

Otto Warburg
International Summer School And
Research Symposium on
Genes, Metabolism, and Systems Modeling
August 30 to September 6, 2012
Shanghai, P.R.China



The CAS-MPG Partner Institute for Computational Biology, Shanghai

Max Planck Institute for Molecular Genetics, Berlin

<http://www.picb.ac.cn/owiss/index.shtml>

Otto Warburg International Summer School and Research Symposium on

Genes, Metabolism, and Systems Modeling

August 30 to September 6, 2012

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This program brings together researchers and PhD students from different backgrounds (including molecular biology, bioinformatics, biological physics, and mathematics) to discuss recent advances in metabolism and gene regulation in an interactive environment. The program focuses on high-level teaching and topical research seminars.

Invited speakers:

Alexander Bockmayr	Freie Universität Berlin
Paul Jensen	University of Virginia
Edda Klipp	Humboldt-Universität zu Berlin
Ina Koch	Johann Wolfgang Goethe-University Frankfurt a. Main
Satoru Miyano	The University of Tokyo
Eytan Ruppin	Tel Aviv University
Denis Thieffry	Institut de Biologie de l'Ecole normale supérieure
Lorenz Wernisch	MRC Biostatistics Unit
Bartek Wilczynski	University of Warsaw

Scientific Coordinators:

Martin Vingron, Jun Yan

Max Planck Institute for Molecular Genetics, Berlin
The CAS-MPG Partner Institute for Computational Biology, Shanghai

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General information

Hope Hotel: Your hotel room rate from 29th Aug. to 6th Sep. will be covered by summer school. You need pay the deposit and other fees if occur.

Add: 500 Zhaojiabang Road. Shanghai.

Tel: 86+21+64716060

Welcome dinner: will take place at Yelixiali Restaurant in 680 Zhaojiabang Road.

Speaker dinner: will take place at Nanling Restaurant in 168 Yueyang Road.

Other Lunch and dinner: will take place at the second floor of the canteen in 320 Yueyang Road.

Registration:

14:00—18:00, Thursday 30th August

300 room of main building, 320 Yueyang Road

Sightseeing:

Monday, 3th September

Morning: Shanghai Museum

Afternoon: Yu Garden

Evening: Cruise

Program

Time	Thursday 30th Aug	Friday 31th Aug	Saturday 1st Sep	Sunday 2nd Sep	Monday 3rd Sep	Tuesday 4th Sep	Wednesday 5th Sep	Thursday 6th Sep
09:00-10:30		Lecture: Paul Jensen	Lecture: Alexander Bockmayr	Lecture: Eytan Ruppin	One Day Sightseeing	Lecture: Edda Klipp	Lecture: Satoru Miyano	Talk: Xinguang Zhu
10:30-10:50		Coffee Break				Coffee Break		
10:50-12:20		Lecture: Denis Thieffry	Lecture: Edda Klipp	Lecture: Edda Klipp		Lecture: Lorenz Wernisch	Lecture: Bartek Wilczynski	Talk: Jin Yang
12:20-13:50		Lunch				Lunch		
13:50-15:20		Lecture: Lorenz Wernisch	Lecture: Ina Koch	Lecture: Denis Thieffry		Lecture: Ina Koch	Student Presentation	Lecture: Denis Thieffry
15:20-15:40	14:00-18:00 Registration	Coffee Break				Coffee Break		
15:40-17:10		Poster	Lecture: Paul Jensen	Student Presentation		Poster	Lecture: Alexander Bockmayr	Goodbye
17:10-18:40	18:00-20:00 Welcome Dinner	Dinner		Introductory Lecture: Satoru Miyano		Dinner		
19:00-20:30		Lecture: Bartek Wilczynski	Lecture: Eytan Ruppin	Student Dinner Speaker Dinner		Lecture: Alexander Bockmayr	Talk: Jun Yan	

Class room location: All lectures, talks and poster sessions will take place in the Mingde Hall of Shanghai Information center for life sciences, CAS. 319 Yueyang Road, Xuhui District, Shanghai, P.R.China

Lectures

Paul Jensen

Lecture one: Metabolic model construction and refinement

Stoichiometric modeling -- gene/protein/reaction relationships, thermodynamics for reaction reversibility, charge balancing, compartmentalization, objective development (de novo and experimental); refining with experimental data -- lethality screening, uptake rate measurement, ¹³C flux determination, metabolomics and expression data.

