Title: Introduction to Systems Biology

Tentative Preface

The book, 'Introduction to Systems Biology', is intended to be a readable introductory text for undergraduate and graduate students who are interested in comprehensive biological systems. Since genomics, transcriptomics, proteomics and other omics analyses provide enormous amounts of biological data, systematic instruction containing explanations of underlying biological meanings through computational methods is required to explain the complex biological mechanisms and to build strategies for their application to biological problems. I hope that this book presents a clear and intuitive illustration of the topics on Systems Biology and further introduces using computational methods in studying complex biological systems.

The book begins with an introductory chapter on Systems Biology. The entire experimental omics tools are briefly described in the second section. The third and forth sections introduce the reader to challenging computational approaches to understand biological dynamic systems. These last two chapters provide ideas of theoretical and modeling optimization in systemic research on biology by presenting most algorithms as implementations, including the up-to-date full range of bioinformatic programs, and illustrating available successful applications.

We intend to provide a broad overview of the field with key examples and typical approaches of experimental design (both wet-lab and computational). Such a format is perfect as a resource book and a book providing a glimpse of the state-of-the-art in Systems Biology, but it also provides biologists with a readable introductory text for new systemic approaches for their own researches.

Contents included in this book -

•   Experimental Techniques for Systems Biology:

o   Quantitative measurements for systems biology
o   Gene expression profilings
o   Proteomics
o   Interactomics
o   Quantitative microscopy and imaging methods
o   Metabolomics
o   Phenomics
o   Localizomics
o   Network Dynamics
o   *In vitro* reconstituted systems

•   Theoretical and Modeling Techniques:

o Metabolic control theory & biochemical network theory
o Application of theory to biological systems
o Biological engineering theory
o Robustness, modularity and evolvability
o Network construction and dynamics
o Spatiotemporal systems
o Bifurcation analysis
o Modeling of signaling and metabolic networks

- Methods and Software Platforms for Systems Biology:

o Computational algorithms for systems biology
o Methods for modeling and simulating biochemical networks
o Software platforms for systems biology
o Databases for systems biology
o Visualization of networks and dynamics
o Application of modeling to drug development

Title: **Introduction to Systems Biology**

Tentative Table of Contents

I. Introduction

1. **A General View of Molecular Technology and How It is Changing Biology (or Systems Biology and New Technologies Enable Predictive and Preventative Medicine)**
    -   Leroy Hood, Institute for Systems Biology, USA
    -   lhood@systemsbiology.org
    -   Institute for Systems Biology, Seattle, WA 98103-8904, USA
    -   Hood L, Heath JR, Phelps ME, Lin B. Systems biology and new technologies enable predictive and preventative medicine. Science. 2004 Oct 22;306(5696):640-3.
    -   Bonneau R, Baliga NS, Deutsch EW, Shannon P, Hood L. Comprehensive de novo structure prediction in a systems-biology context for the archaea Halobacterium sp. NRC-1. Genome Biol. 2004;5(8):R52. Epub 2004 Jul 12.
    -   Systems biology, proteomics, and the future of health care: toward predictive, preventative, and personalized medicine. J Proteome Res. 2004 Mar-Apr;3(2):179-96. Review.
    -   NanoSystems biology. Mol Imaging Biol. 2003 Sep-Oct;5(5):312-25. Review.

2. **Hypothesis-Generating Science in the Post-Genomic Era**
    -   Stephen G. Oliver, School of Biological Sciences, University of Manchester, Oxford Road, Manchester M13 9PL, UK
    -   steve.oliver@man.ac.uk
    -   Taylor CF, Paton NW, … Hubbard SJ, Oliver SG. A systematic approach to modeling, capturing, and disseminating proteomics experimental data. Nat Biotechnol. 2003 Mar;21(3):247-54.
    -   Kell DB, Oliver SG. Here is the evidence, now what is the hypothesis? The complementary roles of inductive and hypothesis-driven science in the post-genomic era. Bioessays. 2004 Jan;26(1):99-105.
    -   Castrillo JI, Oliver SG. Yeast as a touchstone in post-genomic research: strategies for integrative analysis in functional genomics. J Biochem Mol Biol. 2004 Jan 31;37(1):93-106. Review.

3. **Systems-Biological Approach for Understanding Cellular Functions (accepted)**
    -   Hiroaki Kitano, ERATO Kitano Symbiotic Systems Project and The Systems Biology Institute, Japan
    -   kitano@symbio.jst.go.jp, kitano@csl.sony.co.jp

- Systems Biology Group Tokyo & Caltech Unit, ERATO Kitano Symbiotic Systems Project, Japan Science and Technology Corporation, M-31 Suite 6A, 6-31-15, Jingumae Shibuya-ku, Tokyo, 150-0001, Japan
- Sony Computer Science Laboratories, Inc., 3-14-13 Higashi-Gotanda, Shinagawa, Tokyo 141-0022, Japan.
- Morohashi M, Winn AE, Borisuk MT, Bolouri H, Doyle J, Kitano H. Robustness as a measure of plausibility in models of biochemical networks. J Theor Biol. 2002 May 7;216(1):19-30.
- Kitano H. Cancer as a robust system: implications for anticancer therapy. Nat Rev Cancer. 2004 Mar;4(3):227-35. Review.

4. **Systems Biology in the Ocean (accepted)**
   - Edward F. Delong, Massachusetts Institute of Technology, Cambridge, MA 02139, USA
   - delong@mit.edu, Phone 617-253-5271, FAX 617-258-8850
   - Dept. of Civil and Environmental Engineering & Division of Biological Engineering, Massachusetts Institute of Technology
   - Mailing Address: 48-427 MIT, 15 Vassar St., Cambridge, MA. 02139, USA
   - Hallam SJ, Putnam N, Preston CM, Detter JC, Rokhsar D, Richardson PM, DeLong EF. Reverse methanogenesis: testing the hypothesis with environmental genomics. Science. 2004 Sep 3;305(5689):1457-62.
   - Delong EF. Microbiology: reconstructing the wild types. Nature. 2004 Mar 4;428(6978):25-6.

II. Experimental Techniques for Systems Biology

A. Genomics

5. **Logical Circuitry of Genomic Regulatory Interactions (accepted)**
   - Sorin Istrail, Applied Biosystems/Celera, USA
   - Sorin.Istrail@celera.com; (240)453-3668 phone, (240)453-3324 fax
   - Advanced Research and Technology, Applied Biosystems/Celera Genomics, Rockville, MD 20850
   - Also has an appointment as Research Associate in Biology, Caltech
   - Optimal haplotype block-free selection of tagging SNPs for genome-wide association studies. Genome Res. 2004 Aug;14(8):1633-40.
   - Whole-genome shotgun assembly and comparison of human genome assemblies. Proc Natl Acad Sci U S A. 2004 Feb 17;101(7):1916-21. Epub 2004 Feb 09.

