



The Abdus Salam  
International Centre for Theoretical Physics

United Nations  
Educational, Scientific  
and Cultural Organization

International Atomic  
Energy Agency



SMR.1656 - 36

**School and Workshop on  
Structure and Function of Complex Networks**

**16 - 28 May 2005**

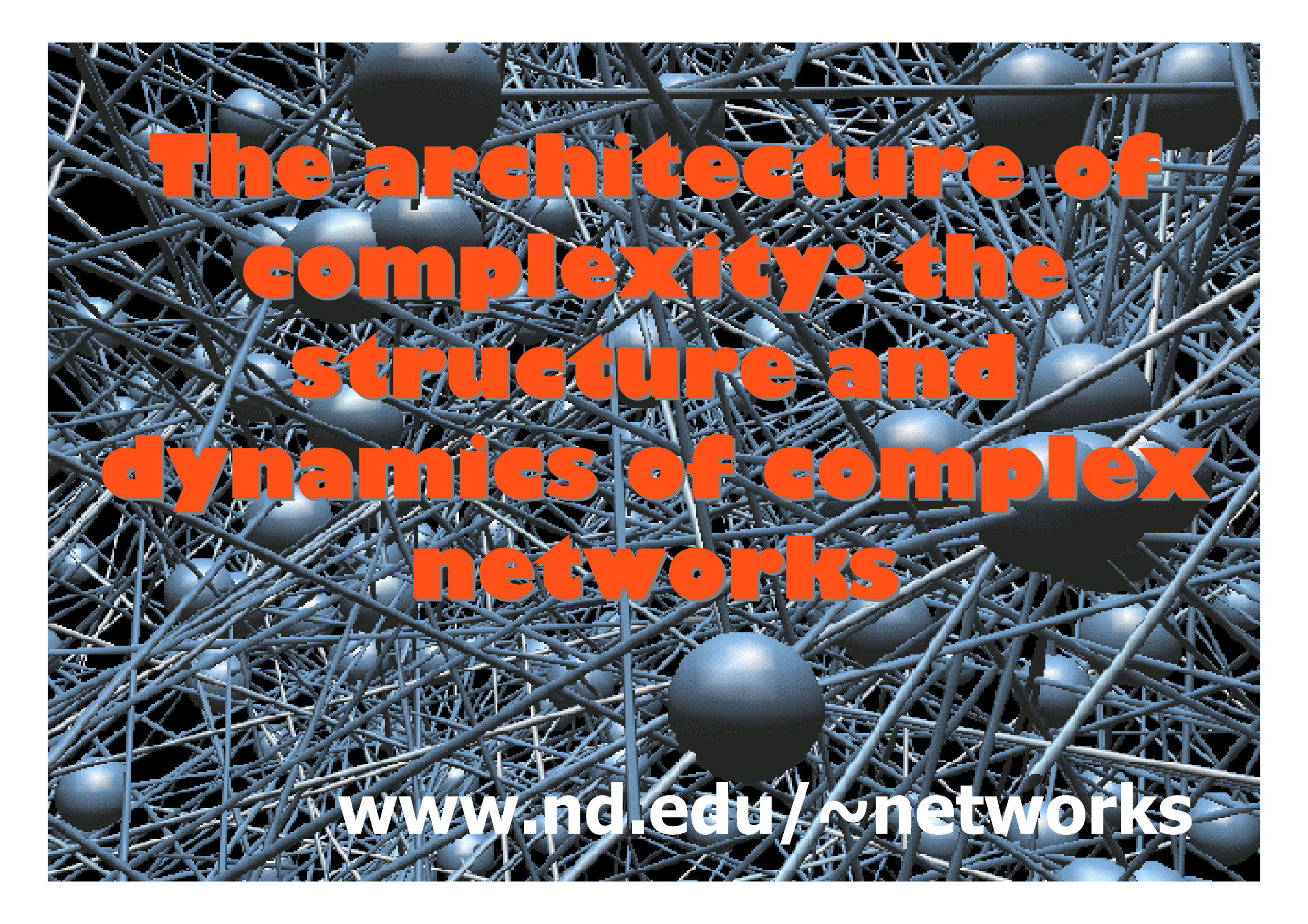
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**The Architecture of Complexity:  
The Structure and Dynamics of Complex Networks  
(Public Lecture)**

**Albert-Laszlo BARABASI  
University of Notre Dame  
Department of Physics  
IN 46556 Notre Dame  
U.S.A.**

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These are preliminary lecture notes, intended only for distribution to participants

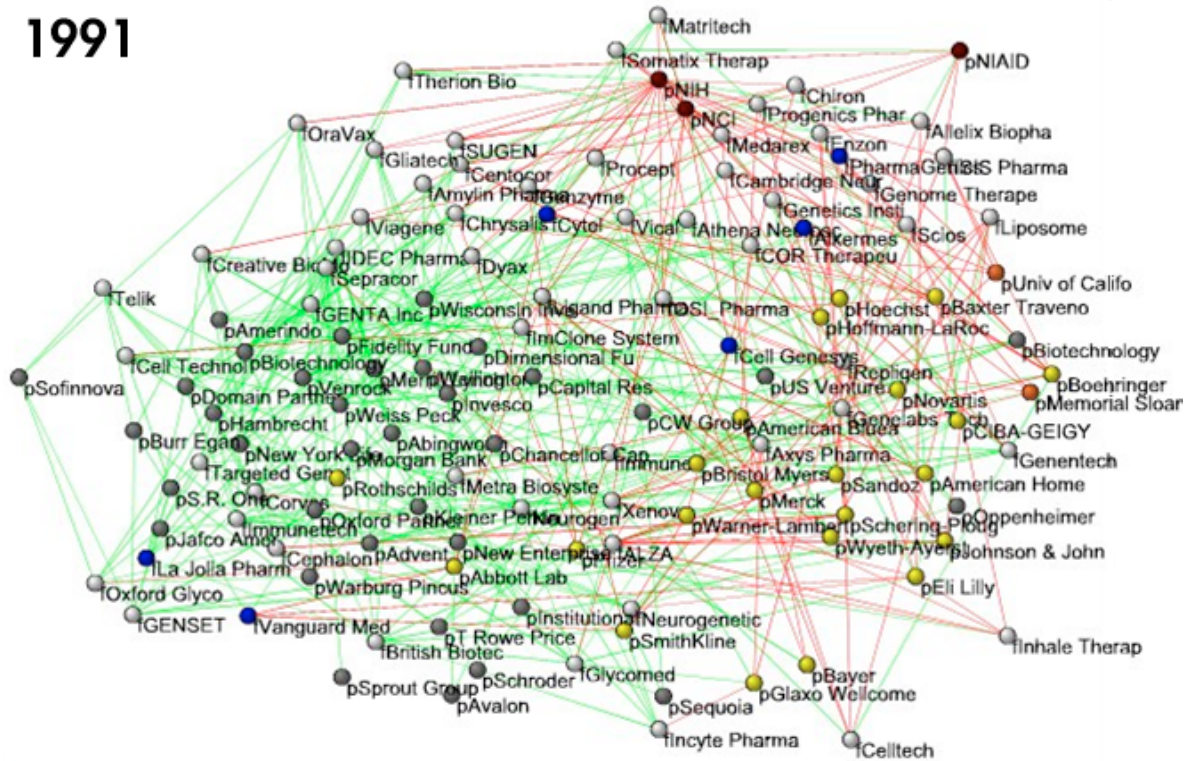


**The architecture of  
complexity: the  
structure and  
dynamics of complex  
networks**

[www.nd.edu/~networks](http://www.nd.edu/~networks)

# Business ties in US biotech-industry

1991

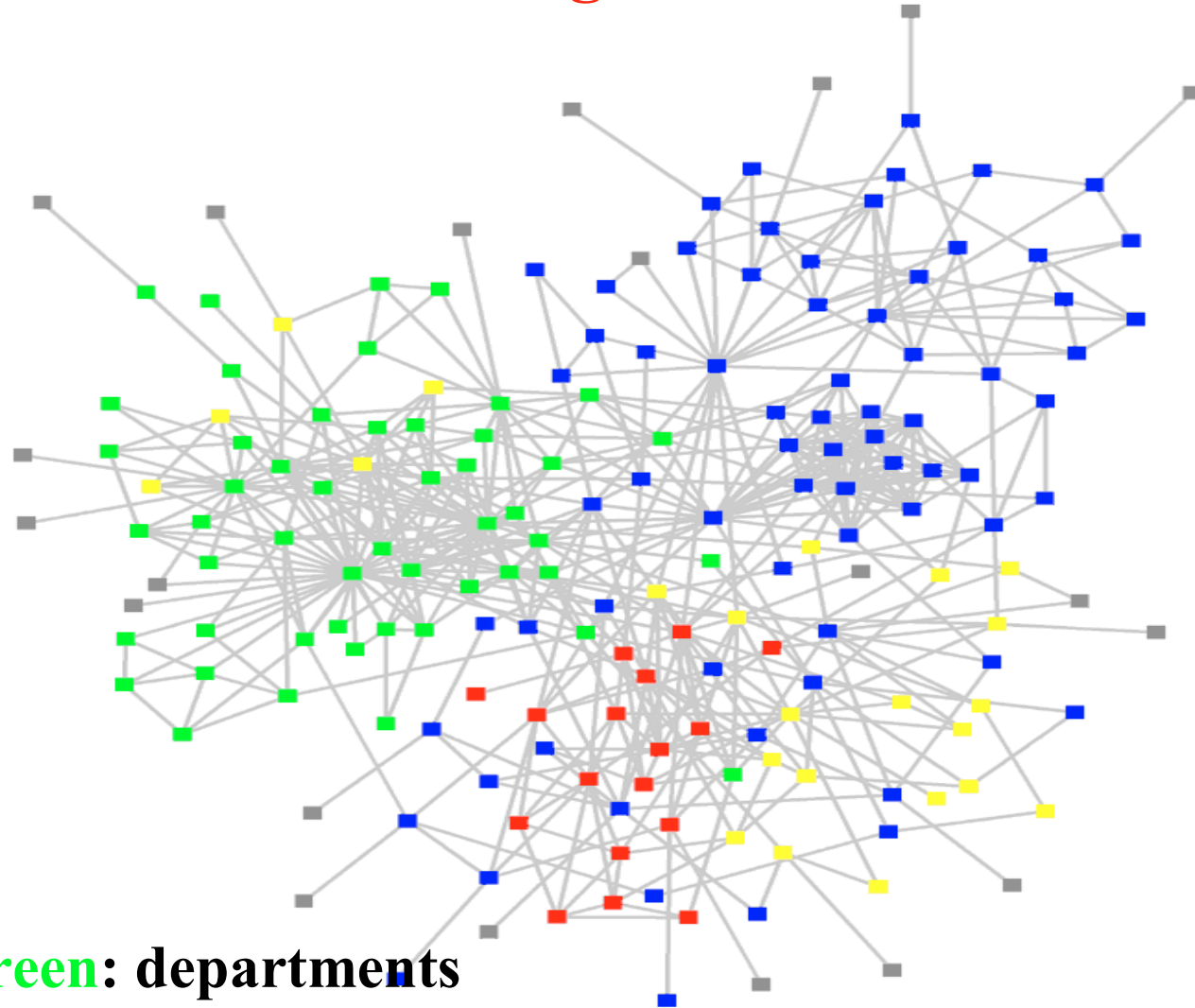


Nodes: companies: investment  
 pharma  
 research labs  
 public  
 biotechnology

Links: financial  
 R&D collaborations

<http://ecclectic.ss.uci.edu/~drwhite/Movie>

# Structure of an organization



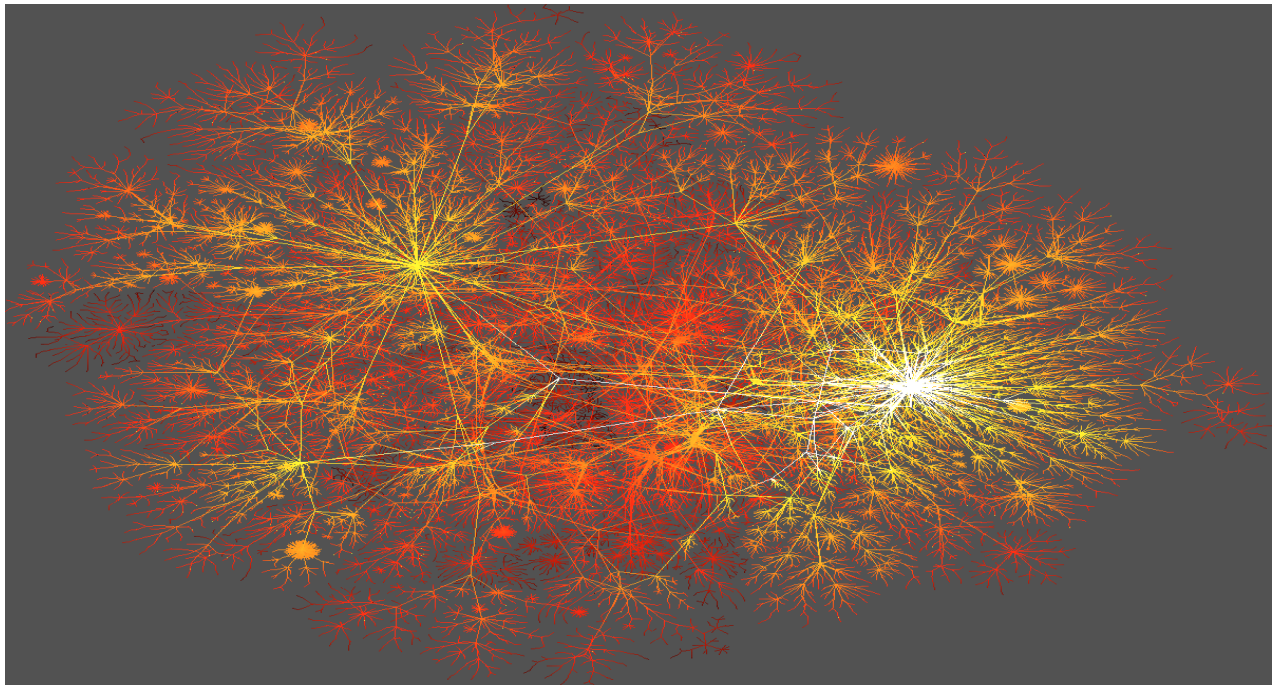
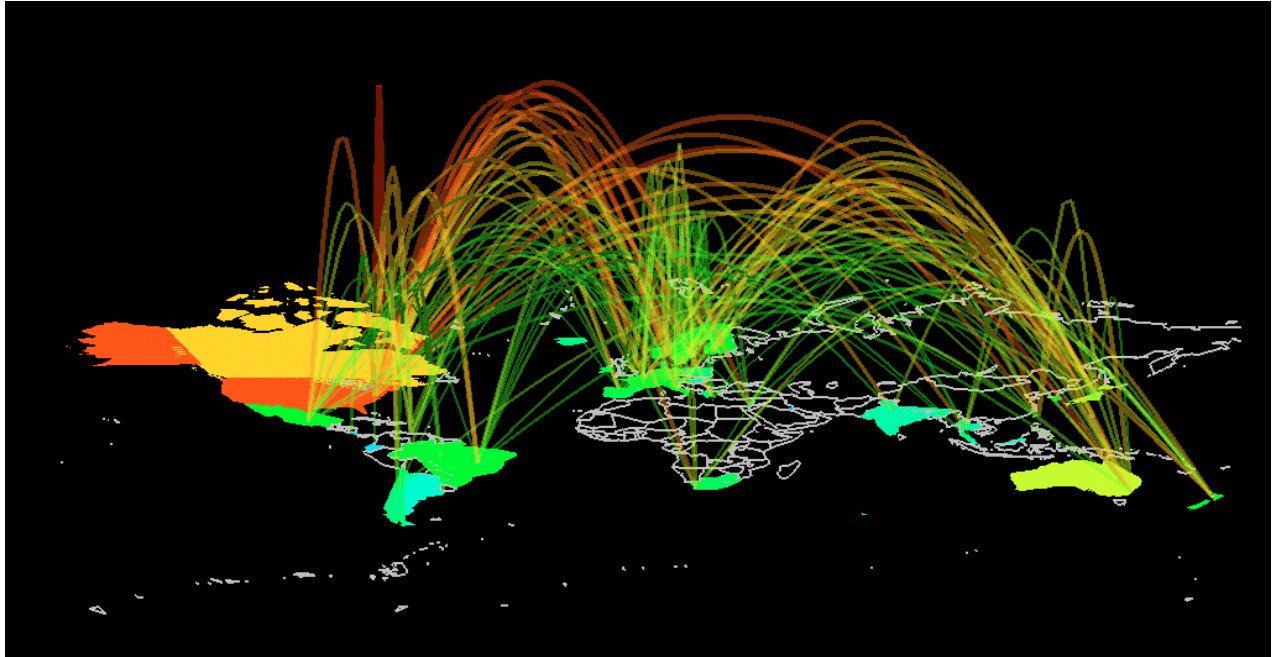
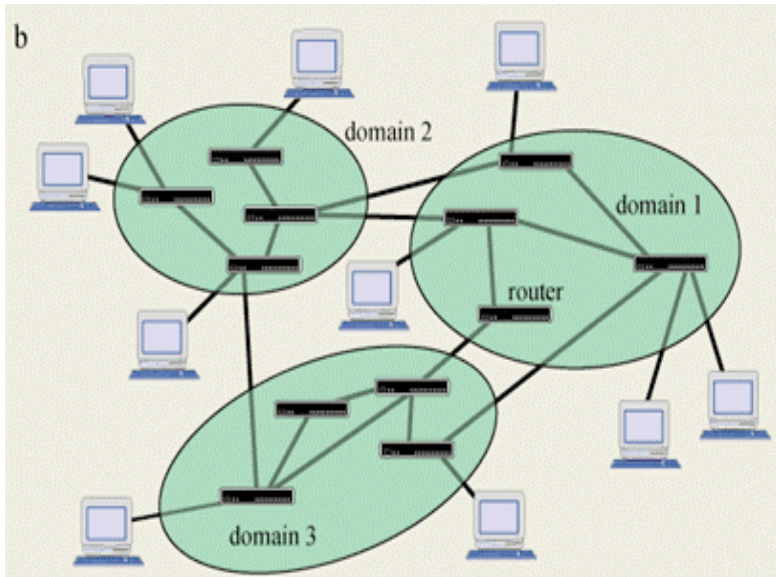
**Red, blue, or green:** departments

