
Acronyms

1. Introduction to complex systems and networks
2. Types of networks
3. Structural properties of networks
4. Network models

TYPES OF NETWORKS

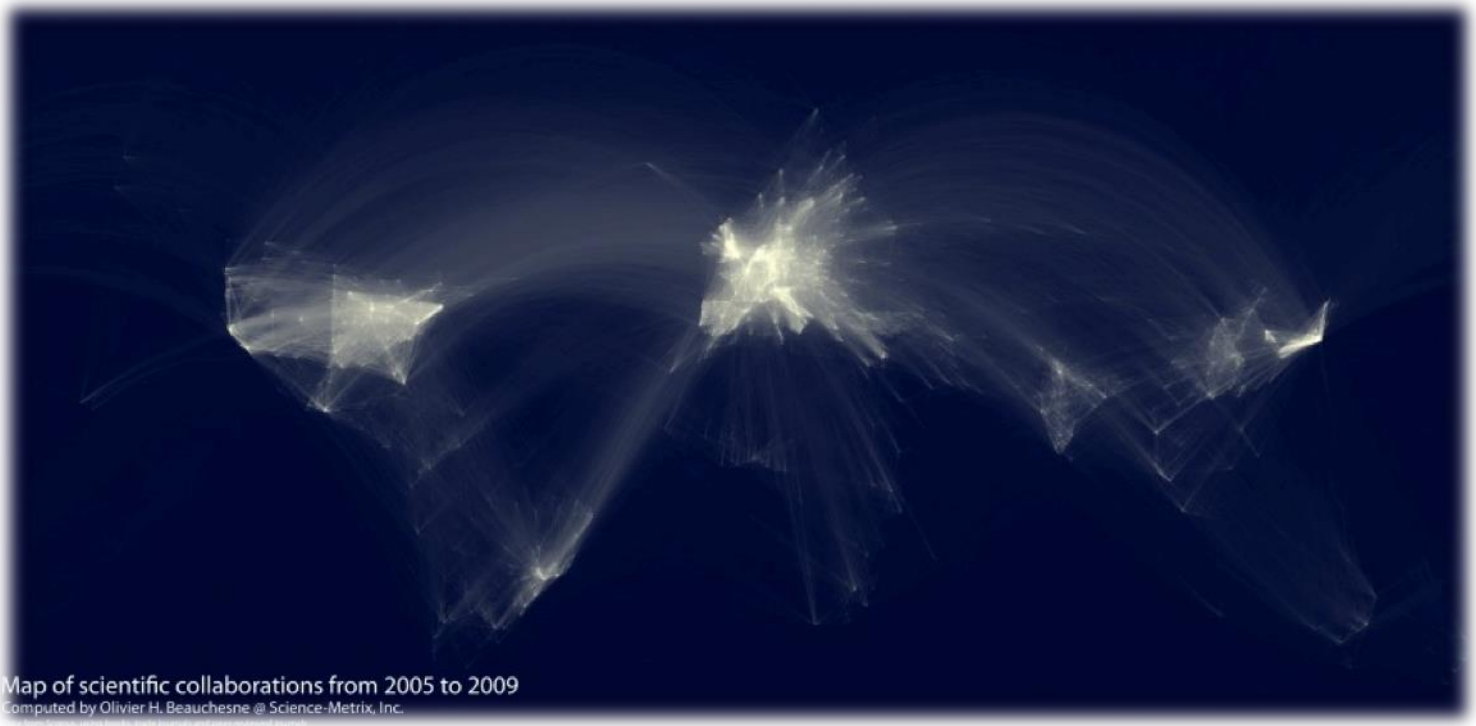
SOCIETY | **Factoid:** **A. Social network**