Lecture two: Applications of genome-scale models

Rational strain design (optimization and elementary mode based methods), adaptive evolution, drug targeting, symbiosis and microbial communities.

Eytan Ruppin

Lecture One: Methods for integrating omics data within genome scale metabolic models

Given pertaining omics data of the context investigated (e.g., gene expression or proteomics in a specific disease), I will describe methods for using it to: (a) infer the most likely metabolic state (iMAT, Shlomi et al, 2008); (b) build a metabolic sub-model (MBA, Jerby et al, 2009) an (c) infer potential drug targets (MTA, Yizhak et al, submitted).

Lecture Two: Their application to study metabolic alterations in aging and cancer.

I will then proceed to describe applications of these methods to study cancer (Folger et al, 2011, Frezza et al, 2011) and aging metabolism (Yizhak et al, submitted).

Reading List

1. Network based prediction of human tissue specific metabolism (T. Shlomi, M.N Cabili, M.J. Herrgard, B.O. Palsson, E. Ruppin) Nature Biotechnology, doi: 10.1038/nbt.1487, August 2008.
2. Computational reconstruction of tissue-specific metabolic models: Application to human liver metabolism (L. Jerby, T. Shlomi*, E. Ruppin*) Molecular Systems Biology (MSB), 6, Article number 401; doi: 10.1038/msb.2010.56, September 2010.
*equal contribution.
3. Predicting selective drug targets in cancer through metabolic networks (O. Folger, L. Jerby, C. Frezza, E. Gottlieb, E. Ruppin*, T. Shlomi*) Molecular Systems Biology (MSB), doi:10.1038/msb.2011.35, 2011. *equal contribution.
4. Haem oxygenase is synthetically lethal with the mitochondrial tumour suppressor fumarate hydratase (C. Frezza, L. Zheng, O. Folger, K. Rajagopalan, E.D. MacKenzie, L. Jerby, M. Micaroni, B. Chaneton, J. Adam, A. Hedley, G. Kalna, I.P.M. Tomlinson, P.J. Pollard, D.G. Watson, R.J. Deberardinis, T. Shlomi*, E. Ruppin*, E. Gottlieb) Nature, 17 Aug 2011 (doi:10.1038/nature10363). *equal contribution.

Bartek Wilczynski

Lecture one: Learning Bayesian Network structure from data

We will discuss different approaches to discovering the structure of a Bayesian Network from experimental data. We will start from the problem statement with some motivating examples. Then we will discuss the classical results regarding the complexity of the problem, together with the typical heuristic approaches. Lastly, we will discuss some special cases, like dynamic Bayesian Networks, where the optimal solution can be found.

Lecture two: Using Bayesian Networks for Chromatin state classification

Chromatin modifications are one of key aspects of gene regulation at the level of transcription. As we gather more and more data regarding different chromatin modifications on a genomic scale (histone marks, chromatin associated proteins, insulator proteins, etc.), we need computational approaches to represent and classify different observations with distinct regulatory states. In the process, we need to formulate and solve new computational problems regarding chromatin state prediction and classification. In this talk we will discuss some approaches to these issues using Bayesian networks as for supervised learning and classification.

Alexander Bockmayr

Lecture one: Metabolic pathway analysis from a mathematical viewpoint

We present the basic mathematical concepts underlying the constraint-based analysis of metabolic networks at steady-state: flux cone, flux balance analysis (FBA), flux

variability analysis (FVA), flux coupling analysis (FCA), elementary flux modes, extreme pathways, and minimal metabolic behaviors. On the algorithmic side, we will focus on linear programming and mixed-integer linear programming methods.

Lecture two: Model checking and parameter inference for Thomas models of gene regulatory networks

We discuss the formalization in temporal logic of dynamic properties in discrete models and their formal verification by model checking. In particular, we show how model checking can be used in parameter inference for Thomas models based on discrete time series.

Lecture three: Comparing Boolean, multi-valued and piecewise affine differential equation models of gene regulatory networks

We compare and contrast different qualitative modeling approaches for gene regulatory networks. On the one hand, we relate Boolean and multi-valued discrete models, on the other hand, multi-valued discrete and piecewise affine differential equation models. We show that even if models in different formalisms are based on equivalent information, the resulting qualitative dynamics may be different. In particular, we establish that high-level dynamic properties such as reachability or the number and type of attractors may depend on the underlying modeling formalism.

