

## Contents

Preface XVII

List of Contributors XIX

1 Introduction 1

1.1 The History of Magnetism in Medicine 3

*Urs Häfeli*

1.1.1 Origins 3

1.1.2 First Medical Uses of Magnets 4

1.1.3 Use of Attracting Forces of Magnets in Medicine 5

1.1.4 Treatment of Nervous Diseases and Mesmerism 10

1.1.5 Other Medical Uses of Magnets and Magnetism 13

1.1.6 The Influence of Magnetic Fields on Man 18

*References* 22

1.2 Basic Physical Principles 26

*Dmitri Berkov*

1.2.1 Introduction 26

1.2.2 The Electromagnetic Field Concept and Maxwell Equations 27

1.2.2.1 Maxwell Equations in a General Case of Time-Dependent Fields 27

1.2.2.2 Constant (Time-Independent) Fields: Electro- and Magnetostatics 29

1.2.2.3 Electric and Magnetic Potentials: Concept of a Dipole 30

1.2.2.4 Force, Torque and Energy in Magnetic Field 35

1.2.3 Magnetic Field in Condensed Matter: General Concepts 38

1.2.3.1 Maxwell Equations in Condensed Matter: Magnetization 38

1.2.3.2 Classification of Materials According to their Magnetic Properties 40

1.2.3.3 Mean Field Theory of Ferromagnetism 42

1.2.4 Magnetic Field in Condensed Matter: Special Topics 44

1.2.4.1 Magnetic Energy Contributions 44

1.2.4.2 Magnetic Domains and Domain Walls 51

1.2.4.3 Magnetization Curves and Hysteresis Loops 53

1.2.4.4	Single-Domain Particles and Superparamagnetism	56
1.2.4.5	Irreversible Magnetic Relaxation	59
1.2.4.6	Reconstruction of Magnetization Distribution Inside a Body from Magnetic Field Measurements	61
	Appendix	63
	References	64
<b>1.3</b>	<b>Creating and Measuring Magnetic Fields</b>	<b>65</b>
	<i>Wilfried Andrä and Hannes Nowak</i>	
1.3.1	Introduction	65
1.3.2	The Generation of Magnetic Fields	65
1.3.3	The Measurement of Magnetic Fields	70
1.3.4	Discussion	74
	References	74
<b>1.4</b>	<b>Safety Aspects of Magnetic Fields</b>	<b>76</b>
	<i>Jürgen H. Bernhardt and Gunnar Brix</i>	
1.4.1	Introduction	76
1.4.2	Risk Evaluation and Guidance on Protection	76
1.4.2.1	Evaluation Process	77
1.4.2.2	Development of Guidance on Protection	77
1.4.3	Static and Extremely Slowly Time-Varying Magnetic Fields	78
1.4.3.1	Interaction Mechanisms and Biological Bases for Limiting Exposure	78
1.4.3.2	Epidemiology	80
1.4.3.3	Safety Aspects and Exposure Levels	81
1.4.4	Time-Varying Magnetic Fields	81
1.4.4.1	Interaction Mechanisms and Biological Bases for Limiting Exposure	81
1.4.4.2	Epidemiology	83
1.4.4.3	Safety Aspects and Exposure Levels	84
1.4.5	Electromagnetic Fields	84
1.4.5.1	Interaction Mechanisms and Biological Bases for Limiting Exposure	84
1.4.5.2	Epidemiology	88
1.4.5.3	Safety Aspects and Exposure Limits	89
1.4.6	Protection of Patients and Volunteers Undergoing MR Procedures	89
1.4.6.1	Static Magnetic Fields	90
1.4.6.2	Time-Varying Magnetic Gradient Fields	90
1.4.6.3	Radiofrequency Electromagnetic Fields	91
1.4.6.4	Contraindications	93
	References	94

