PACIFIC SYMPOSIUM ON BIOCOMPUTING 2011

2011 marks the 16th Pacific Symposium on Biocomputing. The impact of two major biomedical research trends are clearly seen in this year's conference. First, the national push towards "translational research" for moving discovery from bench to bedside is manifest in the sessions on integration of biological & clinical data and on personal genomics. Second, the revolution in DNA sequencing similarly impacts our sessions on data integration, genomewide association studies, microbiomes, personal genomics and many of the others too! Thus, we present a conference in which biocomputation is at the forefront of work aimed at bringing the fruits of the genome projects to practical applications. Other sessions focus on the emerging fields of synthetic biology and multiscale modeling. It is an exciting time for the application of computational and informatics technologies to the key problems facing biomedical science.

Indeed, computation has become a recognized component of virtually all major biomedical research efforts, as a cadre of scientists dually trained in biology & medicine as well as computer science, statistics and engineering approach problems of data analysis, fusion, and the generation of new knowledge. The NIH recently renewed the "National Centers for Biomedical Computation" program (http://www.ncbcs.org/). This program grew out of the 1999 "BISTI Report" (Biomedical Information Science and Technology Initiative) which recommended (1) a National Centers program, (2) a program on the principles of information storage, curation, analysis and retrieval, (3) the provision of additional resources for investigators creating and apply biomedical computing tools, (4) the creation of a scaleable national computation, while also disseminating software and data they produce to others via training sessions, workshops and collaborative research relationships. A key function of the centers is to provide a milieu in which biocomputing professional can develop. The PSB meeting is proud to also contribute to the creation of a cadre of skilled professional scientists and engineers, but providing pre-meeting tutorials, travel support for students and post-doctoral fellowships, and opportunities for "bottom up" organization of new sessions.

We would like to thank our keynote speakers. Dr. Vijay Pande, Associate Professor of Chemistry will talk about recent progress in large scale simulation of biological macromolecules. Our keynote in the area of Ethical, Legal and Social Implications of Technology will be Ellen Wright Clayton, the Rosalind E. Franklin Professor of Genetics & Health Policy, and Professor of Law and Pediatrics, at Vanderbilt University. Professor Clayton is a leader in law and genetics.

PSB provides sessions focusing on emerging areas in biomedical computation. These sessions are often conceived at the meeting as people discuss the opportunities for new and exciting sessions. The efforts of a dedicated group of leaders has produced an outstanding set of sessions, with associated introductory tutorials. These organizers provide the scientific core of PSB, and their sessions are as follows:

Computational Methods Integrating Diverse Biological and Clinical Data for Translational Science Gurkan Bebek, Mark Chance, Mehmet Koyuturk, Nathan D. Price

Genome-wide association mapping and rare alleles: from population genomics to personalized medicine Francisco M. De La Vega, Carlos D. Bustamante, Suzanne M. Leal

Microbiome studies: Understanding how the dominant form of life affects us James Foster, Jason Moore

Multi-scale Modelling of Biosystems: from Molecular to Mesoscale Julie Bernauer, Samuel Flores, Xuhui Huang, Seokmin Shin, Ruhong Zhou

Personal Genomics Can Alkan, Emidio Capriotti, Fereydoun Hormozdiari, Eleazar Eskin, Maricel G. Kann

Reverse Engineering and Synthesis of Biomolecular Systems Gil Alterovitz, Silvio Cavalcanti, May Wang, and Marco F. Ramoni With regards to the *Reverse Engineering and Synthesis of Biomolecular Systems* session, we were saddened by the unexpected death of our friend and colleague Dr. Marco Ramoni. Marco was an internationally known computer scientist and Bayesian theorist whose contributions ranged from new understanding of the genetic mechanisms of stroke and asthma to developing novel methodologies. He was a senior faculty member of the Children's Hospital Informatics Program and an Associate Professor of Pediatrics and Medicine at Harvard Medical School and Associate Director of Bioinformatics in Harvard Partners Center for Genetics and Genomics. He will be missed.

We are also pleased to present three workshops, in which investigators with a common interest come together to exchange results and new ideas in a format that is more informal than the peer-reviewed sessions. For this year, the workshops and their organizers are:

Mining the Pharmacogenomics Literature Kevin Bretonnel Cohen, Yael Garten, Udo Hahn, Nigam H. Shah

Identification of Aberrant Pathway and Network Activity from High-Throughput Data Michael Ochs, Rachel Karchin, Habtom Ressom, Robert Gentleman

Validation and Modeling of Electron Cryo-microscopy Structures of Biological Nanomachines Wah Chiu, Helen Berman, Steven Ludtke, Gerard Kleywegt

Finally, we are happy to welcome a new group for a birds-of-a-feather meeting on "Systems Pharmacogenomics." This session is sponsored by the NIH Pharmacogenomics Research Network Statistical Analysis Resource (P-STAR), which is lead by Dr. Marylyn Ritchie under NIH HL065962.

