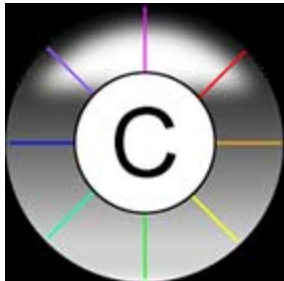
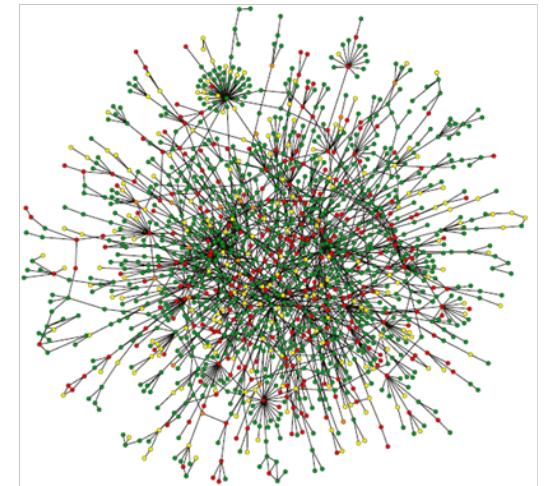


Visualizing Networks: Cytoscape



Prat Thiru



Outline

- Introduction to Networks
- Network Basics
- Visualization
- Inferences
- Cytoscape
- Demo

Why (Biological) Networks?

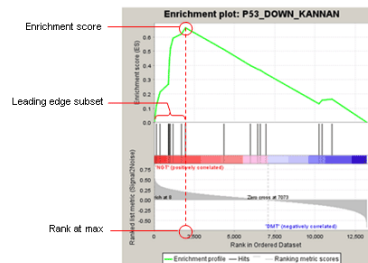
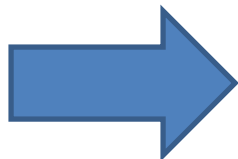
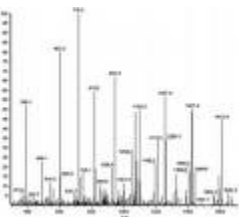
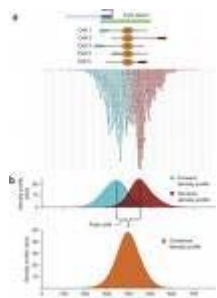
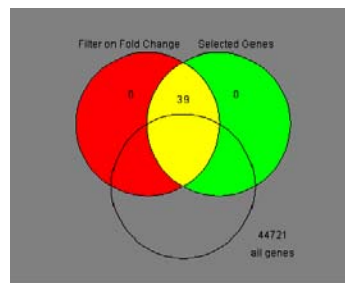
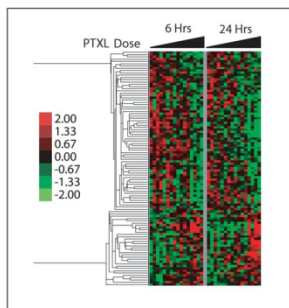
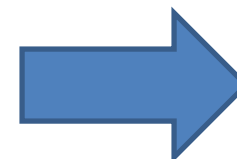
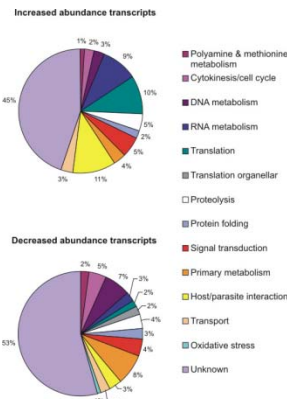
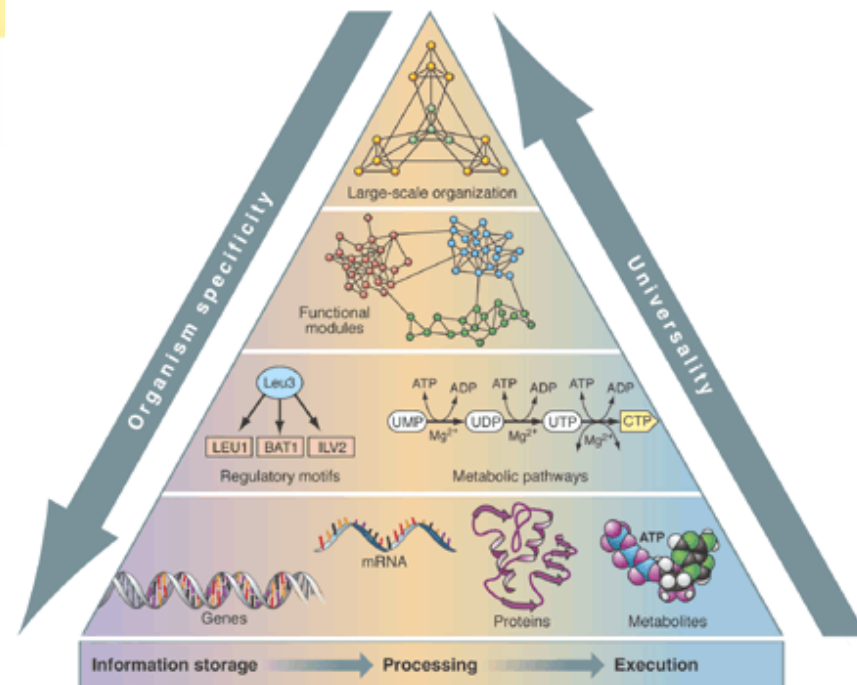
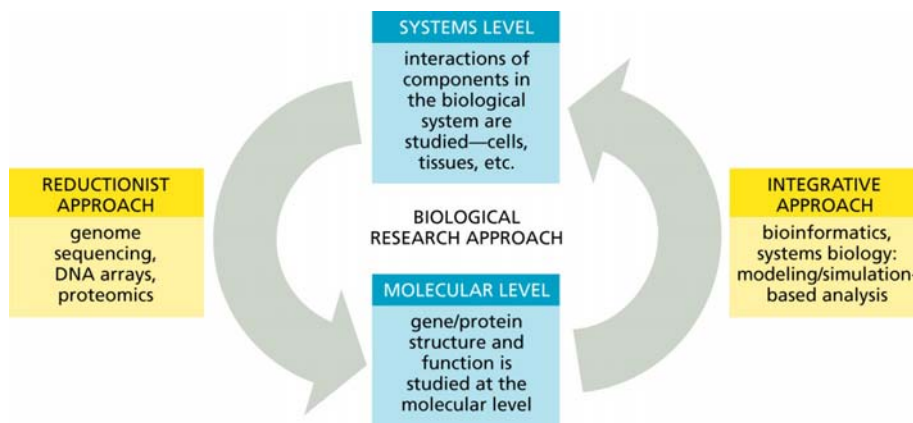


