Networks

NETWORKS AND INTERACTIONS

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Network

- Biological systems are often represented as networks.
- Networks are complex sets of binary interactions or relations between different entities.
- Every biological entity has interactions with other biological entities.
- **The purpose:**

  - Systems biology aims to understand biological entities at the **systemic** levels
  - Analyzing the **relationships** not only as individual components,

    but also as **interacting** systems and their **properties**

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Graph Theory

- the study of graphs, mathematical structures used to model pairwise relations between objects.
- A graph is made up of vertices, nodes, or points which are connected by edges, arcs, or lines.

Graph Types ; edge properties

- **NODES ->** Represent different entities: proteins or genes
- **EDGES ->** Convey information about the links between the nodes

Network Edges Types

- **Undirected edges**

  - Is found in Protein-Protein Interaction networks (PPINs)
  - The relationship between the nodes is a simple connection
  - Without a given 'flow' implied, since the evidence behind the relationship only tells us that A binds B.

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- **Directed edges**

- In metabolic or gene regulation networks
- There is a clear flow of signal implied
- The network can be organized hierarchically.

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• Weighted edges

- Directed or undirected edges can also have weight or a quantitative value associated with them.
- Used to describe concepts such as:

  reliability of an interaction

  a gene quantitative expression change than another

  how closely related two genes are in terms of sequence similarity

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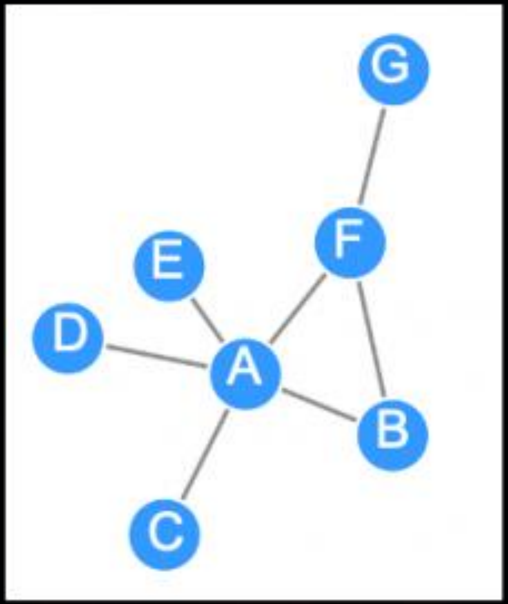
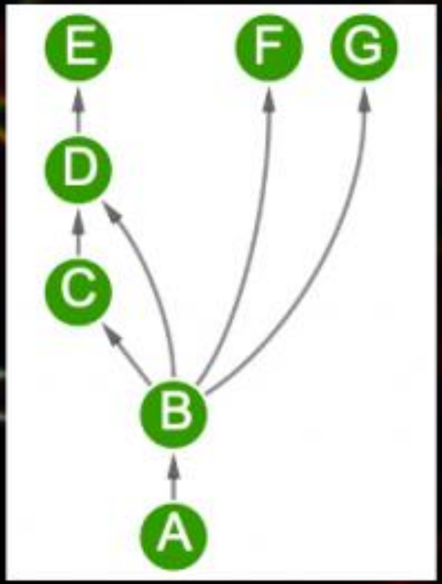
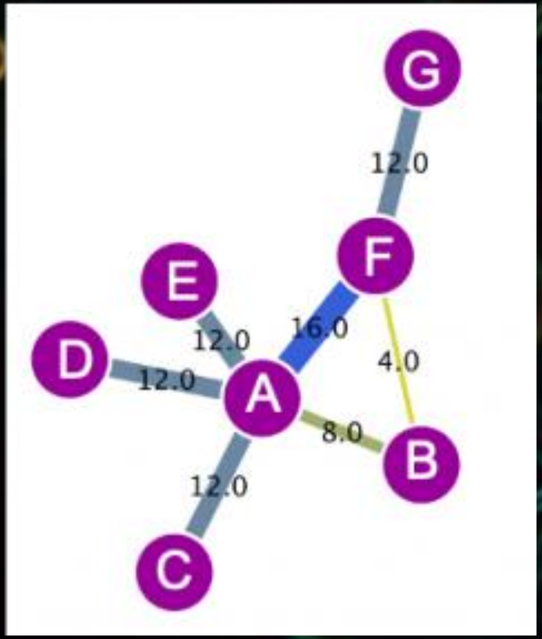


