

Thomas M. Deserno
Editor

BIOLOGICAL AND MEDICAL PHYSICS, BIOMEDICAL ENGINEERING

Biomedical Image Processing

 Springer

BIOLOGICAL AND MEDICAL PHYSICS, BIOMEDICAL ENGINEERING

For further volumes:
<http://www.springer.com/series/3740>

BIOLOGICAL AND MEDICAL PHYSICS, BIOMEDICAL ENGINEERING

The fields of biological and medical physics and biomedical engineering are broad, multidisciplinary and dynamic. They lie at the crossroads of frontier research in physics, biology, chemistry, and medicine. The Biological and Medical Physics, Biomedical Engineering Series is intended to be comprehensive, covering a broad range of topics important to the study of the physical, chemical and biological sciences. Its goal is to provide scientists and engineers with textbooks, monographs, and reference works to address the growing need for information.

Books in the series emphasize established and emergent areas of science including molecular, membrane, and mathematical biophysics; photosynthetic energy harvesting and conversion; information processing; physical principles of genetics; sensory communications; automata networks, neural networks, and cellular automata. Equally important will be coverage of applied aspects of biological and medical physics and biomedical engineering such as molecular electronic components and devices, biosensors, medicine, imaging, physical principles of renewable energy production, advanced prostheses, and environmental control and engineering.

Editor-in-Chief:

Elias Greenbaum, Oak Ridge National Laboratory, Oak Ridge, Tennessee, USA

Editorial Board:

Masuo Aizawa, Department of Bioengineering,
Tokyo Institute of Technology, Yokohama, Japan

Olaf S. Andersen, Department of Physiology,
Biophysics & Molecular Medicine,
Cornell University, New York, USA

Robert H. Austin, Department of Physics,
Princeton University, Princeton, New Jersey, USA

James Barber, Department of Biochemistry,
Imperial College of Science, Technology
and Medicine, London, England

Howard C. Berg, Department of Molecular
and Cellular Biology, Harvard University,
Cambridge, Massachusetts, USA

Victor Bloomfield, Department of Biochemistry,
University of Minnesota, St. Paul, Minnesota, USA

Robert Callender, Department of Biochemistry,
Albert Einstein College of Medicine,
Bronx, New York, USA

Britton Chance, Department of Biochemistry/
Biophysics, University of Pennsylvania,
Philadelphia, Pennsylvania, USA

Steven Chu, Lawrence Berkeley National
Laboratory, Berkeley, California, USA

Louis J. DeFelice, Department of Pharmacology,
Vanderbilt University, Nashville, Tennessee, USA

Johann Deisenhofer, Howard Hughes Medical
Institute, The University of Texas, Dallas,
Texas, USA

George Feher, Department of Physics,
University of California, San Diego, La Jolla,
California, USA

Hans Frauenfelder,
Los Alamos National Laboratory,
Los Alamos, New Mexico, USA

Ivar Giaever, Rensselaer Polytechnic Institute,
Troy, New York, USA

Sol M. Gruner, Cornell University,
Ithaca, New York, USA

Judith Herzfeld, Department of Chemistry,
Brandeis University, Waltham, Massachusetts, USA

Mark S. Humayun, Doheny Eye Institute,
Los Angeles, California, USA

Pierre Joliot, Institut de Biologie
Physico-Chimique, Fondation Edmond
de Rothschild, Paris, France

Lajos Keszthelyi, Institute of Biophysics, Hungarian
Academy of Sciences, Szeged, Hungary

Robert S. Knox, Department of Physics
and Astronomy, University of Rochester, Rochester,
New York, USA

Aaron Lewis, Department of Applied Physics,
Hebrew University, Jerusalem, Israel

Stuart M. Lindsay, Department of Physics
and Astronomy, Arizona State University,
Tempe, Arizona, USA

David Mauzerall, Rockefeller University,
New York, New York, USA

Eugenie V. Mielczarek, Department of Physics
and Astronomy, George Mason University, Fairfax,
Virginia, USA

Markolf Niemz, Medical Faculty Mannheim,
University of Heidelberg, Mannheim, Germany

