The complexity of cellular networks

Warning: Statistical physics.
It only works on average.

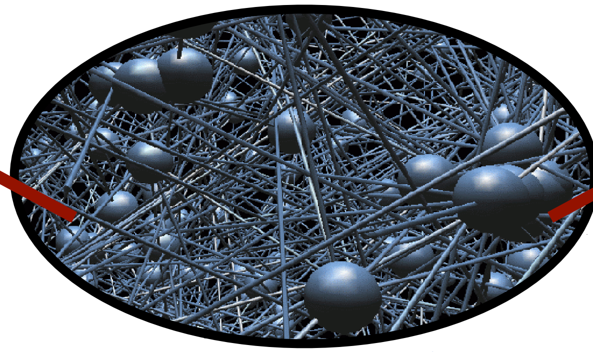
http://regan.med.harvard.edu/CVBR-course.php

1. Meet complex networks

- Complexity and networks -

Many different components

- atoms, particles
- spins, oscillators
- cells, DNA, proteins



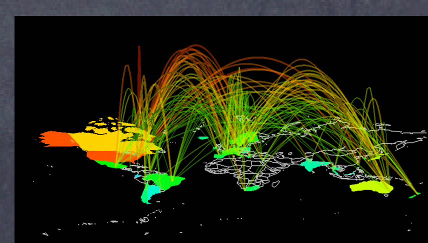
A variety of interactions

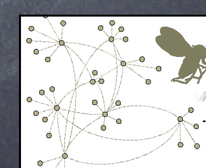
- gravity
- electromagnetism
- genetic regulation
- signaling

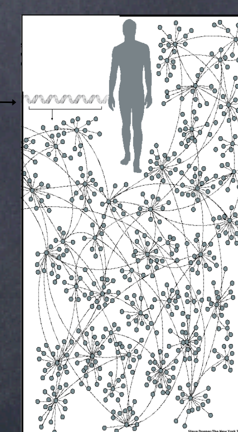
System as a whole: NETWORK

Complexity in:

- topology of interactions
- time evolution of the structure
- dynamics on the structure





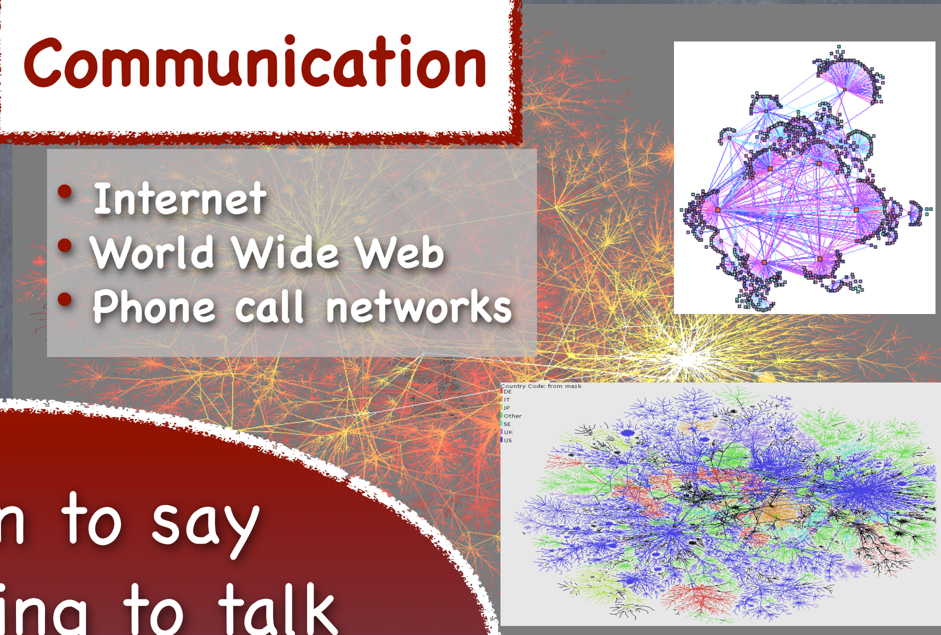


- Meet these networks -

Society

- Friendships, sexual contacts
- Co-authorship, citations
- Movie actors, business
- Co-authorship, citations
- Movie actors, business

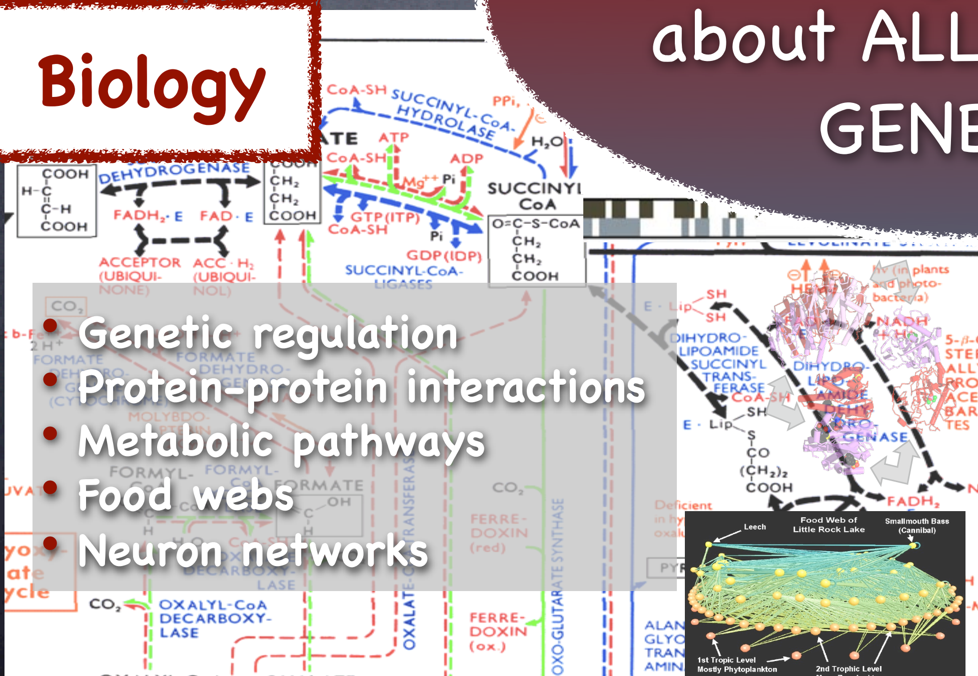
Communication



- Internet
- World Wide Web
- Phone call networks

You mean to say you are going to talk about ALL these? In GENERAL?

Biology



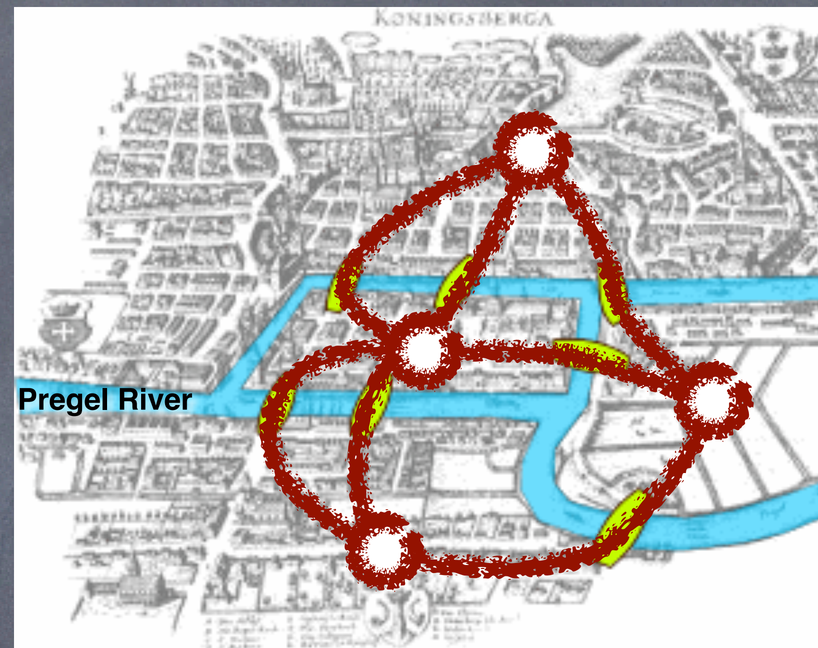
- Genetic regulation
- Protein-protein interactions
- Metabolic pathways
- Food webs
- Neuron networks

- Airline routes
- Word webs
- Power grid

- How it all begun -

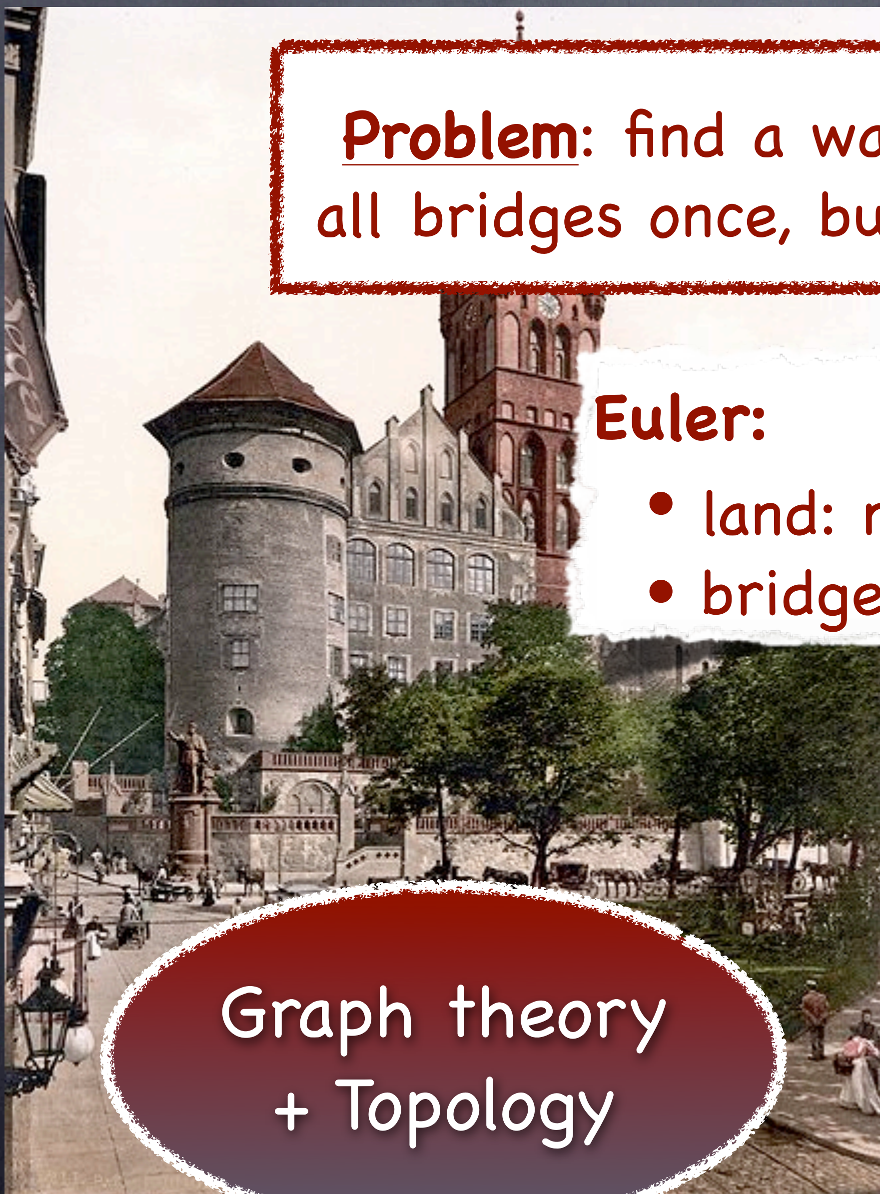
Königsberg, capital of East Prussia

1730's, Euler's time



- How it all begun -

Königsberg, capital of East Prussia



1730's, Euler's time

Problem: find a walk to cross all bridges once, but only once.

Euler:

- land: nodes
- bridges: graph

Graph theory
+ Topology

Solution: a general theorem.

- Eulerian paths only exist on graphs with no odd degree nodes, or exactly 2 odd degree nodes.
- => none for old Königsberg

- Social science knows we network -

Stanley Milgram's experiment, Harvard, 1967

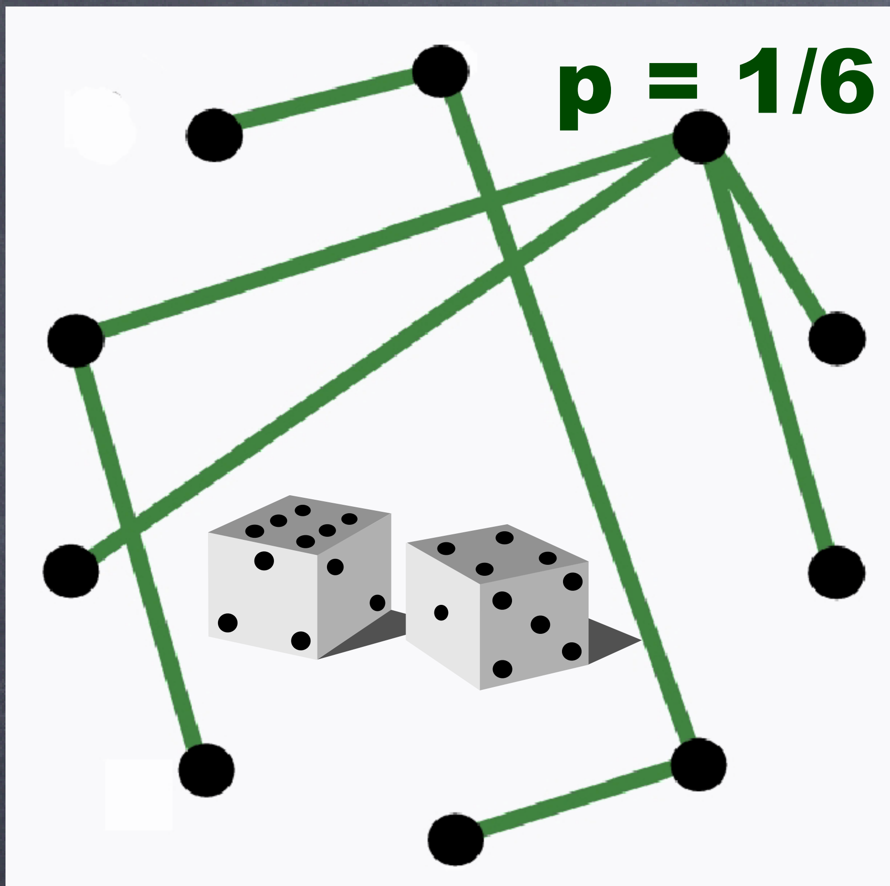
- random individuals in starting towns
- information packet: **target** name, occupation and city (about study, instructions)
- **if you know** target, mail package to target
- if not: mail it to a **personal aqquaintance** you think might know him
- send back trancking postcard