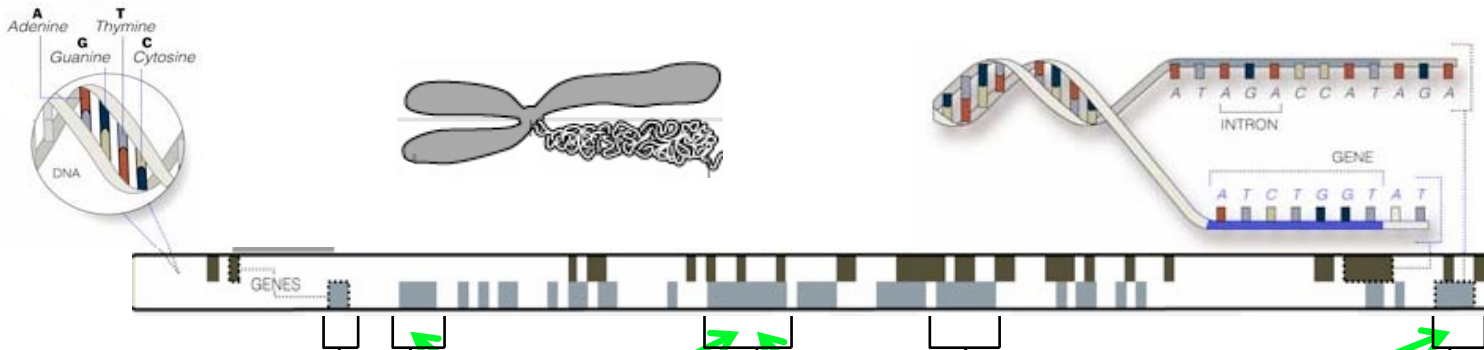
**Yellow:** consultants

**Grey:** external experts



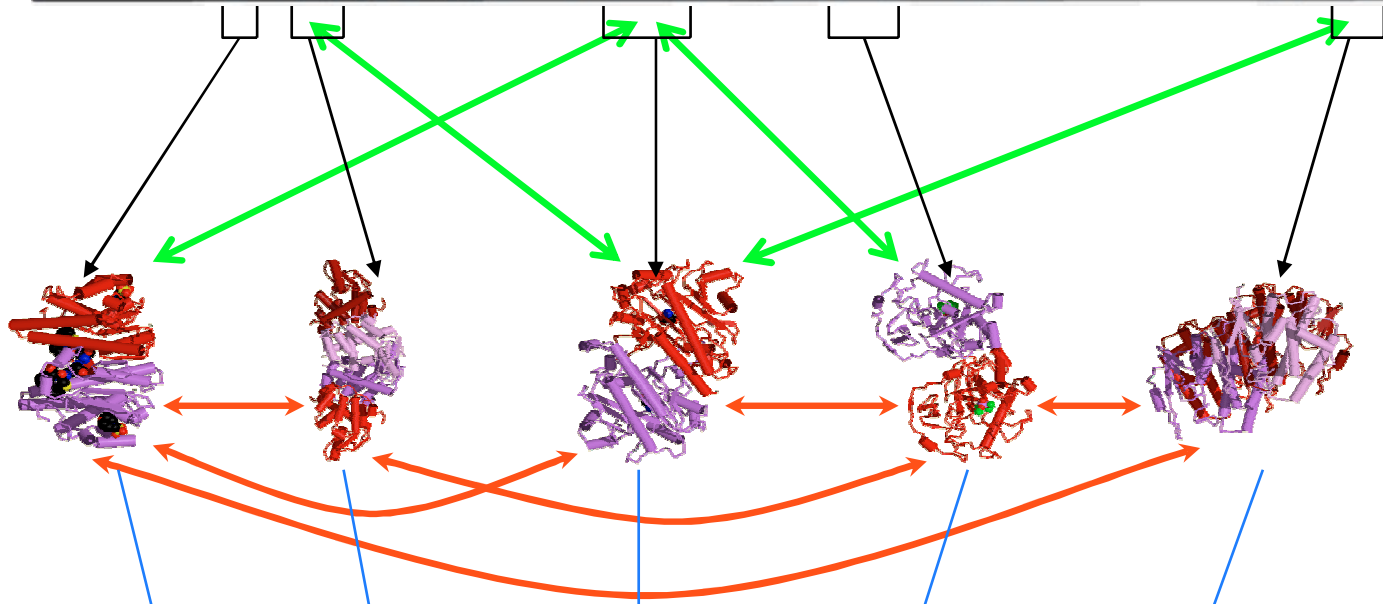
# Internet





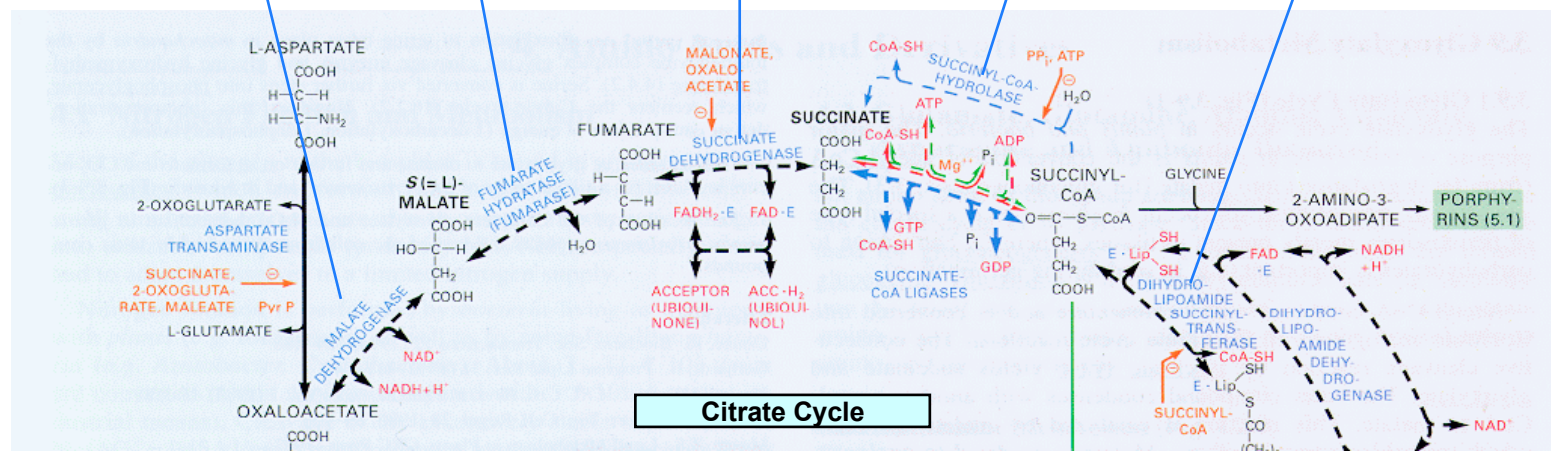
# GENOME

protein-gene interactions



# PROTEOME

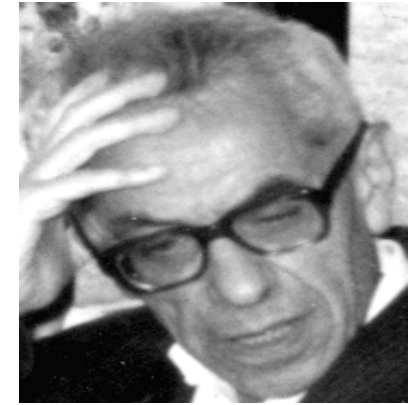
protein-protein interactions



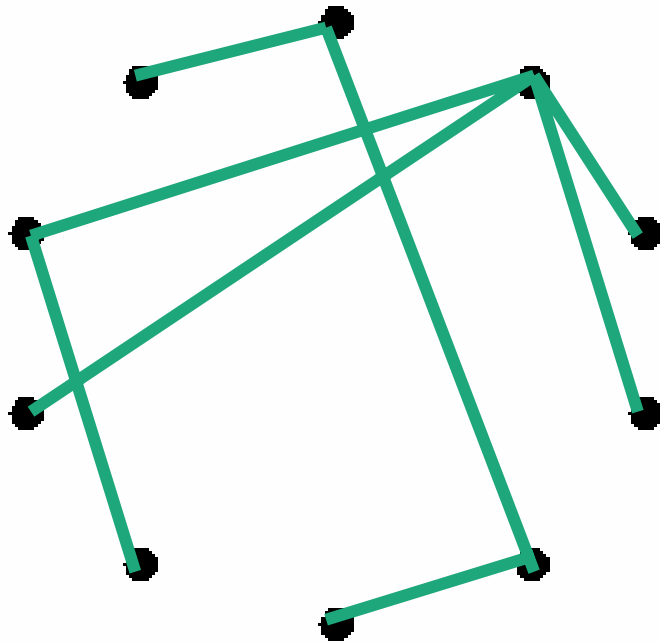
# METABOLISM

Bio-chemical reactions

# Erdős-Rényi model (1960)



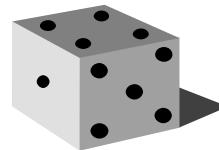
**Pál Erdős**  
(1913-1996)