<b>2</b>	<b>Biomagnetism</b>	97
<b>2.1</b>	<b>Introduction</b>	99
	<i>Hannes Nowak</i>	
<b>2.2</b>	<b>Biomagnetic Instrumentation</b>	101
	<i>Hannes Nowak</i>	
2.2.1	History	101
2.2.2	Biomagnetic Fields	102
2.2.3	SQUID Sensor	104
2.2.4	Shielding: Magnetically and Electrically Shielded Rooms	109
2.2.5	Gradiometers	113
2.2.6	Dewar/Cryostat	116
2.2.7	Commercial Biomagnetic Measurement Devices	117
2.2.7.1	4-D Neuroimaging	118
2.2.7.2	VSM MedTech Ltd.	126
2.2.7.3	Elekta Neuromag®	132
2.2.7.4	Advanced Technologies Biomagnetics (AtB) s.r.l.	139
2.2.7.5	CardioMag Imaging™	142
2.2.7.6	Tristan Technologies, Inc.	144
2.2.7.7	Philips Research, Hamburg	146
2.2.8	Special Biomagnetic Measurement Devices	148
2.2.8.1	Micro-SQUID Systems	148
2.2.8.2	The Jena 16-Channel Micro-SQUID Device	149
2.2.8.3	Planar Gradiometers	149
2.2.8.4	Japanese 256-Channel Device (SSL-Project)	151
2.2.8.5	Vector-Magnetometers	151
2.2.8.6	Biomagnetic Devices with Cryocooler	152
2.2.9	High-Temperature Superconductivity	152
2.2.10	Perspectives	154
	<i>References</i>	155
<b>2.3</b>	<b>Cardiomagnetism</b>	164
	<i>Gerhard Stroink, Birgit Hailer, and Peter Van Leeuwen</i>	
2.3.1	Introduction	164
2.3.1.1	Historical Background	164
2.3.1.2	Electrophysiology	165
2.3.2	Forward Solutions	167
2.3.2.1	Introduction	167
2.3.2.2	Single Current Dipole in an Infinite Homogeneous Conductive Medium	167
2.3.2.3	Current Dipole in a Realistic Torso	170
2.3.2.4	Extended Source Models	172
2.3.2.5	Summary	175

2.3.3	Inverse Solutions	175
2.3.3.1	Introduction	175
2.3.3.2	Model Data Using the Current Dipole as Source Model	176
2.3.3.3	Model Data Using Distributed Sources as Source Model: Imaging	178
2.3.3.4	Summary	179
2.3.4	Validation	180
2.3.5	Clinical Applications of Magnetocardiography	183
2.3.6	Ischemic Heart Disease	183
2.3.6.1	Analysis of MCG Signal Morphology	184
2.3.6.2	Determination of Time Intervals	185
2.3.6.3	Parameters of the Magnetic Field	186
2.3.6.4	Source Parameters	189
2.3.6.5	Conclusion	191
2.3.7	Hypertensive Cardiovascular Disease	191
2.3.7.1	Conclusion	193
2.3.8	Cardiomyopathy	193
2.3.8.1	Conclusion	194
2.3.9	Cardiac Arrhythmias	194
2.3.9.1	Atrial Arrhythmias	195
2.3.9.2	Ventricular Pre-Excitation	196
2.3.9.3	Ventricular Arrhythmias	197
2.3.9.4	Risk Stratification for Malignant Arrhythmias After MI	198
2.3.9.5	Conclusion	200
2.3.10	Clinical Conclusions	200
	<i>References</i>	201
<b>2.4</b>	<b>Neuromagnetism</b>	210
	<i>Thomas R. Knösche, Nobukazu Nakasato, Michael Eiselt, and Jens Haueisen</i>	
2.4.1	Introduction	210
2.4.2	The Generation of Magnetic Signals by the Brain	211
2.4.2.1	Introduction	211
2.4.2.2	Technical Development and Limits of Detection	211
2.4.2.3	Electrophysiology of Brain Cells	212
2.4.2.4	Extracellular Space	215
2.4.2.5	Pathophysiology	216
2.4.2.6	Final Remarks	217
2.4.3	Analysis of Neuromagnetic Fields	218
2.4.3.1	Signal Analysis	218
2.4.3.2	Modeling and Source Reconstruction	222
2.4.4	The Investigation of the Primary Sensory and Motor Systems	230
2.4.4.1	Introduction	230
2.4.4.2	Somatosensory System	230

