CONTENTS

Preface xv
Contributors xvii

1 Evaluation of Spectroscopic Images 1
Patrick W.T. Krooshof, Geert J. Postma, Willem J. Melssen, and Lutgarde M.C. Buydens

1.1 Introduction, 1

1.2 Data Analysis, 2
   1.2.1 Similarity Measures, 3
   1.2.2 Unsupervised Pattern Recognition, 4
       1.2.2.1 Partitional Clustering, 4
       1.2.2.2 Hierarchical Clustering, 6
       1.2.2.3 Density-Based Clustering, 7
   1.2.3 Supervised Pattern Recognition, 9
       1.2.3.1 Probability of Class Membership, 9

1.3 Applications, 11
   1.3.1 Brain Tumor Diagnosis, 11
   1.3.2 MRS Data Processing, 12
       1.3.2.1 Removing MRS Artifacts, 12
       1.3.2.2 MRS Data Quantitation, 13
   1.3.3 MRI Data Processing, 14
       1.3.3.1 Image Registration, 15
   1.3.4 Combining MRI and MRS Data, 16
1.3.4.1 Reference Data Set, 16
1.3.5 Probability of Class Memberships, 17
1.3.6 Class Membership of Individual Voxels, 18
1.3.7 Classification of Individual Voxels, 20
1.3.8 Clustering into Segments, 22
1.3.9 Classification of Segments, 23
1.3.10 Future Directions, 24

References, 25

2 Evaluation of Tomographic Data 30
Jörg van den Hoff

2.1 Introduction, 30
2.2 Image Reconstruction, 33
2.3 Image Data Representation: Pixel Size and Image Resolution, 34
2.4 Consequences of Limited Spatial Resolution, 39
2.5 Tomographic Data Evaluation: Tasks, 46
  2.5.1 Software Tools, 46
  2.5.2 Data Access, 47
  2.5.3 Image Processing, 47
    2.5.3.1 Slice Averaging, 48
    2.5.3.2 Image Smoothing, 48
    2.5.3.3 Coregistration and Resampling, 51
  2.5.4 Visualization, 52
    2.5.4.1 Maximum Intensity Projection (MIP), 52
    2.5.4.2 Volume Rendering and Segmentation, 54
  2.5.5 Dynamic Tomographic Data, 56
    2.5.5.1 Parametric Imaging, 57
    2.5.5.2 Compartment Modeling of Tomographic Data, 57

2.6 Summary, 61

References, 61

3 X-Ray Imaging 63
Volker Hietschold

3.1 Basics, 63
  3.1.1 History, 63
  3.1.2 Basic Physics, 64

3.2 Instrumentation, 66
  3.2.1 Components, 66
    3.2.1.1 Beam Generation, 66
CONTENTS

3.2.1.2 Reduction of Scattered Radiation, 67
3.2.1.3 Image Detection, 69

3.3 Clinical Applications, 76
3.3.1 Diagnostic Devices, 76
    3.3.1.1 Projection Radiography, 76
    3.3.1.2 Mammography, 78
    3.3.1.3 Fluoroscopy, 81
    3.3.1.4 Angiography, 82
    3.3.1.5 Portable Devices, 84
3.3.2 High Voltage and Image Quality, 85
3.3.3 Tomography/Tomosynthesis, 87
3.3.4 Dual Energy Imaging, 87
3.3.5 Computer Applications, 88
3.3.6 Interventional Radiology, 92

3.4 Radiation Exposure to Patients and Employees, 92

References, 95

4 Computed Tomography
Stefan Ulzheimer and Thomas Flohr

4.1 Basics, 97
    4.1.1 History, 97
    4.1.2 Basic Physics and Image Reconstruction, 100

4.2 Instrumentation, 102
    4.2.1 Gantry, 102
    4.2.2 X-ray Tube and Generator, 103
    4.2.3 MDCT Detector Design and Slice Collimation, 103
    4.2.4 Data Rates and Data Transmission, 107
    4.2.5 Dual Source CT, 107

4.3 Measurement Techniques, 109
    4.3.1 MDCT Sequential (Axial) Scanning, 109
    4.3.2 MDCT Spiral (Helical) Scanning, 109
    4.3.2.1 Pitch, 110
    4.3.2.2 Collimated and Effective Slice Width, 110
    4.3.2.3 Multislice Linear Interpolation and z-Filtering, 111
    4.3.2.4 Three-Dimensional Backprojection and Adaptive Multiple Plane Reconstruction (AMPR), 114
    4.3.2.5 Double z-Sampling, 114
    4.3.3 ECG-Triggered and ECG-Gated Cardiovascular CT, 115
    4.3.3.1 Principles of ECG-Triggering and ECG-Gating, 115
    4.3.3.2 ECG-Gated Single-Segment and Multisegment Reconstruction, 118
CONTENTS

5.12 Magnetic Resonance Spectroscopy, 161
  5.12.1 Single Voxel Spectroscopy, 163
  5.12.2 Spectroscopic Imaging, 163

5.13 MR Hardware, 164
  5.13.1 Magnets, 164
  5.13.2 Shimming, 167
  5.13.3 Rf Shielding, 168
  5.13.4 Gradient System, 168
  5.13.5 MR Electronics—The Console, 169
  5.13.6 Rf Coils, 170