6. **Complexity of cis-Regulatory Logics from Simple Molecular Interactions (accepted)**
   - Ulrich Gerland, Nicolas Buchler and Terence Hwa, UCSD, USA
   - hwa@ucsd.edu

- Department of Physics and Center for Theoretical Biological Physics, University of California at San Diego, La Jolla, CA 92093-0319, USA
- Buchler NE, Gerland U, Hwa T. On schemes of combinatorial transcription logic. Proc Natl Acad Sci U S A. 2003 Apr 29;100(9):5136-41. Epub 2003 Apr 17.
- Arndt PF, Hwa T. Regional and time-resolved mutation patterns of the human genome. Bioinformatics. 2004 Jul 10;20(10):1482-5.

B. Transcriptomics

7. Dynamic Transcriptome of Mouse (accepted)
- Yoshihide Hayashizaki, Genome Exploration Group, RIKEN Genomic Sciences Center, Japan
- yosihide@gsc.riken.go.jp (secretary: Ms. Miki Nishikawa mknishi@gsc.riken.jp)
- Genome Exploration Research Group, Genomic Science Center (GSC), RIKEN, 1-7-22 Suehiro-cho, Tsurumi-ku, Yokohama, 230-0045 Japan
- Hayashizaki Y, Kanamori M. Dynamic transcriptome of mice. Trends Biotechnol. 2004 Apr;22(4):161-7
- Hayashizaki Y. The Riken mouse genome encyclopedia project. C R Biol. 2003 Oct-Nov;326(10-11):923-9. Review

8. Learning Biology from Genome-Wide Expression Data
- Naama Barkai, Molecular Genetics, Weizmann Institute of Science, Israel
- naama.barkai@weizmann.ac.il
- Department of Molecular Genetics, Weizmann Institute of Science, 76100 Rehovot, Israel
- Ihmels J, Levy R, Barkai N. Principles of transcriptional control in the metabolic network of Saccharomyces cerevisiae. Nat Biotechnol. 2004 Jan;22(1):86-92. Epub 2003 Nov 30.
- Bergmann S, Ihmels J, Barkai N. Iterative signature algorithm for the analysis of large-scale gene expression data.

9. Dissecting Transcriptional Control Networks (accepted)
- Anirvan M Sengupta, BioMaPS Institute, Rutgers University, Piscataway, NJ 08854, USA
- anirvans@physics.rutgers.edu
- BioMaPS Institute, Rutgers University, Piscataway, NJ 08854, USA.
- Sengupta AM, Djordjevic M, Shraiman BI. Specificity and robustness in transcription control networks. Proc Natl Acad Sci U S A. 2002 Feb 19;99(4):2072-7.
- Nagaraj VH, O'Flanagan RA, Bruning AR, Mathias JR, Vershon AK, Sengupta AM. Combined analysis of expression data and transcription factor binding sites in the yeast genome. BMC Genomics. 2004 Aug 26;5(1):59.

10. Understanding Cellular Signaling Networks in Mouse (accepted)
- Xiaocui Zhu and Sangdun Choi, Division of Biology, California Institute of Technology, Pasadena, CA 91125, USA
- schoi@caltech.edu
- Division of Biology, 147-75, California Institute of Technology, Pasadena, CA 91125, USA
- Zhu X, Hart R, Choi S. Analysis of the major patterns of B cell gene expression changes in response to short-term stimulation with 33 single ligands. J. Immunology. 173(12) / Dec 15, 2004.
- Park PJ, Cao YA, Lee SY, Kim JW, Chang MS, Hart R, Choi S. Current issues for DNA microarrays: platform comparison, double linear amplification, and universal RNA reference. J Biotechnol. 2004 Sep 9;112(3):225-45.

11. Predicting Gene Expression from Sequence
- Saeed Tavazoie, Lewis-Sigler Institute for Integrative Genomics and Department of Molecular Biology, Princeton University, Princeton
- tavazoie@molbio.princeton.edu
- Lewis-Sigler Institute for Integrative Genomics and Department of Molecular Biology, Princeton University, Princeton, NJ 08544, USA.
- Beer MA, Tavazoie S. Predicting gene expression from sequence. Cell. 2004 Apr 16;117(2):185-98.
- Jim K, Parmar K, Singh M, Tavazoie S. A cross-genomic approach for systematic mapping of phenotypic traits to genes. Genome Res. 2004 Jan;14(1):109-15.
- Pritsker M, Liu YC, Beer MA, Tavazoie S. Whole-genome discovery of transcription factor binding sites by network-level conservation. Genome Res. 2004 Jan;14(1):99-108. Epub 2003 Dec 12.

C. Proteomics

12. Proteomics (or Nanotechnology-Based Innovation in Tissue Proteomics)
- Lance A. Liotta, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892-1500, USA.
- lance@helix.nih.gov
- Geho DH, Lahar N, Ferrari M, Petricoin EF, Liotta LA. Opportunities for nanotechnology-based innovation in tissue proteomics. Biomed Microdevices. 2004 Sep;6(3):231-9.
- Interewicz B, Olszewski WL, Leak LV, Petricoin EF, Liotta LA. Profiling of normal human leg lymph proteins using the 2-D electrophoresis and SELDI-TOF mass spectrophotometry approach. Lymphology. 2004 Jun;37(2):65-72.
- Espina V, Woodhouse EC, Wulfkuhle J, Asmussen HD, Petricoin EF 3rd, Liotta LA. Protein microarray detection strategies: focus on direct

detection technologies. J Immunol Methods. 2004 Jul;290(1-2):121-33. Review.

13. Integrated System for Rapid Proteomics Analyses
- Pierre Thibault, IRIC-Institut de recherches en immunologie et cancer, Pavillon Roger-Gaudry, Université de Montréal, Canada
- pierre.thibault@umontreal.ca, Tel: 514-343-6910, Fax: 514-343-7780
- Chaire de recherche du Canada en Proteomique, IRIC-Institut de recherches en immunologie et cancer, Pavillon Roger-Gaudry, Université de Montréal, C.P. 6128, succursale Centre-Ville, Montréal, QC H3C 3J7, Canada
- Li J, Tremblay TL, Harrison J, Thibault P. Integrated system for rapid proteomics analyses using microfluidic devices coupled to anoelectrospray mass spectrometry. Methods Mol Biol. 2004;276:305-24.
- Kearney P, Thibault P. Bioinformatics meets proteomics--bridging the gap between mass spectrometry data analysis and cell biology. J Bioinform Comput Biol. 2003 Apr;1(1):183-200.

