Systems Biology: A Personal View
III. Networks: Basic concepts

Sitabhra Sinha

IMSc Chennai

Ubiquity of Networks

Networks appear at all scales in biology

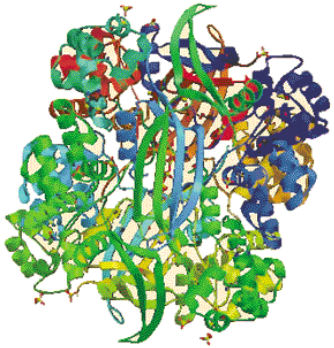
Proteins

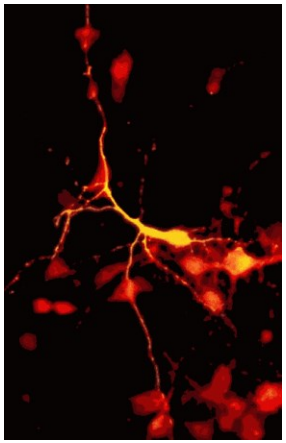
Intra-cellular signalling

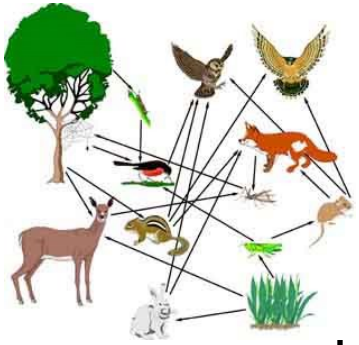
Neuronal communication

Epidemics

Food webs







10^{-9} m 10^{-6} m 10^{-3} m 1 m 10^{3} m 10^{6} m

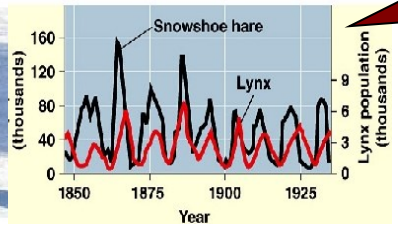
Molecules **Cells** **Organisms** **Populations** **Ecologies**

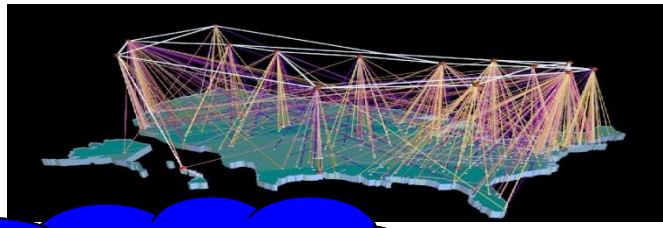
Nonlinear dynamics,
Game-theory strategies

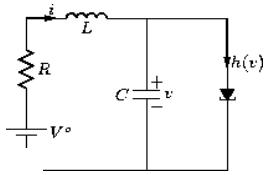
Synchronization,
Consensus,
Cooperation

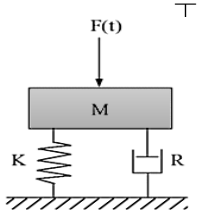
Nodal dynamics

Dynamics on Complex Networks









Complex Networks

Ordering,
Diffusion,
Contagion Spreading

Complexity of dynamics

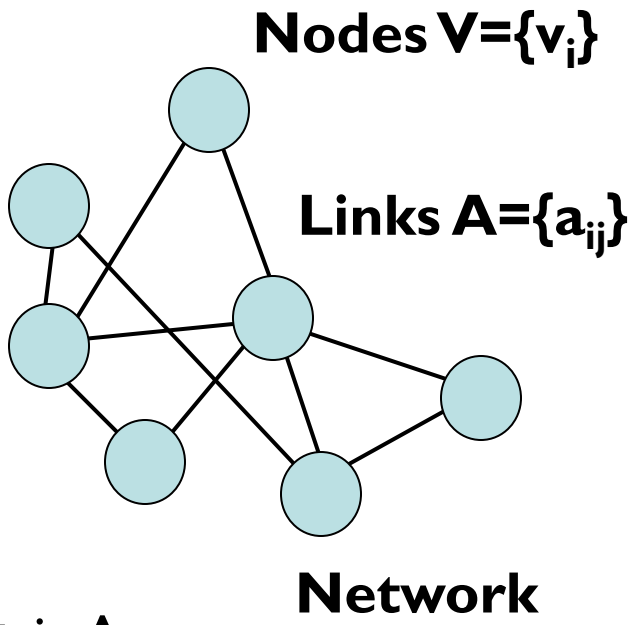
Complexity of interconnection

What is a network ?

