

# METHODS IN MOLECULAR BIOLOGY™

*Series Editor*  
**John M. Walker**  
**School of Life Sciences**  
**University of Hertfordshire**  
**Hatfield, Hertfordshire, AL10 9AB, UK**

For further volumes:  
<http://www.springer.com/series/7651>



# **Functional Genomics**

## **Methods and Protocols**

**Second Edition**

Edited by

**Michael Kaufmann and Claudia Klinger**

*Private Universität, Witten/Herdecke gGmbH, Witten, Germany*

 **Humana Press**

*Editors*

Michael Kaufmann, Ph.D.  
Witten/Herdecke University  
Faculty of Health  
School of Medicine  
Center for Biomedical Education and Research  
Institute for Medical Biochemistry  
The Protein Chemistry Group  
58448 Witten  
Stockumer Str. 10  
Germany  
mika@uni-wh.de

Claudia Klinger, Ph.D.  
Witten/Herdecke University  
Faculty of Health  
School of Medicine  
Center for Biomedical Education and Research  
Institute for Medical Biochemistry  
The Protein Chemistry Group  
58448 Witten  
Stockumer Str. 10  
Germany  
cklinger@uni-wh.de

ISSN 1064-3745                      e-ISSN 1940-6029  
ISBN 978-1-61779-423-0          e-ISBN 978-1-61779-424-7  
DOI 10.1007/978-1-61779-424-7  
Springer New York Dordrecht Heidelberg London

Library of Congress Control Number: 2011940130

© Springer Science+Business Media, LLC 2012

All rights reserved. This work may not be translated or copied in whole or in part without the written permission of the publisher (Humana Press, c/o Springer Science+Business Media, LLC, 233 Spring Street, New York, NY 10013, USA), except for brief excerpts in connection with reviews or scholarly analysis. Use in connection with any form of information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed is forbidden.

The use in this publication of trade names, trademarks, service marks, and similar terms, even if they are not identified as such, is not to be taken as an expression of opinion as to whether or not they are subject to proprietary rights.

Printed on acid-free paper

Humana Press is part of Springer Science+Business Media ([www.springer.com](http://www.springer.com))

---

## Preface

The Life Sciences are undergoing more than ever an accelerating evolution currently culminating in the -omics era characterized by the development of a multitude of high-throughput methods that are now getting to be routinely applied in the modern biochemistry lab. While the basic principles of classic analytical methods, such as Northern or Western blot analysis, are still dominating, the individual methods have advanced and continuously morphed into sophisticated techniques, such as expression profiling of whole genomes via DNA microarrays or the use of delicate protein chips to specifically detect thousands of macromolecules simultaneously during one single experiment. Those innovative techniques are capable of delivering tremendous amounts of data accompanied by the need of only trace amounts of samples and at a minimum in both personnel and material costs. The progress in almost every aspect of computer hardware technology obeys Moore's law, i.e., computer performance still grows exponentially at doubling times in the range of months rather than years. In fact, these advances are an indispensable prerequisite to handle data sets typically obtained by today's procedures applied in the field of Functional Genomics.

Now, after almost a decade has passed by since the first edition of this book has been released, the pace in progress of biochemical and biotechnological high-throughput methodologies ultimately requires the release of an updated version. Compared to the first edition, the scope of this book has been extended considerably, now no longer just dealing with DNA microarrays as the pioneering technology that then initiated the establishment of the formerly new field of Functional Genomics. Instead, due to the methodological expansion of Functional Genomics, other high-throughput techniques, for instance those involved in analyzing proteins and metabolites, are also included.

Functional Genomics can be distinguished from Comparative Genomics by its focus on the dynamic aspects of the transcriptome, proteome, and metabolome, respectively. Nevertheless, it is noticeable that in the literature the two disciplines are frequently mentioned in the same breath which prompted us to open this volume with a chapter about Bioinformatics, although with a strong focus on computational tools suitable to make functional predictions. In contrast to most other publications in the field, the following paragraphs are structured with attention to the nature of the biochemical target molecules rather than the different laboratory methods under consideration, i.e., each chapter contains separate discussions about the analysis of DNA, RNA, proteins, and metabolites. Although we are aware that this strategy cannot completely exclude redundancies, we feel that they at least can be reduced to a minimum. Overall, each individual contribution is intended to be self-contained and largely independent from the other chapters of the book. Ideally, each chapter can be seen as a unit of its own which consequently reduces the importance of the order of chapters.