2.4.4.3	Auditory System	232
2.4.4.4	Visual System	232
2.4.4.5	Olfactory and Gustatory System	234
2.4.4.6	Motor System	235
2.4.4.7	Perspectives	235
2.4.5	Neuromagnetic Fields and Brain Science: Cognitive Functions	235
2.4.5.1	Brain Correlates of Cognition: Components and Localizations	237
2.4.5.2	Human Communication	238
2.4.5.3	Recognition of Objects: Perceptual Binding	241
2.4.5.4	Actions: Planning, Execution, Perception, and Imagery	242
2.4.5.5	Attention	242
2.4.5.6	Memory	243
2.4.5.7	Emotions	244
2.4.6	Clinical Applications	244
2.4.6.1	Introduction	244
2.4.6.2	Somatosensory Evoked Fields (SEFs)	244
2.4.6.3	Auditory Evoked Fields (AEFs)	247
2.4.6.4	Visually Evoked Magnetic Fields (VEFs)	249
2.4.6.5	Language-Related Fields (LRFs)	251
2.4.6.6	Spontaneous Brain Activity in Epilepsy	251
2.4.6.7	Spontaneous Brain Activity in Structural Brain Lesions and Ischemia	255
2.4.6.8	Perspectives	256
	<i>References</i>	256
<b>2.5</b>	<b>Fetal Magnetography</b>	<b>268</b>
	<i>Uwe Schneider and Ekkehard Schleussner</i>	
2.5.1	Fetal Magnetocardiography	268
2.5.1.1	General	268
2.5.1.2	Fetal Cardiac Physiology	268
2.5.1.3	Methodical Approaches	269
2.5.1.4	Standards and International Reference Values	273
2.5.1.5	Monitoring Fetal Cardiac Function: A Brief Comparison of Methods	274
2.5.1.6	Complementary Role in Clinical Diagnosis	274
2.5.1.7	Clinical Research	276
2.5.1.8	Perspectives	277
2.5.2	Fetal Magnetoencephalography	279
2.5.2.1	General Aspects	279
2.5.2.2	Development of Senses	281
2.5.2.3	Applications of fMEG	282
2.5.2.4	Developmental Aspects of Fetal Evoked Responses	283
2.5.2.5	Perspectives	285
	<i>References</i>	286

<b>3</b>	<b>Magnetic Resonance</b>	<b>291</b>
<b>3.1</b>	<b>Introduction</b>	<b>293</b>
	<i>Werner A. Kaiser</i>	
<b>3.2</b>	<b>Physical Principles and Technology of Magnetic Resonance Imaging</b>	<b>297</b>
	<i>Arnulf Oppelt</i>	
3.2.1	Historical Overview	297
3.2.2	Basic Physical Principles of NMR	298
3.2.3	The NMR Signal	301
3.2.4	Nuclear Relaxation	306
3.2.5	Signal-to-Noise Ratio	309
3.2.6	Magnetic Resonance Imaging	311
3.2.7	Selective Excitation	314
3.2.8	Partial Acquisition Techniques	317
3.2.9	Pulse Sequence and Contrast	318
3.2.10	Imaging of Flow	324
3.2.11	Diffusion Imaging	326
3.2.12	MR Spectroscopy	327
3.2.13	System Design Considerations	329
3.2.14	Magnets	331
3.2.15	Shimming	334
3.2.16	Gradient System	335
3.2.17	RF-System	336
3.2.18	Conclusions	339
	<i>References</i>	<i>340</i>
<b>3.3</b>	<b>Modern Applications of MRI in Medical Sciences</b>	<b>343</b>
3.3.1	New MRI Techniques for Cardiovascular Imaging	343
	<i>Debiao Li and Andrew C. Larson</i>	
3.3.1.1	Introduction	343
3.3.1.2	Cardiovascular Morphology	343
3.3.1.3	Cardiac Function and Flow	344
3.3.1.4	Perfusion	349
3.3.1.5	Delayed-Enhancement Imaging	351
3.3.1.6	Coronary MR Angiography	352
3.3.1.7	Coronary Artery Wall Imaging	357
	<i>References</i>	<i>359</i>
3.3.2	Functional Magnetic Resonance Imaging (fMRI)	362
	<i>Oliver Speck, Axel Schreiber, Clemens Janz, and Jürgen Hennig</i>	
3.3.2.1	Physiological and Physical Basis	362
3.3.2.2	Methods for fMRI	363
3.3.2.3	The fMRI Experiment	364