Six degrees of separation

- 64 of the 296 letters made it
- average path length : 5.5 or 6

- Paul Erdős rethinks graph theory -

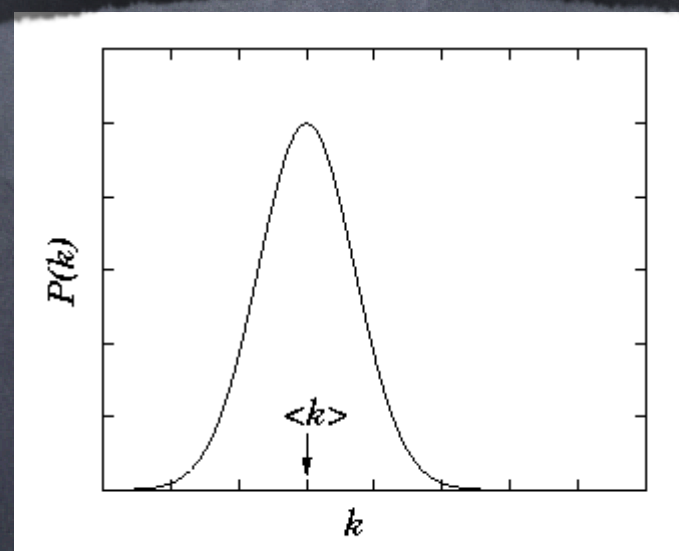
1950's: the Erdős-Rényi Random Network



- **statistical** approach
- the **null model** of large real networks
- **threshold** probability value:
  - ➡ percolation transition **<k>=1**
  - ➡ one giant connected component
  - ➡ Poisson degree distribution
  - ➡ **SMALL WORLD**

$$P(k) \simeq e^{-pN} \frac{(pN)^k}{k!}$$

$$< d >_{i,j} \sim \log(N)$$

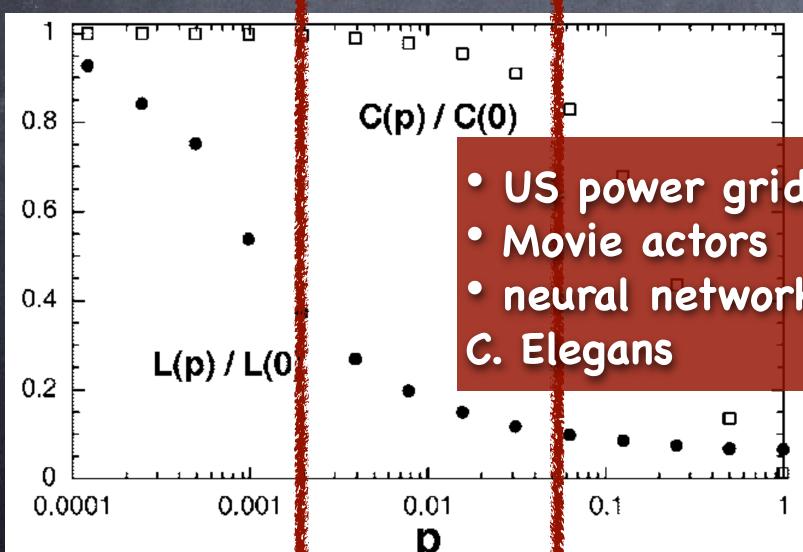


- Birth of modern complex networks -

OK: birth of our modern interest in them

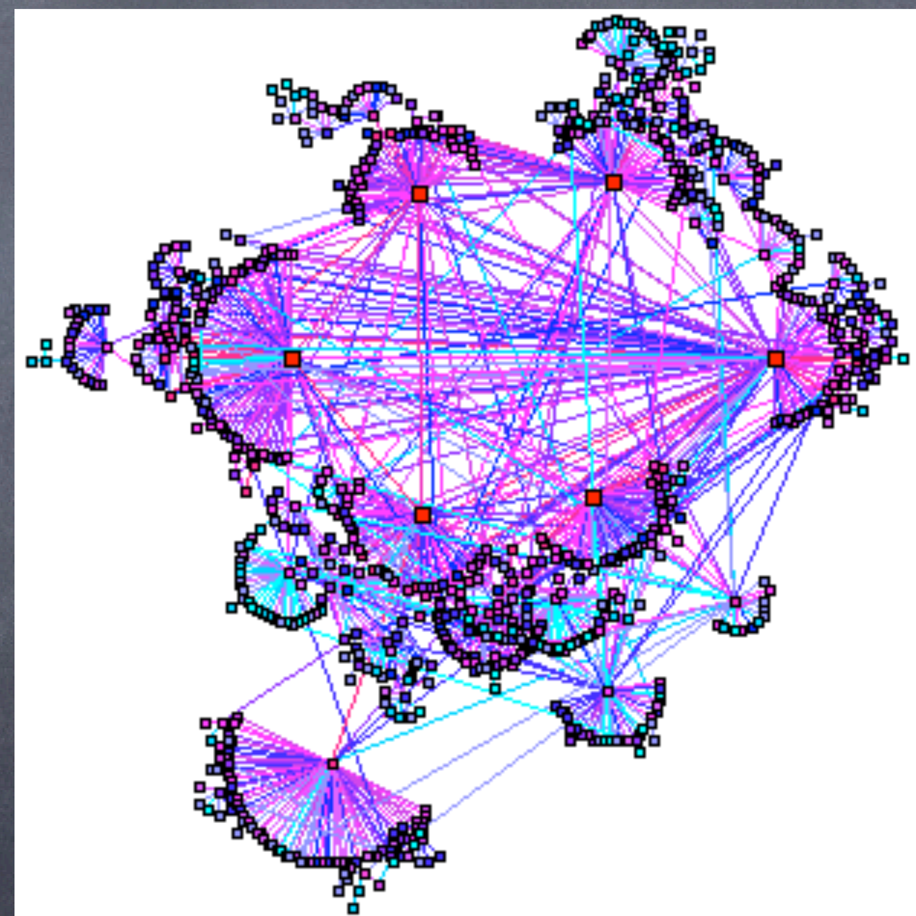
1998 Watts and Strogatz:
Small World Networks

- high clustering
- short average paths



- US power grid
- Movie actors
- neural network of C. Elegans

1999 Barabasi and Albert:
Scale-Free Networks



- WWW, U Notre Dame

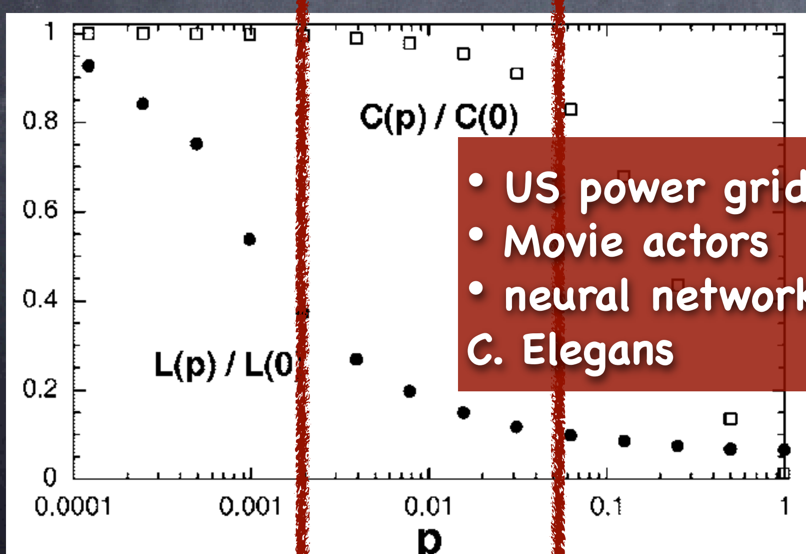
- Birth of modern complex networks -

OK: birth of our modern interest in them

1998 Watts and Strogatz:

Small World Networks

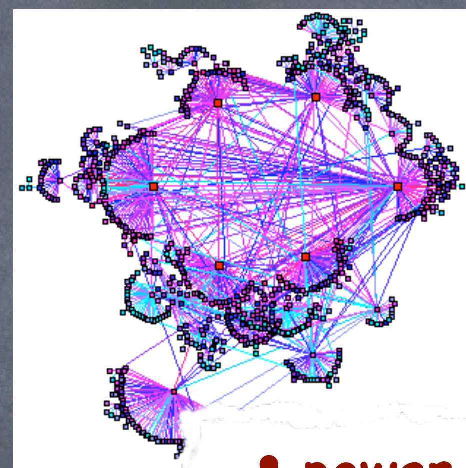
- high clustering
- short average paths

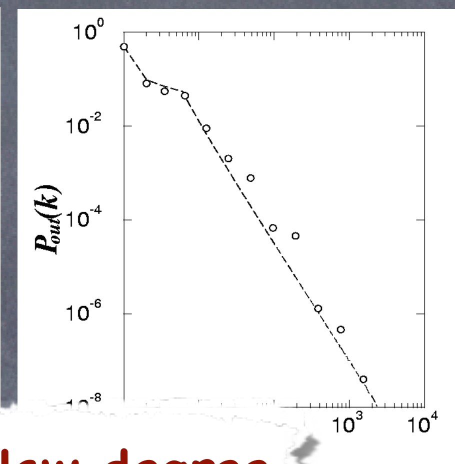


- US power grid
- Movie actors
- neural network of C. Elegans

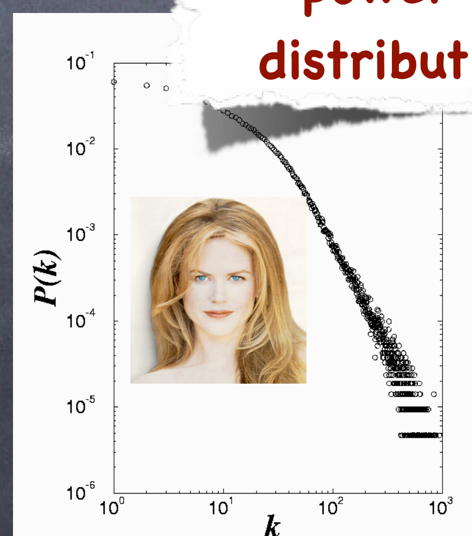
1999 Barabasi and Albert:

Scale-Free Networks



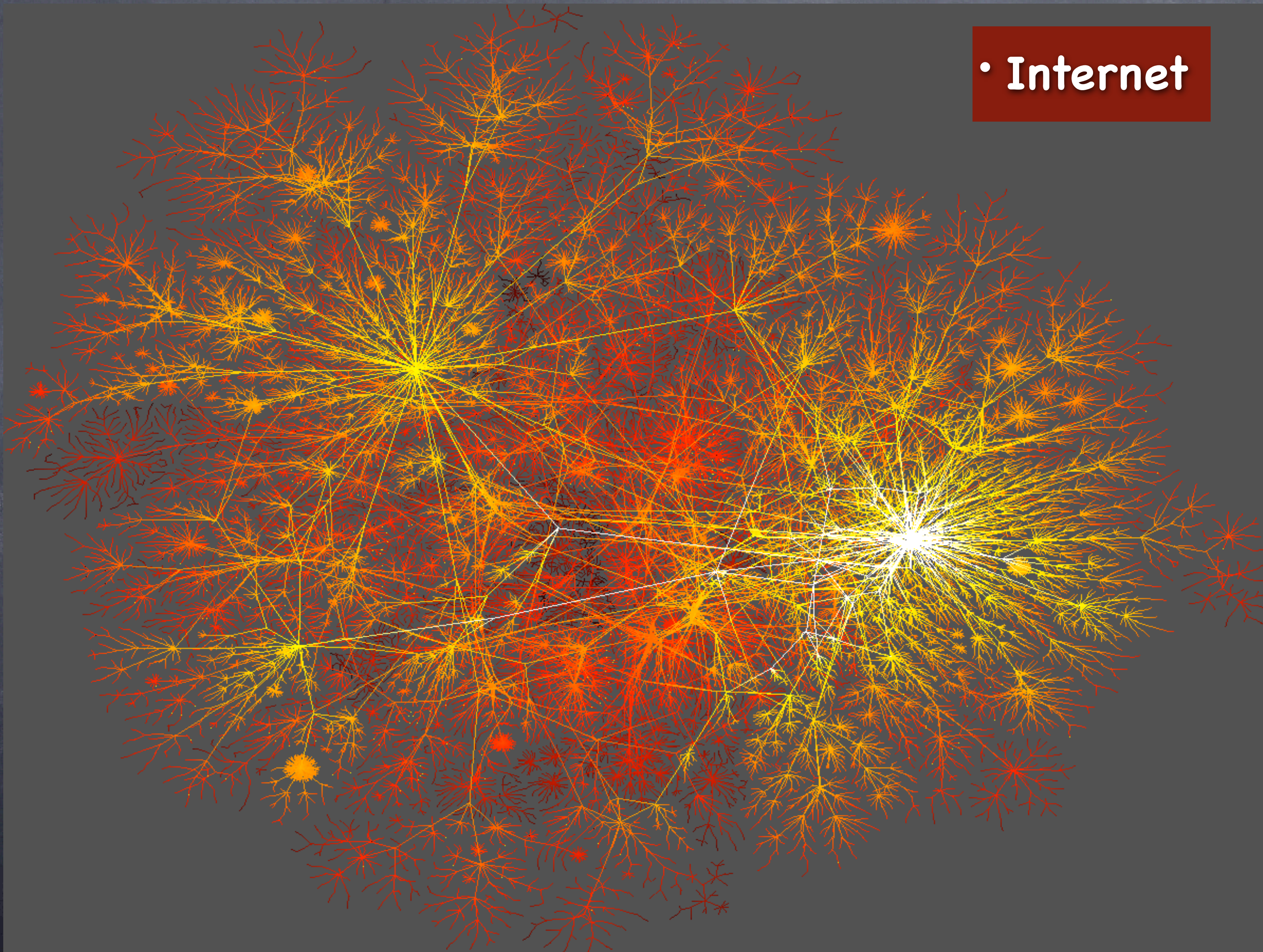


- power law degree distribution!



