The Fifth IEEE International Conference on Systems Biology (IEEE ISB 2011)

Local Organizer

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Organizers

Sponsors

September 2-4, 2011
Zhuhai, Guangdong, China

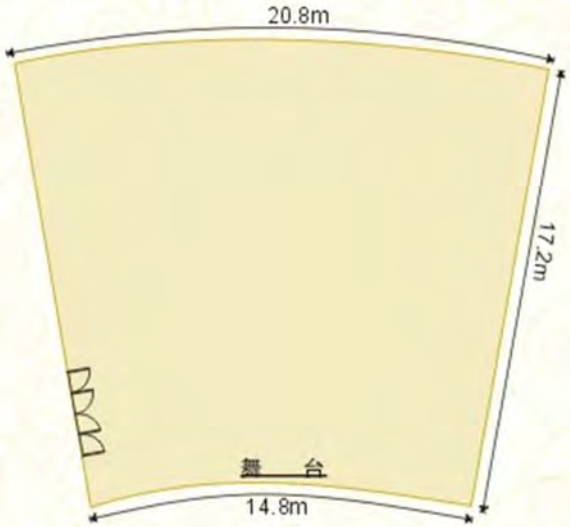
ISB2011 Sessions Locations

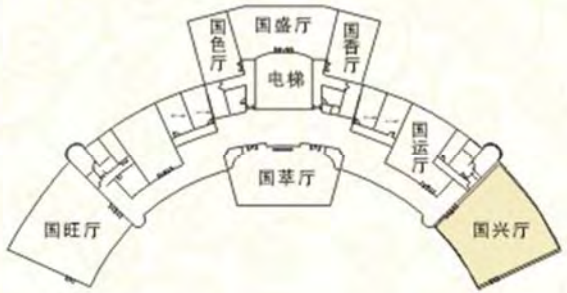
Date		Guo Xing Room	Guo Se Room
September 1 Thursday	**15:00-23:00**	Registration	
	18:00-19:00	Welcome reception	
	19:00-21:30	Board member meeting for Computational Systems Biology Society in ORSC	
September 2 Friday	**Morning 08:00-12:30**	ISB P1 ISB P2	
	Afternoon 13:30-18:30	ISB A1 ISB A2	ISB B1 ISB B2
	Evening 18:30-21:00	Dinner	
September 3 Satursday	**Morning 08:30-12:30**	ISB A3 ISB A4	ISB B3 ISB B4
	Afternoon 13:30-18:30	ISB P3	
		ISB A5	ISB B5
		ISB A6	ISB B6
	Evening 18:30-21:00	Banquet	
September 4 Sunday	**8:00-18:00**	One day sightseeing to Macao city	

Guo Xing Room

国兴厅

4F 国兴厅 Guoxing Room





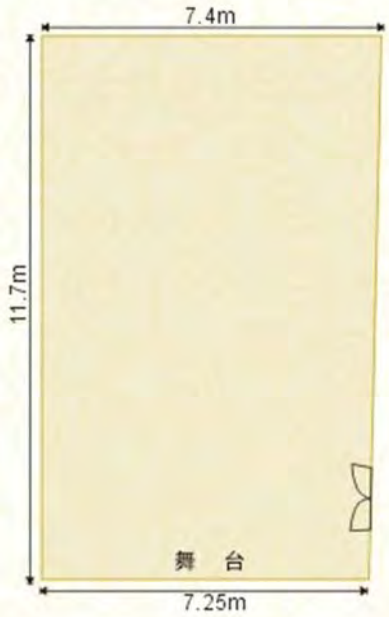
会场面积/Area:302m²
会场楼高/High:3.25m
舞台横幅/Banner:6.4X0.6m
舞台背景/Background:6.4X2.5m

会议厅名 Venue	戏院型 Theatre	课桌型 Classroom	回字型 Hollow	U型 UShape	自助餐 Buffet	酒会 Cocktail	中式围餐 Banquet
国兴厅 Guoxing Room	200	120	50	45	150	设座150人 不设座200人	12

Guo Se Room

国色厅

4F 国色厅 Guose Room



会场面积/Area：97m²
会场楼高/High：2.9m
舞台横幅/Banner：6.4X0.6m
舞台背景/Background：5X2.5m

会议厅名 Venue	戏院型 Theatre	课桌型 Classroom	回字型 Hollow	U型 UShape	自助餐 Buffet	酒会 Cocktail	中式围餐 Banquet
国色厅 Guose Room	60	36	30	30	—	—	—

ISB2011 Schedule

September 1 Thursday	15:00-23:30	Registration (hotel lobby at Zhuhai Dehan Hotel)	
	18:00-19:00	Welcome reception (Zhuhai Dehan Hotel)	
	19:00-21:30	Board member meeting for Computational Systems Biology Society (Guo Se Room in Dehan	
September 2 Friday	08:00-08:30	Opening Session(Guo Xing Room in Zhuhai Dehan Hotel)	
	08:30-10:10	ISB Plenary Session P1 (Guo Xing Room in Zhuhai Dehan Hotel)	
	10:10-10:40	Coffee break	
	10:40-12:20	ISB Plenary Session P2 (Guo Xing Room in Zhuhai Dehan Hotel)	
	12:30-13:30	Lunch (Zhuhai Dehan Hotel)	
	13:30-15:50	ISB Session A1(Guo Xing Room)	ISB Session B1(Guo Se Room)
		Network Medicine I	Structural Systems Biology
	15:50-16:10	Coffee break	
	16:10-18:30	ISB Session A2(Guo Xing Room)	ISB Session B2(Guo Se Room)
		Network Medicine II	Dynamics in Systems Biology I
	18:30-21:00	Dinner (Zhuhai Dehan Hotel)	
September 3 Saturday	08:30-10:10	ISB Session A3(Guo Xing Room)	ISB Session B3(Guo Se Room)
		Network Biology I	Dynamics in Systems Biology II
	10:10-10:40	Coffee break	
	10:40-12:20	ISB Session A4(Guo Xing Room)	ISB Session B4(Guo Se Room)
		Network Biology II	Next Generation Data Analysis
	12:30-13:30	Lunch (Zhuhai Dehan Hotel)	
	13:30-14:20	ISB Plenary Session P3 (Guo Xing Room in Zhuhai Dehan Hotel)	
	14:20-14:40	Break and Discussions	
	14:40-16:20	ISB Session A5(Guo Xing Room)	ISB Session B5(Guo Se Room)
		Network Biology III	Machine Learning Methods
	16:20-16:40	Coffee break	
	16:40-18:20	ISB Session A6(Guo Xing Room)	ISB Session B6(Guo Se Room)
		Bioinformatics I	Bioinformatics II
	18:30-21:00	Banquet	
September 4 Sunday	08:00-18:00	One day excursion in Macao city	

ISB 2011 Program

September 2-4, Zhuhai, Guangdong, China

September 1 (Thursday) Registration

15:00-23:30 Registration, Participants arrival in Zhuhai, check in Zhuhai Dehan Hotel, and Registration package pick up (Hotel Lobby at Zhuhai Dehan Hotel).

18:00-19:00 Welcome Reception (Zhuhai Dehan Hotel)

19:00-21:30 Board member Meeting for Computational Systems Biology Society of ORSC (Guo Se Room in Zhuhai Dehan Hotel)

September 2 (Friday) Technical sessions

07:30-11:30 Registration for late arrivals *(*Hotel Lobby at Zhuhai Dehan Hotel*)*

08:00-08:30 Opening Session for ISB2011 and opening ceremony for Computational Systems Biology Society of ORSC (Guo Xing Room at Zhuhai Dehan Hotel)

Chair: Luonan Chen

8:30-10:10 ISB Plenary Session P1 (Guo Xing Room at Zhuhai Dehan Hotel)

Chair: Luonan Chen

8:30-9:20 TBD

Yijun Ruan

Genomic Technologies, Genome Institute of Singapore, Singapore

Abstract:

9:20-10:10 *A systems biology approach to understanding complex gene regulation in Alzheimer's brain*

Weixiong Zhang

Computer Science and of Genetics, Washington University in Saint Louis, USA

Abstract: Late-onset Alzheimer's disease (AD) is the most common and devastating dementia of the brain. It starts with progressive memory impairment with deficits in executive functioning, language, visual-spatial abilities, personality, behavior and self-care. AD affects a large portion of the aging population around the world and causes serious public health problems. Unfortunately, due to its polygenic nature (meaning that a large number of genes are involved), AD has not yielded to conventional strategies for elucidating genetic mechanisms and for identifying genetic risk factors. My talk will consist of two parts. The first part will focus on our approach to and findings on AD. After briefly describing the AD pathology and AD-related pathways, I will present a general systems-biology approach to complex diseases, such as AD. I will particularly discuss our study on a set of laser-captured single cell-type microarray gene expression data from normal and AD brains, and our results that connect AD with cardiovascular diseases and diabetes. In the second part of my talk, I will discuss one of the two key components of our systems-biology approach, i.e., a method for constructing a co-expression network from microarray gene expression data and a method for identifying community structures (modules) from the network. This analysis helped us identify a co-expressed (and also co-regulated) gene module that contains a large number of disease associated genes.

10:10-10:40 Coffee break

10:40-12:20 ISB Plenary Session P2 (Guo Xing Room at Zhuhai Dehan Hotel)
Chair: Xiang-Sun Zhang

10:40-11:30 *Distance Geometry Problem and Its Applications to Protein Structures*

Yaxiang Yuan
Institute of Computational Mathematics and Scientific/Engineering Computing, Chinese Academy of Sciences, China

Abstract: In this talk, I will discuss the distance geometry problem and its applications to protein structures. The distance geometry problem has many applications such as sensor network localization, image recognition and protein structure identification. We will discuss some theoretical properties of the distance geometry problem, and review numerical methods for this interesting problem. In particular we will discuss a special class of algorithms, namely the gometric build-up algorithms for the solution of the distance geometry problem in protein modeling. Our approach is to minimize the least squares of the errors. I will also discuss techniques for preventing the accumulation of the rounding errors in the geometric build-up calculations. Numerical results on a set of protein structurs are also given to show the efficiency of the geometric build-up approach.

11:30-12:20 *Personal cancer genomes and transcriptomes: lessons learned from lung and liver tumors*

Zemin Zhang
Genentech Inc., USA

Abstract: Next-generation sequencing technologies have greatly reduced the barrier for whole genome and transcriptome analyses of human cancer samples. Using the Complete Genomics platform for whole genome sequencing and the Illumina platform for RNA Seq, we have analyzed multiple lung and liver tumor samples and cell lines. From the comprehensive lung cancer mutational landscape encompassing point mutations, structural variations and copy number alterations, we observed a distinct pattern of selection in various genomic regions and further revealed cigarette smoking as a major source of DNA damaging. Analysis of hepatitis B virus-infected liver cancer patients demonstrated frequent and complex viral DNA integration events in the human genome. We observed a diverse collection of genomic and transcriptional perturbations near viral integration sites, suggesting that widespread viral integration substantially expands carcinogenic opportunities in HBV-infected individuals. We also discuss how such work will pave road for identifying new genomic biomarkers for personalized cancer therapy.

12:00-13:30 Lunch break

13:30-15:50 ISB Session A1 (Guo Xing Room at Zhuhai Dehan Hotel)
Topic: Network Medicine I
Chair: Huarong Zhou

13:30-13:50 *Parallel metabolomics of urine and serum revealed systematic alteration associated with renal disease*

Xianfu Gao, Wanjia Chen, Rongxia Li, Minfeng Wang, Chunlei Chen, Rong Zeng , Yueyi Deng
Key Laboratory of Systems Biology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for B iological Sciences, Chinese Academy of Sciences, China

Paper ID: 68

Abstract: **Background:** Membranous nephropathy is an important glomerular disease characterized by podocyte injury and proteinuria, but no metabolomics research was reported as yet. Here, we performed a parallel metabolomics study, based on human urine and serum, to comprehensively profile systematic metabolic alterations, identify differential metabolites, and understand the pathogenic mechanism of membranous nephropathy. **Results:** There were obvious metabolic distinctions between the membranous nephropathy patients with urine protein lower than 3.5 g/24h (LUPM) and those higher than 3.5 g/24h (HUPM) by PLS-DA model analysis. In total, 26 urine metabolites and 9 serum metabolites were identified to account for such differences, and the majority of metabolites was significantly increased in HUPM patients whether for urines or for serums. Combining the results of urine with serum, all differential metabolites were classified to 5 classes. This classification helps globally insight the systematic metabolic alteration before and after blood flowing through kidney. Citric acid and 4 amino acids were markedly increased only in the serum samples of HUPM patients, implying more impaired filtration function of kidneys of HUPM patients than LUPM patients. The dicarboxylic acids, phenolic acids, and

cholesterol were significantly elevated only in urines of HUPM patients, suggesting more severe oxidative attacks than LUPM patients. **Conclusion:** Parallel metabolomics of urine and serum revealed the systematic metabolic variations associated with LUPM and HUPM patients, where HUPM patients suffered more severe injury of kidney function and oxidative stresses than LUPM patients. This research exhibited a promising application of parallel metabolomics in renal diseases.

13:50-14:10 *The early warning signal of complex diseases based on the network transition entropy*

Rui Liu, Luonan Chen, Kazuyuki Aihara
Collaborative Research Center for Innovative Mathematical Modelling, Institute of Industrial Science, University of Tokyo, Tokyo 153-8505, Japan

Paper ID: 76

Abstract: Many evidences suggested that during the progression of complex diseases, the deteriorations are generally not smooth but abrupt, which may cause a critical transition from one state to another at a tipping point, corresponding to a bifurcation of the dynamical system for the underlying organism. A pre-disease state is assumed to exist before reaching the tipping point between a normal state and a disease state. Since the predisease state is defined as a limit of the normal state, which represents an early-warning signal of the disease, it is crucial to identify such a state so that remedial actions can be executed to avoid the abrupt transition to the disease state. Although most complex diseases are model free, and usually only small samples are available due to clinical limitations, we propose that an index called the network transition entropy (NTE) may serving as an early-warning indicator for predicting the critical transition. Although the theoretical deviation is based on the dynamical network biomarker (DNB), the application of NTE is DNB free.