V. Adrian Parsegian, Physical Science Laboratory,
National Institutes of Health, Bethesda,
Maryland, USA

Linda S. Powers, University of Arizona,
Tucson, Arizona, USA

Earl W. Prohofsky, Department of Physics,
Purdue University, West Lafayette, Indiana, USA

Andrew Rubin, Department of Biophysics, Moscow
State University, Moscow, Russia

Michael Seibert, National Renewable Energy
Laboratory, Golden, Colorado, USA

David Thomas, Department of Biochemistry,
University of Minnesota Medical School,
Minneapolis, Minnesota, USA

Thomas M. Deserno
Editor

Biomedical Image Processing

With 254 Figures



Springer

Editor

Dr. Thomas M. Deserno

RWTH Aachen

Institut für Medizinische Informatik

Pauwelsstr. 30

52074 Aachen, Germany

E-mail: deserno@ieee.org

Biological and Medical Physics, Biomedical Engineering ISSN 1618-7210

ISBN 978-3-642-15815-5

e-ISBN 978-3-642-15816-2

DOI 10.1007/978-3-642-15816-2

Springer Heidelberg Dordrecht London New York

Library of Congress Control Number: 2011921516

© Springer-Verlag Berlin Heidelberg 2011

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilm or in any other way, and storage in data banks. Duplication of this publication or parts thereof is permitted only under the provisions of the German Copyright Law of September 9, 1965, in its current version, and permission for use must always be obtained from Springer. Violations are liable to prosecution under the German Copyright Law.

The use of general descriptive names, registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Cover design: eStudio Calamar Steinen

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

To Verena – the beauty and the beauty of images

Preface

YATBIP: Yet another textbook on biomedical image processing? – Hopefully not. . .

Based on the tutorial *SC086 – Fundamentals of Medical Image Processing* regularly offered at the International SPIE Symposium on Medical Imaging, the Springer-Verlag Series Editor of *Biological and Medical Physics, Medical Engineering* invited me in January 2009 to compile this book. Actually, the idea of providing a “suitable” textbook – comprehensive but short, up-to-date but essential, and detailed but illustrative – for novices like experts, and at reasonable costs, is not new. For years, the lack of any such textbook in image processing covering all of the special needs in biology and medicine is evident. In any teaching lecture, tutorial as well as graduate class. I’m always asked by the students to suggest literature but cannot answer satisfyingly, simply because there isn’t a “suitable” textbook yet.

So we aimed at compiling a high-quality collection of chapters, written for scientists, researchers, lectures and graduate students as well, covering the recent advantages in the broad field of biomedical imaging and image processing in an exemplary way. In February 2009, several fruitful discussions with colleagues at SPIE Medical Imaging convinced me to face the challenge, and I started recruiting author teams for contributions. Finally, 47 authors from 11 nations all over the world collaborated – all of them leading experts in their field. Intensive efforts were made to direct all authors towards a similar style of presentation and equal degree of technical details. Beside some written guidelines, the overview chapter was provided to the authors as an example before they started writing. All authors first provided a short outline and a detailed table of content, which were distributed between all contributors together with a strictly enforced time line. In October 2009, submission of chapters started, and each manuscript was edited carefully. Editor requests have been processed by the authors improving completeness and clarity of presentation, and finally in June 2010, the manuscript was submitted to the publisher.

Fig. 1. *Eierlegende Wollmilchsau*. Every morning, this special animal provides a cooked egg with chilled fresh milk. Its wool is used for high-quality clothes and the meat for excellent dining. It is the first *all-in-one* approach documented in history (Courtesy of: <http://neulehrer.wordpress.com/>)



As a result, this book has appeared as uniform monograph with an overview chapter contributed by the editor, followed by some twenty chapters focusing on particular parts selected from biomedical imaging and image processing. Each chapter gives an introduction and overview of recent trends in its field and provides particular case examples, usually taken from the author’s own research.

Primarily addressing engineers and system developers in computer sciences, the book covers the entire processing pipeline of biomedical imaging. In particular, the following parts are included, with about three chapters in each of it:

1. Image formation
2. Image enhancement
3. Feature extraction and selection
4. Segmentation
5. Classification and measurements
6. Image data visualization
7. Image management and integration
8. Evaluation and customizing

Many people might object me at this point, because we clearly aimed at reaching the unreachable. In Germany, we have the common phrase “*eierlegende Wollmilchsau*”, a metaphor that directly translates to “egg-providing wool-milk-pig” describing the union of all benefits (Fig. 1).