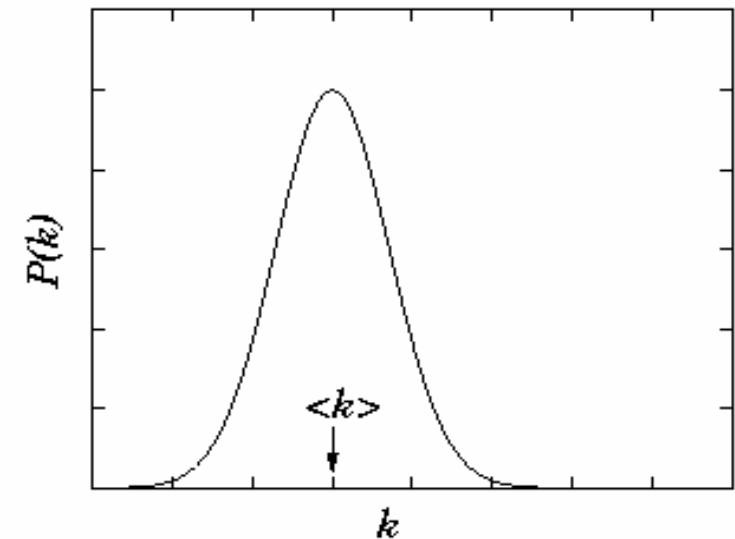
Connect with  
probability  $p$

$$p=1/6$$
$$N=10 \langle k \rangle$$
$$\sim 1.5$$

Poisson distribution



- Democratic
- Random



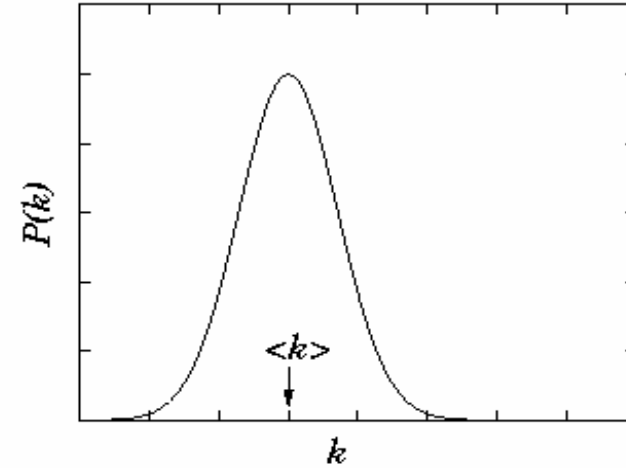


# World Wide Web

**Exponential Network**

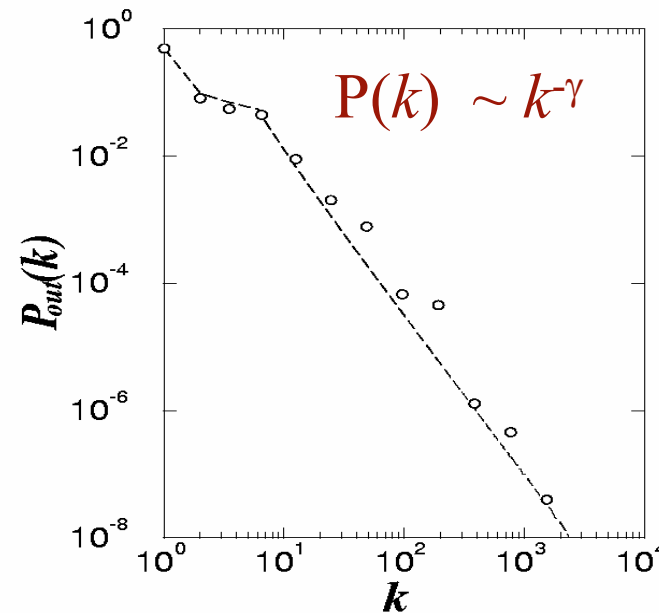


United States



**Expected**

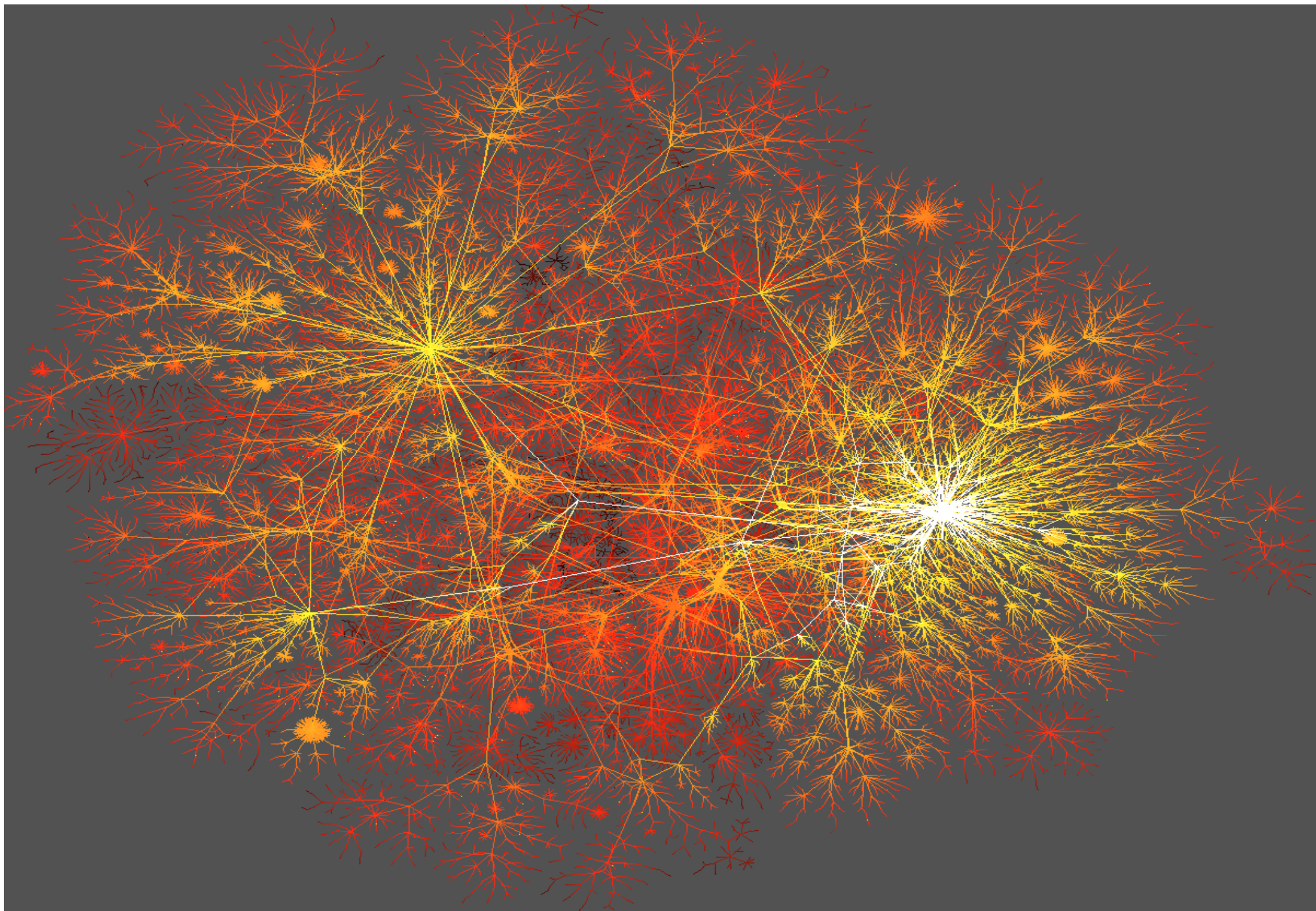
**Scale-free Network**



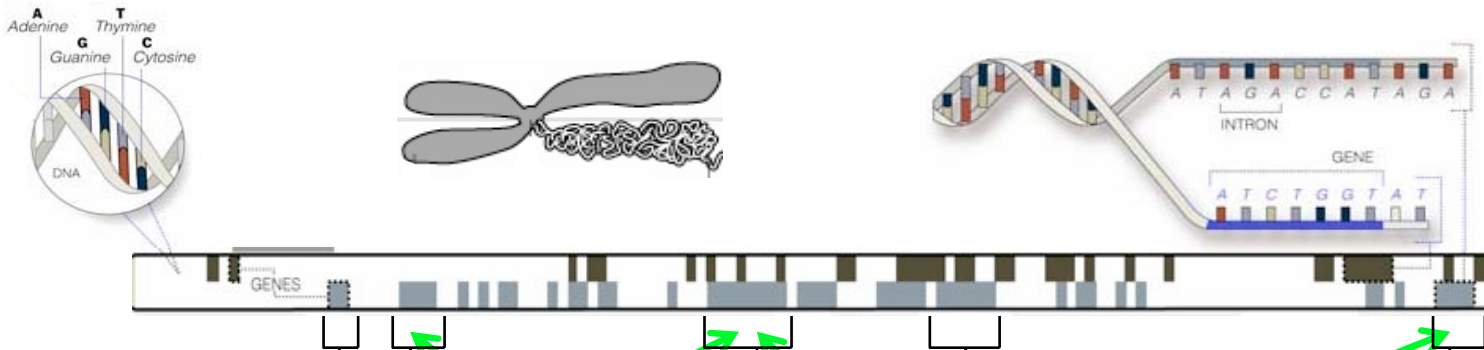
**Found**

R. Albert, H. Jeong, A-L Barabasi, *Nature*, **401** 130 (1999).







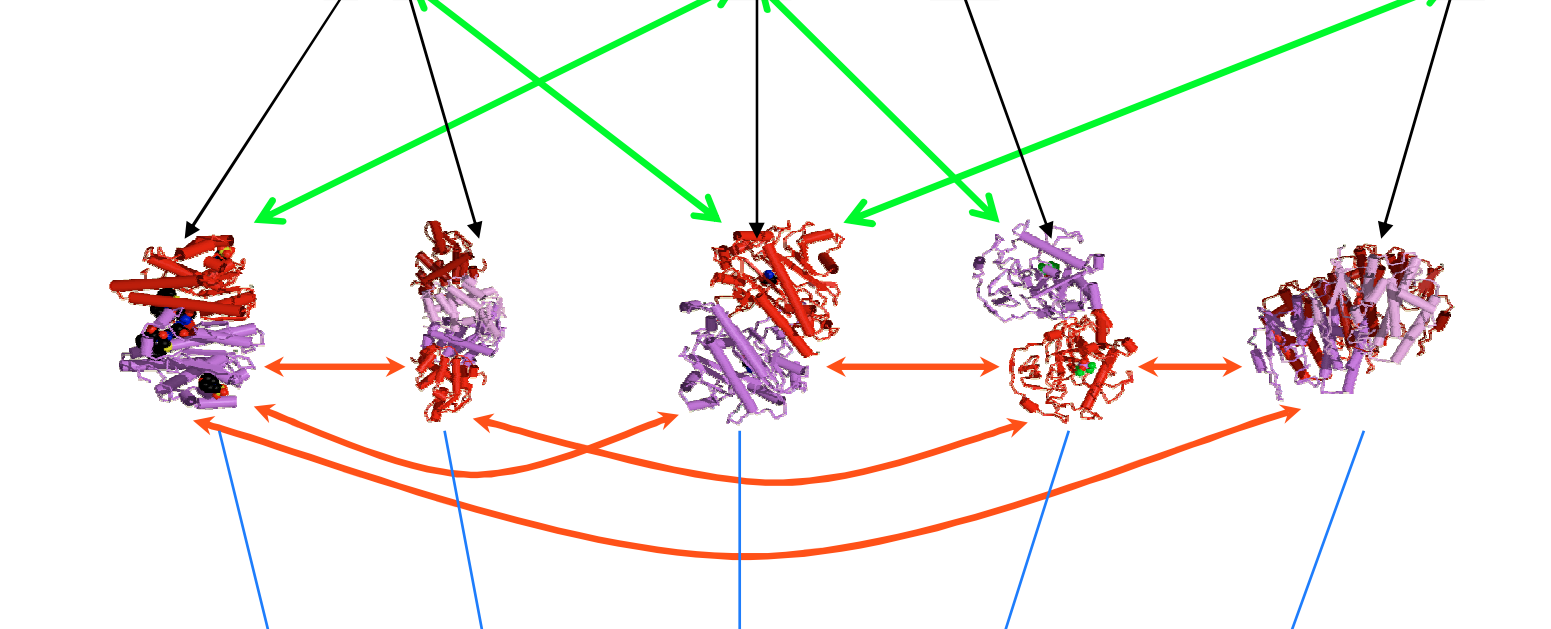


# GENOME

protein-gene interactions

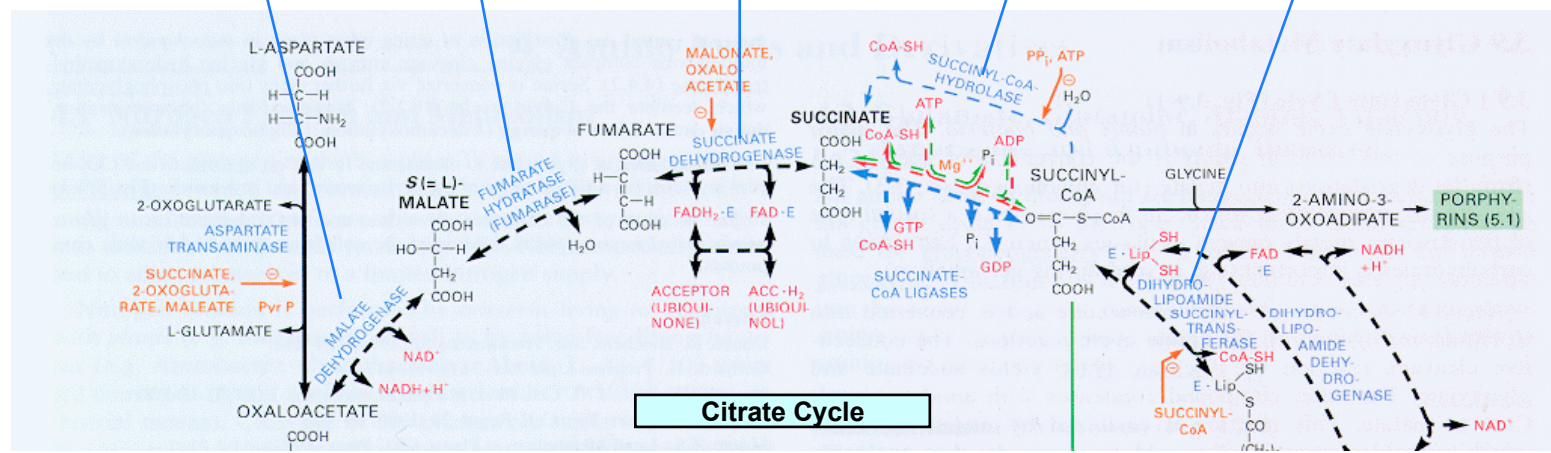
# PROTEOME

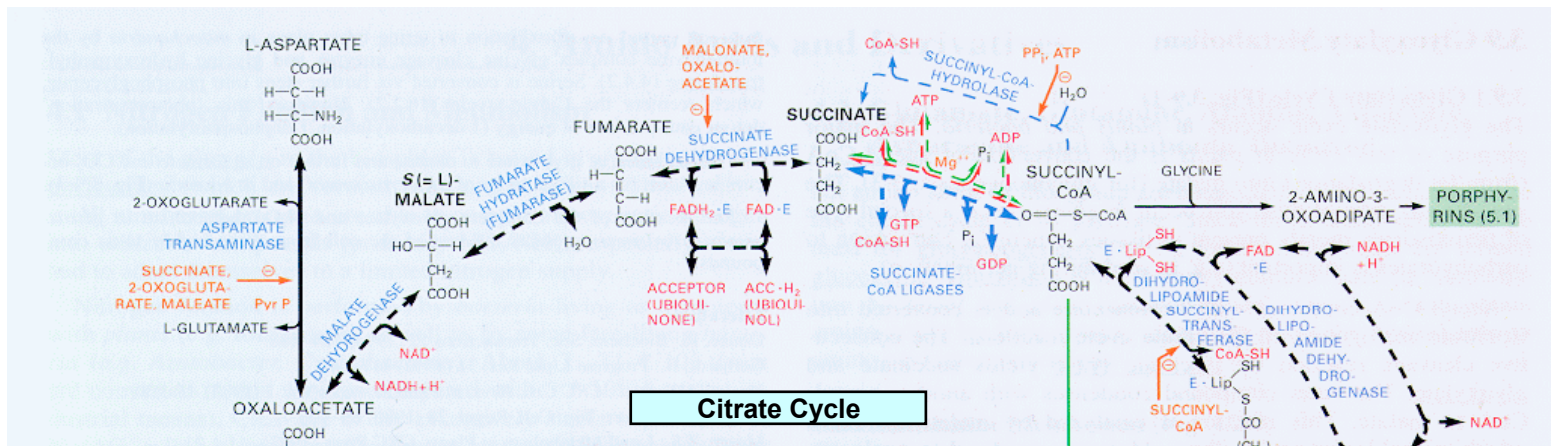
protein-protein interactions



# METABOLISM

Bio-chemical reactions





# METABOLISM

## Bio-chemical reactions



# Biochemical Pathways

1

2

3

4

5

6

7

8

9

10

A

B

C

D

E

F

G

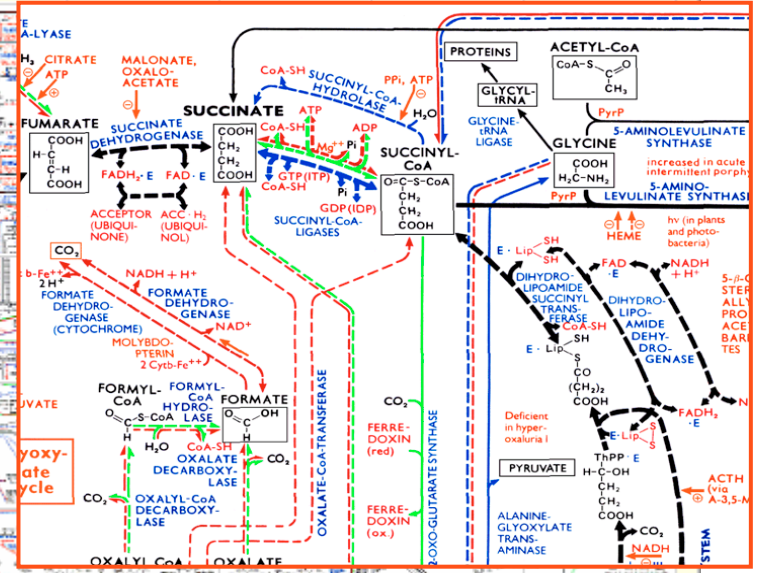
H

I

J

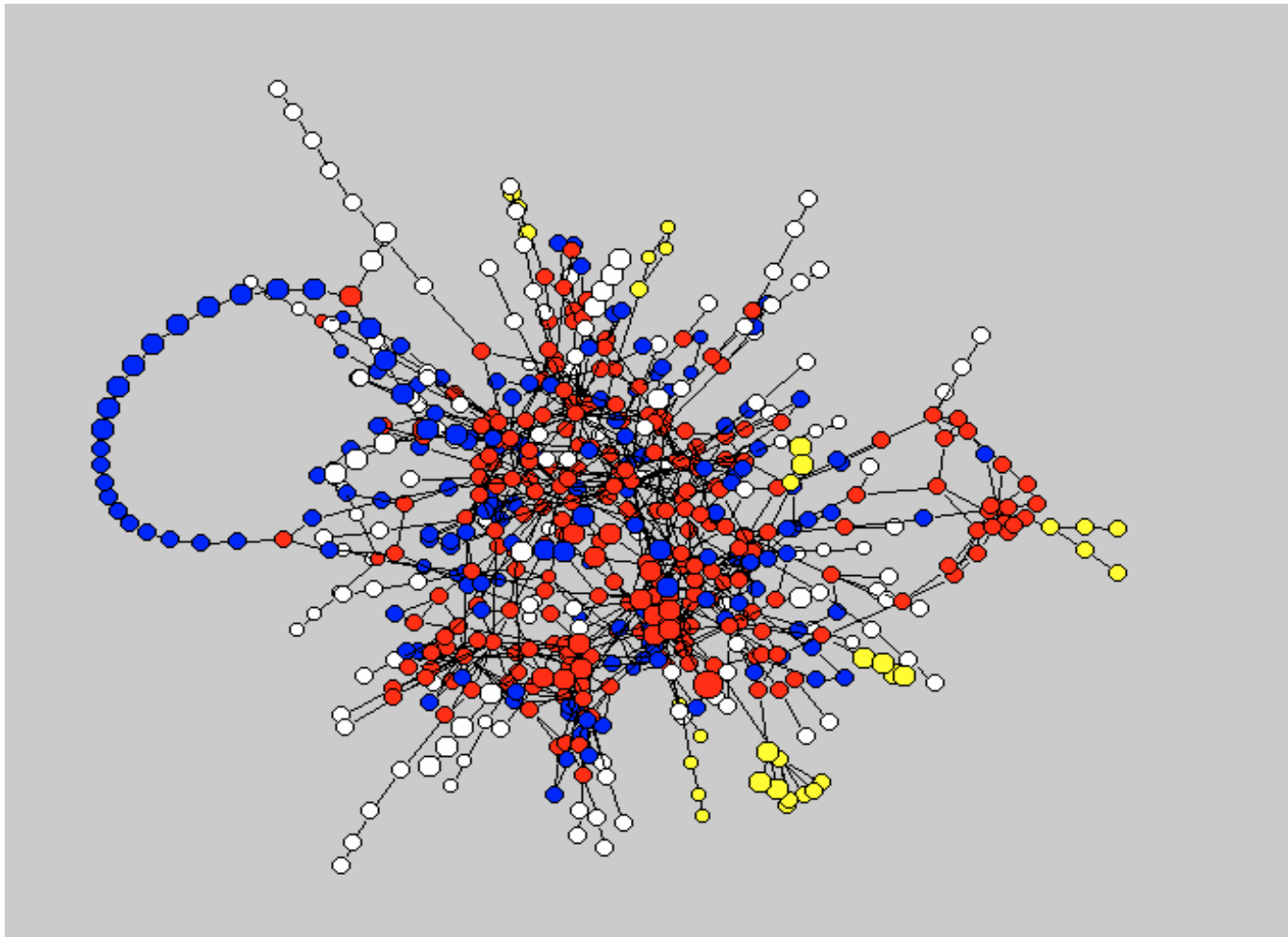
K

L

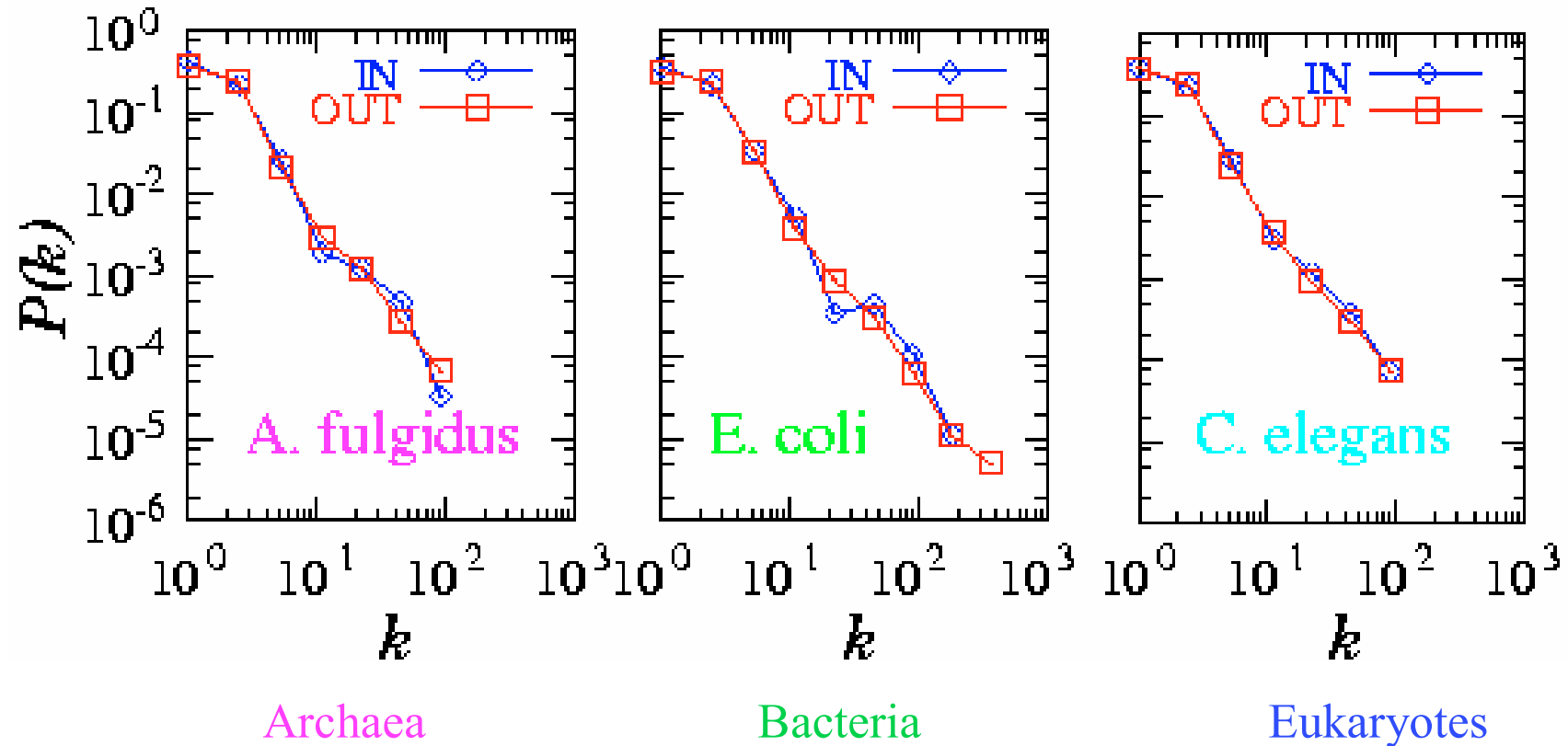


# Metabolic Network

Nodes: chemicals (substrates)  
Links: bio-chemical reactions

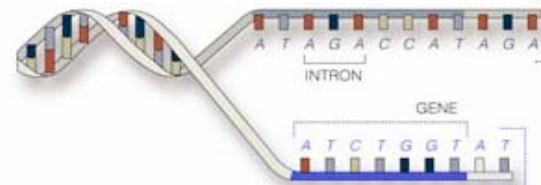
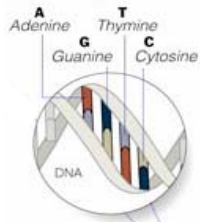


# Metabolic network



Organisms from all three domains of life have a scale-free topology!