The “Social Graph” behind Facebook

MAP OF SCIENTIFIC COLLABORATIONS

B. Information network

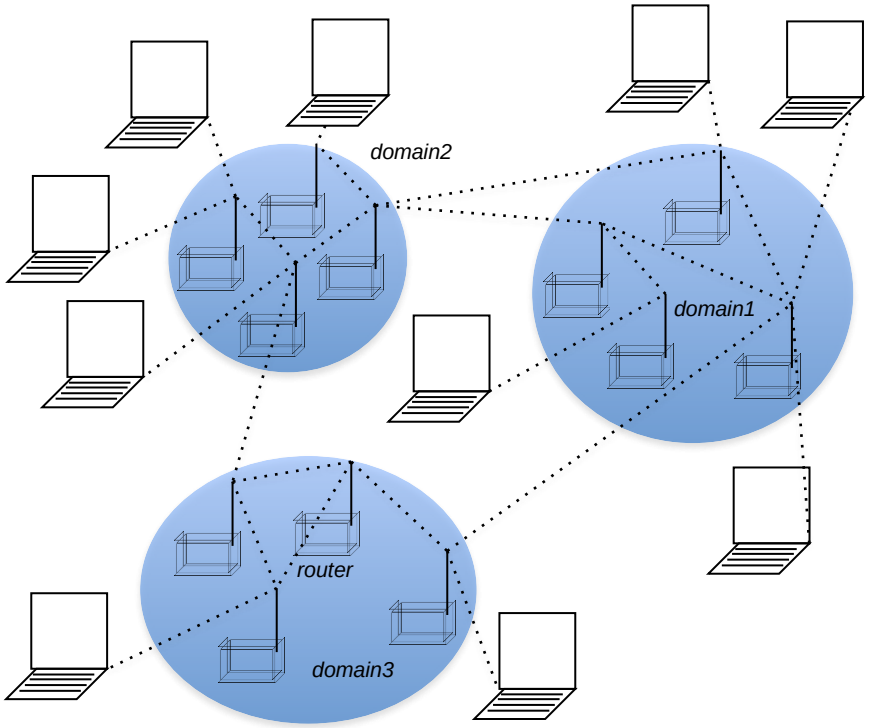
Citation Network



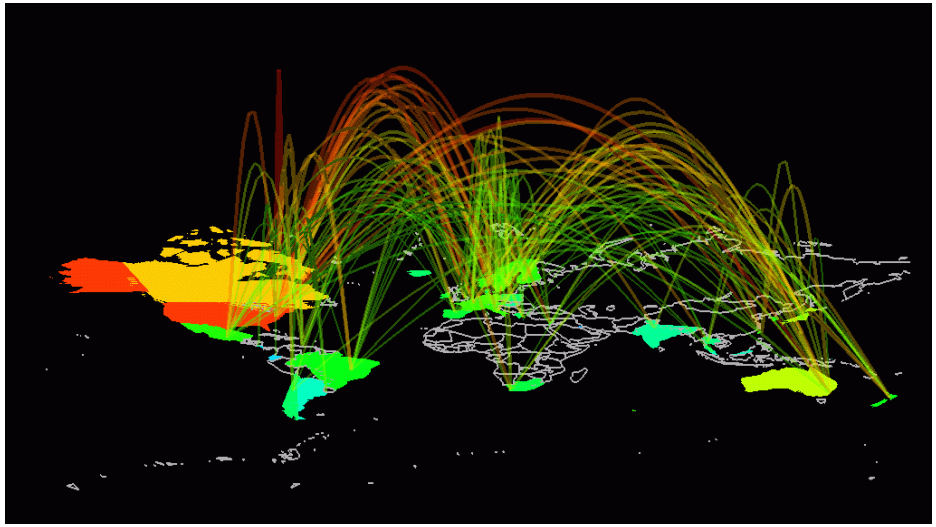
Beauchesne, Olivier H. *Map of Scientific Collaborations* from 2005 to 2009