Tiffany Murray continues expertly to manage the peer review process and assembly of the proceedings. We thank the National Institutes of Health and the International Society for Computational Biology (ISCB) for travel grant support. We are particularly grateful to BJ McKay-Morrison at ISCB for her assistance. We also acknowledge the many busy researchers who reviewed the submitted manuscripts on a very tight schedule. The partial list following this preface does not include many who wished to remain anonymous, and of course we apologize to any who may have been left out by mistake.

We look forward to a great meeting once again.

Aloha!

Pacific Symposium on Biocomputing Co-Chairs, September 29, 2010

Russ B. Altman Departments of Bioengineering, Genetics & Medicine, Stanford University

A. Keith Dunker

Department of Biochemistry and Molecular Biology, Indiana University School of Medicine

Lawrence Hunter

Department of Pharmacology, University of Colorado Health Sciences Center

Teri E. Klein

Department of Genetics, Stanford University

Thanks to the reviewers...

Finally, we wish to thank the scores of reviewers. PSB requires that every paper in this volume be reviewed by at least three independent referees. Since there is a large volume of submitted papers, paper reviews require a great deal of work from many people. We are grateful to all of you listed below and to anyone whose name we may have accidentally omitted or who wished to remain anonymous.

Gary Bader Ranjit Bahadur Gurkan Bebek Julie Bernauer Greg Bowman Sharon Browning Mike Brudno John Bunge Anita Burgun Jun Cai Ali Cakmak Sukmohinder Chahal Jack Chen Xian-Ming Chen Cheng Cheng Jacques Chomilier Bradlev Coe Sarah Cohen Boulakia Markus Covert Phuong Dao Pavel Das Mariza De Andrade James Faeder Michael Feig Juan Fernandez-Recio Pawel Gajer Jean Garnier Christopher Haiman Farhad Hormozdiari Bryan Howie Joanna Howson Xuhui Huang Yin-Fu Huang Jui-Hung Hung Thomas Ioerger Andy Itsara Asif Javed

Hui Jiang Eun Yong Kang Ulas Karaoz Parminder Kaur Alon Keinan Sadik Khuder Ken Kidd Sungwan Kim Carl Kingsford Rob Knight Mehmet Koyutürk Charu Gupta Kumar Sadhir Kumar Douglas Lauffenburger Jose Lazano Seunghak Lee Jing Li Qian-Zhong Li Xin Li Liming Liang Pu Liu Ivan Viktorovich Maly Elena Marchiori Eden Martin Andrew McPherson Jason Mezev Karen Nelson Mohammed Orloff Badri Padhukasahasram Andrew Pakstis John Pani Vishal Patel Lynette Phillips Mihai Pop Nathan D. Price Kriti Puniyani Jeroen Raes

Ben Raphael Soumya Raychaudhuri David Reif Marylyn Ritchie Masaki Sasai Dan Schaid Ursel Schuette Josiah Seaman Dong Shen Jana Shen Seokmin Shin Daniel Silva Mitchell Sogin Jean-Marc Stayert Yan Sun Min-Han Tan Nelson Tang Nicholas Tatonetti Cheryl Thompson Duygu Ucar Jerome Waldispuhl Kai Wang Kesheng Wang George Weinstock Dahlia Weiss Scott Weiss Zhen Xia Lei Xie Gokhan Yavas Seungtai Yoon Deniz Yorukoglu Ye Yuzhen GQ Zhang Zemin Zhang Hoghyu Zhao Jasmine Zhou

Prefacev
COMPUTATIONAL METHODS INTEGRATING DIVERSE BIOLOGICAL AND CLINICAL DATA FOR TRANSLATIONAL SCIENCE
Session Introduction
Towards Integrative Gene Prioritization in Alzheimer's Disease
 Systems Biology Analyses of Gene Expression and Genome Wide Association Study Data in Obstructive Sleep Apnea
Finding Most Likely Haplotypes in General Pedigrees through Parallel Search with Dynamic Load Balancing
<i>Dynamic, Multi-Level Network Models of Clinical Trials</i> 38 Marco D. Sorani, Geoffrey T. Manley, J. Claude Hemphill, Sergio E. Baranzini
Mining Functionally Relevant Gene Sets for Analyzing Physiologically Novel Clinical Expression Data
Genotype Phenotype Mapping in RNA Viruses - Disjunctive Normal Form Learning
GENOME-WIDE ASSOCIATION MAPPING AND RARE ALLELES: FROM POPULATION GENOMICS TO PERSONALIZED MEDICINE
Session Introduction
An Application and Empirical Comparison of Statistical Analysis Methods for Associating Rare Variants to a Complex Phenotype
Haplotype Phasing by Multi-Assembly of Shared Haplotypes: Phase-Dependent Interactions Between Rare Variants

