

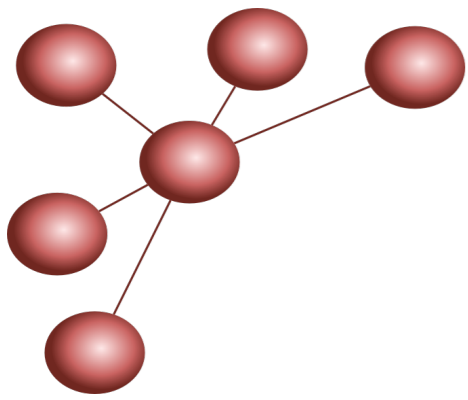
DUBii 2019

Introduction to Network Science

Introduction to Network Biology

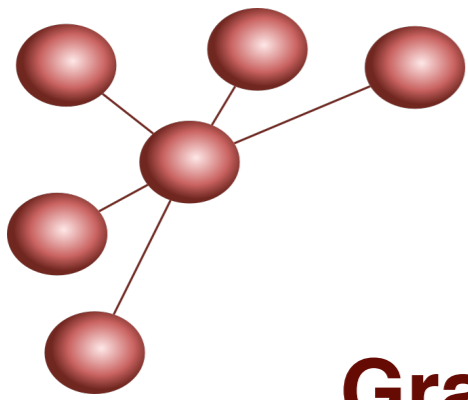
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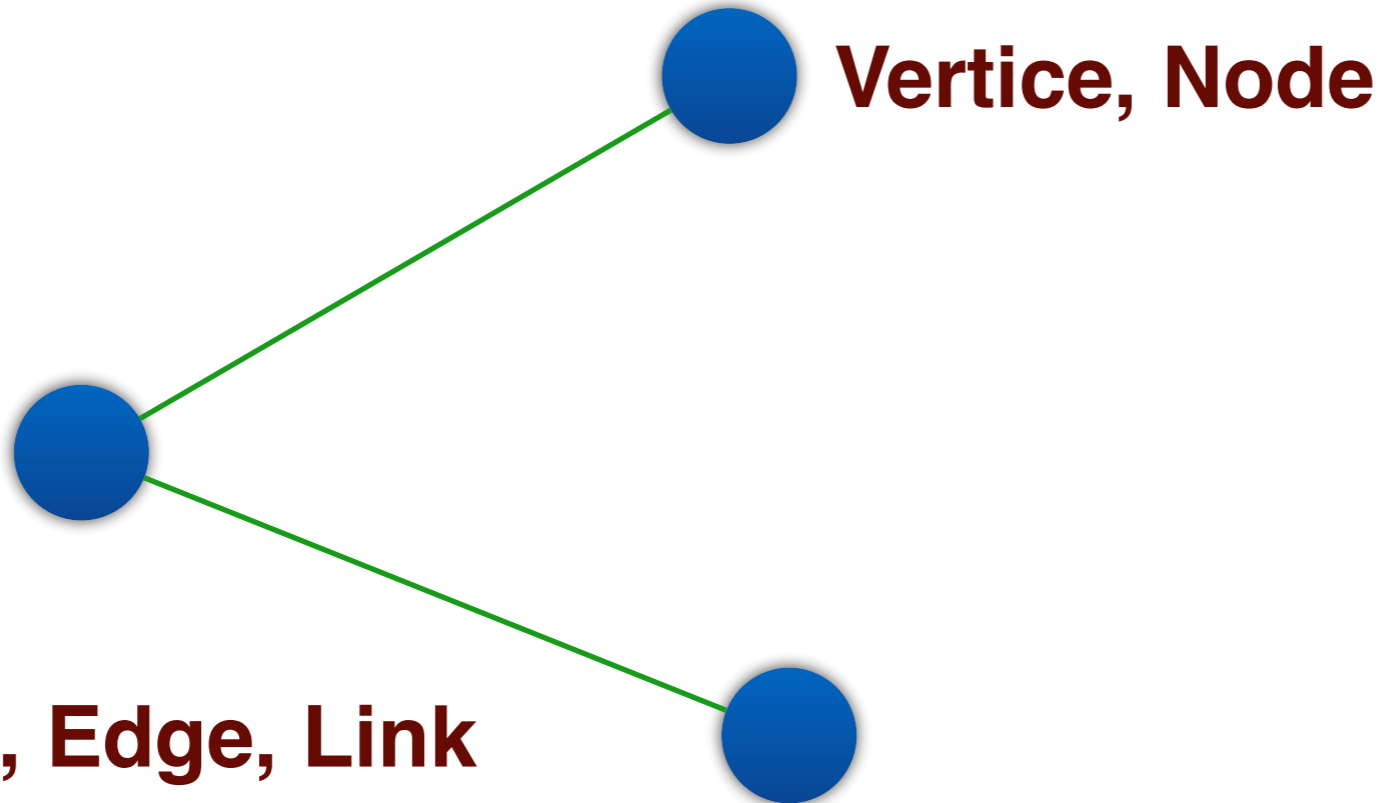
Network Science

- **Start 21th century**
- **Roots on graph theory**
- **In the context of data production and computer sciences**



