

Network analysis

using  **Cytoscape**

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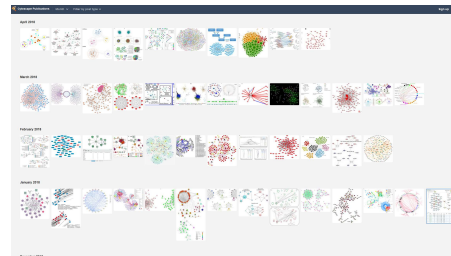
Outline

- Introduction to (biological) networks
 - Graph analysis
 - Properties of biological networks
 - PPI detection methods
- Cytoscape basics
 - Sources for PPI
 - Import & export
 - Selection and styling
 - data integration
 - Enrichments
- Hands-on examples

Widely studied networks

- [Biological networks](#)
- The internet
- Social networks

Molecular networks: most frequent application of Cytoscape



(Biological) networks

- Network: a system with sub-units that are linked into a whole
- Biological network: any network that applies to biological systems
- A mathematical representation of connections found in ecological/ evolutionary/ physiological studies

Graph: a structure of related objects

- $G = (V, E)$
- A set of V vertices/ nodes, with a set of E edges /arcs/ lines
- An edge is associated with two vertices
- Edges: directed, undirected, weighted



Network Representations

List

Protein1	Type	Protein2
ProteinA	pp	ProteinB
ProteinA	pp	ProteinD
ProteinC	pd	ProteinD
ProteinE	pp	ProteinG

Graph with nodes (proteins) and edges (connections)

Matrix (rows, columns)

	A	B	C	D	E	F	G
A	0	1	1	1	1	0	1
B	1	0	0	0	0	1	0
C	1	0	0	1	0	0	0
D	1	0	1	0	0	0	0
E	1	0	0	0	1	0	0
F	0	1	0	0	0	0	0
G	1	0	0	0	1	0	0

Graph theory: some definitions

Degree

Shortest path

Centrality

Molecular networks

- Metabolic networks
- Signalling networks
- Gene regulatory networks

Protein-protein interaction networks

- Protein-protein interactions: physical, selective, biological context dependent
- Interactome: All PPIs of an organism/ organ/ biological condition

Rapid Accumulation of PPI Data

Physical, non redundant protein-protein interactions
Taken from BioGrid stats, Feb. 2010 to Feb. 2018

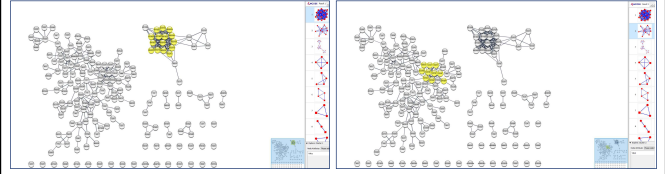
Information quantity - BioGrid

Name	Date modified	Type	Size
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BIOGRID-ORGANISM Homo_sapiens_3.4.118.mtab	3/30/2018 5:46:PM	Text Document	172,258 KB
BIOGRID-ORGANISM Drosophila_melanogaster_3.4.118.mtab	3/30/2018 5:19:PM	Text Document	82,262 KB
BIOGRID-ORGANISM Escherichia_coli_K12_MG1622_3.4.118.mtab	3/30/2018 5:20:PM	Text Document	78,913 KB
BIOGRID-ORGANISM Neurospora_crassa_strain_7242_3.4.118.mtab	3/30/2018 5:24:PM	Text Document	54,615 KB
BIOGRID-ORGANISM Arabidopsis_thaliana_Columbia_3.4.118.mtab	3/30/2018 5:20:PM	Text Document	52,174 KB
BIOGRID-ORGANISM Mus_musculus_3.4.118.mtab	3/30/2018 5:42:PM	Text Document	37,463 KB
BIOGRID-ORGANISM Caenorhabditis_elegans_3.4.118.mtab	3/30/2018 5:24:PM	Text Document	3,926 KB
BIOGRID-ORGANISM Rattus_norvegicus_3.4.118.mtab	3/30/2018 5:21:PM	Text Document	2,711 KB
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BIOGRID-ORGANISM Erwinia_rastrii_3.4.118.mtab	3/30/2018 5:23:PM	Text Document	35 KB

PPI networks properties

Small world effect
Scale free networks
High transitivity

Communities/ clusters/ modules

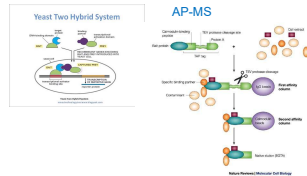
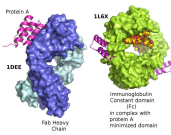