- 3.3.2.4 Data Analysis 365
- 3.3.2.5 Current Results in fMRI 368
- 3.3.2.6 Perspectives 374
- References* 374
  
- 3.3.3 New MRI Techniques for the Detection of Acute Cerebral Ischemia 378  
*Michael E. Moseley, Roland Bammer, and Joachim Röther*
- 3.3.3.1 Introduction 378
- 3.3.3.2 Evolution of DWI Changes in Stroke 379
- 3.3.3.3 DWI in Clinical Practice 381
- 3.3.3.4 Improvements and Pulse Sequences for DWI and DTI 383
- 3.3.3.5 Functional DWI in Brain Mapping 392
- 3.3.3.6 Conclusion and Future Outlook 393
- References* 393
  
- 3.3.4 Clinical Applications at Ultrahigh Fields 398  
*Petra Schmalbrock and Donald W. Chakeres*
- 3.3.4.1 Potential and Challenges with Ultrahigh Field MRI 398
- 3.3.4.2 Image Characteristics in Normal Brain 402
- 3.3.4.3 Applications for Neuropathology 406
- 3.3.4.4 Conclusion and Outlook 410
- References* 411
  
- 3.3.5 Interventional Magnetic Resonance Imaging: Concepts, Systems, and Applications 416  
*Clifford R. Weiss and Jonathan S. Lewin*
- 3.3.5.1 Introduction 416
- 3.3.5.2 Imaging System Development 417
- 3.3.5.3 Supplemental Technical Developments 420
- 3.3.5.4 Specific Applications 423
- 3.3.5.5 Conclusions and Outlook 433
- References* 434
  
- 3.3.6 New Approaches in Diagnostic and Therapeutic MR Mammography 437  
*Werner A. Kaiser, Stefan O.R. Pfeleiderer, Karl-Heinz Herrmann, and Jürgen R. Reichenbach*
- 3.3.6.1 Introduction 437
- 3.3.6.2 Diagnostic MR Mammography 438
- 3.3.6.3 Current Limits and Disadvantages 441
- 3.3.6.4 New Approaches to Diagnostic MR Mammography 442
- 3.3.6.5 Minimally Invasive Procedures: Biopsy and Therapy 445
- 3.3.6.6 MRI-Guided Percutaneous Minimally Invasive Therapy of Breast Lesions 447

3.3.6.7	New Perspectives	449
3.3.6.8	Conclusion	450
	References	451
3.3.7	MR Spectroscopy	456
	<i>Peter Bachert</i>	
3.3.7.1	Introduction	456
3.3.7.2	High-Resolution Nuclear Magnetic Resonance Spectroscopy <i>In Vivo</i>	456
3.3.7.3	Metabolic Information and Clinical Application: <i>In-Vivo</i> $^1\text{H}$ MRS	460
3.3.7.4	Metabolic Information and Clinical Application: <i>In-Vivo</i> $^{13}\text{C}$ MRS	469
3.3.7.5	Metabolic Information and Clinical Application: <i>In-Vivo</i> $^{19}\text{F}$ MRS	469
3.3.7.6	Metabolic Information and Clinical Application: <i>In-Vivo</i> $^{31}\text{P}$ MRS	471
3.3.7.7	Application of MRS in Diagnostics and Clinical Research: Conclusions and Perspectives	472
	References	474
4	<b>Magnetic Substances and Externally Applied Fields</b>	477
4.1	<b>Introduction</b>	479
	<i>Wilfried Andrä</i>	
	References	480
4.2	<b>Magnetic Monitoring as a Diagnostic Method for Investigating Motility in the Human Digestive System</b>	481
	<i>Hendryk Richert, Olaf Kosch, and Peter Görnert</i>	
4.2.1	Introduction	481
4.2.2	Conventional Investigation Methods of the Human GI Tract	482
4.2.3	Magnetic Markers	483
4.2.3.1	Inverse Monitoring	484
4.2.3.2	Theoretical Background	484
4.2.3.3	Forward Monitoring	485
4.2.4	Magnetic Monitoring Systems	486
4.2.4.1	Magnetic Monitoring with Three Magnetic Sensors	486
4.2.4.2	Magnetic Marker Monitoring Using Biomagnetic SQUID Measurement System	487
4.2.4.3	Magnetic Monitoring with Multiple AMR-Sensors	488
4.2.4.4	Comparison of the Measuring Methods	489
4.2.4.5	Information Content of Magnetic Monitoring Investigations	490
4.2.4.6	Motility Pattern of the GI System	491
4.2.4.7	Absorption Processes Inside the GI Tract	493
4.2.5	Conclusion and Outlook	494
	References	496