You as the reader shall judge our success realizing this all-in-one approach: YATBIP or *eierlegende Wollmilchsau*? Any feedback is deeply welcome and should be directed personally to me as the editor.

Facing now the final manuscript, I want to thank Claus Ascheron for encouraging me to initiate this project, and all contributors for timely delivering their high-quality material and appropriately responding to the editorial remarks and suggestions. Jens Hoffmann was assisting me in L^AT_EX programming and Max Jung helped in text and image conversion and optimization.

Also, I want to mention Peter Jentsch and Dirk Bartz, who have passed away during the very last iterations of the manuscript, which leaves me behind speechless. We have included the obituaries in the next pages.

Obituaries



Prof. Dr. Peter Jensch died unexpectedly during the period of the proof-reading of this book chapter on April 15, 2010 after a fulfilling life. Peter Jensch was the initiator of the DICOM research activities at the OFFIS - Institute for Information Technology, Oldenburg, Germany, in the early 1990s and was pushing this topic forward for the rest of his life. The most popular result of this engagement is the well-known Open Source DICOM toolkit DCMTK that is hosted and maintained by OFFIS since 1993. Against this background, all members of the DICOM team at OFFIS

would like to thank Peter Jensch for establishing this extraordinary project and for being such a likeable, energetic boss, mentor, and colleague to us. Without him, OFFIS would not be the popular name in the world of DICOM it is today and we all would not have such encouraging opportunities and research projects we still enjoy. As Chap. 17 of this book is the last publication Peter Jensch participated in and since the content of this chapter is the very topic that strongly influenced his work, we like to use this opportunity to express our sincere gratitude to Peter Jensch.

Oldenburg, June 2010

*Michael Onken
Marco Eichelberg
Jörg Riesmeier*



Prof. Dr. Dirk Bartz died unexpectedly on March 28, 2010 while attending the thirtieth Vattenfall Berlin Half Marathon. Running half-marathon in Berlin was one of his favorite activities.

During his academic career, Dirk strongly supported the idea of building a German Interest Group on Medical Visualization and actively took part the whole time giving advice to many students; particularly supporting female researchers was an important issue. Furthermore, Dirk organized many tutorials at Visualization, Eurographics, and Computer-Assisted Radiology and Surgery (CARS).

In 2005, I was very glad that Dirk joined the effort of writing a textbook on “Visualization in Medicine”. For an 18 month period, we communicated daily on the various aspects of the book. It was enlightening and a pleasure to discuss with Dirk all the time. He was always perfectly reliable and good-humored even in situations where he had a very high workload.

In the end of 2006, Dirk became appointed as Full Professor for Computer-Assisted Surgery at the International Center for Computer-Assisted Surgery (ICCAS), Leipzig, Germany, and started to build a new research group. He focused on visualization techniques, such as illustrative rendering, perceptual studies (from Dirk I learned the term “psychophysical studies”), and applications in neurosurgery and Ear, Nose and Throat (ENT) surgery.

Dirk belonged to the core team which tried to establish a new workshop series “Visual Computing in Biology and Medicine”. It was quite natural that Dirk would host the second event, scheduled to take place in July in Leipzig. Until the very last days of his life, he discussed strategies for this workshop.

Dirk was only 42 years old, leaving behind Heidi, his wife, and his two little sons.

Magedeburg, June 2010

Berhard Preim

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

<i>Zang-Hee Cho, Young-Don Son, Young-Bo Kim,</i>	
<i>and Seung-Schik Yoo</i>	
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, Leticia Rittner, Romaric Audigier,</i> <i>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

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 Rath, 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

Michael Onken, Marco Eichelberg, Jörg Riesmeier, and Peter Jensch ... 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 HongTu Le,</i>		
<i>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 Enhancememt	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

- 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

List of Contributors

Mostafa Analoui

Healthcare and Life Sciences
The Livingston Group
New York, NY, USA
analoui@yahoo.com