14:10-14:30 *Phenotype-Difference Oriented Identification of Molecular Functions for Diabetes Progression in Goto-Kakizaki Rat*

Guanying Piao, Bangguo Qian, Shigeru Saito, Zhi-Ping Liu, Tao Zeng, Yong Wang, Jiarui Wu, Huarong Zhou, Luonan Chen and Katsuhisa Horimoto
Key Laboratory of Systems Biology, SIBS-Novo Nordisk Translational Research Centre for Pre-Diabetes, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200233, China

Paper ID: 33

Abstract: In general, molecular signatures of diseases are estimated by comparing the two sets of molecular data measured for the samples with distinctive phenotypes, and then molecular functions of the diseases are characterized by the following analyses of the signatures. Unfortunately, ambiguous relationships between molecular signatures and functions are observed in some cases, due to a posteriori justification from molecular level to phenotype level. Here, we propose a method for detecting molecular functions of the disease by a deductive justification from phenotype level to molecular level, and illustrate its performance by applying our method to the gene expression and phenotype data sets for diabetes progression in Goto-Kakizaki rat. By our method, the functions identified by the previous studies were well covered, and furthermore, some implications for molecular mechanisms were obtained. Our phenotype-difference oriented method provides some clues to bridge directly a gap between molecular signatures and phenotype data in diabetes.

14:30-14:50 *Predicting microRNA targets by integrating sequence and expression data in cancer*

Naifang Su, Yufu Wang, Minping Qian, and Minghua Deng
LMAM, School of Mathematical Sciences, Peking University, Beijing, China

Paper ID: 52

Abstract: Gene regulation is a key factor in gaining a full understanding of molecular biology. microRNA (miRNA), a novel class of non-coding RNA, has recently been found to be one crucial class of post-transactional regulators, and play important parts in cancer. One essential step to understand the regulatory effect of miRNAs is the reliable prediction of their target mRNAs. Typically, the predictions are solely based on sequence information, which unavoidably have high false detection rates. Here we develop a new algorithm called HCTarget, which predict miRNA targets by integrating the typical algorithm and the paired expression profiles of miRNA and mRNA. HCTarget formulates a linear model to characterize the relationship between mRNA and miRNA, and use a Markov Chain Monto Carlo algorithm to learn the target probabilities. When applying HCtarget to the expression data in multiple myeloma, we predict target genes for ten cancer related miRNAs. The experimental verification and a loss of function study of hsa-miR-16 validate our predictions. Compared with the previous approaches, our target sets have increased functional enrichment. Meanwhile, our predicted target pair hsa-miR-19b and SULF1 plays an important role in multiple myeloma. Therefore, HCtarget is a reliable and effective approach to predict miRNA target genes, and could improve our comprehensive understanding of gene regulation.

14:50-15:10 *microRNA expression analysis reveals significant biological pathways in human prostate cancer*

Yifei Tang, Jiajia Chen, Cheng Luo, Antti Kaipia, Bairong Shen
Center for Systems Biology, Center for Systems Biology, Soochow University, Suzhou, China
Paper ID: 50
Abstract: MicroRNAs (miRNAs) are reported to play essential roles in cancer initiation and progression and microarray technologies are intensively applied to study the miRNA expression profile in cancer. It is very common that the set of differentially expressed miRNAs related to the same cancer identified from different laboratories varies widely. Meanwhile, how the altered miRNAs coordinately contribute to the cause of prostate cancer is still not clear. In this study, we collected and processed four human prostate cancer associated miRNA microarray expression datasets with newly developed cancer outlier detection methods to identify differentially expressed miRNAs (DE-miRNAs). The targets of these DE-miRNAs were then extracted from database or predicted by bioinformatics prediction and then mapped to functional databases for enrichment analysis and overlapping comparison. Newly developed outlier detection methods were found to be more appropriate than t-test in cancer research, and the consistency of independent prostate cancer expression profiles at pathway or gene-set level was shown higher than that at gene (i.e. miRNA here) level. Furthermore, we identified 41 Gene Ontology terms, 4 KEGG pathways and 77 GeneGO pathways which are associated with prostate cancer. Among the top 15 GeneGO pathways, 5 were reported previously and the rest could be putative ones. Our analyses showed that more appropriate outlier detection methods should be used to detect oncogenes or oncomiRNAs that are altered only in a subset of samples. We proved that expression signatures of independent microarray experiments are more consistent rather at pathway level than at miRNA / gene level. We also found that the utilization of similar meta-analysis methods between miRNA and mRNA profiling atasets result in the detection of the same pathways.

15:10-15:30 *Antiallodynic effects of microglial interleukin-1β inhibition in the spinal cord*
Yu-Xia Chu, Min Wang, Ming Yao, Xin-Mei Zhou, Xia-Ying Du, Xiao Wan, Zi-Fang Li, Meng-Jia Zhu, Xiao Chen
Department of Physiology College of Medicine, Jiaxing University Jiaxing, China
Paper ID: 37
Abstract: Microglia play a pivotal role in synaptic plasticity of chronic pain. In this study, the potential role of interleukin 1beta (IL-1β), mainly released by microglia in early stage of nerve injury, in mechanical allodynia induced by tetanic stimulation of the sciatic nerve (TSS) was examined. Mechanical allodynia was observed on both ipsilateral and contralateral sides of TSS. Moreover, the expression of the microglial marker Iba-1 and the proinflammatory cytokine IL-1β were significantly increased. Intrathecal injection of the IL-1 receptor antagonist (IL-1ra, 3.5 μg/ml, 20 μl/rat) 30 min before TSS significantly inhibited bilateral mechanical allodynia on day 3, 5 and 7 after TSS. Immunohistochemistry showed that IL-1β was colocalized with the microglial marker OX-42 in the spinal superficial dorsal horn, but not with the astrocytic marker GFAP and the neuronal marker NeuN on day 4 following TSS. The results demonstrate that microglial IL-1β participates in the hypersensitivity of pain behaviors induced by TSS.

15:30-15:50 *Copy Number Detection Using Self-weighted Least Square Regression*
Xiaorong Yang and Ke-Ang Fu
College of Statistics & Mathematics, Zhejiang Gongshang University, Hangzhou, 310018, China
Paper ID: 11
Abstract: In this article, an efficient algorithm to detect the breakpoints in DNA copy number alterations is considered. In view of the influence of the heavy noises, the self-weighted least square estimation is adopted to downweight the covariance matrix of the wild observations (outliers), which ensure the convergence between the estimated parameters and the true values. The proposed approach makes use of the most of the data itself to reduces the complexity of the model, and presents an insightful discussion for discovery of copy number alterations.

13:30-15:50 ISB Session B1 (Guo Se Room at Zhuhai Dehan Hotel)
Topic: Structural Systems Biology
Chair: Jiangning Song

13:30-13:50 *Gradient-based high precision alignment of cryo-electron subtomograms*
Min Xu and Frank Alber
Program in Molecular and Computational Biology, University of Southern California, Los Angeles, CA 90089, USA
Paper ID: 61
Abstract: Whole cell cryo-electron tomography emerges as an important component for structural system biology approaches. It allows the localization and structural characterization of macromolecular complexes in near living conditions. However, the method is hampered by low resolution, missing data and low signal-to-noise ratio (SNR).

To overcome some of these difficulties one can align and average a large sets of subtomograms. Existing alignment methods are mostly based on an exhaustive scanning and sampling of all but discrete relative rotations and translations of one subtomogram with respect to the other. In this paper, we propose a gradient-guided alignment method based on two subtomogram similarity measures. We also propose a stochastic parallel optimization framework, which increases significantly the efficiency for the simultaneous refinement of multiple alignment candidates. Results on simulated data of model complexes and experimental structures of protein complexes show that even for highly distorted subtomograms and with only a small number of very sparsely distributed initial alignment seeds, our method can accurately recover true transformations with a significantly higher precision than scanning based alignment methods.

13:50-14:10 *Characterizing criticality of proteins by system dynamics Using Escherichia coli central carbon metabolism as a working example*

Ru-Dong Li and Lei Liu
Key Laboratory of Systems Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China

Paper ID: 16

Abstract: Systems biology calls for studying system-level properties of genes and proteins rather than their individual chemical/biological properties. Up to date, most studies aiming at this goal are confined to topology-based approach. However, proteins have tertiary structures and specific functional roles, especially in metabolic systems. Thus topological properties such as connectivity, path length, etc., are not good surrogates for protein properties. In the present work, we developed a method to directly assess protein system-level properties based on system dynamics and in silico knockout tests. Applying the method to E. coli central carbon metabolic system, we found that transaldolase and transketolase-b had great impact on the system in terms of both system states and dynamical stability, while glucose-6-phosphate isomerase exerted very little influence. This finding is highly consistent with experimental characterization of metabolic essentiality. We also found that enzymes could affect a distant metabolite or enzyme even greater than a close neighbor. Our work may create a new angle for evaluating protein criticality in a system.

14:10-14:30 *A General Shape Equation for Local Regular Structure of Biomolecular Chains*

Liu Hong and Jinzhi Lei
Zhou Pei-Yuan Center for Applied Mathematics, Tsinghua University, Beijing, China, 100084

Paper ID: 39

Abstract: A general shape equation for the local regular structure of biomolecular chains at the equilibrium state is established. It predicts a general relationship between the structural curvature and torsion, which only concerns about the elastic property of the molecular chain, and is independent of variable conformations of real biomolecules. Solutions corresponding to *alpha*-helix and *beta*-hairpin in proteins, helical DNA, as well as spiral molecules are discussed, which show a fairly well agreement with experimental data.

14:30-14:50 *Predicting functional impact of single amino acid polymorphisms by integrating sequence and structural features*

Mingjun Wang, Hong-Bin Shen, Tatsuya Akutsu, Jiangning Song
State Engineering Laboratory for Industrial Enzymes, Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences, Tianjin 300308, China

Paper ID: 5

Abstract: Single amino acid polymorphisms (SAPs) are the most abundant form of known genetic variations associated with human diseases. It is of great interest to study the sequence-structure-function relationship underlying SAPs. In this work, we collected the human variant data from three databases and divided them into three categories, i.e. cancer somatic mutations (CSM), Mendelian disease-related variant (SVD) and neutral polymorphisms (SVP). We built support vector machine (SVM) classifiers to predict these three classes of SAPs, using the optimal features selected by a random forest algorithm. Consequently, 280 sequence-derived and structural features were initially extracted from the curated datasets from which 18 optimal candidate features were further selected by random forest. Furthermore, we performed a stepwise feature selection to select characteristic sequence and structural features that are important for predicting each SAPs class. As a result, our predictors achieved a prediction accuracy (ACC) of 84.97, 96.93, 86.98 and 88.24%, for the three classes, CSM, SVD and SVP, respectively. Performance comparison with other previously developed tools such as SIFT, SNAP and Polyphen2 indicates that our method provides a favorable performance with higher Sensitivity scores and Matthew's correlation coefficients (MCC). These results indicate that the prediction performance of SAPs classifiers can be effectively improved by feature selection. Moreover, division of SAPs into three respective categories and construction of accurate SVM-based classifiers for each class provides a practically useful way for investigating the difference between Mendelian disease-related variants and cancer somatic mutations.

14:50-15:10 *Heavy metal tolerance of an Antarctic bacterial strain O5 and its antioxidant enzyme*

activity changes induced by Cu2+

Min Wang, Guangfeng Kan, Cuijuan Shi, Qiuju Xie, Yingying Huang, Zhenhuan Lei
School of the Ocean, Harbin Institute of Technology at Weihai, Weihai 264209, China

Paper ID: 64

Abstract: Under the heavy metal polluted circumstances, microorganisms certainly have some changes in terms of species, quantity, community structure and diversity to adapt the environments. Now, many heavy metal tolerant microbe groups have been studied. In the study, a heavy metal tolerant and psychrophilic bacterium strain from Antarctica was screened. Based on 16S rDNA sequence analysis, this strain belongs to *Planococcus*, named as *Planococcus* sp. O5. The capacity of antimetal of *Planococcus* sp. O5 is Pb^{2+} > Cu^{2+} > Hg^{2+} > Cd^{2+} > Zn^{2+}, and the MICs is 320 mg/L, 130 mg/L, 80 mg/L, 80 mg/L and 40 mg/L, respectively. Lipid peroxidation (indicated by malonydialdehyde content) happened in strain O5 induced with Cu^{2+}. At the same time, the antioxidation enzyme activity (such as SOD, POD and CAT) had stimulus-controlled improvement, which is a certain protection against heavy metals. Therefore, as an important feature adapting the stress environments, the activity of antimetal, can reflect the adaptive strategy of microorganism to some extent. This paper studied the activity of antimetal and antioxidation of a bacterial strain, which can help us better understand the bacteria how to adapt the extreme environments.

15:10-15:30 *FastPval: a fast and memory efficient program to calculate very low p-values from empirical distribution*

Mulin Jun Li and Junwen Wang
Department of Biochemistry, LKS Faculty of Medicine,HKU,Hong Kong SAR, China

Paper ID: 28

Abstract: Resampling methods, such as permutation and bootstrap, have been widely used to generate an empirical distribution for assessing the statistical significance of a measurement. However, to obtain a very low p-value, a large size of resampling is required, where computing speed, memory and storage consumption become bottlenecks, and sometimes become impossible, even on a computer cluster. We have developed a multiple stage p-value calculating program called FastPval that can efficiently calculate very low (up to 10-9) p-values from a large number of resampled measurements. With only two input files and a few parameter settings from the users, the program can compute p-values from empirical distribution very efficiently, even on a personal computer. When tested on the order of 109 resampled data, our method only uses 52.94% the time used by the conventional method, implemented by standard quicksort and binary search algorithms, and consumes only 0.11% of the memory and storage. Furthermore, our method can be applied to extra large datasets that the conventional method fails to calculate. The accuracy of the method was tested on data generated from Normal, Poison and Gumbel distributions and was found to be no different from the exact ranking approach. We have applied our method to finding of transcription factor binding sites (TFBS) in promoter region and genome wide association studies (GWAS). It is proved a better computational efficiency and extensive application in bioinformatics statistical measurement. The FastPval executable file, the java GUI and source code, and the java web start server with example data and introduction, are available at http://wanglab.hku.hk/pvalue.