Reading List

1. Terzer M, Maynard ND, Covert MW, Stelling J. Genome-scale metabolic networks
Wiley Interdiscip Rev Syst Biol Med. 2009 Nov-Dec;1(3):285-97

Orth JD, Thiele I, Palsson BØ. What is flux balance analysis? Nat Biotechnol. 2010 Mar;28(3):245-8

2. Bernot G, Comet JP, Richard A, Guespin J. Application of formal methods to biological regulatory networks: extending Thomas' asynchronous logical approach with temporal logic J Theor Biol. 2004 Aug 7;229(3):339-47

Klarner H, Siebert H, Bockmayr A. Time Series Dependent Analysis of Unparametrized Thomas Networks. IEEE/ACM Transactions on Computational Biology and Bioinformatics, 16 April 2012.

3. Jamshidi S, Siebert H, Bockmayr A. Comparing Discrete and Piecewise Affine Differential Equation Models of Gene Regulatory Networks. Information Processing in Cells and Tissues, IPCAT 2012, Cambridge, UK. Springer, LNCS 7223, 17-24, 2012

Denis Thieffry

Lectures :

1. Logical modelling of cellular regulatory/signalling networks
2. From logical models to (discrete) Petri nets
3. Logical modelling of cell fate decisions

Logical modelling constitutes a flexible framework to build qualitative predictive models, which can be readily analysed or simulated as such, and potentially used as

scaffolds to build more quantitative (continuous or stochastic) models.

We use Multi-valued Decision Diagrams to implement (multi-level) logical updating rules in the modelling software GINsim. This representation enabled the development of efficient algorithms for the identification of stable states, or yet to identify specific (positive or negative) regulatory circuits involved in specific dynamical properties (e.g., multiple attractors or sustained oscillations).

To cope with larger molecular networks, we have implemented a flexible reduction method conserving the attractors of the original model into our software GINsim. Furthermore, we have delineated an incremental, compositional strategy to build large models by combining logical models for simpler regulatory modules.

Simulations of logical models leads to state transition graphs, which may become too large to handle or difficult to interpret, even after model reduction. To ease their analysis, we have developed and implemented an algorithm to compact state transition graph during their calculation. The resulting (compressed) hierarchical state transition graph provide interesting insights regarding the transitions underlying important decisions (choice between alternative attractors).

Finally, logical models can be transposed into other powerful discrete modelling frameworks, including logical constraint programming and Petri nets, thereby enabling the use of complementary methods and software tools to check the consistency between a model specification and dynamical constraints (formally expressed using a temporal logics such as CTL or LTL).

Reading list

1. Chaouiya C (2007). Petri net modelling of biological networks. Briefings Bioinfo 8:

210-9.

2. Chaouiya C, Naldi A, Thieffry D (2012). Logical modelling of gene regulatory networks with GINsim. *Methods Mol Biol* 804: 463-79.
3. Naldi A, Carneiro J, Chaouiya C, Thieffry D (2010). Diversity and plasticity of Th cell types predicted from regulatory network modelling. *PLoS Comput Biol* 6: e1000912.
4. Sánchez L, Chaouiya C, Thieffry D (2008). Segmenting the fly embryo: logical analysis of the role of the Segment Polarity cross-regulatory module. *Int J Dev Biol* 52: 1059-75.
5. Simão E, Remy E, Thieffry D, Chaouiya (2005). Qualitative Modelling of Regulated Metabolic Pathways: Application to the Tryptophan Biosynthesis in E. Coli. *Bioinformatics* 21: ii190-6.
6. Thieffry D (2007). Dynamical roles of biological regulatory circuits. *Briefings Bioinfo* 8: 220-5.

Ina Koch

Lecture one: Introduction to Petri nets

Petri net formalism has been developed to describe causal systems with concurrent processes. Mainly applied to technical systems or financial processes, since about 20 years Petri nets have been used to model biochemical systems at different levels of abstraction.

In my lecture, I will introduce basic definitions and terms of Petri nets. This covers discrete as well as stochastic and continuous Petri nets. I will discuss static and dynamic properties which are important for the application to biology. Analysis and simulation methods will be introduced.

A further focus will be the definition of functional modules that can be used for network reduction and also as building blocks in synthetic biology. In this context, steady-state based definitions are of special interest. Therefore, I will explain invariants, elementary modes, maximal common transition sets, transition clusters, minimal cut sets, and enzyme subsets.

To analyze the entire system's behavior, the reachability analysis will be introduced and discussed.

