

The Challenges of Systems Biology Community Efforts to Harness Biological Complexity

Editors

GUSTAVO STOLOVITZKY, PASCAL KAHLEM, AND ANDREA CALIFANO

This volume is the result of the Second Dialogue on Reverse Engineering Assessment and Methods (DREAM2) Challenges, posed to the systems biology community between July and October, 2007; the DREAM2 Conference, held on December 3–4, 2007 at the New York Academy of Sciences in New York; and the ENFIN-DREAM Conference, Assessment of Computational Methods in Systems Biology, held on April 28–29, 2008 in Madrid, Spain.

CONTENTS

Preface. *By* Gustavo Stolovitzky, Pascal Kahlem, and Andrea Califano ix

Part I.

Selected Papers from the ENFIN-DREAM Joint Conference

- Ranking Genes by Their Co-expression to Subsets of Pathway Members. *By*
Priti Adler, Hedi Peterson, Phaedra Agius, Jüri Reimand, and Jaak Vilo 1
- Creating Reference Datasets for Systems Biology Applications Using Text Mining.
By Martin Krallinger, Ana Maria Rojas, and Alfonso Valencia 14

Selected Papers from the DREAM2 Conference

Transcriptional Modules and Regulatory Networks

- The Condition-Dependent Transcriptional Network in *Escherichia coli*. *By* Karen
Lemmens, Tijl De Bie, Thomas Dhollander, Pieter Monsieurs, Bart De
Moor, Julio Collado-Vides, Kristof Engelen, and Kathleen Marchal 29
- Reverse-Engineering Transcriptional Modules from Gene Expression Data. *By*
Tom Michoel, Riet De Smet, Anagha Joshi, Kathleen Marchal, and Yves Van
de Peer 36

Signaling and Metabolic Networks

- Specification of Spatial Relationships in Directed Graphs of Cell Signaling
Networks. *By* Azi Lipshtat, Susana R. Neves, and Ravi Iyengar 44

Uncovering Metabolic Objectives Pursued by Changes of Enzyme Levels. <i>By Sabrina Hoffmann and Hermann-Georg Holzhütter</i>	57
<i>Biological Network Models</i>	
Modeling of Gene Regulatory Network Dynamics Using Threshold Logic. <i>By Tejswati Gowda, Sarma Vrudhula, and Seungehan Kim</i>	71
Global Robustness and Identifiability of Random, Scale-Free, and Small-World Networks. <i>By Yunchen Gong and Zhaolei Zhang</i>	82
<i>Reverse Engineering Algorithms</i>	
The Five-Gene-Network Data Analysis with Local Causal Discovery Algorithm Using Causal Bayesian Networks. <i>By Changwon Yoo and Erik M. Brilz</i>	93
Combining Multiple Results of a Reverse-Engineering Algorithm: Application to the DREAM Five-Gene Network Challenge. <i>By Daniel Marbach, Claudio Mattiussi, and Dario Floreano</i>	102
Network Inference by Combining Biologically Motivated Regulatory Constraints with Penalized Regression. <i>By Fabio Parisi, Heinz Koeppl, and Felix Naef</i> ..	114
<i>Computation Tools for Reverse Engineering</i>	
A Gene Network Simulator to Assess Reverse Engineering Algorithms. <i>By Barbara Di Camillo, Gianna Toffolo, and Claudio Cobelli</i>	125
A Network Inference Workflow Applied to Virulence-Related Processes in <i>Salmonella typhimurium</i>. <i>By Ronald C. Taylor, Mudita Singhal, Jennifer Weller, Saeed Khoshnevis, Liang Shi, and Jason McDermott</i>	143

Part II.

Best Performer Papers from the DREAM2 Challenges

Overview of the DREAM2 Challenges

Lessons from the DREAM2 Challenges: A Community Effort to Assess Biological Network Inference. <i>By Gustavo Stolovitzky, Robert J. Prill, and Andrea Califano</i>	159
---	-----

The BCL6 Target Discovery Challenge Best Performer Papers

DREAM2 Challenge: Integrated Multi-Array Supervised Learning Algorithm for BCL6 Transcriptional Targets Prediction. <i>By W.H. Lee, V. Narang, H. Xu, F. Lin, K.C. Chin, and W.K. Sung</i>	196
A Data Integration Framework for Prediction of Transcription Factor Targets: A BCL6 Case Study. <i>By Matti Nykter, Harri Lähdesmäki, Alistair Rust, Vestein Thorsson, and Ilya Shmulevich</i>	205

Inferring Direct Regulatory Targets of a Transcription Factor in the DREAM2 Challenge. <i>By</i> Vinsensius B. Vega, Xing Yi Woo, Habib Hamidi, Hock Chuan Yeo, Zhen Xuan Yeo, Guillaume Bourque, and Neil D. Clarke	215
<i>The Protein-Protein Interaction Challenge Best Performer Paper</i>	
A Probabilistic Graph-Theoretic Approach to Integrate Multiple Predictions for the Protein-Protein Subnetwork Prediction Challenge. <i>By</i> Hon Nian Chua, Willy Hugo, Guimei Liu, Xiaoli Li, Limsoon Wong, and See-Kiong Ng	224
<i>The Five Gene Network Challenges Best Performer Papers</i>	
Replaying the Evolutionary Tape: Biomimetic Reverse Engineering of Gene Networks. <i>By</i> Daniel Marbach, Claudio Mattiussi, and Dario Floreano	234
Inferring Gene Networks: Dream or Nightmare? Part 1: Challenges 1 and 3. <i>By</i> Angela Baralla, Wiesława I. Mentzen, and Alberto de la Fuente	246
<i>The in Silico Network Challenges Best Performer Papers</i>	
NIRest: A Tool for Gene Network and Mode of Action Inference. <i>By</i> Mario Lauria, Francesco Iorio, and Diego di Bernardo	257
Reverse Engineering of Gene Networks with LASSO and Nonlinear Basis Functions. <i>By</i> Mika Gustafsson, Michael Hörnquist, Jesper Lundström, Johan Björkegren, and Jesper Tegnér	265
Prediction of Pairwise Gene Interaction Using Threshold Logic. <i>By</i> Tejaswi Gowda, Sarma Vrudhula, and Seungchan Kim	276
Inferring Gene Networks: Dream or Nightmare? Part 2: Challenges 4 and 5. <i>By</i> Alan Scheinine, Wiesława I. Mentzen, Giorgio Fotia, Enrico Pieroni, Fabio Maggio, Gianmaria Mancosu, and Alberto de la Fuente	287
<i>The Genome Scale Challenge Best Performer Paper</i>	
Inference of Regulatory Gene Interactions from Expression Data Using Three-Way Mutual Information. <i>By</i> John Watkinson, Kuo-ching Liang, Xiadong Wang, Tian Zheng, and Dimitris Anastassiou	302
Index of Contributors	315

The New York Academy of Sciences believes it has a responsibility to provide an open forum for discussion of scientific questions. The positions taken by the participants in the reported conferences are their own and not necessarily those of the Academy. The Academy has no intent to influence legislation by providing such forums.