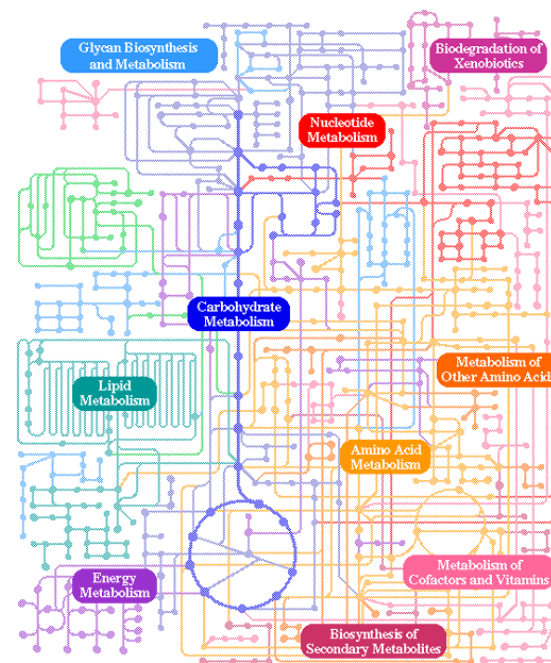
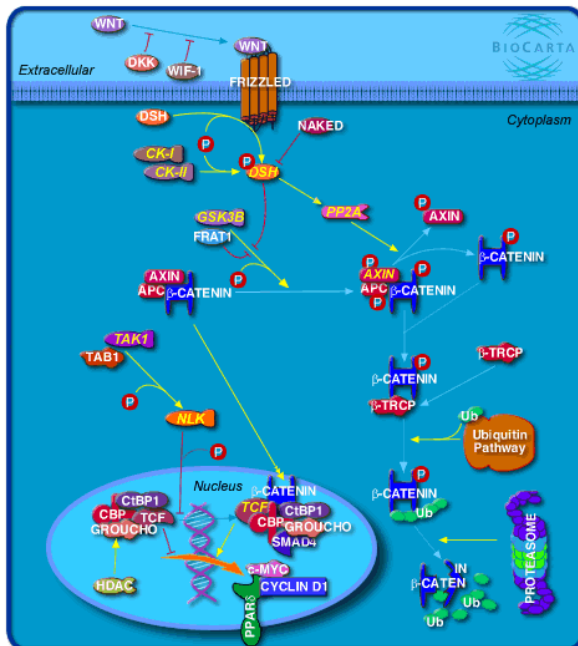
Fig 1: Enrichment plot: P53_DOWN_KANNAN
 Profile of the Running ES Score & Positions of GeneSet Members on the Rank Ordered List