To illustrate the introduced terms and definitions, biological examples will be used, in particular part of the main carbon metabolism in *Solanum tuberosum* (potato tubers).

Lecture two: Applications of Petri net formalism to biology

This lecture is dedicated to special applications of Petri nets to model biochemical networks. I will consider metabolic systems, signal transduction and gene regulatory networks. The examples cover the metabolism of the combined glycolysis and pentose phosphate pathway in erythrocytes, the pheromone response pathway in *Saccharomyces cerevisiae* (baker's yeast), and the signal transduction and gene regulatory processes downstream the dystrophin gene in Duchenne Muscular Dystrophy. For all examples, I will discuss advantages and limits.

Also new aspects of Petri net applications will be introduced and discussed, for example fuzzy Petri nets, or modeling of complex assembly processes of the spliceosome. Finally, our new software tool MonaLisa which is especially designed to edit, analyze, and animate biochemical Petri nets.

Satoru Miyano

Lecture one: Introductory lecture

Lecture two: Statistical modeling and cancer

Reading list

"The Elements of Statistical Learning" by Trevor Hastie, Robert Tibshirani, Jerome Friedman, Springer

<http://www-stat.stanford.edu/~tibs/ElemStatLearn/>

Lorenz Wernisch

Lecture one: Introductory lecture on Bayesian Network

Bayesian and related network modelling principles and biological examples but no inference or estimation algorithms.

Lecture two: Specific research topics on Bayesian inference, regulatory networks, interaction networks

1. Simplified modeling of stochastic dynamical systems using flow cytometry data.
2. Bayesian structural equation modelling for epidemiological/immunological regulation networks.
3. Gaussian process modelling of time series gene expression data in Mycobacterium combined with metabolic network flux analysis.
4. PP interaction graph analysis for interpretation of Array CGH and expression data from cancer samples.

Edda Klipp

Lectures

1. Introduction into dynamic modeling with ODEs (dynamics, stability, bifurcations,...)
2. Modeling of signaling pathways
3. Modeling of the interaction of signaling pathways with other types of pathways including metabolism and cell cycle

Talks

Xinguang Zhu

TBA

Jun Yan

Inter-organ metabolic transport in mammal

Complex organisms have evolved separate organs for specialized metabolic functions so that a metabolite is often synthesized in one organ but further catabolized in another. Membrane transporters, especially solute carrier (Slc) proteins, play important roles in shuttling metabolites in and out of the cells. Here we aim to reconstruct the network of inter-organ metabolic transport on the “-omic” scale. This is realized by systematically analyzing the organ-specific expression of enzymes and Slcs using microarray data and high-resolution in situ hybridization data. We provided convincing evidences that the entire metabolic network is segregated in different tissues and inter-organ transport of metabolites is facilitated by strategically located Slcs. Our study provides us molecular correlates for the known inter-tissue metabolic transport systems as well as the unknown ones.

Jin Yang

Modeling and simulation strategies for complex cell signaling systems

Abstract -- Predictive modeling for large-scale biochemical reaction networks requires proper techniques that can effectively describe and efficiently compute biomolecular interactions of combinatorial complexity. In this talk I will introduce the rule-based modeling framework and simulation methods for studying signal transduction systems with site-specific interaction details. We will first review the need and the state of art of the computational approach using rule-based models. We will then focus on a specific

modeling structure, namely, molecular finite automata, which are programmable and executable machines that model dynamics of biomolecular entities and their interactions involved in signaling systems.

Student Presentation

Presentation 1

Kasia Bozek

PICB, 320 Yueyang Road, Shanghai

Human Metabolic Evolution

Abstract:

Genetic divergence between humans and other primates follows general evolutionary clock and provides only limited number of human-specific features. Phenotypically humans are clearly distinct from other species. What molecular mechanisms are responsible for the distinct human-specific phenotype?

To investigate this, we studied divergence between humans, chimpanzees, macaques and mice at three levels of molecular phenotype: metabolic, lipid and transcriptome. We analyzed metabolic and lipid compositions as well as transcriptome profiles in five tissues: three functionally different brain regions, prefrontal, visual and cerebellar cortex, as well as muscle and kidney. In addition, we assessed the effect of postmortem delay and external effects such as human diet and limited physical activity on primate metabolome.