Respiratory electron transport chain

Lipid homeostasis

PPI detection methods

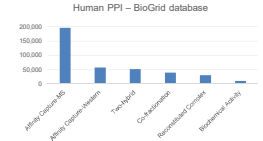
Low throughput, small scale, high resolution → High throughput, large scale, low resolution



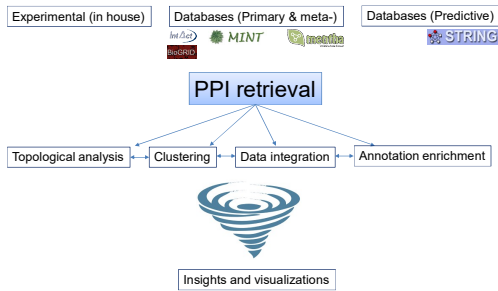
PPI detection methods

197,019
57,106
51,225
39,088
29,827
10,483

Affinity Capture-MS
Affinity Capture-Western
Two-hybrid
Co-fractionation
Reconstituted Complex
Biochemical Activity



Building and analyzing PPINs




The Era of Network Biology




- Parts list
- Blueprint
- Diagnostic tools
- Replace Parts
- Genomics
- Network Medicine
- Metabolomics, proteomics
- Gene Therapy

Part 2




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Added value: Network Environment

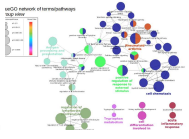
- Visualization
- Relationship between genes and gene sets
- Graph analysis tools
- Data integration
- Open-source, apps

Basic Cytoscape Workflow



Expression
Network
Annotation

Enrichments
Graph analysis

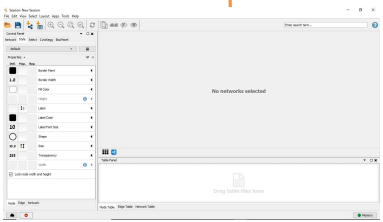


Outline

- ➔ Retrieving networks
- Selection and filtering
- Layouts, clustering
- ➔ Data integration
- Styles
- ➔ Enrichments

➔ Can be done outside Cytoscape

Initial window



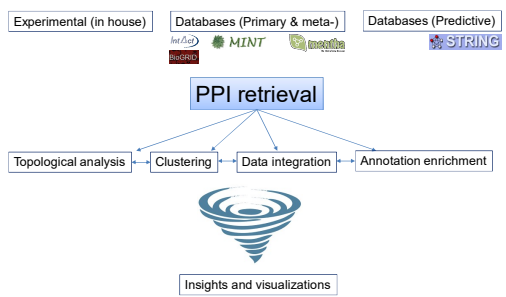
Toolbar: with command buttons, name is shown when mouse hovers