15:30-15:50 *The calibration method research for biology image*

Zilong Liu, Wenli Liu, Rui Chen, Yu Wang, and Ningfang Liao
National Institute of Metrology, Beijing 100013, China

Paper ID: 26

Abstract: Biology image is a main approach of biology research, So the measurement and recognition accurately of biology image, especially the monometer image like cell image, is very important and critical. All these depend on the accurate display of biology image. A key model of standard display function(SDF) for biology image is established at cell level, and measurement images are calibrated by the metrology standard of image using this model. The biology image can be appeared more “true” through this calibration. The SDF of several serial image data at key wavelengths are calibrated using the model, and then these serial data are combined in one image, thus the calibration is achieved. A kind of human erythrocyte image is measured and calibrated correspondly. After calibrated, the chromatism of this image is improved by 3 and the luminance contrast of that is improved by 2.

15:50-16:10 Coffee break

16:10-18:30 ISB Session A2 (Guo Xing Room at Zhuhai Dehan Hotel)

Topic: Network Medicine II

Chair: Bairong Shen

16:10-16:30 *Identification of Master Regulator Candidates for Diabetes Progression in Goto-Kakizaki Rat by a Computational Procedure*

Shigeru Saito, **Yidan Sun**, Zhi-Ping Liu, Yong Wang, Xiao Han, Huarong Zhou, Luonan Chen and Katsuhisa Horimoto
Key Laboratory of Human Functional Genomics of Jiangsu Province, Nanjing Medical University, Nanjing 210029, China
Paper ID: 49
Abstract: Recently, we have identified 39 candidates of active regulatory networks for the diabetes progression in Goto-Kakizaki (GK) rat by using the network screening, which were well consistent with the previous knowledge of regulatory relationship between transcription factors (TFs) and their regulated genes. In addition, we have developed a computational procedure for identifying transcriptional master regulators (MRs) related to special biological phenomena, such as diseases, in conjunction of the network screening and inference. Here, we apply our procedure to identify the MR candidates for diabetes progression in GK rat. First, active TF-gene relationships for three periods in GK rat were detected by the network screening and the network inference, in consideration of TFs with specificity and coverage, and finally only 5 TFs were identified as the candidates of MRs. The limited number of the candidates of MRs promises to perform experiments to verify them.

16:30-16:50 *Context-specific miRNA Regulation Network Predicts Cancer Prognosis*
Xionghui Zhou, Juan Liu, Changning Liu, Simon Rayner, Fengji Liang, Jingfang Ju, Yinghui Li, Shanguang Chen, Jianghui Xiong
School of Computer Science, Wuhan University, Wuhan, P.R. China
Paper ID: 53
Abstract: MicroRNAs can regulate hundreds of target genes and play a pivotal role in a broad range of biological process. However, relatively little is known about how these highly connected miRNAs-target networks are remodelled in the context of various diseases. Here we examine the dynamic alteration of context-specific miRNA regulation to determine whether modified microRNAs regulation on specific biological processes is a useful information source for predicting cancer prognosis. A new concept, Context-specific miRNA activity (CoMi activity) is introduced to describe the statistical difference between the expression level of a miRNA's target genes and non-targets gene within a given gene set (context). The microarray gene expression profile of brain tumors from 356 patients (The Cancer Genome Atlas dataset) was converted into a CoMi activity pattern, and showed significant positive correlation with the corresponding miRNA expression pattern. In a breast cancer cohort, the differential CoMi activity between good prognosis (longer survival) vs bad prognosis patients forms a scale-free network, which highlighted a group of important cancer-related microRNAs and GO terms, e.g. hsa-miR-34a and 'cell adhesion'. Then two breast cancer cohorts were used in outcome prediction in an independent test. Using a popular T-test feature selection method and a support vector machine (SVM) classifier with 10-fold cross-validation, the CoMi activity feature achieves an area under curve (AUC) of 0.7155, better than the AUC value of 0.6339 for feature selection based on mRNA expression. In an independent test, CoMi feature selection achieved an AUC of 0.6874. Survival analysis also shows signatures defined by CoMi activity was predictive of survival and superior to mRNAs signatures. In short, we have demonstrated the first interrogation of dynamic remodeling of context specific miRNAs regulation networks in cancer. The altered microRNAs regulation on specific contexts could be used to predict cancer prognosis and reveal hidden levels of cancer regulation mechanisms.

16:50-17:10 *Numerical Modeling of the Transmission Dynamics of Bird-Flu Epidemic Model*
Wirawan Chinviriyasit, Settapat Chinviriyasit, and Akabut Sirijampa
Department of Mathematics King's Mongkut University of Technology Thonburi, Thailand.
Paper ID: 74
Abstract: A competitive finite-difference method will be constructed and used to solve a modified deterministic model for the spread of bird flu within a given population. Although the developed method in this paper is implicit by construction, it enables the various sub-populations of the model to be monitored explicitly as time t tends to infinity. Furthermore, the method will be seen to be more competitive (in terms of numerical stability) than some well-known methods in the literature. The method is used to to illustrate the effect of bird immigration.

17:10-17:30 *Pathogenesis of axial spondyloarthropathy in a network perspective*
Jing Zhao, Ting-Hong Yang, Jie Chen, and Petter Holme
Department of Mathematics, Logistical Engineering University, Chongqing, Chin;
Department of Natural Medicinal Chemistry Second Military Medical University Shanghai, China
Paper ID: 9
Abstract: Complex chronic diseases are usually not caused by changes in a single causal gene but by an unbalanced regulating network resulting from the dysfunctions of multiple genes or their products. Therefore, network based systems approach can be helpful for the identification of candidate genes related to complex diseases and their relationships. The Axial spondyloarthropathy (SpA) is a group of chronic inflammatory joint

diseases that mainly affects the spine and the sacroiliac joints, yet, the pathogenesis of SpA remains largely unknown. In this paper, we conducted a networked systems study on the pathogenesis of SpA. We integrated data related to SpA, from the OMIM database, proteomics and microarray experiments of SpA, to prioritize SpA candidate disease genes in the context of human protein interactome. Based on the top ranked SpA related genes, we constructed a PPI network and identified potential pathways associated with SpA. The PPI network and pathways reflect the well-known knowledge of SpA, i.e., immune mediated inflammation, as well as imbalanced bone modeling caused new bone formation and bone loss. This study may facilitate our understanding of the SpA pathogenesis from the perspective of network systems.

17:30-17:50 *Dynamics of HBV model with intermittent antiviral therapy*

Ben-gong Zhang, Luonan Chen, and Kazuyuki Aihara
FIRST, Aihara Innovative Mathematical Modelling Project, JST, Japan; Institute of Industrial Science, The University of Tokyo, Japan

Paper ID: 55

Abstract: This paper studies the dynamics of the Hepatitis B virus (HBV) model with intermittent antiviral therapy. We first propose a mathematical model of HBV and then analyze its qualitative and dynamical properties with a new treatment therapy. Combining with the clinical data and theoretical analysis, we show that the intermittent antiviral therapy regimen is one of optimal strategies to treat this kind of complex disease. There are two mainly advantages on this therapy. Firstly, it can delay the drug resistance. Secondly, it can reduce the duration of treatment time comparing with the long term continuous therapy, thereby reducing the adverse side effect. Our results clear provides a new way to treat the HBV disease.

17:50-18:10 *ChIP-Array: Gene Regulation Network Construction from ChIP-seq/chip and mRNA expression data*

Jing Qin, Mulin Li, Panwen Wang, Michael Zhang, Junwen Wang
The University of Hong Kong

Paper ID: 29

Abstract: Chromatin immunoprecipitation (ChIP) coupled with high-throughput techniques (ChIP-X), such as next generation sequencing (ChIP-Seq) and microarray (ChIP–chip), has been successfully used to map active transcription factor binding sites (TFBS) of a transcription factor (TF). The targeted genes can be activated or suppressed by the TF, or are unresponsive to the TF. Microarray technology has been used to measure the actual expression changes of thousands of genes under the perturbation of a TF, but is unable to determine if the affected genes are direct or indirect targets of the TF. Furthermore, both ChIP-X and microarray methods produce a large number of false positives. Combining microarray expression profiling and ChIP-X data allows more effective TFBS analysis for studying the function of a TF. However, current web servers only provide tools to analyze either ChIP-X or expression data, but not both. Here, we present ChIP-Array, a web server that integrates ChIP-X and expression data from human, mouse, yeast, fruit fly and Arabidopsis. This server will assist biologists to detect direct and indirect target genes regulated by a TF of interest and to aid in the functional characterization of the TF. ChIP-Array is available at http://wanglab.hku.hk/ChIP-Array, with free access to academic users.

16:10-18:30 ISB Session B2 (Guo Se Room at Zhuhai Dehan Hotel)

Topic: Dynamics in Systems Biology I

Chair: Ping Ao

16:10-16:30 *Identifying temporal trace of biological process during phase transition*

Tao Zeng, Luonan Chen
Key Laboratory of Systems Biology, SIBS-Novo Nordisk Translational Research Centre for PreDiabetes, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200031

Paper ID: 77

Abstract: Phase transition widely exists in the biological world, such as the transformation of cell cycle phases, cell differentiation stages, cancer development steps, and so on. These are considered as the conversions of a genetic system from one phenotype/genotype to another. In previous studies, the molecular mechanisms of biological phase transition have attracted much attention, in particular, on the different genotypes related to specific phase but less of focus on the cascade of genes' functions during the phase change. However, it is a fundamental but important mission to track the temporal characteristics of a genetic system during specific phase transition or process, which can offer clues for understanding life and advancing its quality. By overcoming the hurdles of traditional time segmentation and temporal biclustering methods, a causal process model (CPM) in the present work is proposed to study the biological phase transition in a systematic way: boundary gene estimation for gene-specific segmentation and temporal block construction for whole data division. After the computational validation on synthetic data, CPM was used to analyze the well-known Yeast cell cycle data to identify the time periods of six phases in two cell cycles, and revealed phase/cycle related biological processes. These primary

results demonstrate that CPM is efficient comparing to traditional methods, and has potential to elucidate the genetic mechanism with more complicated phase transitions.

16:30-16:50 *Kinetics of Muller's Ratchet from Adaptive Landscape Viewpoint*

Shuyun Jiao, Yanbo Wang, Bo Yuan, Ping Ao
Shanghai Center for Systems Biomedicine, Key Laboratory of Systems Biomedicine of Ministry of Education, Shanghai Jiao Tong University, 200240, Shanghai, P.R.China

Paper ID: 7

Abstract: Background: The accumulation of deleterious mutations of a population directly contributes to the fate as to how long the population would exist. Muller's ratchet provides a quantitative framework to study the effect of accumulation. Adaptive landscape as a powerful concept in system biology provides a handle to describe complex and rare biological events. In this article we study the evolutionary process of a population exposed to Muller's ratchet from the new viewpoint of adaptive landscape which allows us estimate the single click of the ratchet starting with an intuitive understanding. Methods: We describe how Wright-Fisher process maps to Muller's ratchet. We analytically construct adaptive landscape from general diffusion equation. It shows that the construction is dynamical and the adaptive landscape is independent of the existence and normalization of the stationary distribution. We generalize the application of diffusion model from adaptive landscape viewpoint. Results: We develop a novel method to describe the
dynamical behavior of the population exposed to Muller's ratchet, and analytically derive the decaying time of the fittest class of populations as a mean first passage time. Most importantly, we describe the absorption phenomenon by adaptive landscape, where the stationary distribution is non-normalizable. These results suggest the method may be used to understand the mechanism of populations evolution and describe the biological processes quantitatively.

16:50-17:10 *Time delay¬accelerated transition of gene switch and ¬enhanced stochastic resonance in a bistable gene regulatory model*

Canjun Wang, Ming Yi, and Keli Yang
Nonlinear Research Institute, Baoji University of Arts and Sciences, Baoji 721016, China

Paper ID: 32

Abstract: The roles of time delay on gene switch and stochastic resonance are systematically explored based on a famous gene transcriptional regulatory model with noises. Our theoretical results show that the time delay can induce the switch, i.e., the TF-A monomer concentration shifts from the high concentration state to the low concentration state ("on"/"off"), and can further accelerate the transition from "on" to"off". Moreover, it is found that the stochastic resonance can be enhanced by the time delay and the correlated noise intensity. However, the additive noise original from the synthesis rate restrains the stochastic resonance. It is very interesting that the resonance bi-peaks structure appears for the large value of the additive noise intensity. The theoretical results by using small-delay timeapproximation approach are consistent well with our numerical simulation.

17:10-17:30 *Synchronization Feature of Coupled cell-cycle Oscillators*

Wei Wang, Xiufen Zou
School of Mathematics and Statistics, Wuhan University, Wuhan430072, China

Paper ID: 48

Abstract: Based on the model of the Xenopus embryonic cell cycle proposed in literature [1], which can exhibit sustained limit cycle oscillations, we first build a multi-cell system of these oscillators that are coupled through a common complex protein that plays an important role in the core regulation of cell-cycle oscillators, and then show synchronization features in this coupled multi-cell system. Through bifurcation analysis and numerical simulations, we give synchronization intervals of the sensitive parameters in the individual oscillator and the coupling parameters in the coupled oscillators. Then, we analyze the effects of these parameters on synchronization time, period and amplitude, and find interesting phenomena, e.g., there are two synchronization intervals of activation coefficient in the Hill function of the activated CDK1 that activates the Plk1, and different synchronization intervals have distinct influences on synchronization time, period and amplitude. More interestingly, we find that the coupled system can switch between a stable state and a stable periodic orbit. These results suggest that the reaction process that the activated cyclin-CDK1 activates the Plk1 has very important influence on the synchronization ability of the coupled system. Our work not only can be viewed as an important step toward the comprehensive understanding for mechanisms of Xenopus embryonic cell cycle and but also can provide the guide for further biological experiments.

