase topics ranging from the basic physical principles of magnetism to the detection and manipulation, synthesis protocols, and natural occurrence of magnetic nanoparticles. Up-to-date examples of their clinical use and research applications in the biomedical fields of sensing by diverse magnetic detection methods, in imaging by MRI, and in therapeutic strategies, such as hyperthermia, are also discussed, providing a thorough introduction to this rapidly developing field. Each chapter features questions, with answers available on the online resources page, key equations and definitions, and numerous illustrations to help readers grasp key concepts. Mathematical tools, together with key literature references, provide a strong underpinning for the material, making it ideal for graduate students, lecturers, medical researchers, and industrial scientific strategists.

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Preface

The last decade has seen dramatic growth in research on applications of magnetic nanoparticles. New avenues of investigation have been developed, such as magnetic actuation and the use of magnetic particles for MRI drug delivery. Furthermore, magnetic nanoparticle-based point-of-care diagnostic systems for the detection of substances ranging from cardiac infarction markers to narcotics have been released to market. International conferences on magnetism and solid-state physics, such as the IEEE International Magnetics Conference (Intermag) and Conference on Magnetism and Magnetic Materials (MMM), have increasingly included sessions solely dedicated to research on magnetic nanoparticles and their applications in life sciences. Concurrently, international conferences in life sciences are also hosting sessions to discuss this research.

As a result of the proliferation of interest in magnetic nanoparticles in so many areas, there is a need for a handbook to be compiled to act as an interdisciplinary lexicon. The goal of this monograph is to provide a first point of reference for the design, synthesis, and application of magnetic nanoparticles in biosensing and medicine, not only for newcomers to this field, but also established scientists looking for potentially new applications of their research.

The eight chapters in this book aim to cover the diverse range of disciplines that together define biomedical applications of magnetic nanoparticles. In Chapter 1, the theory of magnetism, and the properties of magnetic materials and nanoparticles is presented (Ionescu, Llandro, and Ziebeck). This chapter provides an introduction to the origin of magnetism in transition metals and the fundamental magnetic properties exhibited by magnetic nanoparticles that define their behavior in applied magnetic fields.

In Chapter 2, the synthesis of magnetic nanoparticles is described (Tartaj, Veintemillas-Verdaguer, Gonzalez-Carreño, and Serna). In this chapter, a detailed practical guide is given on the best synthesis strategies for making magnetic nanoparticles. The relative advantages and disadvantages of each synthesis strategy are examined to enable the correct selection for the desired application.

In Chapter 3 on magnetic nanoparticle functionalization (Palfreyman), a comprehensive guide to coating and functionalizing magnetic nanoparticles for biomedical applications is provided. Issues that are addressed in this chapter include the advantages and disadvantages of different chemical functionalization strategies, and detailed approaches to quantify the extent of surface coating and loading of ligands on nanoparticles.

In Chapter 4 on manipulating magnetic nanoparticles (Fan, Chien, Schneider, and Hafeli), the application of nanoparticles in targeted medicine is reviewed. These applications include the control of magnetic nanoparticles for the targeted delivery of therapeutics to sites of disease and magnetic hyperthermia. Different approaches to nanoparticle manipulation are presented to provide an approach for future precision control of nanoparticles in medical applications.

Chapter 5 is on modeling the capture of magnetic nanoparticles from flow (Hallmark, Darton, and Pearce). In this chapter, a method of developing a robust model for predicting magnetic nanoparticle behavior in applied magnetic fields in the body is presented. This model offers a method for optimizing magnetic targeting of nanoparticle-linked therapeutics, and highlights the key physical properties of magnetic nanoparticles and their environment that affect targeting.

In Chapter 6, sensing of magnetic nanoparticles by diverse magnetic sensors is described (Sandhu, Southern, S. Cardoso, Knudde, F. A. Cardoso, Freitas, and Kurlyandskaya). This chapter details the underlying physical principles that affect the detection and imaging of magnetic nanoparticles in a number of biomedical sensing applications. It provides insights into how magnetic nanoparticle sensing systems may be developed to provide the most sensitive diagnostic approaches available for potentially revolutionary advances in medical science.

In Chapter 7, the design of nanoparticles for contrast agents in MRI (Lee and Hyeon) is investigated. In this chapter the optimal properties of magnetic nanoparticles for application in the medical imaging area of MRI are described. Different magnetic nanoparticle compositions and coatings are compared to provide a clear guide on material selection for obtaining the best contrast agents.