Romaric Audigier

Laboratoire Vision et Ingénierie
des Contenus, CEA-LIST
romaric.audigier@cea.fr

Paulo M. Azevedo-Marques

Medical School of Ribeirão Preto
University of São Paulo
São Paulo, Brazil
pmarques@fmrp.usp.br

André G.R. Balan

Computer Science, Mathematics
and Cognition Center
Federal University of ABC
São Paulo, Brazil
agrbalan@icmc.usp.br

Dirk Bartz[†]

Innovation Center for Computer
Assisted Surgery (ICCAS)
University of Leipzig
Leipzig, Germany

Pedro H. Bugatti

Computer Science Department
University of São Paulo
São Paulo, Brazil
pbugatti@icmc.usp.br

Zang-Hee Cho

Neuroscience Research Institute
Gachon University of Medicine
and Science, Seoul, Korea
zcho@gachon.ac.kr

Krzysztof Chris Ciesielski

Department of Mathematics
West Virginia University
Morgantown, WV, USA
and

Department of Radiology
University of Pennsylvania
Philadelphia, PA, USA
kcies@math.wvu.edu

Lena Costaridou

Department of Medical Physics
University of Patras
Patras, Greece
costarid@upatras.gr

Hervé Delingette

Asclepios Team, INRIA
Sophia-Antipolis, France
herve.delingette@inria.fr

Thomas M. Deserno

Department of Medical Informatics
RWTH Aachen University
Aachen, Germany
deserno@ieee.org

Jan D'hooge

Department of Cardiovascular
Diseases, Katholieke Universiteit
Leuven, Leuven, Belgium
jan.dhooge@uz.kuleuven.ac.be

Jorge Documet

Image Processing and Informatics
Lab, University of Southern
California, Los Angeles, CA, USA
documet@usc.edu

Marco Eichelberg

OFFIS Institute for Information
Technology, Oldenburg, Germany
eichelberg@offis.de

Hayit Greenspan

Department of Biomedical
Engineering, Tel-Aviv University
Tel-Aviv, Israel
hayit@eng.tau.ac.il

Bart M. ter Haar Romeny

Department of Biomedical
Engineering, Eindhoven
University of Technology
Eindhoven, The Netherlands
b.m.terhaarromeny@tue.nl

Tobias Heimann

French Research Institute
of Computer Science and Automatic
Control, INRIA
Sophia Antipolis Cedex, France
and
German Cancer Research Center
Heidelberg, Germany
t.heimann@dkfz.de

Steven C. Horii

Department of Radiology
University of Pennsylvania
Philadelphia PA, USA
steve.horii@uphs.upenn.edu

Alexander Horsch

Department of Medical Statistics
and Epidemiology, Technische
Universität München
Munich, Germany
and
Computer Science Department
University of Tromsø
Tromsø, Norway
alexander.horsch@tum.de

H.K. (Bernie) Huang

Image Processing and Informatics
Lab, University of Southern
California, Los Angeles, CA, USA
hkhuang@aol.com

Peter Jensch[†]

OFFIS Institute for Information
Technology, Oldenburg, Germany

Jayashree Kalpathy-Cramer

Department of Medical Informatics
and Clinical Epidemiology
Oregon Health & Science University
Portland, OR, USA
kalpathy@ohsu.edu

Young-Bo Kim

Neuroscience Research Institute
Gachon University of Medicine
and Science, Seoul, Korea
neurokim@gachon.ac.kr

Anh HongTu Le

Image Processing and Informatics
Lab, University of Southern
California, Los Angeles, CA, USA
anhhle@usc.edu

Brent J. Liu

Image Processing and Informatics
Lab, University of Southern
California, Los Angeles, CA, USA
brentliu@usc.edu

Murray H. Loew

Biomedical Engineering Program
Department of Electrical
and Computer Engineering
The George Washington University
Washington, DC, USA
loew@gwu.edu

Roberto A. Lotufo

School of Electrical and Computer
Engineering, State University
of Campinas (UNICAMP)
Campinas, Brazil
lotufo@unicamp.br

Rubens C. Machado

Center for Information Technology
Renato Archer (CTI), Ministry
of Science and Technology (MCT)
Campinas, Brazil
rubens.machado@cti.gov.br