Networks: An Integrative Approach



Examples



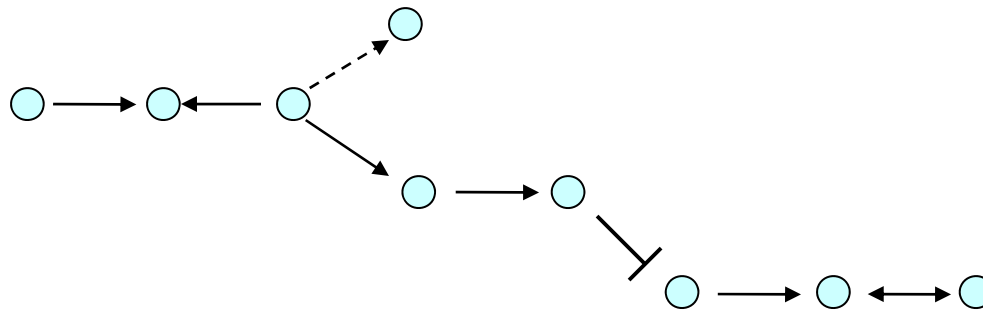
01100 5/5/04 Image source from KEGG

What are Networks?

- Representation of relationships
 - Physical Interactions
 - Regulatory Interactions
 - Genetic Interactions
 - Similarity Relationships

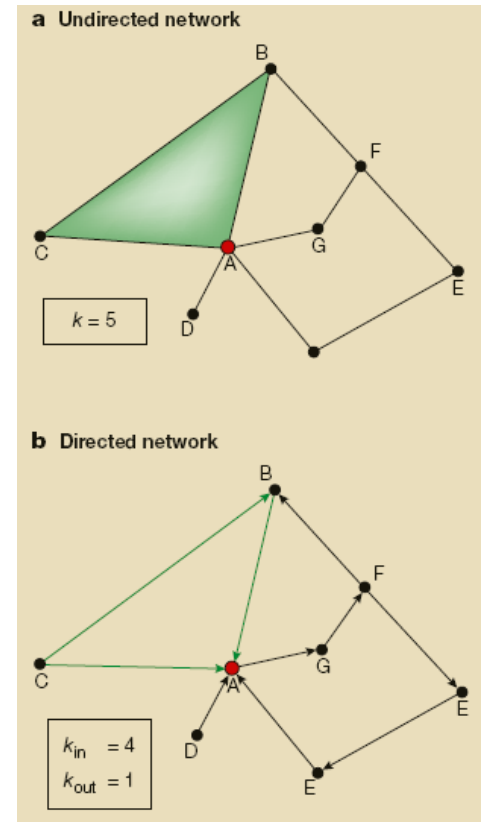
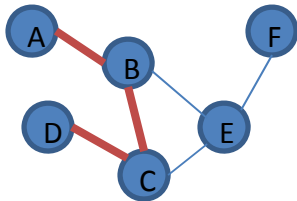
Network Basics