14. Structural Genomics
- Sung-Hou Kim, University of California at Berkeley
- shkim@cchem.berkeley.edu
- Department of Chemistry and Calvin Laboratory, Lawrence Berkeley National Laboratory, University of California at Berkeley, Berkeley, CA 94720, USA
- Zhang C, Kim SH. Overview of structural genomics: from structure to function. Curr Opin Chem Biol. 2003 Feb;7(1):28-32. Review.
- Kim SH, Shin DH, Choi IG, Schulze-Gahmen U, Chen S, Kim R. Structure-based functional inference in structural genomics. J Struct Funct Genomics. 2003;4(2-3):129-35. Review.

D. Interactomics

15. Protein Interactions
- David Eisenberg, UCLA. USA
- david@mbi.ucla.edu
- UCLA-DOE Institute for Genomics and Proteomics, Howard Hughes Medical Institute, Molecular Biology Institute, Box 951570, Los Angeles, California 90095-1570, USA
- Salwinski L, Eisenberg D. In silico simulation of biological network dynamics. Nat Biotechnol. 2004 Aug;22(8):1017-9. Epub 2004 Jul 04.
- Bowers PM, Pellegrini M, Thompson MJ, Fierro J, Yeates TO, Eisenberg D. Prolinks: a database of protein functional linkages derived from coevolution. Genome Biol. 2004;5(5):R35. Epub 2004 Apr 16.

16. Interactome with the Yeast Two-Hybrid System

- Barry Causier, School of Biology, University of Leeds, Leeds LS2 9J7, UK
- b.e.causier@leeds.ac.uk, B.E.Causier@leeds.ac.uk, Phone: +44(0) 113 3432838
- Causier B. Studying the interactome with the yeast two-hybrid system and mass spectrometry. Mass Spectrom Rev. 2004 Sep-Oct;23(5):350-67. Review.
- Causier B, Davies B. Analysing protein-protein interactions with the yeast two-hybrid system. Plant Mol Biol. 2002 Dec;50(6):855-70. Review.

17. Large-Scale Mapping of Genetic Networks
- Charlie Boone, University of Toronto, Canada
- charlie.boone@utoronto.ca
- Banting and Best Department of Medical Research, University of Toronto, Toronto, ON, Canada M5G 1L6
- Global mapping of the yeast genetic interaction network. Science. 2004 Feb 6;303(5659):808-13.
- Integration of chemical-genetic and genetic interaction data links bioactive compounds to cellular target pathways. Nat Biotechnol. 2004 Jan;22(1):62-9. Epub 2003 Dec 07.
- Yeast genomics and proteomics in drug discovery and target validation. Prog Cell Cycle Res. 2003;5:159-66. Review.

E. Metabolomics

18. Dynamic Metabolomics for Systems Biology (accepted)
- Joseph J. Heijnen, Delft University of Technology, The Netherlands
- E-mail: J.Boks@tnw.tudelft.nl (Jenny Boks-Zondervan is his Secretariat), Phone: +31 (0)15 2782342, Fax: +31 (0)15 2782355
- Kluyver Laboratory, Delft University of Technology, The Netherlands
- Wu L, Wang W, van Winden WA, van Gulik WM, Heijnen JJ. A new framework for the estimation of control parameters in metabolic pathways using lin-log kinetics. Eur J Biochem. 2004 Aug;271(16):3348-59.
- Visser D, Heijnen JJ. Dynamic simulation and metabolic re-design of a branched pathway using linlog kinetics. Metab Eng. 2003 Jul;5(3):164-76.
- Visser D, Heijnen JJ. The mathematics of metabolic control analysis revisited. Metab Eng. 2002 Apr;4(2):114-23. Review.

19. From Gene Expression to Metabolic Fluxes (accepted)
- Jens Nielsen, Technical University of Denmark, Lyngby, Denmark
- jn@biocentrum.dtu.dk
- Center for Microbial Biotechnology, BioCentrum-DTU, Technical University of Denmark, Building 223, DK-2800 Kgs, Lyngby
- Patil KR, Akesson M, Nielsen J. Use of genome-scale microbial models for metabolic engineering. Curr Opin Biotechnol. 2004 Feb;15(1):64-9.

- Bro C, Nielsen J. Impact of 'ome' analyses on inverse metabolic engineering. Metab Eng. 2004 Jul;6(3):204-11
- Bro C, Regenberg B, Nielsen J. Genome-wide transcriptional response of a Saccharomyces cerevisiae strain with an altered redox metabolism. Biotechnol Bioeng. 2004 Feb 5;85(3):269-76.

20. Reconstruction and Structural Analysis of Metabolic and Regulatory Networks (accepted)
- An-Ping Zeng, German Research Centre for Biotechnology, Germany
- aze@gbf.de
- Biochemical Engineering Division, GBF-German Research Centre for Biotechnology, Braunschweig
- Sun J, Zeng AP. IdentiCS--identification of coding sequence and in silico reconstruction of the metabolic network directly from unannotated low-coverage bacterial genome sequence. BMC Bioinformatics. 2004 Aug 16;5(1):112.
- Ma HW, Zhao XM, Yuan YJ, Zeng AP. Decomposition of metabolic network into functional modules based on the global connectivity structure of reaction graph. Bioinformatics. 2004 Aug 12;20(12):1870-6. Epub 2004 Mar 22.

F. Phenomics

21. Genome-Scale Assessment of Phenotypic Changes during Adaptive Evolution (accepted)
- Bernhard Palsson, University of California San Diego, La Jolla, CA, USA
- bpalsson@be-research.ucsd.edu; FAX (858) 822-3120
- Department of Bioengineering, University of California, San Diego, San Diego, California 92092-0412, USA
- Fong SS, Palsson BO. Metabolic gene-deletion strains of Escherichia coli evolve to computationally predicted growth phenotypes. Nat Genet. 2004 Oct;36(10):1056-8. Epub 2004 Sep 26.
- Reed JL, Palsson BO. Genome-Scale In Silico Models of E. coli Have Multiple Equivalent Phenotypic States: Assessment of Correlated Reaction Subsets That Comprise Network States. Genome Res. 2004 Sep;14(9):1797-805.
- Papin JA, Stelling J, Price ND, Klamt S, Schuster S, Palsson BO. Comparison of network-based pathway analysis methods. Trends Biotechnol. 2004 Aug;22(8):400-5.