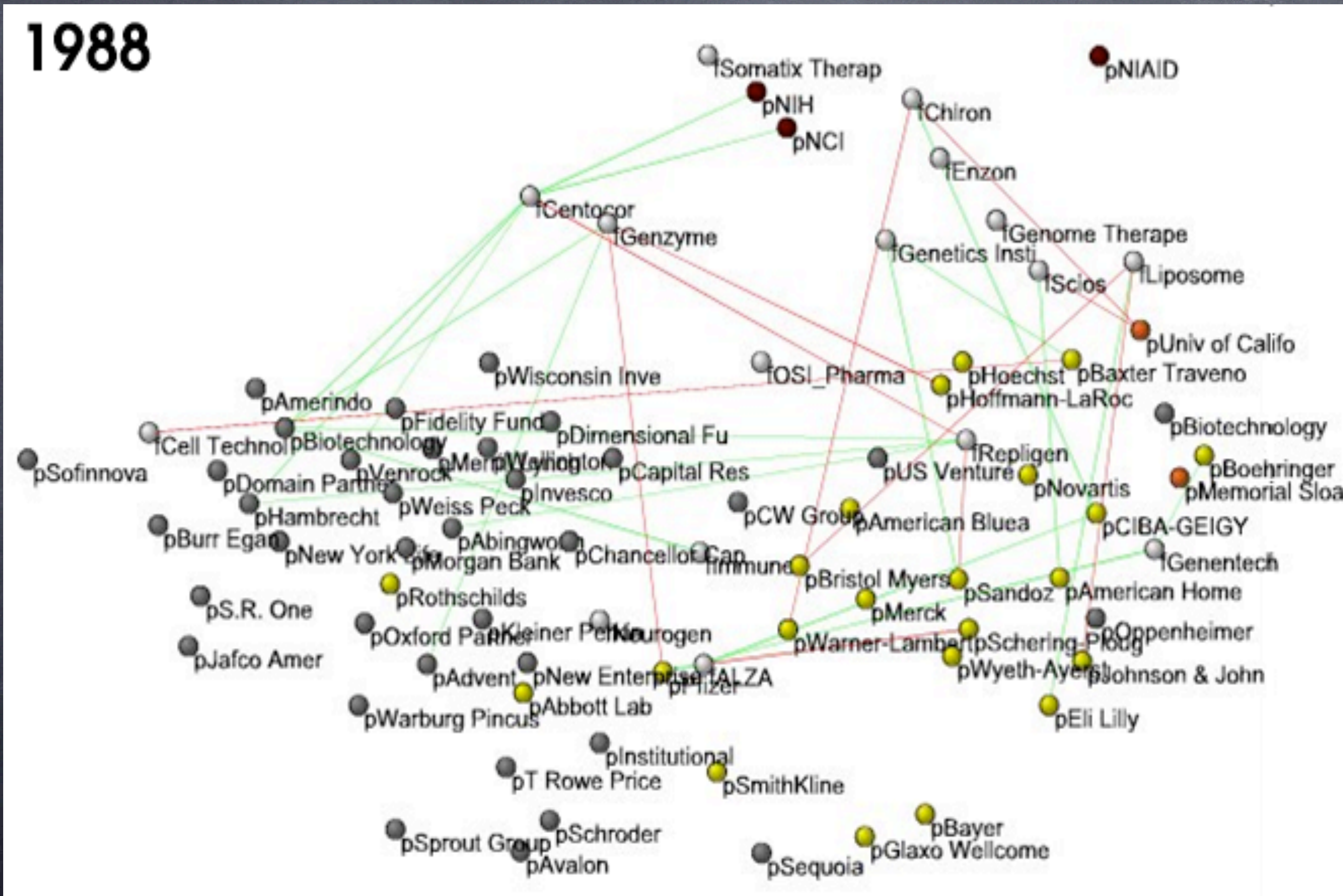
- BA model
  - ➡ growth
  - ➡ preferential attachment

