

Contents

1 Fundamentals of Biomedical Image Processing	
<i>Thomas M. Deserno</i>	1
1.1 Introduction	1
1.1.1 Steps of Image Processing	2
1.1.2 Remarks on Terminology	3
1.1.3 Biomedical Image Processing	4
1.2 Medical Image Formation	4
1.2.1 Basic Physics	5
1.2.2 Imaging Modalities	6
1.2.3 Digitalization	13
1.3 Image Enhancement	16
1.3.1 Histogram Transforms	16
1.3.2 Convolution	18
1.3.3 Mathematical Morphology	18
1.3.4 Calibration	19
1.3.5 Registration	20
1.4 Image Data Visualization	22
1.4.1 Marching Cube Algorithm	23
1.4.2 Surface Rendering	23
1.4.3 Volume Rendering	23
1.5 Visual Feature Extraction	25
1.5.1 Data Level	25
1.5.2 Pixel Level	25
1.5.3 Edge Level	25
1.5.4 Texture Level	26
1.5.5 Region Level	26
1.6 Segmentation	27
1.6.1 Pixel-Based Segmentation	27
1.6.2 Edge-Based Segmentation	30
1.6.3 Region-Based Segmentation	31

1.6.4	Over- and Under-Segmentation	32
1.6.5	Model-Based Segmentation	34
1.7	Classification	37
1.7.1	Statistic Classifiers	39
1.7.2	Syntactic Classifiers	39
1.7.3	Computational Intelligence-Based Classifiers	40
1.8	Quantitative Measurements and Interpretation	41
1.8.1	Partial Volume Effect	42
1.8.2	Euclidean Paradigm	42
1.8.3	Scene Analysis	42
1.8.4	Examples	43
1.9	Image Management	45
1.9.1	Archiving	45
1.9.2	Communication	45
1.9.3	Retrieval	47
1.10	Conclusion and Outlook	48
	References	49

Part I Image Formation

2 Fusion of PET and MRI for Hybrid Imaging

Zang-Hee Cho, Young-Don Son, Young-Bo Kim,

and Seung-Schik Yoo	55	
2.1	Introduction	55
2.2	Positron Emission Tomography	57
2.2.1	Basic Principles	57
2.2.2	Image Reconstruction	59
2.2.3	Signal Optimization	59
2.2.4	High-Resolution Research Tomograph	60
2.3	Magnetic Resonance Imaging	62
2.3.1	Basic Principles	62
2.3.2	Image Reconstruction	63
2.3.3	Signal Optimization	64
2.3.4	High-Field MRI	65
2.4	Hybrid PET Fusion System	67
2.4.1	PET/CT Systems	68
2.4.2	PET/MRI Systems	68
2.4.3	High-Resolution Fusion	70
2.4.4	PET/MRI Fusion Algorithm	72
2.5	Conclusions	76
	References	76

3 Cardiac 4D Ultrasound Imaging

<i>Jan D'hooge</i>	81
3.1 The Role of Ultrasound in Clinical Cardiology	81
3.2 Principles of Ultrasound Image Formation	82
3.2.1 The Pulse-Echo Measurement	82
3.2.2 Gray Scale Encoding	83
3.2.3 Gray Scale Imaging	85
3.2.4 Phased Array Transducer Technology	85
3.3 Limitations of 2D Cardiac Ultrasound.....	86
3.3.1 Complex Anatomy (Congenital Heart Disease)	87
3.3.2 Geometric Assumptions to Assess Volumes	88
3.3.3 Out-of-Plane Motion and Foreshortening	89
3.4 Approaches Towards 3D Cardiac Ultrasound	89
3.4.1 Freehand 3D Ultrasound	90
3.4.2 Prospective Gating	90
3.4.3 Retrospective Gating	91
3.4.4 Two-Dimensional Arrays	92
3.5 Validation of 3D Cardiac Ultrasound Methodologies	95
3.6 Emerging Technologies	96
3.6.1 Transesophageal 3D Imaging.....	96
3.6.2 True Real-Time Volumetric Imaging	97
3.7 Remaining Challenges in 4D Cardiac Ultrasound	98
3.7.1 Resolution.....	98
3.7.2 Image Quality	99
3.7.3 Data Visualization and Interaction	101
3.7.4 Segmentation/Automated Analysis	101
References	102

