Department of Computer Science, UC Irvine

ICS 288A: Biological Networks

Winter 2009

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Lectures:

Time	Place
TuTh 12:30- 1:50p	DBH 1423

Office Hours: By appointment. The best way to reach me is by e-mail.

Marking Scheme:

(1) 15% homework
(2) 30% class participation
(3) 55% final project
(project proposal 5%; 40 minute presentation 15%; written report 35%)

Recommended Texts:

a) Jurisica and Wigle (Editors), "Knowledge Discovery in Proteomics", CRC Press, 2005.
b) Bornholdt and Schuster (Editors), "Handbook of Graphs and Networks: From the Genome to the Internet", Wiley, 2003.
c) A list of papers selected by Prof. Przulj (see below).
d) "LEDA: A Platform for Combinatorial and Geometric Computing", by Kurt Mehlhorn, Stefan Näher, Cambridge University Press, 1999.

Course Overview and Goals:

Vast amounts of biological network data have recently been generated allowing increasing numbers of system level studies of biological structures and processes. Various mathematical and computational tools are being developed to analyze these data with the goal of better understanding of biological processes, disease, and contributing to the time and cost effectiveness of biological experimentation. This course will give an overview of the existing types of biological network data, point to sources of errors and biases in the data, and introduce the current literature on graph theoretic modeling and discrete algorithmic analyses applied to these data. The course will also present an impartial overview of the works of several major network biology labs around the world (e.g. Uri Alon, M. Vidal, M. Tyers, M. Stumpf, J. Doyle, A-L Barabasi etc.).

Topics Outline:

The course will cover the following topics:

a) Types of biological networks: metabolic, signaling, protein-protein interaction, etc.

b) Major databases storing biological network data (e.g. MINT, DIP, HPRD, GRID, MIPS, KEGG).
c) Sources of noise and biases in various types of the biological network data (e.g. biotechnological biases and limitations, effects of sampling).
d) Computational challenges in network analysis: introduction to basic graph theoretic and computational complexity concepts such as subgraph isomorphism and NP-completeness.
e) Properties of large networks: global (e.g. degree distribution, clustering coefficient, average diameter) and local (e.g. network motifs and graphlets).
f) Network models: various types of random graphs (e.g. Erdos-Renyi, small-world, scale-free, hierarchical, geometric) and network growth models (e.g. preferential attachment).
g) Network motifs: techniques for their detection (exhaustive and heuristic network search algorithms) and biological function (e.g. feed-forward loops in transcriptional regulation networks).
h) Interplay of network topology and function (e.g. "lethality" and "centrality", "synthetic lethality" and network "redundancy", graph theoretic pathway models).
i) From models to heuristic algorithms (e.g. exploiting network model properties for "optimal" walks through a network, or detection of small network substructures).
j) Graph alignment heuristics (e.g. PathBLAST).
k) Network evolution (e.g. gene duplication and divergence in biological network growth models).
l) Clustering problems in biological networks (e.g. detection of protein complexes).
m) Software tools and libraries for network analysis (e.g. LEDA, Pajek).

Online course evaluations:

The winter 2009 quarter online evaluation window will be open at the end of the quarter.

Reading Materials (to be updated later in the course):

1. A.-L. Barabasi and Z. N. Oltvai, "Network Biology: Understanding the Cell's Functional Organization", Nature Reviews Genetics, vol 5, 2004.
2. S. Maslov and K. Sneppen, "Specificity and Stability in Topology of Protein Networks", Science 269, 2002.
3. H. Jeong, S. P. Mason, and A.-L. Barabasi, "Lethality and centrality in protein networks", Nature 411, 2001.
4. S. Coulomb, M. Bauer, D. Bernard, and M.-C. Marsolier-Kergoat, "Mutational robustness is only weakly related to the toplogy of protein interaction networks", CNET 2004.
5. H. Jeong, B. Tombor, R. Albert, Z. N. Oltvai, and A.-L. Barabasi, "The large-scale organization of metabolic networks", Nature 407, 2000.
6. R. Tanaka, "Scale-Rich Metabolic Networks", Physical Review Letters 94, 2005.
7. R. Milo, S. Shen-Orr, S. Itzkovitz, N. Kashtan, D. Chklovskii, and U. Alon, "Network Motifs: Simple Building Blocks of Complex Networks", Science 289, 2002.
8. S. Shen-Orr, R. Milo, S. Mangan, and U. Alon, "Network motifs in the transcriptional regulation network of *E. coli*", Nature Genetics 31, 2002.
9. R. Milo *et al.*, "Superfamilies of Evolved and Designed Networks", Science 303, 2004.
10. Y. Artzy-Randrup, S. J. Fleishman, N. Ben-Tal, and L. Stone, "Comment on "Network Motifs: Simple Building Blocks of Complex Networks" and "Superfamilies of Evolved and Designed Networks"", Science 305, 2004.