- Graphs with nodes (or vertices) and edges
- Nodes: Proteins, Genes, RNA, or other biomolecule
- Edges: nature of interaction



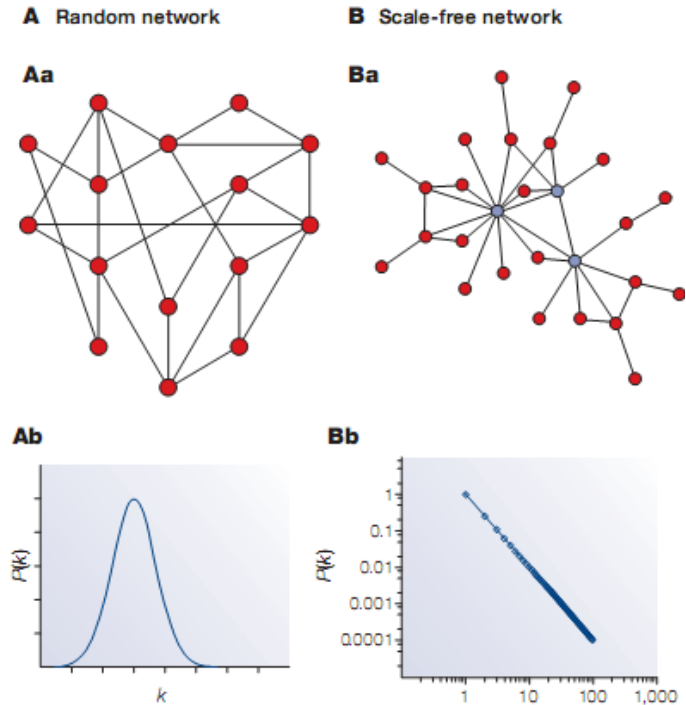
Network Basics

- Directed vs Undirected Network
- Degree (k): number of links the node has to other nodes
 - Incoming degree k_{in}
 - Outgoing degree k_{out}
- Shortest Path: fewest links or edges between two nodes



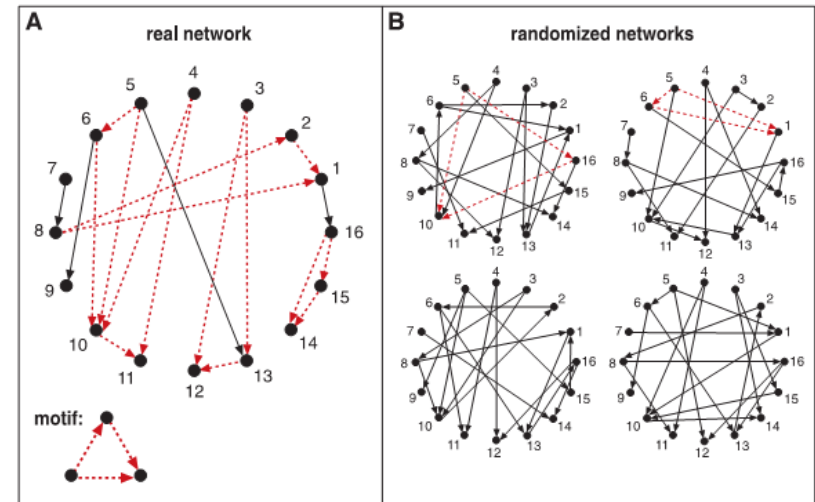
Network Basics: Biological Network Properties

- Scale-free
 - degree distribution follows the power-law
 - few highly interconnected nodes
- Small-world
 - most nodes can be reached from every other by a small number of steps
- Modular
 - group of physically or functionally linked molecules that work together to achieve a distinct function



Network Basics: Motifs

- A pattern that occurs more often than in randomized networks
- eg. feed-forward loop