Part II Image Enhancement

4 Morphological Image Processing Applied in Biomedicine

<i>Roberto A. Lotufo, Letícia Rittner, Romaric Audigier, Rubens C. Machado, and André V. Saúde</i>	107
4.1 Introduction	107
4.2 Binary Morphology	108
4.2.1 Erosion and Dilation.....	108
4.2.2 Opening and Closing	110
4.2.3 Morphological Reconstruction from Markers	111
4.2.4 Reconstruction from Opening	112
4.3 Gray-Scale Operations	114
4.3.1 Erosion and Dilation.....	115
4.3.2 Opening and Closing	116
4.3.3 Component Filters and Morphological Reconstruction	119
4.3.4 Regional Maxima	121

4.4	Watershed Segmentation	122
4.4.1	Classical Watershed Transform	122
4.4.2	Filtering the Minima	123
4.4.3	Watershed from Markers	124
4.4.4	Inner and Outer Markers	125
4.5	Segmentation of Diffusion MRI	126
4.6	Conclusions	128
	References	128

5 Medical Image Registration

	<i>Daniel Rueckert and Julia A. Schnabel</i>	131
5.1	Introduction	131
5.2	Transformation Model	132
5.2.1	Rigid Transformation	133
5.2.2	Affine Transformation	133
5.2.3	Projective Transformation	134
5.2.4	Non-Rigid Transformation: Parametric Models	134
5.2.5	Non-Rigid Transformation: Non-Parametric Models	138
5.3	Registration Basis	139
5.3.1	Feature-Based Registration	140
5.3.2	Voxel-Based Registration	141
5.4	Optimization	144
5.5	Validation of Registration	144
5.6	Application	146
5.6.1	Intra-Subject Registration	146
5.6.2	Inter-Subject Registration	147
5.7	Summary and Conclusions	149
	References	150

Part III Feature Extraction and Selection

6 Texture in Biomedical Images

	<i>Maria Petrou</i>	157
6.1	Introduction	157
6.2	Characterizing the Texture of Swatches	158
6.2.1	From Grammars to Markov Random Fields	158
6.2.2	From Markov Random Fields to Fractals	159
6.2.3	From Markov Random Fields to Gibbs Distributions	159
6.2.4	Co-occurrence Matrices	160
6.2.5	Generalized Co-occurrence Matrices	161
6.2.6	Orientation Histograms	162
6.2.7	Textons	163
6.2.8	Features from the Discrete Fourier Transform	163
6.3	Simultaneous Texture Segmentation and Recognition	165

6.3.1	From Spatio-Frequency to Spatio-Structural Space	166
6.3.2	Statistical Spatio-Structural Space	168
6.3.3	Monogenic Signal	169
6.3.4	From Monogenic Signal Back to Gabor Functions	170
6.3.5	Beyond Spatial Patterns into Gray Value Distributions	171
6.4	Examples of the Use of Texture Features in Biomedical Applications	172
6.4.1	Mammography	172
6.4.2	Brain Image Data	173
6.5	Discussion and Conclusions	174
	References	175
7 Multi-Scale and Multi-Orientation Medical Image Analysis		
<i>Bart M. ter Haar Romeny</i>	177
7.1	Introduction	177
7.2	The Necessity of Scale	178
7.2.1	The Optimal Aperture Function	178
7.2.2	Derivatives of Sampled, Discrete Data, Such as Images	180
7.3	Differential Invariants	181
7.3.1	Gauge Coordinates	181
7.3.2	Invariants from Tensor Contraction	182
7.4	Second Order Image Structure and Features	183
7.4.1	Isophote Curvature	183
7.4.2	Flowline Curvature	184
7.4.3	Corners	184
7.4.4	Principal Curvatures	185
7.4.5	The Shape Index	186
7.5	Third Order Image Structure: T-Junctions	187
7.6	Adaptive Blurring and Geometry-Driven Diffusion	187
7.7	Edge Focusing	189
7.8	Orientation Analysis	190
7.9	Applications	192
7.9.1	Catheter Detection	192
7.9.2	Endocard Contour Detection	193
7.9.3	Denoising of Crossing Lines	193
7.10	Conclusion	194
	References	195
8 Feature Extraction and Selection for Decision Making		
<i>Agma J.M. Traina, Caetano Traina Jr., André G.R. Balan, Marcela X. Ribeiro, Pedro H. Bugatti, Carolina Y.V. Watanabe, and Paulo M. Azevedo-Marques</i>	197
8.1	Introduction	197
8.2	Image Representation	198
8.2.1	Medical Image Segmentation and Feature Extraction	199
8.2.2	Color Features	201