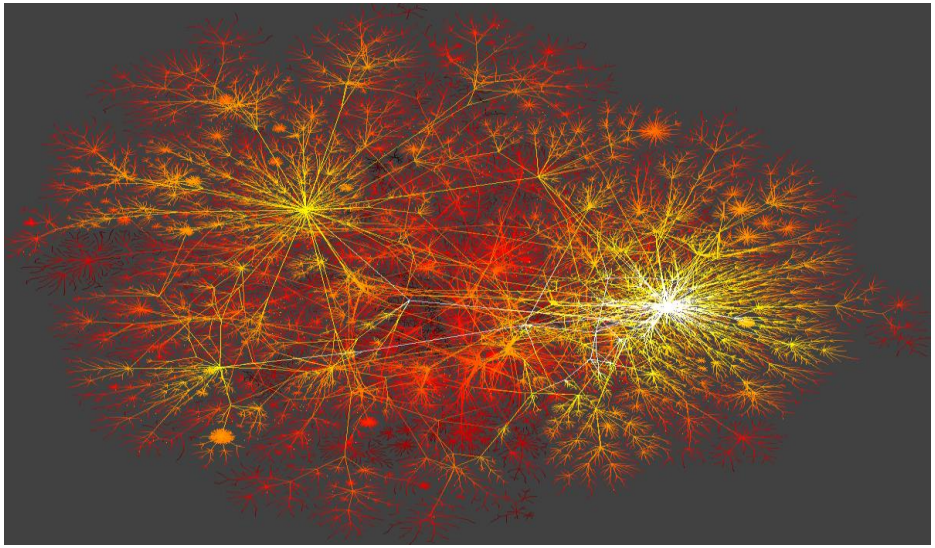
INTERNET

B. World Wide Web Network



World-wide internet traffic





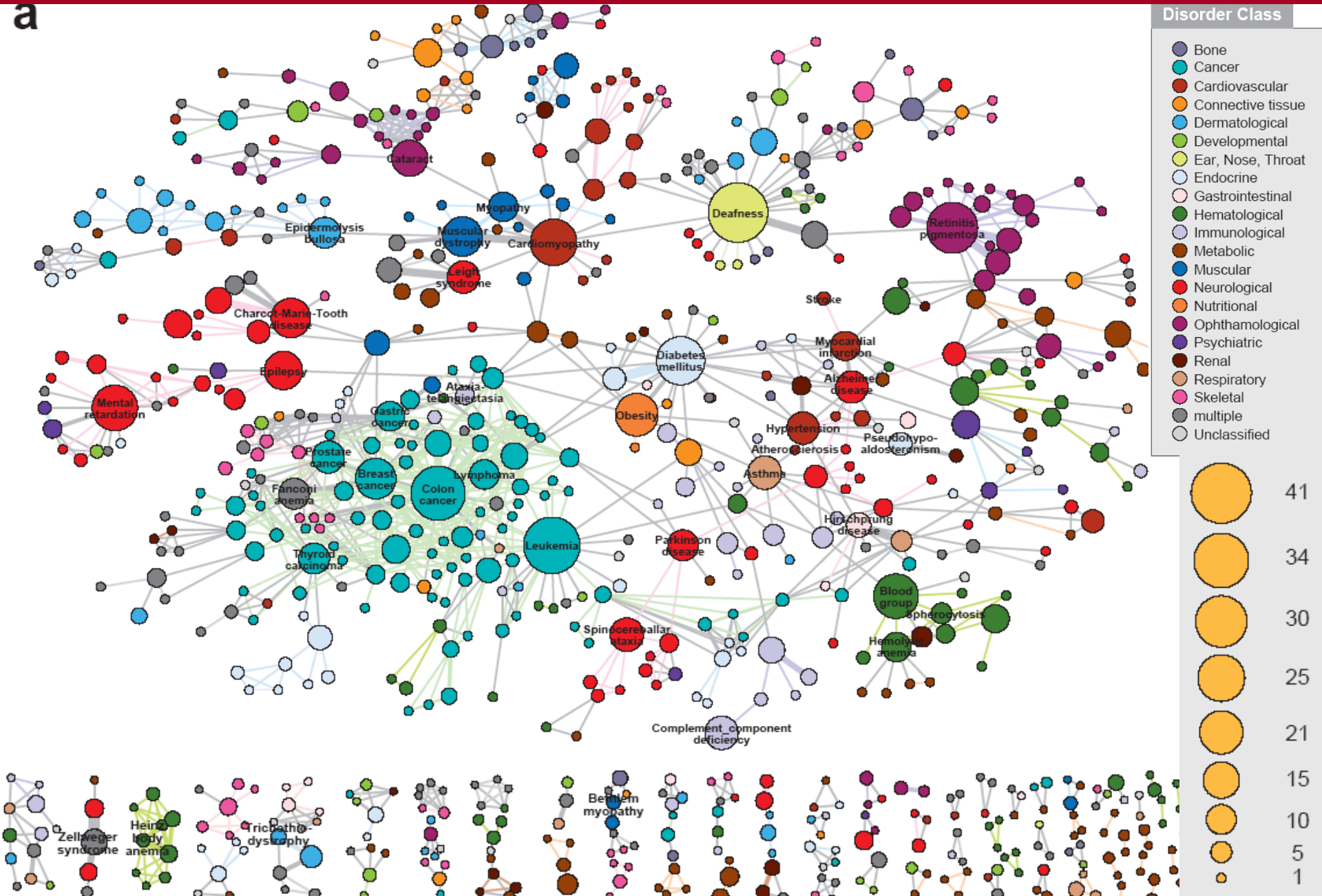
Internet connectivity


IMPACT

THE TOOLS OF MODERN NETWORK THEORY

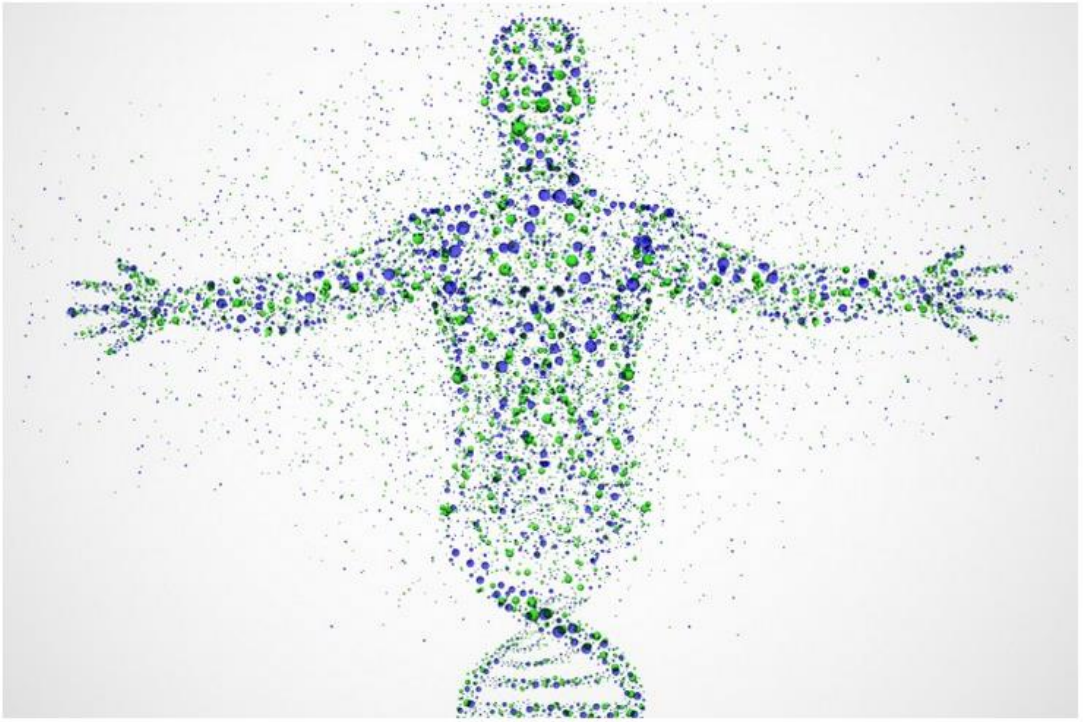
- Graph theory
- Social network theory
- Statistical physics
- Computer science
- Biology
- Statistics

HUMAN DISEASE NETWORK



Northeastern researchers connect diseases based on their molecular similarities

February 23, 2015 by Northeastern News



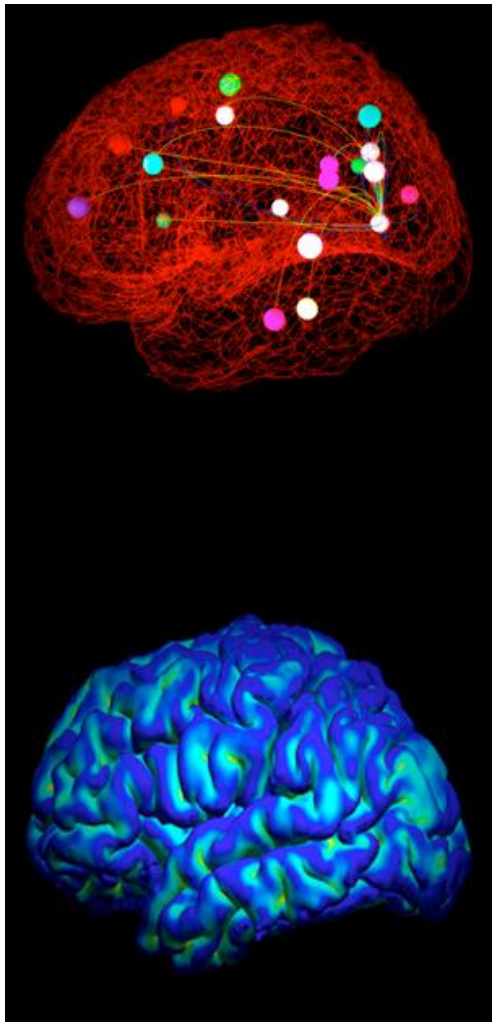
Menche offered an example of the power of the network map, explaining that doctors typically diagnose patients based on symptoms described by the patient. But using the network map, he said, could make it possible to find out what is happening in the gene product interactions to cause the particular ailment.

BRAIN RESEARCH

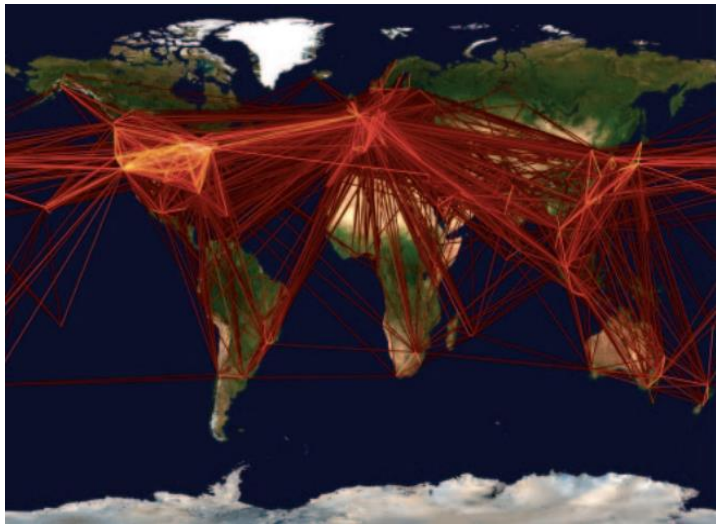
In September 2010 the National Institutes of Health awarded $40 million to researchers at Harvard, Washington University in St. Louis, the University of Minnesota and UCLA, to develop the technologies that could systematically map out brain circuits.