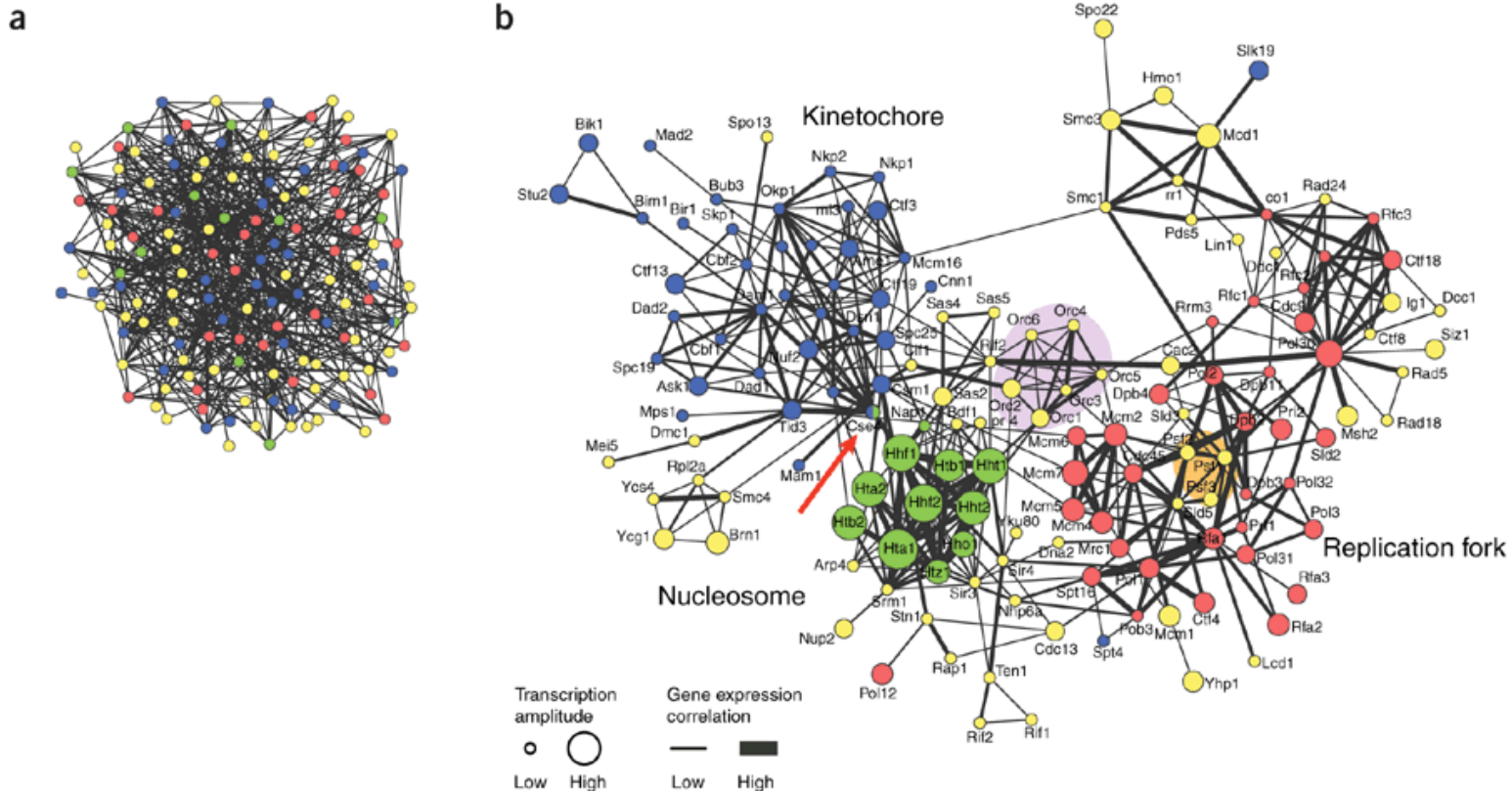
Visualization: Layout

- Use layout algorithm
 - Force-directed
 - Spring-embedded
- Most visualization software contains many layout options
- Large networks with many edges/nodes results in *hairball* – breakdown the network into smaller parts.