8.2.3	Texture Features	203
8.2.4	Shape Features	204
8.3	Image Features and Distance Functions	205
8.3.1	Similarity Search and Metric Spaces	206
8.3.2	Distance Functions	206
8.3.3	Case Study: Evaluating Distance Functions for Separating Data	208
8.4	Feature Selection	210
8.4.1	Curse of Dimensionality	211
8.4.2	Traditional Algorithm for Feature Selection	211
8.4.3	Combined Feature Selection and Discretization	213
8.5	Association Rule Mining	215
8.5.1	Definition	215
8.5.2	Case Study: Improving Computer-Aided Diagnosis by Association Rule Mining	215
8.6	Conclusions	220
	References	221

Part IV Segmentation

9 Parametric and Non-Parametric Clustering for Segmentation

<i>Hayit Greenspan and Tanveer Syeda-Mahmood</i>	227	
9.1	Introduction	227
9.2	Image Modeling and Segmentation	229
9.2.1	Image Modeling	230
9.2.2	Segmentation	230
9.2.3	State of the Art	231
9.3	Probabilistic Modeling of Feature Space	231
9.3.1	Gaussian Mixture Models	232
9.3.2	Expectation Maximization	232
9.3.3	Visualization	233
9.4	Using GMMs for Brain Tissue and Lesion Segmentation	234
9.4.1	Application Domain	234
9.4.2	Spatial Constraints	234
9.4.3	Modeling Spatial Constraints Through GMM	235
9.4.4	Tissue Segmentation	238
9.4.5	Lesion Segmentation	238
9.5	Non-Parametric Clustering Approaches to Segmentation	240
9.5.1	Description of the Feature Space	241
9.5.2	Clustering Intensity, Geometry, and Motion	243
9.6	Using Non-Parametric Clustering for Cardiac Ultrasound	245
9.6.1	Application Domain	245
9.6.2	Cardiac Motion Estimation	246
9.6.3	Segmentation of Meaningful Regions	246

9.7 Discussion	248
References	248
10 Region-Based Segmentation: Fuzzy Connectedness, Graph Cut and Related Algorithms	
<i>Krzysztof Chris Ciesielski and Jayaram K. Udupa</i>	251
10.1 Introduction and Overview	251
10.1.1 Digital Image Scene	252
10.1.2 Topological and Graph-Theoretical Scene Representations	253
10.1.3 Digital Image	253
10.1.4 Delineated Objects	254
10.2 Threshold-Indicated Fuzzy Connected Objects	254
10.2.1 Absolute Fuzzy Connectedness Objects	255
10.2.2 Robustness of Objects	256
10.2.3 Algorithm for Delineating Objects	256
10.3 Optimization in Foreground-Background Case	257
10.3.1 Relative Fuzzy Connectedness	258
10.3.2 Algorithm for Delineating Objects	259
10.3.3 Graph Cut Delineation	259
10.4 Segmentation of Multiple Objects	262
10.4.1 Relative Fuzzy Connectedness	262
10.4.2 Iterative Relative Fuzzy Connectedness	263
10.4.3 Algorithm for Iterative Relative Fuzzy Connectedness	265
10.4.4 Variants of IRFC	266
10.5 Scale-Based and Vectorial Fuzzy Connectedness	266
10.6 Affinity Functions in Fuzzy Connectedness	267
10.6.1 Equivalent Affinities	267
10.6.2 Essential Parameters in Affinity Functions	269
10.7 Other Delineation Algorithms	270
10.7.1 Generalized Graph Cut	270
10.7.2 Level Set vs. Generalized Graph Cut	271
10.8 Medical Image Examples	273
10.9 Concluding Remarks	276
References	276
11 Model-Based Segmentation	
<i>Tobias Heimann and Hervé Delingette</i>	279
11.1 Introduction	279
11.2 Deformable Simplex Meshes	281
11.2.1 Internal Forces on Simplex Meshes	282
11.2.2 Image Forces	283
11.2.3 Globally Constrained Deformation	285
11.2.4 3D+t Deformable Simplex Meshes	286
11.2.5 Advanced Segmentation Strategies	288
11.2.6 Geometric Representations for Model-Based Segmentation	290