Control Panel: Network, style, select

Network Panel: opens with links to demos

Table Panel: node, edge, and network data

Building and analyzing PPIs



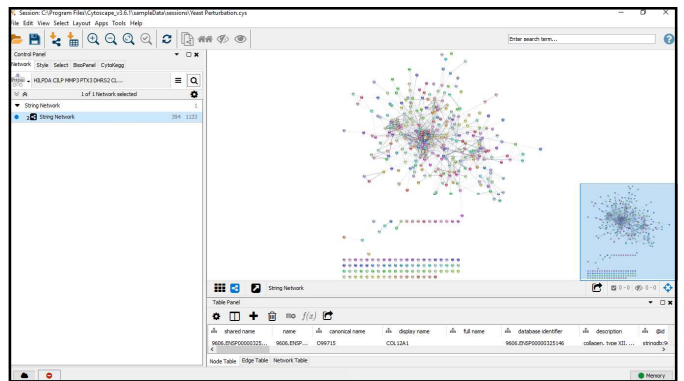
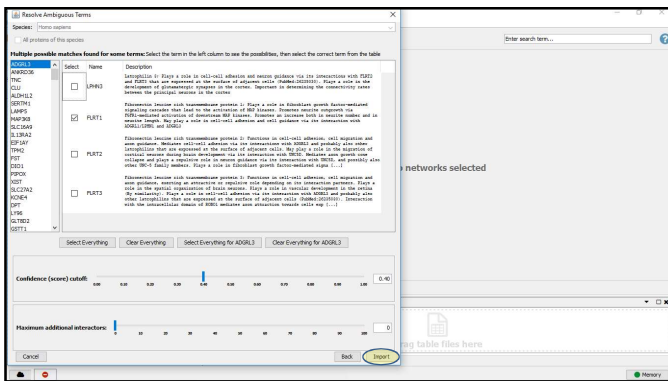
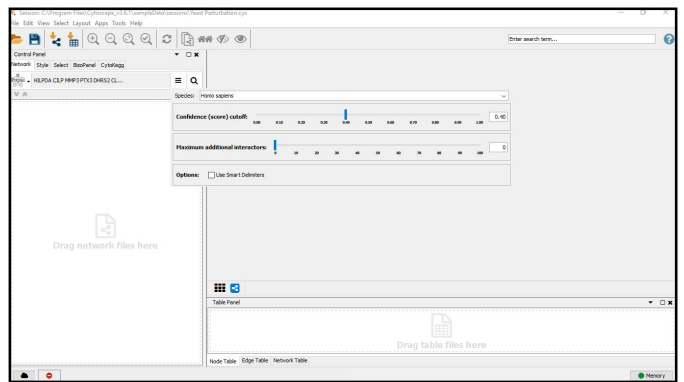
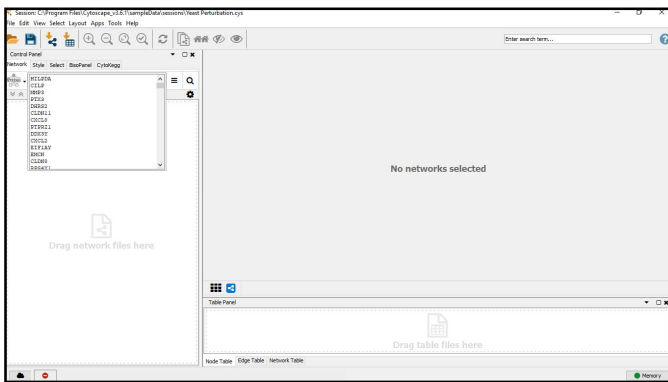
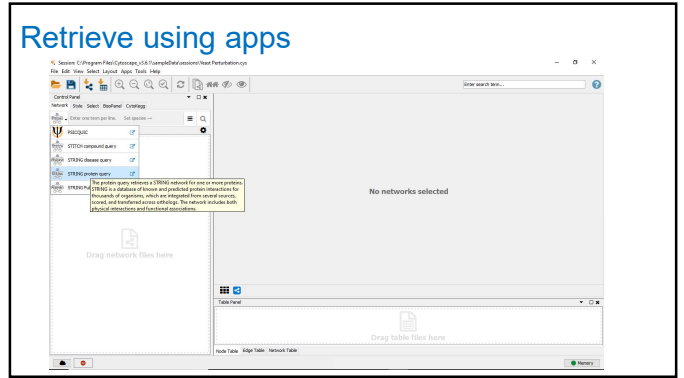
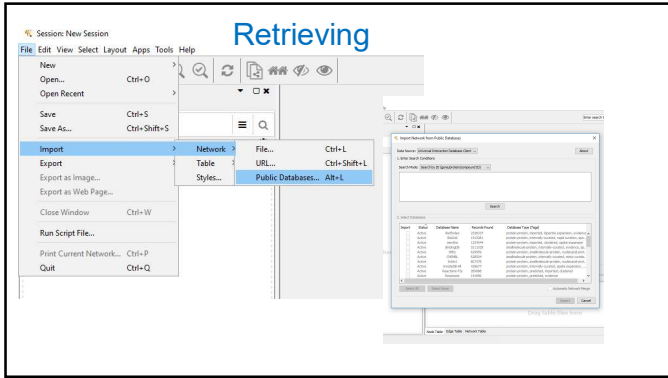
Experimental (in house) | Databases (Primary & meta-) | Databases (Predictive)