- Explosion of data -

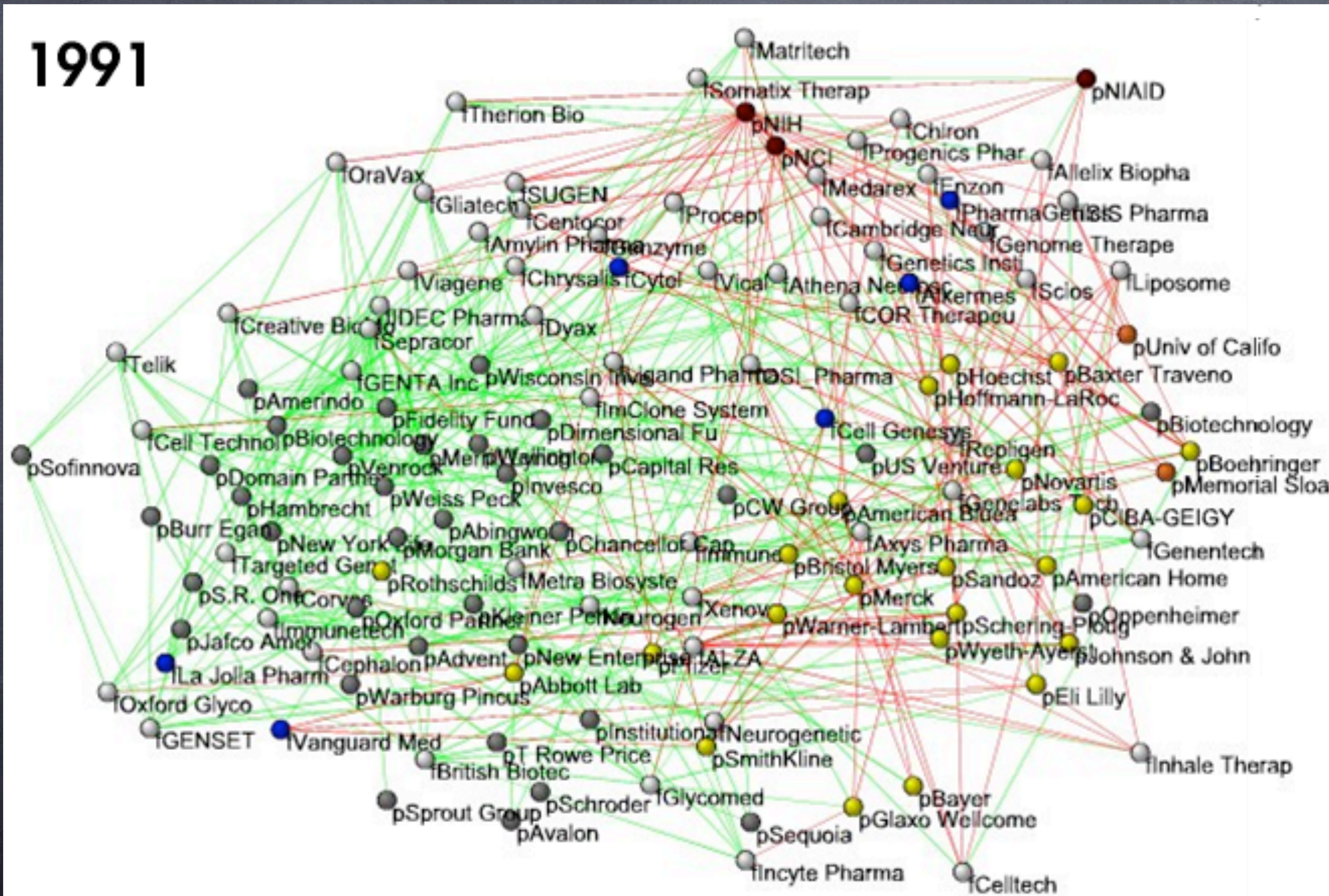


• Internet

Business ties in US biotech-industry

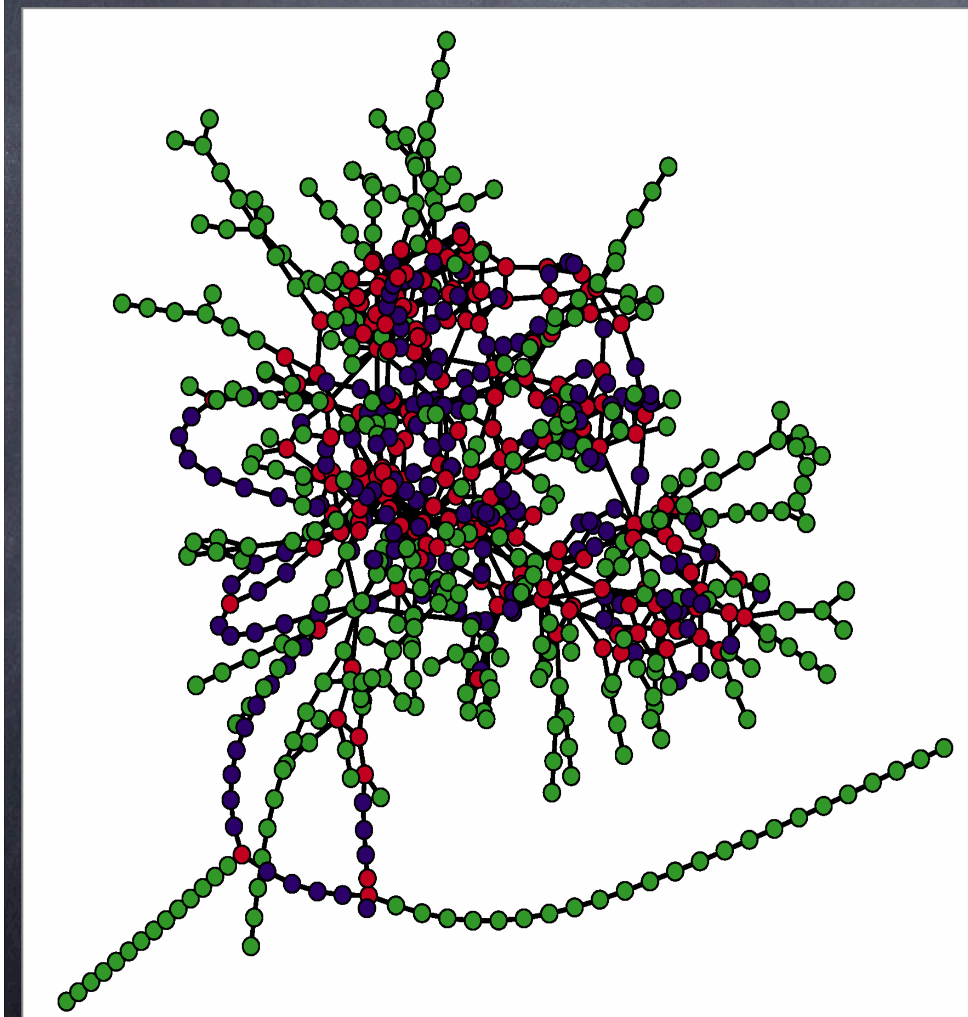


Business ties in US biotech-industry

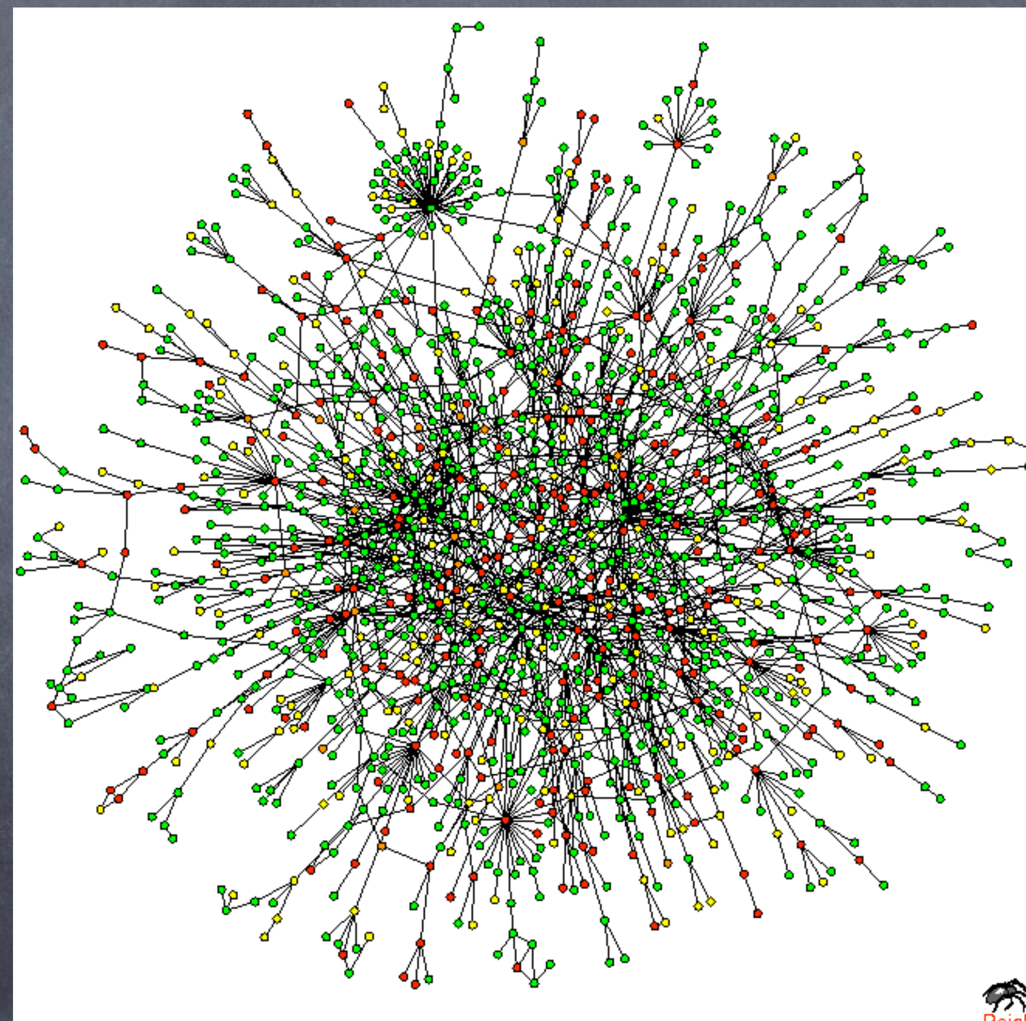


- In biology, too -

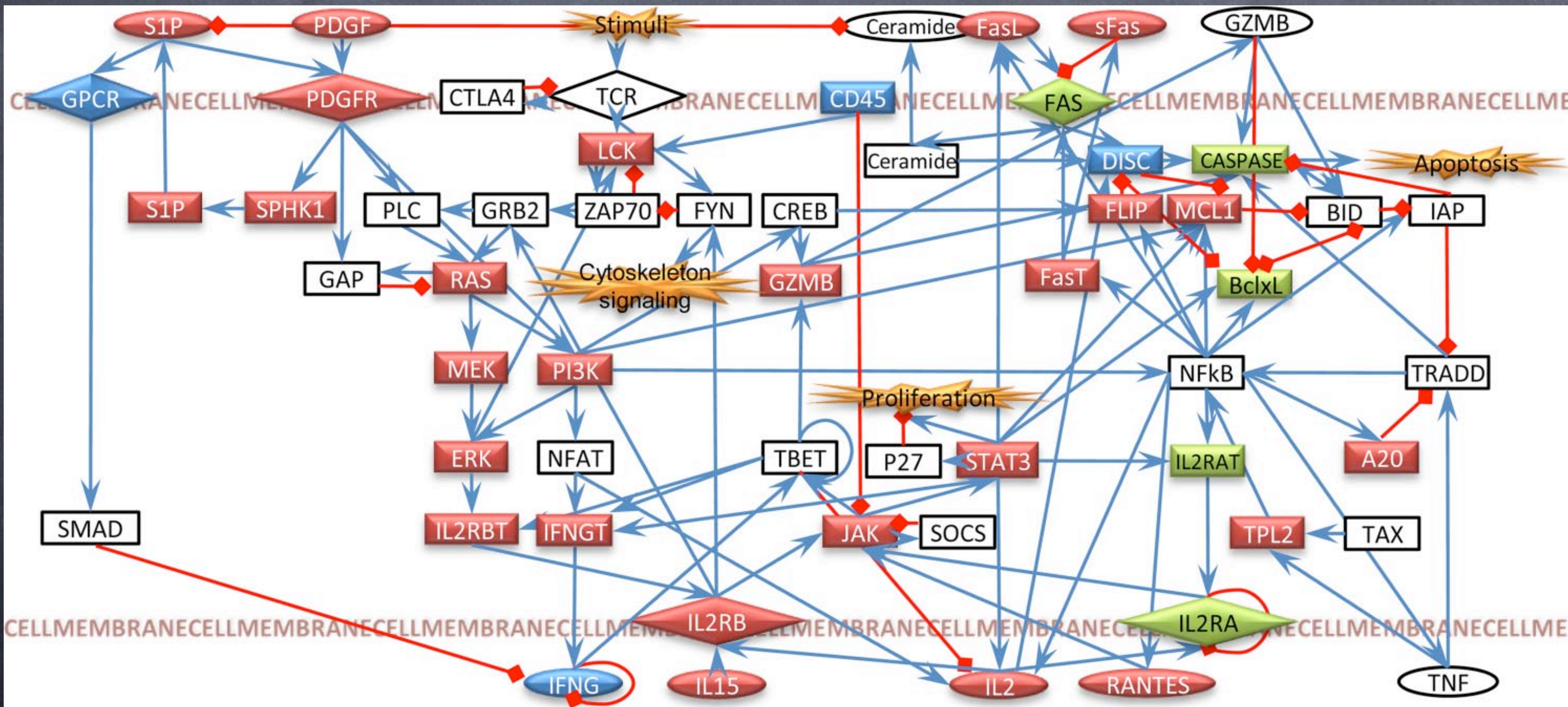
Metabolic network, E. Coli



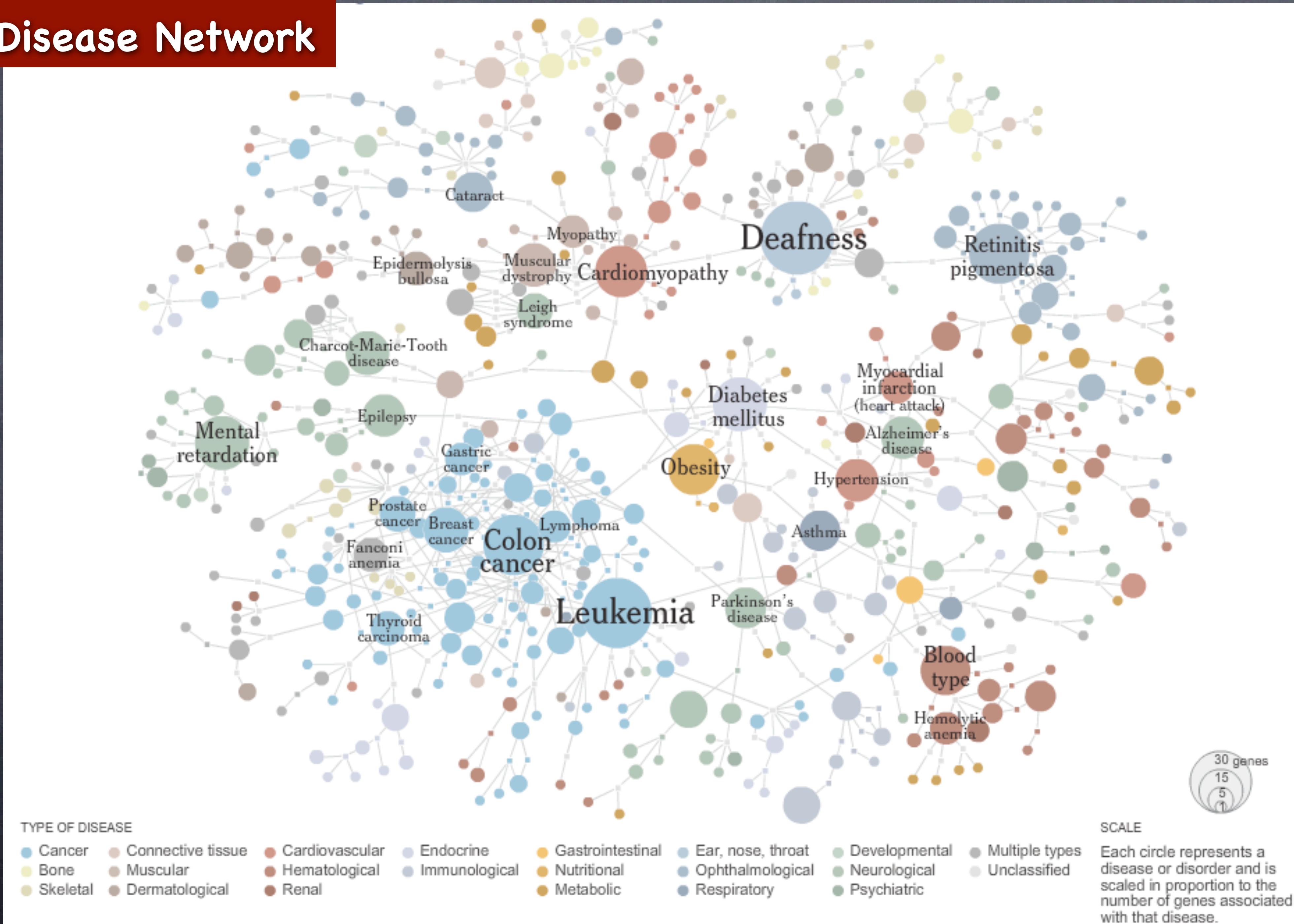
Protein Interaction network, Yeast



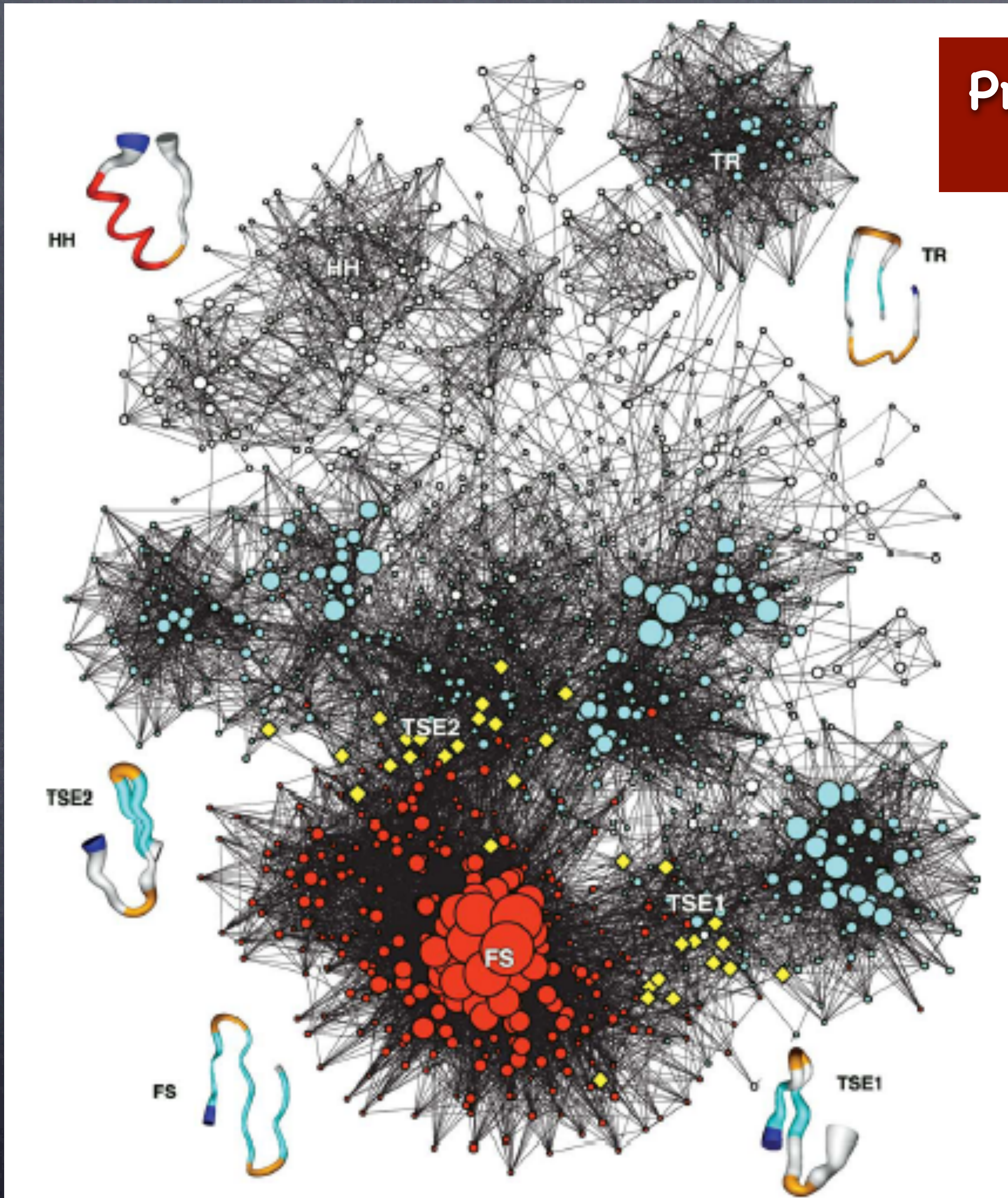
Survival signaling in large granular lymphocye leukemia