An Evaluation of Power to Detect Low-frequency Variant Associations Using Allele-Matching Tests that Account for Uncertainty	0
Eleftheria Zeggini, Jennifer L. Asimit	
Penalized Regression for Genome-wide Association Screening of Sequence Data	6
MICROBIOME STUDIES: UNDERSTANDING HOW THE DOMINANT FORM OF LIFE AFFECTS US	
Session Introduction	8
Estimating the Number of Species with Catchall	1
A Framework for Analysis of Metagenomic Sequencing Data	1
Visualization and Statistical Comparisons of Microbial Communities Using R Packages on Phylochip Data	2
 Human Microbiome Visualization Using 3D Technology	4
Comparing Bacterial Communities Inferred from 16S rRNA Gene Sequencing and Shotgun Metagenomics	5
MULTI-SCALE MODELLING OF BIOSYSTEMS: FROM MOLECULAR TO MESOSCALE	
Session Introduction	7
Computational Generation Inhibitor-Bound Conformers of P38 Map Kinase and Comparison with Experiments	1
Molecular Dynamics Simulations of the Full Triple Helical Region of Collagen Type I Provide an Atomic Scale View of the Protein's Regional Heterogeneity	3
Structural Insights Into Pre-Translocation Ribosome Motions	5

New Conformational Search Method Using Genetic Algorithm and Knot Theory for Proteins......217 Yoshitake Sakae, Tomoyuki Hiroyasu, Mitsunori Miki, Yuko Okamoto

PERSONAL GENOMICS

Session Introduction	229
Can Alkan, Emidio Capriotti, Eleazar Eskin, Fereydoun Hormozdiari, Maricel G. Kann	
The Reference Human Genome Demonstrates High Risk of Type 1 Diabetes and Other Disorders	231
Rong Chen, Atul J. Butte	
Matching Cancer Genomes to Established Cell Lines for Personalized Oncology Joel T. Dudley, Rong Chen, Atul J. Butte	243
Use of Biological Knowledge to Inform the Analysis of Gene-Gene Interactions Involved in Modulating Virologic Failure with Efavirenz-Containing Treatment Regimens in ART-Naïve ACTG Clinical Trials Participants Benjamin J. Grady, Eric C. Torstenson, Paul J. Mclaren, Paul W. De Bakker, David W. Haas, Gregory K. Robbins, Roy M. Gulick, Richard Haubrich, Heather Ribaudo, Marylyn D. Ritchie	253
Visual Integration of Results from a Large DNA Biobank (BioVU) Using Synthesis-View Sarah Pendergrass, Scott M. Dudek, Dan M. Roden, Dana C. Crawford, Marylyn D. Ritchie	265
Multivariate Analysis of Regulatory SNPs: Empowering Personal Genomics by Considering Cis Epistasis and Heterogeneity Stephen D. Turner, William S. Bush	- 276
Haplotype Inference from Single Short Sequence Reads Using a Population Genealogical History Model Jin Zhang, Yufeng Wu	288
REVERSE ENGINEERING AND SYNTHESIS OF BIOMOLECULAR SYSTEMS	
Session Introduction	300
Gil Alterovitz, Silvio Cavalcanti, Taro M. Muso, Marco F. Ramoni, May Wang	
Binary Counting with Chemical Reactions	302
Aleksandra Kharam, Hua Jiang, Marc Riedel	

Defining the Players in Higher-Order Networks: Predictive Modeling for Reverse Engineering Functional Influence Networks Jason E. McDermott, Michelle Archuleta, Susan L. Stevens, Mary P. Stenzel-Poore, Antonio Sanfilippo	314
Rate-Independent Constructs for Chemical Computation Philip Senum, Marc Riedel	326
Towards Real-Time Control of Gene Expression: Controlling the HOG Signaling Cascade Jannis Uhlendorf, Samuel Bottani, Francois Fages, Pascal Hersen, Gregory Batt	338
Identifying Targets for Intervention by Analyzing Basins of Attraction Michael P Verdicchio, Seungchan Kim	350
MINING THE PHARMACOGENOMICS LITERATURE	
Workshop Introduction Kevin Bretonnel Cohen, Yael Garten, Udo Hahn, Nigam H. Shah	362
IDENTIFICATION OF ABERRANT PATHWAY AND NETWORK ACTIVITY FROM HIGH-THROUGHPUT DATA	
Workshop Introduction Michael Ochs, Rachel Karchin, Habtom Ressom, Robert Gentleman	364
VALIDATION AND MODELING OF ELECTRON CRYO-MICROSCOPY STRUCTURES OF BIOLOGICAL NANOMACHINES	
Workshop Introduction	360