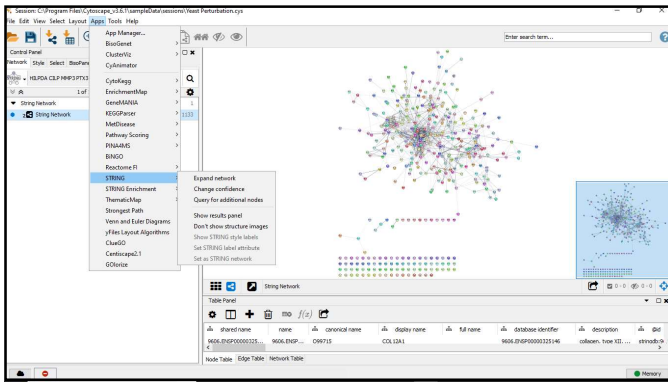
bioGRID | MINT | metaMINT | STRING

PPI retrieval

Topological analysis | Clustering | Data integration | Annotation enrichment

Insights and visualizations





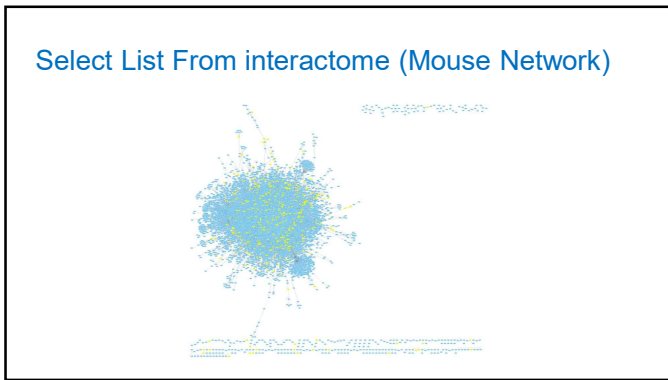
Selection/ filtering

- By column, degree, or topology

Selection by column (nodes/ edges)

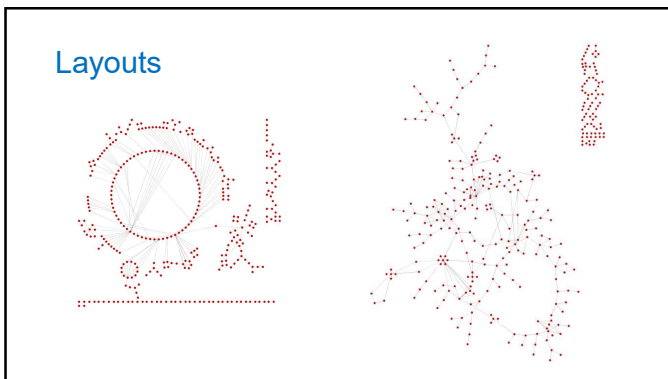
See topology
Stylize

Make new network



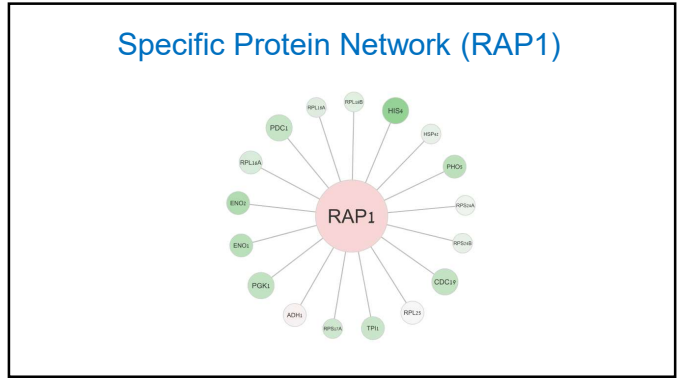
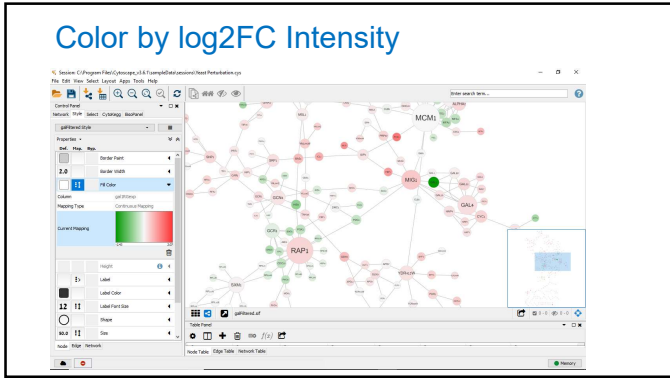
Selection of Up-regulated

The screenshot shows the STRING database interface. A red box highlights the 'Up-regulated' filter in the 'Filter' section. The network graph shows nodes and edges, with some nodes highlighted in yellow. Below the graph, there is a table with columns: 'name', 'accession name', 'display name', 'EJ name', 'database identifier', 'description', and 'ID'.



Network Analyzer+ Node Size by Degree

The screenshot shows the Network Analyzer+ interface. The network graph has nodes of varying sizes, where larger nodes represent a higher degree. Labels like 'MCM1', 'MGI1', 'GAL4', 'RAP1', and 'TOR1A1B' are visible on the graph.