11. R. Milo, S. Itzkovitz, N. Kashtan, R. Levitt, and U. Alon, "Response to Comment on "Network Motifs: Simple Building Blocks of Complex Networks" and "Superfamilies of Evolved and Designed Networks"", Science 305, 2004.
12. N. Kashtan, S. Itzkovitz, R. Milo, and U. Alon, "Network motifs in biological networks: Roles and Generalizations", Quantitative Biology.
13. N. Kashtan, S. Itzkovitz, R. Milo, and U. Alon, "Efficient sampling algorithm for estimating subgraph concentrations and detecing network motifs", Bioinformatics 20 (11), 2004.
14. N. Przulj, D. G. Cornail, and I. Jurisica, "Modeling Interactome: Scale-Free or Geometric?", Bioinformatics 20 (18), 2004.
15. N. Przulj, D. G. Cornail, and I. Jurisica, "Efficient estimation of graphlet frequency distributions in protein-protein interaction networks", Bioinformatics, 2006, doi:10.1093/bioinformatics/btl030.
16. S. Wuchty, Z. N. Oltvai, and A.-L. Barabasi, "Evolutionary conservation of motif constituents in the yeast protein interaction network", Nature Genetics 35 (2), 2003.
17. C. Song, S. Havlin, and H. A. Makse, "Self-similarity of complex networks", Nature 433, 2005.
18. S. Itzkovitz *at al*., "Coarse-Graining and Self-Dissimilarity of Complex Networks", Phys Rev E 71, 016127 (2005).
19. M. Stumpf, C. Wiuf, and R. May, "Subnets of scale-free networks are not scale-free: Sampling properties of networks", PNAS 102 (12), 2005.
20. J.-D. Han, D. Dupuy, N. Bertin, M. E. Cusick, and M. Vidal, "Effect of sampling on topology predictions of protein-protein interaction networks", Nature Biotechnology 23 (7), 2005.
21. A. Vazquez, A. Flammini, A. Maritan, and A. Vespignani, "Modeling of protein interaction networks", Complexus 1, 2003.
22. C. von Mering *et al*., "Comparative assessment of large-scale data sets of protein-protein interactions", Nature 417, 2002.
23. J. Berg and M. Lassig, "Local graph alignment and motif search in biological networks", PNAS 101 (41), 2004.
24. B. P. Kelley *et al*., "Conserved pathways within bacteria and yeast as revealed by global protein network alignment", PNAS 100 (20), 2003.
25. E. F. Keller, "Revisiting 'scale-free' networks", BioEssays 27: 1060-8, 2005.
26. E. de Silva and M. P. H. Stumpf, "Complex networks and simple models in biology", Journal of the Royal Society Interface 2: 419-430, 2005.
27. M. A. M. de Aguiar and Y. Bar-Yam, "Spectral analysis and the dynamic response of complex networks", Physical Review E 71: 016106, 2005.
28. J-F Rual et al., "Towards a proteome-scale map of the human protein-protein interaction network", Nature, 2005, doi:10.1038/nature04209.
29. U. Stelzl et al., "A Human Protein-Protein Interaction Network: A Resource for Annotating the Proteome", Cell 122: 957-68, 2005.
30. S. Suthram, T. Sittler, and T. Ideker, "The Plasmodium protein network diverges from those of other eukaryotes", Nature 438 (3): 108-12, 2005.
31. R. Guimera and L. A. N. Amaral, "Functional cartography of complex metabolic networks", Nature 433: 895-900, 2005.
32. J. S. Mattick and M. J. Gagen, "Accelerating Networks", Science 307: 856-8, 2005.
33. J. Mintseris and Z. Weng, "Structure, function, and evolution of transient and obligate protein-protein interactions", PNAS 102 (31): 10930-10935, 2005.
34. H. B. Fraser, "Modularity and evolutionary constraint on proteins", Nature Genetics 37 (4): 351-2, 2005.