The book is useful for all scientists who plan to establish or extend one of the technologies described here in their own labs. Although short introductions of the basic principles of each procedure are not omitted, the focus of each chapter lies mainly on the practical aspects of each method enabling the reader to easily acquire all the equipment and materials needed

and to successfully perform the experiments autonomously. As often as possible original lab protocols are included, making it easier to reproduce the respective procedures.

Finally, we would like to thank all the contributors for their time, patience, and endurance that undoubtedly was necessary to do such an excellent work. Regarding the reader, we hope that this book will satisfy its intention of being one of the pieces helping him to perform his experiments successfully, which, with respect to everyday lab experience, unfortunately is often an exception rather than the rule in a scientist's real life.

*Witten, Germany*

*Michael Kaufmann  
Claudia Klinger*

---

# Contents

<i>Preface</i> . . . . .	<i>v</i>
<i>Contributors</i> . . . . .	<i>xi</i>
PART I BIOINFORMATICS	
1 Prediction of Protein Tertiary Structures Using MUFOLD . . . . .	3
<i>Jingfen Zhang, Zhiquan He, Qingguo Wang, Bogdan Barz, Ioan Kosztin, Yi Shang, and Dong Xu</i>	
2 Prediction of Protein Functions . . . . .	15
<i>Roy D. Sleator</i>	
3 Genome-Wide Screens for Expressed Hypothetical Proteins . . . . .	25
<i>Claus Desler, Jon Ambæk Durhuus, and Lene Juel Rasmussen</i>	
4 Self-Custom-Made SFP Arrays for Nonmodel Organisms . . . . .	39
<i>Ron Ophir and Amir Sherman</i>	
PART II DNA ANALYSIS	
5 Construction and Analysis of Full-Length and Normalized cDNA Libraries from Citrus . . . . .	51
<i>M. Carmen Marques and Miguel A. Perez-Amador</i>	
6 Assembling Linear DNA Templates for In Vitro Transcription and Translation . . . . .	67
<i>Viktor Stein, Miriam Kaltenbach, and Florian Hollfelder</i>	
7 Automated Computational Analysis of Genome-Wide DNA Methylation Profiling Data from HELP-Tagging Assays . . . . .	79
<i>Qiang Jing, Andrew McLellan, John M. Greally, and Masako Suzuki</i>	
PART III RNA ANALYSIS	
8 Detection of RNA Editing Events in Human Cells Using High-Throughput Sequencing . . . . .	91
<i>Iouri Chepelev</i>	
9 Comparative Study of Differential Gene Expression in Closely Related Bacterial Species by Comparative Hybridization . . . . .	103
<i>Ruisheng An and Parwinder S. Grewal</i>	
10 Whole-Genome RT-qPCR MicroRNA Expression Profiling . . . . .	121
<i>Pieter Mestdagh, Stefaan Derveaux, and Jo Vandesompele</i>	
11 Using Quantitative Real-Time Reverse Transcriptase Polymerase Chain Reaction to Validate Gene Regulation by PTTG . . . . .	131
<i>Siva Kumar Panguluri and Sham S. Kakar</i>	

- 12 FRET-Based Real-Time DNA Microarrays . . . . . 147  
*Arjang Hassibi, Haris Vikalo, José Luis Riechmann,  
 and Babak Hassibi*

#### PART IV PROTEIN ANALYSIS I: QUANTIFICATION AND IDENTIFICATION

- 13 2-D Gel Electrophoresis: Constructing 2D-Gel  
 Proteome Reference Maps . . . . . 163  
*Maria Paola Simula, Agata Notarpietro, Giuseppe Toffoli,  
 and Valli De Re*
- 14 The Use of Antigen Microarrays in Antibody Profiling . . . . . 175  
*Krisztián Papp and József Prechl*
- 15 Limited Proteolysis in Proteomics Using  
 Protease-Immobilized Microreactors. . . . . 187  
*Hiroshi Yamaguchi, Masaya Miyazaki, and Hideaki Maeda*
- 16 Mass Spectrometry for Protein Quantification in Biomarker Discovery . . . . . 199  
*Mu Wang and Jinsam You*