James G. Malcolm

Department of Psychiatry, Brigham
and Women's Hospital, Harvard
Medical School, Boston, MA, USA
malcolm@bwh.harvard.edu

Henning Müller

University of Applied Sciences
Western Switzerland (HES-SO)
Sierre, Switzerland
and
University and Hospitals of Geneva
Geneva, Switzerland
henning.mueller@hevs.ch

Michael Onken

OFFIS Institute for Information
Technology, Oldenburg, Germany
onken@offis.de

Maria Petrou

Informatics and Telematics Institute
Centre for Research
and Technology Hellas (CERTH)
Thessaloniki, Greece
petrou@iti.gr

Bernhard Preim

Department of Simulation and
Graphics, University of Magdeburg
Magdeburg, Germany
preim@isg.cs.uni-magdeburg.de

Yogesh Rath

Department of Psychiatry, Brigham
and Women's Hospital
Harvard Medical School
Boston, MA, USA
yogesh@bwh.harvard.edu

Marcela X. Ribeiro

Computer Science Department
University of São Paulo
São Paulo, Brazil
mxavier@icmc.usp.br

Jörg Riesmeier

ICSMED AG, Oldenburg, Germany
riesmeier@icsmed.de

Leticia Rittner

School of Electrical and Computer
Engineering, State University
of Campinas (UNICAMP)
Campinas, Brazil
lrittner@dca.fee.unicamp.br

Daniel Rueckert

Department of Computing, Imperial
College London, London, UK
d.rueckert@imperial.ac.uk

André V. Saúde

Department of Computer Science
Federal University of Lavras
Lavras, Minas Gerais, Brazil
saude@dcc.ufla.br

Julia A. Schnabel

Institute of Biomedical Engineering
Department of Engineering
Science, University of Oxford
Oxford, UK
julia.schnabel@eng.ox.ac.uk

Young-Don Son

Neuroscience Research Institute
Gachon University of Medicine
and Science, Seoul, Korea
ydson@gachon.ac.kr

Tanveer Syeda-Mahmood

IBM Almaden Research Center
San Jose, CA, USA
stf@almaden.ibm.com

Agma J.M. Traina

Computer Science Department
University of São Paulo
São Paulo, Brazil
agma@icmc.usp.br

Caetano Traina

Computer Science Department
University of São Paulo
São Paulo, Brazil
caetano@icmc.usp.br

Jayaram K. Udupa

Department of Radiology
University of Pennsylvania
Philadelphia, PA, USA
jay@mail.med.upenn.edu

Carolina Y.V. Watanabe

Computer Science Department
University of São Paulo
São Paulo, Brazil
carolina@icmc.usp.br

Carl-Fredrik Westin

Department of Radiology
Brigham and Women's Hospital
Harvard Medical School
Boston, MA, USA
westin@bwh.harvard.edu

Ivo Wolf

Department of Medical Informatics
Mannheim University of Applied
Science, Mannheim, Germany
i.wolf@hs-mannheim.de

Seung-Schik Yoo

Department of Radiology
Brigham and Women's Hospital
Harvard Medical School
Boston, MA, USA
yoo@bwh.harvard.edu

Acronyms

1D	One-Dimensional
2D	Two-Dimensional
3D	Three-Dimensional
4D	Four-Dimensional
AAM	Active Appearance Model
AAPM	American Association of Physicists in Medicine
ABCD	Asymmetry, Border, Color, and Differential structures
ACE	Associative Classifier Engine
ACR	American College of Radiology
ACSE	Association Control Service Element
ADNI	Alzheimer's Disease Neuroimaging Initiative
AE	Application Entity
AFC	Absolute Fuzzy Connectedness
AHA	American Heart Association
AIF	Arterial Input Function
AJAX	Asynchronous Javascript XML
AJCC	American Joint Committee on Cancer
ALM	Acral Lentiginous Melanoma
AMN	Atypical Melanocytic Nevi
ANN	Artificial Neural Network
AOM	Area Overlap Measure
APD	Avalanche Photodiode
API	Application Programming Interface
ASCF	Alternating Sequential Component Filter
ASD	Atrial Septal Defect
ASF	Alternating Sequential Filter
ASM	Active Shape Model
AVD	Absolute Volumetric Difference