Undirected edges



Directed edges



Weighted edges

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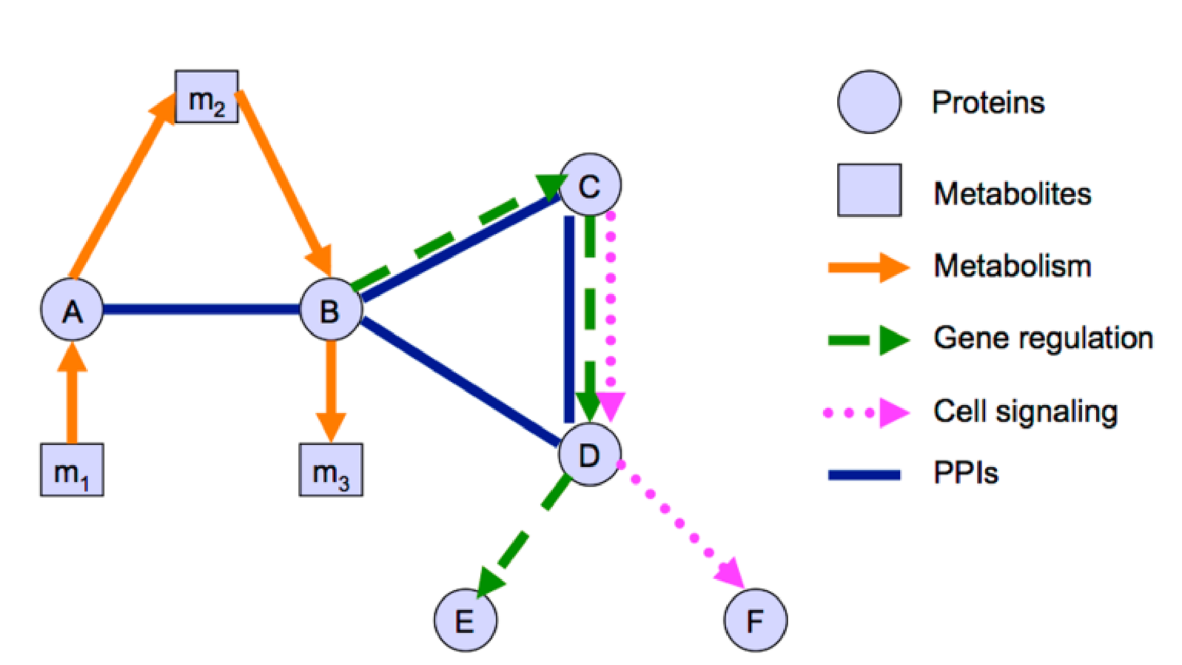
Biological networks

- **Modeling:** make the connections and interactions as a biological model.