17:30-17:50 *Intrinsic Noise Induced State Transition in Coupled Positive and Negative Feedback Genetic Circuit*

Pei Wang, Jinhu Lv, Yuhuan Zhang, and Maciej J. Ogorzalek
Sch. Math. Stat. Wuhan University, Wuhan 430072, China

Paper ID: 73

Abstract: It is well known that gene regulatory circuits can be modeled by the deterministic or stochastic

approach. In this paper, a three-component coupled positive and negative feedback genetic circuit is firstly modeled deterministically by Hill kinetics. Then, a corresponding stochastic model is also investigated by using Gellispie's stochastic simulation. Some typical dynamical behaviors of the genetic circuit are further discussed based on the bifurcation analysis of deterministic system, including monostability, bistability, excitability, and oscillation. This paper aims to further investigate the effect of intrinsic noise inherently in stochastic models on steady states transition. It includes: i) For the parameters in deterministically bistable region, intrinsic noise may induce bistable switch for the not too large system volume, which can be observed by the generation of a new stable steady state; ii) For the parameters in deterministically excitable region, intrinsic noise may induce periodic switch for the very large system volume, which can be observed by the stabilization of another unstable steady state and the switching between two stable states; iii) When time delays are introduced in these two models, similar phenomena can be observed. The above results will certainly increase the understanding of the inner relationships between different modeling for the genetic circuit. It sheds some light on the real- world engineering applications, such as the engineering design of synthetic circuits.

17:50-18:10 *Detecting Coherent Local Patterns from Time Series Gene Expression Data by a Temporal Biclustering Method*

Ji-Bin Qu, Xiang-Sun Zhang, Ling-Yun Wu, Yong Wang, and Luonan Chen
Institute of Applied Mathematics Academy of Mathematics and Systems Science, CAS . Beijing 100190

Paper ID: 81

Abstract: Time-series gene expression data analysis plays an important role in bioinformatics. In this paper, we propose a biclustering method to detect local expression patterns in time-series gene expression data by performing clustering on both gene and time dimensions. Our method aims to find gene subsets which show coherent expression profiles in some time subsets which have a consecutive order in a bicluster. Specifically, our temporal biclustering method is composed of a discretization procedure and a follow-up sequence alignment, which can identify similar local expression profiles and further reveal coherent local relations such as complementary and timelagged coherence. We apply our method to yeast cell cycle data, and find several biologically important biclusters.

18:10-18:30 *A Quantitative Framework of Transcriptional Dynamics by Integrating Multiple Sources of Knowledge*

Shu-Qiang Wang and Han-Xiong Li
Department of Manufacturing Engineering and Engineering, Management City University of Hong Kong,Hong Kong

Paper ID: 57

Abstract: A key challenge in the post genome era is to identify genome-wide transcriptional regulatory networks, which specify the interactions between transcription factors and their target genes. In this work, a regulatory model based binding energy is proposed to quantify the transcriptional regulatory network. Multiple quantities, including binding affinity and the activity level of transcription factor (TF) are incorporated into a general learning model. The sequence features of the promoter and the possible occupancy of nucleosomes are exploited to estimate the binding probability of regulators. Comparing with the previous models that only employ microarray data, the proposed model can bridge the gap between the relative background frequency of the observed nucleotide and the gene's transcription rate. Experimental results show that the proposed model can effectively identify the parameters and the activity level of TF. Moreover, the kinetic parameters introduced in the proposed model can reveal more biological sense than some previous models can do.

18:30-20:30 -Dinner at Zhuhai Dehan Hotel

September 3 (Saturday) Technical sessions

8:30-10:10 ISB Session A3 (Guo Xing Room at Zhuhai Dehan Hotel)

Topic: Network Biology I

Chair: Lin Gao

08:30-08:50 *Neural fate decisions mediated by Notch-Delta signaling*

Ruiqi Wang, Kaihui Liu, and Luonan Chen
Institute of Systems Biology, Shanghai University, Shanghai 200444, China
Paper ID: 69
Abstract: In the developing nervous system, the expression of proneural genes, i.e., *Hes1*, *Neurogenin-2* (*Ngn2*), and *Deltalike-1* (*Dll1*), oscillates in neural progenitors with a period of 2–3 h, but is persistent in postmitotic neurons. In this paper, we present a computational model for neural fate decisions based on intertwined Notch-Delta signaling involving the Hes1, Notch, and Dll1 proteins. In agreement with experimental observations, the model predicts that Notch-Delta signaling plays critical roles in regulating the choice between remaining as a progenitor and embarking on neural differentiation.

08:50-09:10 *Detecting B-cell lymphomas dysregulation modules based on molecular interaction network*

Fu-Yan Hu and Xingming Zhao
Department of Mathematics, Institute of Systems Biology, Shanghai University, Shanghai, China
Paper ID: 25
Abstract: Identifying dysregulation modules for complex diseases, such as B-cell lymphomas, can provide insights into the mechanisms of diseases and help to identify novel drug targets. In this work, based on molecular interaction network, we applied a network flow model to identify the dysregulation modules for three subtypes of non-Hodgkin's lymphomas, including Burkitt's lymphoma (BL), follicular lymphoma (FL), and mantle cell lymphoma (MCL). In our identified dysregulation modules, there are multiple genes that were reported in literature to be related to B-cell lymphomas, which demonstrate that our presented method is really effective for identifying dysregulation modules related to diseases.

09:10-09:30 *Analysis of Gene Expression Profile Triggered by Signal Peptide of Eosinophil Cationic Protein ECPsp triggers gene expression*

Yu-Shu Liu, Chung-Hsaio Chao, Hao-Teng Chang, Yong Wang, Margaret Dah-Tsyr Chang, and Tun-Wen Pai
Graduate Institute of Molecular Systems Biomedicine, College of Medicine, China Medical University, Taichung, Taiwan
Paper ID: 38
Abstract: The signal peptide of eosinophil cationic protein (ECPsp) is known to play an important role in translocating ECP to extracellular space. However, we previously discovered that ECPsp has a novel function of inhibiting microbial growth and regulating the gene expression of tumor growth factor-alpha (TGF-α) and epidermal growth factor receptor (EGFR) in mammalian cells. In the present study, we first generated a DNA microarray dataset, which showed that ECPsp up-regulated inflammatory molecules including cytokines, chemokines, interferon-induced molecules, and Toll-like receptors. We then generated a function linkage network by integrating the microarray dataset with the KEGG pathway database, and discovered that STAT1, an important factor regulating cytokine expression and release, served as a hub to connect the pathways of cytokine stimulation (TGF-α and EGFR) and inflammatory responses. Furthermore, integrating the ECPsp interactome dataset with the functional linkage network elucidated that STAT1 served as a hub to connect 3 functional clusters, including cell proliferation and survival, protein translational regulation, and inflammatory responses. Our approach involving experimental and computational systems biology provided predicted pathways and potential regulation for further characterization of the novel function of ECPsp under inflammatory conditions.

09:30-09:50 *Inferring Domain-Domain Interactions Using an Extended Parsimony Model*

Chen Chen, Jun-Fei Zhao, Qiang Huang, Rui-Sheng Wang, and Xiang-Sun Zhang
National Center for Mathematics and Interdisciplinary Sciences, Institute of Applied Mathematics, Academy of Mathematics and Systems Science, CAS, Beijing 100190
Paper ID: 78
Abstract: High-throughput technologies have produced a large number of protein-protein interactions (PPIs) for different species. As protein domains are functional and structural units of proteins, many computational efforts have been made to identify domain-domain interactions (DDIs) from PPIs. Parsimony assumption is widely used in computational biology as the evolution of the nature is considered as a continuous optimization process. In the context of identifying DDIs, parsimony methods try to find a minimal set of DDIs that can explain the observed PPIs. This category of methods are promising since they can be formulated and solved easily. Besides, researches have shown that they could detect specific DDIs , which is often hard for many probabilistic methods. In this paper, we revisit the parsimony model by presenting two important extensions. First, 'complex networks' as an emerging concept is incorporated as prior knowledge into the parsimony model. With this improvement, the prediction accuracy increases, which to some extent enhances the biological meaning of the common property of complex networks. Second, two randomization tests are designed to show the parsimony nature of the DDIs in mediating PPIs, which corroborates the model validation.

09:50-10:10 *Detecting protein complexes in PPI networks: the roles of interactions*

Xiaoke Ma and Lin Gao

School of Computer Science and Technology, Xidian University, 710071, PR China

Paper ID: 13

Abstract: Studying protein complexes is very important in biological processes since it helps reveal the structure-functionality relationships in protein complexes. Most of the available algorithms are based on the assumption that dense subgraphs correspond to complexes, fail to take into account the inherence organization within protein complex and the roles of edges. To investigate the roles of edges in PPI networks, we show that the edges connecting less similar vertices in topology are more significant in maintaining the global connectivity, indicating the weak ties phenomenon in PPI networks. By using the concept of bridgeness, a reliable virtual network is constructed, in which each maximal clique corresponds to a core. By this notion, the detection of the protein complexes is transformed into a

classic all-clique problem. A novel core-attachment based method is developed, which detects the cores and attachments, respectively. Finally, a comprehensive comparison between the existing algorithms and our algorithm has been made by comparing the predicted complexes against benchmark complexes. The experimental results on the yeast PPI network show that the proposed method outperforms the state-of-the-art algorithms and analysis of detected modules by the present algorithm suggests that most of these modules have well biological significance in context of complexes, implying that the role of interactions is a critical and promising factor in extracting protein complexes.

08:30-10:10 ISB Session B3 (Guo Se Room at Zhuhai Dehan Hotel)

Topic: Dynamics in Systems Biology II

Chair: Tianshou Zhou

08:30-08:50 *Mathematical analysis of malaria transmission model with nonlinear incidences*

Pariyaporn Roop-o, Settapat Chinviriyasit, Waraporn Chatanin, and Wirawan Chinviriyasit

Department of mathematics, King Mongkut's University of Technology Thonburi, Thailand.

Paper ID: 75

Abstract: In this paper, an epidemic model with nonlinear incidences is proposed to describe the dynamics of malaria transmission. The stability of the system can be controlled by the threshold number R_0 which governs the existence and stability of the endemic equilibrium. It is found that the disease-free equilibrium point is locally asymptotically stable when the reproduction number $R_0 < 1$ and the disease always dies out. For $R_0 > 1$, the disease-free equilibrium becomes unstable and the endemic equilibrium is locally asymptotically stable using the general theory of competitive system and compound matrices. Numerical results are shown that the contribution of the nonlinear saturating incidence to the basic reproduction number provides important guidelines for accessing control of malaria diseases.

08:50-09:10 *Extrinsic vs. Intrinsic Noises in Phage Lambda Genetic Switch*

Wei Tian, Hongyuan Zhu, Xue Lei and Ping Ao

Shanghai Center for Systems Biomedicine, Key Laboratory of Systems Biomedicine of Ministry of Education, Shanghai Jiao Tong University, 200240, Shanghai, P.R. China

Paper ID: 17

Abstract: Noises in biological modeling may be classified into two kinds: intrinsic noise, which derives from the variability in dominant molecular interaction and is responsible for the given phenomenon, and extrinsic noise, which arises from other sources, like fluctuations in the environment and so on. Phage lambda is a simple model organism that exhibits important noisy characteristics. It lives in either lysogenic state or lytic state after infecting a bacterium, that is determined by a genetic switch. The mathematical modeling of this genetic switch typically only considers intrinsic noise, though a previous study by one of present authors suggested the critical role of extrinsic noise. In the present study by comparing theoretical results of phage lambda in lysogeny with experiment data, we first achieve good numerical agreements of five constrains of phage lambda for averaged variables. This success indicates that current dominant molecular agents are right. In addition, we confirm the existence of extrinsic noise in lambda genetic switch and find it surprisingly large. This finding calls for an extension of the current mathematical model to better describe the noises. We also point out some possible sources of extrinsic noise.

09:10-09:30 *Bifurcation of an Epidemic Model with Sub-optimal Immunity and Saturated Recovery Rate*

Chang Phang and Yong Hong Wu

Department of Science and Mathematics, Faculty of Science, Technology and Human Development. Universiti Tun Hussein Onn Malaysia.
Paper ID: 41
Abstract: In this paper, we study the bifurcation of an epidemic model with sub-optimal immunity and saturated treatment/recovery rate. Different from classical models, sub-optimal models are more realistic to explain the microparasite infections disease such as Pertussis and Influenza A. By carrying out the bifurcation analysis of the model, we show that for certain values of the model parameters, Hopf bifurcation, Bogdonov- Takens bifurcation and its associated homoclinic bifurcation occur. By studying the bifurcation curves, we can predict the persistence or extinction of diseases.

09:30-09:50 *WinBEST-KIT for Analyzing Multilayer and Multicellular Systems*
Tatsuya Sekiguchi and **Masahiro Okamoto**
Department of Life Sciences and Informatics, Faculty of Engineering, Maebashi Institute of Technology, Maebashi, Gunma 371-0816, Japan
Paper ID: 43
Abstract: Previously, we developed a biochemical reaction simulator called WinBEST-KIT (Biochemical Engineering System analyzing Tool-KIT, which runs under Microsoft Windows) for analyzing complicated metabolic pathways. WinBEST-KIT provides an integrated simulation environment for experimental researchers in metabolic engineering. A particularly notable feature of WinBEST-KIT is that users can easily define and customize reaction symbols in the graphical user interface. Users can use their original kinetic equations, in addition to the pre-installed standard kinetic equations, to represent unknown kinetic mechanisms as reaction steps. However, owing to the increasing size of reaction systems to be analyzed in metabolic pathways, large-scale reaction systems must be divided into several arbitrary compartmental reaction systems and procedures are needed, such as multilayered hierarchical representation, to describe the interactions between the compartmental reaction systems. Accordingly, in this study, we developed a new version of WinBEST-KIT that enables users to construct several arbitrary reaction schemes as layers, to connect the layers, and to analyze the interactions between them. This hierarchical representation is effective for constructing multilayered mathematical models of biochemical systems, such as genome–enzyme–metabolite systems, reaction cascade systems, and multicellular systems.