- 4.3 Remote-Controlled Drug Delivery in the Gastrointestinal Tract 499**  
*Wilfried Andrä and Christoph Werner*
- 4.3.1 Introduction 499
- 4.3.2 Physical Principles Used or Proposed for Remote Controlled Release 500
- 4.3.2.1 Capsules Designed for Drug Release under the Guiding or Withholding Influence of a Magnetic Field 500
- 4.3.2.2 Capsules Using Mechanical Forces of Magnetic Fields to Open a Container 501
- 4.3.2.3 Capsule Operation Triggered by an Alternating (AC) Magnetic Field 501
- 4.3.2.4 Application of Rotating Magnetic Fields 503
- 4.3.3 Discussion and Outlook 504
- 4.3.3.1 Capsules already Used for Animal and Human Studies 504
- 4.3.3.2 Outlook 507
- References 508*
- 4.4 Magnetic Stimulation 511**  
*Shoogo Ueno and Minoru Fujiki*
- 4.4.1 Introduction 511
- 4.4.2 History 511
- 4.4.2.1 History of Magnetic Stimulation 511
- 4.4.2.2 The Beginnings of Magnetic Brain Stimulation 512
- 4.4.3 Principle of Transcranial Magnetic Stimulation 513
- 4.4.3.1 Vectorial and Localized Magnetic Stimulation: A Computer Simulation Study 513
- 4.4.3.2 Physiological Principle 516
- 4.4.3.3 Functional Mapping of the Human Motor Cortex 517
- 4.4.3.4 Inhibition–Excitation Balance 520
- 4.4.4 Clinical and Preclinical Application of TMS 521
- 4.4.4.1 Targeting Method 521
- 4.4.4.2 Representative Neurosurgical Case 522
- 4.4.4.3 Cellular–Molecular Level 523
- References 525*
- 4.5 Liver Iron Susceptometry 529**  
*Roland Fischer and David E. Farrell*
- 4.5.1 Introduction 529
- 4.5.2 Iron Metabolism and Iron Overload 529
- 4.5.3 Technical Developments of Biomagnetic Liver Susceptometry 531
- 4.5.3.1 DC-Field Low- $T_C$  SQUID Biosusceptometer 531
- 4.5.3.2 AC-Field SQUID Biosusceptometer 532
- 4.5.3.3 Room-Temperature Biosusceptometer 534
- 4.5.3.4 High- $T_C$  Biosusceptometer 534

- 4.5.4 Physical and Biochemical Basics 535
- 4.5.5 Magnetostatic Principles 537
- 4.5.6 Calibration and Validation 538
- 4.5.7 Magnetic Background and Noise Problems 540
- 4.5.8 Alternative Methods 541
- 4.5.9 Medical Applications 542
  - 4.5.9.1 Measurement Procedures 542
  - 4.5.9.2 Primary Hemochromatosis 542
  - 4.5.9.3 Iron-Deficiency Anemia 543
  - 4.5.9.4 Secondary Hemochromatosis 543
  - 4.5.9.5 Long-Term Iron Chelation 543
  - 4.5.9.6 Future Applications 544
- 4.5.10 Summary and Outlook 544
  - References* 545
  