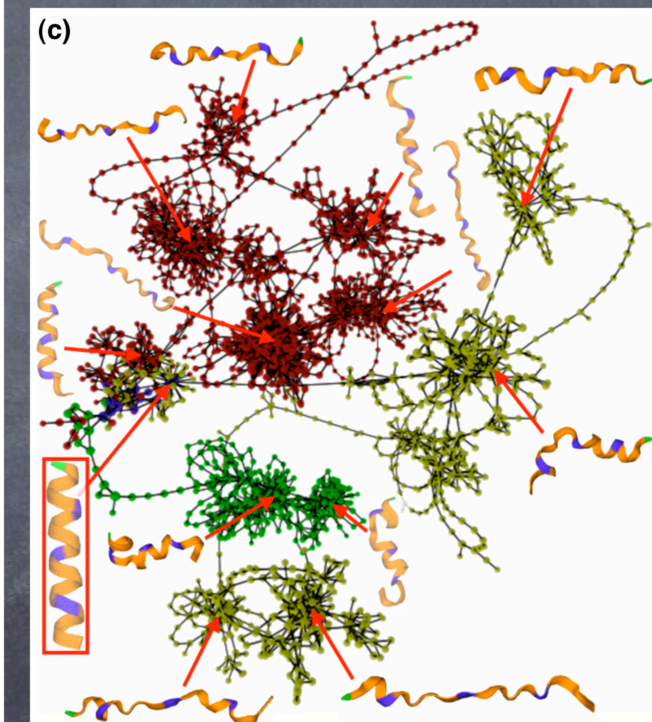


Disease Network

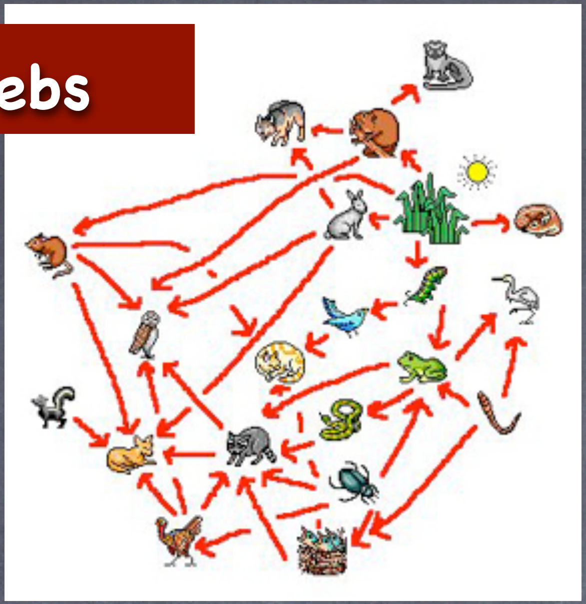


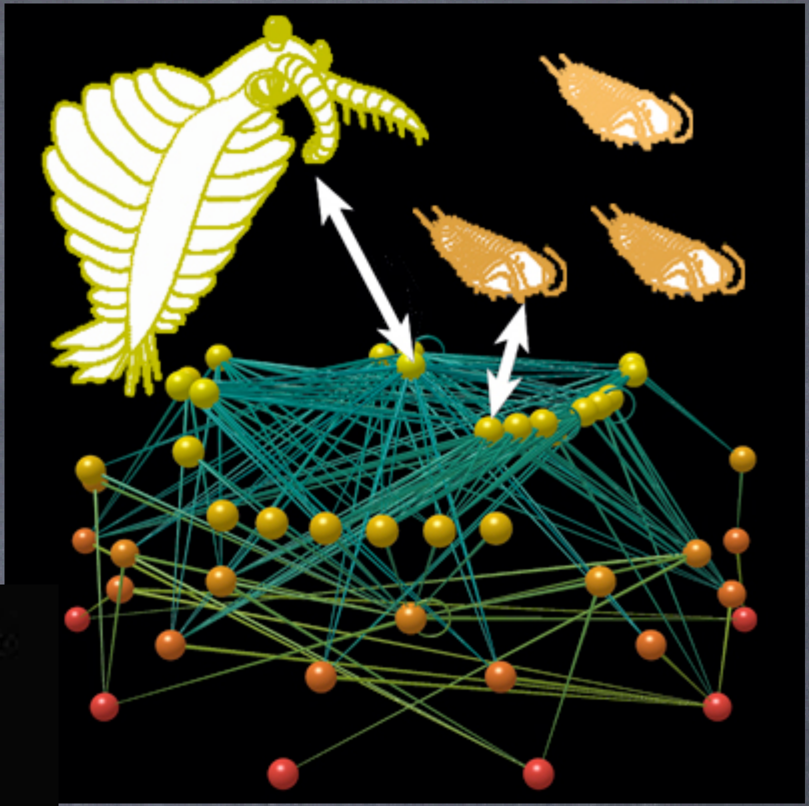
Protein folding pathways

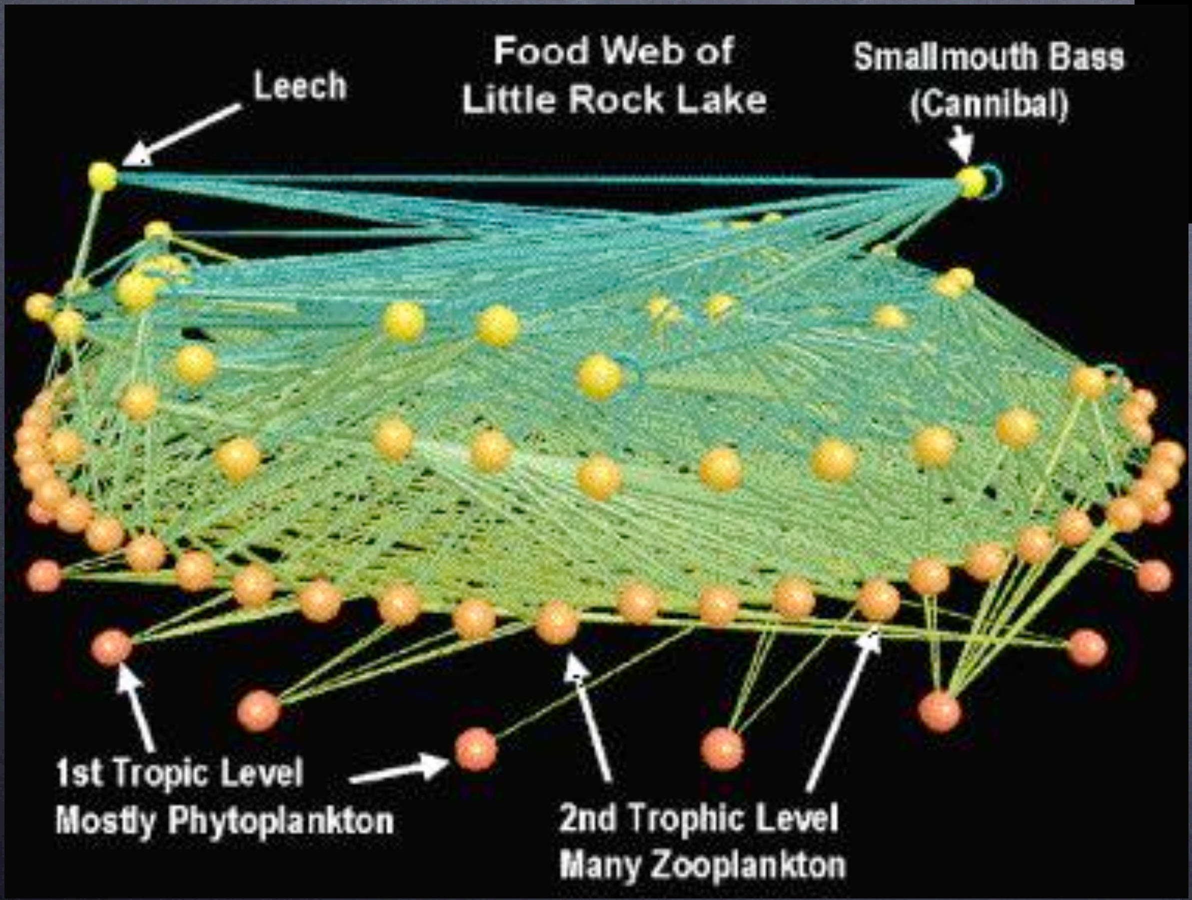




Food webs







Food Web of
Little Rock Lake
Leech
Smallmouth Bass
(Cannibal)
1st Tropic Level
Mostly Phytoplankton
2nd Trophic Level
Many Zooplankton

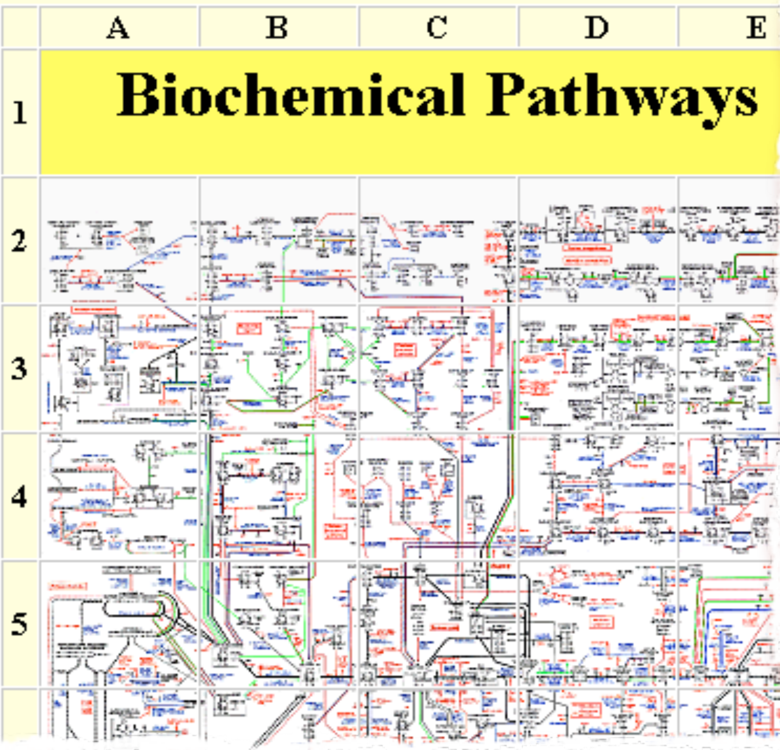
You mean to say you are going to talk about ALL these? In GENERAL?

STRUCTURAL UNIVERSALITIES

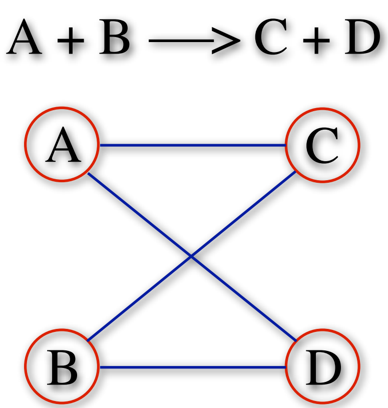
EVOLUTION OF STRUCTURE

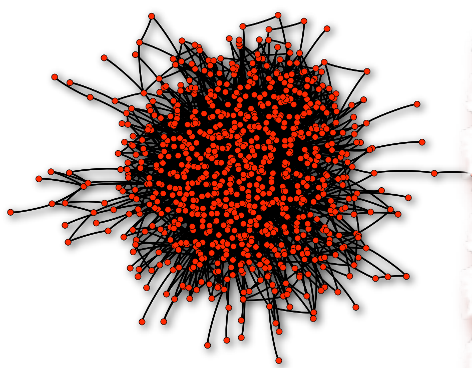
WHAT DO THEY DO? (and how?)

- Let's use an example -



- **Simple graph** (metabolites - nodes; reactions - links)
  - **=> degree properties**
  - **=> paths and their statistics**
  - **=> clustering, motifs**
  - **=> degree mixing patterns**
  - **=> communities, hierarchy, fractals**

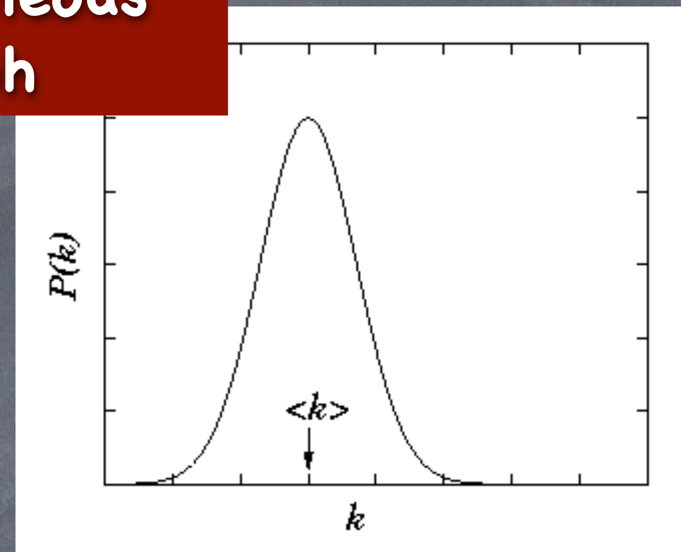


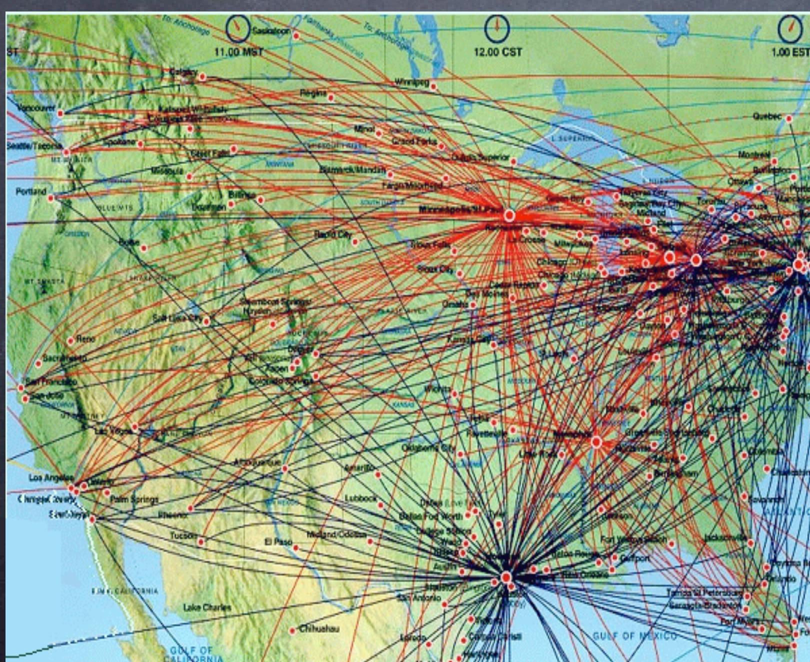


- **Directed graph** (one-way reactions)
- **Weighted graph** (rates, concentrations)
- **Bipartite graph** (both metabolites and reactions are network nodes)

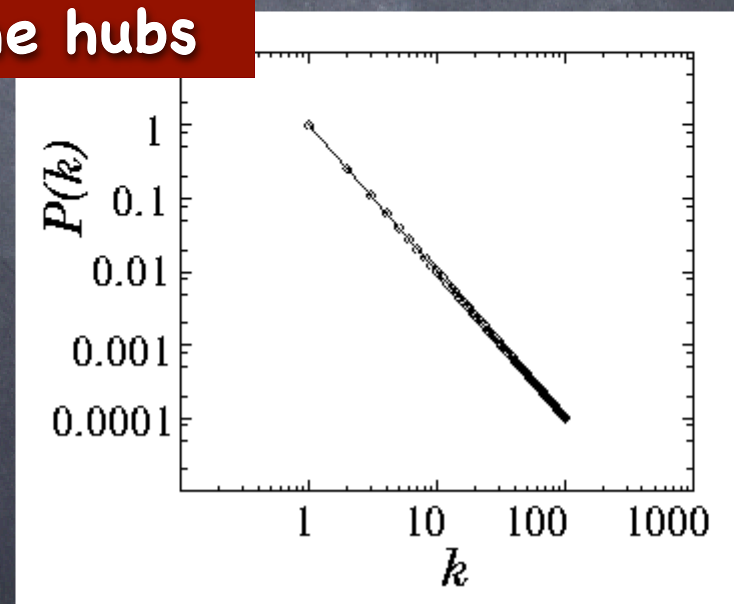
- Degree distribution and its claim to fame -

Homogeneous graph





Meet the hubs

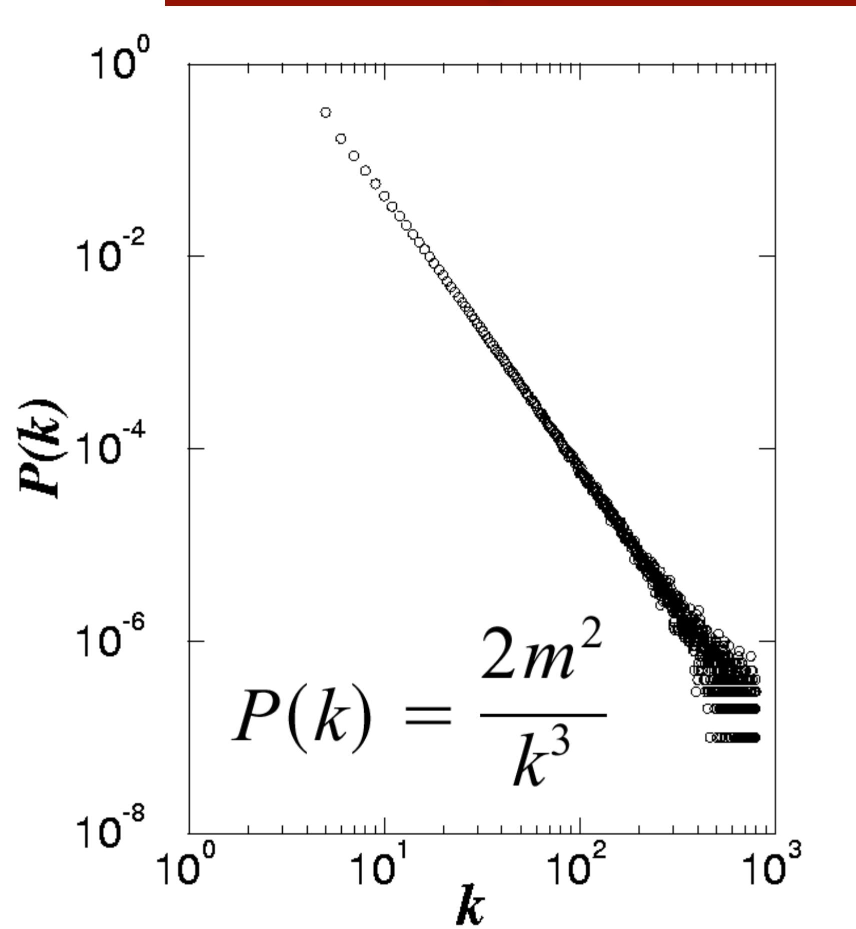


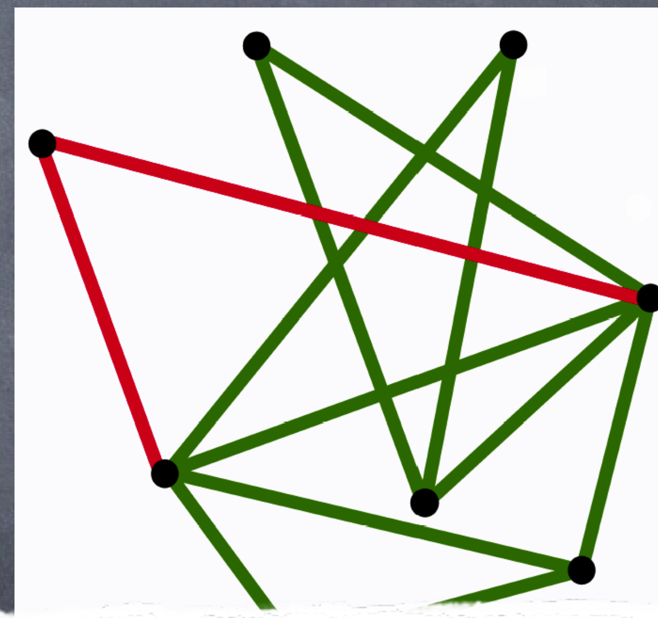
- Rich gets richer -

1999, Barabasi & Albert **Scale-Free Model**

- **Networks grow**
- **New nodes pick popular old nodes:** preferential attachment