# Bio-Map

## GENOME

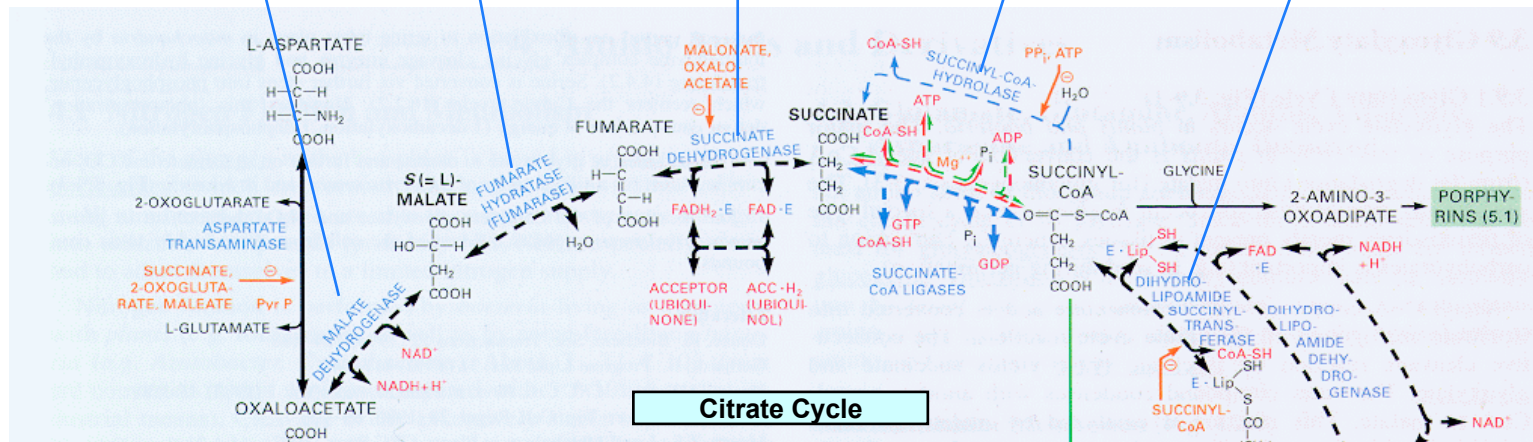
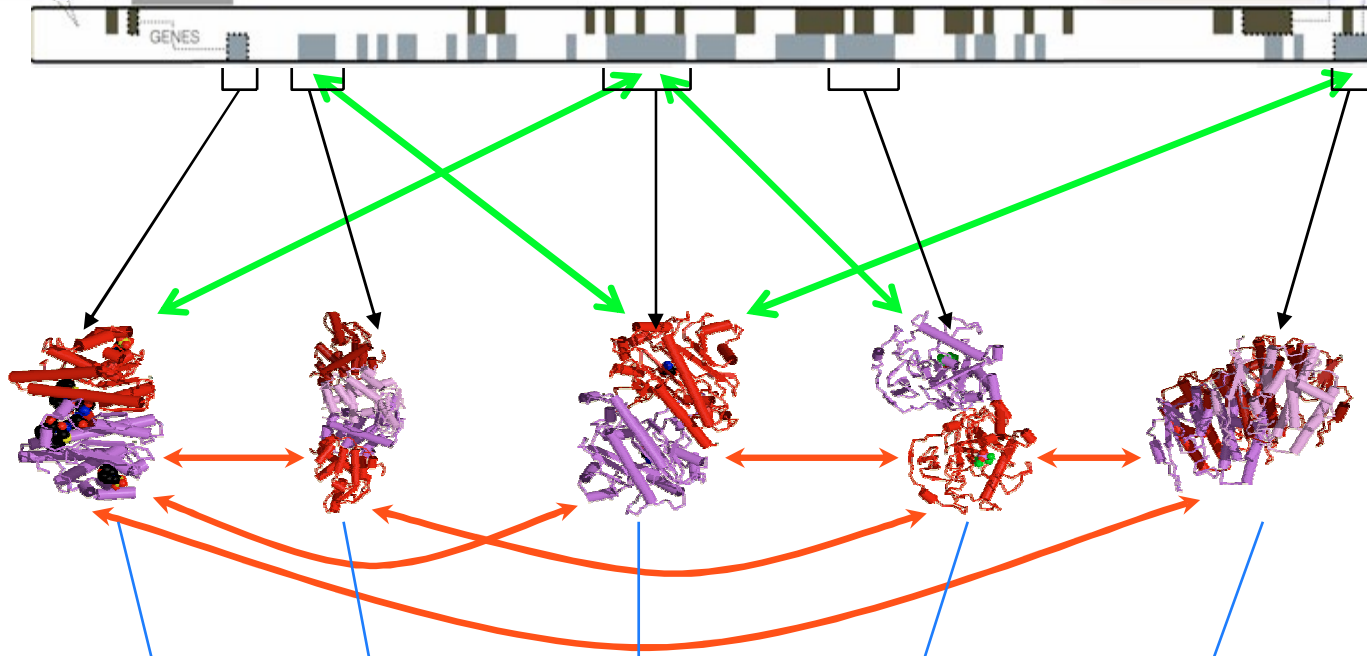
protein-gene interactions

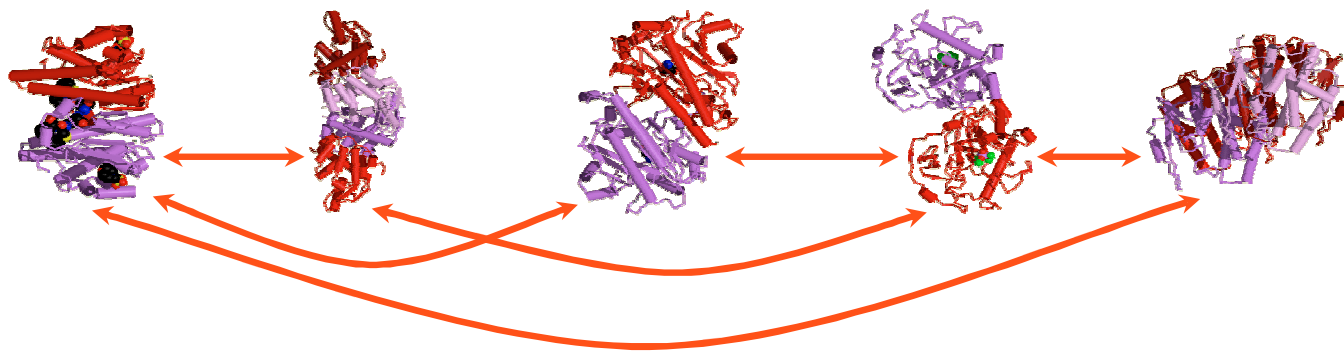
## PROTEOME

protein-protein interactions

## METABOLISM

Bio-chemical reactions



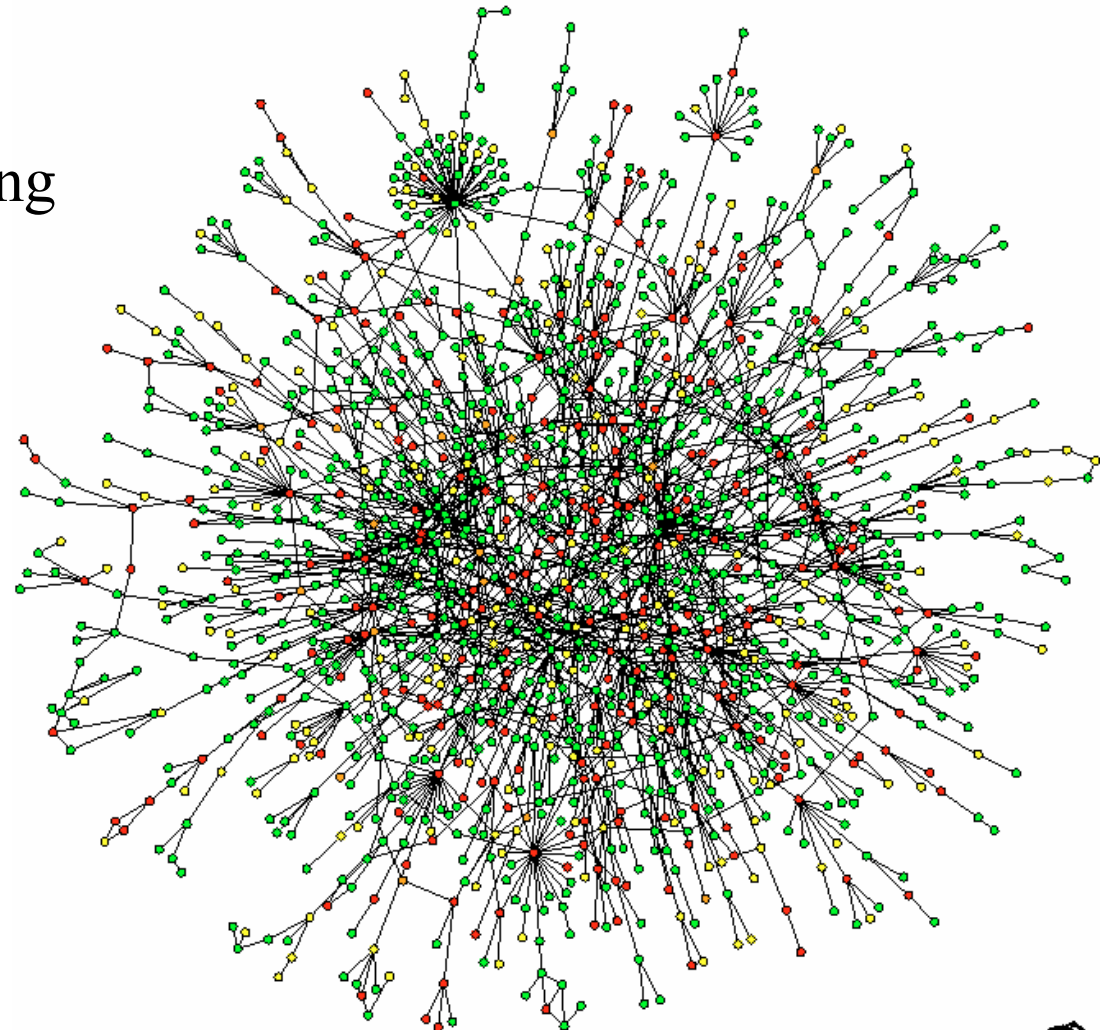
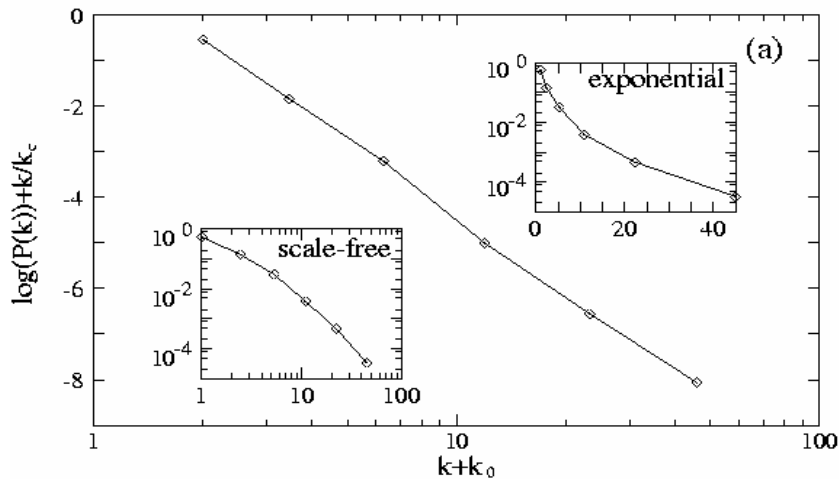


**PROTEOME**  
**protein-protein**  
**interactions**

# Topology of the protein network

Nodes: proteins

Links: physical interactions-binding



$$P(k) \sim (k + k_0)^{-\gamma} \exp\left(-\frac{k + k_0}{k_\tau}\right)$$

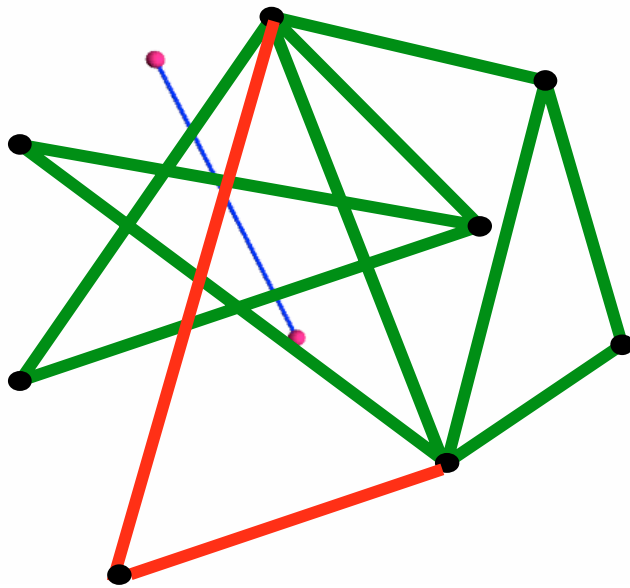
# Origin of SF networks: Growth and preferential attachment

(1) Networks continuously expand by the addition of new nodes

WWW : addition of new documents

(2) New nodes prefer to link to highly connected nodes.

WWW : linking to well known sites



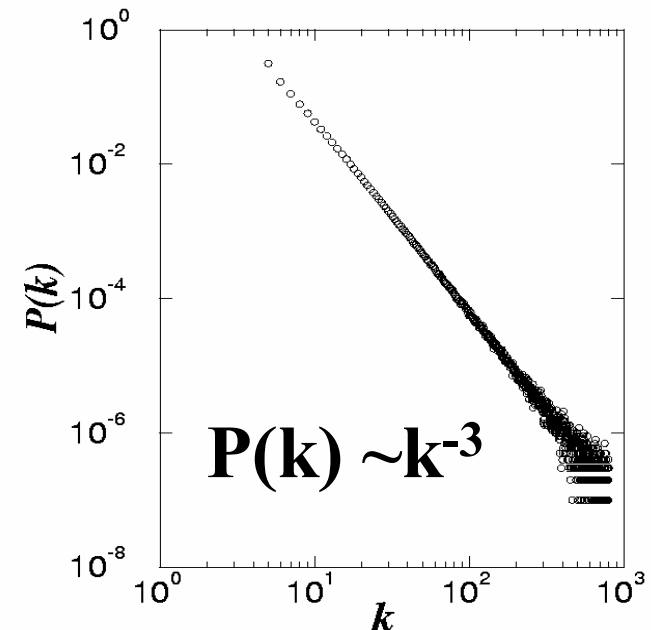
Barabási & Albert, *Science* **286**, 509 (1999)

**GROWTH:**

add a new node with  $m$  links

**PREFERENTIAL ATTACHMENT:** the probability that a node connects to a node with  $k$  links is proportional to  $k$ .

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



# Can Latecomers Make It? Fitness Model

SF model:  $k(t) \sim t^{1/2}$   $\longrightarrow$  (first mover advantage)

Real systems: nodes compete for links -- *fitness*

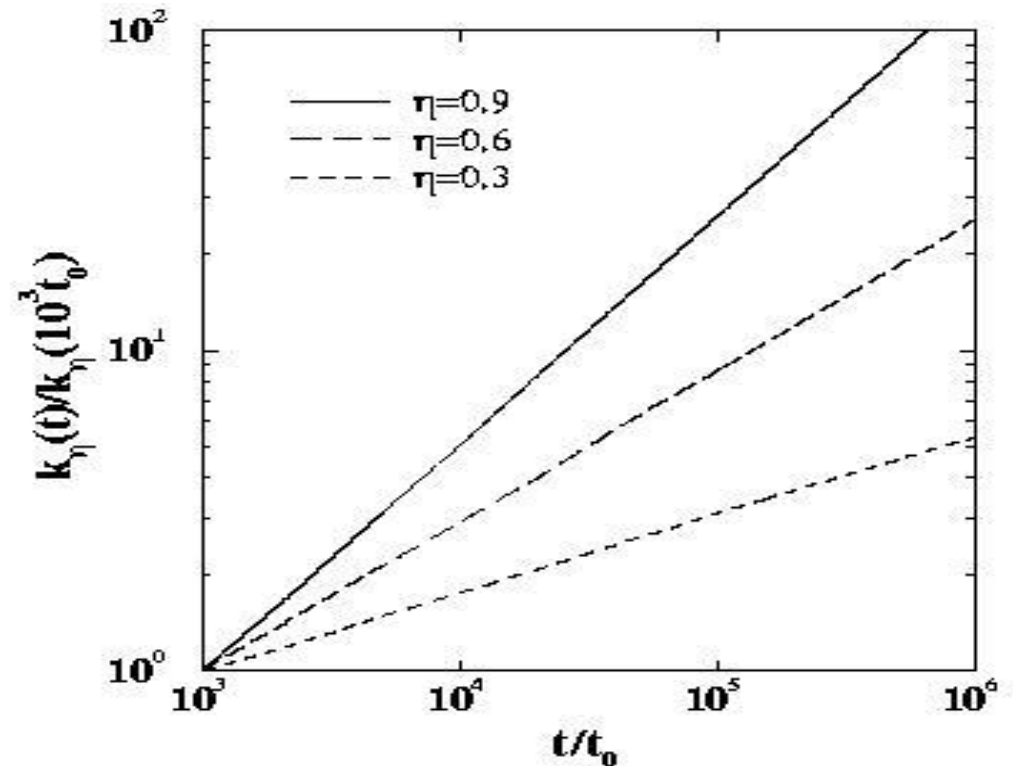
Fitness Model: fitness ( $\eta$ )

$$\Pi(k_i) \cong \frac{\eta_i k_i}{\sum_j \eta_j k_j}$$

$$k(\eta, t) \sim t^{\beta(\eta)}$$

where

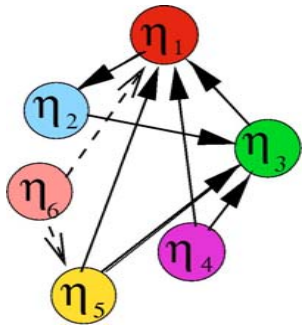
$$\beta(\eta) = \eta/C \quad \int d\eta \rho(\eta) \frac{1}{C/\eta - 1} = 1$$