- 4.6 Magnetic Hyperthermia and Thermoablation 550**  
*Rudolf Hergt and Wilfried Andrä*
  - 4.6.1 Introduction 550
  - 4.6.2 Physical Principles of Magnetic Particle Heating 551
    - 4.6.2.1 Losses during Magnetization Reversal within the Particles 552
    - 4.6.2.2 Losses Caused by Rotational Motion of Particles 554
    - 4.6.2.3 Thermal Relaxation Effects in Magnetic Nanoparticles 555
    - 4.6.2.4 Eddy Current Effects 558
  - 4.6.3 Physical-Technical Implementation of the Therapy 559
    - 4.6.3.1 Demand of Specific Heating Power 559
    - 4.6.3.2 Parameters of the Alternating Magnetic Field 561
    - 4.6.3.3 Optimization of the Magnetic Material 561
  - 4.6.4 Biomedical Status of Magnetic Particle Hyperthermia 564
    - 4.6.4.1 Studies with Animals and Cell Cultures 564
    - 4.6.4.2 Application to Human Patients 565
  - References* 567
  
- 4.7 Magnetic Cell Separation for Research and Clinical Applications 571**  
*Michael Apel, Uwe A.O. Heinlein, Stefan Miltenyi, Jürgen Schmitz, and John D.M. Campbell*
  - 4.7.1 Introduction 571
  - 4.7.2 MACS® Technology 572
    - 4.7.2.1 The Concept 572
    - 4.7.2.2 Magnetic Separation Strategies 572
    - 4.7.2.3 Magnetic Labeling Strategies and Reagents 574
    - 4.7.2.4 Superparamagnetic MicroBeads 575
    - 4.7.2.5 Column Technology and Research Separators 576
    - 4.7.2.6 CliniMACS® Plus Instrument, and Accessories 577

- 4.7.3 Magnetic Cell Sorting for Clinical Applications 580
  - 4.7.3.1 Stem Cell Enrichment for Graft Engineering in Hematological Disorders 580
  - 4.7.3.2 NK Cells: CD56 and CD3 583
  - 4.7.3.3 T-Cell Subset Graft Engineering Strategies 583
  - 4.7.3.4 Antigen-Specific T Cells: Cytokine Capture System 585
  - 4.7.3.5 Dendritic Cells (DC): CD14-derived DC, BDCA-1, BDCA-4 586
  - 4.7.3.6 Into the Future: Cardiac Regeneration Using CD133<sup>+</sup> Stem Cells 589
- References 591
  
- 4.8 Magnetic Drug Targeting 596**  
*Christoph Alexiou and Roland Jurgons*
  - 4.8.1 Background and History of Magnetic Drug Targeting 596
  - 4.8.2 Regional Chemotherapies for Cancer Treatment 598
  - 4.8.3 Current Applications of Magnetic Drug Targeting 599
    - 4.8.3.1 *In-Vitro* Studies 600
    - 4.8.3.2 *In-Vivo* Studies 600
  - 4.8.4 Outlook 602
- References 602
  
- 4.9 New Fields of Application 606**  
*Wilfried Andrä and Urs Häfeli*
  - 4.9.1 Introduction 606
  - 4.9.2 Magnetic Particle Imaging (MPI) 606
  - 4.9.3 Magnetically Modulated Optical Nanoprobes 608
  - 4.9.4 Magnetic Guidance 608
    - 4.9.4.1 Small Particles Guided by Extracorporeally Generated Field Gradients 609
    - 4.9.4.2 Field Gradients Generated by Magnetic Implants 610
    - 4.9.4.3 Magnetic Devices Moved by Alternating or Rotating Magnetic Fields 610
- References 611
  
- 5 Conclusions and Perspectives 613**  
*Jens Haueisen*
  
- Index 617**