The Human Connectome Project (HCP) with the ambitious goal to construct a map of the complete structural and functional neural connections in vivo within and across individuals.

http://www.humanconnectomeproject.org/overview/

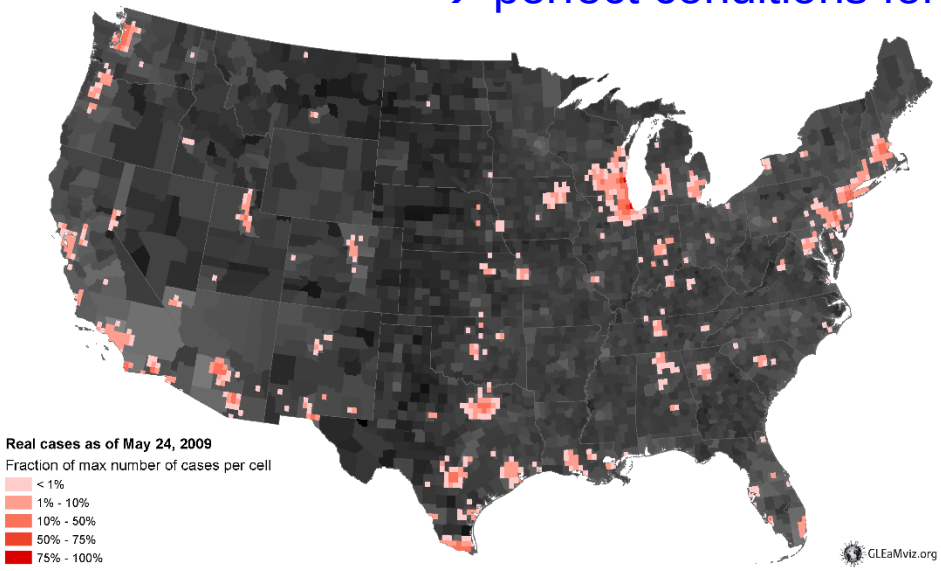


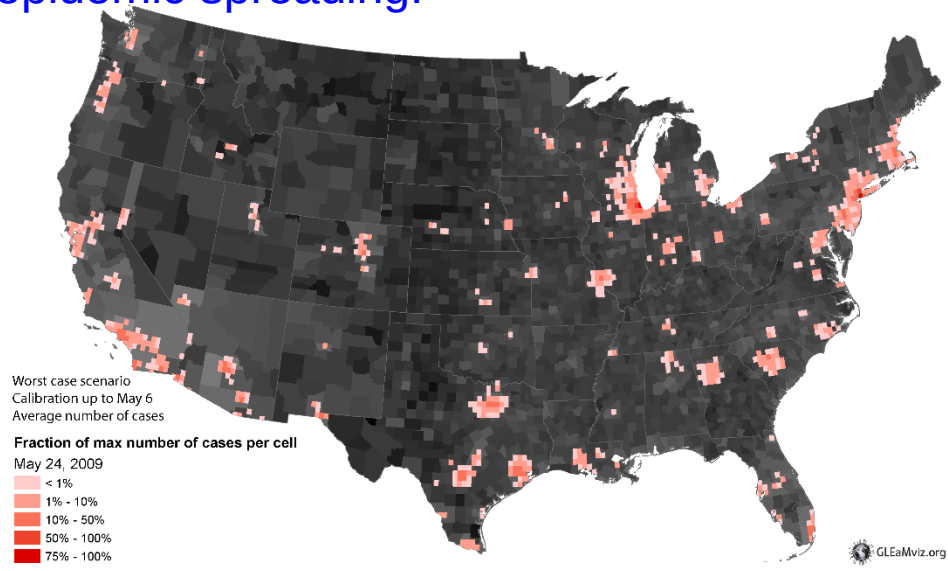
Real



Projected

→ perfect conditions for epidemic spreading.





Alessandro Vespignani
Vittoria Colizza

https://www.youtube.com/watch?v=5uEBl2x78SI

Local Researchers Forecast Spread Of Ebola

November 17, 2014 8:25 PM **By Christina Hager**

Filed Under: CBS Boston, Christina Hager, Ebola, Northeastern University, UMass Memorial Medical Center, WBZ

A Northeastern University researcher tracks the spread of Ebola. (WBZ-TV)

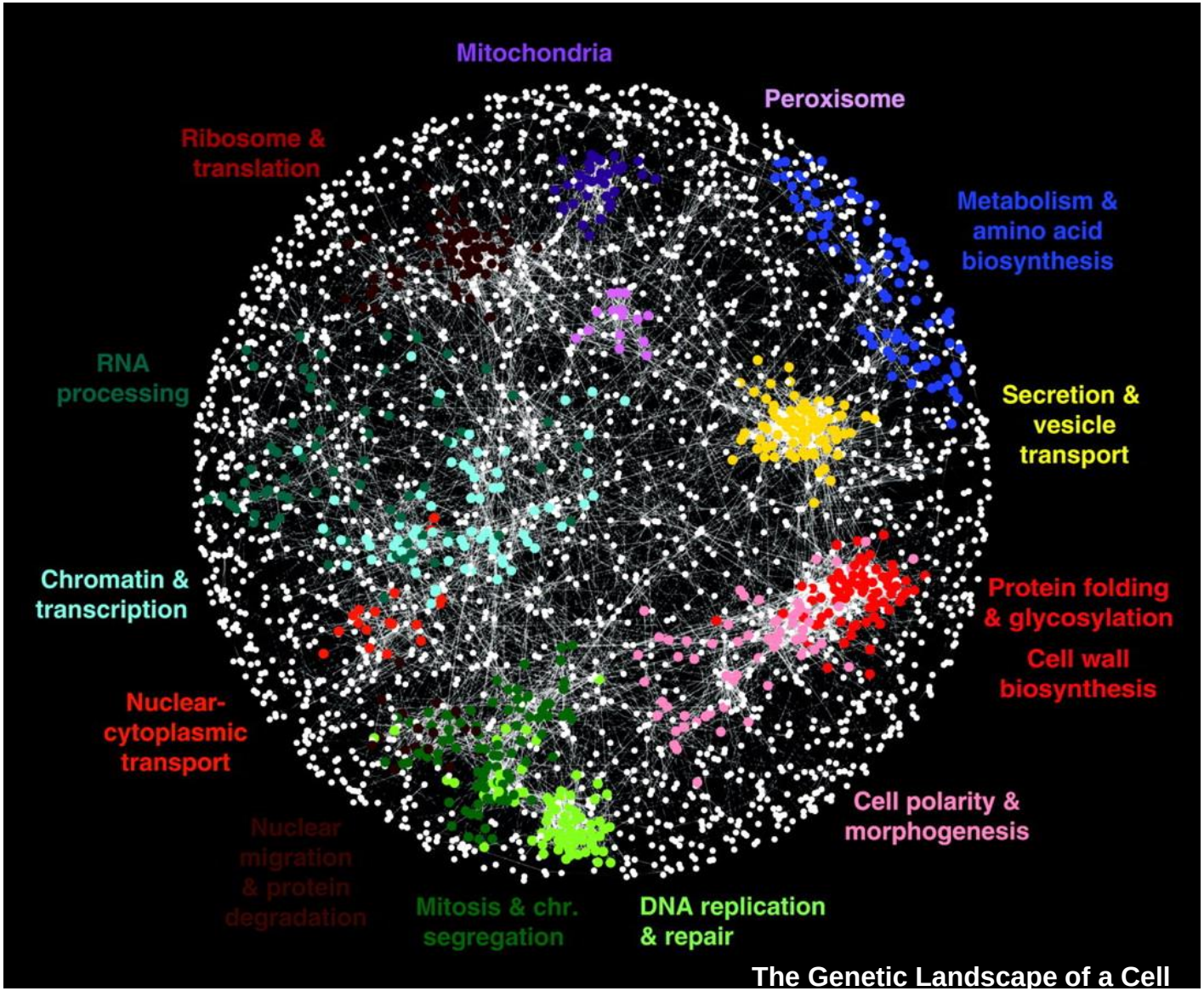
BOSTON (CBS) — Don't be surprised if there are a few more Ebola cases in the United States in the next couple months.

