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Interdisciplinary dialogue for education, collaboration, and innovation: Intelligent Biology and Medicine in and beyond 2013

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Abstract

The 2013 International Conference on Intelligent Biology and Medicine (ICIBM 2013) was held on August 11-13, 2013 in Nashville, Tennessee, USA. The conference included six scientific sessions, two tutorial sessions, one workshop, two poster sessions, and four keynote presentations that covered cutting-edge research topics in bioinformatics, systems biology, computational medicine, and intelligent computing. Here, we present a summary of the conference and an editorial report of the supplements to *BMC Genomics* and *BMC Systems Biology* that include 19 research papers selected from ICIBM 2013.

Introduction

Built upon the success of last year's conference [1-4], the 2013 International Conference on Intelligent Biology and Medicine (ICIBM 2013) was held on August 11-13, 2013 in Nashville, Tennessee, USA. The primary goal of the conference remains to foster interdisciplinary and multidisciplinary research and to provide education and training opportunities to students and junior investigators who are interested in bioinformatics, systems biology, or intelligent computing. The conference brought together more than 110 participants with diverse backgrounds spanning biology, medicine, computer science, bioengineering, statistics, and mathematics, among others.

We received 65 manuscript and 37 abstract submissions. Compared to last year, we continue to have steady submissions on topic areas including biological network analysis, network medicine, and next-generation sequencing (NGS) data analysis. An emerging research area at ICIBM is proteomics-based research and applications. Thanks to grant support from the National Science Foundation, we were able to provide 21 travel awards to trainees from 19 universities across both the USA and international institutions. The travel awards were selected by the Award Committee from a substantial number of outstanding manuscripts and abstracts that spanned the wide variety of research subjects. In the following section, we present a summary of the scientific program of the conference and an editorial report of the supplements to *BMC Genomics* and *BMC Systems Biology*.

ICIBM 2013 scientific program

The scientific program included four keynote speakers who are world renowned leaders in biomedical informatics, pharmacogenomics, bioinformatics, and systems biology, six scientific sessions, two poster sessions, two tutorials, and one workshop. Here, we briefly review the keynote speakers' lectures followed by the workshop, tutorials, and regular scientific sessions.

Four keynote speakers presented their pioneering research and shared their perspectives of relevant research fields. These speakers were Dr. Lucila Ohno-Machado from the University of California, San Diego, Dr. Dan M. Roden from Vanderbilt University, Dr. A. Keith Dunker from Indiana University, and Dr. Yixue Li from the Chinese Academy of Sciences.

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"*Sharing clinical and genomic data for research: Is it simply a matter of trust?*" Dr. Ohno-Machado presented different models for sharing clinical and genomic data for research, which are designed to accommodate highly diverse policies. She also discussed how her group is currently implementing these models in several projects, such as the University of California Research eXchange initiative. Dr. Ohno-Machado is the Associate Dean for Informatics and Technology at the School of Medicine, University of California, San Diego, the founding Chief of the Division of Biomedical Informatics, and a Professor of Medicine. She is an elected fellow of the American Institute for Medical and Biological Engineering, the American College of Medical Informatics, and the American Society for Clinical Investigation. She is the Editor-In-Chief of the Journal of the American Medical Informatics Association. Her research focuses on predictive modeling, particularly including the evaluation of individualized probabilistic estimates for risk assessment and prognosis.

"*Genetic variation modulating drug response: discovery and implementation*" Dr. Roden introduced BioVU, a resource that links DNA extracted from clinically-obtained blood samples to their de-identified electronic medical record (EMR). BioVU not only enables the discovery of new genomic variants associated with specific clinical phenotypes, but also new phenotypes associated with specific genotypes (i.e. genetic pleiotropy) in an approach Dr. Roden and his team termed "phenome-wide association study" (PheWAS). Dr. Roden also presented the Vanderbilt PREDICT (Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment) program that empowers patients and doctors with the genetic information needed to predict and help prevent adverse side effects of drugs. Dr. Roden served as the Director of the Vanderbilt Arrhythmia Service, the director of the Division of Clinical Pharmacology (1992-2004), and in 2006 was named the Assistant Vice-Chancellor for Personalized Medicine. Dr. Roden has been elected to membership in the American Society for Clinical Investigation and the Association of American Physicians, and he is a fellow of the American Association for the Advancement of Science.

"*An intrinsically disordered protein Swiss-Knife-like toolkit for signaling diversification*" Dr. A. Keith Dunker provided a comprehensive review of intrinsically disordered proteins (IDPs) and their critical role as a multifaceted, Swiss-Knife-like toolkit that enables swift (on an evolutionary time scale) diversification of cell signaling to facilitate the development of metazoans and their rapid evolution. Dr. Dunker is a Professor of Biochemistry and Molecular Biology at Indiana University, where he launched the Center for Computational Biology and Bioinformatics and served as its Director. He is best known for his research in understanding IDPs using bioinformatics approaches and laboratory experiments. He and his collaborators were the first to consider these proteins as a distinct class with important biological functions.