09:50-10:10 *Finding Optimal Control Policy by Using Dynamic Programming in Conjunction with State Reduction*
Xi Chen and Wai-Ki Ching
AMAC Laboratory, Department of Mathematics, The University of Hong Kong, Hong Kong, China
Paper ID: 60
Abstract: In this paper we study the problem of finding optimal control policy for probabilistic Boolean networks (PBNs). Previous works have been done by using dynamic programmingbased (DP) method. However, due to the high computational complexity of PBNs, DP method is computationally inefficient for large networks. Inspired by the state reduction strategies studied in [10], we consider using dynamic programming in conjunction with state reduction approach to reduce the computational cost of DP method. Numerical examples are given to demonstrate the efficiency of our proposed method.

10:10-10:40 Coffee break

10:40-12:20 ISB Session A4 (Guo Xing Room at Zhuhai Dehan Hotel)
Topic: Network Biology II
Chair: Xiufen Zou

10:40-11:00 *NRProF: Neural Response Based Protein Function Prediction Algorithm*
Hari Krishna Yalamanchili, Junwen Wang, and Quan-Wu Xiao
Department of Biochemistry, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China.
Paper ID: 8
Abstract: A large amount of proteomic data is being generated due to the advancements in high-throughput genome sequencing. But the rate of functional annotation of these sequences falls far behind. To fill the gap between the number of sequences and their annotations, fast and accurate automated annotation methods are

required. Many methods, such as GOblet, GOfigure, and Gotcha, are designed based on the BLAST search. Unfortunately, the sequence coverage of these methods is low as they cannot detect the remote homologues. The lack of annotation coverage of the existing methods advocates novel methods to improve protein function prediction. Here we present a automated protein functional assignment method based on the neural response algorithm, which simulates the neuronal
behavior of the visual cortex in the human brain. The main idea of this algorithm is to define a distance metric that corresponds to the similarity of the subsequences and reflects how the human brain can distinguish different sequences. Given query protein, we predict the most similar target protein using a two layered neural response algorithm and thereby assigned the GO term of the target protein to the query. Our method predicted and ranked the actual leaf GO term among the top 5 probable GO terms with 87.66% accuracy. Results of the 5-fold cross validation and the comparison with PFP and FFPred servers indicate the prominent performance by our method. The NRProF program, the dataset, and help files are available at http://www.jjwanglab.org/NRProF/.

11:00-11:20 *Systematic Reconstruction of Splicing Regulatory Modules by Integrating Many RNA-Seq Datasets*

Chao Dai, Wenyuan Li, Juan Liu, and Xianghong Jasmine Zhou
School of Computer, Wuhan University, Wuhan 430072, PR China

Paper ID: 59

Abstract: Alternative splicing is a ubiquitous gene regulatory mechanism that dramatically increases the complexity of the proteome. In this paper we study splicing module, which we define as a set of cassette exons co-regulated by the same splicing factors. We have designed a tensor-based approach to identify co-splicing clusters that appear frequently across multiple conditions, thus very likely to represent splicing modules – a unit in the splicing regulatory network. In particular, we model each RNA-seq dataset as a co-splicing network, where the nodes represent exons and the edges are weighted by the correlations between exon inclusion rate profiles. We apply our tensor-based method to the 19 co-splicing networks derived from RNA-seq datasets and identify an atlas of frequent co-splicing clusters. We demonstrate that these identified clusters represent splicing modules by validating against four biological knowledge databases. The likelihood that a frequent co-splicing cluster is biologically meaningful increases with its recurrence across multiple datasets, highlighting the importance of the integrative approach. We also demonstrate that the co-splicing clusters reveal novel functional groups which cannot be identified by co-expression clusters, and that the same exons can dynamically participate in different pathways depending on different conditions and different other exons that are co-spliced.

11:20-11:40 *Dynamic remodeling of context-specific miRNAs regulation networks facilitate in silico cancer drug screening*

Lida Zhu, Fengji Liang, Juan Liu, Simon Rayner, Yinghui Li, Shanguang Chen, Jianghui Xiong
School of Computer Science, Wuhan University, Wuhan, P.R. China

Paper ID: 63

Abstract: **Background:** Much effort has been expended in exploring the connections between transcriptome, disease and drug, based on the premise that drug induced perturbations in the transcriptome will affect the phenotype and finally help to cure a disease. MicroRNAs (miRNAs) play a key role in the regulation of the transcriptome and have been identified as a key mediator in human disease and drug response. However, even if miRNA expression can be precisely detected, the information regarding miRNAs action on a particular part of the transcriptome is still lacking. Here, we introduced a novel concept, the Context-specific MiRNA activity (CoMi activity), to reflect a miRNA's regulation effect on a context specific gene set, by calculating the statistical difference between the distributions of its target gene expression and non-target gene expression. In this study we investigate whether CoMi activity could provide a novel perspective on miRNA mechanisms of action in disease and drug response, and facilitate *in silico* drug screening. **Results:** Using breast cancer as an example, we examined the CoMi activity based on a Gene Ontology (GO) term as context. Then we constructed a differential CoMi activity network (cancer vs. normal), based on the comi activity represents as a link between miRNAs and GO terms. (e.g. hsa-miR-27a's regulation on GO term "apoptosis"). The topological analysis of the generated network demonstrated that the cancer specific CoMi network is a scale free network. The highly connected nodes highlighted a group of known onco-miRNAs (e.g. hsa-miR-183*) and tumor suppressor miRNAs (e.g. hsa-miR-34a), as well as some well-known cancer related GO biological processes (e.g. apoptosis). Interestingly, we found that chemotherapeutic drug treatment can counteract the dis-regulated CoMi activity in the cancer-specific network. For instance, 100% of down-regulated CoMi activities in a "core" breast cancer network contains apoptosis- related GO terms that could be counteracted by Paclitaxel treatment. To perform *in silico* drug screening, the similarity of a query CoMi activity signature (e.g. differential CoMi activity in cancer vs. normal) to each of the reference CoMi activities (converted from reference mRNAs expression profiles in the Connectivity Map) was assessed. We found that the most negatively correlated compounds significantly overlapped with known cancer drugs. **Conclusions:** By defining a Stability Index for *in silico* drug screening, we found CoMi activity signatures strikingly outperformed the traditional CMAP method or mRNA-based signatures. Thus, the dynamic remodeling of context-specific miRNAs regulation network could reveal the hidden miRNAs that act as key mediators of drug action and facilitate *in silico* cancer drug screening.

11:40-12:00 *Exploring drug combinations in a drug-cocktail network*

Ke-Jia Xu, Fu-Yan Hu, Jiangning Song, and Xingming Zhao
Department of Mathematics, Institute of Systems Biology, Shanghai University, Shanghai 200444, China

Paper ID: 80

Abstract: Combination of different agents is widely used clinically to combat complex diseases with improved therapy and decreased side effects. It is necessary to understand the underlying mechanisms of drug combinations. In this work, we proposed a network-based approach to investigate drug combinations. Our results showed that the agents in an effective combination tend to have more similar therapeutic effects and more interaction partners in a 'drug-cocktail network' than random combination networks. Based on our results, we further developed a statistical model termed as Drug Combination Predictor (DCPred) by using the topological features of the drugcocktail network, and assessed its prediction performance by making full use of a well-prepared dataset containing all known effective drug combinations extracted from the Drug Combination Database (DCDB). As a result, our model achieved the overall best AUC (Area Under the Curve) score of 0.92. Our findings provide useful insights into the underlying rules of effective drug combinations and offer important clues as to how to accelerate the discovery process of new combination drugs in the future.

10:40-12:20 ISB Session B4 (Guo Se Room at Zhuhai Dehan Hotel)

Topic: Next Generation Data Analysis

Chair: Paul Horton

10:40-11:00 *EpiRegNet: constructing epigenetic regulatory networks from high throughput gene expression data for humans*

Junwen Wang, **Yan Wang**, and Panwen Wang
The University of Hong Kong

Paper ID: 10

Abstract: The advances of high throughput methods, such as microarray gene profiling and RNA-seq, have enabled researchers to identify thousands of differentially expressed genes under a certain perturbation. Much work has been done to understand the genetic factors that contribute to the expression changes by searching the over-represented regulatory motifs in the promoter regions of these genes. However, the changes could also be caused by epigenetic regulation, especially histone modifications, and no web server has been constructed to study the epigenetic factors that are responsible for gene expression changes. Here, we present a web tool for this purpose. Provided with different categories of genes (e. g. up, down regulated or no changed genes), the server will find epigenetic factors that are responsible for the difference among the categories, and construct an epigenetic regulatory network. Furthermore, it will perform co-localization analysis between these epigenetic factors and transcription factors, which were collected from large scale experimental ChIP-seq or computational predicted data. The network can be visualized by a user friendly interface and the data are downloadable in batch. The server currently supports 12 cell types in human, including ESC and CD4+ T cells, and will expand as more public data are available. It also allows user to create a self-defined cell type, upload and analyze multiple ChIP-seq. It is freely available to academic users at http://jjwanglab.org/EpiRegNet.

11:00-11:20 *Next generation sequencing has lower sequence coverage and poorer SNP-detection capability in the regulatory regions*

Weixin Wang, Zhi Wei and Junwen Wang
The University of Hong Kong

Paper ID: 27

Abstract: The rapid development of next generation sequencing (NGS) technology provides a new chance to extend the scale and resolution of genomic research. How to efficiently map millions of short reads to the reference genome and how to make accurate SNP calls are two major challenges in taking full advantage of NGS. In this article, we reviewed the current software tools for mapping and SNP calling, and evaluated their performance on samples from The Cancer Genome Atlas (TCGA) project. We found that BWA and Bowtie are superior to the other alignment tools in comprehensive performance, while SOAP2 has the fastest alignment speed and SHRiMP has the highest coverage. Furthermore, we showed that next-generation sequencing platform has significantly lower coverage and poorer SNP-calling performance in the CpG islands, promoter and 5'-UTR regions of the genome. NGS experiments targeting for these regions should have higher sequencing depth than the normal genomic region.

11:20-11:40 *Parallel-META: A High-Performance Computational Pipeline for Metagenomic Data Analysis*

Xiaoquan Su, Jian Xu, Kang Ning
Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Sciences,

Qingdao, Shandong, China
Paper ID: 45
Abstract: Metagenomics method directly sequences and analyzes genome information from microbial communities. There are usually more than hundreds of genomes from different microbial species in the same community, and the main computational tasks for metagenomics data analysis include taxonomical and functional component of these genomes in the microbial community. Metagenomic data analysis is both data- and computation- intensive, which requires extensive computational power. Most of the current metagenomic data analysis softwares were designed to be used on a single computer, which could not match with the fast increasing number of large metagenomic projects' computational requirements. Therefore, advanced computational methods and pipelines have to be developed to cope with such need for efficient analyses. In this paper, we proposed Parallel-META, a GPU- and multi-core-CPU-based open-source pipeline for metagenomic data analysis, which enabled the efficient and parallel analysis of multiple metagenomic datasets. In Parallel-META, the similarity-based database search was parallelized based on GPU computing and multi-core CPU computing optimization. Experiments have shown that Parallel-META has at least 15 times speed-up compared to traditional metagenomic data analysis method, with the same accuracy of the results (http://www.bioenergychina.org:8800/).

11:40-12:00 *Genomic signatures for metagenomic data analysis: exploiting the reverse complementarity of tetranucleotides*

Fabio Gori, Dimitrios Mavroedis, Mike S.M. Jetten, and Elena Marchiori
Radboud University Nijmegen, iCIS, Nijmegen, The Netherlands
Paper ID: 40
Abstract: Metagenomics studies microbial communities by analyzing their genomic content directly sequenced from the environment. To this aim metagenomic datasets, consisting of many short DNA or RNA fragments, are computationally analyzed using statistical and machine learning methods with the general purpose of binning or taxonomic annotation. Many of these methods act on features derived from the data through a genomic signature, where a typical genomic signature of a fragment is a vector whose entries specify the frequency with which oligonucleotides appear in that fragment. In this article we analyze experimentally the ability of existing genomic signatures to facilitate the discrimination between fragments belonging to different genomes. We also propose new genomic signatures that take into account that fragments can have been sequenced from both strands of a genome; this is achieved by exploiting the reverse complementarity of oligonucleotides. We conduct extensive experiments on in silico sampled genomic fragments in order to assess comparatively the effectiveness of existing genomic signatures and
those proposed in this article. Results of the experiments indicate that the direct use of the reverse complementarity of tetranucleotides in the definition of a genome signatures allows to have performances comparable to the best existing signatures using less features. Therefore the proposed genomic signatures provide an alternative set of features for analyzing metagenomic data. Online Supplementary material is available at http://www.cs.ru.nl/ gori/signature metagenomics/.

12:00-12:20 *A Similarity Network approach for analyzing the marine microbial diversity*

Wei Chen, Yongmei Cheng, Shaowu Zhang, Liyang Hao, Peng Ding
College of Automation, Northwestern Polytechnical University, 710072, Xi'an, China
Paper ID: 47
Abstract: The microbes in the world's oceans are most abundant organisms on earth, playing an important role in the maintenance the balance of marine ecology. However, little knowledge of ecological interdependencies is known due to the limitation of current method for large-scale data and narrow surveys done for marine microbes while microbe exhibited significant inter-lineage associations naturally. Here we present a similarity network-based method to represent and analyze potential interactions among the marine microbes based on the 16S rRNA sequences. A set of parameters such as network degrees, short path, clustering coefficient and so on, are computed to characterize the similarity network topology. A few core sub networks (or network motifs) were found which show that microbe in the marine environment has a cluster propensity and evolutionary relatedness, meanwhile, the variable of network motif also indicated that the microbial diversity has a regional difference. These results show the network-based methods are effective for advance understanding the complexity and function of the marine microbial community after experiment technical.