That's according to a Northeastern University researcher who's created a forecasting map to predict the spread of the deadly disease. He warns it's not an exact science, and says a vaccine could change everything.

"We have projections for one or two cases at the most during November, December," Alessandro Vespignani said.

GENE NETWORK

A correlation-based network connecting genes with similar genetic interaction profiles



STRUCTURAL PROPRIETIES OF NETWORKS

Here we define the most basic network measures that allow us to compare and characterize different complex networks.

NETWORKS OR GRAPHS?

network often refers to real systems

- www,
- social network
- metabolic network.

Language: (Network, node, link)

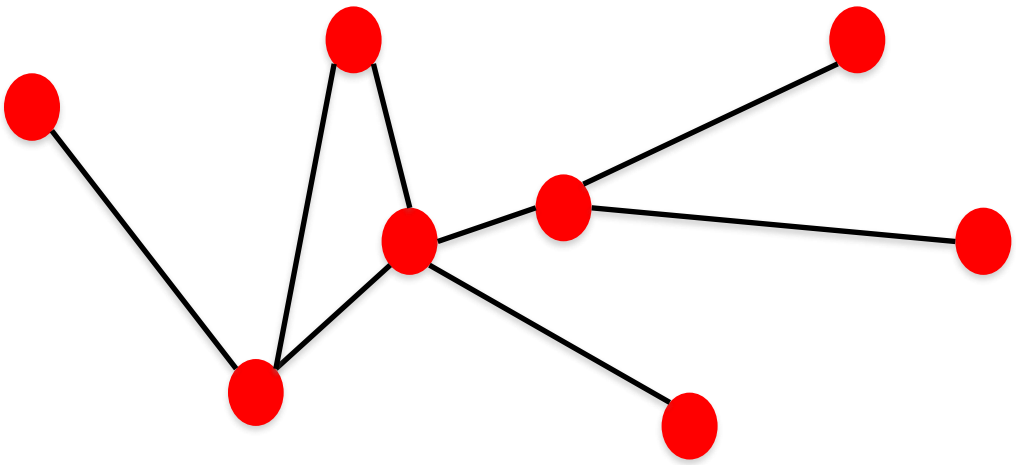
graph: mathematical representation of a network

- web graph,
- social graph (a Facebook term)

Language: (Graph, vertex, edge)

Graph theory-the field of mathematics that deal with mathematical foundations of networks

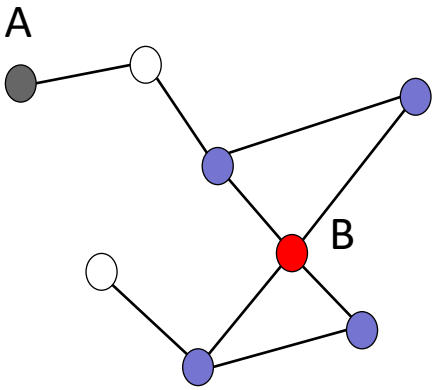
COMPONENTS OF A COMPLEX SYSTEM



- **components**: nodes, vertices N
- **interactions**: links, edges L
- **system**: network, graph (N, L)

GRAPH PROPERTIES: NODE DEGREES

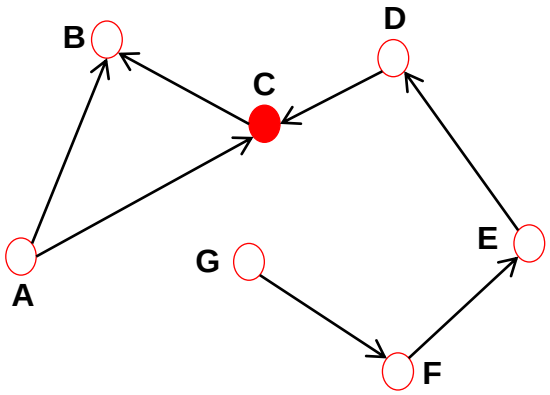
Undirected



Node degree: the number of links connected to the node.

$$k_A = 1 \qquad k_B = 4$$

Directed



In *directed networks* we can define an in-degree and out-degree. The (total) degree is the sum of in- and out-degree.

$$k_C^{in} = 2 \qquad k_C^{out} = 1 \qquad k_C = 3$$

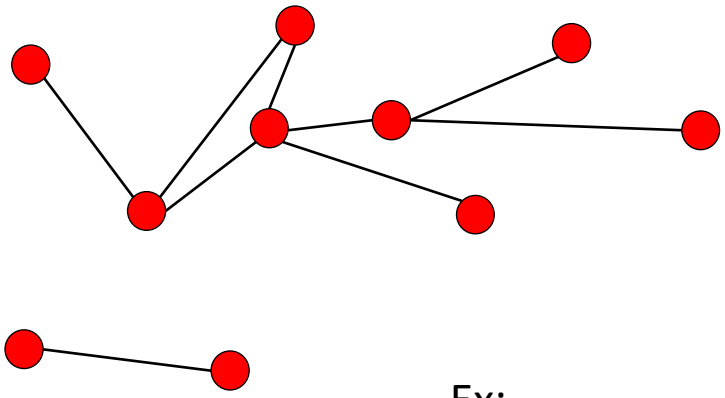
Source: a node with $k^{in} = 0$; Sink: a node with $k^{out} = 0$.