"*Genome sequences of wild and domestic bactrian camels*" Dr. Yixue Li presented draft genome sequences from both a wild and a domestic *Bactrian* camel. The study by Dr. Li and his team reveals the evolutionary history of camels and provides insights on the genetic basis of camels' remarkable salt tolerance and unusual immune system. Dr. Li is the Director of the Shanghai Center for Bioinformation Technology, Vice Director and Professor of the Key Laboratory of Systems Biology at Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences. Dr. Li's research interests include bioinformatics, systems biology, and computational biology.

ICIBM 2013 included one workshop and two tutorials for educational purposes, all of which were much appreciated by the conference participants.

"*Workshop on Next-Generation Sequencing*" This workshop was organized by Dr. Kun Huang from The Ohio State University and Dr. Dongxiao Zhu from Wayne State University. The workshop brought together active researchers in the NGS field and provided an opportunity for them to introduce cutting edge technologies and novel computational methodologies, discuss challenges and opportunities, and interact with the attendees. This workshop had three sessions and nine talks. A majority of the talks introduced new methods for NGS data analysis, including genotype calling, identifying spontaneous mutations in bacteria, metagenomic mining, peak-calling in ChIP-Seq experiments, network-based detection of cancer driver genes, and analysis of allele specific expression. Others presented interesting applications of NGS technologies to studies in autism spectrum disorder, cancer, and pharmacogenomics.

"*Tutorial I: Introduction to Proteome Informatics*" This tutorial was organized by Dr. David L. Tabb from Vanderbilt University, and it had four instructors. The workshop introduced major elements of the protein identification and quantitation pipelines and describes a strategy for proteogenomic experiments with both RNA-Seq and proteomic data. The workshop provided a useful overview of proteome informatics for computer scientists, bioinformaticians, and statisticians who have not previously worked with proteomics data sets.

"*Tutorial II: Pathway and Network Analysis Tutorial*" This tutorial was provided by Dr. Alexander Pico from the Gladstone Institutes and Dr. Jing Wang from Vanderbilt University. Dr. Pico provided a general introduction to WikiPathways, a collaborative platform for building, curating, and distributing biological pathway knowledge for the research community. He also provided a brief

introduction to the powerful network visualization tool Cytoscape. Dr. Wang introduced NetGestalt, a novel web-based data integration framework that allows simultaneous presentation of large-scale experimental and annotation data from various sources in the context of biological networks to facilitate data visualization, analysis, and interpretation.

ICIBM 2013 had six regular scientific sessions for researchers to showcase their original works in the areas of bioinformatics, systems biology, medical informatics, and intelligent computing. The presenters were chosen through a rigorous review process, and their work stood out among the submissions as novel and significant. These sessions were:

Session I: Next Generation Sequencing (NGS): Analysis and Tools
Session II: Network Analysis
Session III: Genomics
Session IV: Systems Biology
Session V: Computational Medicine
Session VI: Intelligent Computing

The details of each session, including session chairs, speakers, and the title and abstract of each talk, are available online [5] and in the conference program book. Here, we provide an editorial report of the supplements to *BMC Genomics* and *BMC Systems Biology* that include 19 research papers selected from 65 manuscripts submitted to ICIBM 2013. Each manuscript was reviewed by at least two reviewers (most by three reviewers) and went through two rounds of reviews. Among the 19 selected papers, 8 are devoted to network analysis methods and their applications to disease studies. Four papers describe new development or careful evaluation of methods for NGS data analysis. Two papers employ proteomic or proteogenomic approaches in human cancer studies. The other papers cover a diverse range of topics.