$$\Pi(k_i) = \frac{k_i}{\sum_j k_j}$$





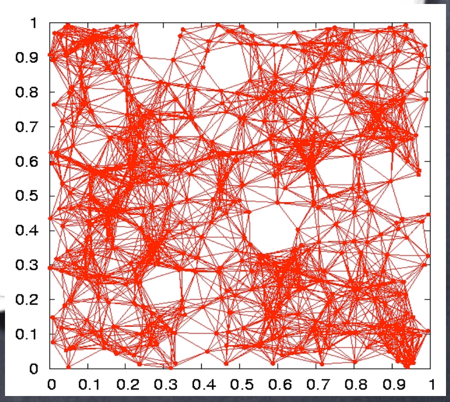
1965, Price, scietific citation network

➡ measures powerlaw

➡ builds model: cited papers get more citations

- Statistical physics gets its hands on scale-free models -

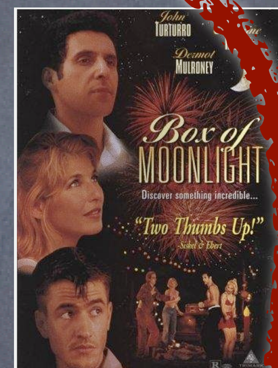
- **linear preferential attachment: critical for powerlaws**
- **fitness-based attachment models: math similar to BEC**
- **other growth models that result in preff. attachment**
- **configuration model:** ensemble of all networks with a given degree distribution
  - ➡ scale-free networks are ultra-small: $\langle d \rangle \sim \log(\log N)$
  - ➡ vanishing number of triangles
- **physical constraints on link length**
  - ➡ large cost of length forbids hubs
  - ➡ complex models for spatially embedded scale-free networks



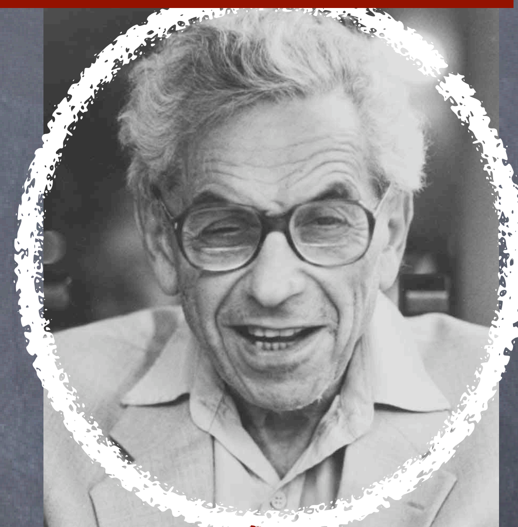
- Paths in a small world -

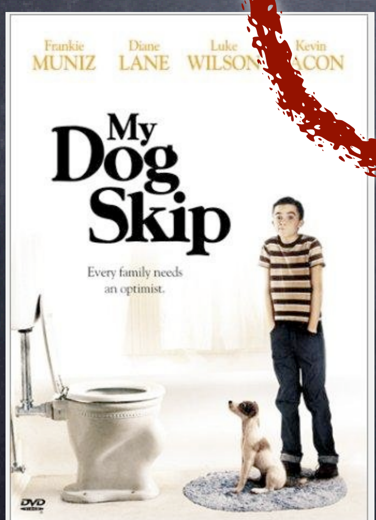
The Kevin Bacon game

John Turturro



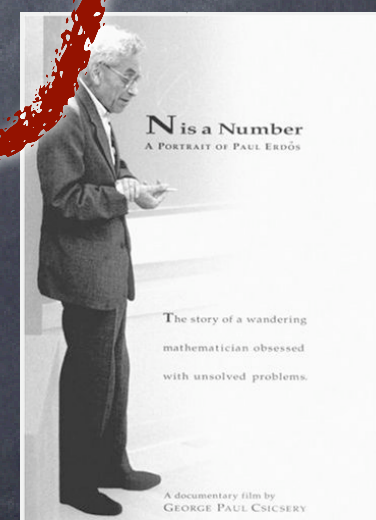
The Erdős Number





Clint Howard

Gene Patterson

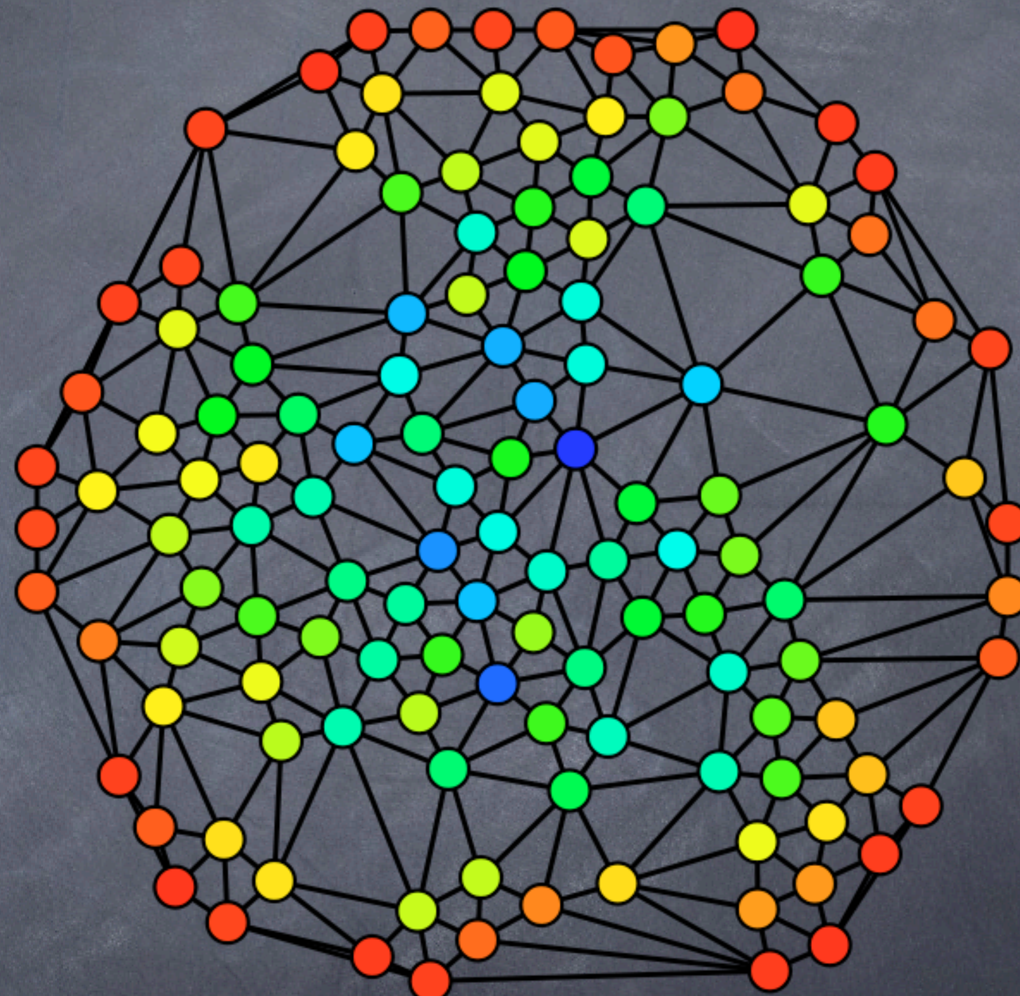


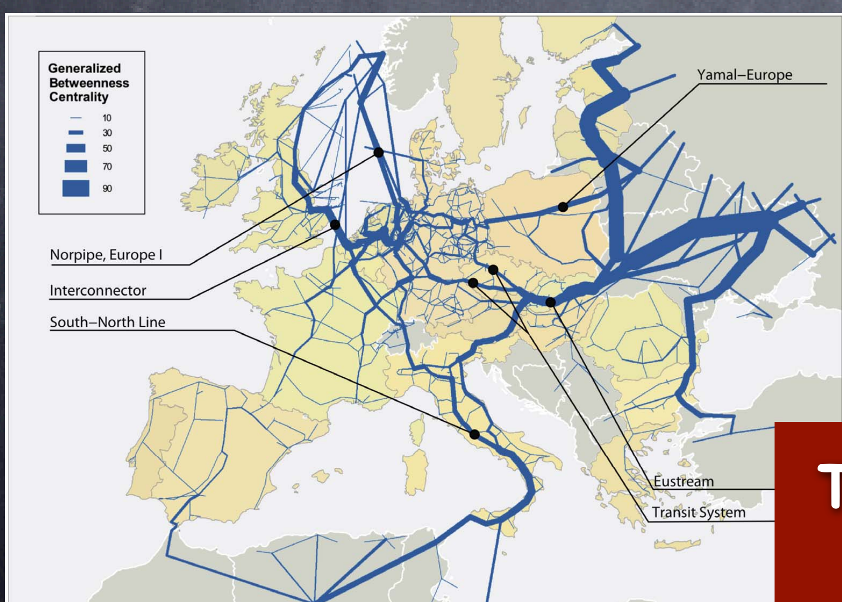
Erdős has a Bacon number of 4

- Centrality, or betweenness -

- Number of shortest paths through a node or link

Crutial measure for flow

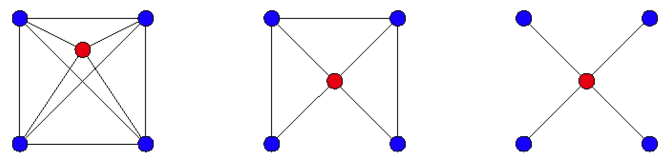




Trans-European gas network

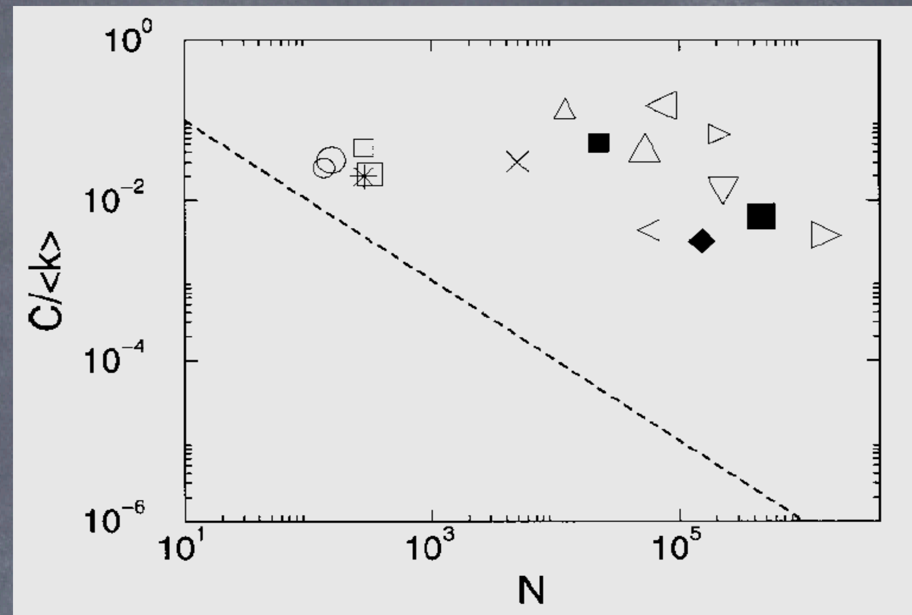
- The clustering coefficient and motifs -

- **Fraction of connected neighbours**

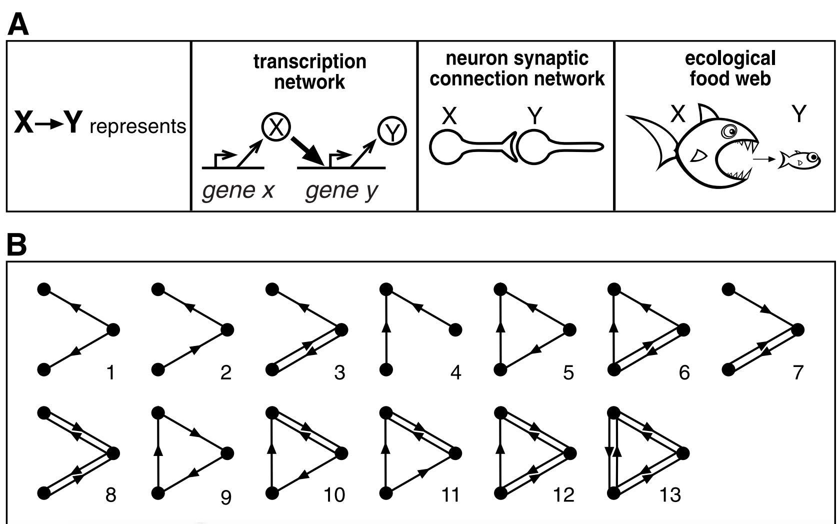


C=1 C=1/2 C=0

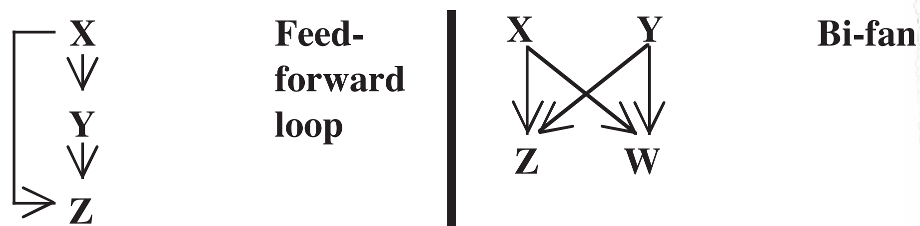
$$C_i = \frac{2 n_i}{k_i (k_i - 1)}$$



- **Motif:** pattern of connection between any triplet / quadruplet /...