# Bose-Einstein Condensation in Evolving Networks

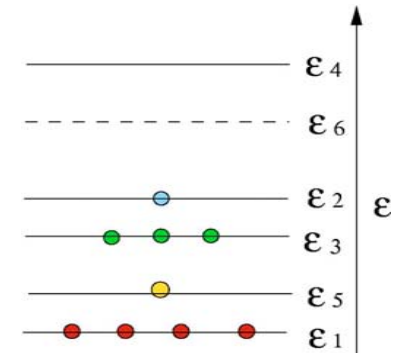
Network



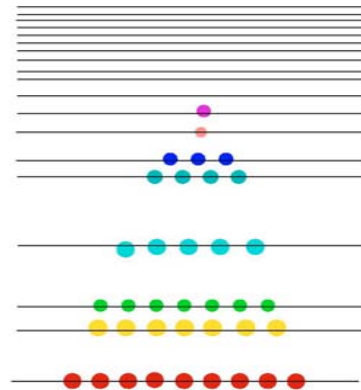
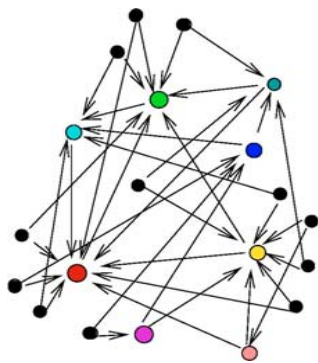
$$\Pi_i = \frac{\eta_i k_i}{\sum_j \eta_j k_j}$$

$$\begin{aligned} \eta &\longrightarrow e^{-\beta\varepsilon} \\ k_{in}(\eta) &\longrightarrow n(\varepsilon) = \frac{1}{e^{-\beta\varepsilon} - 1} \\ \rho(\eta) &\longrightarrow g(\varepsilon) \end{aligned}$$

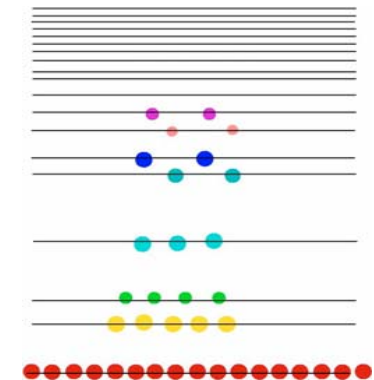
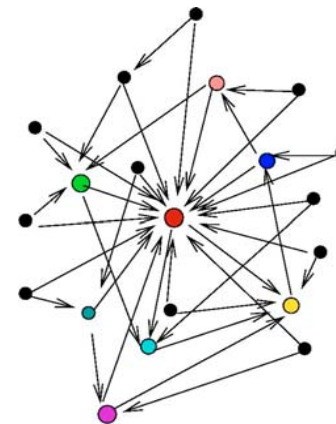
Bose gas



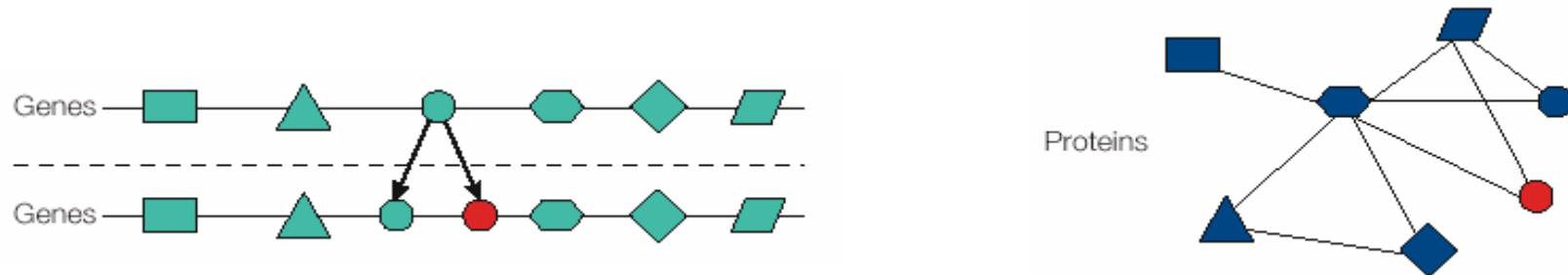
Fit-gets-rich



Bose-Einstein condensation



# Origin of the scale-free topology in the cell: Gene Duplication



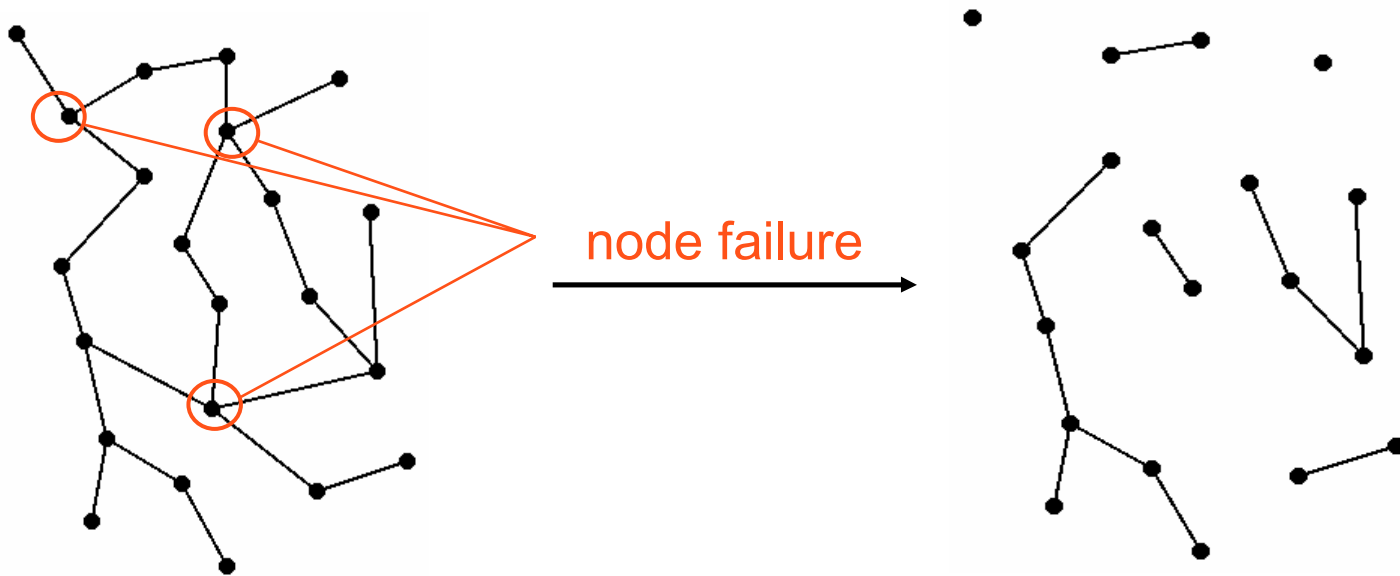
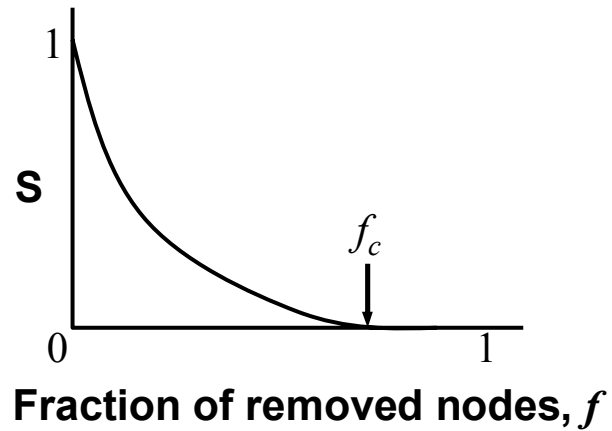
**Proteins with more interactions are more likely to obtain new links:**

$$\Pi(k) \sim k \quad (\text{preferential attachment})$$

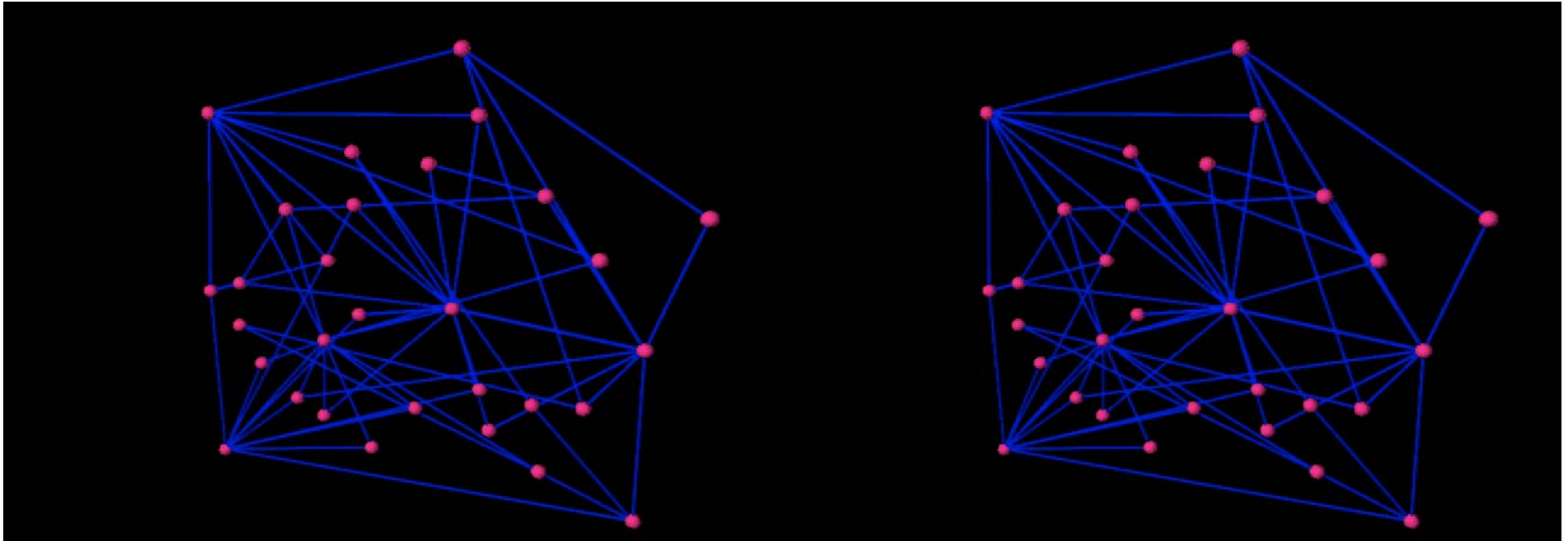
Wagner 2001; Vazquez *et al.* 2003; Sole *et al.* 2001; Rzhetsky & Gomez 2001;  
Qian *et al.* 2001; Bhan *et al.* 2002.

# Robustness

Complex systems maintain their basic functions even under errors and failures  
(cell  $\rightarrow$  mutations; Internet  $\rightarrow$  router breakdowns)

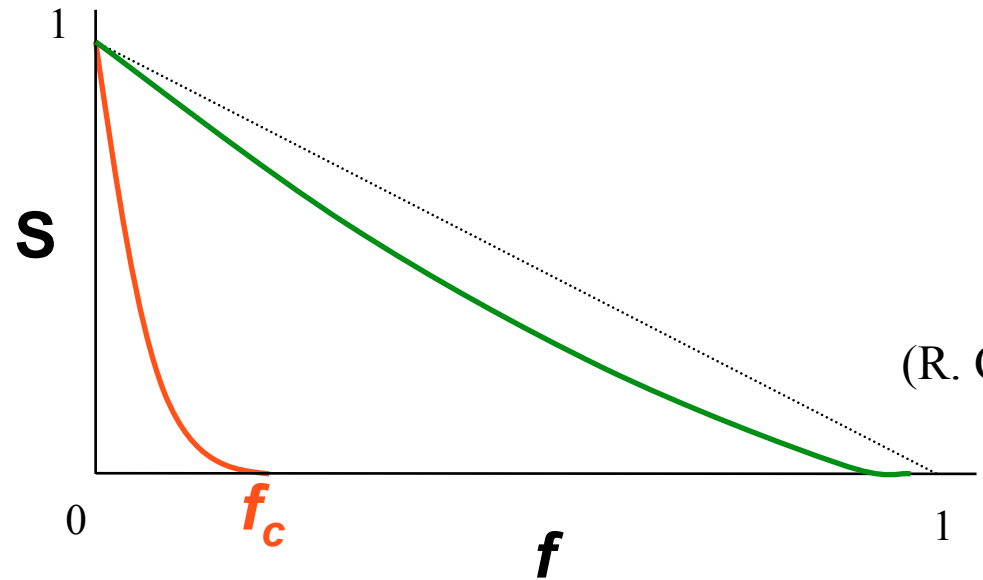


# Robustness of scale-free networks



Attacks

Failures



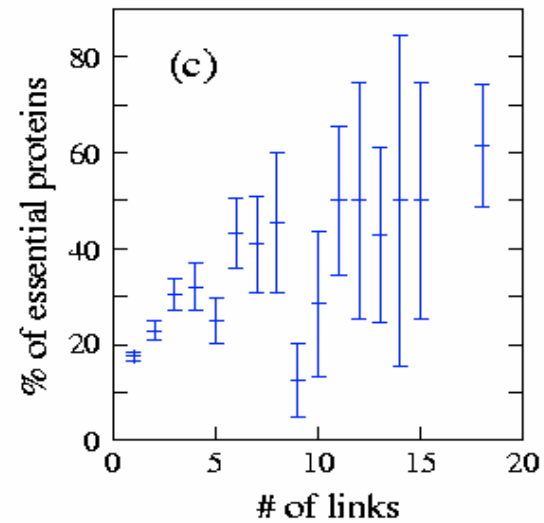
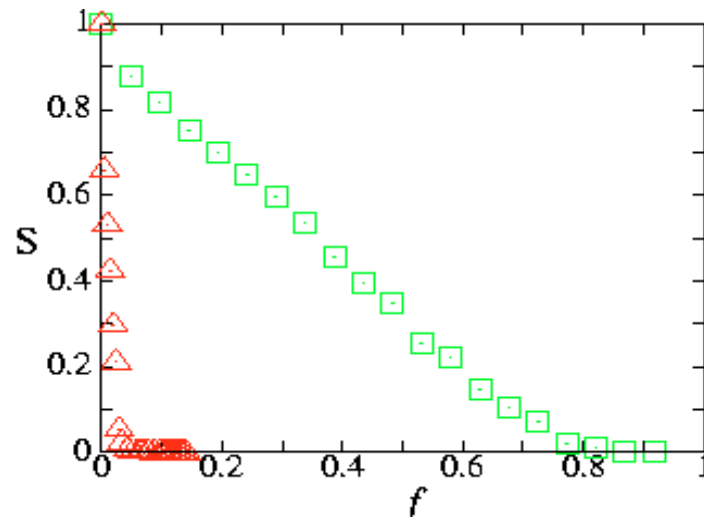
$$\gamma \leq 3 : f_c = 1$$

(R. Cohen et al PRL, 2000)

Albert, Jeong, Barabasi, *Nature* **406** 378 (2000); H

# Yeast protein network

## - lethality and topological position -



Highly connected proteins are more **essential (lethal)**...

H. Jeong, S.P. Mason, A.-L. Barabasi, Z.N. Oltvai, Nature 411, 41-42 (2001)



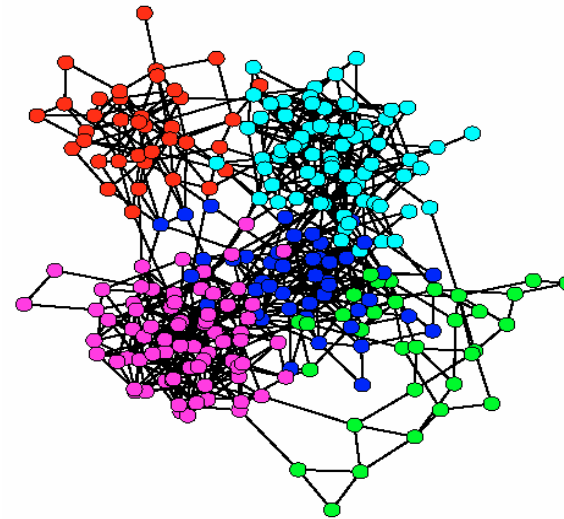
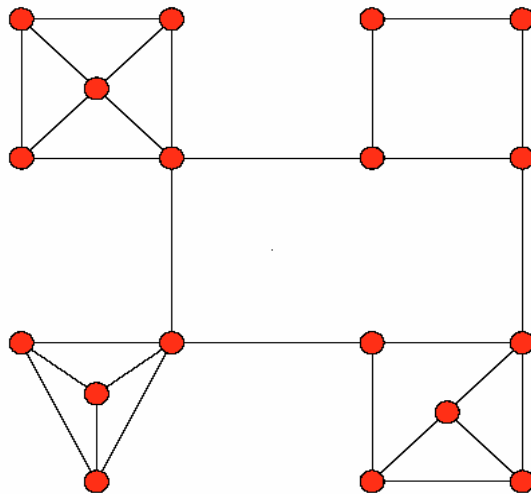
# Modularity in Cellular Networks

## ➤ Hypothesis:

Biological functions are carried by discrete functional modules.