XVIII Contents

11.3	Statistical Models of Shape and Appearance	291
11.3.1	Shape Representation	292
11.3.2	Point Correspondence	292
11.3.3	Construction of Statistical Shape Models	295
11.3.4	Modeling Object Appearance	297
11.3.5	Local Search Algorithms	298
11.4	Conclusion	300
	References	301

Part V Classification and Measurements

12 Melanoma Diagnosis

<i>Alexander Horsch</i>	307	
12.1	The Cutaneous Melanoma	307
12.1.1	Medical Basics	307
12.1.2	Relevance of Early Diagnosis	309
12.2	State of the Art in CM Diagnosis	309
12.2.1	Diagnostic Algorithms	309
12.2.2	Imaging Techniques	311
12.2.3	Diagnostic Accuracies	313
12.3	Dermoscopy Image Analysis	314
12.3.1	Image Analysis Approaches	314
12.3.2	Segmentation of Skin Lesions	315
12.3.3	Feature Extraction	316
12.3.4	Feature Visualization	317
12.3.5	Classification Methods	319
12.4	Commercial Systems	322
12.4.1	System Design Principles	322
12.4.2	Image Capture Devices	323
12.4.3	Dermoscopy Computer Systems	324
12.5	Evaluation Issues	324
12.5.1	Case Databases	325
12.5.2	Evaluation Methods	325
12.6	Conclusion	325
	References	326

13 CADx Mammography

<i>Lena Costaridou</i>	329	
13.1	Introduction	329
13.2	Basic Terms and Definitions	330
13.2.1	Breast Imaging Modalities	330
13.2.2	Mammographic Lesions	331
13.2.3	CADe Schemes	332
13.2.4	CADx Architectures	333

13.3 CADx Schemes in X-ray Mammography	335
13.3.1 Morphology Analysis of MC Clusters	335
13.3.2 Texture Analysis of MC Clusters	338
13.3.3 Morphology and Texture Analysis of Masses	339
13.4 CADx Schemes in Breast Ultrasound	341
13.5 CADx Schemes in Breast MRI	344
13.6 Application Examples	346
13.6.1 Segmentation Accuracy on MC Cluster Content	346
13.6.2 Heterogeneity of Enhancement Kinetics in DCE-MRI	349
13.7 Discussion and Conclusions	351
References	353

14 Quantitative Medical Image Analysis for Clinical Development of Therapeutics

<i>Mostafa Analoui</i>	359
14.1 Introduction	359
14.2 Key Issues in Drug Research and Clinical Development	361
14.2.1 Biological Marker	361
14.2.2 Imaging Modality	362
14.3 Quantitative Image Analysis	363
14.3.1 Assessment of Osteoarthritis	364
14.3.2 Assessment of Carotid Atherosclerosis	365
14.3.3 Assessment of Cancer	367
14.4 Managing Variability in Imaging Biomarkers	369
14.4.1 Technical Validation	370
14.4.2 Standard Operation Procedures	371
14.4.3 Regulatory Issues	372
14.5 Future Directions	373
References	374

Part VI Image Data Visualization

15 Visualization and Exploration of Segmented Anatomic Structures

<i>Dirk Bartz and Bernhard Preim</i>	379
15.1 Introduction	379
15.2 Indirect and Direct Volume Rendering	380
15.2.1 Indirect Volume Rendering	380
15.2.2 Rendering of Multiple Objects	380
15.2.3 Direct Volume Rendering	382
15.2.4 Rendering of Segmented Data	383
15.2.5 Discussion	384
15.3 Generation of Smooth and Accurate Surface Models	386
15.3.1 Mesh Smoothing with Fairing	386
15.3.2 Improving Mesh Quality	388