Components = Nodes or Vertices

Interactions = Links or Edges

System = Network or Graph



Network structure is defined by *adjacency matrix* A

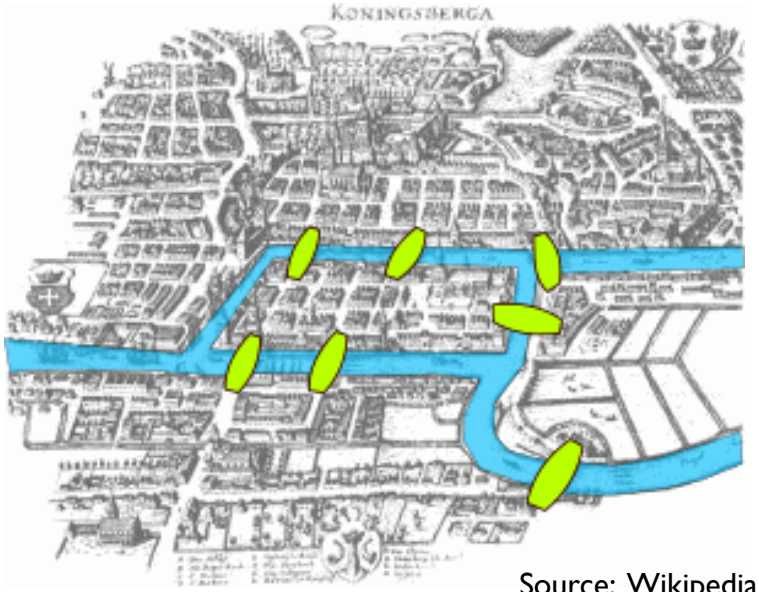
A_{ij} = 1, if a link exists between i and j ($\neq$ i)

= 0, otherwise

What is a *complex* network ?

Other than regular networks (d-dimensional lattice) or homogeneous random networks

Using the concept of networks:
From the 7 bridges of Konigsberg…



Source: Wikipedia

Problem: to find a walk through the city that would cross each bridge once and only once.
Euler: the problem has **no** solution.

Source: Wikipedia

Leonard Euler (1707-1783)

Led to foundation of Graph theory: the study of mathematical structures called graphs that model pairwise relations between objects

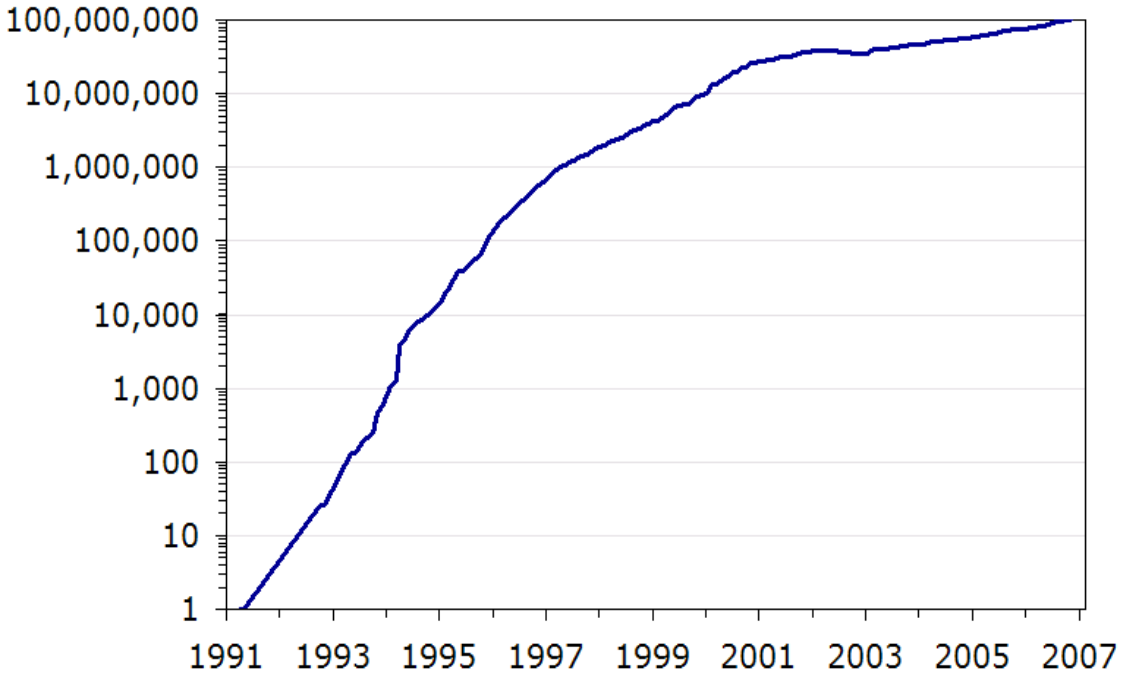
Using the concept of networks:

…to searching the World Wide Web

When the World Wide Web (WWW) was first proposed, it was widely assumed that its utility was limited because it would be impossible to efficiently access the vast quantity of information distributed throughout the entire network

Like searching for a needle in a haystack most of the time what you will find will be completely irrelevant to what you want !