5.14 MRI Safety, 171
  5.14.1 Magnet Safety, 171
  5.14.2 Gradient Safety, 173

5.15 Imaging Artefacts in MRI, 173
  5.15.1 High Field Effects, 174

5.16 Advanced MR Technology and Its Possible Future, 175

References, 175

6 Toward A 3D View of Cellular Architecture: Correlative Light Microscopy and Electron Tomography 180
Jack A. Valentijn, Linda F. van Driel, Karen A. Jansen, Karine M. Valentijn, and Abraham J. Koster

6.1 Introduction, 180

6.2 Historical Perspective, 181

6.3 Stains for CLEM, 182

6.4 Probes for CLEM, 183
  6.4.1 Probes to Detect Exogenous Proteins, 183
    6.4.1.1 Green Fluorescent Protein, 183
    6.4.1.2 Tetracysteine Tags, 186
    6.4.1.3 Theme Variations: Split GFP and GFP-4C, 187
  6.4.2 Probes to Detect Endogenous Proteins, 188
    6.4.2.1 Antifluorochrome Antibodies, 189
    6.4.2.2 Combined Fluorescent and Gold Probes, 189
    6.4.2.3 Quantum Dots, 190
    6.4.2.4 Dendrimers, 191
  6.4.3 Probes to Detect Nonproteinaceous Molecules, 192

6.5 CLEM Applications, 193
  6.5.1 Diagnostic Electron Microscopy, 193
  6.5.2 Ultrastructural Neuroanatomy, 194
7 Tracer Imaging 215

Rainer Hinz

7.1 Introduction, 215
7.2 Instrumentation, 216
  7.2.1 Radioisotope Production, 216
  7.2.2 Radiochemistry and Radiopharmacy, 219
  7.2.3 Imaging Devices, 220
  7.2.4 Peripheral Detectors and Bioanalysis, 225
7.3 Measurement Techniques, 228
  7.3.1 Tomographic Image Reconstruction, 228
  7.3.2 Quantification Methods, 229
    7.3.2.1 The Flow Model, 230
    7.3.2.2 The Irreversible Model for Deoxyglucose, 230
    7.3.2.3 The Neurorxceptor Binding Model, 233
7.4 Applications, 234
  7.4.1 Neuroscience, 234
    7.4.1.1 Cerebral Blood Flow, 234
    7.4.1.2 Neurotransmitter Systems, 235
    7.4.1.3 Metabolic and Other Processes, 238
  7.4.2 Cardiology, 240
  7.4.3 Oncology, 240
    7.4.3.1 Angiogenesis, 240
    7.4.3.2 Proliferation, 241
    7.4.3.3 Hypoxia, 241
    7.4.3.4 Apoptosis, 242
    7.4.3.5 Receptor Imaging, 242
    7.4.3.6 Imaging Gene Therapy, 243
  7.4.4 Molecular Imaging for Research in Drug Development, 243
  7.4.5 Small Animal Imaging, 244

References, 244
8 Fluorescence Imaging 248

Nikolaos C. Deliolanis, Christian P. Schultz, and Vasilis Ntziachristos

8.1 Introduction, 248
8.2 Contrast Mechanisms, 249
  8.2.1 Endogenous Contrast, 249
  8.2.2 Exogenous Contrast, 251
8.3 Direct Methods: Fluorescent Probes, 251
8.4 Indirect Methods: Fluorescent Proteins, 252
8.5 Microscopy, 253
  8.5.1 Optical Microscopy, 253
  8.5.2 Fluorescence Microscopy, 254
8.6 Macroscopic Imaging/Tomography, 260
8.7 Planar Imaging, 260
8.8 Tomography, 262
  8.8.1 Diffuse Optical Tomography, 266
  8.8.2 Fluorescence Tomography, 266
8.9 Conclusion, 267

References, 268

9 Infrared and Raman Spectroscopic Imaging 275

Gerald Steiner

9.1 Introduction, 275
9.2 Instrumentation, 278
  9.2.1 Infrared Imaging, 278
  9.2.2 Near-Infrared Imaging, 281
9.3 Raman Imaging, 282
9.4 Sampling Techniques, 283
9.5 Data Analysis and Image Evaluation, 285
  9.5.1 Data Preprocessing, 287
  9.5.2 Feature Selection, 287
  9.5.3 Spectral Classification, 288
  9.5.4 Image Processing Including Pattern Recognition, 292
9.6 Applications, 292
  9.6.1 Single Cells, 292
9.6.2 Tissue Sections, 292
  9.6.2.1 Brain Tissue, 294
  9.6.2.2 Skin Tissue, 295
  9.6.2.3 Breast Tissue, 298
  9.6.2.4 Bone Tissue, 299
9.6.3 Diagnosis of Hemodynamics, 300