Graph, Network, Web

Definition

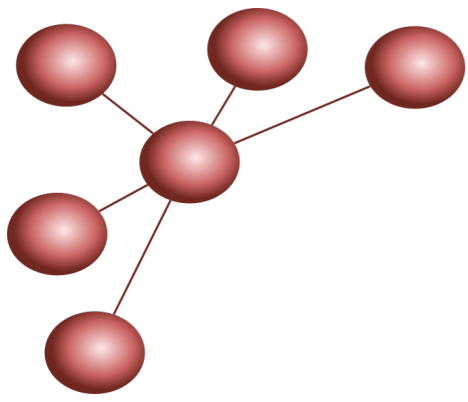


Vertice, Node

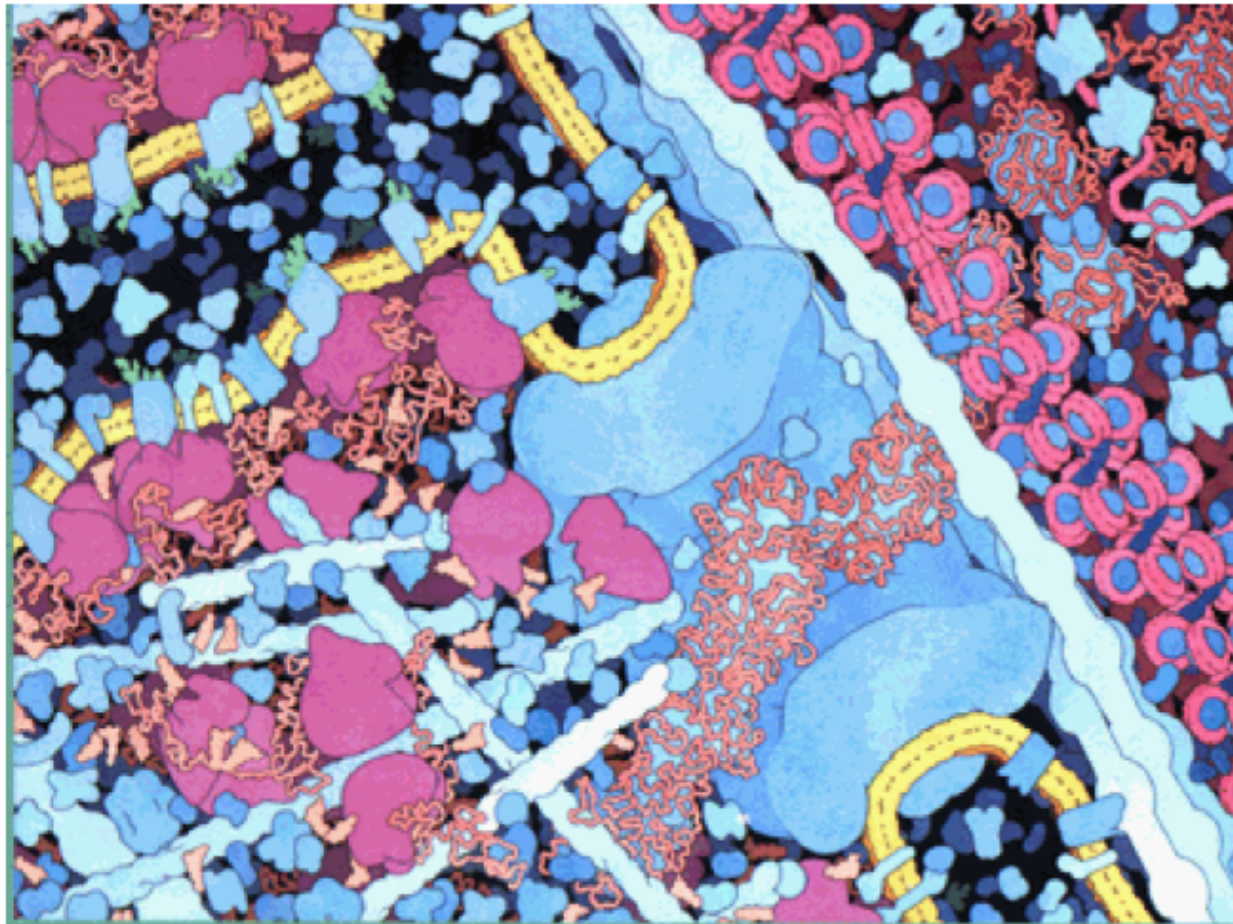
Interaction, Edge, Link

$$G = \{V, E\}$$

Topology, Motifs ...



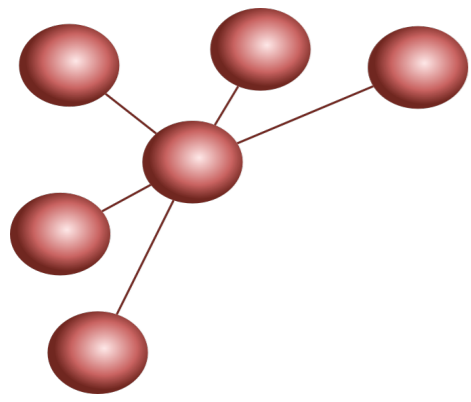
Macromolecules do not act isolated, but interact with each other to perform their functions



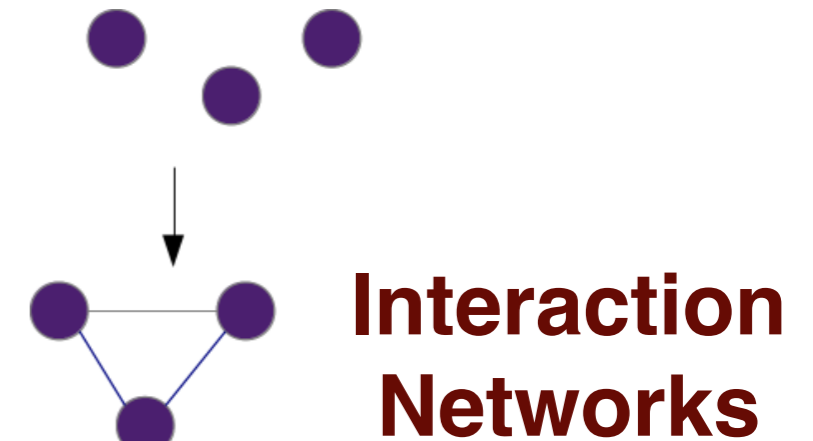
**Molecular interactions:
Protein-Protein
Protein-DNA
Protein-RNA
Protein-Lipid
...**

Transient, stable, obligatory ...

Systems Biology because living organisms are complex systems



**Systems component : genes/
proteins**

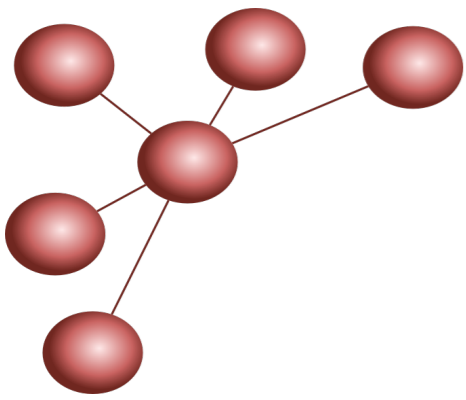


Emerging properties : phenotypes

- **Global/collective behavior cannot be deduced from the knowledge on the components**
- **Phenotype does not emerge from isolated biological molecules but from their interactions**

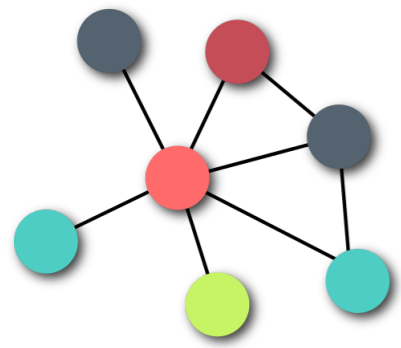
Exemple :





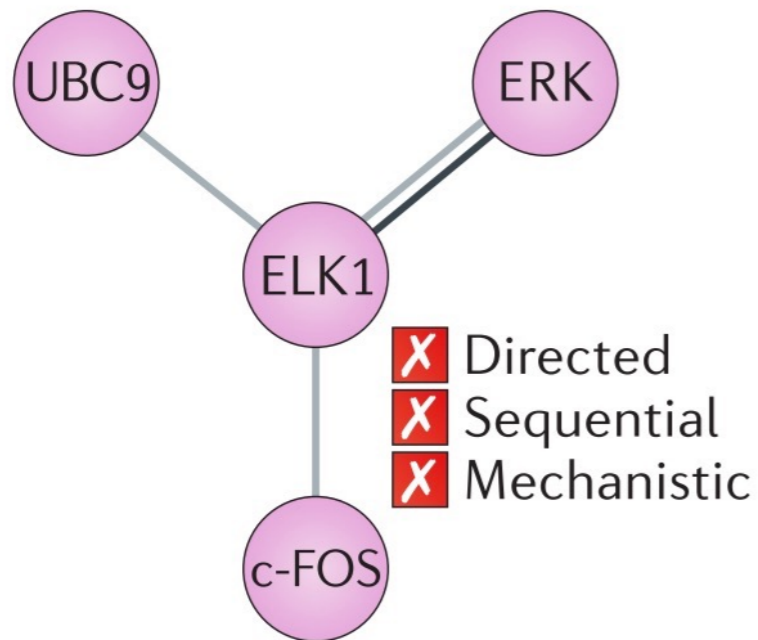
Biological Networks

- From literature, knowledge, curation
- From large-scale interaction experiments
- From inference from large-scale experiments