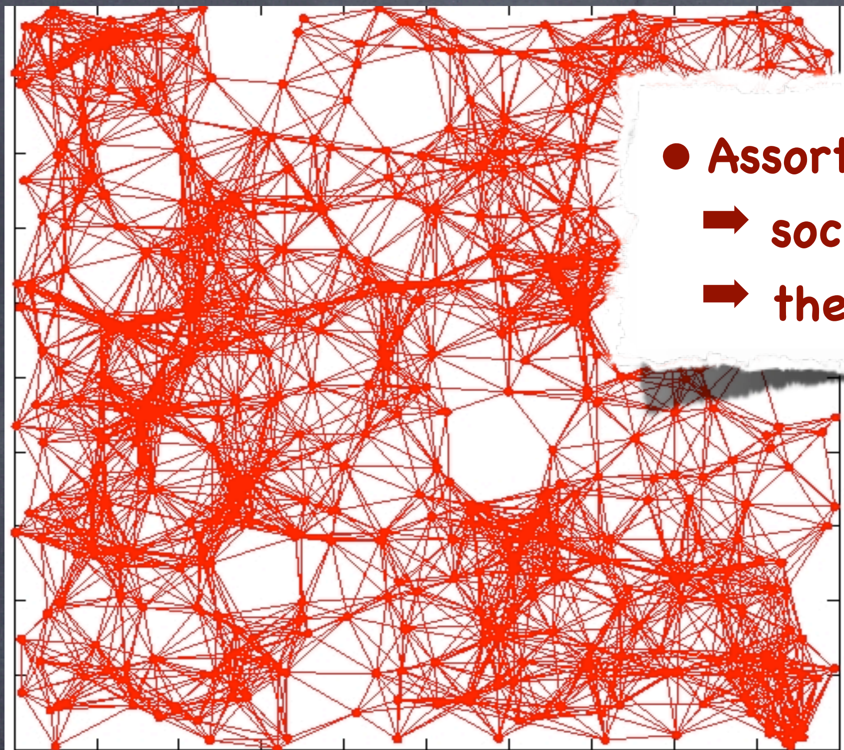


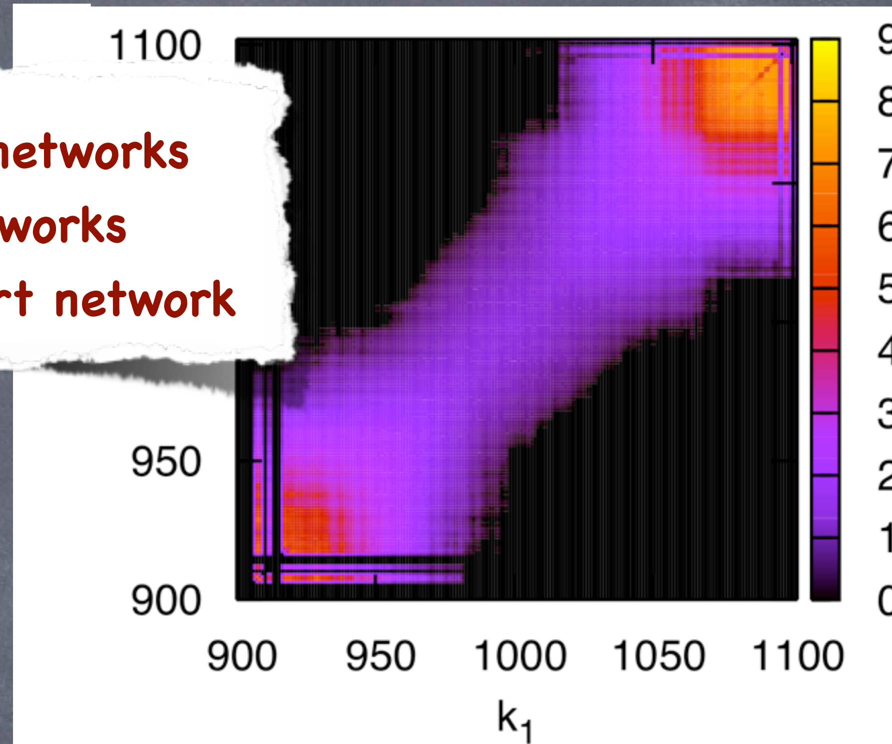
Transctiptional regulation:



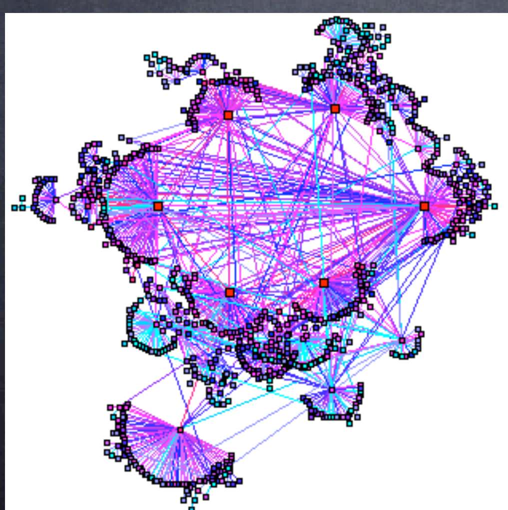
40	7 ± 3	10	203	47 ± 12	13
70	11 ± 4	14	1812	300 ± 40	41