22. Phenome Mapping with an ORFeome-based RNAi Library
- Marc Vidal, Center for Cancer Systems Biology and Department of Cancer Biology, Dana-Farber Cancer Institute, and Department of Genetics, Harvard Medical School
- marc_vidal@dfci.harvard.edu

- Center for Cancer Systems Biology and Department of Cancer Biology, Dana-Farber Cancer Institute, and Department of Genetics, Harvard Medical School, Boston, Massachusetts 02115, USA.
- Dupuy D, Li QR, Deplancke B, Boxem M, Hao T, Lamesch P, Sequerra R, Bosak S, Doucette-Stamm L, Hope IA, Hill DE, Walhout AJ, Vidal M. A first version of the Caenorhabditis elegans Promoterome. Genome Res. 2004 Oct;14(10B):2169-75.
- Rual JF, Ceron J, Koreth J, Hao T, Nicot AS, Hirozane-Kishikawa T, Vandenhaute J, Orkin SH, Hill DE, van den Heuvel S, Vidal M. Toward improving Caenorhabditis elegans phenome mapping with an ORFeome-based RNAi library. Genome Res. 2004 Oct;14(10B):2162-8.
- Rual JF, Hirozane-Kishikawa T, Hao T, Bertin N, Li S, Dricot A, Li N, Rosenberg J, Lamesch P, Vidalain PO, Clingingsmith TR, Hartley JL, Esposito D, Cheo D, Moore T, Simmons B, Sequerra R, Bosak S, Doucette-Stamm L, Le Peuch C, Vandenhaute J, Cusick ME, Albala JS, Hill DE, Vidal M. Human ORFeome version 1.1: a platform for reverse proteomics. Genome Res. 2004 Oct;14(10B):2128-35.
- Brasch MA, Hartley JL, Vidal M. ORFeome cloning and systems biology: standardized mass production of the parts from the parts-list. Genome Res. 2004 Oct;14(10B):2001-9.

23. Bacterial Persistence: A Phenotypic Switch Revealed by Microfluidics (accepted)
- Nathalie Q. Balaban, The Rockefeller University, New York, USA
- nathalieqb@phys.huji.ac.il
- Laboratory of Living Matter and Center for Studies in Physics and Biology, Rockefeller University, 1230 York Avenue, New York, NY 10021, USA.
- Racah Institute for Physics, Hebrew University, Jerusalem 91904, Israel.
- Balaban NQ, Merrin J, Chait R, Kowalik L, Leibler S. Bacterial persistence as a phenotypic switch. Science. 2004 Sep 10;305(5690):1622-5. Epub 2004 Aug 12.
- Bershadsky AD, Balaban NQ, Geiger B. Adhesion-dependent cell mechanosensitivity. Annu Rev Cell Dev Biol. 2003;19:677-95. Review.

G. Localizomics

24. Interpretation of Protein Subcellular Locations
- Robert F. Murphy, Department of Biological Sciences, and Center for Automated Learning and Discovery, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, PA 15213, USA.
- murphy@cmu.edu
- Murphy RF. Automated interpretation of protein subcellular location patterns: implications for early cancer detection and assessment. Ann N Y Acad Sci. 2004 May;1020:124-31.

- Hu Y, Murphy RF. Automated interpretation of subcellular patterns from immunofluorescence microscopy. J Immunol Methods. 2004 Jul;290(1-2):93-105.
- Huang K, Murphy RF. Boosting accuracy of automated classification of fluorescence microscope images for location proteomics. BMC Bioinformatics. 2004 Jun 18;5(1):78.
- Huang K, Murphy RF. From quantitative microscopy to automated image understanding. J Biomed Opt. 2004 Sep-Oct;9(5):893-912

25. Fluorescence Imaging of Signaling Networks
- Mary N. Teruel, Department of Molecular Pharmacology, Stanford University School of Medicine, 269 Campus Drive, Room 3230, Stanford, CA 94305, USA
- mteruel@stanford.edu
- Meyer T, Teruel MN. Fluorescence imaging of signaling networks. Trends Cell Biol. 2003 Feb;13(2):101-6. Review.
- Teruel MN, Meyer T. Parallel single-cell monitoring of receptor-triggered membrane translocation of a calcium-sensing protein module. Science. 2002 Mar 8;295(5561):1910-2.
- Tengholm A, Teruel MN, Meyer T. Single cell imaging of PI3K activity and glucose transporter insertion into the plasma membrane by dual color evanescent wave microscopy. Sci STKE. 2003 Feb 11;2003(169):PL4. Print 2003 Feb 11.

H. Signaling Networks

26. Temporal and Spatial Control of Signaling in the Interferon-r/jak/Stat1 Pathway (accepted)
- Uwe Vinkemeier and Thomas Höfer, Humboldt University Berlin, Germany
- thomas.hoefer@biologie.hu-berlin.de
- Department of Theoretical Biophysics, Institute of Biology, Humboldt University Berlin, Invalidenstrasse 42, 10115, Berlin, Germany
- Mariani L, Lohning M, Radbruch A, Hofer T. Related Articles, Links
- Transcriptional control networks of cell differentiation: insights from helper T lymphocytes. Prog Biophys Mol Biol. 2004 Sep;86(1):45-76.
- Salazar C, Hofer T. Allosteric regulation of the transcription factor NFAT1 by multiple phosphorylation sites: a mathematical analysis. J Mol Biol. 2003 Mar 14;327(1):31-45.
- Hofer T, Venance L, Giaume C. Control and plasticity of intercellular calcium waves in astrocytes: a modeling approach. J Neurosci. 2002 Jun 15;22(12):4850-9.

27. Employing Systems Biology to Quantify Receptor Tyrosine Kinase Signaling in Time and Space (accepted)

- Boris N Kholodenko, Thomas Jefferson University, Philadelphia, PA, USA
- Boris.Kholodenko@jefferson.edu
- Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, 1020 Locust Street, Philadelphia, PA 19107, USA
- Kholodenko BN. Four-dimensional organization of protein kinase signaling cascades: the roles of diffusion, endocytosis and molecular motors. J Exp Biol. 2003 Jun;206(Pt 12):2073-82. Review.
- Kholodenko BN, Kiyatkin A, Bruggeman FJ, Sontag E, Westerhoff HV, Hoek JB. Untangling the wires: a strategy to trace functional interactions in signaling and gene networks. Proc Natl Acad Sci U S A. 2002 Oct 1;99(20):12841-6.
- Kholodenko BN. MAP kinase cascade signaling and endocytic trafficking: a marriage of convenience? Trends Cell Biol. 2002 Apr;12(4):173-7. Review.

28. Propagating Chemical Waves Within and Among Cells
- Howard R. Petty, University of Michigan, Ann Arbor, MI, USA
- hpetty@umich.edu
- Departments of Ophthalmology and Visual Sciences, University of Michigan Medical School, Ann Arbor, MI 48105
- Petty HR. Detection of cytokine signal transduction "cross-talk" in leukocyte activation. Methods Mol Biol. 2004;249:219-28.
- Albrecht E, Kindzelskii AL, Petty HR. Signal processing times in neutrophil activation: dependence on ligand concentration and the relative phase of metabolic oscillations. Biophys Chem. 2003 Dec 1;106(3):211-9.

29. Modeling Cell Cycle Controls: An Example of the "Last Step" of Computational Molecular Biology (accepted)
- Bela Novak and John Tyson, Virginia Tech, USA
- tyson@vt.edu, Tel 540-231-4662, Fax 540-231-9307
- Bela Novak <bnovak@mail.bme.hu>
- Department of Biology, M.C. 0406, Virginia Polytechnic Institute & State University, Blacksburg VA 24061, USA
- Novak BB, Tyson JJ. A model for restriction point control of the mammalian cell cycle. J Theor Biol. 2004 Oct 21;230(4):563-79.
- Battogtokh D, Tyson JJ. Bifurcation analysis of a model of the budding yeast cell cycle. Chaos. 2004 Sep;14(3):653-61.