GRAPH PROPERTIES: DEGREE DISTRIBUTION

Degree distribution P(k): probability that a randomly chosen vertex has degree k

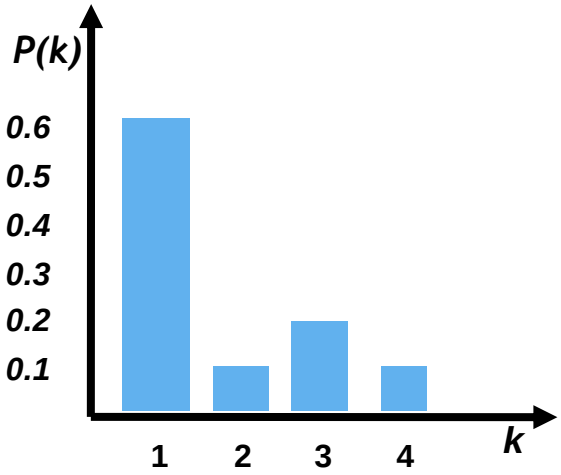
N_k = # nodes with degree k

$P(k) = N_k / N$ ❾ **plot**



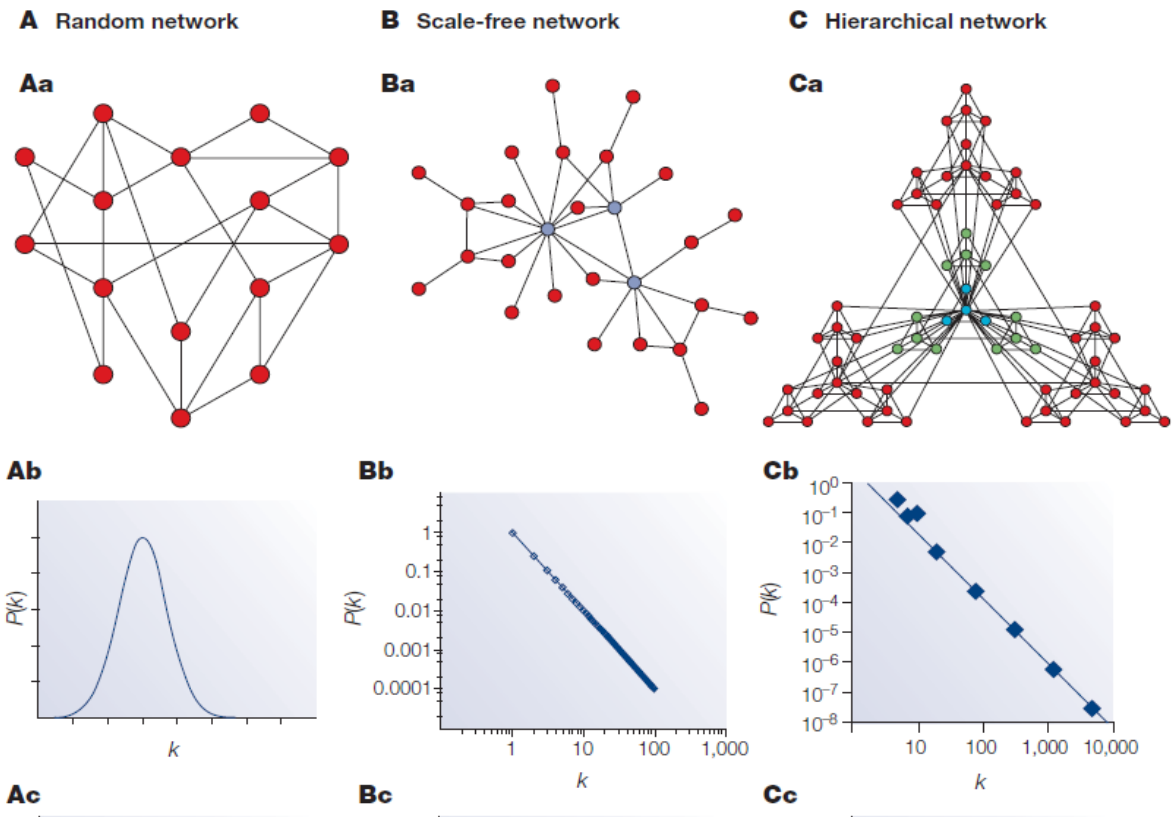
Ex:

(total of 10 nodes)



The degree distribution allows us to distinguish between different classes of networks.

Network Models

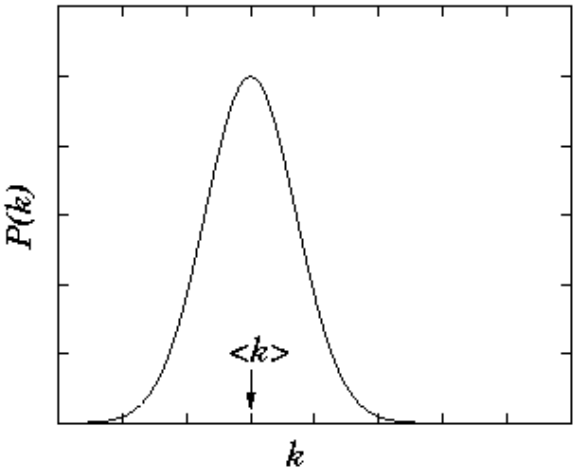


Indicates that the most nodes have roughly the same number of links

Most nodes have only a few links. A few nodes have a large number of links, which are called hubs.