#### PART V PROTEIN ANALYSIS II: FUNCTIONAL CHARACTERIZATION

- 17 High-Throughput Microtitre Plate-Based Assay  
 for DNA Topoisomerases . . . . . 229  
*James A. Taylor, Nicolas P. Burton, and Anthony Maxwell*
- 18 Microscale Thermophoresis as a Sensitive Method to Quantify Protein:  
 Nucleic Acid Interactions in Solution . . . . . 241  
*Karina Zillner, Moran Jerabek-Willemsen, Stefan Duhr,  
 Dieter Braun, Gernot Längst, and Philipp Baaske*
- 19 Bioluminescence Resonance Energy Transfer: An Emerging Tool  
 for the Detection of Protein-Protein Interaction in Living Cells . . . . . 253  
*Soren W. Gersting, Amelie S. Lotz-Havla, and Ania C. Muntau*
- 20 LuMPIS: Luciferase-Based MBP-Pull-Down Protein Interaction  
 Screening System . . . . . 265  
*Maria G. Vizoso Pinto and Armin Baiker*
- 21 Yeast Two-Hybrid Screens: Improvement of Array-Based Screening  
 Results by N- and C-terminally Tagged Fusion Proteins . . . . . 277  
*Thorsten Stellberger, Roman Häuser, Peter Uetz,  
 and Albrecht von Brunn*
- 22 Inducible microRNA-Mediated Knockdown of the Endogenous  
 Human Lamin A/C Gene . . . . . 289  
*Ina Weidenfeld*
- 23 Multiple-Gene Silencing Using Antisense RNAs in *Escherichia coli* . . . . . 307  
*Nobutaka Nakashima, Shan Goh, Liam Good, and Tomohiro Tamura*
- 24 Functional Screen of Zebrafish Deubiquitylating Enzymes  
 by Morpholino Knockdown and In Situ Hybridization . . . . . 321  
*William Ka Fai Tse and Yun-Jin Jiang*



25 Silencing of Gene Expression by Gymnotic Delivery  
of Antisense Oligonucleotides. . . . . 333  
*Harris S. Soifer, Troels Koch, Johnathan Lai, Bo Hansen,  
Anja Hoeg, Henrik Oerum, and C.A. Stein*

26 Polycistronic Expression of Interfering RNAs from RNA  
Polymerase III Promoters . . . . . 347  
*Laura F. Steel and Viraj R. Sanghvi*

PART VI METABOLITE ANALYSIS

27 Metabolite Analysis of *Cannabis sativa* L. by NMR Spectroscopy . . . . . 363  
*Isvett Josefina Flores-Sanchez, Young Hae Choi, and Robert Verpoorte*

28 Metabolome Analysis of Gram-Positive Bacteria  
such as *Staphylococcus aureus* by GC-MS and LC-MS . . . . . 377  
*Manuel Liebeke, Kirsten Dörries, Hanna Meyer, and Michael Lalk*

29 Metabolic Fingerprinting Using Comprehensive Two-Dimensional  
Gas Chromatography – Time-of-Flight Mass Spectrometry . . . . . 399  
*Martin F. Almstetter, Peter J. Oefner, and Katja Dettmer*