12:30-13:30 Lunch break

13:30-14:20 ISB Plenary Session P3 (Guo Xing Room at Zhuhai Dehan Hotel)

Chair: Katsuhisa Horimoto

13:30-14:20 *TBD*

Makoto Asashima
Research Center for Stem Cell Engineering, National Institute of Advanced Industrial Science Technology (AIST), Japan; Department of Life Sciences (Biology), Graduate School of Arts and Sciences, The University of Tokyo, Japan; Center for Research and Development Strategy, Japan Science and Technology Agency (JST)

Abstract:

14:20-14:40 Break and Discussions

14:40-16:20 ISB Session A5 (Guo Xing Room at Zhuhai Dehan Hotel)

Topic: Network Biology III

Chair: Yan Zhang

14:40-15:00 *Robustness of CDK2 in Triggering Cellular Senescence based on Probability of DNA-damaged Cells Passing G1/S Checkpoint*

Hong Ling, Sandhya Samarasinghe, and Don Kulasiri
Centre for Advanced Computational Solutions (C-fACS) Lincoln University
Christchurch, New Zealand

Paper ID: 1

Abstract: Recent experiments have shown that cellular senescence, a mechanism employed by cells for thwarting cell proliferation, plays an important role in protecting cells against cancer; therefore, a deeper understanding of cellular senescence can lead to effective cancer treatment. Inhibition of CDK2 is thought to be the critical trigger for cellular senescence. In this study, we first implement a mathematical model of G1/S transition involving the DNA-damage pathway and show that cellular senescence can be achieved by lowering CDK2. The robustness of CDK2 in triggering cellular senescence is determined from the probability (β) of DNA-damaged cells passing G1/S checkpoint for normal CDK2 and CDK2-deficient situations based on different thresholds of the peak time of two important biomarkers, CycE and E2F. The comparison of the values of β under the normal CDK2 and lower CDK2 levels reveals that reducing CDK2 levels can decrease the percentage of damaged cells passing G1/S checkpoint; more importantly, 50% reduction of CDK2 achieves 65% reduction in the percentage of damaged cells passing the G1/S checkpoint. These results point out that the developed model can highlight the possibility of lowering the bar for cellular senescence by reducing CDK2 levels. The results of investigation of β for the different thresholds of the peak times of other biomarkers show that β is insensitive to these perturbations of the peak time indicating that CDK2 activity is robust in lowering the senescence bar for low and high levels of DNA-damage. Furthermore, a mathematical formulation of robustness indicates that the robustness of CDK2 -triggered senescence increases with decreasing levels of CDK2, and is slightly greater for low-level DNA damage condition.

15:00-15:20 *Inferring gene regulatory networks from multiple time course gene expression datasets*

Bo-Lin Chen, Li-Zhi Liu, Fang-Xiang Wu
Division of Biomedical Engineering, University of Saskatchewan, Saskatoon, SK S7N 5A9, Canada

Paper ID: 3

Abstract: We proposed a scheme to infer gene regulatory networks from multiple time course gene expression datasets. As the scarcity of time course data, most current methods usually making the inferred gene regulatory network structure as an illposed one, and typically cannot handle multiple experimental datasets directly. On the other hand, gene expression data generated by different groups worldwide are increasingly accumulated. In this paper, we first formulate the inference of sparse and stable gene regulatory networks as a constraint optimization problem, which can be easily solved by a given single dataset. Then, two methods of network combination are proposed, which can combine structures inferred from various experimental datasets. After that, the parameters in gene regulatory network with that structure are estimated by solving another optimization problem. Finally, we test and validate our methods on synthetic datasets in a series of numerical experiments in terms of the structure accuracy and the model error.

15:20-15:40 *A Modified Newton's Method for Inverse Problem of Probabilistic Boolean Networks with Gene Perturbations*

Wen Li, Wai-Ki Ching, and Lu-Bin Cui

School of Mathematical Sciences, South China Normal University, Guangzhou, China, 510631.
Paper ID: 44
Abstract: Modeling genetic regulatory networks is an important research issue in systems biology. Many mathematical models have been proposed, and among these models, Boolean Network (BN) and its extension Probabilistic Boolean Network (PBN) are popular. In this paper we consider the problem constructing PBNs with gene perturbations. We propose a modified Newton's method to get the gene perturbation probability of the captured problem. Numerical experiments are given to demonstrate both effectiveness and efficiency of our proposed method.

15:40-16:00 *An edge based core-attachment method to detect protein complexes in PPI networks*
Wang Yu, Gao Lin, and Chen Zhe
School of Computer Science and Technology, Xidian University, Xi'an,710071, China
Paper ID: 18
Abstract: Characterization and identification of protein complexes in protein-protein interaction (PPI) networks is important in understanding cellular processes. With the core-attachment concept, a novel core-attachment algorithm is proposed by characterizing the protein complex core from the perspective of edges. We reinvite a protein complex core to be a set of closely interrelated edges rather than a set of interrelated proteins. We first identify the edges must belong to a core, and then partition these edges to extract cores. After that, we select the attachments for each complex core to form a protein complex. Finally, we evaluate the performance of our algorithm by applying it on two different yeast PPI networks. The experimental results show that our algorithm outperforms the MCL, CPM, CoAch in terms of number of precisely predicted protein complexes, localization as well as GO semantic similarity. Our proposed method is validated as an effective algorithm in identifying protein complexes and can provide more insights for future biological study. It proves that edge community is a better topological characterization of protein complex.

16:00-16:20 *A Dynamical Method to Extract Communities Induced by Low or Middle-degree Nodes*
Junhua Zhang, Zhi-Ping Liu, Xiang-Sun Zhang, and Luonan Chen.
Key Laboratory of Random Complex Structures and Data Science, Academy of Mathematics and Systems Science, Chinese Academy of Sciences, Beijing 100190, China
Paper ID: 70
Abstract: Many networks are proved to have community structure. Dense communities have been intensively investigated in recent years, oppositely seldom attention has been paid to sparse ones, which refer to those communities induced by low or middle-degree nodes rather than high-degree components. Recently, it has gradually been recognized that sparse community is also an important structure in biological networks because most disease genes and drug targets are within it. In this paper, we propose a dynamical method to extract sparse communities in complex networks by constructing local synchronization properties of phase oscillators. Compared to dense communities, sparse ones provide more general building and functional blocks in the networks without emphasis on the dominance of internal degrees over outside ones as well as the constraints of high degree connectors.

14:40-16:20 ISB Session B5 (Guo Se Room at Zhuhai Dehan Hotel)

Topic: Machine Learning Methods

Chair: Xingming Zhao

14:40-15:00 *Identifying Biomarkers for Acupuncture Treatment via an Optimization Model*
Yong Wang, Qiao-Feng Wu, Chen Chen, Xian-Zhong Yan, Shu-Guang Yu, Xiang-Sun Zhang, Fan-Rong Liang
National Center for Mathematics and Interdisciplinary Sciences, Academy of Mathematics and Systems Science, Chinese Academy of Sciences, Beijing, China 100190
Paper ID: 67
Abstract: Identifying biomarkers for acupuncture treatment is crucial to understand the mechanism of acupuncture effect at molecular level. In this study, we investigate the metabolic profiles of acupuncture treatment on several meridian points in human. To identify the subsets of metabolites that best characterize the acupuncture effect for each meridian point, a linear programming based model is proposed to identify biomarkers from the high-dimensional metabolic data. Specifically, we use nearest centroid as prototype to simultaneously minimize the number of selected features and leave-one-out cross validation error of the classifier. As a result, we reveal novel metabolite biomarkers for acupuncture treatment. Our result demonstrates that metabolic profiling might be

a promising method to investigating the molecular mechanism of acupuncture. Comparison with other existing methods shows the efficiency and effectiveness of our new method. In addition, the method proposed in this paper is general and can be used in other high-dimensional applications, such as cancer genomics.

15:00-15:20 *Protein Interaction Prediction for Mouse PDZ Domains Using Dipeptide Composition Features*

Songyot Nakariyakul, Zhi-Ping Liu, and Luonan Chen
Key Laboratory of Systems Biology, SIBS-Novo Nordisk Translational Research Centre for PreDiabetes, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200031, China; Department of Electrical and Computer Engineering, Thammasat University, Khlong Luang, Pathumthani 12120, Thailand

Paper ID: 36

Abstract: The PDZ domain is one of the largest families of protein domains that are involved in targeting and routing specific proteins in signaling pathways. PDZ domains mediate protein-protein interactions by binding the C-terminal
peptides of their target proteins. Using the dipeptide feature encoding, we develop a PDZ domain interaction predictor using a support vector machine that achieves a high accuracy rate of 82.49%. Since most of the dipeptide compositions are redundant and irrelevant, we propose a new hybrid feature selection technique to select only a subset of these compositions that are useful for interaction prediction. Our experimental results show that only approximately 25% of dipeptide features are needed and that our method increases the accuracy by 3%. The selected dipeptide features are analyzed and shown to have important roles on specificity pattern of PDZ domains.

15:20-15:40 *Evolutionary sequence divergence predicts protein sub-cellular localization signals*

Yoshinori Fukasawa, Ross KK Leung, Stephen KW Tsui, and Paul Horton
Department of Computational Biology, Graduate School of Frontier Sciences, University of Tokyo, Kashiwa, Japan

Paper ID: 65

Abstract: Protein sub-cellular localization is a central problem in understanding cell biology and has been the focus of intense research. In order to predict localization from amino acid sequence a myriad of features have been tried: including amino acid composition, sequence similarity, the presence of certain motifs or domains, and many others. Surprisingly, sequence conservation of sorting motifs has not yet been employed, despite its extensive use for tasks such as the prediction of transcription factor binding sites. Here, we flip the problem around, and present a proof of concept for the idea that the *lack* of sequence conservation can be a useful feature for localization prediction.

15:40-16:00 *Discriminative Random Field Approach to Prediction of Protein Residue Contacts*

Mayumi Kamada, Morihiro Hayashida, Jiangning Song, and Tatsuya Akutsu
Bioinformatics Center, Institute for Chemical Research, Kyoto University, Gokasho, Uji, Kyoto, 611-0011, Japan

Paper ID: 62

Abstract: Understanding of interactions of proteins is important to reveal networks and functions of molecules. Many investigations have been conducted to analyze interactions and contacts between residues. It is supported that residues at interacting sites have co-evolved with those at the corresponding residues in the partner protein to keep the interactions between the proteins. Therefore, mutual information (MI) between residues calculated from multiple sequence alignments of homologous proteins is considered to be useful for identifying contact residues in interacting proteins. In our previous work, we proposed a prediction method for protein-protein interactions using mutual information and conditional random fields (CRFs), and confirmed its usefulness. The discriminative random field (DRF) is a special type of CRFs, and can recognize some specific characteristic regions in an image. Since the matrix consisted of mutual information between residues in two interacting proteins can be regarded as an image, we propose a prediction method for protein residue contacts using DRF models with mutual information. To validate our method, we perform computational experiments for several interactions between Pfam domains. The results suggest that the proposed DRF-based method with MI is useful for predicting protein residue contacts compared with that using the corresponding Markov random field (MRF) model.

16:00-16:20 *Evaluating the denoising techniques in protein-protein interaction prediction*

Yong-Cui Wang, Xian-Wen Ren, Nai-Yang Deng, and Xiang-Sun Zhang
Key Laboratory of Adaptation and Evolution of Plateau Biota, Northwest Institute of Plateau Biology, Chinese Academy of Science, Xining, China, 810001

Paper ID: 19

Abstract: The past decades witnessed extensive efforts to study the relationships among proteins. Particularly, sequence-based protein-protein interactions (PPIs) prediction is fundamentally important in speeding up the

process of mapping interactomes of organisms. The composition vectors are usually constructed to encode proteins as real-value vectors, which is feeding to a machine learning framework. However, the composition vector value might be highly correlated to the distribution of amino acids, i.e., amino acids which are frequently observed in nature tend to have a large value of composition vector. Thus formulation to estimate the noise may be needed during representations. Here, we introduce two kinds of denoising composition vectors, which are efficient in construction of phylogenetic trees, to eliminate the noise. When validating these two denoising composition vectors on *Escherichia coli* (*E:coli*) and *Saccharomyces cerevisiae* (*S:cerevisiae*) randomly and artificial negative datasets, respectively, the predictive performance is not improved, and even worse than non-denoised prediction. These results suggest that, the denoising formulation efficient in phylogenetic trees construction can not improve the PPIs prediction, that is, what is noise is dependent on the applications.

16:20-16:40 Coffee break

16:40-18:20 ISB Session A6 (Guo Xing Room at Zhuhai Dehan Hotel)

Topic: Bioinformatics I

Chair: Tun-Wen Pai

16:40-17:00 *Identifying Positional Homologs as Bidirectional Best Hits of Sequence and Gene Context Similarity*

Melvin Zhang and **Hon Wai Leong**
Department of Computer Science, National University of Singapore, 13 Computing Drive, Singapore 117417

Paper ID: 34

Abstract: Identifying corresponding genes (orthologs) in different species is an important step in genome-wide comparative analysis. In particular, one-to-one correspondences between genes in different species greatly simplify certain problems such as transfer of function annotation and genome rearrangement studies. Positional homologs are the direct descendants of a single ancestral gene in the most recent common ancestor and by definition form one-to-one correspondence. In this work, we present a simple yet effective method (BBH-LS) for the identification of positional homologs from the comparative analysis of two genomes. Our BBH-LS method integrates sequence similarity and gene context similarity in order to get more accurate ortholog assignments. Specifically, BBH-LS applies the bidirectional best hit heuristic to a combination of sequence similarity and gene context similarity scores. We applied our method to the human, mouse, and rat genomes and found that BBH-LS produced the best results when using both sequence and gene context information equally. Compared to the state-of-the-art algorithms, such as MSOAR2, BBH-LS is able to identify more positional homologs with fewer false positives.