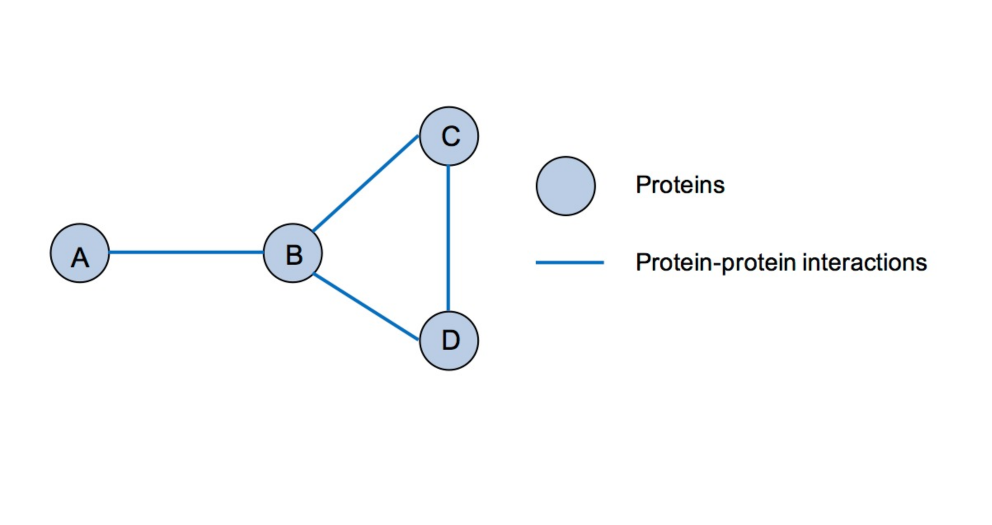


Some of the most common types of biological networks

1. Protein-protein interaction networks (PPI)

nodes = proteins

edges = physical / functional interactions



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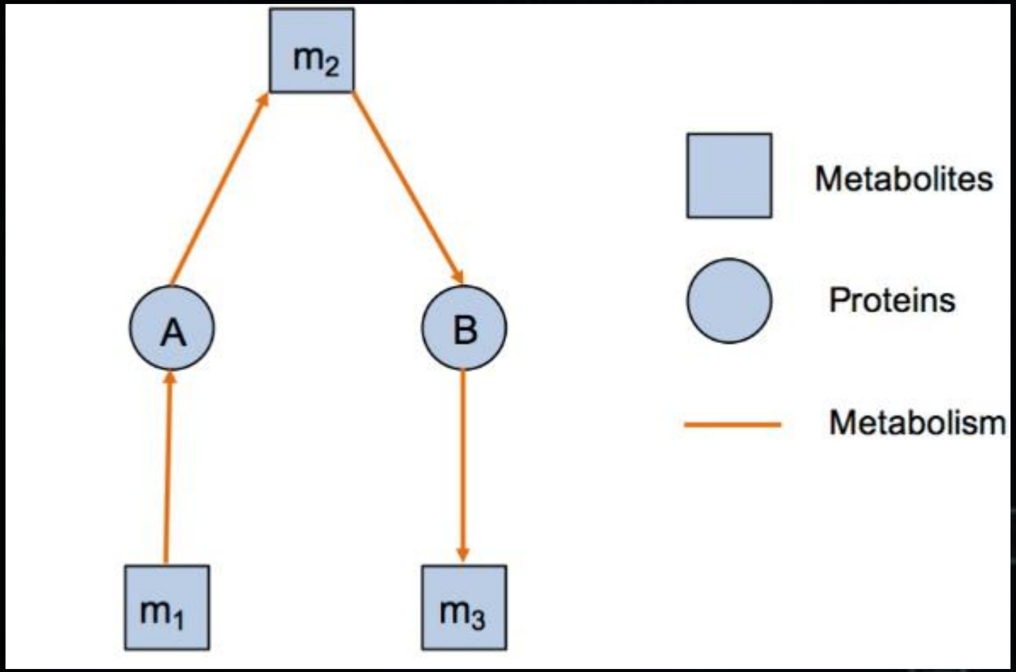
2. Metabolic networks

- modeling of cellular metabolisms.

nodes = proteins and enzymes
edges = metabolism / metabolic interaction



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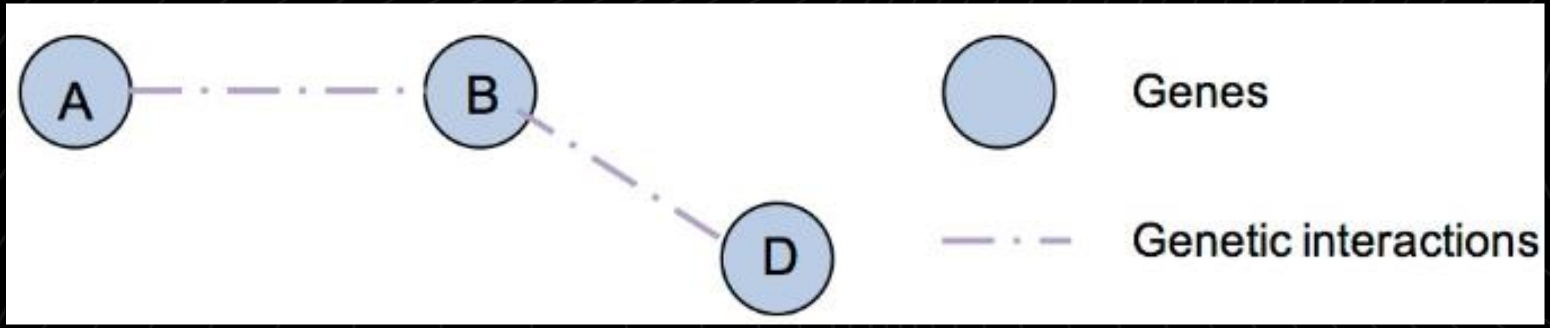
3. Genetic interaction networks