30. Structure and Evolution of Transcriptional Regulatory Networks (accepted)
- M Madan Babu, MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK
- madanm@mrc-lmb.cam.ac.uk
- MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK

- Teichmann SA, Babu MM. Gene regulatory network growth by duplication. Nat Genet. 2004 May;36(5):492-6. Epub 2004 Apr 11.
- Babu MM, Luscombe NM, Aravind L, Gerstein M, Teichmann SA. Structure and evolution of transcriptional regulatory networks. Curr Opin Struct Biol. 2004 Jun;14(3):283-91.

III. Theoretical and Modeling Techniques

31. Multilevel Description of Biological Networks (or On Switches, Gates and Clocks: Life in the Time of Systems Biology)
- Stanislas Leibler, Rockefeller University, USA
- E-mail: Administrative Secretary (Kirk, Shannon): kirks@rockefeller.edu
- Laboratory of Living Matter and Center for Studies in Physics and Biology, Rockefeller University, 1230 York Avenue, New York, NY 10021, USA.
- Balaban NQ, Merrin J, Chait R, Kowalik L, Leibler S. Bacterial persistence as a phenotypic switch. Science. 2004 Sep 10;305(5690):1622-5. Epub 2004 Aug 12.
- Mihalcescu I, Hsing W, Leibler S. Resilient circadian oscillator revealed in individual cyanobacteria. Nature. 2004 Jul 1;430(6995):81-5.
- Vilar JM, Guet CC, Leibler S. Modeling network dynamics: the lac operon, a case study. J Cell Biol. 2003 May 12;161(3):471-6. Review.
- Vilar JM, Leibler S. DNA looping and physical constraints on transcription regulation. J Mol Biol. 2003 Aug 29;331(5):981-9.

32. Bringing Genomes to Life: The Use of Genome-Scale *in silico* Models (accepted)
- Bernhard O. Palsson, Dept of Bioengineering, University of California, San Diego, USA
- bpalsson@be-research.ucsd.edu; FAX (858) 822-3120
- Department of Bioengineering, University of California, San Diego, San Diego, California 92092-0412, USA
- Reed JL, Palsson BO. Genome-Scale In Silico Models of E. coli Have Multiple Equivalent Phenotypic States: Assessment of Correlated Reaction Subsets That Comprise Network States. Genome Res. 2004 Sep;14(9):1797-805.
- Papin JA, Stelling J, Price ND, Klamt S, Schuster S, Palsson BO. Comparison of network-based pathway analysis methods. Trends Biotechnol. 2004 Aug;22(8):400-5.
- Price ND, Schellenberger J, Palsson BO. Uniform sampling of steady-state flux spaces: means to design experiments and to interpret enzymopathies. Biophys J. 2004 Oct;87(4):2172-86.

33. Bayesian Network Approach to Cell Signaling Pathway Modeling
- Douglas A. Lauffenburger, Biological Engineering Division, Massachusetts Institute of Technology
- lauffen@mit.edu
- Biological Engineering Division, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

- Sachs K, Gifford D, Jaakkola T, Sorger P, Lauffenburger DA. Bayesian network approach to cell signaling pathway modeling. Sci STKE. 2002 Sep 3;2002(148):PE38.
- Maly IV, Wiley HS, Lauffenburger DA. Self-organization of polarized cell signaling via autocrine circuits: computational model analysis. Biophys J. 2004 Jan;86(1 Pt 1):10-22.
- Prudhomme W, Daley GQ, Zandstra P, Lauffenburger DA. Multivariate proteomic analysis of murine embryonic stem cell self-renewal versus differentiation signaling. Proc Natl Acad Sci U S A. 2004 Mar 2;101(9):2900-5. Epub 2004 Feb 20.
- Ideker T, Lauffenburger D. Building with a scaffold: emerging strategies for high- to low-level cellular modeling. Trends Biotechnol. 2003 Jun;21(6):255-62.

34. Scale Free Networks
- Albert-Laszlo Barabasi and Zoltan Oltvai, University of Notre Dame/North Western University
- alb@nd.edu, zno008@northwestern.edu
- Barabasi: Department of Physics, University of Notre Dame, Notre Dame, Indiana 46556, USA., alb@nd.edu
- Oltvai: Department of Pathology, Northwestern University, Chicago, Illinois 60611, USA., zno008@northwestern.edu
- Barabasi AL, Oltvai ZN. Network biology: understanding the cell's functional organization. Nat Rev Genet. 2004 Feb;5(2):101-13. Review.
- Dobrin R, Beg QK, Barabasi AL, Oltvai ZN. Aggregation of topological motifs in the Escherichia coli transcriptional regulatory network. BMC Bioinformatics. 2004 Jan 30;5(1):10.
- Yook SH, Oltvai ZN, Barabasi AL. Functional and topological characterization of protein interaction networks. Proteomics. 2004 Apr;4(4):928-42.
- Almaas E, Kovacs B, Vicsek T, Oltvai ZN, Barabasi AL. Global organization of metabolic fluxes in the bacterium Escherichia coli. Nature. 2004 Feb 26;427(6977):839-43.

35. Networks of Epistatic Interactions (accepted)
- Roy Kishony, Bauer Center for Genomics Research, Harvard University
- rkishony@CGR.Harvard.edu, 617-496-3112, 617-495-2196 (fax)
- Bauer Center for Genomics Research, Harvard University, 7 Divinity Ave, Cambridge, MA 02138
- Roy Kishony and Stanislas Leibler. Environmental stresses can alleviate the average deleterious effect of mutations. Journal of Biology 2003; 2:14

36. Modules in Biological Networks
- Eran Segal, Stanford University

- eran@cs.stanford.edu
- Computer Science Department, Stanford University, Stanford, California 94305, USA
- Segal E, Friedman N, Koller D, Regev A. A module map showing conditional activity of expression modules in cancer. Nat Genet. 2004 Oct;36(10):1090-8. Epub 2004 Sep 26.
- Segal E, Yelensky R, Koller D. Genome-wide discovery of transcriptional modules from DNA sequence and gene expression. Bioinformatics. 2003;19 Suppl 1:i273-82.
- Segal E, Shapira M, Regev A, Pe'er D, Botstein D, Koller D, Friedman N. Module networks: identifying regulatory modules and their condition-specific regulators from gene expression data. Nat Genet. 2003 Jun;34(2):166-76.