17:00-15:20 *Comparative genomics revealed a novel DNA-binding regulatory protein involved in homologous recombination in bacteria*

Yang Gao and Yan Zhang
Computer Network Information Center, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100005 China

Paper ID: 35

Abstract: Homologous recombination is a fundamental cellular process that is most widely used by cells to rearrange genes and accurately repair DNA double-strand breaks. It may result in the formation of a critical intermediate named Holliday junction, which is a four-way DNA junction and needs to be resolved to allow chromosome segregation. Different Holliday junction resolution systems and enzymes have been characterized from all three domains of life. In bacteria, the RuvABC complex is the most important resolution system. In this study, we conducted comparative genomics studies to identify a novel DNA-binding protein, YebC, which may serve as a key regulator of RuvABC resolvasome. On the other hand, the presence of YebC orthologs in some organisms lacking RuvC implied that it might participate in other biological processes. Further phylogenetic analysis of YebC protein sequences revealed two functionally different subtypes of this family: YebC_I and YebC_II. Only YebC_I subgroup may play an important role in regulating RuvABC gene expression in bacteria. Investigation of YebC-like proteins in eukaryotes suggested that they may have originated from YebC_II proteins and evolved a new function as a specific translational activator in mitochondria. Finally, additional phylum-specific genes associated with Holliday junction resolution were predicted. Overall, this study provides new insight into the basic mechanism of Holliday junction resolution and homologous recombination in bacteria.

17:20-17:40 *The preservation of bidirectional promoter architecture in eukaryotes - functional or co-regulation constraint?*

Chao Xu, Jiajia Chen and Bairong Shen
Center for systems biology, Soochow University, Suzhou, China

Paper ID: 51

Abstract: The bidirectional promoter architecture has been reported in many organisms, and the conservation of bidirectional arrangement has also been studied in several former researches. However, the explanation for the evolutionary conservation about this genomic structure is still insufficient. In this study the large scale identification and pathway enrichment analysis for bidirectional genes were performed in several eukaryotes, and the comparative analysis of this arrangement between human and mouse were dissected for the purpose of discovering the drive force of the preservation of this genomic structure. The comparative analysis about the gene expression and biological functions between human and mouse bidirectional genes were performed. It was observed that the selective constraint of this architecture mainly derives from the function bias of bidirectional genes rather than the co-regulation between paired genes. The results of our analyses indicated that the bidirectional genes are conserved in pathway level and the potential selective constraints of bidirectional architecture conservation comes from the gene function preference rather
than the co-regulation of paired genes' expression.

17:40-18:00 *A linear programming model for identifying non-redundant biomarkers based on gene expression profiles*

Xianwen Ren, Yong Wang, Luonan Chen and Xiang-Sun Zhang
State Key Laboratory for Molecular Virology and Genetic Engineering, Institute of Pathogen Biology, Chinese Academy Medical Sciences and Peking Union Medical College, Beijing, 100730, China

Paper ID: 56

Abstract: With the development of high-throughput technologies, e.g. microarrays and the second generation sequencing technologies, gene expression profiles have been applied widely to characterize the functional states of various samples at different conditions. This is especially important for clinical biomarker identification that is vital to the understanding of the pathogenesis of a certain disease and the subsequent therapies. Because of the complexity of multi-gene disorders, a single biomarker or a set of separate biomarkers often fails to discriminate the samples correctly. Moreover, biomarker identification and class assignment of diseases are intrinsically linked while the current solutions to these two tasks are generally separated. Motivated by these issues, we give out a novel model based on linear programming in this study to simultaneously identify the most meaningful biomarkers and classify accurately the disease types for patients. Results on a few real data sets suggest the effectiveness and advantages of our method.

18:00-18:20 *Cross-species identification of hydroxylation sites for ARD and FIH interaction*

Ying-Tsang Lo, Tsan-Huang Shih, Han-Jia Lin,Tun-Wen Pai, Margaret Dah-Tsyr Chang
Dept.of Computer Science and Engineering, 2Institute of Bioscience and Biotechnology，Center of Excellence for Marine Bioenvironment and Biotechnology, Nation Taiwan Ocean University, Keelung, Taiwan

Paper ID: 71

Abstract: Ankyrin repeat domain (ARD) proteins contain various numbers of internal repeat units. They are considered as one important factor to influence hypoxia response through hydroxylation interaction with Factor Inhibiting HIF (FIH) enzymes which can repress HIF under normoxia environment. In this study, we adopted sequence based method and applied conserved hydroxylation motif patterns for identifying ASN/ASP/HIS hydroxylation sites on ARDs. First, a set of known ARD proteins was collected, and all corresponding repeat units were manually constructed and verified by removing redundant units. All extracted segments served as fundamental seed units to retrieve all ARDs proteins from 5 different species. Those ARD candidates were automatically segmented and a conserved hydroxylation motif pattern was applied for identifying all hydroxylation sites. As a result, the retrieval performance for ARDs achieved a sensitivity of 82% and a specificity of 98% for human species based on a testing dataset of 1,244 protein sequences. For hydroxylation site prediction, a sensitivity of 72.2% and a positive prediction value of 62% were achieved based on a set of 18 experimentally verified hydroxylation residues.

16:40-18:20 ISB Session B6 (Guo Se Room at Zhuhai Dehan Hotel)

Topic: Bioinformatics II

Chair: Masahiro Okamoto

16:40-17:00 *Analyzing Time-Course Gene Expression Data Using Profile-State Hidden Markov Model*

Qiang Huang, Ling-Yun Wu, Ji-Bin Qu and Xiang-Sun Zhang
National Center for Mathematics and Interdisciplinary Sciences, Institute of Applied Mathematics, Academy of Mathematics and Systems Science, CAS, Beijing 100190

Paper ID: 72

Abstract: As the high-throughput experimental techniques such as microarray and next generation sequencing (NGS) developing, we can get more and more gene expression data. The gene expression data analysis is one of the fundamental tasks in bioinformatics. In this paper, we propose a new profile state hidden Markov model (HMM) for analyzing time-course gene expression data, which gives a new point of view to explain the variation of gene expression and regulation in different time. This model addresses the bicluster problem efficiently and can identify the irregular shape and overlapping biclusters. The comprehensive computational experiments on simulated and real data show that the new method is valid and useful.

17:00-17:20 *The role of GSH depletion in resveratrol induced HeLa cell apoptosis*

Bo Zhang, Xiao-qin Wang, Hanying Chen, Qiusheng Zheng, Xin Li
University of Shihezi, School of Pharmaceutical Sciences Shihezi 832002, China

Paper ID: 2

Abstract: The dual role of Resveratrol (Rsv) in cell apoptosis was recently reported by its anti/pro-oxidant activities. The involvement of ROS and GSH was thus investigated in Rsv-induced HeLa cell apoptosis. Rsv, higher than 10μM, elevated the intracellular ROS but reduced $O_{2^{\cdot-}}$ and GSH levels. ROS scavengers (Tempol, catalase) could not inhibit the apoptosis. Treatment with GSH modulators DTT or BSO were resulted up-regulation or down-regualtion GSH levels, but both enhanced Rsv-induced HeLa cell apoptosis. However, BSO could not prevent the DTT+Rsv treated HeLa cells from apoptosis. Further, Rsv-induced HeLa cell apoptosis was accompanied by activation of caspase 3 but not caspase 9, neither did the loss of mitochondrial membrane potential. Conclusively, the changes of ROS by Rsv were not tightly correlated with apoptosis in HeLa cells. However, intracellular GSH levels are partially related to Rsv-induced HeLa cell apoptosis via a mitochondrial independent manner.

17:20-17:40 *FaSD: A fast and accurate SNP detection algorithm for next-generation sequencing data*

Feng Xu, Weixin Wang, Pak Chung Sham, and Junwen Wang
Department of Biochemistry, LKS Faculty of Medicine,HKU,Hong Kong SAR, China

Paper ID: 30

Abstract: One of the major applications of Next Generation Sequencing (NGS) technology is to detect single nucleotide polymorphisms (SNPs). Several tools have been developed to call SNPs based on NGS outputs and reference genome. However, most of them require high sequencing depth, which is expensive to obtain. Here, we propose a novel SNP-detection program, FaSD, to call SNPs from low depth NGS data. Evaluated on two independent datasets from The Cancer Genome Atlas (TCGA) project with Affymetrix and Illumina SNP arrays as golden standard, FaSD showed superior performance over current state-of-the-art SNP calling software, including SOAPsnp, Maq, and SNVmix2. FaSD is particularly effective in calling SNPs when the sequencing depths are low.

17:40-18:00 *RNADAP—RNA-Seq Data Annotation Pipeline*

Zunming Liu, Jingfa Xiao, Jiayan Wu, Jun Yu
CAS Key Laboratory of Genome Sciences and Information, Beijing Institute of Genomics, Chinese Academy of Sciences, Beijing, China

Paper ID: 21

Abstract: RNA-Seq has become one of the most important new approaches for gene expression analysis as well as transcriptome analysis. The issue of how to analysis RNA-Seq data is one of the biggest challenges for current transcriptomics research. In this study, we develop an RNA-Seq data annotation pipeline named RNADAP, which is an efficient transcriptomes analysis tool to evaluate gene expression quantization in isoform level and compatible for reads data from different platforms. RNADAP is a typical Java application so the pipeline could be carried out on Windows as well as Linux. The installation process is convenient and user can grasp it very easily with a friendly user interface.

RNADAP is a free, open-source software and written in Java. All source code, instructions, testing data and additional scripts are available at http://rnadap.sourceforge.net/.

18:00-18:20 *An identification of secondary structure conserved elements in mammalian syntenic regions*

Toutai Mituyama
Computational Biology Research Center, AIST, Tokyo, Japan

Paper ID: 79

Abstract: 3,361 putative RNA secondary structure conserved regions were identified from mammalian syntenies by using leading-edge RNA sequence data analysis tools. The identified candidates are found to be concentrated in transcription factor binding sites of various genes, which infer secondary structure conserved elements play certain roles for transcription regulation.

18:30-20:00 Banquet & Performance

September 4 (Sunday) Social Program: One-day tour to Macao city

8:00 Departure at Zhuhai Dehan hotel Lobby

18:00 Return back to Zhuhai Dehan hotel Lobby

*The above program subjects to revision based on further information and Ad Hoc presentation requests.

Makoto Asashima

Fellow and Director of Research Center for Stem Cell Engineering
National Institute of Advanced Industrial Science and Technology (AIST)

Emeritus and Visiting Professor
Department of Life Sciences (Biology), Graduate School of Arts and Sciences, The University of Tokyo

Principal Fellow
Center for Research and Development Strategy, Japan Science and Technology Agency (JST)

Education
Graduated from Tokyo University for Education in March, 1967
Finished the graduate courses at the University of Tokyo
Master of Science from the University of Tokyo in March 1969
Doctor of Science from the University of Tokyo in March 1972(Ph.D.)

Professional career
Research Assistant of Institute of Molecularbiology, Free University of Berlin (Germany) (Apr.1972-Sep.1974)
Associate Professor of Yokohama City University, Faculty of Arts and Sciences (Oct.1974-Dec.1985)
Professor at Yokohama City University, Faculty of Arts and Sciences (Jan.1985-Mar.1993)
Professor at The University of Tokyo, Faculty of Arts and Sciences (Apr.1993-Mar.1995)
Professor at The University of Tokyo, Graduate School of Arts and Sciences (Apr.1995-Jan.2003)
Dean and Head at The University of Tokyo, Graduate School of Arts and Sciences (Feb.2003-2005)
Vice-President of Science Council of Japan (Oct.4,2005- Sep.2008)
Director of Life Sciences Network in the University of Tokyo (Oct.1,2005-Mar.31,2007)
Director of Center for Structuring Life Sciences in the University of Tokyo (Apr.1,2006-Mar.31,2007)
Director, Organ Development Research Laboratory in National Institute of Advanced Industrial Science and Technology(AIST) (Apr.1,2006-)
Managing Director, Executive Vice President, Visiting Professor in the University of Tokyo (Apr.1,2007-Mar.31,2009)
Fellow, Organ Development Research Laboratory in National Institute of Advanced Industrial Science and Technology(AIST) (Apr.1,2009-Mar.31,2010)
Principal Fellow, Center for Research and Development Strategy, Japan Science and Technology Agency (JST) (July,2009-)
Fellow and Director, Research Center for Stem Cell Engineering (SCRC), AIST (Apr.1,2010-)

Academic activity
Japanese Society of Developmental Biology (President, 2003-2006)
Japanese Society of Zoological Science(President, 2003-2006)
Japanese Society of Cell Biology (Council)
Japanese Society of Space Biology (President, 2002-2006)
Japanese Society of Molecular Biology

International Society of Developmental Biologists (Academic council member)
Development Growth and Differentiation (Editor)
Cell Structure and Function (Editor)
Int. J. Developmental Biology (Associate editor)
The Japanese Society for Regenerative Medicine(Director)
The Japanese Society of Inflammation and Regeneration(honorary member)

Prizes
Prize of Japanese Society of Zoological Science in 1990
Prize of Inoue Academic Foundation (with gold medal) in 1990
Prize of Kihara Memorial Academic Foundation (Silver Flower design with gold frame) in 1994
Siebold Prize (Germany; President Weiszeker) in 1994
Toray Science Prize (with gold medal) in 1999
Mochida Medical Science Prize (with gold medal) in 1999
Naito Memorial Science Prize (with gold medal) in 2000
Prize of Japanese Society of Bioindustry in 2000
Uehara Prize (with gold medal) in 2000
Imperial Prizes and Japan Academy (with silver pot) from Society of Japan Academy in 2001
Purple Ribbon Prize (Academic field called as Shiji-hosho) from the Japanese Government in 2001
The prince Hitachi Prize for comparative oncology (with special medal) in 2002
Erwin-Stein-Preises (Germany: Erwin-Stein-Stiftung)in 2008
Award of Bunka Koro Sha (cultural contributor) from Ministry of Education, Culture, Sports, Science and Technology in 2008

Professional
Developmental Biology, Cell Biology, Zoological Science 1. Mechanism of early development of vertebrate using from experimental biology to molecular biology
Control of Organogenesis in vitro
Molecular biology of cell differentiation and embryonic development
Cloning and analysis of organ specifid genes and early embryonic development
Organogenesis and regenerative medicine
Space Biology in Life Science

Books
Organizer-A milestone of a half-century from Spemann (Elsevier/North-Holland, in 1978)
The Vertebrate Organizer (Springer, in 2004)
Handbook of Stem Cells (Elsevier, in 2004)Stem Cells from Hydra to Man (Springer, in 2008)
Development and its Mechanism (Idemitsu Press, in 1983)
Modern biology (Riko-Gakusha, in 1988)
Developmental biology (Asakura-Press, in 1996)
Mechanism of Developmental Biology (Iwanami-Press, in 1998)
Fundamental of Molecular biology (Shokabo-Press, in 2000)
Other 20 books

Yaxiang Yuan

Professor, Institute of Computational Mathematics and Scientific/Engineering Computing, Chinese Academy of Sciences, China
President, Operations Research Society of China

EDUCATION

UNDERGRADUATE B.Sc. Department of Mathematics, Xiangtan University, Hunan, China, 1981.
GRADUATE Graduate School of the Chinese Academy of Sciences, March - December 1982. under Professor Feng Kang and Professor Xi Shao-lin
Ph.D. STUDY Department of Applied Mathematics and Theoretical Physics and Pembroke College, University of Cambridge, England, January 1983 - May 1986 (under Professor M.J.D. Powell FRS).
TRAINING PROGRAM Executive Development Center, College of Commerce and Business Administration, University of Illinois at Champaign-Urbana, USA, August 1995, Training Program for Research Institute Directors of Chinese Academy of Sciences.