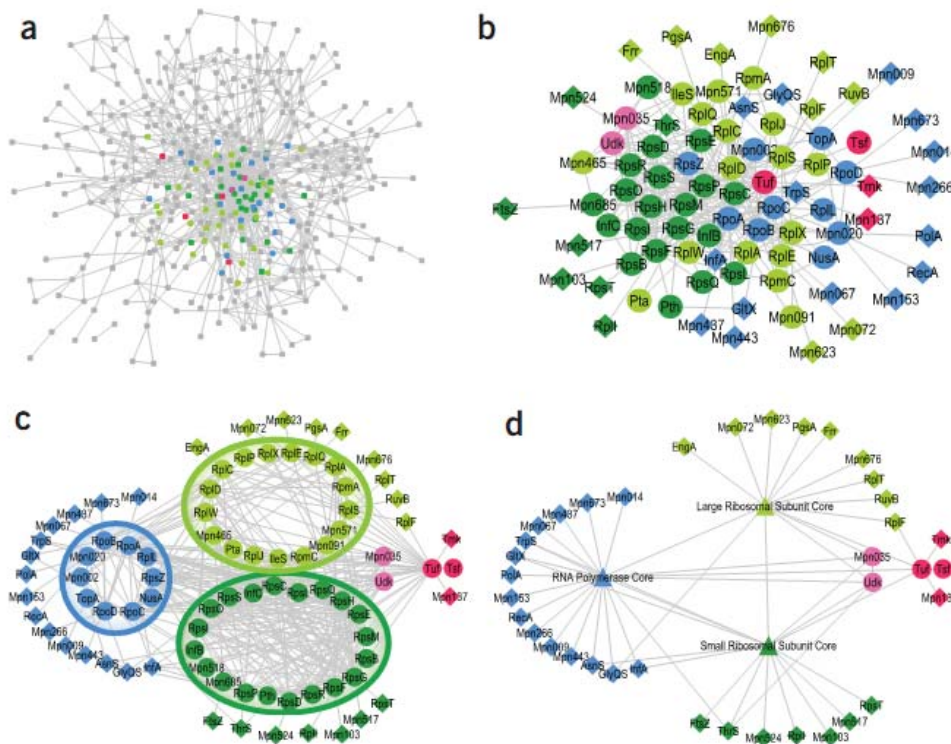
Visualization: Features

- Draw edges and nodes with different visual features (eg. shapes, colors, sizes, edge thickness)
- Examples:
 - Node color to represent cellular localization
 - Protein colored based on similar function
 - Edge thickness based on correlation data

Visualization: Layout and Features



Visualization: Layout and Features



Inferences of Networks

- Protein Function Prediction
 - *guilt by association*
 - Infer protein function based on interactions
 - Neighboring nodes should be annotated
- Highly Interconnected Nodes
 - hubs
 - dense cluster => characteristic of protein complexes or pathways
 - Indispensable
- Global System Relationships

Limitations

- Difficult to capture temporal and concentration information in a static representation
- All relationships might not be represented in pairwise edges

Cytoscape

- Freely available open source Java-based software for visualizing and analyzing network
- Made public in July 2002
- Latest version is 2.7.0
- Win/Mac/Linux
- Easy to install
- 918 citations (Apr 2010)
- Core functions:
 - network layout and querying
 - expression profile integration
 - linking of network to different databases
- Additional functionality by plugins
 - <http://www.cytoscape.org/plugins2.php>

Cytoscape Consortium



Cytoscape

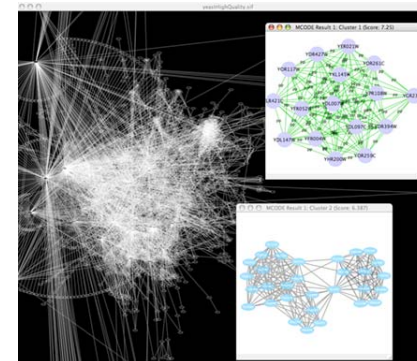
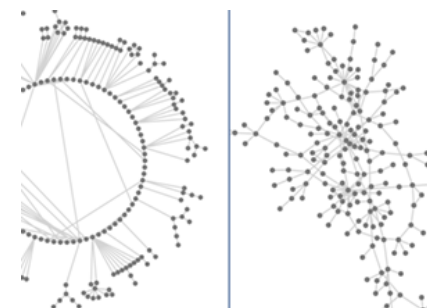
File Formats