Represent the functional interactions between pairs of genes in an organism

- Nodes = Genes
- Edges = Genetic interactions
- are useful for understanding the relation between genotype and phenotype



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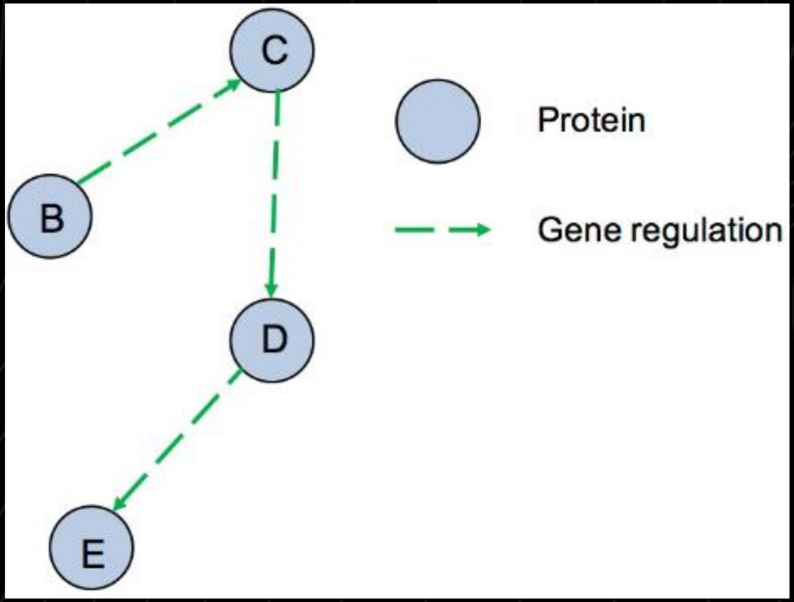
4. Gene / Transcriptional Regulatory networks

- Gene regulatory network (signed network)
- Regulatory interactions inter genes
- Nodes = genes or proteins
- Edges = activator / inhibitor interactions



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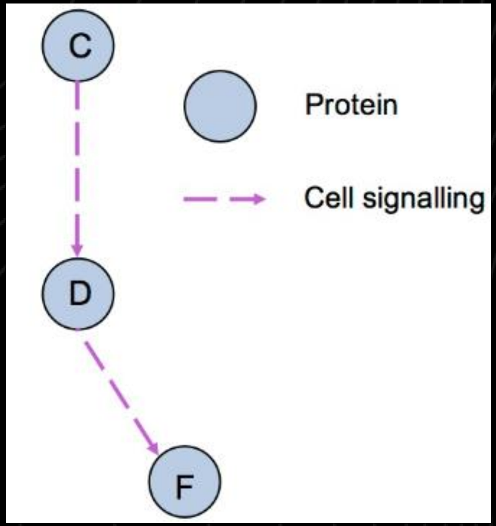
5. Cell signalling networks