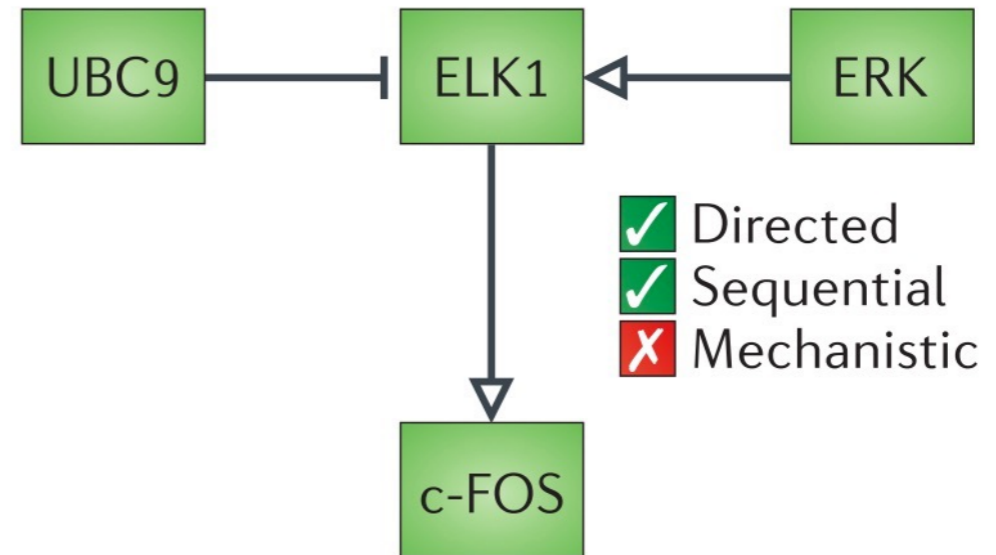


2 main types of networks to represent biological information flow

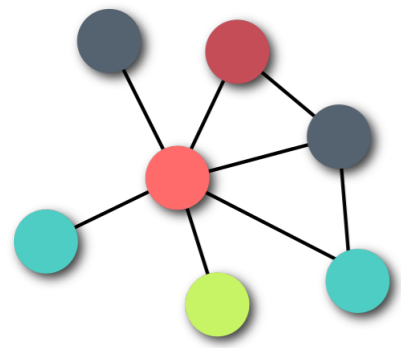
a Interaction network



b Activity flows

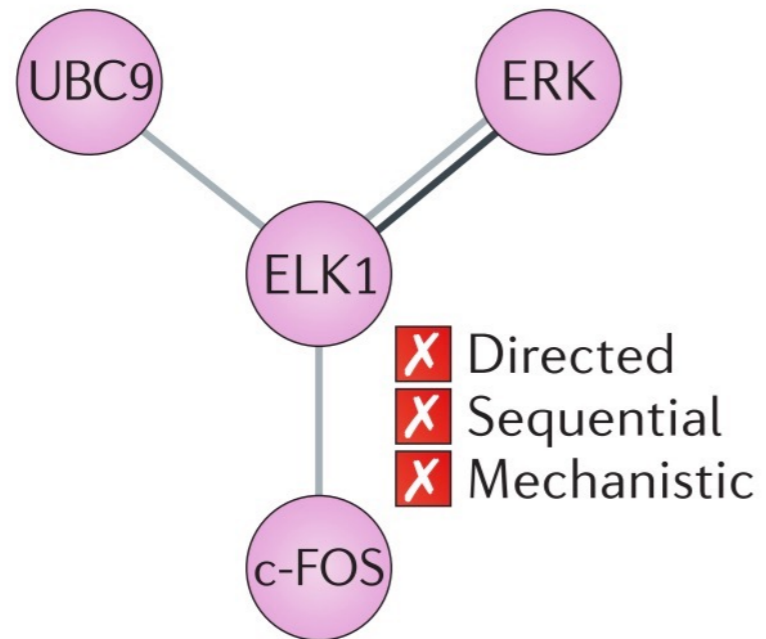


Le Novère et al. 2015