*Index*. . . . . 413



---

## Contributors

- MARTIN F. ALMSTETTER • *Institute of Functional Genomics, University of Regensburg, Josef-Engert-Str. 9, Regensburg 93053, Germany*
- RUI SHENG AN • *Department of Entomology, The Ohio State University, 1680 Madison Ave, Wooster, OH 44691, USA*
- PHILIPP BAASKE • *NanoTemper Technologies GmbH, Floessergasse 4, München 81369, Germany*
- MIGUEL A. PEREZ-AMADOR • *Pérez-Amador Instituto de Biología Molecular y Celular de Plantas, CSIC-Universidad Politécnica de Valencia, Ciudad Politécnica de la Innovación, Ingeniero Fausto Elio s/n, 46022, Valencia, Spain*
- ARMIN BAIKER • *Bavarian Health and Food Safety Authority, Oberschleissheim, Germany*
- BOGDAN BARZ • *Department of Physics and Astronomy, University of Missouri, Columbia, MO, USA*
- DIETER BRAUN • *Ludwig-Maximilians-Universität München, System Biophysics, München, Germany*
- NICOLAS P. BURTON • *Inspiralis Ltd, Norwich Bioincubator, Norwich Research Park, Colney, Norwich NR4 7UH, UK*
- IOURI CHEPELEV • *Laboratory of Molecular Immunology, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD 20892, USA*
- YOUNG HAE CHOI • *Pharmacognosy Department/Metabolomics, Gorlaeus Laboratories, Institute of Biology, Leiden University, P.O. Box 9502, RA Leiden 2300, The Netherlands*
- VALLI DE RE • *Experimental and Clinical Pharmacology Unit, CRO Centro di Riferimento Oncologico, IRCCS National Cancer Institute, via F. Gallini 2, Aviano (PN) 33081, Italy*
- STEEFAAN DERVEAUX • *Center for Medical Genetics, Ghent University, De Pintelaan 185, Ghent 9000, Belgium*
- CLAUS DESLER • *Center for Healthy Aging, University of Copenhagen, Blegdamsvej 3, Copenhagen 2200, Denmark*
- KATJA DETTMER • *Institute of Functional Genomics, University of Regensburg, Josef-Engert-Str. 9, Regensburg 93053, Germany*
- KIRSTEN DÖRRIES • *Institute of Pharmacy, Ernst-Moritz-Arndt-Universität Greifswald, Friedrich-Ludwig-Jahn-Str. 17, Greifswald 17487, Germany*
- STEFAN DUHR • *NanoTemper Technologies GmbH, München, Germany*
- JON AMBÆK DURHUUS • *Center for Healthy Aging, Faculty of Health Sciences, University of Copenhagen, Copenhagen N 2200, Denmark*
- ISVETT JOSEFINA FLORES-SANCHEZ • *Institute of Biological Chemistry, Washington State University, Pullman, WA, USA*
- SHAN GOH • *Department of Pathology and Infectious Diseases, Royal Veterinary College, University of London, London, UK*

- LIAM GOOD • *Department of Pathology and Infectious Diseases, Royal Veterinary College, University of London, London, UK*
- JOHN M. GREALLY • *Albert Einstein College of Medicine, Price 322, 1301 Morris Park Avenue, Bronx, NY 10461, USA*
- PARWINDER S. GREWAL • *Department of Entomology, The Ohio State University, 1680 Madison Ave, Wooster, OH 44691, USA*
- ROMAN HÄUSER • *Institute of Toxicology and Genetics, Karlsruhe Institute of Technology (KIT), Eggenstein-Leopoldshafen 76344, Germany*
- BO HANSEN • *Santaris Pharma, Kogle Alle 6, Horsholm DK-2970, Denmark*
- ARJANG HASSIBI • *Institute for Cellular and Molecular Biology, University of Texas, 1 University Station C8800, Austin, TX 78712-0323, USA*
- BABAK HASSIBI • *Electrical Engineering Department, California Institute of Technology, Pasadena, CA 91125, USA*
- ZHIQUAN HE • *Department of Computer Science, University of Missouri, Columbia, MO, USA*
- ANJA HOEG • *Santaris Pharma, Kogle Alle 6, Horsholm DK-2970, Denmark*
- FLORIAN HOLLFELDER • *Department of Biochemistry, University of Cambridge, 80 Tennis Court Road, Cambridge, CB2 1GA, UK*
- MORAN JERABEK-WILLEMSSEN • *NanoTemper Technologies GmbH, München, Germany*
- YUN-JIN JIANG • *Institute of Molecular and Genomic Medicine, National Health Research Institutes, 35 Keyan Road, Zhunan Town, Miaoli County 35053, Taiwan*
- QIANG JING • *Departments of Genetics (Computational Genetics) and Center for Epigenomics, Albert Einstein College of Medicine, 1301 Morris Park Avenue, Bronx, NY, USA*
- SHAM S. KAKAR • *Department of Physiology and Biophysics and James Graham Brown cancer Center, University of Louisville, Clinical and Translational Building, Room 322, Louisville, KY 40202, USA*
- MIRIAM KALTENBACH • *Department of Biochemistry, University of Cambridge, 80 Tennis Court Road, Cambridge, CB2 1GA, UK*
- TROELS KOCH • *Santaris Pharma, Kogle Alle 6, Horsholm DK-2970, Denmark*
- IOAN KOSZTIN • *Department of Physics and Astronomy, University of Missouri, Columbia, MO, USA*
- JOHNATHAN LAI • *Santaris Pharma, Kogle Alle 6, Horsholm DK-2970, Denmark*
- GERNOT LÄNGST • *Universität Regensburg, Biochemistry III, Regensburg, Germany*
- MICHAEL LALK • *Institute of Pharmacy, Interfaculty Institute for Genetics and Functional Genomics, University of Greifswald, F.-L.-Jahnstr. 15, Greifswald D-17487, Germany*
- MANUEL LIEBEKE • *Biomolecular Medicine, Department of Surgery and Cancer, Faculty of Medicine, Imperial College London, London SW7 2AZ, UK*
- AMELIE S. LOTZ-HAVLA • *Department of Molecular Pediatrics, Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University, München 80337, Germany*
- HIDEAKI MAEDA • *Measurement Solution Research Center, National Institute of Advanced Industrial Science and Technology, Tosu, Saga, Japan*
- M. CARMEN MARQUES • *Instituto de Biología Molecular y Celular de Plantas (IBMCP), Universidad Politécnica de Valencia (UPV) and Consejo Superior de Investigaciones Científicas (CSIC), CPI 8E, Ingeniero Fausto Elio s/n, Valencia 46022, Spain*