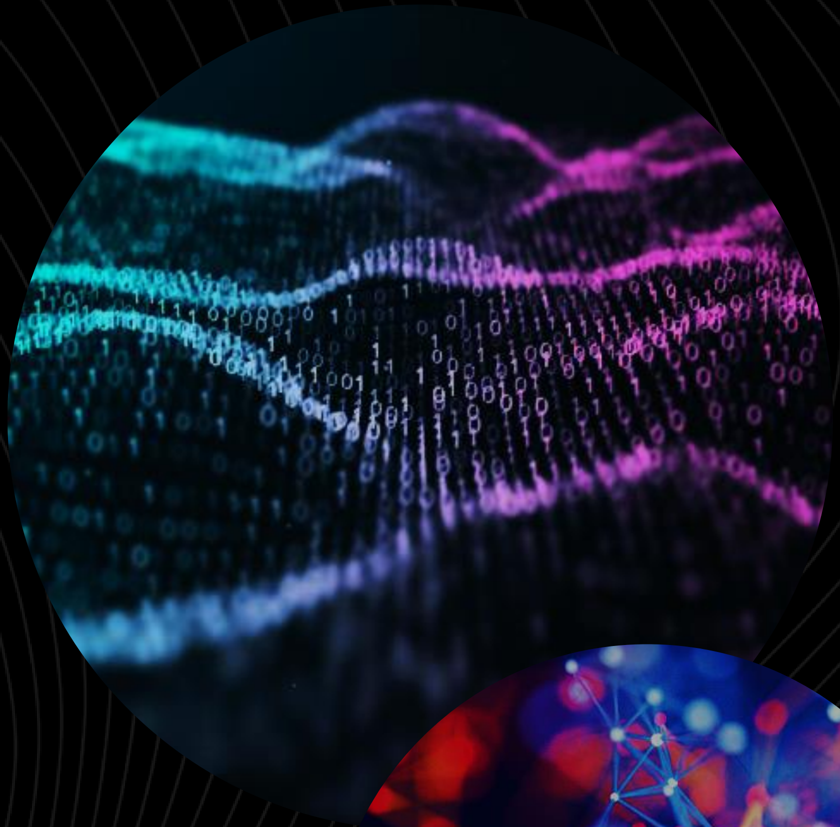
cellular signalling pathways

(signed network)

nodes = proteins

edges = inhibitor / activator connections





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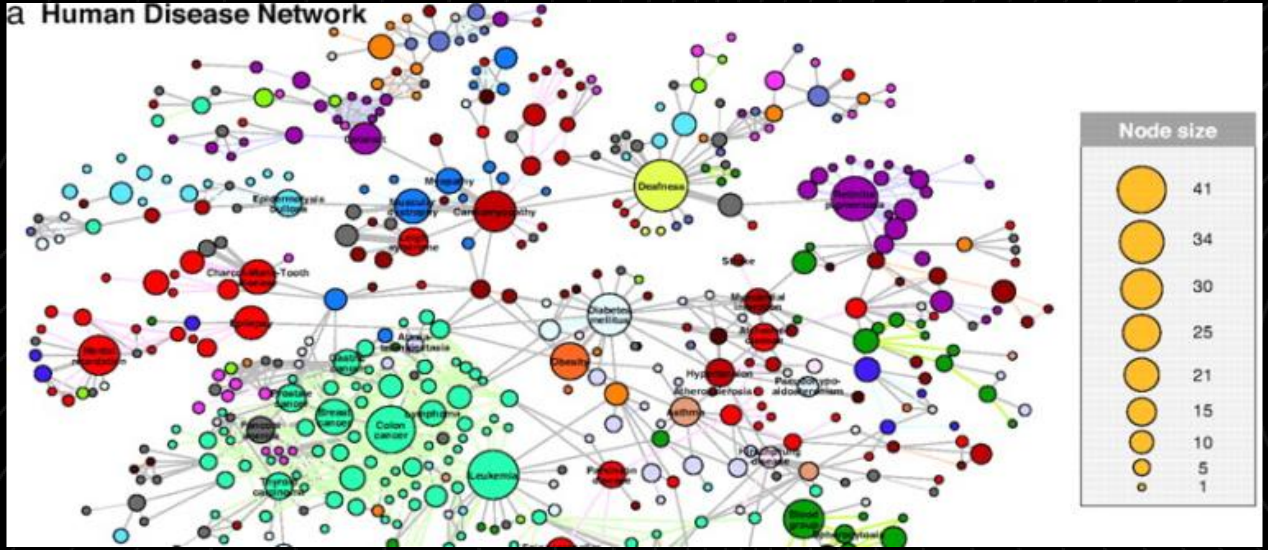
6. Disease Gene Networks

- Each node corresponds to a distinct disorder, colored based on the disorder class.
- The size of each node is proportional to the number of genes in the corresponding disorder.
- The link thickness is proportional to the number of genes shared by the disorders connected by the link.



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Types of graphs

The differences between different types of graphs depends on what can go in Edges.