Cytoscape Applications

Cytoscape App Store

All Apps

Categories

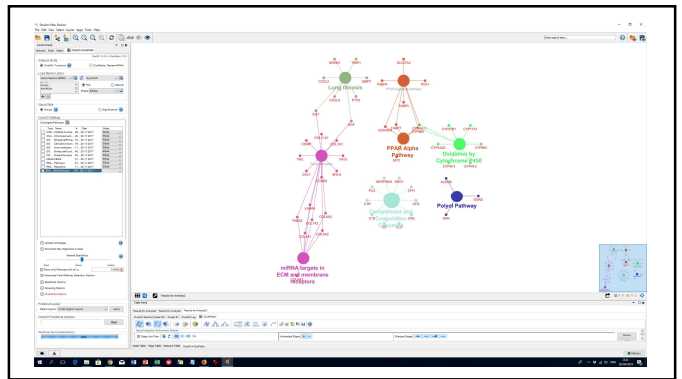
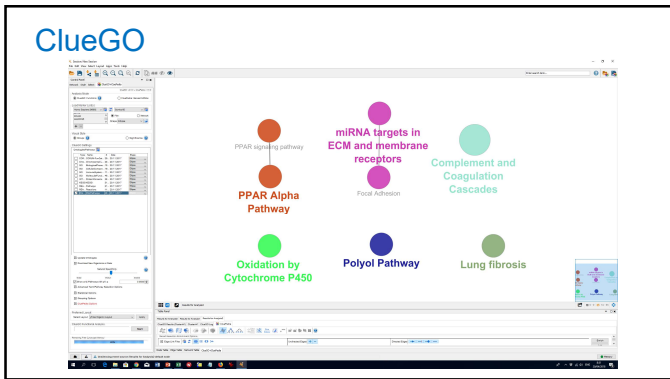
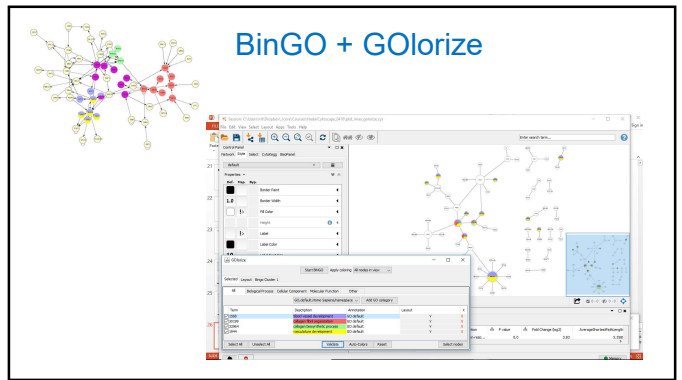
- collections
- data visualization
- network generation
- graph analysis
- network analysis
- online data import
- integrated analysis
- clustering
- systems biology
- layout
- data integration
- enrichment analysis
- visualization
- core app
- network comparison

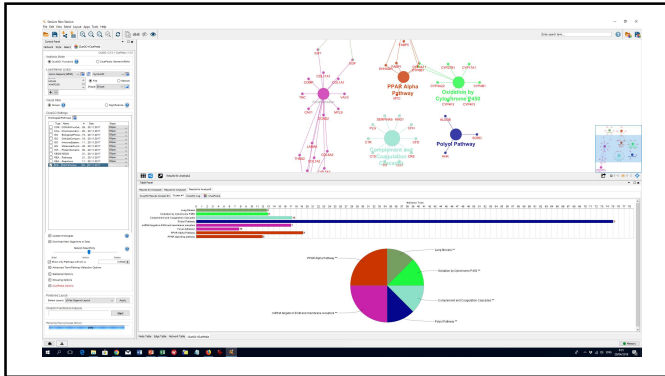
Data visualization

Search for posts about data visualization →
Ask a question about data visualization →

Sort by Name | downloads | votes | newest release

- codApp**: Integration between Cytoscape and the NCBI Conserved Domain
- CHAT**: Identify contextually relevant hubs in biological networks
- ClueGO**: Creates and visualizes a functionally grouped network of
- clusterMaker2**: Multi-algorithm clustering app for Cytoscape
- cy3html**: cy3html visualizes SEMM models (Systems Biology Markup)
- cyBrowser**: Core App: Add HTML Browser to Cytoscape





General tips

- For heavy applications can be slow and memory consuming (yet always improving)
- Save sessions and views
- Sometimes there is inconsistency between Linux/Windows