Growth of number of web pages between 1991-2007

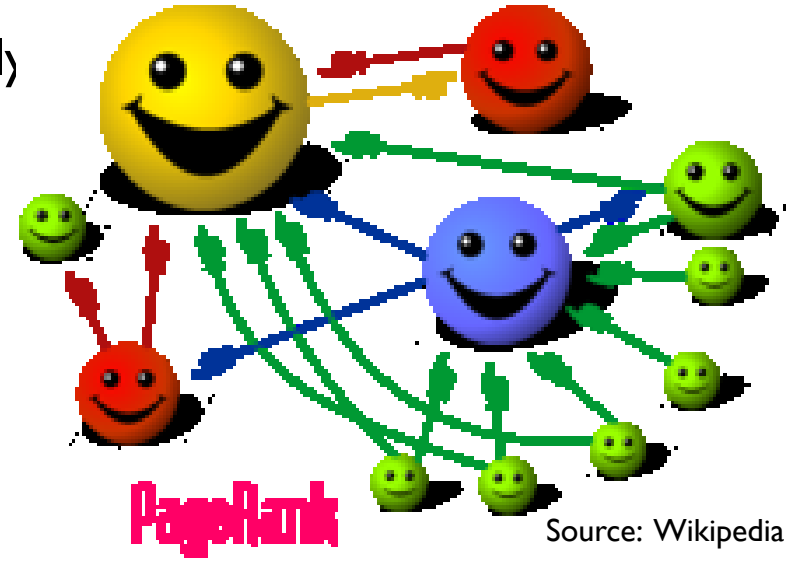


Source:www.useit.com/alertbox/web-growth.html

Using the theory of networks

Google's answer to data deluge

Manually indexed search engines were clearly incapable of handling the exponentially increasing amount of information in the web…
until Google came up with an efficient automated search algorithm that weights the importance of each page according to how many other pages are pointing to it



Source: Wikipedia

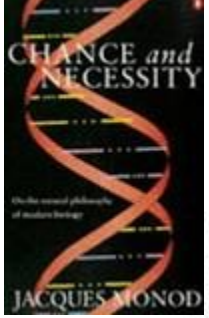
- The page rank algorithm is directly inspired by the graph theoretic concept of node centrality
- importance of a node measured in terms of how extensively it is connected to other important (i.e., having high centrality) nodes.

Thinking about biological problems in terms of networks

Example:

The *system* of genes in a cell that switch each other ON/OFF resulting in a cellular phenotype

Network of genes controlling each other



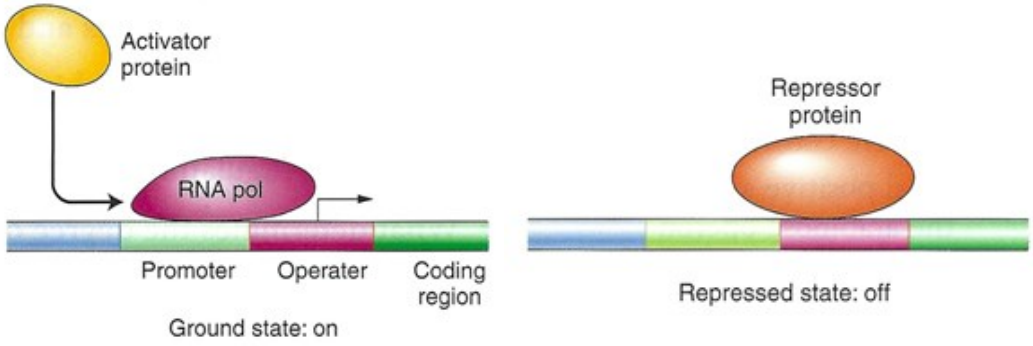
1965

Jacob & Monod: Explained the genetic regulation of enzyme synthesis with their work on *lac* operon in *E coli*

Jacques Monod
(1910 – 1976)

Francois Jacob
(1920 – 2013)

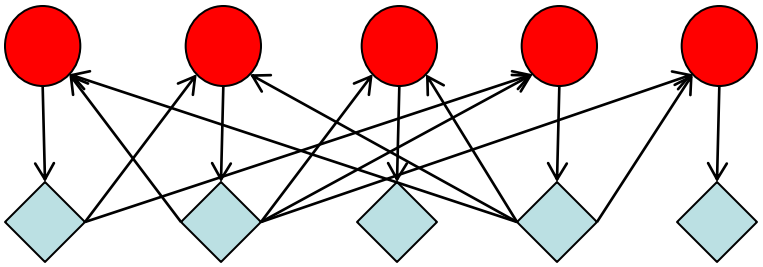
Overview of prokaryotic transcription regulation



www.discoveryandinnovation.com

Genes

TFs



Led to the idea of a **bipartite** network of genes and transcription factors that regulate the expression (switching ON/OFF) of genes: collective activity of the network – expression of different proteins – in a cell differs depending on the cell type (e.g., neuron vs muscle cell)