- ANTHONY MAXWELL • *Department of Biological Chemistry, John Innes Centre, Colney, Norwich NR4 7UH, UK*
- ANDREW McLELLAN • *Departments of Genetics (Computational Genetics) and Center for Epigenomics, Albert Einstein College of Medicine, 1301 Morris Park Avenue, Bronx, NY, USA*
- PIETER MESTDAGH • *Center for Medical Genetics, Ghent University, De Pintelaan 185, Ghent 9000, Belgium*
- HANNA MEYER • *Institute of Pharmacy, Interfaculty Institute for Genetics and Functional Genomics, University of Greifswald, F.-L.-Jahnstr. 15, Greifswald D-17487, Germany*
- MASAYA MIYAZAKI • *Measurement Solution Research Center, National Institute of Advanced Industrial Science and Technology, 807-1 Shuku, Tosu, Saga 841-0052, Japan*
- ANIA C. MUNTAU • *Department of Molecular Pediatrics, Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University, München 80337, Germany*
- NOBUTAKA NAKASHIMA • *Bioproduction Research Institute, National Institute of Advanced Industrial Science and Technology (AIST), 2-17-2-1 Tsukisamu-Higashi, Toyohira-ku, Sapporo 062-8517, Japan*
- AGATA NOTARPIETRO • *Experimental and Clinical Pharmacology Unit, CRO Centro di Riferimento Oncologico, IRCCS National Cancer Institute, via F. Gallini 2, Aviano (PN) 33081, Italy*
- PETER J. OEFNER • *Institute of Functional Genomics, University of Regensburg, Josef-Engert-Str. 9, Regensburg 93053, Germany*
- HENRIK OERUM • *Santaris Pharma, Kogle Alle 6, Horsholm DK-2970, Denmark*
- RON OPHIR • *Institute of Plant Sciences, Agricultural Research Organization, Volcani Research Center, Bet Dagan 50250, Israel*
- SIVA KUMAR PANGULURI • *Department of Anatomical Sciences and Neurobiology, University of Louisville, 500 S Preston Street, HSC A-Tower, room 1001, Louisville, KY 40202, USA*
- KRISZTIÁN PAPP • *Immunology Research Group, ELTE-MTA, Pazmany P.s. 1C, Budapest H-1117, Hungary*
- JÓZSEF PRECHL • *Immunology Research Group, ELTE-MTA, Pazmany P.s. 1C, Budapest H-1117, Hungary*
- LENE JUEL RASMUSSEN • *Center for Healthy Aging, Faculty of Health Sciences, University of Copenhagen, Copenhagen N 2200, Denmark*
- JOSÉ LUIS RIECHMANN • *Division of Biology, California Institute of Technology, Pasadena, CA 91125, USA*
- VIRAJ R. SANGHVI • *Department of Microbiology and Immunology, Institute for Molecular Medicine and Infectious Disease, Drexel University College of Medicine, 245 North 15th Street, Philadelphia, PA 19102, USA*
- YI SHANG • *Department of Computer Science, University of Missouri, Columbia, MO, USA*
- AMIR SHERMAN • *Institute of Plant Sciences, Agricultural Research Organization, Volcani Research Center, Bet Dagan 50250, Israel*
- MARIA PAOLA SIMULA • *Experimental and Clinical Pharmacology Unit, CRO Centro di Riferimento Oncologico, IRCCS National Cancer Institute, via F. Gallini 2, Aviano (PN) 33081, Italy*