In Chapter 8, magnetotactic bacteria are reviewed (Bazylinski and Trubitsyn). In this chapter, the occurrence of magnetic nanoparticles in nature and how these biological systems are able to produce endogenous magnetic nanoparticles are investigated. The harnessing of these systems is discussed to provide a scalable and low-cost approach to yield biomagnetic nanoparticles with tailored magnetic properties for biomedical applications.

We believe that the collaboration and exchange of ideas driving the interdisciplinary field of magnetic nanoparticle research that we have outlined in this book will help to provide the next generation of diagnostics and treatment strategies for improved medical care in the future.

Abbreviations

a	Real-space lattice parameter
a_0	Bohr radius
AFM	Atomic force microscopy
AF	Antiferromagnetic
AMR	Anisotropic magnetoresistance
AP	Antiparallel
α	Demagnetization factor (-)
α	Magnet-to-vessel distance
α_H	Modified Hooge parameter
$\boldsymbol{B}$	Magnetic flux (T)
$\lvert\boldsymbol{B}\rvert$	Absolute magnetic flux (T)
β_{di}	Integral width
B_{hf}	Magnetic hyperfine field
B_J	Brillouin function
C	Curie constant
CDF	Cation diffusion facilitator
CLIO	Cross-linked iron oxide nanoparticle
CMOS	Complementary metal oxide semiconductor
CNT	Carbon nanotube
CT	Computed tomography
ChT	Chemotherapy
CIP	Current in plane
COC	Cyclo olefin copolymer
CPP	Current perpendicular to plane
χ	Susceptibility
χ_{eff}	Effective magnetic susceptibility
χ_{Landau}	Landau susceptibility
χ_{Larmor}	Larmor diamagnetic susceptibility
χ_v	Volume susceptibility (-)
χ_{VV}	Susceptibility arising from Van Vleck paramagnetism
χ_o^p	Pauli susceptibility
D	Hydrodynamic drag (N)
d	Diameter

Da	Dalton, measure of molecular mass (1 Da = 1.6605×10^{-27} kg)
DEP	Dielectrophoretic force
DIC	Diisopropylcarbodiimide
DMF	Dimethylformamide
DMSA	Dimercaptosuccinic acid
DNA	Deoxyribonucleic acid
DOPA	3,4,-dihydroxyl-L-phenylalanine
DOTA	1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid
DUV	Deep ultraviolet
DSPE	1,2-distearoyl-sn-glycero-3-phosphoethanolamine
DTPA	Diethylene triamine pentaacetic acid
dts	Double-triangular shaped (anisotropic crystals)
D_V	Volume-weighted domain size
$\boldsymbol{E}$	Electric field
e	1.6021765×10^{-19} C, the unit charge for the carrier i.e. an electron
E_B	Energy barrier
EDC	1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride
E_{dip}	Dipole-dipole energy
EEW	Electric explosion of wire
E_F	Fermi energy
EGF	Epidermal growth factor
emu	Electromagnetic unit
E_n	Energy of the *n*th electron shell
EPR	Enhanced permeation and retention
ESION	Extremely small iron oxide nanoparticles < 4 nm in size
E_{strain}	Magnetostriction energy
ε	Adhesion energy (m^2 kg/s^2)
ε_m	Permittivity of the medium
ε_0	Permittivity of free space
η	Viscosity (Pa s)
η_K	Kerr ellipticity
$\boldsymbol{F}$	Force
Fab	Fragment antigen-binding (region)
FC	Field cooled
Fc	Fragment crystallizable (region)
FDA	Food and Drug Administration
F_{grad}	Gradient force
$\boldsymbol{F}_h$	Shear force (N)
FION	Ferrimagnetic iron oxide nanoparticle
$\boldsymbol{F}_m$	Magnetic force (N)
FM	Ferromagnetic
Fmoc	Fluorenylmethyloxycarbonyl
$\boldsymbol{F}_r$	Resultant force acting on an immobilized nanoparticle (N)