Web Service Clients



Visualization



Network Visualization Software

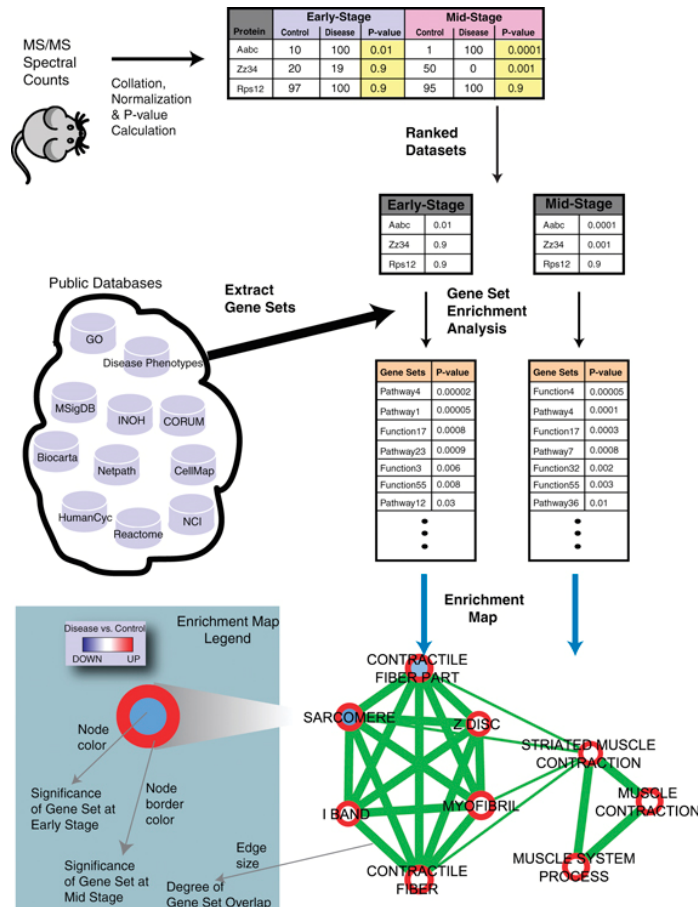
Name	Cost	Description	URL
BioLayout Express 3D	Free	Generation and cluster analysis of networks with 2D/3D visualization	http://www.bioblayout.org/
BiologicalNetworks	Free	Analysis suite; visualizes networks and heat map; abundance data	http://www.bioblogicalnetworks.org/
Cytoscape	Free	Network analysis; extensive list of plug-ins for advanced visualization	http://www.cytoscape.org/
Ingenuity Pathways	\$	Full analysis suite; network and pathway a	http://www.ingenuity.com/pathwaya
Medusa	Free	Basic network visualization tool	http://coot.embl.de/medusa/
GeneGO	\$	Full analysis suite; network and pathway visualizations	http://www.genego.com/
Ondex	Free	Integrative workbench: large network visualizations; abundance data	http://www.ondex.org/
Osprey	Free	Tool for visualization of interaction networks	http://tinyurl.com/osprey1/
Pajek	Free	Generic network visualization and analysis tool	http://pajek.imfm.si/
ProViz	Free	Software for visualization and exploration of interaction networks	http://tinyurl.com/proviz/