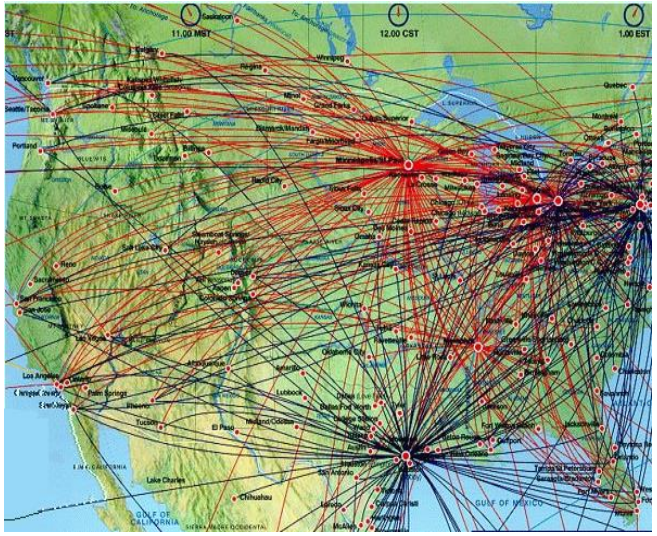
What does the difference mean? Visual representation.

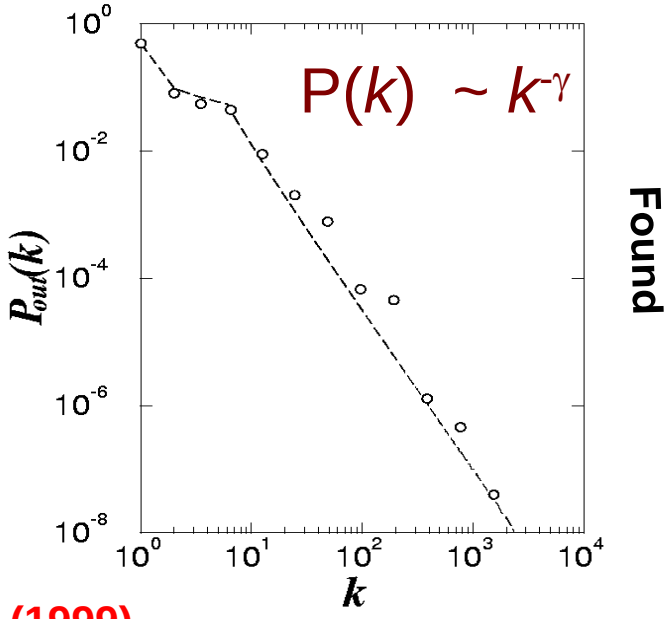
Exponential Network



Expected

Scale-free Network

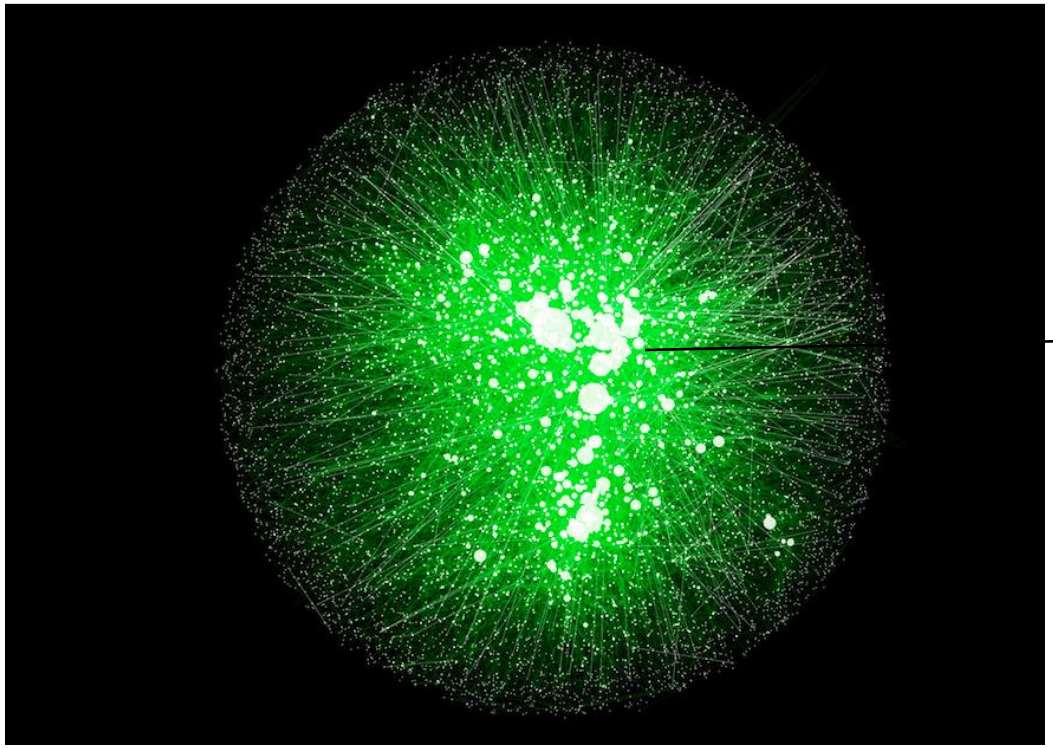




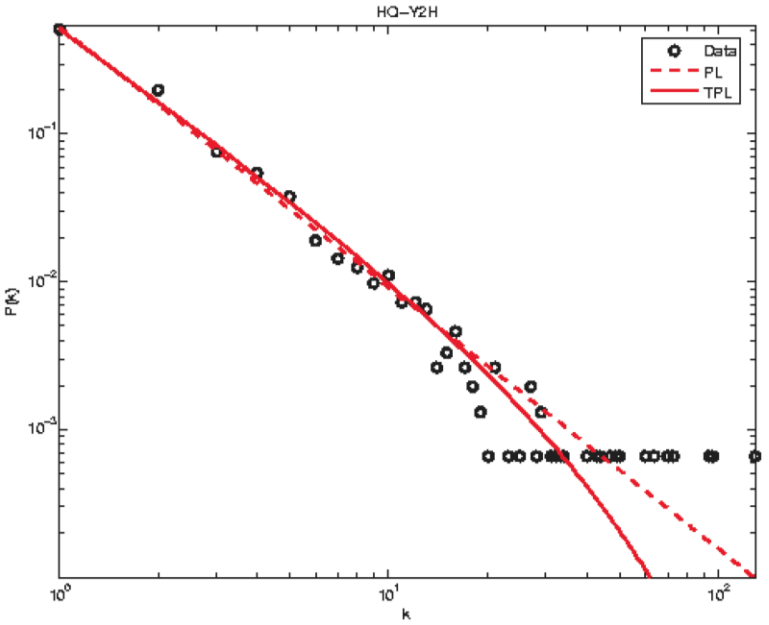
Found

R. Albert, H. Jeong, A-L Barabasi, *Nature*, 401 130 (1999).

HUMAN INTERACTOME



hubs



Rual *et al.* Nature 2005; Stelze *et al.* Cell 2005

CLUSTERING COEFFICIENT

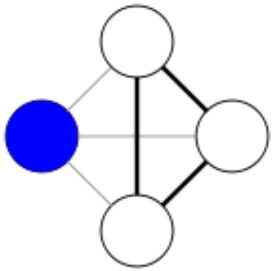
Clustering coefficient:

what portion of your neighbors are connected?

