# Lecture Notes in Bioinformatics

4532

Edited by S. Istrail, P. Pevzner, and M. Waterman

Editorial Board: A. Apostolico S. Brunak M. Gelfand T. Lengauer S. Miyano G. Myers M.-F. Sagot D. Sankoff R. Shamir T. Speed M. Vingron W. Wong

Subseries of Lecture Notes in Computer Science

Trey Ideker Vineet Bafna (Eds.)

# Systems Biology and Computational Proteomics

Joint RECOMB 2006 Satellite Workshops on Systems Biology and on Computational Proteomics San Diego, CA, USA, December 1-3, 2006 Revised Selected Papers



#### Series Editors

Sorin Istrail, Brown University, Providence, RI, USA Pavel Pevzner, University of California, San Diego, CA, USA Michael Waterman, University of Southern California, Los Angeles, CA, USA

#### Volume Editors

Trey Ideker University of California Department of Bioengineering San Diego, CA 92093, USA E-mail: tideker@ucsd.edu

Vineet Bafna University of California Computer Science and Engineering Dept. San Diego, CA 92093, USA E-mail: ybafna@cs.ucsd.edu

Library of Congress Control Number: 2007931338

CR Subject Classification (1998): F.2, G.3, E.1, H.2.8, J.3

LNCS Sublibrary: SL 8 – Bioinformatics

ISSN 0302-9743

ISBN-10 3-540-73059-1 Springer Berlin Heidelberg New York ISBN-13 978-3-540-73059-0 Springer Berlin Heidelberg New York

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, re-use of illustrations, recitation, broadcasting, reproduction on microfilms 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.

Springer is a part of Springer Science+Business Media

springer.com

© Springer-Verlag Berlin Heidelberg 2007 Printed in Germany

Typesetting: Camera-ready by author, data conversion by Scientific Publishing Services, Chennai, India Printed on acid-free paper SPIN: 12076215 06/3180 5 4 3 2 1 0

### **Preface**

The RECOMB Satellite Conferences on Systems Biology and Computational Proteomics were held December 1–3, 2006, at La Jolla, California. The Systems Biology meeting brought researchers together on various aspects of systems biology, including integration of genome-wide microarray, proteomic, and metabolomic data, inference and comparison of biological networks, and model testing through design of experiments. Specific topics included:

- Pathway mapping and evolution in protein interaction networks
- Inference of protein signaling networks for understanding cellular responses and developmental programs
- Model prediction of drug mechanism of action and toxicity
- Multi-scale methods which bridge abstract and detailed models
- Systematic design of genome-scale experiments
- Modeling and recognition of regulatory elements
- Identification and modeling of *cis*-regulatory regions
- Modeling the structure and function of regulatory regions
- Comparative genomics of regulation

With the sequencing of the genome, and subsequent identification of the parts list (the gene and their protein products), there is a renewed emphasis on studying the proteome. This year, the computational proteomics meeting focused on on computational mass spectrometry. Mass spectrometry is emerging as a key technology for proteomics. The last few years have seen tremendous improvement in the quality and quantity of available peptide mass spectrometry data, as well as the realization that advanced computational approaches are critical to the success of this technology. The conference explored the use of this technology in various proteomic applications, including, but not limited to: protein identification and quantification in specific cellular environments; structural genomics; networks of protein interaction; post-translational modifications; and others.

We received approximately 50 full paper submissions to the joint workshops. After review, a total of 20 were invited for oral presentations, adding to 14 plenary talks. These papers appear either as extended abstracts in this volume or are published in the journal *Molecular Systems Biology*.

Finally, we gratefully acknowledge support from our sponsors: the International Society for Computational Biology, RECOMB Steering Committee, the California Institute for Telecommunications and Information Technology (Calit2), the UC Discovery Program, and Pfizer La Jolla.