15.4	Visualization of Vascular Structures	389
15.4.1	Surface-based Vessel Visualization	390
15.4.2	Model-based Surface Visualization of Vascular Structures	390
15.4.3	Volume Rendering of Vascular Structures	392
15.5	Virtual Endoscopy	394
15.5.1	Graphical Representation	395
15.5.2	Interaction Model	396
15.5.3	User Interface	396
15.5.4	Case Study: Virtual Colonoscopy	397
15.6	Conclusions	397
	References	398

16 Processing and Visualization of Diffusion MRI

<i>James G. Malcolm, Yogesh Rathi, and Carl-Fredrik Westin</i>	403	
16.1	Introduction	403
16.2	Modeling	404
16.2.1	Imaging the Tissue	404
16.2.2	Parametric Models	405
16.2.3	Non-parametric Models	405
16.2.4	Regularization	407
16.2.5	Characterizing Tissue	407
16.3	Tractography	408
16.3.1	Deterministic Tractography	408
16.3.2	Probabilistic Tractography	409
16.3.3	Global Tractography	411
16.3.4	Validation	412
16.4	Applications	413
16.4.1	Volume Segmentation	413
16.4.2	Fiber Clustering	414
16.4.3	Connectivity	416
16.4.4	Tissue Analysis	417
16.5	Summary	418
	References	419

Part VII Image Management and Integration

17 Digital Imaging and Communications in Medicine

<i>Michael Onken, Marco Eichelberg, Jörg Riesmeier, and Peter Jensch</i>	427	
17.1	DICOM Basics	427
17.1.1	Introduction and Overview	428
17.1.2	Information Objects	428
17.1.3	Display Pipeline	430
17.1.4	Network and Media Services	433
17.1.5	Conformance	437

17.2	Advanced DICOM Services	438
17.2.1	Advanced Image Display Services	438
17.2.2	DICOM Structured Reporting	442
17.2.3	Application Hosting	447
17.3	Conclusions and Outlook	452
	References	453
18	PACS-Based Computer-Aided Detection and Diagnosis	
	<i>H.K. (Bernie) Huang, Brent J. Liu, Anh Hong Tu Le, and Jorge Documet</i>	455
18.1	Introduction	455
18.2	The Need for CAD-PACS Integration	456
18.2.1	Approaches of CAD-PACS Integration	457
18.2.2	CAD Software	459
18.3	DICOM Standard and IHE Workflow Profiles	459
18.3.1	DICOM Structured Reporting	460
18.3.2	IHE Profiles	461
18.4	The CAD-PACS TM Toolkit	461
18.4.1	Concept	462
18.4.2	Structure, Components, and Editions	462
18.5	Example of CAD-PACS Integration	463
18.5.1	The Digital Hand Atlas	463
18.5.2	CAD Evaluation in a Laboratory Setting	464
18.5.3	CAD Evaluation in a Clinical Environment	465
18.5.4	CAD-PACS Integration Using DICOM-SR	466
18.6	Conclusion	467
	References	469
19	Content-Based Medical Image Retrieval	
	<i>Henning Müller and Thomas M. Deserno</i>	471
19.1	Introduction	471
19.1.1	Motivation and History	472
19.1.2	Query-by-Example(s) Paradigm	472
19.2	General Image Retrieval	473
19.2.1	Classification vs. Retrieval	473
19.2.2	System Components and Computation	474
19.2.3	Features and Signatures	474
19.2.4	Distance and Similarity Measures	476
19.3	Medical Image Retrieval	476
19.3.1	Application Fields	477
19.3.2	Types of Images	477
19.3.3	Image Preprocessing	478
19.3.4	Visual and Non-Visual Image Features	478
19.3.5	Database Architectures	479
19.3.6	User Interfaces and Interaction	480
19.3.7	Interfacing with Clinical Information Systems	480