DEGREES

B.Sc., Xiangtan University, China, 1982.
Ph.D., University of Cambridge, England, 1986.

PREVIOUS EMPLOYMENTS/POSITIONS

Rutherford Research Fellow, Fitzwilliam College, University of Cambridge, England, from October 1985 to September 1988.
Professor, Computing Center, the Chinese Academy of Sciences , Beijing, China, from November 1988 to Feb. 1995
Director, State Key Laboratory of Scientific/Engineering Computing, Chinese Academy of Sciences, from Sept 1996 to Oct 2005
Director, Institute of Computational Mathematics and Scientific/Engineering Computing, Chinese Academy of Sciences, from March 1995 to April 2007.
Vice President, Academy of Mathematics and System Sciences, Chinese Academy of Sciences, from Dec 1998 to March 2007.

ACADEMIC VISITINGS

Department of Computer Science, University of Colorado at Boulder, U.S.A. from September 1990 to February 1991.
Department of Electrical Engineering and Computer Science, Northwestern University, Illinois, U.S.A., March to August, 1991.
Institute of Angewante Mathematik und Statistik, Universitaet der Wuerzburg, Germany, from July 1992 to June 1993. (Humboldt Fellow)
Department of Mathematics, Honk Kong Baptist College, January to May, 1994.
Department of Mathematics, Federal University of Parana, Brazil, March to May, 1997.
Department of Applied Mathematics and Theoretical Physics, University of Cambridge, October 2007 to September 2008.
Department of Angewandte Informatik, Unviersity Bayreuth, Germany, May-August, 2010 (supported by Humboldt Foundation)

TEACHING EXPERIENCE

Supervising Part II ``Numerical Analysis'' and ``Approximation Methods'' at University of Cambridge, 1984-1988.

Lecturing ``Numerical Methods for Optimization'' and ``Matrix Computations'' at the Graduate School of the Chinese Academy of Sciences, 1989--.

Lecturing ``Numerical Methods for Constrained Optimization'' for graduate students at University of Colorado at Boulder, Fall 1990.

AWARDS, ETC.

First prize in Universities Mathematics Competition, Hunan, China, 1980.
J.T. Knight Prize, University of Cambridge, England, 1983.
L. Fox Prize, London, England, 1985.
Second grade Natural Science Prize, the Chinese Academy of Sciences, 1989.
Young Scientist Award, Chinese Academy of Sciences, 1993
Feng Kang Prize, Beijing, 1995
Young Scientist Award of China, 1996.
First grade Science and Technology Advance Award, Beijing.
National Excellent Science and Technolgy Worker, 2005.
Second Grade, National Natural Science Award of China, 2006.

INVITED LECTURES

Plenary Lecture, the 4th International Congress on Industrial and Applied Mathematics(Edinburgh, UK, 1999)
Invited Lecture, The Third Asian Mathematical Conference(Malina, Philippines, 2000)
Keynote Lecture, INFORMS International Conference, (Hong Kong, 2006)

PROFESSIONAL BODIES:

SIAM Journal of Optimization, associate editor, 2007--.
Mathematics of Computation , member of editorial board, 2010-;
Journal of Scientific Computing , member of editorial board, 2007-;
Optimization and Engineering (Kluwer), member of editorial board, 2002-.
Optimization Methods and Software (Taylor and Francis), member of editorial board, 1993-.
Science in China and Chinese Science Bulletin , member of editorial board, 1996-
Systems Science and Mathematical Sciences, member of editorial board, 1995-
Control, Optimisation and Calculus of Variations(ESAIM), member of editorial board, 2003-2005.
Journal of Computational Mathematics (VSP), member of editorial board, 1988-; Associate Editor-in-Chief, 1994-2006.
Chinese Mathematical Society, vice president, 2000-2007.
China SIAM, member of executive committee, 1995-1999; vice president, 2000-2008.
Chinese Operational Research Society, member of executive committee, 1997-2000; vice president, 2000-2004; president, 2004-
Chinese Computational Mathematics Society, member of the council, 1990-1997.
International Congress of Mathematicians 2002, General Secretary.

SOCIAL ACTIVITY:

President of the Chinese Students and Scholars Association of University of Cambridge, from October 1984 to September 1985 and from October 1986 to September 1987.
Member of the Executive Committee of the All-China Youth Federation , from August 1990 -- July 2007.
Member of the Youth Committee of the Western Returned Scholars Association, 1992 -- 2000.
Vice President of the Western Returned Scholars Association & President of the UK branch of WRSA, 1999 -- 2007.
Member of the executive committee of the Chinese Association of Alexander von Humboldt Follows, from 1995.

Zemin Zhang

Principal Scientist: Bioinformatics & Computational Biology, Genentech Inc., USA

Education/Background

University of California, San Francisco, Postdoctoral Fellow 1995-1998
Pennsylvania State University, Biochemistry and Molecular Biology, Ph.D 1989-1995
China-United States Biochemistry and Molecular Biology Training Program 1988-1989
Nankai University, Genetics, B.S 1984-1988

Awards & Honors

Sigma Xi Research Gran 1995
CUSBEA Scholar 1989
Tianjin Intercollegiate Scholarship 1988
Nankai College Scholarship 1987

Weixiong Zhang

Professor, Computer Science and of Genetics, Washington University in Saint Louis, USA

Education:

Ph.D. University of California at Los Angeles (UCLA)
B.S. Tsinghua University, Beijing, China

Research Interests:

Computational systems biology (machine learning/datamining methods and their applications to molecular biology and genomics - e.g., cis-element identification, gene identification and selection, non-coding small RNAs and their regulatory functions, gene regulatory networks, stress tolerance and regulation in plants, cancer, neurodegenerative diseases (e.g., Alzheimer's disease), and haplotype inference)

Artificial Intelligence (heuristic search, phase transitions in complex systems, planning and scheduling, constraint satisfaction and optimization, resource allocation in multi-agent systems and sensor networks)

Combinatorial optimization (e.g., Traveling Salesman and Boolean satisfiability) and search algorithms

Journal editorial duties

Artificial Intelligence (Associate editor, 2009-present; Editorial board member, 2007-present)
J. of Alzheimer's Disease (Associate editor, 2009-present)
PLoS Computational Biology (Associate editor, 2008-present)
The Open Systems Biology Journal (Advisory board member, 2008-present)
J. of Artificial Intelligence Research - JAIR (Editorial board member, 2005-present)
AI Communications - The European Journal on Artificial Intelligence (Associate editor, 2004-present)

Yijun Ruan

Senior Group Leader, Assoc Director, Genomic Technologies, Genome Institute of Singapore

Education

1995-1996	Post-doctoral Fellow, Program of Gene Discovery and Gene Expression, Monsanto Company, St Louis, Missouri, USA
1990-1994	Doctor of philosophy in Plant Molecular Biology, University of Maryland, College Park, Maryland, USA
1982-1985	MS in Microbiology, Huazhong Agricultural University, Wuhan, China
1978-1982	BS in Microbiology, Huazhong Agricultural University, Wuhan, China

Professional Appointments

2006	Adjunct Professor, National University of Singapore, Singapore
2003	Associate Director, Genome Technology Genome Institute of Singapore
2002	Senior Group Leader, Genome Technology and Biology Genome Institute of Singapore
1999-2002	Director, Core Genomics and Applications Large Scale Biology Corporation, Vacaville, California, USA
1996-1999	Senior Scientist, Genome Technology, Monsanto Company, St. Louis, Missouri, USA

Honors and Awards

2006	National Science Award 2006, Singapore
1998-2001	Rockefeller Foundation Fellow Helped China to initiate rice functional genomics research sponsored by Rockefeller Foundation under a rice biotech fellowship program.
1995	Carroll E. Cox Graduate Research Excellence Award, University of Maryland, 1995. For the best Ph.D dissertation in biology submitted in 1994

Research Focus

My primary interest is to elucidate the structures and dynamics of all functional DNA elements in complex genomes through transcriptome characterizations and genome interrogation. To facilitate such understanding we have developed paired-end-ditag (PET) based high throughput and high precision DNA sequencing and mapping methodologies. We are applying these sequencing-based measurements to address complex biological questions such as how cancer cells progress and how stem cells maintain their unique properties. Another major interest of mine is to discover previously uncharacterized microbial genes and genomes that are relevant to human health. To this end, we have established a metagenome analysis capability that includes a filtration system for isolating uncultured microbes, shotgun and PET sequencing of metagenomes to uncover viral and bacterial genome sequences from a variety of environment settings and cavities of the human body.

2011 IEEE International Conference on Systems Biology (ISB)

Zhuhai, China, September 2–4, 2011

Edited by

Luonan Chen
Xiang-Sun Zhang
Ling-Yun Wu
Yong Wang

2011 IEEE International Conference on Systems Biology (ISB)

IEEE Catalog Number CFP11ISB-ART
ISBN 978-1-4577-1666-9

Additional copies of this publication are available from

Curran Associates, Inc.
57 Morehouse Lane
Red Hook, NY 12571 USA
+1 845 758 0400
+1 845 758 2633 (FAX)
Email: curran@proceedings.com

ABOUT ISB 2011

THEME AND SCOPE

The 5th IEEE International Conference on Systems Biology (ISB 2011), organized by Chinese Academy of Sciences and Sun Yat-Sen University will be held in Zhuhai, China, September 2-4, 2011. The conference is sponsored by National Natural Science Foundation of China (NSFC), Japan Society for the Promotion of Science (JSPS), Academy of Mathematics and Systems Sciences of CAS (AMSS), Shanghai Institutes for Biological Sciences of CAS (SIBS), Sun Yat-Sen University University, Computational Systems Biology Society of ORSC, Systems Biology Technical Committee of IEEE SMC Society, and also sponsored by IEEE SMC Society.

Systems Biology and Bioinformatics have become intensive research topics in the recent past decade and attracted great many leading scientists working in Biology, Physics, Mathematics and Computer Science. Optimization, Statistics, and many other mathematical methods have been widely used in the field. Following the successful OSB 2007-2009 and ISB 2010, the purpose of ISB 2011 is to extend the international forum for scientists, researchers, educators, and practitioners to exchange ideas and approaches, to present research findings and state-of-the-art solutions in this interdisciplinary field, including mathematical methods and its applications in biosciences and researches on various aspects of Systems Biology, such as integration of genome-wide microarray, proteomic, and metabolomic data, inference and comparison of biological networks, and model testing through design of experiments.

The purpose of ISB 2011 is to provide an international forum for scientists, researchers to exchange ideas and approaches, including theoretical methodology development and its applications in biosciences and researches on various aspects of Computational Systems Biology. Themes of the ISB 2011 will be interdisciplinary by its nature and focus on bridging opportunities between mathematical methods and Systems Biology studies. We are particularly interested in submissions that report on theoretical, experimental and applied research motivated by systems biology problems. Typical, but not exclusive, topics of interest are:

- Gene Regulatory Networks
- Protein Interaction Networks
- Metabolic Networks
- Signaling Networks
- Comparative Genomics
- Functional Genomics
- Metagenomics
- Genome-Wide Association Study
- Promoter Analysis and Discovery
- Biomarker Identification and Drug Discovery
- Evolution and Phylogenetics
- Non-coding RNAs
- Proteomics
- Protein Structures and Functions
- Microbial Community Analysis
- Qualitative Analysis of Biological Systems
- Quantitative Models of Cellular and Multi-Cellular Systems
- Designing and Modeling Synthetic Biological Systems
- Nonlinear Dynamics and Analysis of Biological Systems
- Designing Synthetic Biological Circuits
- High Performance Computing for Biological Data Analysis
- Data Mining and Machine Learning for Biological Data
- Information Theory and Statistical Analysis
- Systems Biology of Cancer and Metastasis
- Brain Systems Biology
- Systems Neuro-Informatics

COMMITTEES

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  - Kwang-Hyun Cho (Korea Advanced Institute of Science and Technology, Korea)
  - Xiang-Sun Zhang (Chinese Academy of Sciences, China)

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- Program Committee
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  - Yu Xia (Boston University, USA)
  - Dong Xu (University of Missouri-Columbia, USA)
  - Xiang-Sun Zhang (Chinese Academy of Sciences, China)
  - Yaoqi Zhou (Indiana University-Purdue University Indianapolis, USA)

PROCEEDING PAPERS AND CONTRIBUTING AUTHORS

Sixty-five full papers in this volume cover wide range of computational systems biology. Authors of these papers come from China mainland, Hong Kong, Taiwan, Australia, Canada, Finland, Japan, Korea, Malaysia, Netherlands, New Zealand, Poland, Singapore, Sweden, Thailand, United Kingdom, United States. Many active researchers in various areas contributed their overview and introduction in their fields besides specific deep research achievements.

Contents

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