December 2007 Vineet Bafna
Trey Ideker

## Organization

## Program Committee

Annette Adler Agilent

John Aitchison Institute of Systems Biology

Gary Bader Memorial Sloan-Kettering Cancer Center

Vineet Bafna (Co-chair) University of California, San Diego Ron Beavis University of British Columbia Marshall Bern Palo Alto Research Center

Tim Chen University of Southern California Eric Davidson California Institute of Technology

Nathan Edwards University of Maryland

Keith Elliston Genstruct

Eleazar Eskin University of California, San Diego

Tim Galitski Institute of Systems Biology

Mark Gerstein Yale University

Jeff Hasty University of California, San Diego

Ralf Herwig Max Planck Institute for Molecular Genetics

Leroy Hood Institute for Systems Biology
Trey Ideker (Co-chair) University of California, San Diego

Janette Jones Unilever SEAC

Peter Karp Bioinformatics Research Group, SRI Intl

Stuart Kim Stanford University

Edda Klipp Max Planck Institute for Molecular Genetics

Oliver Kohlbacher Universität Tübingen

Douglas Lauffenburger Massachusetts Institute of Technology Mike Levine University of California, Berkeley Bin Ma University of Western Ontario

Edward Marcotte University of Texas

Andrew McCulloch University of California, San Diego

Satoru Miyano University of Tokyo Alexey Nesvizhskii University of Michigan William Noble University of Washington

Bernhard Palsson University of California, San Diego

Dana Pe'er Harvard Medical School

Pavel Pevzner University of California, San Diego Tzachi Pilpel Weizmann Institute of Science

Teresa M. Przytycka NIH/NLM/NCBI
Ben Raphael Brown University
Knut Reinert Freie Universität Berlin
Cenk Sahinalp Simon Fraser University
Ron Shamir Tel Aviv University

#### VIII Organization

Roded Sharan Tel Aviv University

Alfonso Valencia Centro Nacional de Biotecnologia

Guy Warner Unilever SEAC

Christopher Workman Technical University of Denmark John Yates The Scripps Research Institute

Ralf Zimmer Institut für Informatik

## RECOMB Systems Biology Steering Committee

Trey Ideker (Chair) University of California, San Diego

Ron Shamir Tel Aviv University Satoru Miyano University of Tokyo

Douglas Lauffenburger Massachusetts Institute of Technology

Leroy Hood Institute for Systems Biology

## **RECOMB Computational Proteomics Steering Committee**

Vineet Bafna (Chair)

John Yates

Tim Chen

Pavel Pevzner

University of California, San Diego
The Scripps Research Institute
University of Southern California
University of California, San Diego

## Organizing Committee

Vineet Bafna University of California, San Diego Trey Ideker University of California, San Diego Nuno Bandeira University of California, San Diego

Thomas Lemberger MSB BJ Morrison McKay ISMB

Samantha Smeraglia University of California, San Diego Shaojie Zhang University of California, San Diego

## **Sponsoring Institutions**

The International Society for Computational Biology

Molecular Systems Biology

The UC Discovery Grant

Pfizer Inc.

The UCSD Jacobs School of Engineering

Calit2: California Institute for Telecommunications and Information Technology

# Table of Contents

Not All Scale Free Networks Are Born Equal: The Role of the Seed Graph in PPI Network Emulation	1
Probabilistic Paths for Protein Complex Inference	14
Markov Additive Chains and Applications to Fragment Statistics for Peptide Mass Fingerprinting	29
A Context-Specific Network of Protein-DNA and Protein-Protein Interactions Reveals New Regulatory Motifs in Human B Cells	42
Identification and Evaluation of Functional Modules in Gene Co-expression Networks	57
A Linear Discrete Dynamic System Model for Temporal Gene Interaction and Regulatory Network Influence in Response to Bioethanol Conversion Inhibitor HMF for Ethanologenic Yeast	77
A Computational Approach for the Identification of Site-Specific Protein Glycosylations Through Ion-Trap Mass Spectrometry  Yin Wu, Yehia Mechref, Iveta Klouckova, Milos V. Novotny, and Haixu Tang	96
De Novo Signaling Pathway Predictions Based on Protein-Protein Interaction, Targeted Therapy and Protein Microarray Analysis  Derek Ruths, Jen-Te Tseng, Luay Nakhleh, and Prahlad T. Ram	108
Alignment of Mass Spectrometry Data by Clique Finding and Optimization	119
Author Index	131