❖ Hartwell, L.-H., Hopfield, J. J., Leibler, S., & Murray, A. W. (1999).

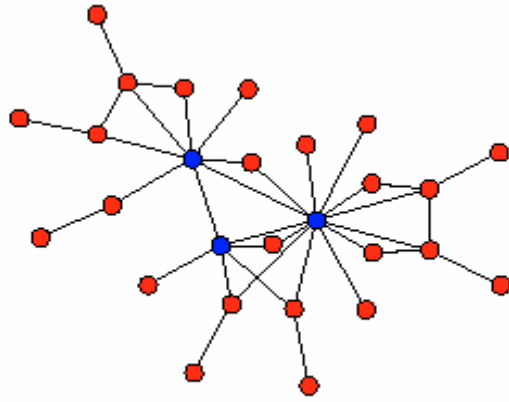
## ➤ Traditional view of modularity:



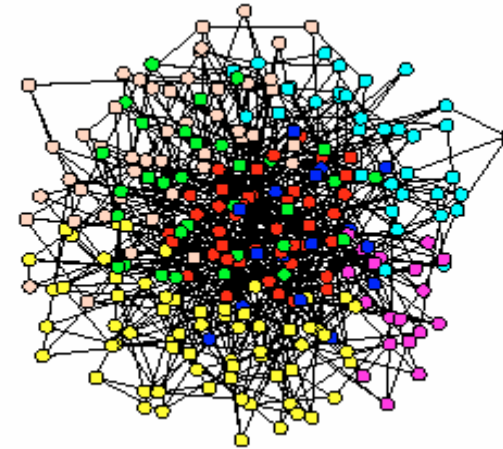
➤ Question: Is modularity a myth, or a structural property of biological networks?  
(are biological networks fundamentally modular?)

# Modular vs. Scale-free Topology

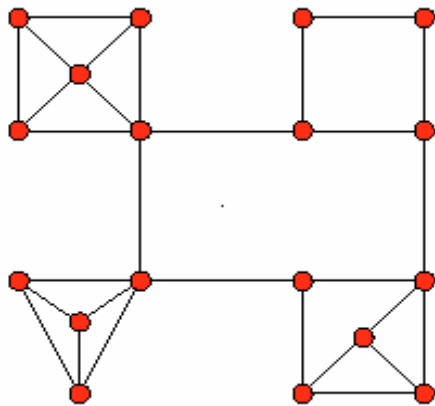
(a)



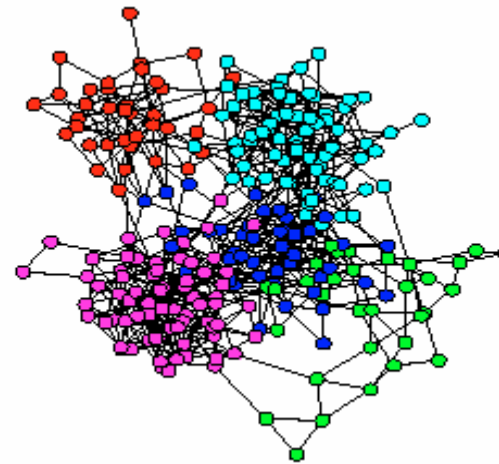
Scale-free



(b)



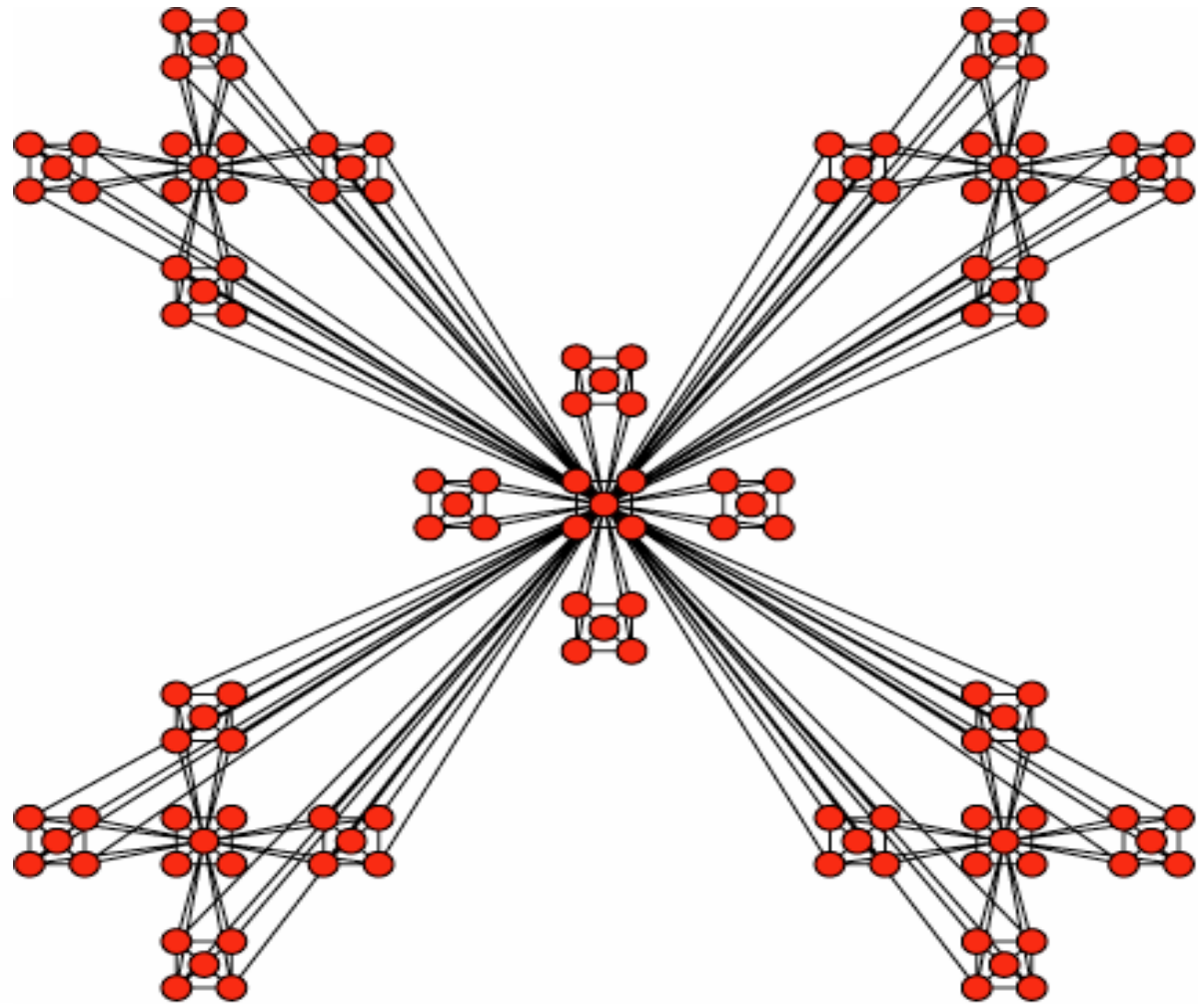
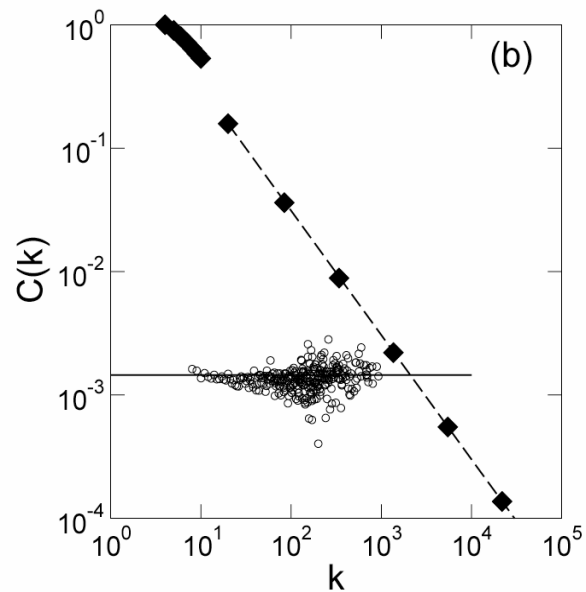
Modular



# Hierarchical Networks

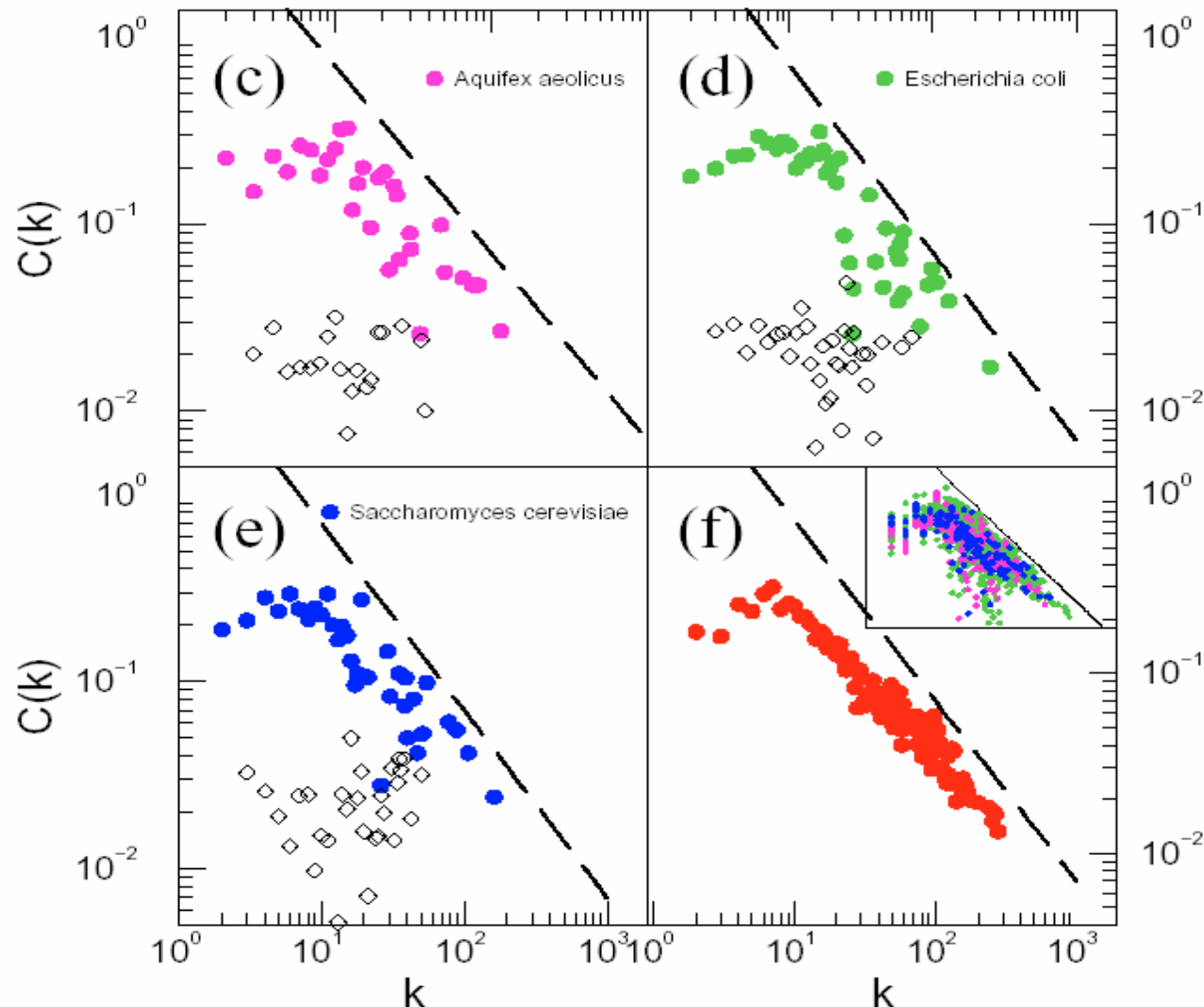
## 3. Clustering coefficient scales

$$C(k) \sim k^{-1}$$



$C(k) = \frac{\text{\# links between } k \text{ neighbors}}{k(k-1)/2}$

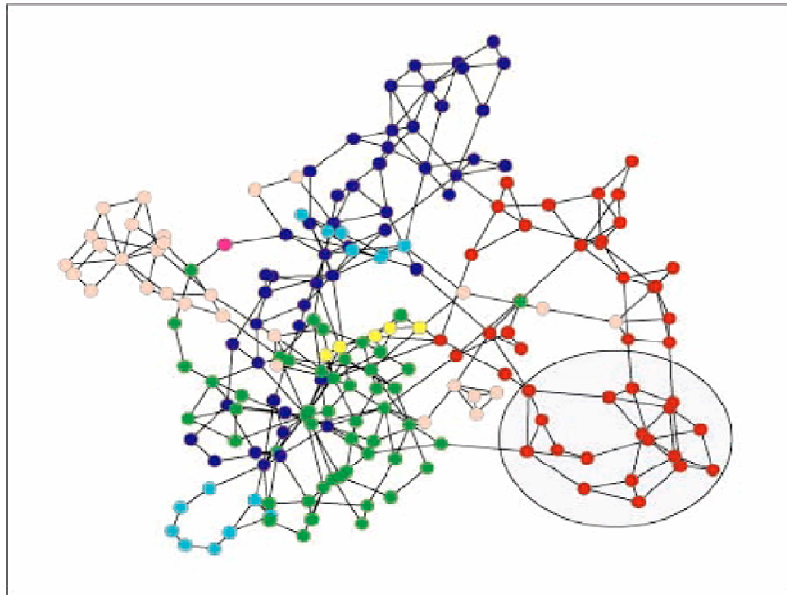
## Scaling of the clustering coefficient $C(k)$



**The metabolism forms a hierarchical network.**

Ravasz, Somera, Mongru, Oltvai, A-L. B, *Science* **297**, 1551 (2002).

# Characterizing the links



**Metabolism:**  
**Flux Balance Analysis (Palsson)**  
**Metabolic flux for each reaction**

*Balance Equations:*

A:  $-v_1 - b_1 = 0$

B:  $v_1 + v_4 - v_2 - v_3 = 0$

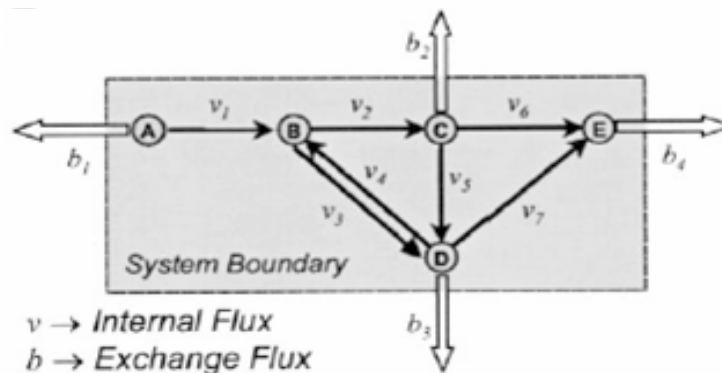
C:  $v_2 - v_5 - v_6 - b_2 = 0$

D:  $v_3 + v_5 - v_4 - v_7 - b_3 = 0$

E:  $v_6 + v_7 - b_4 = 0$

**Matrix Notation**

**$S \cdot v = 0$**

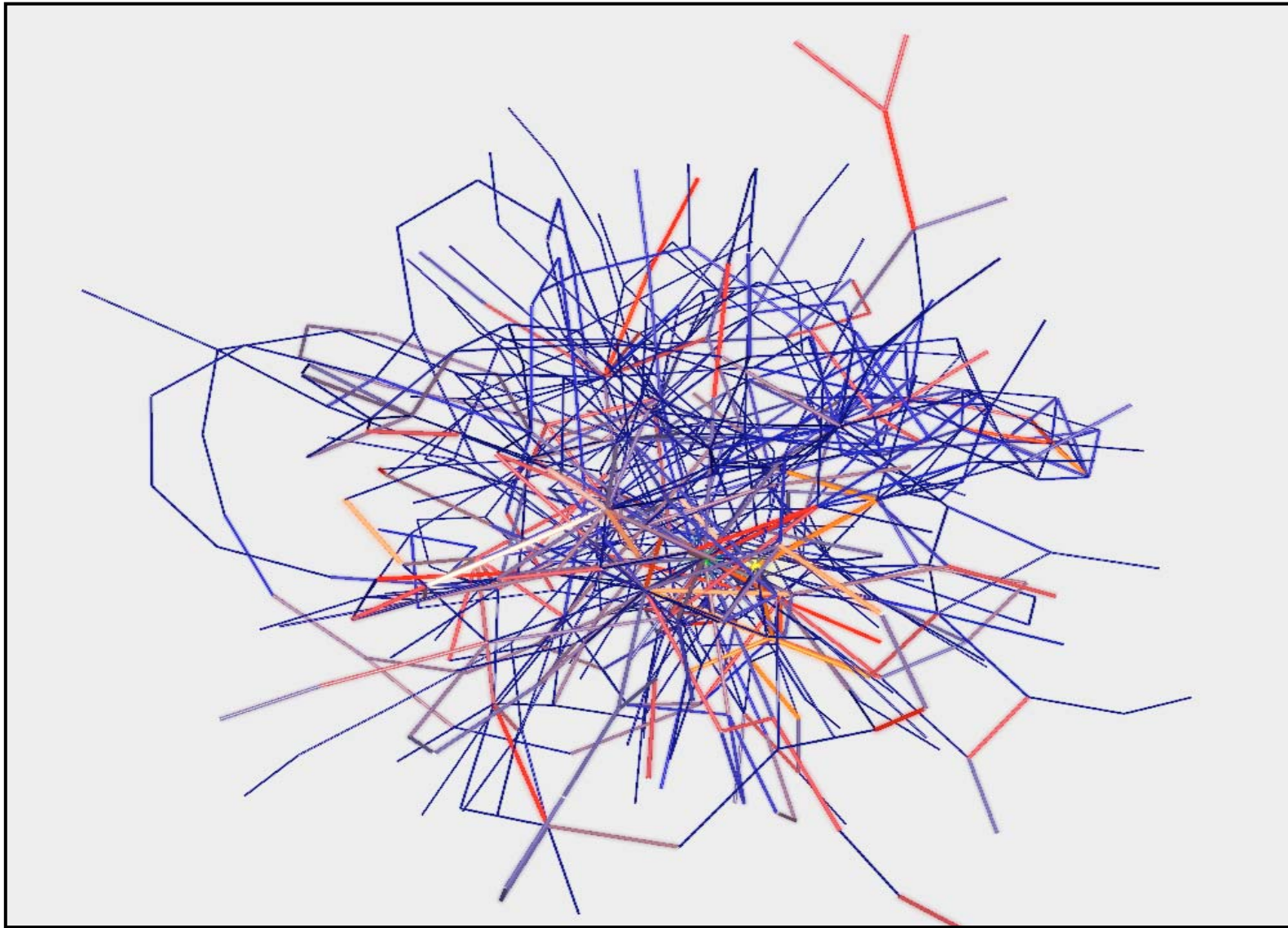


Edwards, J. S. & Palsson, B. O. *PNAS* **97**, 5528 (2000).