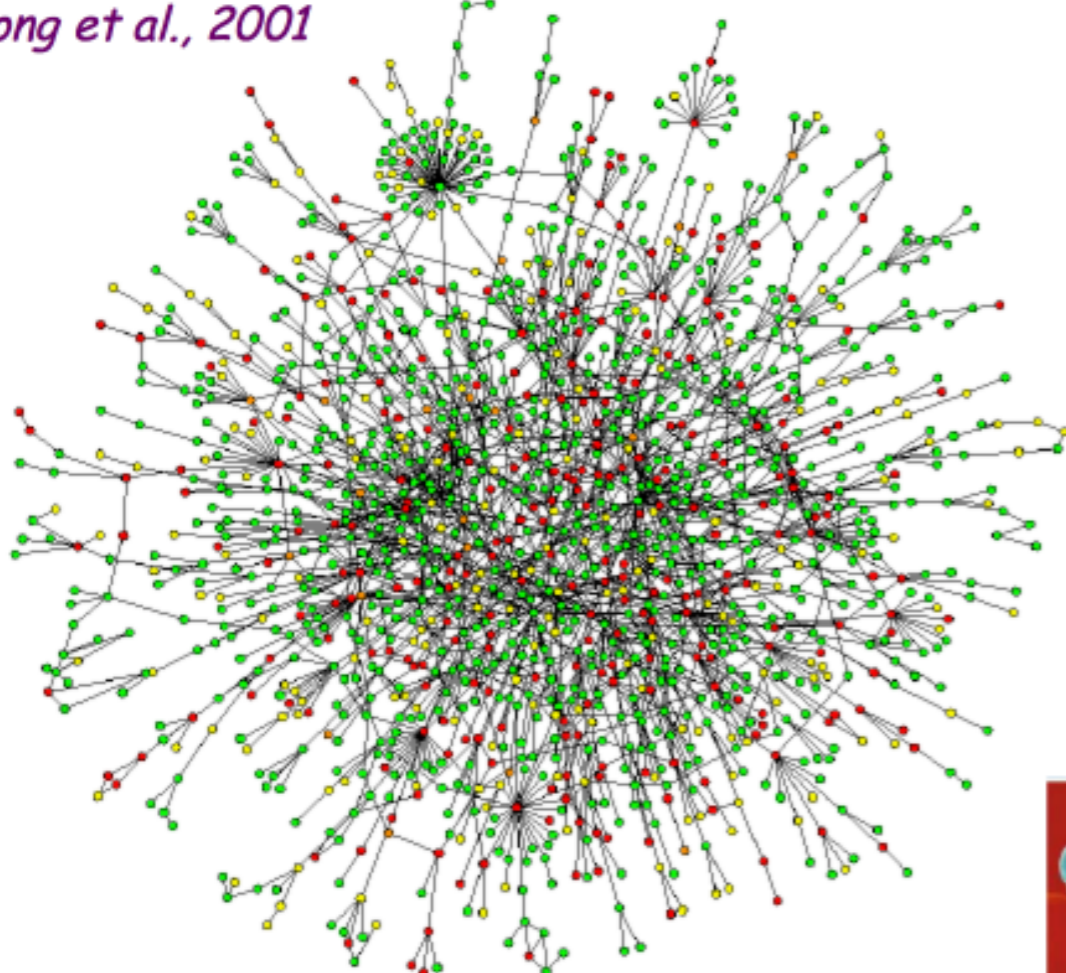
Interaction networks / Interactome

a Interaction network

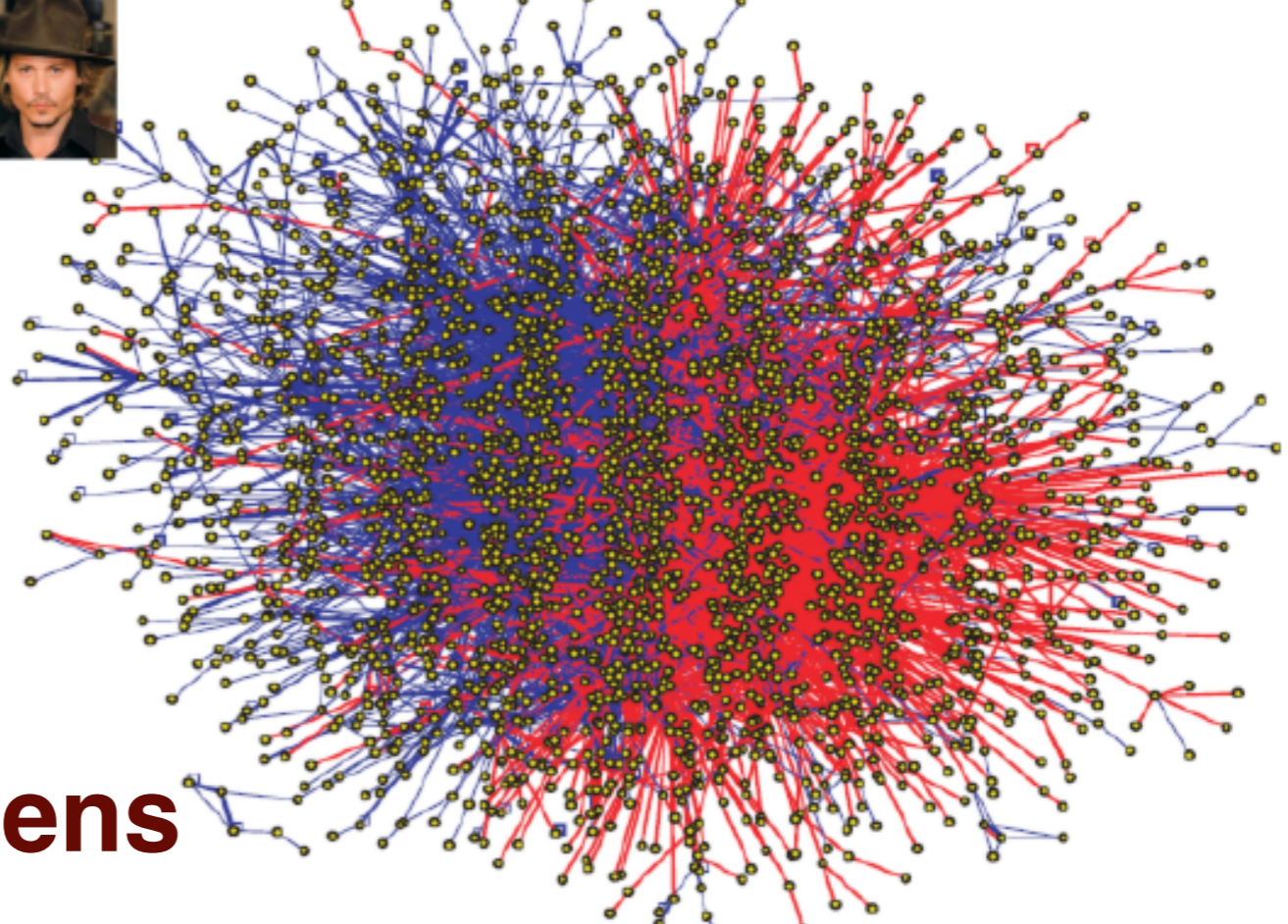
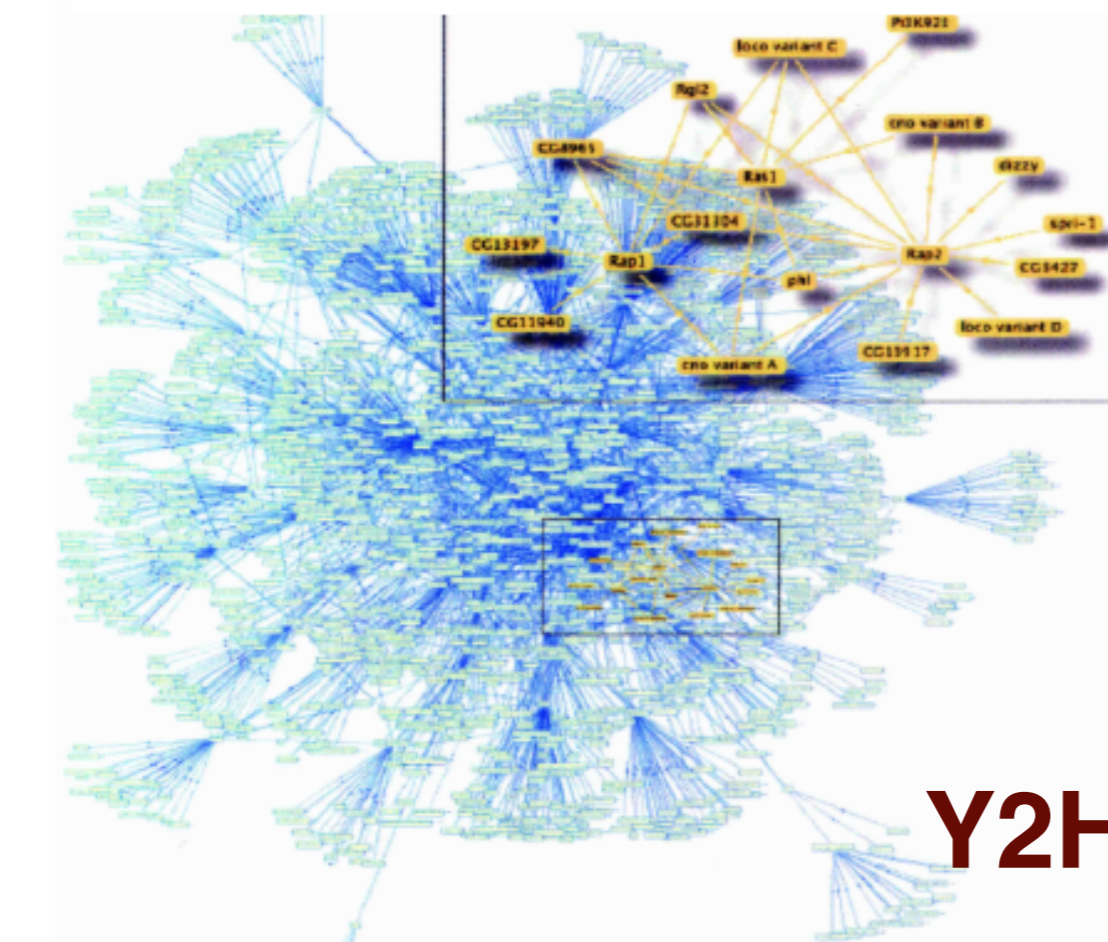
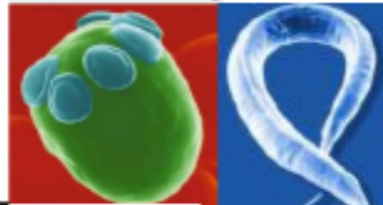
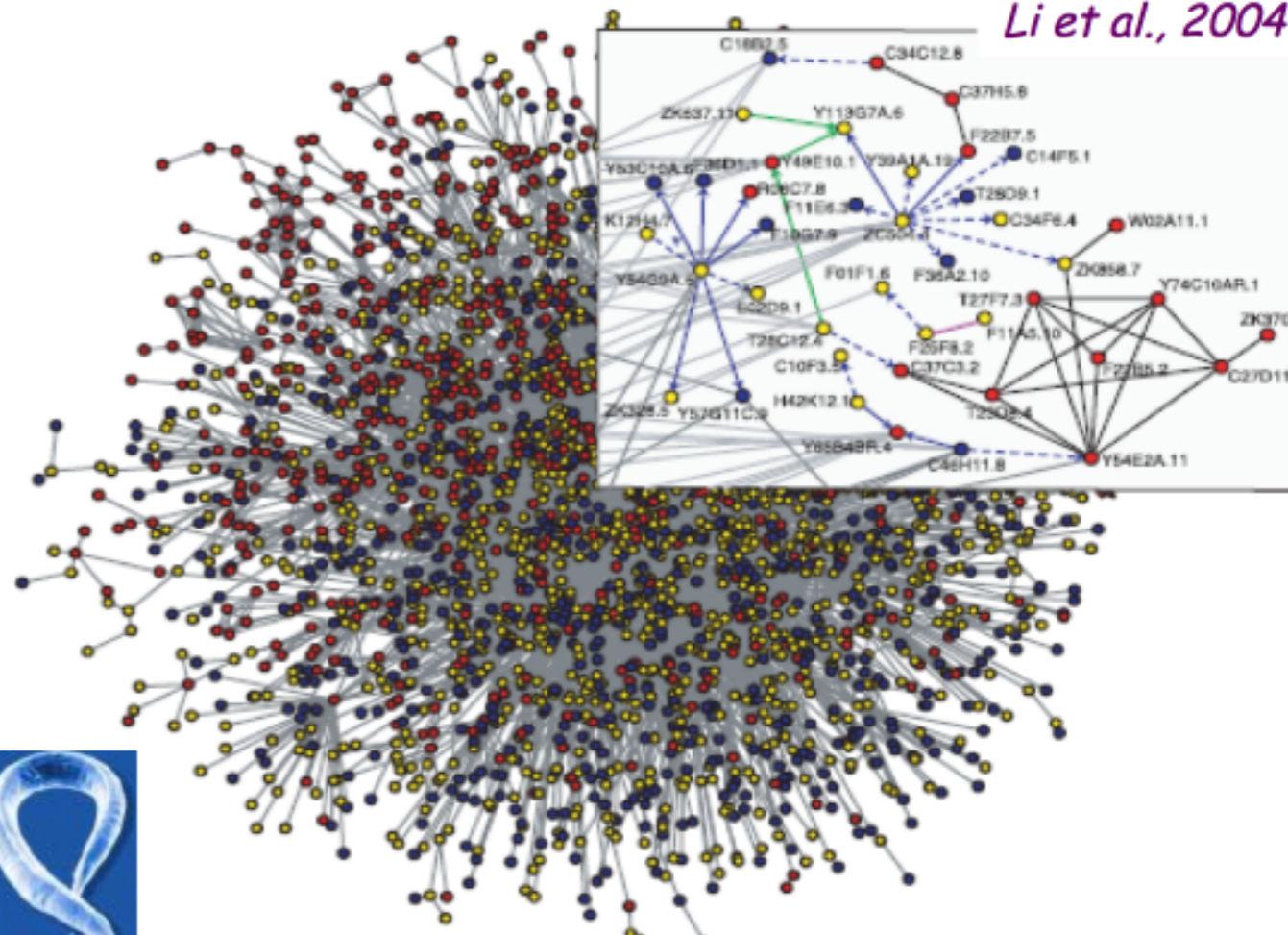