Visualization Tools Comparison

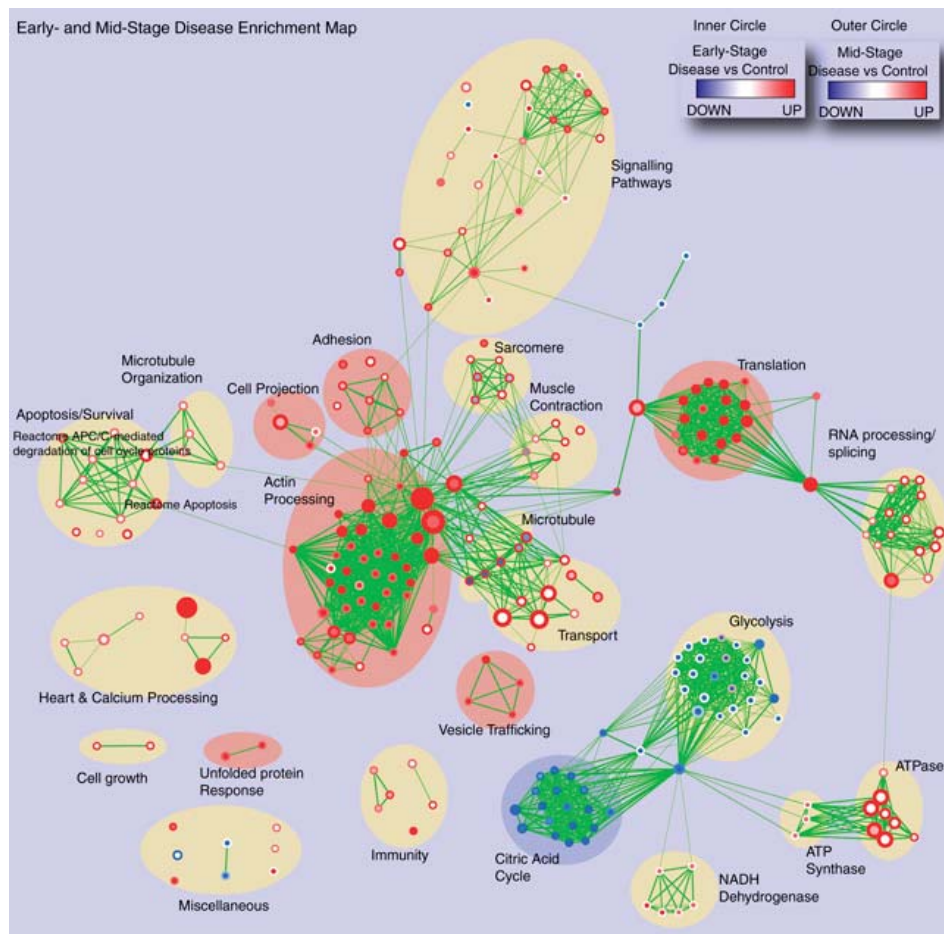
Feature	CY	GM	VA	OS	CD	AR	IN	GG	PI	PR	BL	PA
Free for academic use	✓	✓	✓	✓	✓				✓	✓	✓	✓
Free for commercial use	✓	✓	✓		✓				✓	✓	✓	
Open source	✓	✓							✓	✓	✓	
Curated pathway/network content		✓		✓		✓	✓	✓				
Standard file format support	✓		✓		✓				✓	✓		✓
User-defined networks/pathways	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Functionality to infer new pathways	✓		✓			✓		✓	✓			
GO/pathway enrichment analysis	✓	✓	✓				✓	✓				
Automated graph layout	✓		✓	✓	✓	✓	✓	✓			✓	✓
Complex criteria for visual properties		✓				✓	✓	✓			✓	✓
Multiple visual styles	✓		✓	✓		✓	✓	✓			✓	✓
Advanced node selection	✓		✓	✓		✓	✓	✓	✓	✓	✓	✓
Customizable gene/protein database		✓	✓			✓		✓	✓			
Rich graphical annotation		✓	✓				✓	✓				✓
Statistical network analysis	✓		✓				✓	✓	✓		✓	
Extensible functionality: plugins or API	✓		✓		✓	✓	✓	✓	✓			
Quantitative pathway simulation					✓	✓						

CY, Cytoscape³¹; GM, GenMAPP²⁶; VA, VisANT²⁴; OS, Osprey²³ (<http://biodata.mshri.on.ca/osprey/>); CD, CellDesigner²⁵; AR, Ariadne Genomics Pathway Studio; IN, Ingenuity Pathways Analysis; GG, GeneGo; PI, PIANA (<http://sbi.imim.es/piana/>); PR, ProViz (<http://cbi.labri.fr/eng/proviz.htm>); BL, BioLayout; PA, PATIKA.

Cytoscape Example



Cytoscape Example



Pathway Databases

- BioCyc
 - <http://biocyc.org/>
- Kyoto Encyclopedia of Genes and Genomes (KEGG)
 - <http://www.genome.jp/kegg/>
- Pathguide
 - <http://www.pathguide.org/>
- Reactome
 - <http://www.reactome.org/>

Demo

- Uploading Network
- Adding annotation
- Viewing gene expression data
- BiNGO plugin