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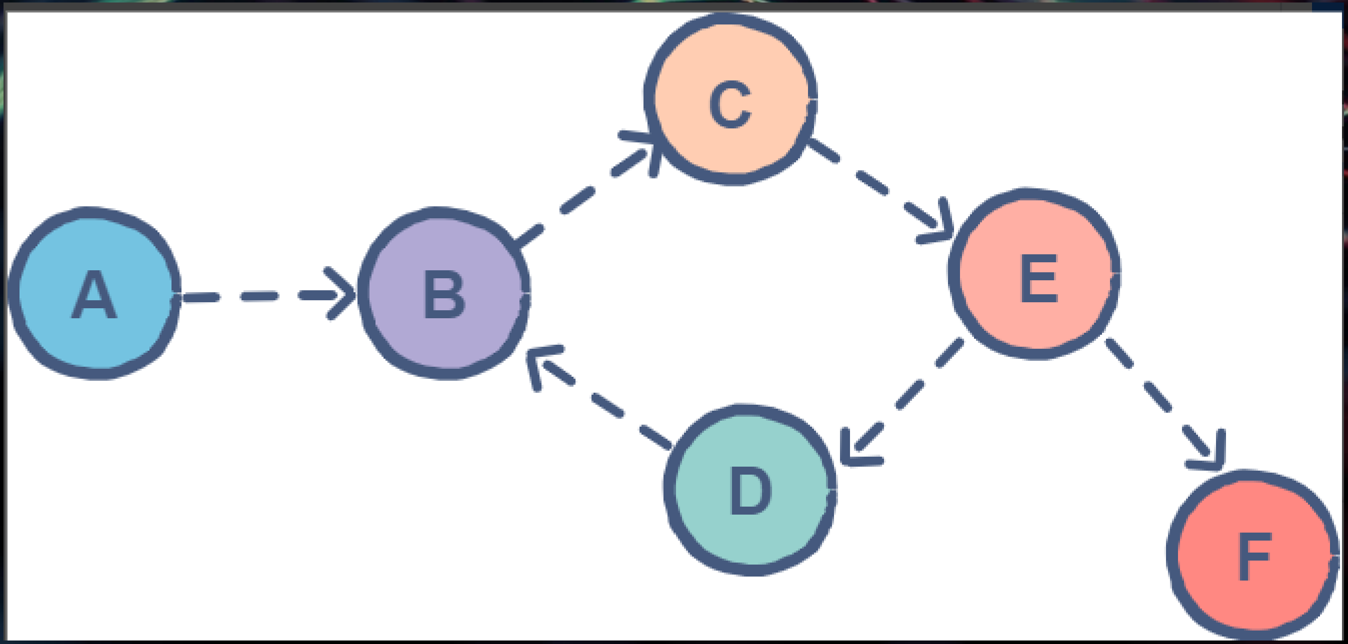
1. Directed graphs (signed)

- Digraph : each element of edge is an ordered pair.

- **As <u>arrows</u> from a source, head, or initial vertex to a sink, tail, or terminal vertex.**

- **Each of these two vertices is called an endpoint of the edge.**



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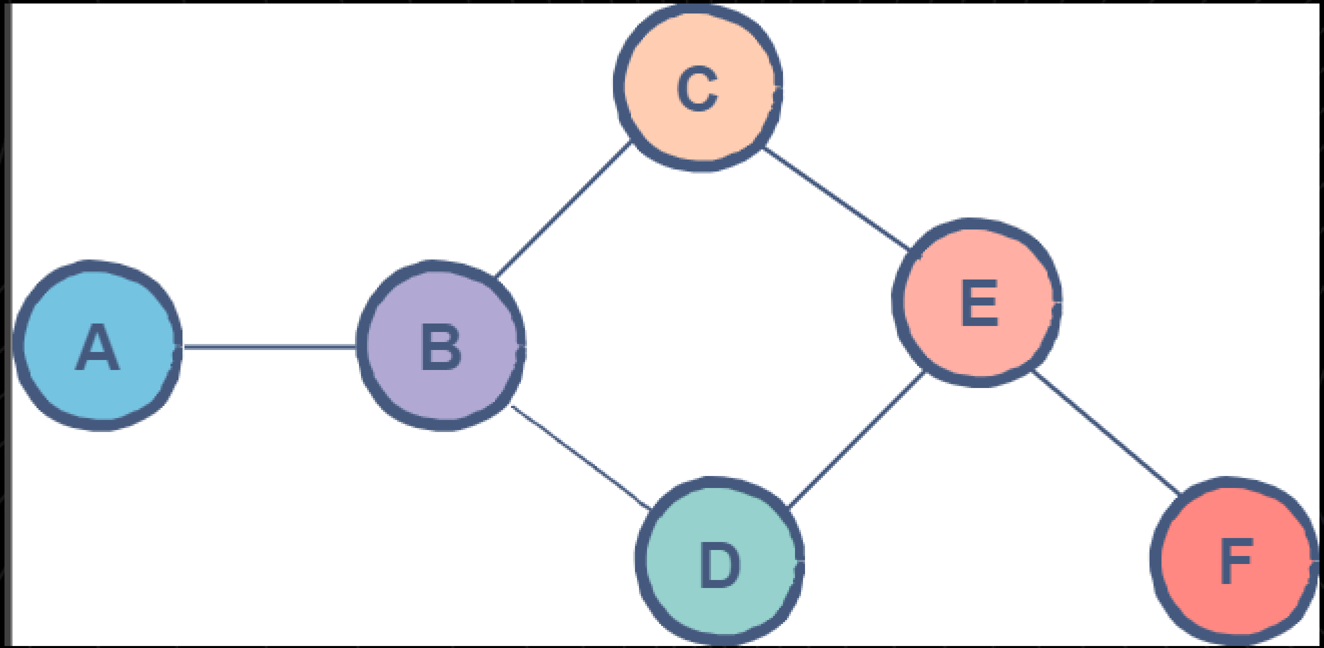
2. Undirected graphs