Le Novère et al. 2015

Jeong et al., 2001



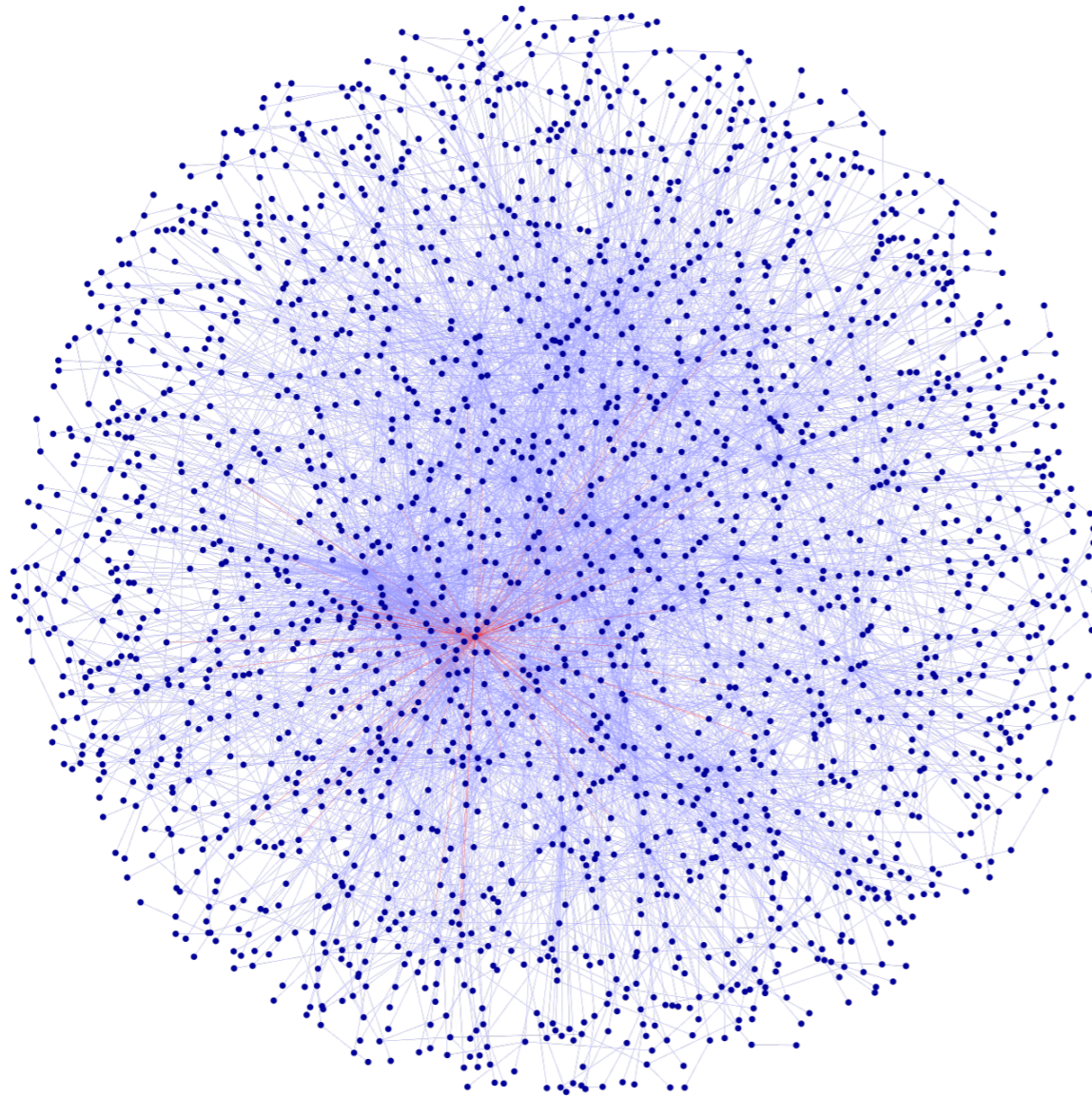
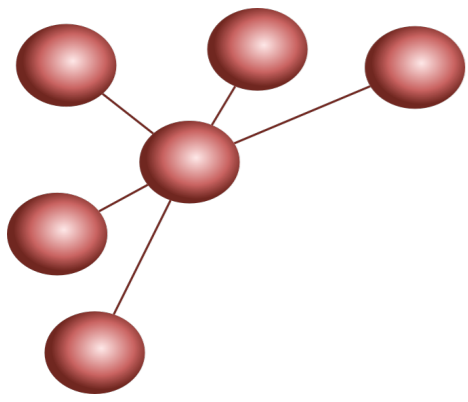
Li et al., 2004