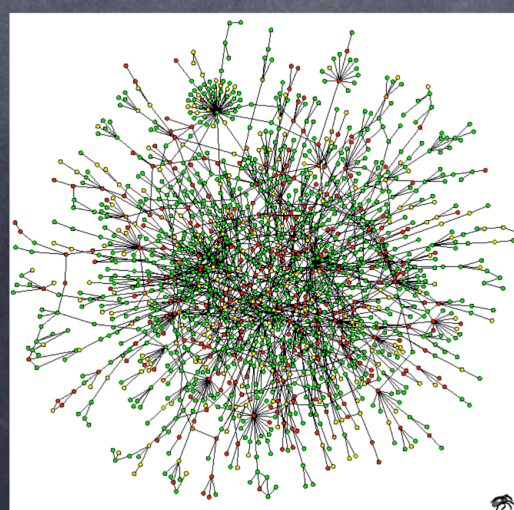
- Degree correlations -





- **Assortative networks**
  - ➡ social networks
  - ➡ the airport network

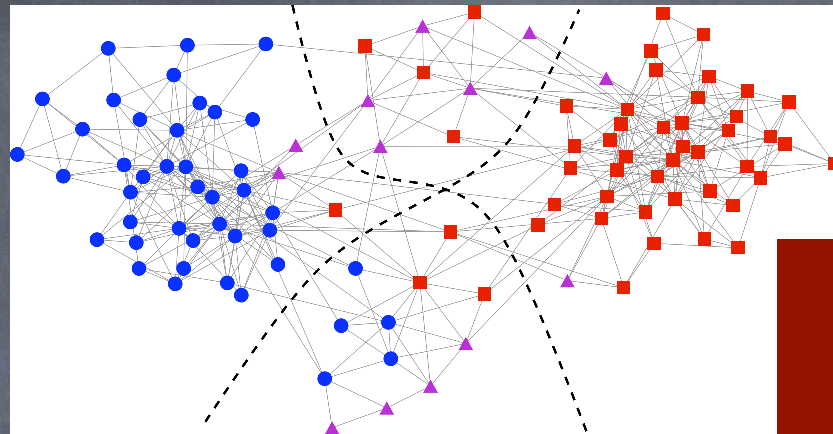




- **Disassortative networks**
  - ➡ biological networks
  - ➡ communication

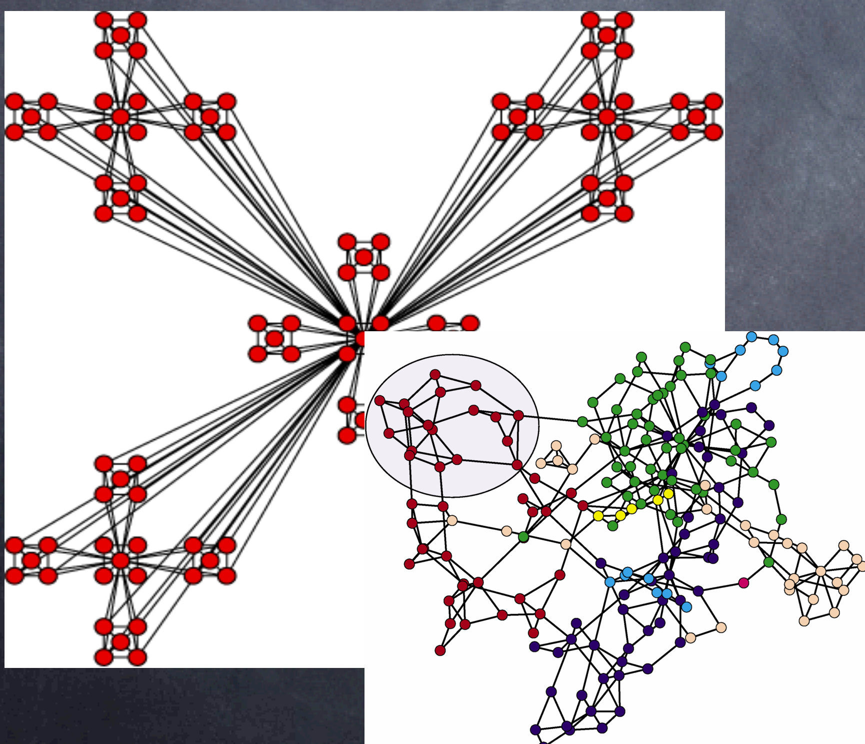
- Modular organization -

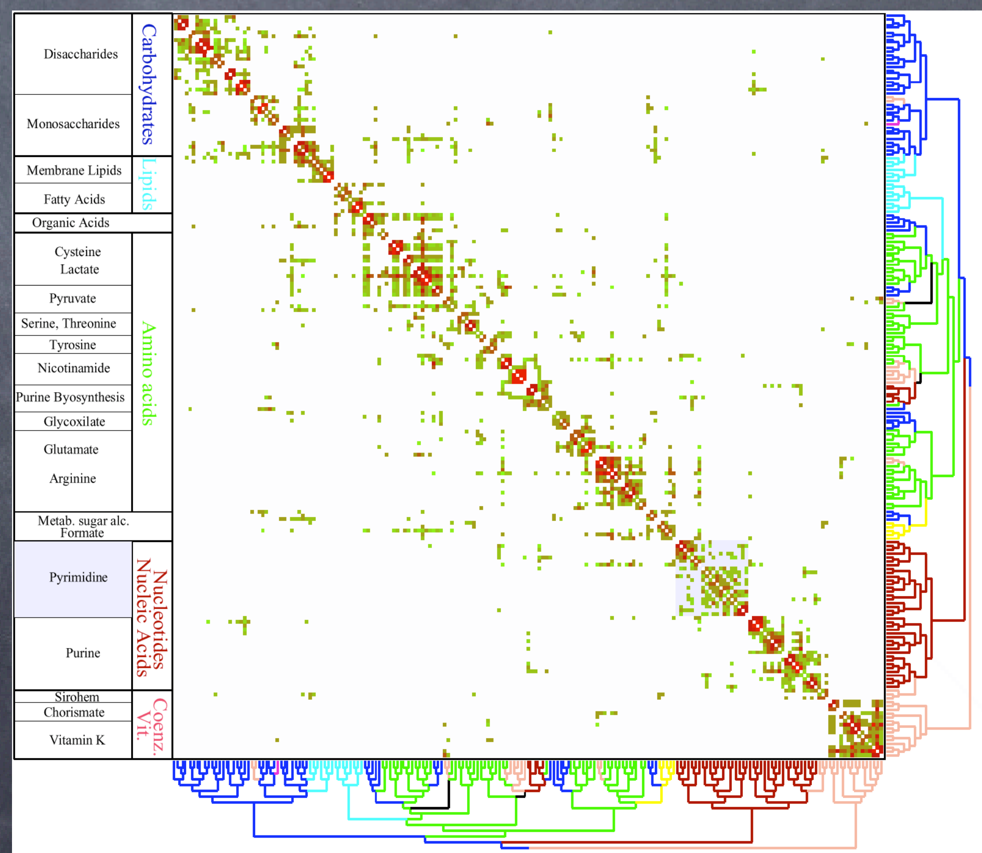
- **Communities**



Books on American politics

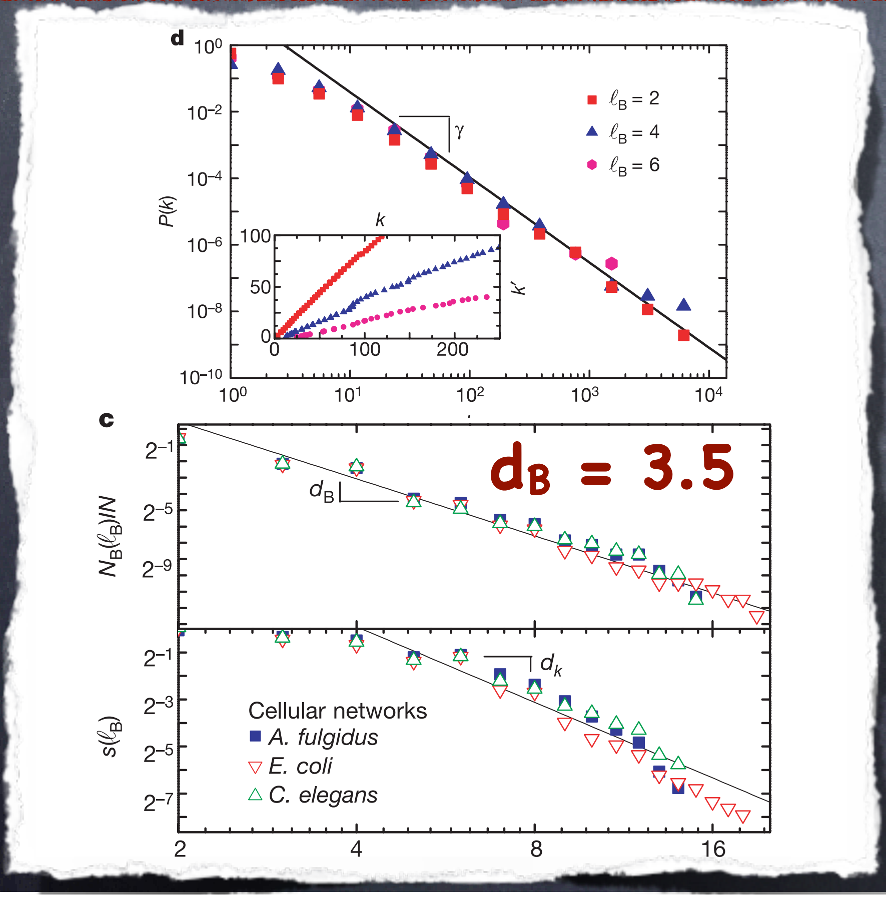
- **Hierarchy**

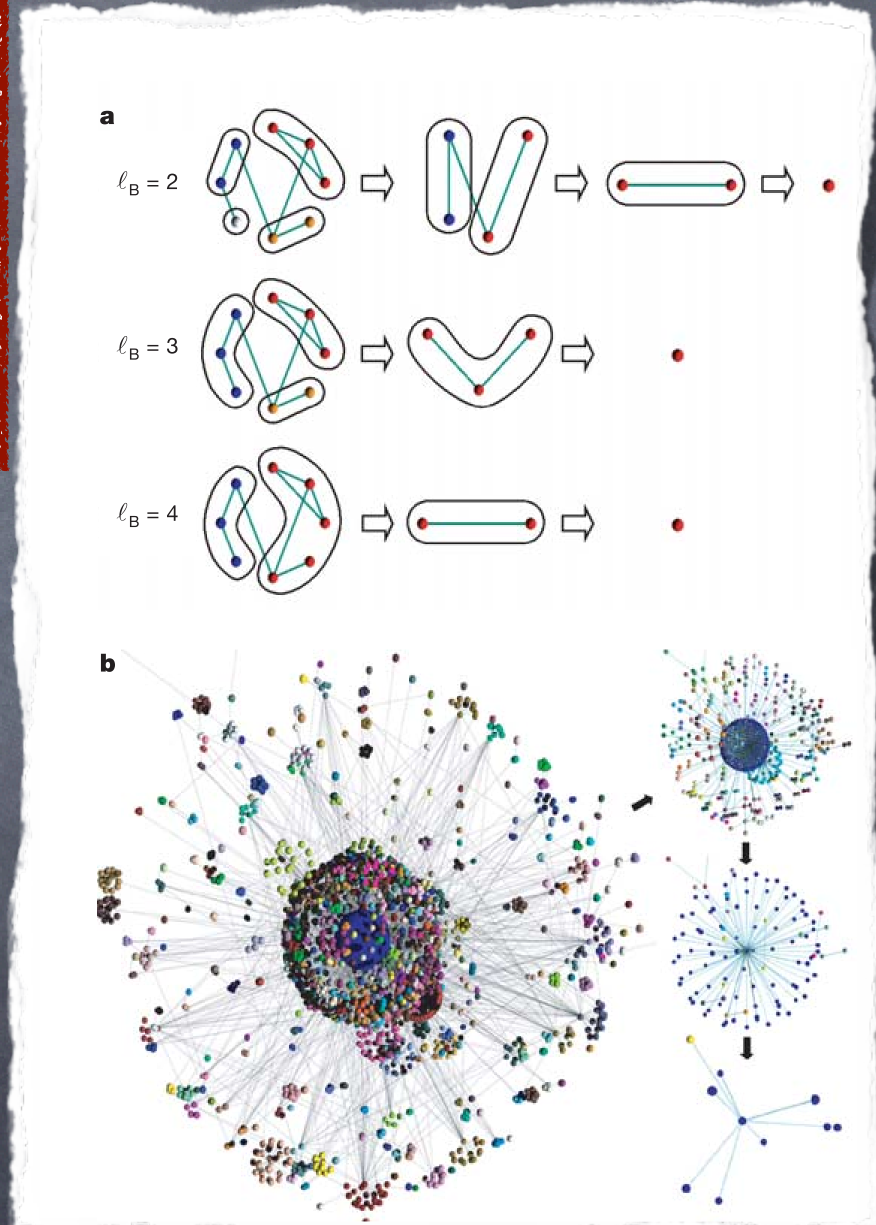




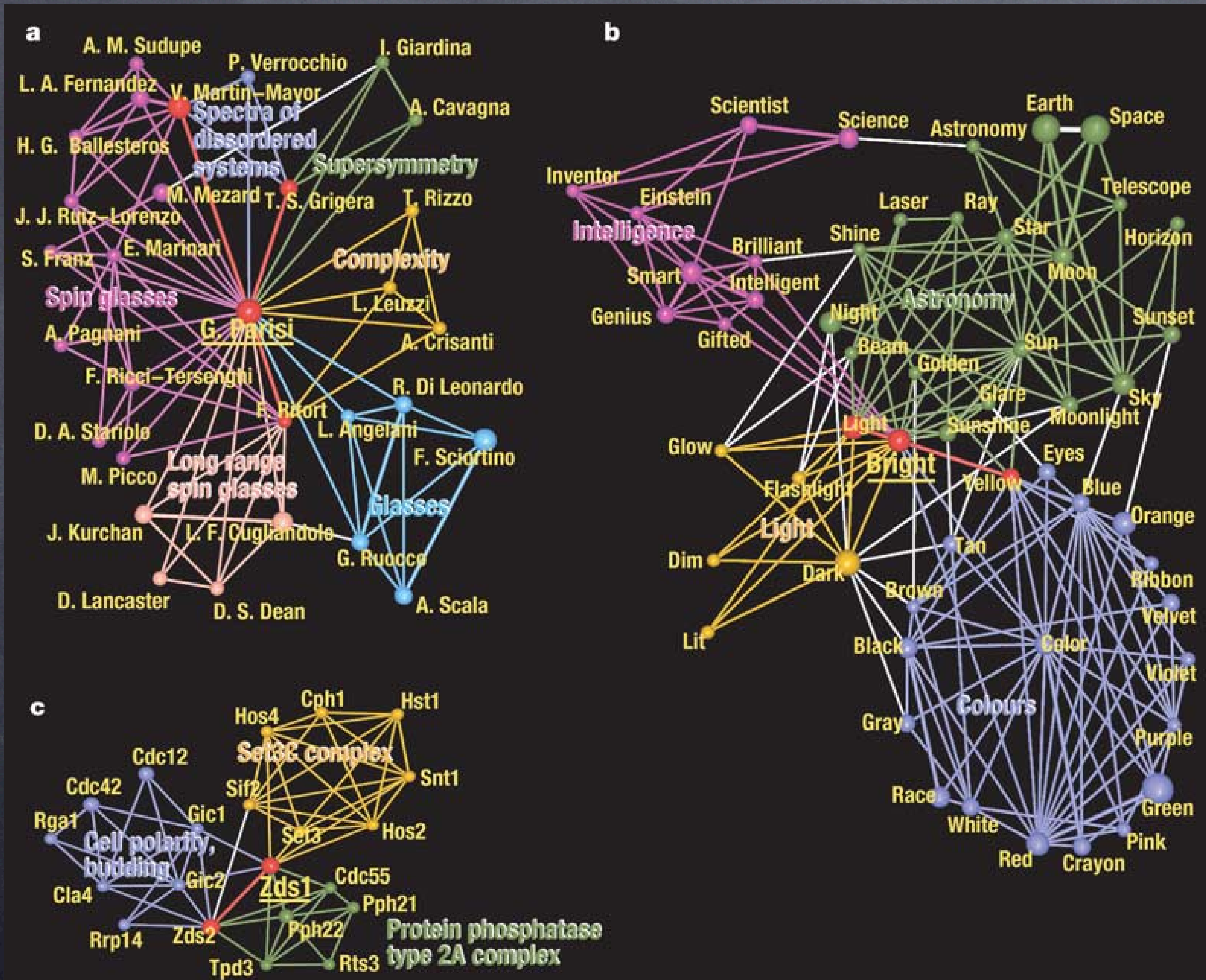
- Self similarity and fratal networks -

- **Fractals hidden in networks**
  ➡ degree distribution invariant under reduction
  ➡ power law decay of fox numbers vs box size

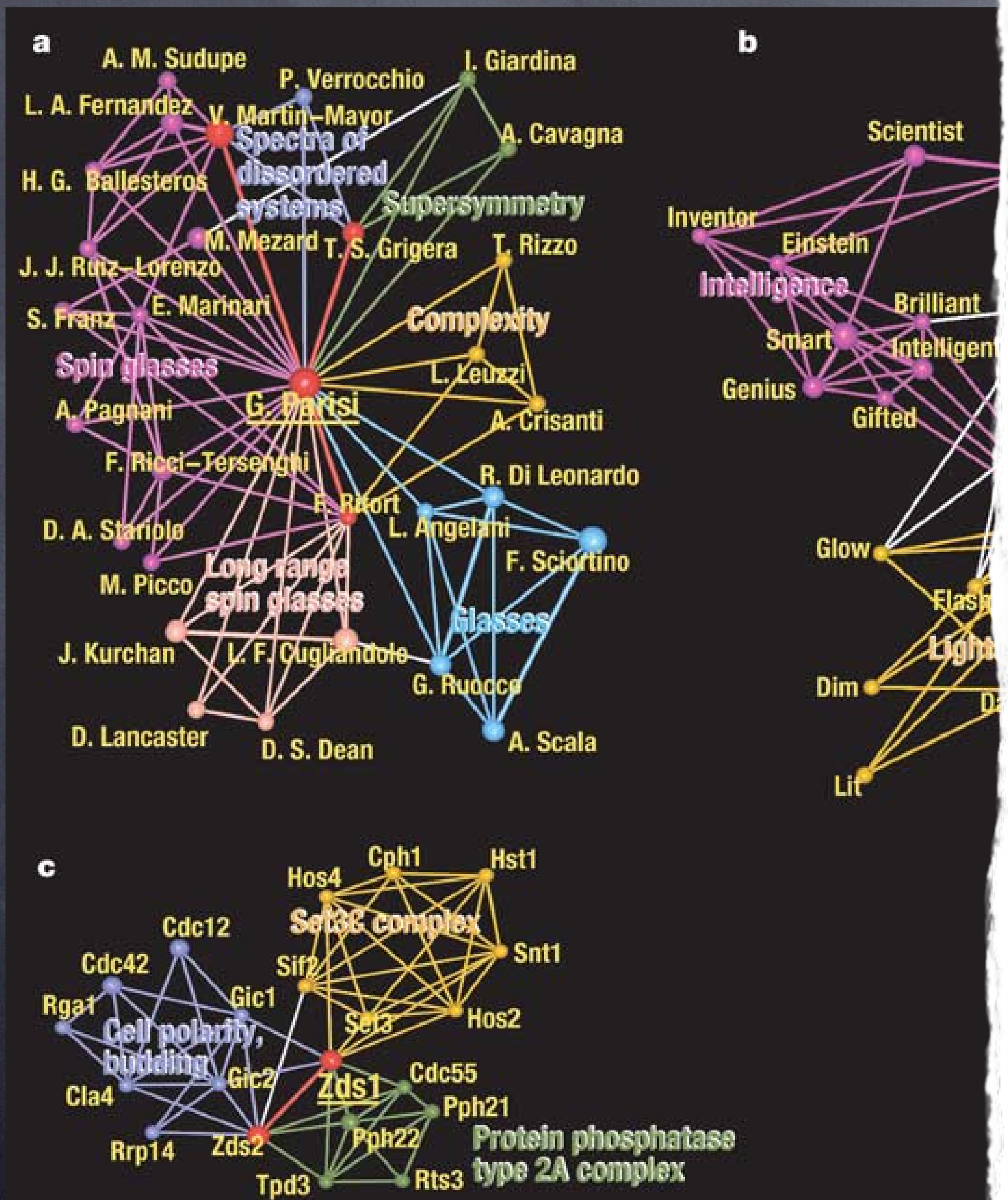


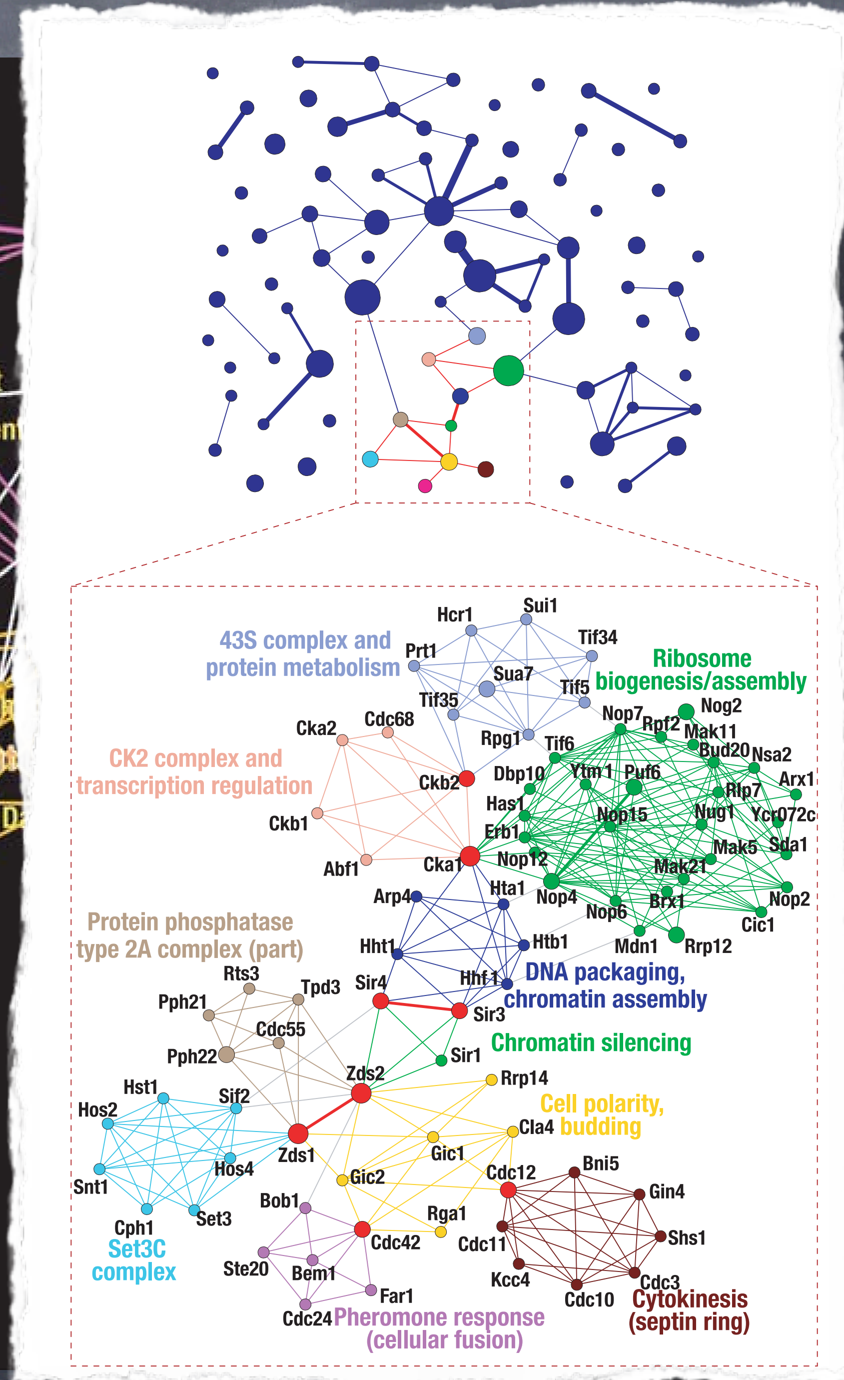


- Overlapping communities -



- Overlapping communities -





2. Dynamics on complex networks

April 13
12 PM