Random Boolean Network

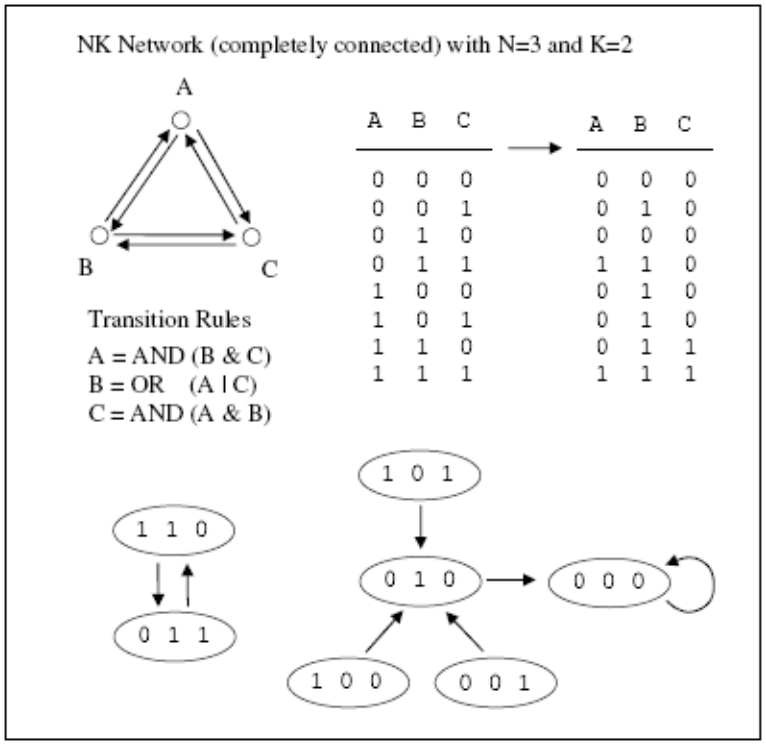
Model for explaining how the collective switching of genes can lead to different cellular phenotypes

S A Kauffman (1969) Metabolic stability and epigenesis in randomly constructed genetic nets. *Journal of Theoretical Biology*, 22:437-467.

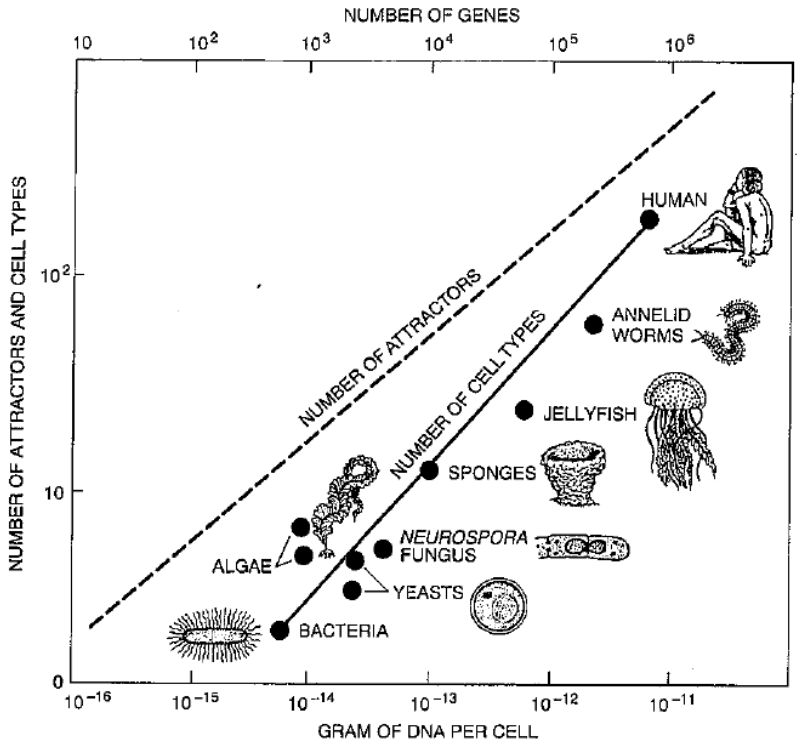
N Boolean variables each of whose states are determined by a boolean function taking inputs from a subset of size K variables

www.anisn.it

Stuart Kauffman (1939 -)



wiki.cas-group.net



Kauffman, Scientific American (1991)

The set of functions defines a directed network on N nodes

2^N possible network states for binary variables