37. Mathematical Modeling of Metabolic Diseases Caused by Enzyme Deficiencies (accepted)

- Hermann-Georg Holzhütter, Humboldt University Berlin, Germany
- hermann-georg.holzhuetter@charite.de
- Humboldt-University Berlin, Medical School (Charite), Institute of Biochemistry, Berlin, Germany.
- Holzhutter HG. The principle of flux minimization and its application to estimate stationary fluxes in metabolic networks. Eur J Biochem. 2004 Jul;271(14):2905-22.
- Peters B, Holzhutter HG. In vitro phototoxicity testing: development and validation of a new concentration response analysis software and biostatistical analyses related to the use of various prediction models. Altern Lab Anim. 2002 Jul-Aug;30(4):415-32.

38. Reconstructing Genetic Regulatory Networks using Gene Expression Profiling and State Space Models (accepted)

- David Wild, Keck Graduate Institute, USA; Co-authors: Zoubin Ghahramani (Gatsby Computational Neuroscience Unit, University College London), Matthew Beal (Dept of Computer Science and Engineering, SUNY Buffalo)
- david_wild@kgi.edu
- Co-authors: Dr. Zoubin Ghahramani, Gatsby Computational Neuroscience Unit, University College London (zoubin@gatsby.ucl.ac.uk) and Dr. Matthew Beal, Dept of Computer Science and Engineering, SUNY Buffalo
- Keck Graduate Institute, 535 Watson Drive, Claremont, CA 91711, USA
- Beal MJ, Falciani F, Ghahramani Z, Rangel C, Wild DL. A Bayesian approach to reconstructing genetic regulatory networks with hidden factors. Bioinformatics. 2004 Sep 7

- Dubey A, Hwang S, Rangel C, Rasmussen CE, Ghahramani Z, Wild DL. Clustering protein sequence and structure space with infinite Gaussian mixture models. Pac Symp Biocomput. 2004:399-410.
- Raval A, Ghahramani Z, Wild DL. A Bayesian network model for protein fold and remote homologue recognition. Bioinformatics. 2002 Jun;18(6):788-801.

39. Silicon Cell Initiative (accepted)
- Jacky L. Snoep, University of Stellenbosch/ZA; H.V. Westerhoff, Vrije Universiteit Amsterdam, The Netherlands
- jls@sun.ac.za
- Department of Biochemistry, University of Stellenbosch, Private Bag X1, Matieland 7602, South Africa
- Olivier BG, Snoep JL. Web-based kinetic modelling using JWS Online. Bioinformatics. 2004 Sep 1;20(13):2143-4. Epub 2004 Apr 08.
- Snoep JL, Olivier BG. JWS online cellular systems modelling and microbiology. Microbiology. 2003 Nov;149(Pt 11):3045-7.
- Snoep JL, Olivier BG. Java Web Simulation (JWS); a web based database of kinetic models. Mol Biol Rep. 2002;29(1-2):259-63.

40. Combining Biological Networks to Predict Physical and Genetic Interactions
- Frederick P. Roth, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, 250 Longwood Avenue, Boston, MA 02115
- fritz_roth@hms.harvard.edu
- Wong SL, Zhang LV, Tong AH, Li Z, Goldberg DS, King OD, Lesage G, Vidal M, Andrews B, Bussey H, Boone C, Roth FP. Combining biological networks to predict genetic interactions. Proc Natl Acad Sci U S A. 2004 Nov 2;101(44):15682-7. Epub 2004 Oct 20.
- Asthana S, King OD, Gibbons FD, Roth FP. Predicting protein complex membership using probabilistic network reliability. Genome Res. 2004 Jun;14(6):1170-5. Epub 2004 May 12.
- Zhang LV, Wong SL, King OD, Roth FP. Predicting co-complexed protein pairs using genomic and proteomic data integration. BMC Bioinformatics. 2004 Apr 16;5(1):38.

41. Switches and Metabolic Optimality in Systems Biology (accepted)
- Xiaoxia Lin, Gary Gao, Jeremy Zucker and George Church, Harvard Medical School, USA
- g1m1c1@arep.med.harvard.edu
- "Xiaoxia Lin (Xiaoxia Lin)" <xiaoxia@genetics.med.harvard.edu>, <ygao@receptor.med.harvard.edu>, "'Jeremy Zucker'" <zucker@research.dfci.harvard.edu>, "'Aaron Brandes'" <aaronb@media.mit.edu>

- Professor of Genetics, Harvard Medical School, MIT Health Sciences & Technology & CSBi, Director of the Lipper Center for Computational Genetics, MIT-Harvard DOE Genomes to Life Center, NIH Center for Excellence in Genomic Science, Mail: NRB room 238, 77 Avenue Louis Pasteur, Boston, MA 02115 USA, Phone: (617) 432-1278 Administrative assistant (Cindy Vallaro); -7562 direct line & voice mail
- Harvard Medical School, Department of Genetics, 200 Longwood Ave, Boston, MA, 02115, USA
- Selinger DW, Wright MA, Church GM. On the complete determination of biological systems. Trends Biotechnol. 2003 Jun;21(6):251-4.
- Janse DM, Crosas B, Finley D, Church GM. Localization to the proteasome is sufficient for degradation. J Biol Chem. 2004 May 14;279(20):21415-20. Epub 2004 Mar 23.
- Segre D, Zucker J, Katz J, Lin X, D'Haeseleer P, Rindone WP, Kharchenko P, Nguyen DH, Wright MA, Church GM. From annotated genomes to metabolic flux models and kinetic parameter fitting. OMICS. 2003 Fall;7(3):301-16.

42. Robustness of Genetic Switch (accepted)
- Ping Ao, University of Washington, USA
- aoping@u.washington.edu, fax: (206) 685-8047; ph: (206) 543-7837
- Department of Physics, University of Washington, USA
- Zhu XM, Yin L, Hood L, Ao P. Calculating biological behaviors of epigenetic states in the phage lambda life cycle. Funct Integr Genomics. 2004 Jul;4(3):188-95. Epub 2004 Feb 05.
- Zhu XM, Yin L, Hood L, Ao P. Robustness, Stability and Efficiency of Phage λ Genetic Switch: Dynamical Structure Analysis. Journal of Bioinformatics and Computational Biology v.2 (4) (2004) 785-817

- **IV. Methods and Software Platforms for Systems Biology**

43. Building the Computational Chassis of Virtual Cell (accepted)
- Pawan Dhar, Bioinformatics Institute of Singapore, Singapore
- pk@bii-sg.org, pk@bii.a-star.edu.sg, Tel: (65) 6478 8264, Fax: (65) 6478 9047
- Pawan Dhar, Chee Meng, Sandeep Somani, Li Ye, Anand Sairam, Mandar Chitre, Zhu Hao, Kishore Sakharkar (2004): Cellware – a new modeling and simulation tool for Computational Systems Biology. Bioinformatics 20, 1319-21.
- Dhar Pawan (2004). The Cell equator - more than poles apart. Trends in Biotechnology 22, 103-4
- Zhu H, Huang S, Dhar P. The next step in systems biology: simulating the temporospatial dynamics of molecular network. Bioessays. 2004 Jan;26(1):68-72.
- Zhu H, Sun Y, Rajagopal G, Mondry A, Dhar P. Facilitating arrhythmia simulation: the method of quantitative cellular automata modeling and parallel running. Biomed Eng Online. 2004 Aug 30;3(1):29.
- Meng TC, Somani S, Dhar P. Modeling and simulation of biological systems with stochasticity. In Silico Biol. 2004 Apr 16;4(2):0024