- ROY D. SLEATOR • *Department of Biological Sciences, Cork Institute of Technology, Bishopstown, Cork, Ireland*
- HARRIS S. SOIFER • *Department of Oncology, Montefiore Medical Center, Albert Einstein College of Medicine, 111 East 210th Street, Hofheimer 1st Floor, Bronx, NY 10467, USA*
- LAURA F. STEEL • *Department of Microbiology and Immunology, Institute for Molecular Medicine and Infectious Disease, Drexel University College of Medicine, 245 North 15th Street, Philadelphia, PA 19102, USA*
- C.A. STEIN • *Albert Einstein College of Medicine, Albert Einstein-Montefiore Cancer Center, Montefiore Medical Center, 111 E. 210 St. Bronx, NY 10467, USA*
- VIKTOR STEIN • *Department of Biochemistry, University of Cambridge, 80 Tennis Court Road, Cambridge, CB2 1GA, UK*
- THORSTEN STELLBERGER • *Max-von-Pettenkofer-Institut, Lehrstuhl Virologie, Ludwig-Maximilians-Universität (LMU), München, Germany*
- MASAKO SUZUKI • *Departments of Genetics (Computational Genetics) and Center for Epigenomics, Albert Einstein College of Medicine, 1301 Morris Park Avenue, Bronx, NY, USA*
- TOMOHIRO TAMURA • *Bioproduction Research Institute, National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba, Ibaraki, Japan*
- JAMES A. TAYLOR • *Department of Biological Chemistry, John Innes Centre, Colney, Norwich NR4 7UH, UK*
- GIUSEPPE TOFFOLI • *Experimental and Clinical Pharmacology Unit, CRO Centro di Riferimento Oncologico, IRCCS National Cancer Institute, via F. Gallini 2, Aviano (PN) 33081, Italy*
- WILLIAM KA FAI TSE • *Craniofacial Developmental Biology Laboratory, Center for Regenerative Medicine, Massachusetts General Hospital, Harvard Medical School, 185 Cambridge Street, Boston, MA 02114, USA*
- PETER UETZ • *Center for the Study of Biological Complexity, Virginia Commonwealth University, PO Box 842030, 1015 Floyd Ave. Richmond, VA 23284, USA*
- JO VANDESOMPELE • *Center for Medical Genetics, Ghent University, De Pintelaan 185, Ghent 9000, Belgium*
- ROBERT VERPOORTE • *Pharmacognosy Department/Metabolomics, Gorlaeus Laboratories, Institute of Biology, Leiden University, P.O. Box 9502, RA Leiden 2300, The Netherlands*
- HARIS VIKALO • *Electrical and Computer Engineering Department, University of Texas, Austin, TX 78712, USA*
- MARÍA G. VIZOSO PINTO • *Department of Virology, Max von Pettenkofer-Institute, Pettenkoferstr. 9a, München 80336, Germany*
- ALBRECHT VON BRUNN • *Max-von-Pettenkofer-Institut, Lehrstuhl Virologie, Ludwig-Maximilians-Universität (LMU), Pettenkoferstr. 9a, München 80336, Germany*
- MU WANG • *Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, 635 Barnhill Drive, MS 4053, Indianapolis, IN 46202, USA*

QINGGUO WANG • *Department of Computer Science, University of Missouri, Columbia, MO, USA*

INA WEIDENFELD • *Molecular, Cellular, and Developmental Biology, University of Colorado at Boulder, Campus Box 347, Boulder, CO 80309, USA*

DONG XU • *Department of Computer Science, University of Missouri-Columbia, 201 Engineering Building West, Columbia, MO 65211, USA*

HIROSHI YAMAGUCHI • *Measurement Solution Research Center, National Institute of Advanced Industrial Science and Technology, Tosu, Saga, Japan*

JINSAM YOU • *Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, 635 Barnhill Drive, MS 4053, Indianapolis, IN 46202, USA*

JINGFEN ZHANG • *Department of Computer Science, University of Missouri, Columbia, MO, USA*

KARINA ZILLNER • *Universität Regensburg, Biochemistry III, Regensburg, Germany*