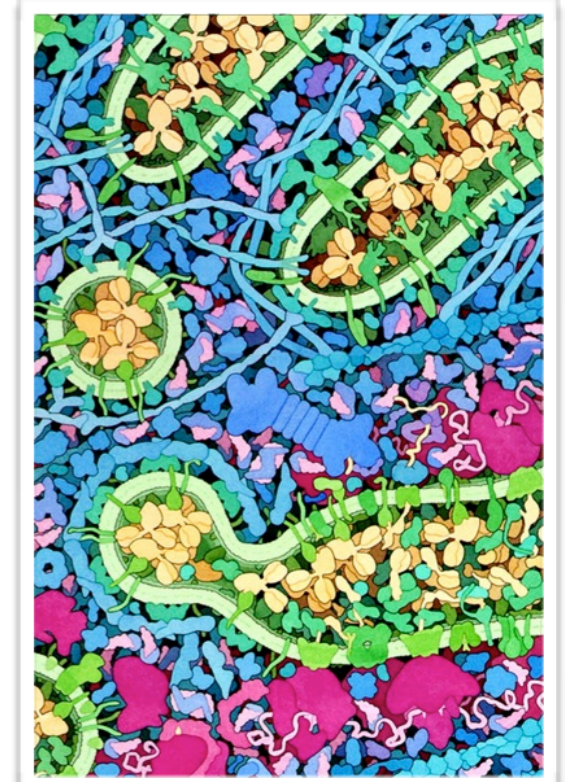
Formstecher et al., 2005

Rual et al., 2005

Y2H screens



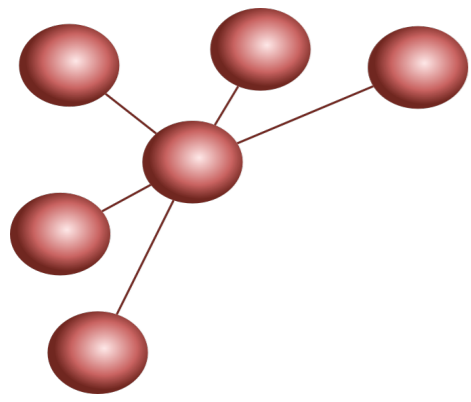
Interactomes



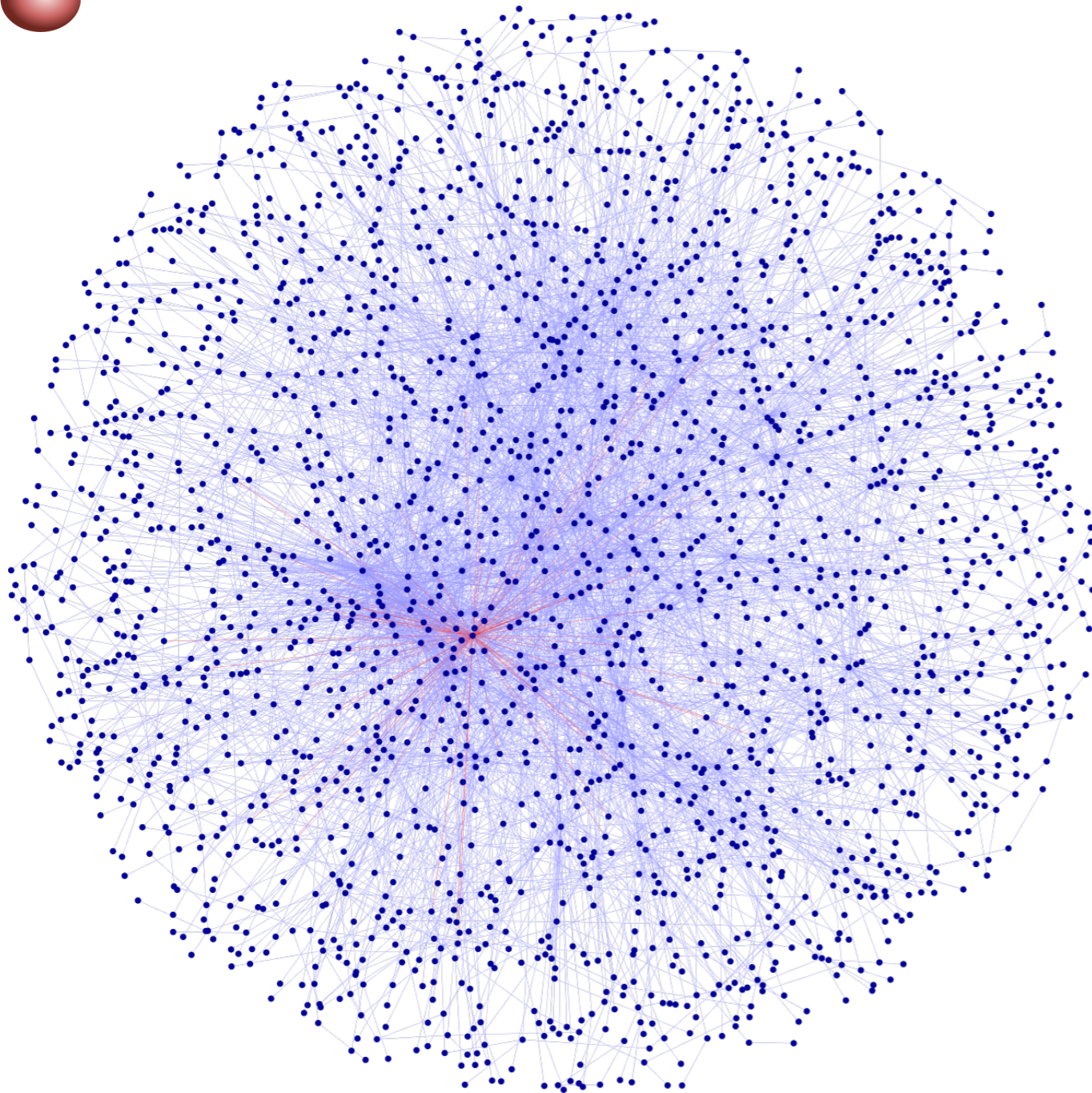
Set of protein-protein interactions detected in an organism

Physical interactions, but physiological interactions ?

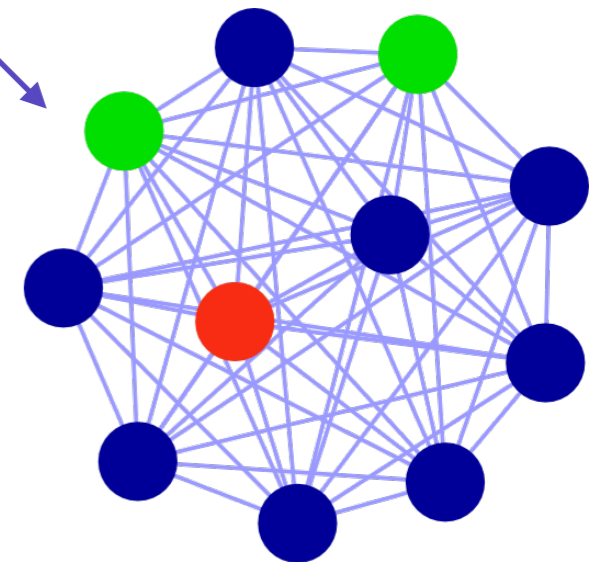
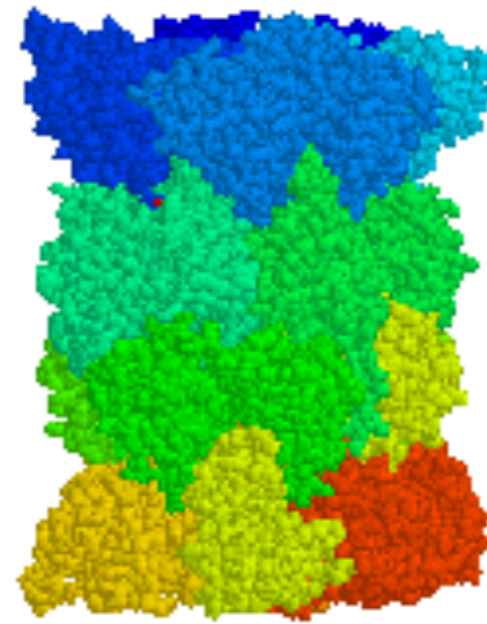
Interactomes are devoid of spatio-temporal information



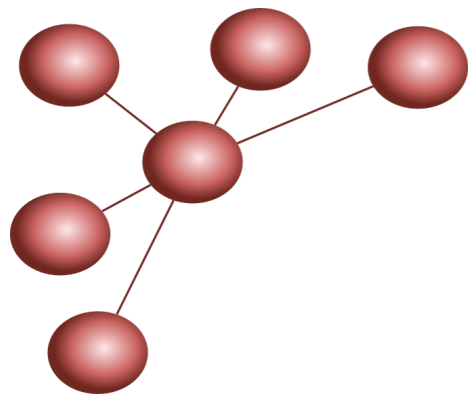
Interactomes



Protein-protein interaction networks



Protein complexes



Interaction databases

Multi-organisms:

DIP (dip.doe-mbi.ucla.edu)

IntAct (www.ebi.ac.uk/intact)

MINT (mint.bio.uniroma2.it/mint)

BioGRID (www.thebiogrid.org)