19.4	Evaluation.....	481
19.4.1	Available Databases	481
19.4.2	Tasks and User Models.....	481
19.4.3	Ground Truth and Gold Standards	482
19.4.4	Benchmarks and Events	483
19.5	Examples for Medical CBIR Systems	483
19.5.1	Medical Gnu Image Finding Tool.....	484
19.5.2	Image Retrieval in Medical Applications.....	484
19.6	Discussion and Conclusions	487
19.6.1	Strengths and Weaknesses of Current Systems	488
19.6.2	Gaps of Medical CBIR Systems	488
19.6.3	Future Developments	488
	References	490

Part VIII Evaluation and Customizing

20 Systematic Evaluations and Ground Truth

<i>Jayashree Kalpathy-Cramer and Henning Müller</i>	497	
20.1	Introduction	497
20.2	Components for Successful Evaluation Campaigns	498
20.2.1	Applications and Realistic Tasks	498
20.2.2	Collections of Images and Ground Truth	499
20.2.3	Application-Specific Metrics	500
20.2.4	Organizational Resources and Participants.....	501
20.3	Evaluation Metrics and Ground Truth	502
20.3.1	Registration	502
20.3.2	Segmentation	503
20.3.3	Retrieval	506
20.4	Examples of Successful Evaluation Campaigns	508
20.4.1	Registration	508
20.4.2	Segmentation	509
20.4.3	Annotation, Classification and Detection	511
20.4.4	Information Retrieval	512
20.4.5	Image Retrieval	512
20.5	Lessons Learned.....	517
20.6	Conclusions.....	517
	References	518

21 Toolkits and Software for Developing Biomedical Image Processing and Analysis Applications

<i>Ivo Wolf</i>	521	
21.1	Introduction	521
21.2	Toolkits	522

21.2.1	The NA-MIC Kit	522
21.2.2	Insight Segmentation and Registration Toolkit	523
21.2.3	The Visualization Toolkit	524
21.2.4	Open Inventor	525
21.2.5	Medical Imaging Interaction Toolkit	526
21.2.6	The Image-Guided Surgery Toolkit	527
21.2.7	The Multimod Application Framework	528
21.2.8	vtkINRIA3D	529
21.2.9	OFFIS DICOM ToolKit	529
21.2.10	Grassroots DICOM Library	530
21.2.11	The Common Toolkit	530
21.2.12	Simulation Open Framework Architecture	530
21.3	Development Environments	531
21.3.1	SCIRun	532
21.3.2	OpenXIP	532
21.3.3	DeVIDE	533
21.3.4	VisTrails	534
21.3.5	LONI Pipeline	534
21.3.6	MeVisLab	535
21.3.7	MATLAB®	535
21.3.8	Interactive Data Language	536
21.4	Extensible Software	537
21.4.1	3D Slicer	537
21.4.2	MITK ExtApp and MITK 3M3	538
21.4.3	Graphical Interface for Medical Image Analysis and Simulation	539
21.4.4	OsiriX	539
21.4.5	ParaView	539
21.4.6	ImageJ and Fiji	540
21.4.7	MIPAV	541
21.4.8	VolView	541
21.4.9	Analyze	541
21.4.10	Amira	542
21.5	Conclusion and Discussion	543
	References	543

22 Image Processing and the Performance Gap

<i>Steven C. Horii and Murray H. Loew</i>	545	
22.1	Introduction	545
22.2	Examples of Clinically Useful Image Processing	546
22.2.1	Windowing and Image Display	546
22.2.2	Contrast and Edge Enhancement	546
22.2.3	Noise Reduction and Color Coding	547
22.2.4	Registration and Segmentation	547
22.2.5	Image Compression and Management	548

XXIV Contents

22.3	Why are there Gaps?	549
22.3.1	The Conservative Radiologist	549
22.3.2	The Busy Radiologist: Digital vs. Analog Workflow	549
22.3.3	The Wary Radiologist: Malpractice Concerns	550
22.3.4	The Skeptical Radiologist: Evidence-Based Requirements	551
22.3.5	Tails, Dogs, and Gaps.....	552
22.4	The Goals of Image Processing for Medical Imaging	553
22.4.1	Automation of Tasks	553
22.4.2	Improvement of Observer Performance	555
22.5	Closing the Gap.....	561
22.5.1	Education	561
22.5.2	Research	562
22.6	Conclusion	563
	References	563
	Index	567