PHYS 597A: Graphs and networks in systems biology

Spring 2008
T Th 9:45 - 11:00 am
103 Osmond Laboratory

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Many complex systems are difficult to describe and understand because they are composed of large numbers of elements interacting in a non-ordered way. A good example is cellular biology: diverse cellular components (genes, proteins, enzymes) participate in various reactions and regulatory interactions, forming a robust system. A very useful representation of complex systems is given by graphs (or networks), where we denote the components with nodes and their interactions by edges. The properties of these interaction graphs can then be analyzed by graph theoretical and statistical mechanics methods and this information can lead to important conclusions about the possible dynamical behaviors of the system.

This class will focus on four main questions:
(i) How do we determine or infer the interaction graphs underlying complex systems?
(ii) How can we characterize the organizational features of large-scale networks?
(iii) What are the mechanisms that determine the common topological features of a wide variety of networks?
(iv) To what degree does the topology of the interaction network underlying a complex system topology determine the dynamical behavior (e.g. steady state or oscillations) of the system?

Throughout the class the focus will be on biological networks and on the connections of network theory to systems biology. Systems biology topics will include inference of regulatory networks from gene expression data; analysis of protein interaction networks, metabolic networks and gene regulatory networks; continuous and discrete dynamical models of signal transduction and gene regulation.

Prerequisites

- MATH 017 (finite mathematics) or similar introduction to probabilities and combinatorics
- MATH 110 (techniques of calculus) or MATH 140B (calculus and biology) or similar introduction to calculus
- BIOL 011 or similar introductory biology
- BMB 211 or similar elementary biochemistry

These are not absolute prerequisites in the sense that the necessary background can be obtained by extra reading during the class. Supporting reading materials will be made available upon request.

Grades

Grades for this class will be based on homework assignments (50%) and work on a project (50%). Weekly homework will include exercises and critical reading assignments. There will be 10 homework assignments, graded on a 1-10 basis. Project topics will be selected from a list of suggestions or can be based on the research interests of participants. Work on terms projects will continue throughout the semester, with an abstract due in March and a draft paper due in April. Each participant will give a 10 minute project presentation during the last 3 classes. The final papers will be due on May 5, at 5 pm.

Main topics covered

1. elements of graph theory: node degree, distances between nodes, clustering, node betweenness, subgraphs, directed graphs
2. graph algorithms and graph analysis/visualization software
3. analysis of cellular networks: gene regulatory networks, signal transduction networks, metabolic networks
4. random graph theory
5. network models and theory: lattices, small-world networks, scale-free networks, evolving networks
6. percolation and flow processes on networks
7. modeling the dynamics of reaction networks and of signal transduction networks
8. inference of gene regulatory networks from gene expression data
9. modeling the dynamics of gene regulatory networks

Important references (copies will be provided)

1. Réka Albert and Albert-László Barabási, Statistical mechanics of complex networks, Reviews of Modern Physics 74, 47-97 (2002).
2. C. Christensen, J. Thakar and R. Albert, Systems-level insights into cellular regulation: inferring, analyzing, and modeling intracellular networks, IET Systems Biology 1, 61-77 (2007).
3. John J. Tyson, Katherine C. Chen and Béla Novák, Sniffers, buzzers, toggles and blinkers: dynamics of regulatory and signaling pathways in the cell, Current Opinion in Cell Biology 15, 221-231 (2003).

Reference books

1. Stefan Bornholdt, Heinz G. Schuster (eds.), Handbook of Graphs and Networks: from the Genome to the Internet (2002).
2. Mark Newman, Albert-László Barabási, Duncan J. Watts (eds.), The Structure and Dynamics of Networks (2006).
3. James M. Bower and Hamid Bolouri (eds.), Computational Modeling of Genetic and Biochemical Networks (2001).
4. Bernhard Palsson, Systems Biology: Properties of Reconstructed Networks (2006).
5. Uri Alon, An Introduction to Systems Biology: Design Principles of Biological Circuits (2006).

Table 1: Preliminary syllabus

Week	Date	Tuesday	Thursday
1	1/14	Introduction	Basic graph measures
2	1/21	Basic graph measures Homework 1 due	Topology of real networks
3	1/28	Topology of cellular networks Homework 2 due	Topology of cellular networks
4	2/4	Random graph theory Homework 3 due	Small-world and scale-free models
5	2/11	Evolving networks Homework 4 due	Evolving cellular networks
6	2/18	Network algorithms and software Homework 5 due	Network resilience
7	2/25	Resilience of cellular networks Homework 6 due	Spreading processes
8	3/3	Epidemic models Homework 7 due	Dynamics of cellular networks
9	3/10	No class	No class
10	3/17	Reaction network dynamics Abstract due	Dynamics of signal transduction
11	3/24	Dynamics of signal transduction Homework 8 due	Discrete and stochastic dynamics
12	3/31	Network inference Homework 9 due	Network inference
13	4/7	Gene regulation - continuous Preliminary paper due	Gene regulation - discrete
14	4/14	Gene regulation - stochastic Homework 10 due	Examples of current models
15	4/21	Examples of current models	Project presentations
16	4/28	Project presentations	Project presentations