Network analysis methods and applications

A large proportion of papers focused on network analysis methods and their application to human disease studies. Udyavar et al. [6] applied the weighted gene co-expression network analysis in a lung cancer study and uncovered a signature of signaling hubs closely associated with the small cell lung cancer (SCLC) phenotype. Among the identified hubs, tyrosine kinase SYK emerged as an unsuspected SCLC oncogenic driver and potential therapeutic target. Yu et al. [7] integrated co-expression and the protein interactome to identify network modules of human diseases. The method outperformed the traditional differential expression approach. Budd et al. [8] used a network-based approach that determines the sum node degree for all experimentally verified microRNA targets in order to identify potential regulators of prostate cancer initiation, progression, and metastasis. Shi et al. [9] developed a two-step approach for gene regulatory network identification, featuring an integrated method to identify modularized regulatory structures and subsequently refine their target genes. Ma et al. [10] developed a tool for modeling and visualizing the relationship between different groups of compounds that share similar differential gene expression signatures, termed "Mode of Actions," regarding their therapeutic effect. They then applied the tool to a breast cancer study. Wu et al. [11] built a weighted disease and drug heterogeneous network based on known disease-gene and drug-target relationships and then clustered the network to identify modules and infer putative drug repositioning candidates. Liu et al. [12] proposed the use of graph-based Laplacian regularized logistic regression to integrate biological networks into disease classification and pathway association problems. The algorithm outperformed elastic net and lasso in the simulation studies. The utility of the algorithm was also validated through its ability in reliably differentiating breast cancer subtypes using a breast cancer dataset from The Cancer Genome Atlas (TCGA) consortium. Finally, Jiang et al. [13] proposed a comprehensive framework at the network level to integrate single nucleotide polymorphism (SNP) annotation, target gene assignment, Gene Ontology classification, pathway enrichment analysis, and regulatory network reconstruction to illustrate the molecular functions of prostate cancer-associated SNPs.

NGS data analysis methods and applications

Several papers presented new methods or thorough evaluations of existing methods for the analysis of data derived from metagenomic sequencing, ChIP-Seq, or RNA-Seq. Srinivasan et al. [14] developed an alignment-free n-gram-based method named MetaID that can accurately identify microorganisms at the strain level and estimate the abundance of each organism in a sample given a metagenomic sequencing dataset. Liu et al. [15] developed a novel quantitative method for comparing two biological ChIP-Seq samples, called QChIPat. Their method has several advantages. First, it considers a control (or input) experiment; second, it incorporates a nonparametric empirical Bayes correction normalization; moreover, it provides the binding pattern information among different enriched regions. Guo et al. [16] designed a comprehensive experiment to evaluate six read count-based RNA-Seq analysis methods (DESeq, DEGseq, edgeR, NBPSeq, TSPM and baySeq) using both real and simulated data. They found the six methods produce similar fold changes and reasonable overlapping of differentially expressed genes. However, all six methods suffered from over-sensitivity. Compared to other methods, edgeR achieved a better balance between speed and accuracy.

Liu et al. [17] analyzed RNA-Seq data from kidney renal clear cell carcinoma at both gene- and isoform-levels in an attempt to uncover cancer-stage-dependent expression signatures. They found that isoform expression profiling provides unique and important information that cannot be detected by gene expression profiles. Furthermore, they showed combining gene and isoform expression signatures helps identify advanced stage cancers, predict clinical outcome, and present a comprehensive view of cancer development and progression.

Proteomics in cancer research

Molecular cancer research has been dominated by genomic technologies during the last decade. With recent advancements in proteomics technologies, proteomics and integrative proteogenomics now play an increasingly important role in this field. Sun et al. [18] created the database CanProFu that comprehensively annotates fusion peptides formed by exon-exon linkage between these pairing genes. They applied the database to mass spectrometry datasets of 40 human non-small cell lung cancer (NSCLC) samples and 39 normal lung samples and identified 11 NSCLC-specific gene fusion events. Zhang et al. [19] presented a peptidomics approach to search for novel alternative splicing isoforms in clinical proteomics. Their results showed that the approach has significant potential in enabling the discovery of new types of high-quality alternative splicing isoform biomarkers. Proteomics datasets have also been used to confirm a SCLC gene expression signature identified from microarray data [6].

Other papers in these supplements cover a diverse range of topics. Dai et al. [20] comprehensively analyzed the sequence origin of Pldi-Ak158810 loci, which originated from the inter-genic regions in mice after the divergence of mice and rats. They found that various factors, including rearrangement and transposable elements, contributed to the formation of the sequence. To address the multiple-test correction problem in expression quantitative trail loci (eQTL) studies, Chakraborty et al. [21] developed an approach that takes advantage of an empirical Bayes method and local false discovery rate (lfdr) calculation. Their method better controls the false positive rate compared to traditional methods. Tyaga et al. [22] developed a 3D QSAR model that allows researchers to correlate the structural features of thiosemicarbazone group with their anticancer cathepsin L inhibitory activity through the development of a robust 3D QSAR model. Wang et al. [23] presented a comprehensive model with 128 features that allows accurate prediction of allergenic proteins. They showed the value of the Maximum Relevance Minimum Redundancy (mRMR) method and Incremental Feature Selection (IFS) procedure in feature selection. Lastly, Wang et al. [24] developed a novel approach to automatically generate meaningful annotations for gene sets that are directly tied to relevant articles in literature.

Conference organization

2013 International Conference on Intelligent Biology and Medicine (ICIBM 2013)

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Competing interests

The authors declare that they have no competing interests.

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