References, 301

10 Coherent Anti-Stokes Raman Scattering Microscopy 304
  Annika Enejder, Christoph Heinrich, Christian Brackmann, Stefan Bernet, and Monika Ritsch-Marte
10.1 Basics, 304
  10.1.1 Introduction, 304
10.2 Theory, 306
10.3 CARS Microscopy in Practice, 309
10.4 Instrumentation, 310
10.5 Laser Sources, 311
10.6 Data Acquisition, 314
10.7 Measurement Techniques, 316
  10.7.1 Excitation Geometry, 316
  10.7.2 Detection Geometry, 318
  10.7.3 Time-Resolved Detection, 319
  10.7.4 Phase-Sensitive Detection, 319
  10.7.5 Amplitude-Modulated Detection, 320
10.8 Applications, 320
  10.8.1 Imaging of Biological Membranes, 321
  10.8.2 Studies of Functional Nutrients, 321
  10.8.3 Lipid Dynamics and Metabolism in Living Cells and Organisms, 322
  10.8.4 Cell Hydrodynamics, 324
  10.8.5 Tumor Cells, 325
  10.8.6 Tissue Imaging, 325
  10.8.7 Imaging of Proteins and DNA, 326
10.9 Conclusions, 326
    References, 327
CONTENTS

11 Biomedical Sonography 331
Georg Schmitz

11.1 Basic Principles, 331
11.1.1 Introduction, 331
11.1.2 Ultrasonic Wave Propagation in Biological Tissues, 332
11.1.3 Diffraction and Radiation of Sound, 333
11.1.4 Acoustic Scattering, 337
11.1.5 Acoustic Losses, 338
11.1.6 Doppler Effect, 339
11.1.7 Nonlinear Wave Propagation, 339
11.1.8 Biological Effects of Ultrasound, 340
11.1.8.1 Thermal Effects, 340
11.1.8.2 Cavitation Effects, 340

11.2 Instrumentation of Real-Time Ultrasound Imaging, 341
11.2.1 Pulse-Echo Imaging Principle, 341
11.2.2 Ultrasonic Transducers, 342
11.2.3 Beamforming, 344
11.2.3.1 Beamforming Electronics, 344
11.2.3.2 Array Beamforming, 345

11.3 Measurement Techniques of Real-Time Ultrasound Imaging, 347
11.3.1 Doppler Measurement Techniques, 347
11.3.1.1 Continuous Wave Doppler, 347
11.3.1.2 Pulsed Wave Doppler, 349
11.3.1.3 Color Doppler Imaging and Power Doppler Imaging, 351
11.3.2 Ultrasound Contrast Agents and Nonlinear Imaging, 353
11.3.2.1 Ultrasound Contrast Media, 353
11.3.2.2 Harmonic Imaging Techniques, 356
11.3.2.3 Perfusion Imaging Techniques, 357
11.3.2.4 Targeted Imaging, 358

11.4 Application Examples of Biomedical Sonography, 359
11.4.1 B-Mode, M-Mode, and 3D Imaging, 359
11.4.2 Flow and Perfusion Imaging, 362

References, 365

12 Acoustic Microscopy for Biomedical Applications 368
Jürgen Bereiter-Hahn

12.1 Sound Waves and Basics of Acoustic Microscopy, 368
12.1.1 Propagation of Sound Waves, 369
12.1.2 Main Applications of Acoustic Microscopy, 371
12.1.3 Parameters to Be Determined and General Introduction into Microscopy with Ultrasound, 371

12.2 Types of Acoustic Microscopy, 372
12.2.1 Scanning Laser Acoustic Microscope (LSAM), 373
12.2.2 Pulse-Echo Mode: Reflection-Based Acoustic Microscopy, 373
   12.2.2.1 Reflected Amplitude Measurements, 379
   12.2.2.2 V(z) Imaging, 380
   12.2.2.3 V(f) Imaging, 382
   12.2.2.4 Interference-Fringe-Based Image Analysis, 383
   12.2.2.5 Determination of Phase and the Complex Amplitude, 386
   12.2.2.6 Combining V(f) with Reflected Amplitude and Phase Imaging, 386
   12.2.2.7 Time-Resolved SAM and Full Signal Analysis, 388

12.3 Biomedical Applications of Acoustic Microscopy, 391
12.3.1 Influence of Fixation on Acoustic Parameters of Cells and Tissues, 391
12.3.2 Acoustic Microscopy of Cells in Culture, 392
12.3.3 Technical Requirements, 393
   12.3.3.1 Mechanical Stability, 393
   12.3.3.2 Frequency, 393
   12.3.3.3 Coupling Fluid, 393
   12.3.3.4 Time of Image Acquisition, 394
12.3.4 What Is Revealed by SAM: Interpretation of SAM Images, 394
   12.3.4.1 Sound Velocity, Elasticity, and the Cytoskeleton, 395
   12.3.4.2 Attenuation, 400
   12.3.4.3 Viewing Subcellular Structures, 401
12.3.5 Conclusions, 401

12.4 Examples of Tissue Investigations using SAM, 403
12.4.1 Hard Tissues, 404
12.4.2 Cardiovascular Tissues, 405
12.4.3 Other Soft Tissues, 406

References, 406

Index