Based on measurements from a total of more than 400 samples, we show (1) existence of distinct metabolic profiles for each tissue; (2) rapid pace of metabolic evolution among species in all tissues; (3) large excess of metabolic divergence on the human evolutionary lineage. While some of human-specific metabolic divergence could be linked to particularities of human lifestyle, such as human diet and lack of exercise, the vast majority of observed changes cannot be explained by these environmental factors. We use gene and metabolite functional annotation in order to link the species- and tissue-specific changes into their potential regulatory pathways.

Through an integrative approach of combining the information on the metabolic, lipid and gene expression levels we aim at constructing a comprehensive picture of human-specific molecular mechanisms in different tissues with a particular focus on those present in brain and potentially involved in human cognitive capacities.

Presentation 2

Roman Brinzanik

MPI for Molecular Genetics, Ihnestr. 63-73

Integrative Omics Data Analysis for the Study of Energy Metabolism in Fruit Fly

Abstract:

The general aims of this exploratory data analysis are to use *Drosophila* as a model system for obesity and to contribute to the systems biology of energy homeostasis. For this purpose we analyze and integrate several – omics data sets of *Drosophila* during starvation. Significant changes in metabolite profiles and their mapping on known metabolic pathways suggest several switches to the degradation of different energy storages. Lipidomics data show differential mobilization of fatty acids. A comparison with genome-wide RNA-seq data allows for new hypotheses on the transcriptional regulation of the metabolic pathways. Promoter analysis of starvation-responsive genes suggests candidates for the regulating transcription factors. This study begins to elucidate a molecular network that controls energy metabolism in *Drosophila*.

Presentation 3

Dorothee Girbig

MPI for Molecular Plant Physiology

Analyzing coordinated stability conditions of metabolic cycles

Abstract:

The ability of a steady state to remain unaltered under perturbations is called stability. A framework for the systematic analysis of stability conditions is structural kinetic modeling (SKM) [1]. It provides a parameterized representation of the system Jacobian, in which the individual parameters encode partial derivatives of the reaction rates in a steady state. Here, a simple normalization step restricts the parameter values to predefined sampling intervals. This enables the combination of SKM with a Monte-Carlo approach in which large numbers of models are created using randomly sampled parameters. The subsequent analysis of the parameter sets leading to stable or unstable models can then provide hints about the conditions that ensure stability in metabolic systems.

In my talk, I will give an introduction to the methodology and present our latest developments for improving the analysis of SKM experiments. We recently presented a machine-learning approach in order to detect patterns of enzyme-metabolite interactions that act together in an orchestrated manner to enable stability [2]. I will also demonstrate how we apply SKM to two types of metabolic cycles in primary metabolism, namely the Calvin-Benson cycle, and the TCA cycle. Here, our main questions concern (1) understanding the coordinated response to perturbations, and (2) the role of allosteric regulators in maintaining stability.

[1] Steuer, R., Gross, T., Selbig, J., and Blasius, B. (2006). Structural kinetic modeling of metabolic networks. *Proceedings of the National Academy of Sciences of the United States of America*, 103(32), 11868–11873.

[2] Girbig, D., Grimbs, S., and Selbig, J. (2012). Systematic analysis of stability patterns in plant primary metabolism. *PLoS ONE*, 7(4), e34686.

Presentation 4

Zhisong He

PICB, 320 Yueyang Road

Expression of LincRNAs in Human Brain

Abstract:

In the past few years, thousands of long intergenic non-coding RNAs (lincRNAs) have been discovered in humans and other species. Although functions of lincRNAs remain largely unknown, several lincRNAs have been shown to act as important regulators, e.g. XIST, HOTAIR and HOTTIP. To gain insight into the roles of lincRNAs in human brain development and aging, we sequenced human brain transcriptome at 14 stages of development and aging distributed over the entire human lifespan using high throughput sequencing (RNA-seq).

Currently there are more than 10,000 human lincRNAs annotated by Ensembl release 64 and in the work of Cabili et al. To further improve the lincRNA annotation, we successfully reconstructed another 552 novel lincRNA gene candidates with our data. Taking all into account, more than 1,300 lincRNAs with evident expression in human brain were identified. Over 1/3 of them had significant expressional changes with age. Based on their expression patterns, we tried to infer lincRNAs functions. Furthermore,

we identified both cis- and trans- regulatory effects of these age-related lincRNAs on the expression of protein-coding genes. The results are also supported by macaque prefrontal cortex transcriptome time series data and by the effect of lincRNA knockdown experiments in mouse. The expression profile and effect consistency between human lincRNAs and their orthologs in other species implies the functional conservation and importance of lincRNAs.