44. MathSBML: A Package for Manipulating SBML-based Biological Models
- Bruce E. Shapiro, Jet Propulsion Laboratory, California Institute of Technology
- bshapiro@caltech.edu
- Jet Propulsion Laboratory, California Institute of Technology, Mail Stop 126-347, 4800 Oak Grove Drive, Pasadena, CA 91109, USA
- Shapiro BE, Hucka M, Finney A, Doyle J. MathSBML: a package for manipulating SBML-based biological models. Bioinformatics. 2004 Nov 1;20(16):2829-31. Epub 2004 Apr 15.
- Shapiro BE, Levchenko A, Meyerowitz EM, Wold BJ, Mjolsness ED. Cellerator: extending a computer algebra system to include biochemical arrows for signal transduction simulations. Bioinformatics. 2003 Mar 22;19(5):677-8.

45. CellML 1.1: A Standard for Biological Model Specification and Reuse
- Catherine M. Lloyd, Bioengineering Institute, University of Auckland, Auckland, New Zealand
- c.lloyd@auckland.ac.nz
- Bioengineering Institute, University of Auckland, Level 6, 70 Symonds Street, Auckland, New Zealand
- Lloyd CM, Halstead MD, Nielsen PF. CellML: its future, present and past. Prog Biophys Mol Biol. 2004 Jun-Jul;85(2-3):433-50. Review.

46. DBRF-MEGN Method: An Algorithm for Deducing Minimum Equivalent Gene Networks from Large-Scale Gene Expression Profiles of Gene Deletion Mutants (accepted)

- Koji Kyoda and Shuichi Onami, Graduate School of Science and Technology, Keio University, Yokohama, Japan
- KK: kyoda@so.bio.keio.ac.jp, SO: sonami@bio.keio.ac.jp
- Graduate School of Science and Technology, Keio University, 3-14-1 Hiyoshi, Kohoku, Yokohama 223-8522, Japan
- Kyoda K, Baba K, Onami S, Kitano H. DBRF-MEGN method: an algorithm for deducing minimum equivalent gene networks from large-scale gene expression profiles of gene deletion mutants. Bioinformatics. 2004 May 27, 20:2662-2675

47. Metabolic Control Analysis: A Tool for Understanding Cellular Behavior, Control and Regulation (or Modelling Cellular Systems with PySCeS) (accepted)

- Jan-Hendrik Hofmeyr, Stellenbosch University, South Africa
- jhsh@maties.sun.ac.za or jhsh@sun.ac.za
- Adress during June-December 2004: Dept. of Molecular Cell Physiology, Faculty of Earth and Life Sciences, Vrije Universiteit Amsterdam, De Boelelaan 1085, NL-1081 HV Amsterdam, The Netherlands (Jannie Hofmeyr jhsh@casema.nl)
- Department of Biochemistry, University of Stellenbosch, Private Bag X1, Matieland 7602, South Africa
- Cornish-Bowden A, Hofmeyr JH. The role of stoichiometric analysis in studies of metabolism: an example. J Theor Biol. 2002 May 21;216(2):179-91.
- Olivier BG, Rohwer JM, Hofmeyr JH. Modelling cellular processes with Python and Scipy. Mol Biol Rep. 2002;29(1-2):249-54.
- Olivier BG, Rohwer JM, Hofmeyr JH. Modelling cellular systems with PySCeS. Bioinformatics. 2004 Sep 28

48. Alternative Designs for a Genetic Switch: Analysis of Switching Times using the Piecewise Power-Law Representation within Biochemical Systems Theory

- Michael Savageau, University of Michigan, USA
- savageau@umich.edu
- Department of Microbiology and Immunology, The University of Michigan Medical School, 5641 Med. Sci. II, Ann Arbor, MI 48109-0620, USA
- Savageau MA. Alternative designs for a genetic switch: analysis of switching times using the piecewise power-law representation. Math Biosci. 2002 Nov-Dec;180:237-53.
- Wall ME, Hlavacek WS, Savageau MA. Design of gene circuits: lessons from bacteria. Nat Rev Genet. 2004 Jan;5(1):34-42. Review

- Wall ME, Hlavacek WS, Savageau MA. Design principles for regulator gene expression in a repressible gene circuit. J Mol Biol. 2003 Sep 26;332(4):861-76.

49. PathBLAST: A Tool for Alignment of Protein Interaction Networks
- Brian P. Kelley and Brent R. Stockwell, Whitehead Institute of Biomedical Research
- stockwell@wi.mit.edu
- Whitehead Institute for Biomedical Research, Nine Cambridge Center, Cambridge, MA 02142-1479, USA
- Kelley BP, Yuan B, Lewitter F, Sharan R, Stockwell BR, Ideker T. PathBLAST: a tool for alignment of protein interaction networks. Nucleic Acids Res. 2004 Jul 1;32(Web Server issue):W83-8.
- Kelley BP, Sharan R, Karp RM, Sittler T, Root DE, Stockwell BR, Ideker T. Conserved pathways within bacteria and yeast as revealed by global protein network alignment. Proc Natl Acad Sci U S A. 2003 Sep 30;100(20):11394-9. Epub 2003 Sep 22.

50. SigPath: Quantitative Modeling of Signaling Pathways
- Fabien Campagne, Weill Cornell Medical College, USA
- fac2003@med.cornell.edu
- Department of Physiology and Biophysics and Institute for Computational Biomedicine, Weill Medical College of Cornell University, New York, NY, 10021, USA.
- Campagne F, Neves S, Chang CW, Skrabanek L, Ram PT, Iyengar R, Weinstein H. Quantitative information management for the biochemical computation of cellular networks. Sci STKE. 2004 Aug 24;2004(248):PL11.
- Campagne F, Bettler E, Vriend G, Weinstein H. Batch mode generation of residue-based diagrams of proteins. Bioinformatics. 2003 Sep 22;19(14):1854-5.

51. Handling and Interpreting Large Gene Lists using HomGL and GOSSIP (accepted)
- Nils Blüthgen, Institute for Theoretical Biology, Humboldt University Berlin, Invalidenstrasse 43, Berlin, D-10115, Germany
- nils.bluethgen@itb.biologie.hu-berlin.de
- Bluthgen N, Kielbasa SM, Cajavec B, Herzel H. HOMGL-comparing genelists across species and with different accession numbers. Bioinformatics. 2004 Jan 1;20(1):125-6.
- Bluthgen N, Herzel H. How robust are switches in intracellular signaling cascades? J Theor Biol. 2003 Dec 7;225(3):293-300.
- Swat M, Kel A, Herzel H. Bifurcation analysis of the regulatory modules of the mammalian G1/S transition. Bioinformatics. 2004 Jul 10;20(10):1506-11.