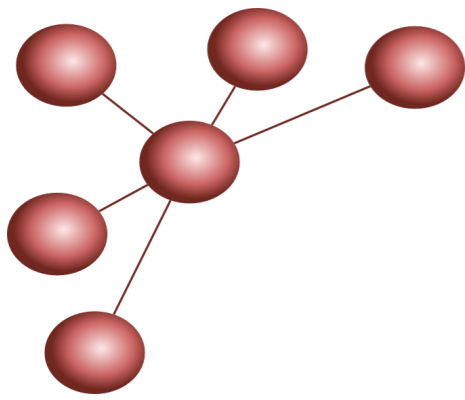
BIND (www.blueprint.org)

Human


Reactome-FI



**International
Molecular
Exchange
Consortium**



Psicquic portal

EMBL-EBI  Services Research Training About us

PSICQUIC View

BRCA2
Examples: BRCA2, Q06609, dmc1, 10831611

Input Form **Browse** Help

[Input Form](#) > [Browse](#)

1,832 binary interactions found for search term *BRCA2*

<input type="checkbox"/> APID Interactomes	<input checked="" type="checkbox"/> BAR-6	<input checked="" type="checkbox"/> bhf-ucl-0	<input type="checkbox"/> BIND
<input checked="" type="checkbox"/> BindingDB-0	<input checked="" type="checkbox"/> BioGrid-322	<input checked="" type="checkbox"/> ChEMBL-0	<input type="checkbox"/> DIP
<input type="checkbox"/> DIP-IMEx	<input type="checkbox"/> DrugBank	<input checked="" type="checkbox"/> EBI-GOA-miRNA-0	<input checked="" type="checkbox"/> EBI-GOA-nonIntAct-65
<input type="checkbox"/> GeneMANIA	<input checked="" type="checkbox"/> HPIDb-0	<input checked="" type="checkbox"/> I2D-0	<input checked="" type="checkbox"/> IMEx-241
<input checked="" type="checkbox"/> InnateDB-0	<input checked="" type="checkbox"/> InnateDB-All-561	<input checked="" type="checkbox"/> IntAct-107	<input type="checkbox"/> Interoprc
<input type="checkbox"/> iRefIndex	<input checked="" type="checkbox"/> MatrixDB-12	<input checked="" type="checkbox"/> MBInfo-0	<input checked="" type="checkbox"/> mentha-380
<input checked="" type="checkbox"/> MINT-84	<input checked="" type="checkbox"/> MPIDB-0	<input checked="" type="checkbox"/> Reactome-0	<input checked="" type="checkbox"/> Reactome-FIs-29
<input type="checkbox"/> Spike	<input type="checkbox"/> TopFind	<input checked="" type="checkbox"/> UniProt-25	<input type="checkbox"/> VirHostNet
<input type="checkbox"/> ZINC			

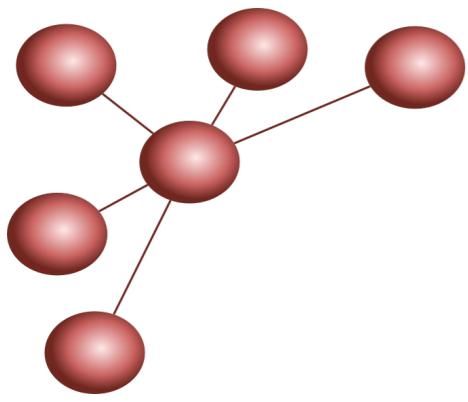
Status of the service

- ONLINE
- OFFLINE
- WARNING: Time out
- ERROR: Unexpected Error

1,832 selected interactions

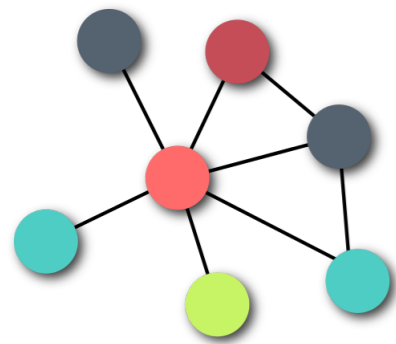
version: 1.4.11

<http://www.ebi.ac.uk/Tools/webservices/psicquic/>



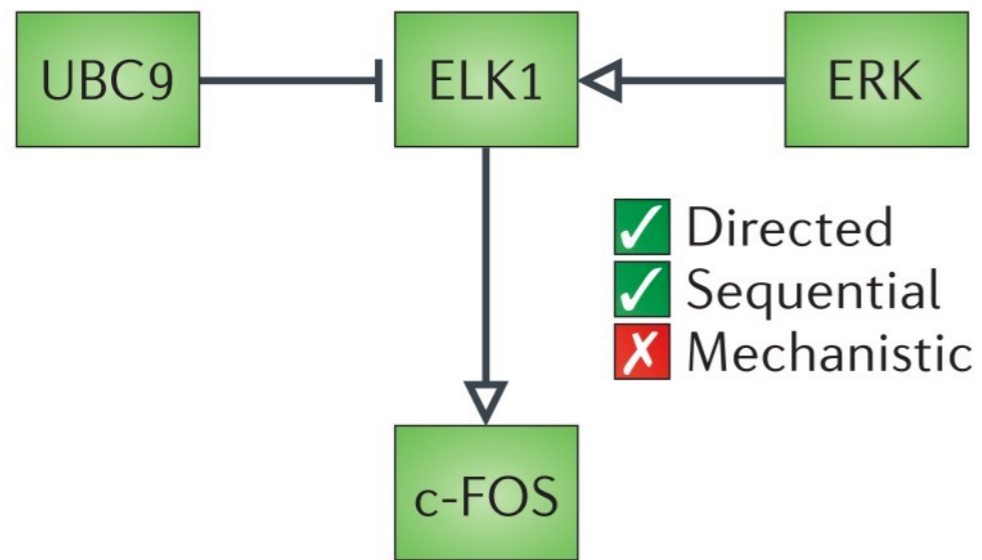
Network inference from -omics data

- Co-expression networks from transcriptomics data => Session #2



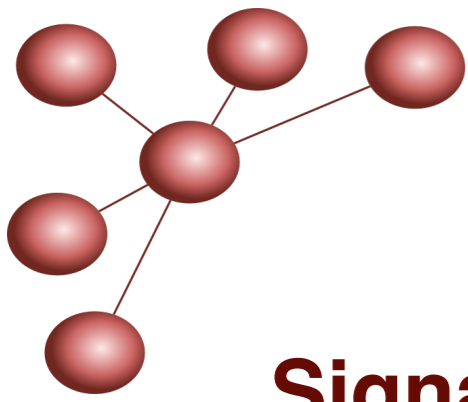
Activity flow / Gene Regulatory Networks / Influence Graphs