Presentation 5

Qiang Li

PICB, 320 Yueyang Road

Systematic Identification of Novel Gene Members of Mammalian Metabolic Pathways

Abstract:

The metabolic functions of known enzymes in the metabolic pathways are among the best studied gene functions so far. However, how these enzymes are regulated and how they are linked to other metabolism-related genes such as metabolite transporters is still unclear. Using the fact that functionally related genes are often co-expressed, we developed an efficient computational method to predict novel genes participating in known metabolic pathways by screening genome-wide expression data. We identified the sets of enzymes associated with consecutive metabolic reactions that also show co-expression. Using these co-expressed consecutive enzymes as query sets or “baits”, we screened the entire mouse microarray datasets in the Gene Expression Omnibus (GEO) database for additional co-expressed genes. Using this method, we also gained insights into the physiological conditions that affect metabolic pathways. Our extended list of co-expressed metabolism-related genes facilitated the identification of their potential regulators using promoter analysis. We further validated that these novel

genes also show spatial co-localizations with known enzymes in metabolic pathways by high-resolution in situ hybridization (ISH) data in E14.5 mouse embryos. Our prediction provided novel gene candidates with putative functional roles in metabolic pathways, which will be further investigated and validated by experiments.

Presentation 6

Guofeng Meng

MPI for Molecular Genetics, Ihnestr. 63-73

GbA: inferring transcriptional regulation with expression data for biological processes

Abstract:

For a biological process, different transcription factors and regulators interact with each other to form the regulatory network, which complicates recovery of the transcriptional regulation. Efficient prediction for regulation between transcription factors and target genes is a crucial initial step for further experimental validation, or even to understand the biological process. Based on philosophy of Guilty by Association, we introduce a novel tool named as GbA, to recover the transcriptional regulation in studied biological process. With GbA, the regulators of target genes are recovered by predicting regulators of their co-expressed genes with over-representation analysis. As evaluations, GbA was applied to three independent biological processes. Predictions were further investigated with true TF binding sites determined by ChIP-seq/chip and microarray data. All the results supported that GbA significantly recovered the true TF-target regulation. By checking the prediction for the same TF in three biological processes, we confirmed that prediction of GbA was condition-specific. We also compared the performance of GbA with position weight matrix based methods and results suggested

that GbA were more efficient to recover the true TF regulation.

Presentation 7

Arne Müller

Freie Universität Berlin Arnimallee 6

Fast Thermodynamically Constrained Flux Variability Analysis

Abstract:

Motivation:

Flux variability analysis is a useful tool to analyze the reliability of results obtained by flux balance analysis on genome-scale metabolic networks. However, in some cases flux variability predicts unbounded flux through some of the reactions in the network. These fluxes violate the second law of thermodynamics. Hence, we are interested in running flux variability analysis incorporating thermodynamic constraints.

Results:

We present a method for efficient flux variability analysis (and flux balance analysis) with thermodynamic constraints on genome-scale metabolic networks. We show that flux balance analysis with thermodynamic constraints is NP-hard. Besides this, we derive a theoretical tractability result which can also be applied to many metabolic networks in practice. We use this tractability result to develop a new constraint programming

algorithm Fast-tFVA for fast flux variability analysis with thermodynamic constraints.

Computational comparisons with previous methods demonstrate the effectiveness of the new method. For flux variability analysis, a speed up of factor 30-300 is achieved.

Presentation 8

Wei Qian

PICB, 320 Yueyang Road

Recent coevolution in human genomes

Abstract:

Recent studies of large-scale genetic polymorphism data in human revealed great number of candidate loci of local adaptation, which is in sheer contrast to the short history since human population divergence. We hypothesize that many signals of recent directional adaptation resulted from co-evolution via gene/protein interaction rather than independent selection events. Using the protein-protein interaction (PPI) network, we found that genes under recent selection preferentially appear at the intermediate regions of PPI network. We then studied the relationship between the selection signals and inter-gene distances on the PPI network. We found that candidate genes of positive selection are significantly enriched for shorter mutual network distances; Furthermore, genes in shorter network distances are more correlated on their population divergence patterns than those further apart on the PPI network. These strongly support the occurrence of gene/gene co-evolution in the recent human evolutionary history. Finally, on the sub-networks of positively selected genes, high genetic divergence correlations are found to strongly cluster around several hub genes, such as PTPN11, GRB2 in Europeans, TGFBR1, UBE2I, EGFR, UBQLN1 in Han Chinese and HIF1A in Africans, suggesting that multiple genes might be co-selected by hitch-hiking on the same selection event, via the connection of hub genes. In summary, our study contributed to inferring recent coevolution in human history and providing candidate interacting proteins that might coevolve for further study.