- Each edge is a two-element subset of node.
- Neighbors = two nodes which are linked by one edge
- The multi-edges are especially important for networks in which two elements can be linked by more than one connection.
- PPI networks



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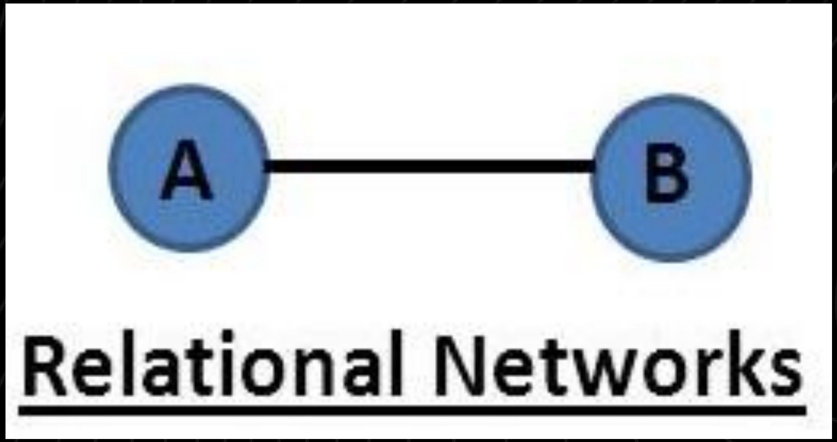
Categories

- Relational networks
  - The relationships between nodes without any direction.
  - Generally undirected (non-causal relationships).
  - Nodes are all the same "type".
  - No signs on edges.



EXAMPLE: protein A is a dimerization part of protein B

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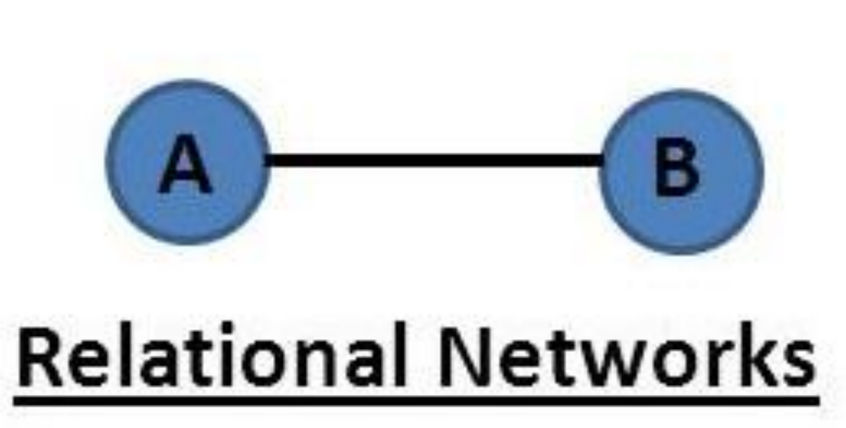
• Correlation networks

- undirected (non-causal)
- Nodes are the same “type”.
- Edges can have signs.