F_{scat}	Scattering force
Fur	Ferric uptake regulator
$\boldsymbol{F_v}$	Volumetric body force term in the Navier–Stokes equations (N/m^3)
FWHM	Full width at half the maximum intensity
ϕ	Volume fraction of nanoparticles in suspension (-)
ϕ_m	Nanoparticle packing fraction (-)
$\boldsymbol{\Phi}_K$	Kerr effect
φ_K	Kerr rotation
G	Modulus of rigidity
G_f	Thermodynamic potential (free energy)
G	Pair distribution function
GC	Graphitic carbon
$\boldsymbol{g}$	Gravitational acceleration vector (m/s^2)
g_J	Landé g-factor
GMI	Giant magnetoimpedance
GMR	Giant magnetoresistance
g_s	Electron spin g-factor (approximately 2.002319)
γ	Phenomenological Hooge's parameter that quantifies the magnitude of noise for a certain device
γ	Electron gyromagnetic ratio: the ratio between the magnetic dipole moment and angular momentum of the free electron
$\boldsymbol{H}$	Magnetic field (A/m)
$\lvert\boldsymbol{H}\rvert$	Absolute magnetic field (A/m)
$\widehat{H}$	Hamiltonian of the system
h	Planck's constant
H_{ac}	Alternating drive field
H_{b}	Nanoparticle fringe field
H_c	Coercive field
H_{dc}	Time invariant dc magnetic field
H_{exch}	Exchange coupling field
H_{ext}	External field
H_{f}	Magnetostatic coupling
HGMS	High-gradient magnetic separation
HGT	Horizontal gene transfer
H_{int}	Internal field
H_{J}	Sense current field
H_{k}	Anisotropy field
H_{keff}	Effective anisotropy field
$\hbar\ell$	Orbital angular momentum
H_{N}	Néel coupling
HOBt	Hydroxybenzotriazole
HPG	Hyperbranched polyglycerol
$\hbar\mathbf{s}$	Electron's intrinsic angular momentum or spin

H_{sw}^0	Switching field at 0 K
IDT	Interdigital transducers
InSb	Indium antimonide
ITO	Indium tin oxide
J_{ij}^{ex}	Exchange constant between two spins $\boldsymbol{s}_i$ and $\boldsymbol{s}_j$
K_L	Kendal fitting parameter
K	Clausius–Mossotti factor
K_1	Cubic anisotropy constant
$\mathrm{k_B}$	Boltzmann constant (= 1.3806×10^{-23} $\mathrm{m^2\ kg/(s\ K)}$)
k	Crystal wavevector
k_P	Power law fluid consistency index (Pa $\mathrm{s^{(n+1)}}$)
K_u	Uniaxial anisotropy
κ	Magnetic softness (-)
L	Capillary length (m)
LDH	Lactate dehydrogenase
LLG	Landau–Lifshitz–Gilbert equation
LOR	Lift-off resist
LSP	Localized surface plasmon
λ_s	Saturation magnetostriction
M	Magnetization
$\boldsymbol{m}$	Magnetic dipole vector (A $\mathrm{m^2}$)
m	Number of Bohr magnetons per particle
MAI	Magnetosome island
MAR	Motional averaging regime
MBE	Molecular beam epitaxy
MDC	Magnetic drug carrier
m_e	Mass of an electron
MEMS	Microelectromechanical systems
MeOx	Metal oxide
MFH	Malignant fibrous histiocytoma
MFM	Magnetic force microscopy
MHC II	Class II major histocompatibility complex
MI	Magnetoimpedance
MMP	Multicellular magnetotactic prokaryotes
MOKE	Magneto-optical Kerr effect
MOF	Metal-organic framework
MR	Magnetoresistive
MRI	Magnetic resonance imaging
MWCNT	Multiwall carbon nanotube
MNP	Magnetic nanoparticles
M_R	Remanence: remanent magnetization after saturation in the absence of any applied field
MRAM	Magnetic random-access memory

MRS	Magnetic relaxation switch
MSC	Mesenchymal stem cells
MSN	Mesoporous silica nanoparticle
M_{sat}	Maximum moment
M_s	Saturation magnetization (A/m)
MTJ	Magnetic tunnel junction
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
M_{ZFC}	Zero-field cooled magnetization
μ	Magnetic permeability
μ_0	Vacuum permeability (T m/A)
μ_B	Bohr magneton
μ_{eff}	Effective paramagnetic moment
$\bar{\mu}_k$	Mean of the Gaussian distribution
μ_r	Relative permeability
n	Power law index (-)
NdFeB	Neodymium iron boron
NEMS	Nanoelectromechanical systems
NHS	N-hydroxysuccinimide
NLM	National Library of Medicine
NM	Non-magnetic
N_A	Avogadro's constant 6.02×10^{23} mol^{-1}
$N_{\uparrow}^{1}$	Spin up electron density of state
n_b	Index of the medium
N_c	Number of carriers in current I
n_h	Number of vacancies in the valence band
NMR	Nuclear magnetic resonance
NP	Nanoparticles
NSF	Nephrogenic systemic fibrosis
OAI	Oxic-anoxic interface
OATZ	Oxic-anoxic transition zone
OGMS	Open-gradient magnetic separation
Ω	Angular velocity
ω_0	Attempt frequency
P	Spin polarization of the FM electrodes
p	Pressure (Pa)
p	Crystal momentum
ΔP	Pressure drop (Pa)
PCC	Pyridinium chlorochromate
PCR	Polymerase chain reaction
PDMS	Polydimethylsiloxane
PEEM	Photoemission electron microscopy
PET	Positron emission tomography
PEG	Polyethylene glycol
PEI	Polyethylenimine