Presentation 9

Qingfeng Song

PICB, 320 Yueyang Road

A new mechanistic model of canopy photosynthesis with a complete description of the canopy architecture

Abstract:

Canopy architecture has been a major target in crop breeding for improved yields. Under elevated atmospheric CO₂ conditions (Ca), whether crop architectures in current elite crop cultivars can be modified for increased canopy CO₂ uptake rate (Ac) is unknown. Here we developed a new model of canopy photosynthesis model, which includes three components: a) a canopy architectural model; b) a forward ray tracing algorithm and c) a steady state biochemical model of C₃ photosynthesis, to study this question. With this model, we demonstrated that the Ac estimated from ‘average’ canopy light conditions is about 25% higher than that from detailed light conditions and theoretically evaluated the influence of canopy architectural on Ac under current and future elevated Ca in rice. Simulations results suggest that to gain an optimal Ac for the rice cultivar we examined the stem height, leaf width, and leaf angles can be potentially manipulated to enhance canopy photosynthesis. This model provides a framework for designing ideal crop architectures to gain optimal Ac under future changing climate conditions. A close linkage between canopy photosynthesis modeling and canopy photosynthesis measurements is required to fully realize the potential of such modeling approach in guiding crop improvements.

Presentation 10

Yichi Xu

320 Yueyang Road

Analysis of molecular signatures in mammalian hibernation

Abstract:

Mammalian hibernators display phenotypes similar to physiological conditions in non-hibernating species under conditions of calorie restriction and fasting, hypoxia,

hypothermia, ischemia-reperfusion, and sleep. However, whether or how similarities are also reflected on molecular and genetic levels is unclear. We identified molecular signatures of torpor and arousal in hibernation using a new custom-designed cDNA microarray for the arctic ground squirrel (*Urocitellus parryii*) and compared them to molecular signatures of selected phenotypes in mouse. Our results show that differential gene expression related to metabolism during torpor is closely related to that during calorie restriction and hypoxia. PPAR α is crucial for metabolic remodeling in hibernation. Genes related to the sleep-wake cycle and temperature response genes induced by hypothermia follow the same expression changes as in torpor-arousal cycle. Increased fatty acid metabolism might contribute to the protection against ischemia-reperfusion injury during hibernation. Further, by comparing with thousands of pharmacological signatures, we identified drugs that may induce similar expression patterns in human cell lines as during hibernation.

Poster Titles

Poster 1

Mahsa Ghanbari

Reconstruction of gene Regulatory Networks

Poster 2

Alexandra Grigore

Flux balance analysis on random metabolic systems

Poster 3

Johannes Helmuth

Transcriptional regulation of ubiquitous and tissue-specific genes

Poster 4

Youtao Lu

Using factor analysis for detection of key molecules that distinguish effective treatments of rheumatoid arthritis

Poster 5

Mingju Lv

The pathway of C4 evolution

Poster 6

Alessandro Mammana

Inferring nucleosome positioning and histone modifications from sequencing data

Poster 7

Annalisa Marsico

A computational method for microRNA promoter recognition

Poster 8

Arne Müller

Fast Thermodynamically Constrained Flux Variability Analysis

Poster 9

Shouneng Peng

Using high density 3D image registration to identify genetic loci associated with facial morphological variations.

Poster 10

Ling Sun

Relating the structure and dynamics of gene regulatory networks

Poster 11

Ruping Sun

Inferring competing endogenous RNA regulation using microRNA regulatory effect score

Poster 12

Minxian Wang

Positive selection on DNA base excision pathway

Poster 13

Yuting Liu

Cold induced RNA-binding proteins influence circadian selection of alternative polyadenylation

Poster 14

Yi Xiao

3D model of leaf light environment

Poster 15

Zheng Yan

New target finding way for special group of microRNA

Poster 16

Xinyi Yang

Gene network reconstruction applied on different types of real data

Poster 17

Bin Zhang

Intermediate size non-coding RNA in the prefrontal cortex of Primates

Poster 18

Qiaoyong Zhong

Novel Tools and Algorithms for Annotating FT-IR Spectral Images

Poster 19

Xiaoyuan Zhou

Diversity of the mouse intestinal microbiome associated with different therapies to Rheumtoid Arthritis

