Phys 597A: Graphs and Networks in Systems Biology

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Networks, networks everywhere

- Network infrastructure, social networking
- Network - a tool for understanding complex systems
- Many **non-identical** elements connected by **diverse** interactions
- Cellular interaction networks: signal transduction, gene regulation, metabolism
- Graph measures provide information on interaction graphs
- Network models explain and predict properties of graph classes
- Network topology influences network robustness and the dynamics of flows
- Dynamics of cellular networks
- Understand emergent properties – synchronization, phase transitions, homeostasis

**Definition of graphs (networks)**

Network (graph): a set of nodes connected by edges
Nodes (vertices): A, B, C...
Edges (links): AC, BC, CD, CJ...

The spatial arrangement of nodes and edges does not matter.
Can be augmented by additional node and edge information.
Many complex systems have an underlying network topology

Internet, router level
- nodes: routers, hosts
- edges: wires, cables, wireless
Q: Which edges are static and which change?

Internet, domain level
- nodes: domains (ISP’s)
- edges: gateway protocols
- Undirected
Q: What is the nature of edges?

Map of the Internet, colored by IP addresses, by William R. Cheswick

The World Wide Web is the higher level of the Internet

- nodes: webpages
- edges: hyperlinks - directed

The WWW is the largest network with topological information available.
The size of the WWW has surpassed 10 billion nodes, it is increasing.
Search engines can index only a small percentage of the Web.

Structure of a website

Color: inferred node clustering

Food webs describe the energy flow within species:

- **Nodes:** species
- **Edges:** predator-prey relationship
- **Directed edges:** process: nutrient flow

Social systems can be regarded as networks:

- **Nodes:** individuals
- **Edges:** social interaction
- **“Six degrees of separation”:** the social distance between people is small

**Actor collaboration**
- **Nodes:** actors
- **Edges:** cast jointly

**Scientific coauthorship**
- **Nodes:** scientists
- **Edges:** wrote a paper

Q: Can you propose an alternative network based on actor/movie or author/paper information?

**Dating network in a high-school**
- **Blue:** boys
- **Pink:** girls

Q: does it surprise you that the network is connected?

**Collaborations at the Santa Fe Institute**

Color: inferred node clustering

Q: what do you think is the basic idea of the clustering algorithm?
Spread of disease in a social network
- black: diseased
- pink: infected
- green: healthy

Q: Where do you think the network mapping started?

Network of free semantic associations
Based on the University of South Florida Word Association, Rhyme and Word Fragment Norms

Map of yeast protein-protein interactions, by Hawoong Jeong
- Red: essential protein
- Yellow: growth-affecting protein
- Green: non-essential protein

Cell metabolism forms a network of reactions
Metabolism: sum of chemical processes by which energy is stored or released.
Metabolic pathway: sequence of enzyme reactions.
- nodes: metabolites
- edges: reactions
Different representations possible.
Cellular processes form networks on many levels

**Reaction networks**
- nodes: substrates, enzymes
- edges: chemical reactions

**Regulatory networks**
- nodes: genes, proteins
- edges: translation ↔ or regulation →, activating or inhibiting

### Two-component signal transduction pathway

### Interaction network of the Drosophila segment polarity genes
Why study networks?

- It is increasingly recognized that complex systems cannot be described in a reductionist view.
- Understanding the behavior of such systems starts with understanding the topology of the corresponding network.
- Topological information is fundamental in constructing realistic models for the function of the network.

Network-related questions:
- How do we determine or infer network topology?
- How can we quantitatively describe large networks?
- How did networks get to be the way they are?
- What are the consequences of a specific network organization?