52. Cross-Species Comparison Using Expression Data (accepted)

- Gaëlle Lelandais and Stéphane Le Crom
- Stéphane Le Crom, lecrom@biologie.ens.fr, Laboratoire de Biologie Moléculaire du Développement, INSERM U368, École Normale Supérieure, 46 rue d'Ulm 75230 Paris Cedex 5 FRANCE
- Gaëlle Lelandais, lelandais@biologie.ens.fr, Laboratoire de Génétique Moléculaire, CNRS UMR8451, École Normale Supérieure, 46 rue d'Ulm 75230 Paris Cedex 5 FRANCE
- Lelandais G, Le Crom S, Devaux F, Vialette S, Church GM, Jacq C, Marc P. Nucleic Acids Res. 2004 Jan 1;32 Database issue:D323-5.
- Marc P, Jacq C. Arrayplot for visualization and normalization of cDNA microarray data. Bioinformatics. 2002 Jun;18(6):888-9.

53. PEDRo: A Database for Storing, Searching and Disseminating Experimental Proteomics Data (accepted)

- Kevin Garwood and Norman Paton, Department of Computer Science, University of Manchester, UK
- garwood@cs.man.ac.uk, Prof. Norman Paton: <norm@cs.man.ac.uk>, Phone: +44 161 275 6910, Fax: +44 161 275 6236
- Department of Computer Science, University of Manchester, Oxford Road, Manchester M13 9PL, United Kingdom
- Garwood K, McLaughlin T, Garwood C, Joens S, Morrison N, Taylor CF, Carroll K, Evans C, Whetton AD, Hart S, Stead D, Yin Z, Brown AJ, Hesketh A, Chater K, Hansson L, Mewissen M, Ghazal P, Howard J, Lilley KS, Gaskell SJ, Brass A, Hubbard SJ, Oliver SG, Paton NW. PEDRo: a database for storing, searching and disseminating experimental proteomics data. BMC Genomics. 2004 Sep 17;5(1):68.
- Garwood KL, Taylor CF, Runte KJ, Brass A, Oliver SG, Paton NW. Pedro: a configurable data entry tool for XML. Bioinformatics. 2004 Oct 12;20(15):2463-5. Epub 2004 Apr 08.

54. Representing and Analyzing Biological Function with aMAZE, A Database of Molecular Interactions and Processes

- Shoshana J. Wodak, Universite Libre de Bruxelles, Belgium
- shosh@ucmb.ulb.ac.be
- Service de Conformation de macromolecules Biologique et Bioinformatique, Centre de Biologie Structurale et Bioinformatique, Universite Libre de Bruxelles, CP 263, Boulevard du Triomphe, 1050 Bruxelles, Belgium
- Wodak SJ, Mendez R. Prediction of protein-protein interactions: the CAPRI experiment, its evaluation and implications. Curr Opin Struct Biol. 2004 Apr;14(2):242-9.
- Lemer C, Antezana E, Couche F, Fays F, Santolaria X, Janky R, Deville Y, Richelle J, Wodak SJ. The aMAZE LightBench: a web interface to a relational database of cellular processes. Nucleic Acids Res. 2004 Jan 1;32 Database issue:D443-8.

- Deville Y, Gilbert D, van Helden J, Wodak SJ. An overview of data models for the analysis of biochemical pathways. Brief Bioinform. 2003 Sep;4(3):246-59.

55. Validating Drug Targets *in silico*: A Role for Control Analysis and Computer Simulation

- David A. Fell, Oxford Brookes Univ., UK
- dfell@brookes.ac.uk
- daf@bms.brookes.ac.uk
- School of Biology and Molecular Science, Oxford Brookes University, Headington, Oxford OX3 OBP, UK
- Fell DA, Wagner A. The small world of metabolism. Nat Biotechnol. 2000 Nov;18(11):1121-2.
- Poolman MG, Assmus HE, Fell DA. Applications of metabolic modelling to plant metabolism. J Exp Bot. 2004 May;55(400):1177-86. Epub 2004 Apr 08.
- Poolman MG, Olcer H, Lloyd JC, Raines CA, Fell DA. Computer modelling and experimental evidence for two steady states in the photosynthetic Calvin cycle. Eur J Biochem. 2001 May;268(10):2810-6.

56. The Virtual Cell Software Environment (accepted)

- Ion I. Moraru and Leslie M. Loew, Department of Physiology, University of Connecticut Health Center
- moraru@panda.uchc.edu, Moraru@NEURON.UCHC.EDU, Tel: 860-679-2908, Fax: 860-679-1269, Cell: 860-978-8528
- Department of Cell Biology, University of Connecticut Health Center, 263 Farmington Ave., Farmington, CT 06030-3505
- Dr. Loew's email: les@volt.uchc.edu
- Center For Biomedical Imaging Technology and National Resource for Cell Analysis and Modeling, Department of Physiology, University of Connecticut Health Center, Farmington, CT 06030, USA
- Moraru II, Schaff JC, Slepchenko BM, Loew LM. The virtual cell: an integrated modeling environment for experimental and computational cell biology. Ann N Y Acad Sci. 2002 Oct;971:595-6.
- Slepchenko BM, Schaff JC, Macara I, Loew LM. Quantitative cell biology with the Virtual Cell. Trends Cell Biol. 2003 Nov;13(11):570-6. Review.

Appendices

1. Useful Websites for Omics and Systems Biology Research
(Example)

Field	Name	Function	Website	Provider
Genomics	BLAST	Similarity Search	http://www.ncbi.nlm.nih.gov/BLAST	NCBI
	…	…		
Transcriptomics				
Proteomics				
Metabolomics				
…	…	…		

2. Software and Databases for Systems Biology
(Example)

Catagory	Name	Function	Platform	Developer/Provider
Modeling	MathSBML	Package for Manipulating SBML-based Biological Models	Web (http://...) UNIX/Windows/ Macintosh/VMS	Bruce E. Shapiro (free)
	CellML 1.1	Biological Model Specification and Reuse	UNIX/Windows	Catherine M. Lloyd (free)
	…	…	…	…
Networks	PathBLAST	Alignment of Protein Interaction Networks		Whitehead Institute
Algorithms	DBRF-MEGN	Deducing Minimum Equivalent Gene Networks from Large-Scale Gene Expression Profiles		Koji Kyoda and Shuichi Onami (free)
Database	PEDRo	Storing, Searching and Disseminating Experimental Proteomics Data		
…	…	…	…	…