EXAMPLE: the changes of A expression can change B expression

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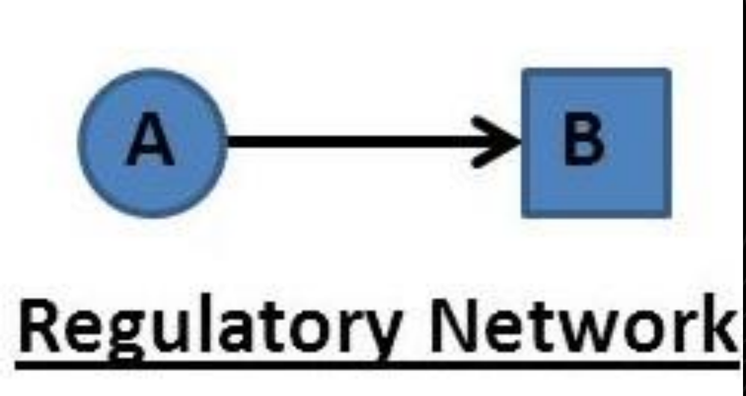
- **Regulatory networks**

  - directed networks (causal relationships)
  - can have variant “types” of nodes
  - Edges can have signs.



EXAMPLE: TF A regulates Gene B

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Degree

- The nodes of a graph can be characterized by the number of edges that they have.

the number of other nodes to which they are adjacent.

In directed networks:

- in-degree => the number of directed edges that point toward the node.
- out-degree => the number of directed edges that start at the node.

- “Scale free” networks

  - A network without a typical degree (or typical scale).

  - The continuously decreasing degree distribution indicates that low-degree nodes have the highest frequencies.

    meaning: probability of attendance of low-degree nodes is high.

    There is a lot of nodes with low degree,

      a few of them interacted with each other

    There is a few nodes with high degree, interacted with a lot of nodes.

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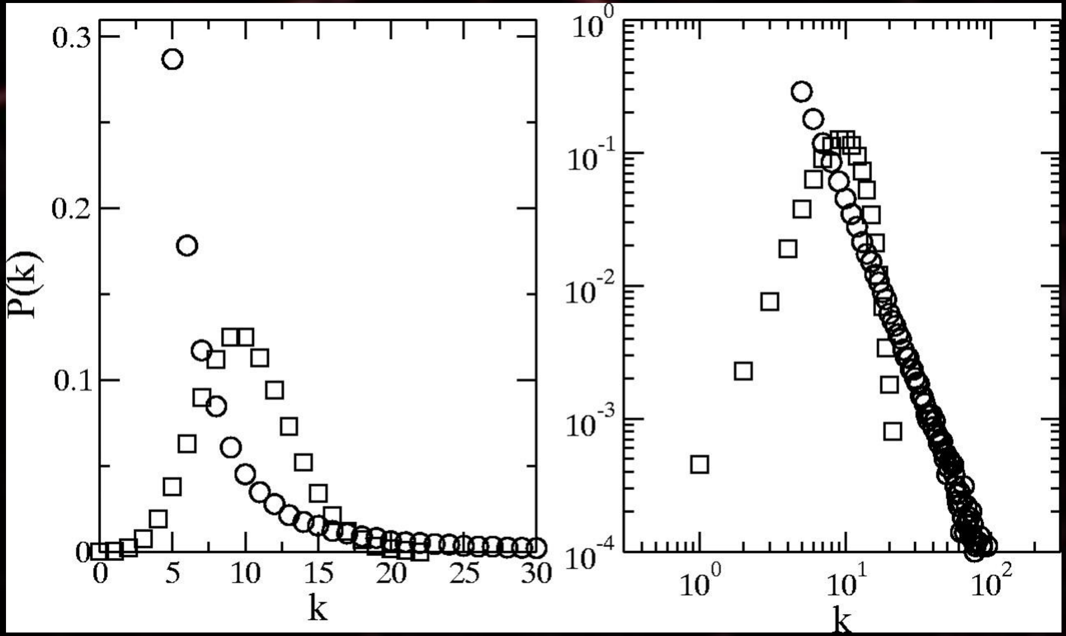
Comparison between the degree distribution of scale-free networks (circles) and random graphs (squares) having the same number of nodes and edges

- The bell shaped = degree distribution of random graphs peaks at the average degree and decreases fast for both smaller and larger degrees.

  indicating that these graphs are statistically homogeneous



- The degree distribution of the scale-free network appears as a straight line on a logarithmic plot.

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- Every sub-networks of whole network

  has the scale-free structure.
- **Hub nodes** = Those few nodes which are connected to many nodes.
- Most of biological networks