Participants

Juliane	Perner	Max Planck Institute for Molecular Genetics
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Wei	Qian	CAS-MPG Partner Institute for Computational Biology
Yimin	Tao	CAS-MPG Partner Institute for Computational Biology
Jiajia	Xu	CAS-MPG Partner Institute for Computational Biology
Yandong	Yin	CAS-MPG Partner Institute for Computational Biology
Xiong	Yang	CAS-MPG Partner Institute for Computational Biology
Zheng	Yan	CAS-MPG Partner Institute for Computational Biology
Kasia	Bozek	CAS-MPG Partner Institute for Computational Biology
Qiaoyong	Zhong	CAS-MPG Partner Institute for Computational Biology
YIng	Zhou	CAS-MPG Partner Institute for Computational Biology
Jinhua	Liu	CAS-MPG Partner Institute for Computational Biology
Yuting	Liu	CAS-MPG Partner Institute for Computational Biology
Mingju	Lv	Shanghai Institutes for Biologic Sciences, Chinese Academic of Science

Bin	Zhang	CAS-MPG Partner Institute for Computational Biology
Meng	Shi	CAS-MPG Partner Institute for Computational Biology
Arne	Müller	Freie Universität Berlin
Hongwen	Xuan	CAS-MPG Partner Institute of Computational Biology
Xiaoyuan	Zhou	CAS-MPG Partner Institute for Computational Biology
Xiaoyang	Dou	CAS-MPG Partner Institute for Computational Biology
Youtao	Lu	CAS-MPG Partner Institute for Computational Biology
Xiaoou	Zhang	CAS-MPG Partner Institute for Computational Biology
Zongfeng	Yang	CAS-MPG Partner Institute for Computational Biology
Xin	Huang	CAS-MPG Partner Institute for Computational Biology
Roman	Brinzanik	MPI for Molecular Genetics
Alessandro	Mammana	Max Planck Institute for Molecular Genetics
Qiao	Lu	CAS-MPG Partner Institute for Computational Biology
Ruiqing	Fu	CAS-MPG Partner Institute for Computational Biology
Minxian	Wang	CAS-MPG Partner Institute for Computational Biology
Zenghua	Fan	CAS-MPG Partner Institute for Computational Biology
Dorothee	Girbig	Max Planck Institute for Molecular Plant Physiology
Yuchen	Wang	CAS-MPG Partner Institute for Computational Biology
Xianbin	Yu	CAS-MPG Partner Institute for Computational Biology
Chang-Peng	Xin	CAS-MPG Partner Institute for Computational Biology
Yu	Wang	CAS-MPG Partner Institute for Computational Biology
Yuting	Wang	CAS-MPG Partner Institute for Computational Biology

Mahsa	Ghanbari	Max Planck Institute for Molecular Genetics
Chen	Ming	CAS-MPG Partner Institute for Computational Biology
Zhijun	Han	CAS-MPG Partner Institute of Computational Biology
Alexandra	Grigore	Freie Universitaet Berlin / Max Planck Institute for Molecular Genetics
Pei	Wu	CAS-MPG Partner Institute of Computational Biology
Yi	Xiao	CAS-MPG Partner Institute for Computational Biology
Xiao	Cui	CAS-MPG Partner Institute for Computational Biology
Wenchao	Hu	CAS-MPG Partner Institute for Computational Biology
Shouneng	Peng	CAS-MPG Partner Institute for Computational Biology
Lian	Deng	CAS-MPG Partner Institute for Computational Biology
Yi	Huang	CAS-MPG Partner Institute for Computational Biology
Xinyi	Yang	CAS-MPG Partner Institute for Computational Biology
Zhisong	He	CAS-MPG Partner Institute for Computational Biology
Lingfeng	Gou	CAS-MPG Partner Institute for Computational Biology
Sile	Hu	CAS-MPG Partner Institute for Computational Biology
Ran	Li	CAS-MPG Partner Institute for Computational Biology
Chen	Yang	CAS-MPG Partner Institute for Computational Biology
Guofeng	Meng	Max Planck Institute for Molecular Genetics
Qiang	Li	CAS-MPG Partner Institute for Computational Biology

Map

PICB Surrounding Map



Notes