Edwards, J. S., Ibarra, R. U. & Palsson, B. O. *Nat Biotechnol* **19**, 125 (2001).

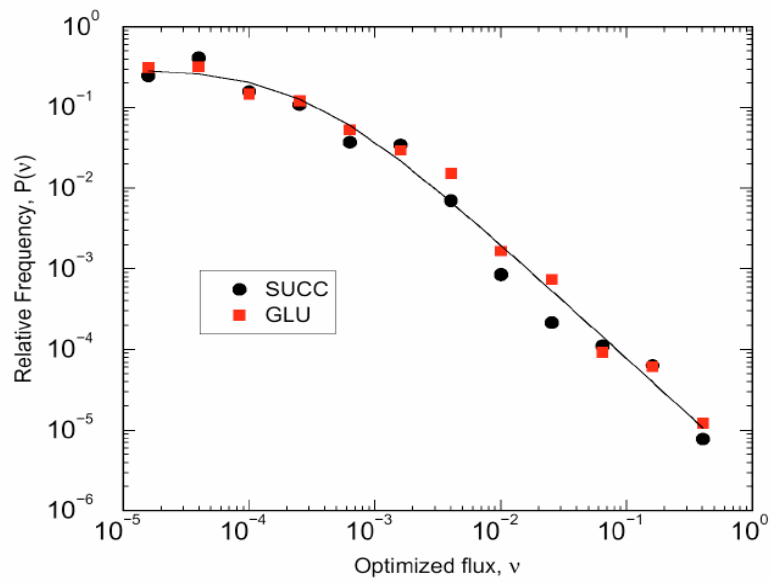
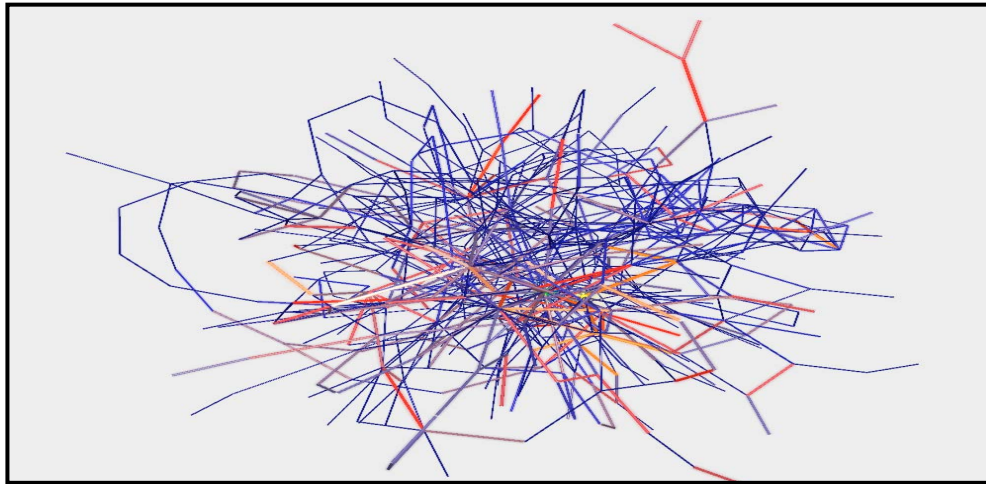
Ibarra, R. U., Edwards, J. S. & Palsson, B. O. *Nature* **420**, 186 (2002).

# Global flux organization in the *E. coli* metabolic network

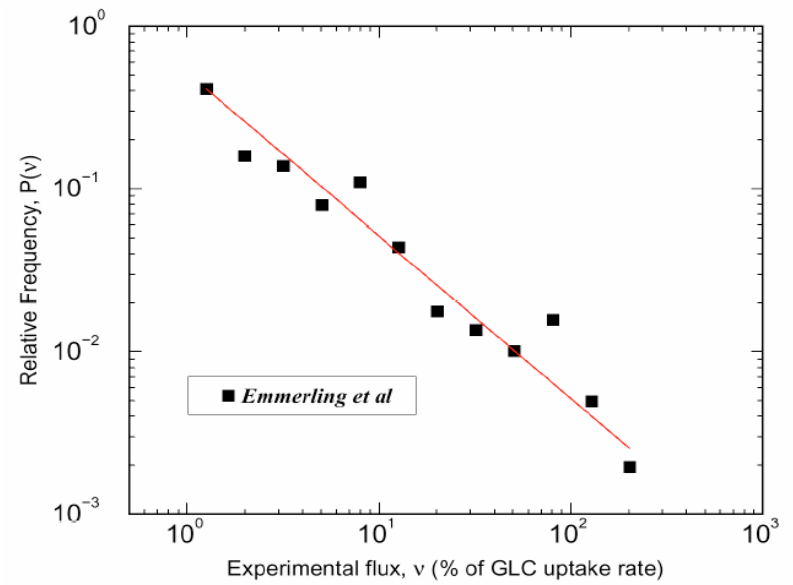


E. Almaas, B. Kovács, T. Vicsek, Z. N. Oltvai, A.-L. B. Nature, 2004.





**SUCC:** Succinate uptake  
**GLU :** Glutamate uptake

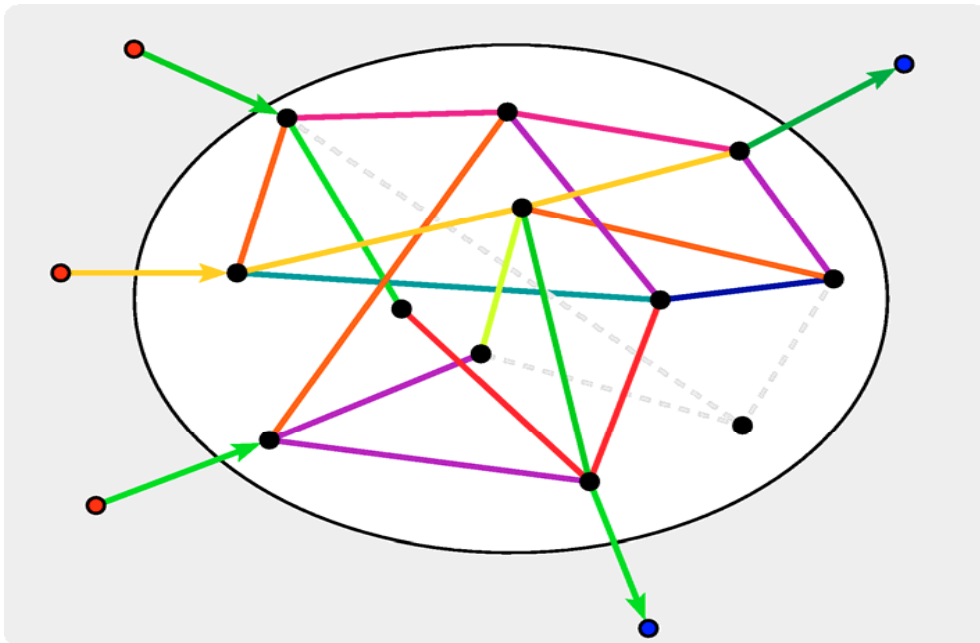


Central Metabolism,  
 Emmerling et. al, *J Bacteriol* **184**, 152 (2002)

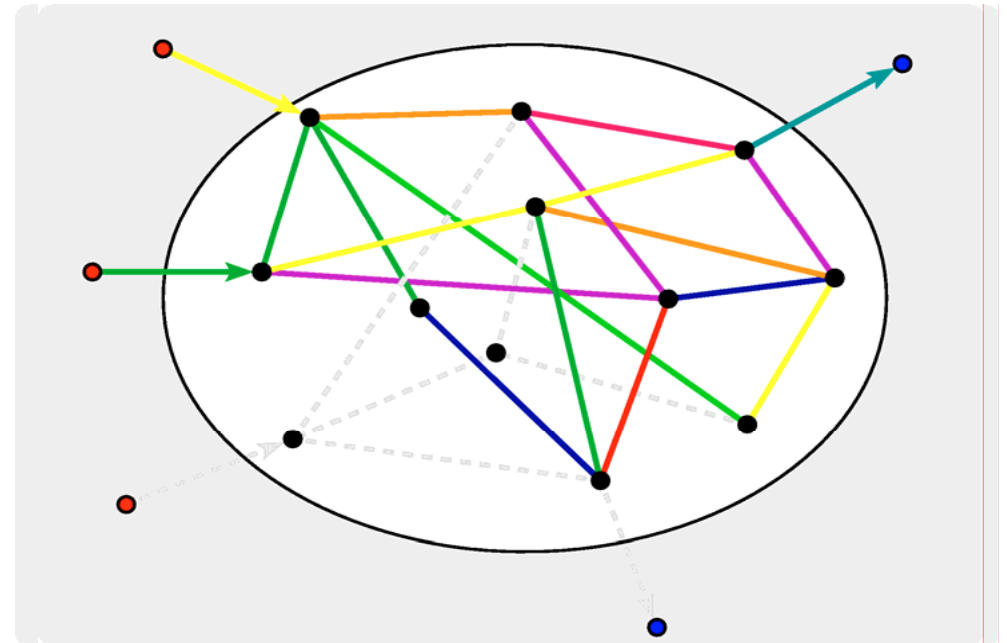
# Network Plasticity

How does the metabolic network adapt to environmental changes?

**Flux plasticity**  
(changes in flux rates)



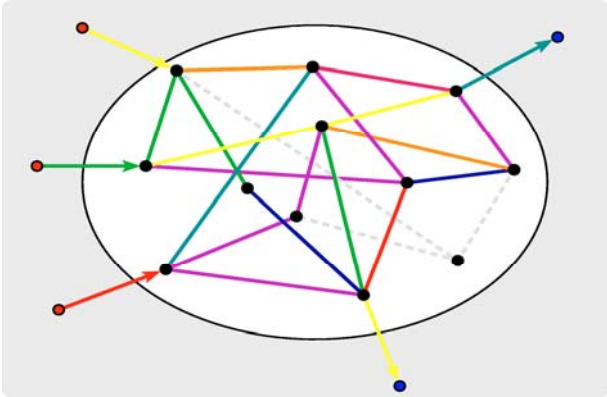
**Structural plasticity**  
(reaction [de-] activation)



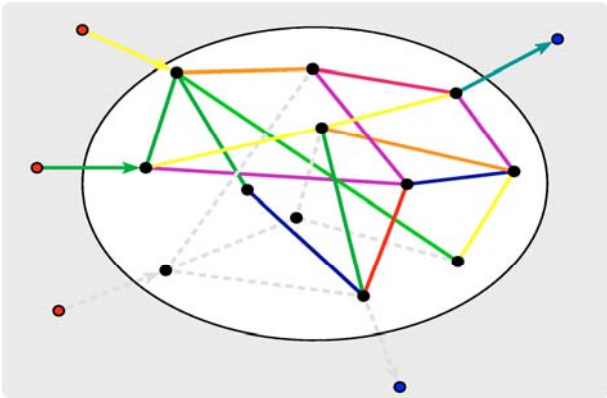


# The Metabolic Core

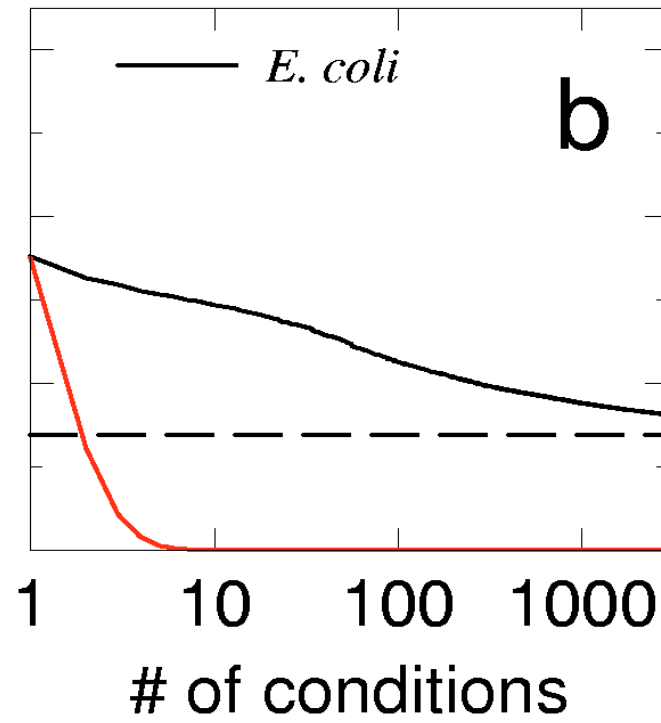
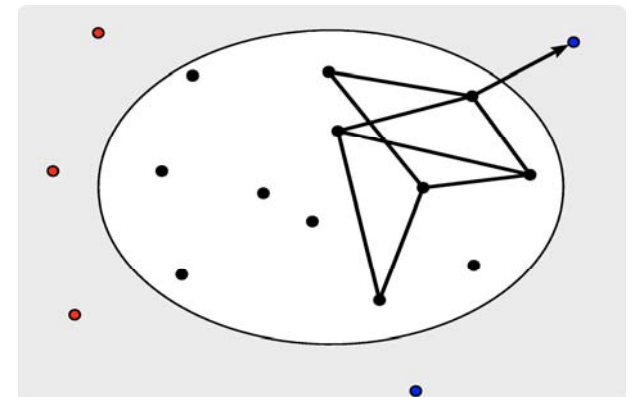
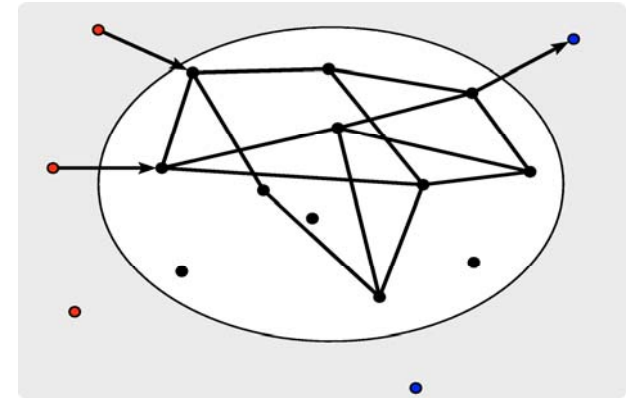
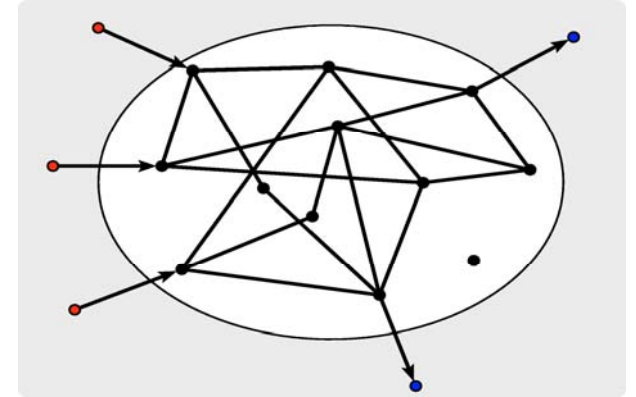
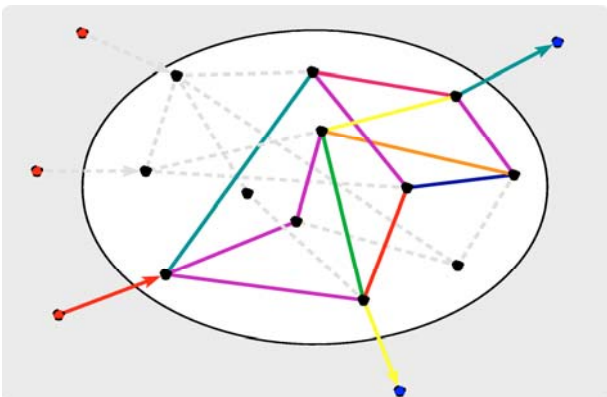
Condition 1