PL-PEG	Phospholipid-poly(ethylene glycol)
PMA	Perpendicular magnetic anisotropy
PMMA	Poly(methyl methacrylate)
PNBP	P-nitrobenzyl pyridine
PS	Polystyrene
PSA	Polysialic acids
PTX	Paclitaxel
PVC	*Planctomycetes-Verrucomicrobia-Chlamydiae*
ψ	Wavefunction
Q	Fluid volumetric flow rate (m^3/s)
q	Charge
R	Capillary radius (m)
R	Resistance
r	Radial coordinate (m)
r_a	Nanoparticle aggregate radius (m)
r_p	Nanoparticle radius (m)
Re	Reynolds number
Re(K)	Real part of the Clausius–Mossotti factor K
RES	Reticuloendothelial system
RF	Radio-frequency
RHT	Regional hyperthermia
RKKY	Ruderman–Kittel–Kasuya–Yosida
RNA	Ribonucleic acid
RT	Radiotherapy
ρ	Density (kg/m^3)
S	Magnetic viscosity
SAM	Self-assembled monolayers
SAR	Specific absorption rate
SAW	Standing acoustic wave
SCID	Severe combined immunodeficiency
SDR	Static dephasing regime
SELEX	Systematic evolution of ligands by exponential enrichment
SEM	Scanning electron microscope
SERS	Surface-enhanced Raman scattering
SIBA	Self-induced back-action
S_M	Isobaric-isothermal magnetic entropy
SNR	Signal-to-noise
SPECT	Single photon emission computed tomography
SPION	Superparamagnetic iron oxide nanoparticle
SPB	Superparamagnetic beads
SPP	Surface plasmon polariton
$\boldsymbol{S}_r$	Atomic spin

ST	Soft tissue
SQUID	Superconducting quantum interference device
SV	Spin valve
σ	Standard deviation of the Gaussian distribution
T	Temperature (K)
T	Torque
t	Time (s)
T_B	Blocking temperature
T_{C}	Transition temperature
T_{E}	Echo time
TEM	Transmission electron microscopy
th	Thickness of immobilized MNP bed (m)
T_{ir}	Irreversibility temperature
T_{N}	Néel temperature
TMR	Tunnel magnetoresistance
TRM	Thermoremanent magnetization
TSHR	Thyroid-stimulating hormone receptor
TT	Thermotherapy
T_{tr}	Transition temperatures
$<T_Z>$	Expectation value of the dipole operator
τ	Relaxation time
τ_{mag}	Magnetic relaxation time
τ_N	"Néel" relaxation time
θ_c	Capture angle (degrees)
$\theta_{c,crit}$	Critical capture angle (degrees)
Θ_f	Free layer
Θ_p	Pinned layer
USPIO	Ultrasmall superparamagnetic iron oxide nanoparticles
UV	Ultraviolet
V	Voltage
v	Velocity (m/s)
V_c	Crystal field potential
$\bar{\upsilon}_f$	Average flow
V_H	Hall voltage
V_p	Particle volume (m^3)
VSM	Vibrating sample magnetometer
W	Electronic band width
WSIO	Water-soluble iron oxide
WSION	Water-soluble iron oxide nanoparticle
x	x-component
ξ	Coherence length
XANES	X-ray absorption near edge structure

XMCD	X-ray magnetic circular dichroism
y	y-component
Z	Total impedance of a ferromagnetic conductor
Z_i	Total number of electrons in the atom or ion
z	z-component
ZFC	Zero field cooled
ζ	Effective electric potential

Brackets indicate the SI unit of the parameter or if (-) the parameter is dimensionless.