b Activity flows

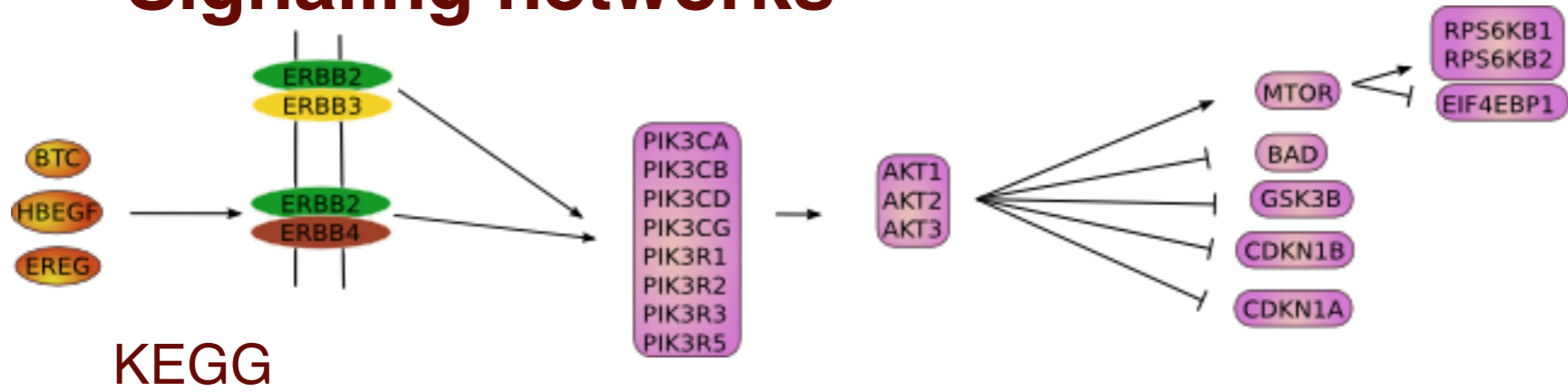


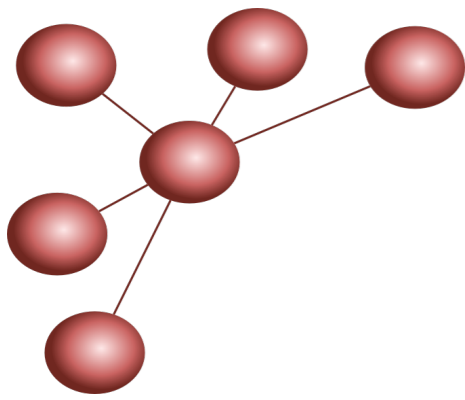
Le Novère et al. 2015

Signaling Networks



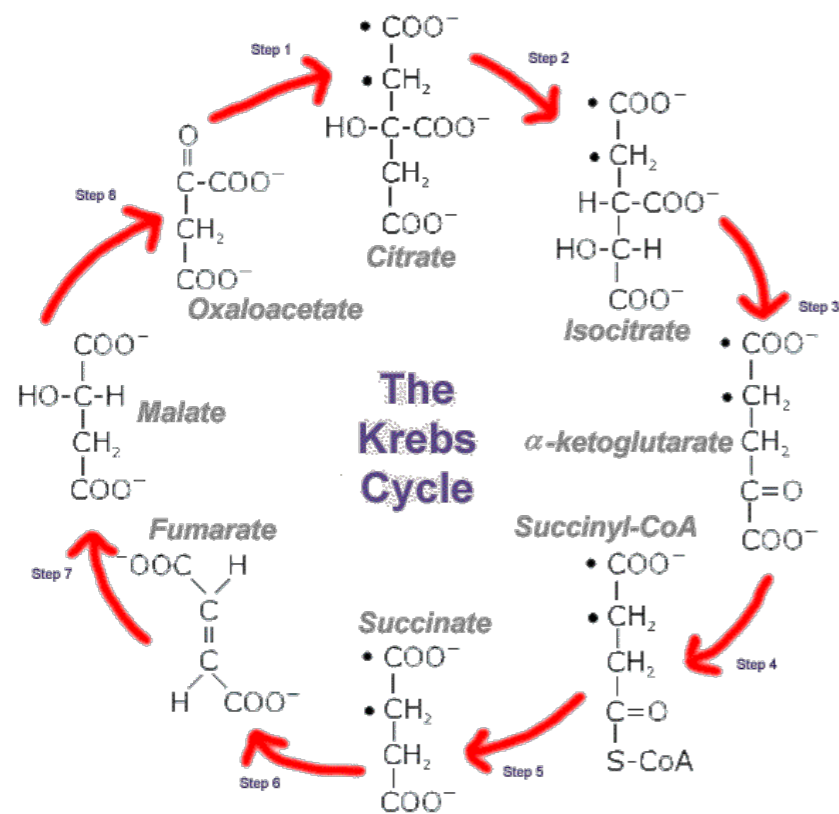
Signaling networks



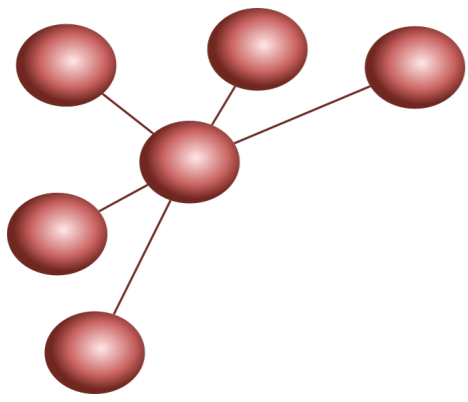


Metabolic networks

2 types of nodes : enzymes & substrates, reaction directional or bidirectional

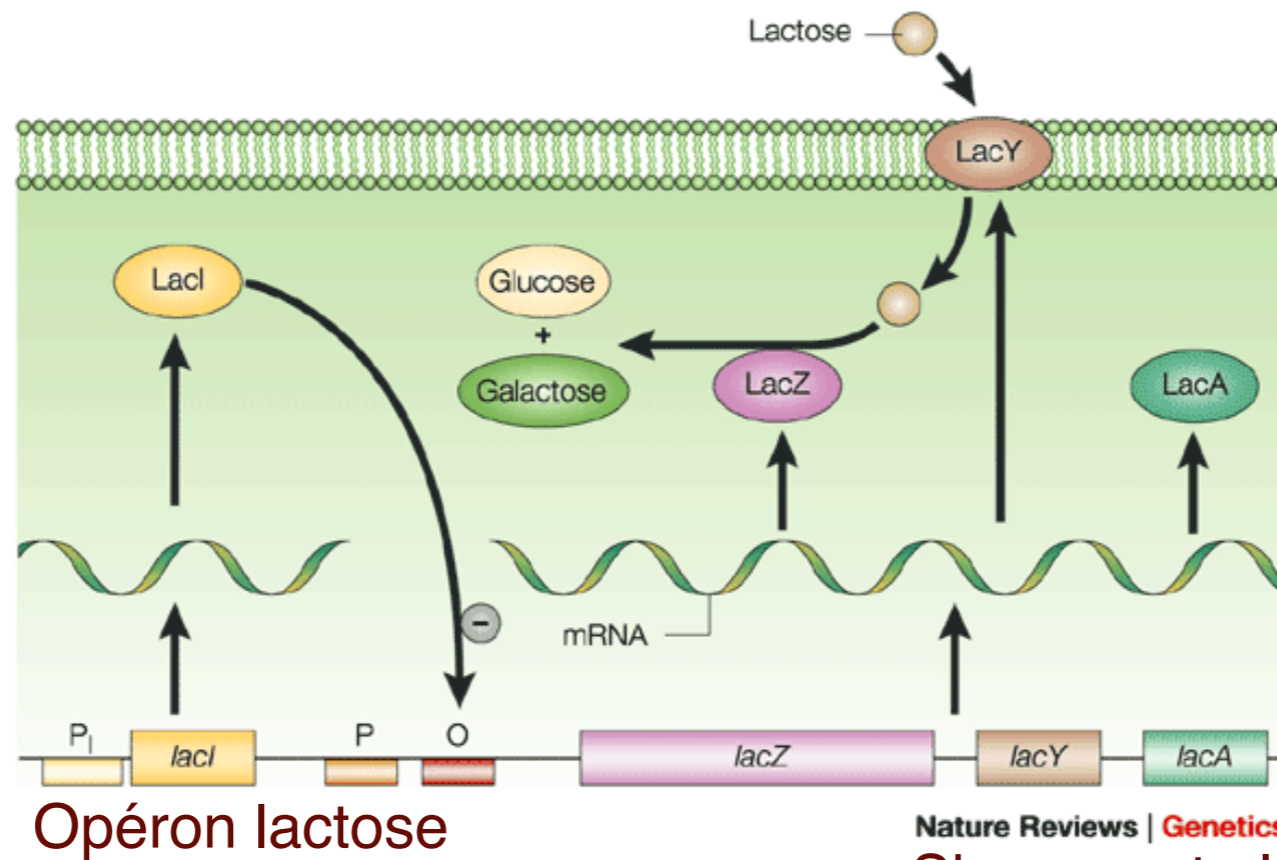


Metabolic Cycle



Gene Regulatory Networks

Operon / Regulatory networks



Opéron lactose

Nature Reviews | Genetics
Shuman et al.