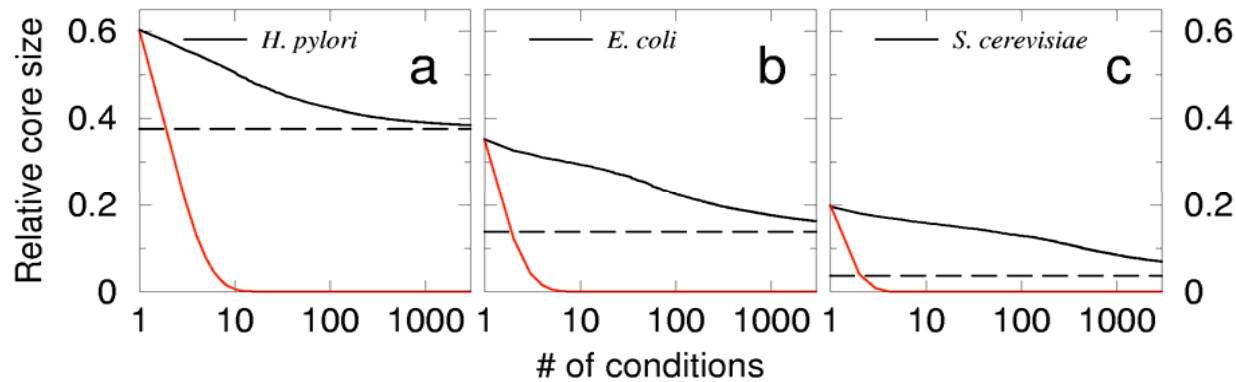
Condition 2



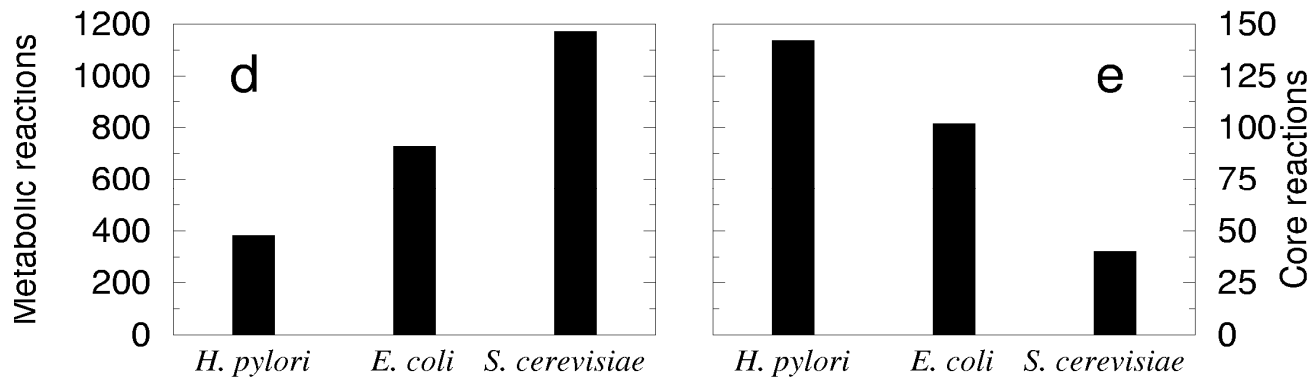
Condition 3



# The Metabolic Core



- A connected set of reactions that are **ALWAYS** active

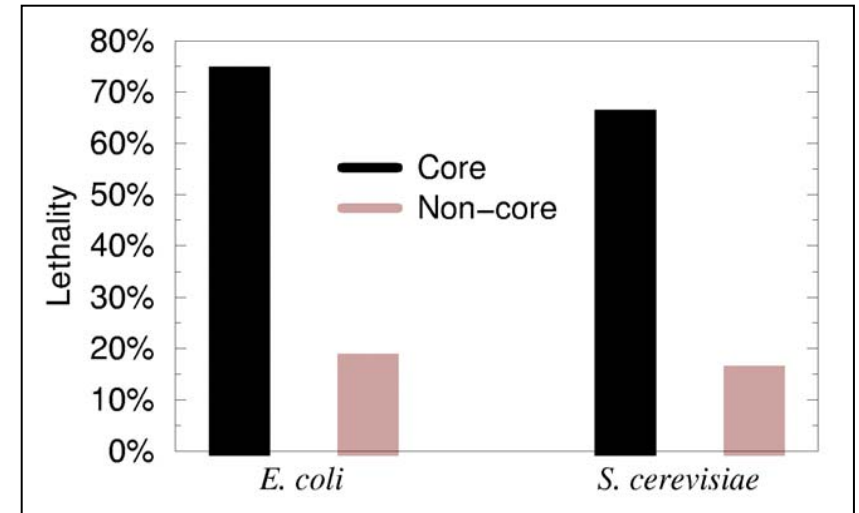


- The larger the network, the smaller the core  
→ a collective network effect

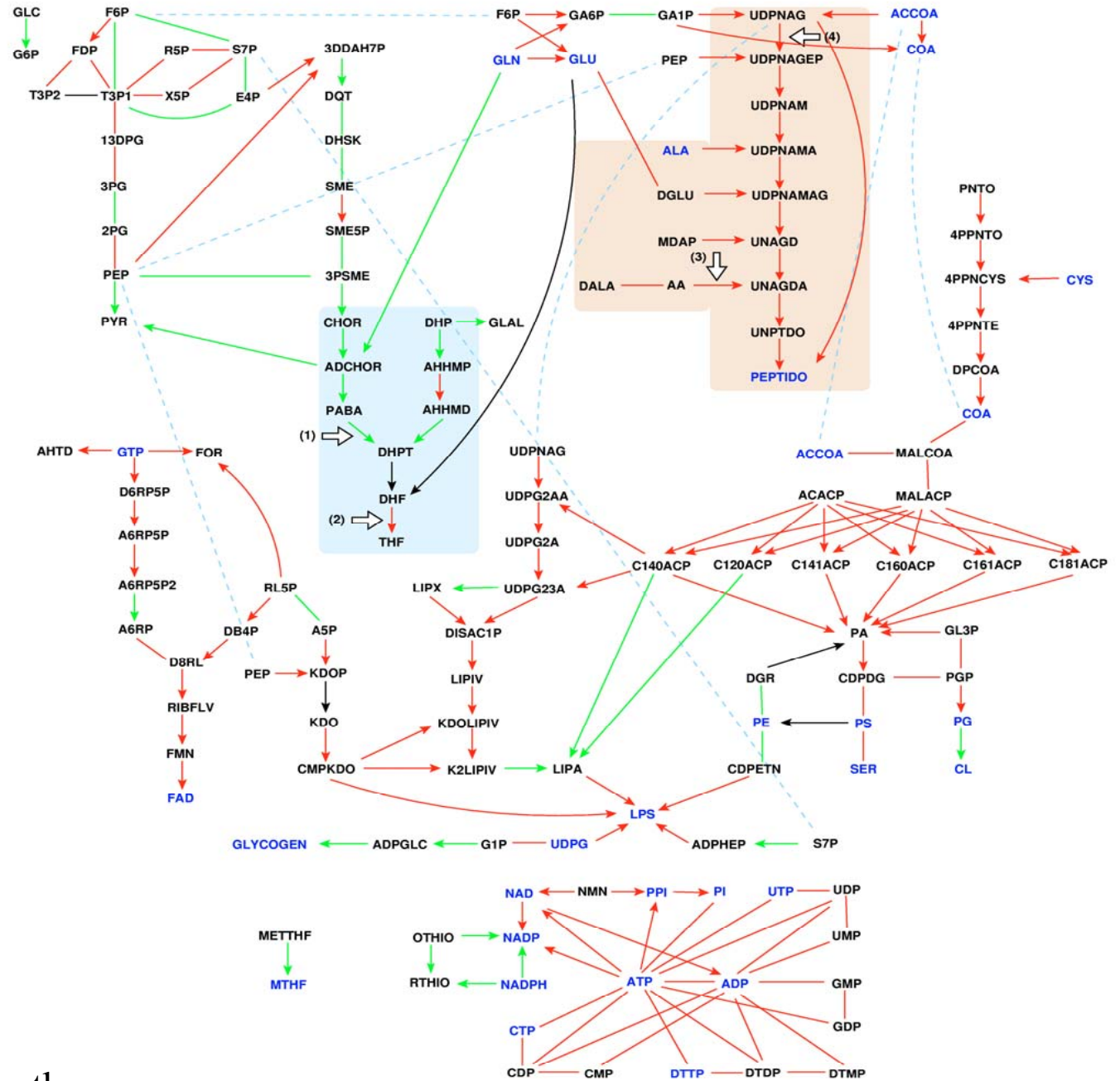
# Characterizing the core

## The core is highly essential:

- *E. coli*: **74%** lethal (18% in non-core)
- Yeast: **66%** lethal (16% non-core)
- The core is evolutionary conserved
- *E. coli* :  
**72%** of core enzymes (47% of non-core)



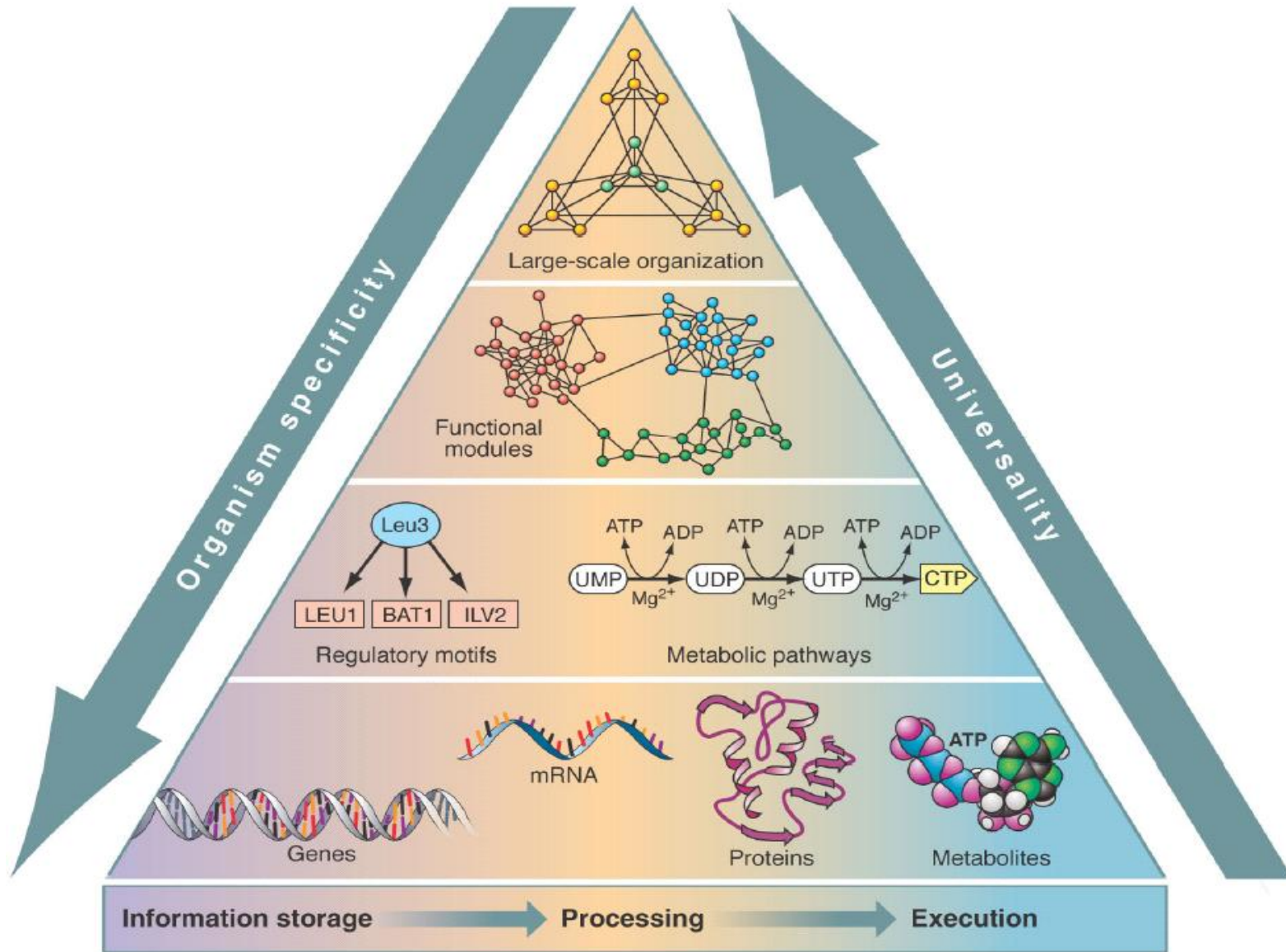
# Core: Antibiotic targets?



Blue: folate biosynthesis pathway

Brown: peptidoglycan biosynthesis pathway

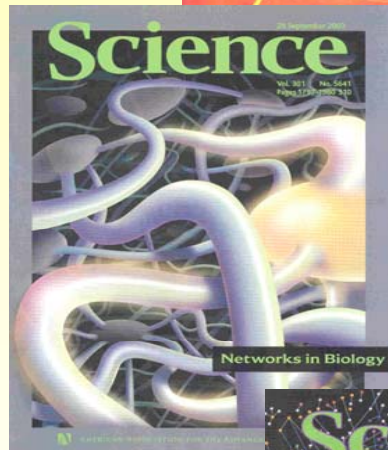
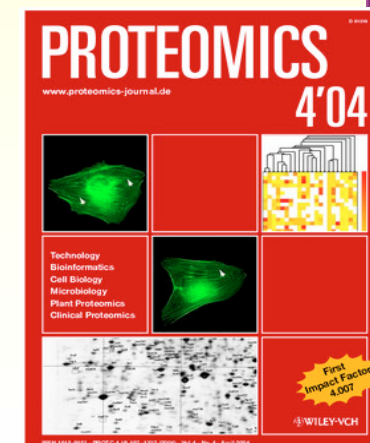
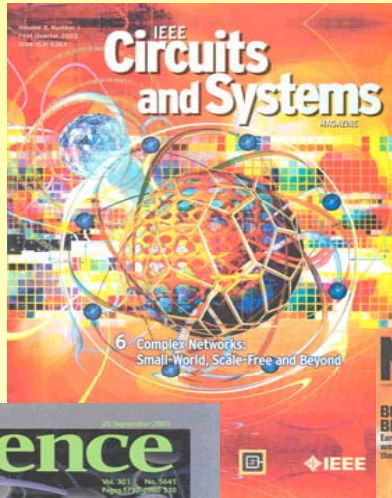
# Life's Complexity Pyramid



Z.N. Oltvai and A.-L. B. (2002).



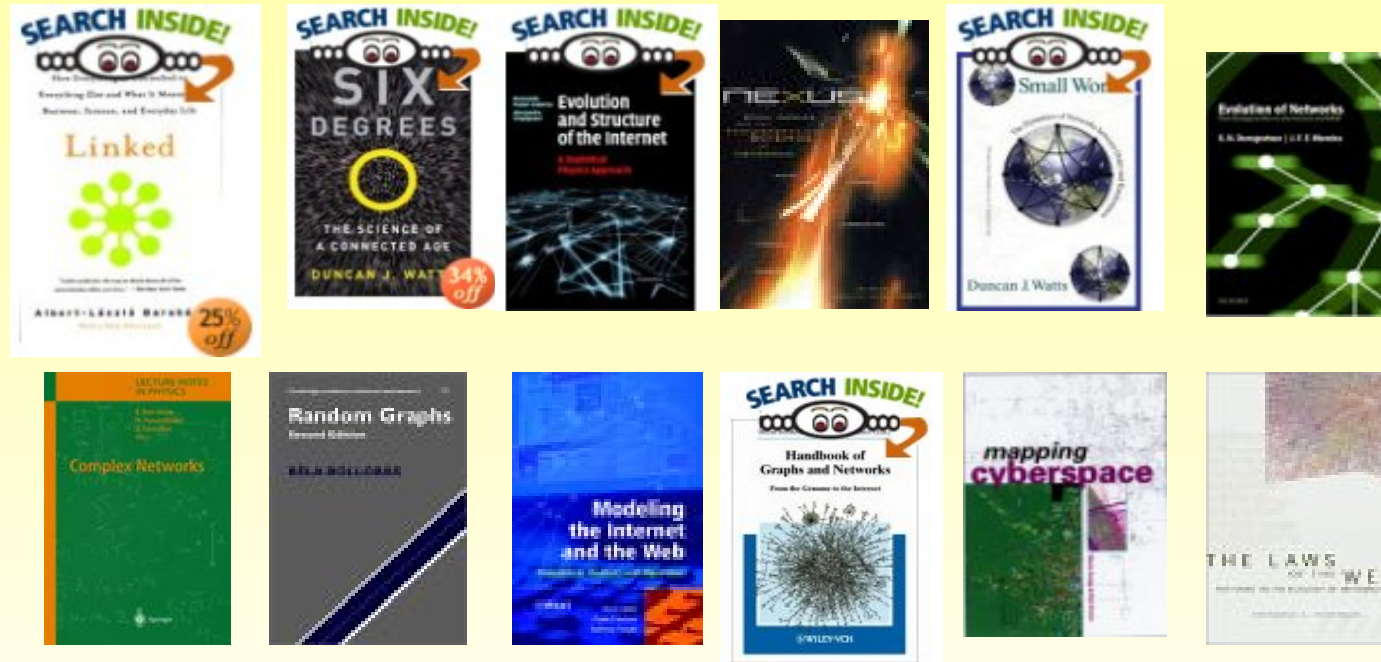
Albert-László Barabási  
Emil T. Hofman Professor of Physics  
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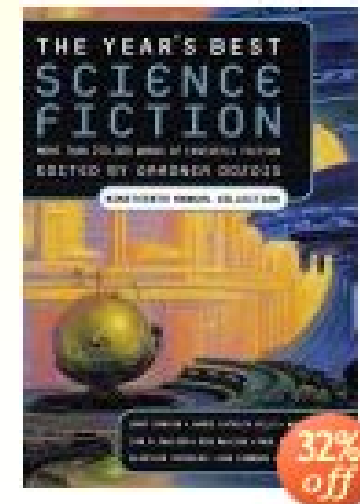
College of Science



→ Over  
20 Books:



→ Science Fiction  
and Visual Arts:





← Museum Exhibit



NRC Panel on “Network Science”

# THE NATIONAL ACADEMIES

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## NRC Panel on “Network Science”

### What is “network science”?

**An attempt to understand networks emerging in nature, technology and society using a unified set of tools and principles.**

### What is new here?

**A recognition that despite their individual differences, a wide range of networks emerge and evolve driven by a *fundamental set of laws and mechanism.***



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## NRC Panel on “Network Science”

### What is next?

#### Network Topology:

quite advanced—much to be learned still

#### Dynamics on networks:

Is there such a degree of universality as we see in the topology?

I hope so--- but still looking for the (...’s) laws here....



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**Réka Albert, Penn State**

**Ginestra Bianconi, Trieste**

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**<http://www.nd.edu/~networks>**

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