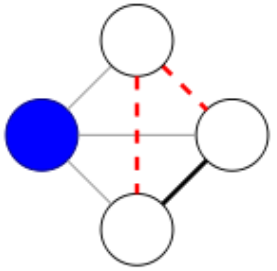
- Node i with degree k_i
- C_i in [0,1]
- Ei number of triangle passing the node

$$C_i = \frac{2e_i}{k_i(k_i - 1)}$$

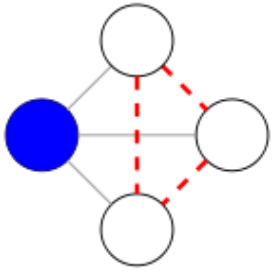
The clustering coefficient of a node is the number of triangles that pass through a node, relative to the maximum number of loops that could pass through the node.



c = 1



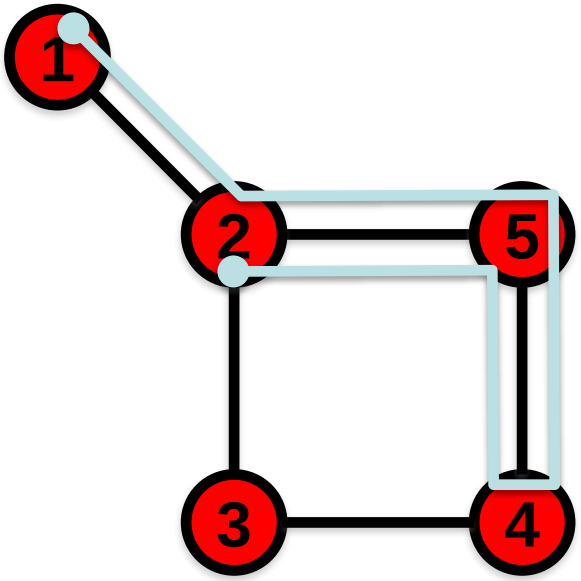
c = 1/3



c = 0

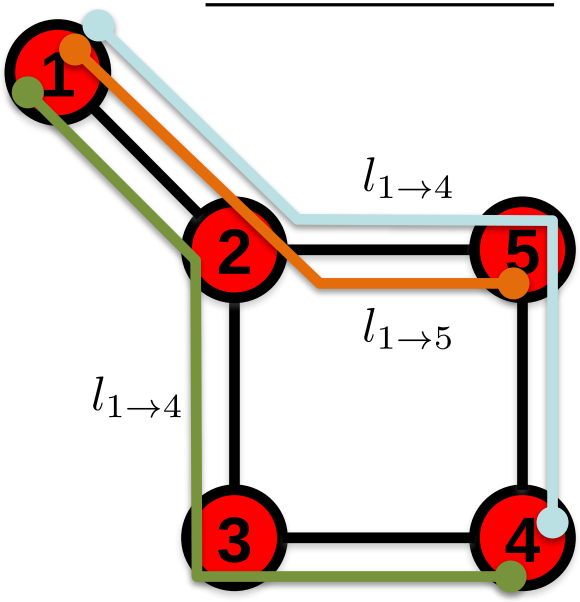
SHORTEST PATH:

Path



A sequence of nodes such that each node is connected to the next node along the path by a link.

Shortest Path



$l_{1\to4} = 3$

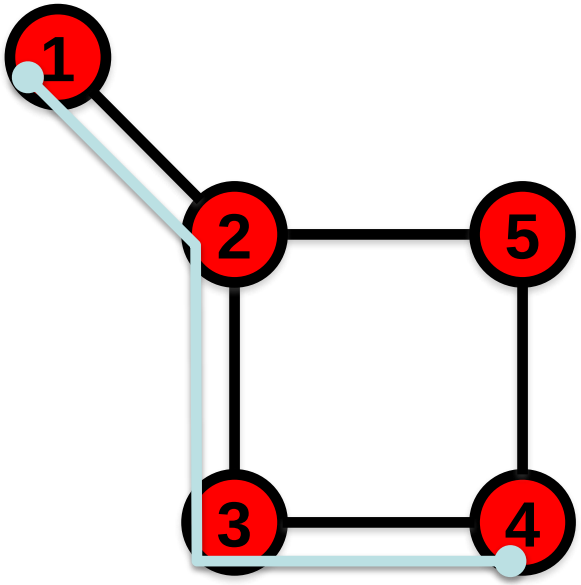
$l_{1\to5} = 2$

The path with the shortest length between two nodes (distance).

Shows if proteins in a network are more connected than by chance

AVERAGE PATH LENGTH:

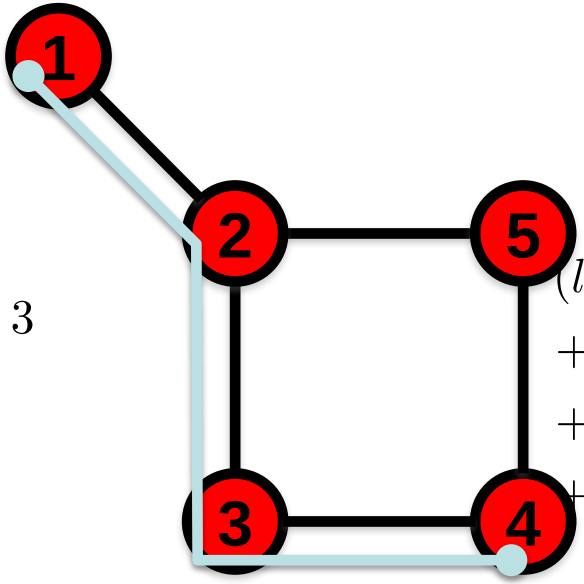
Diameter



$$l_{1\to 4} = 3$$

The longest shortest path in a graph

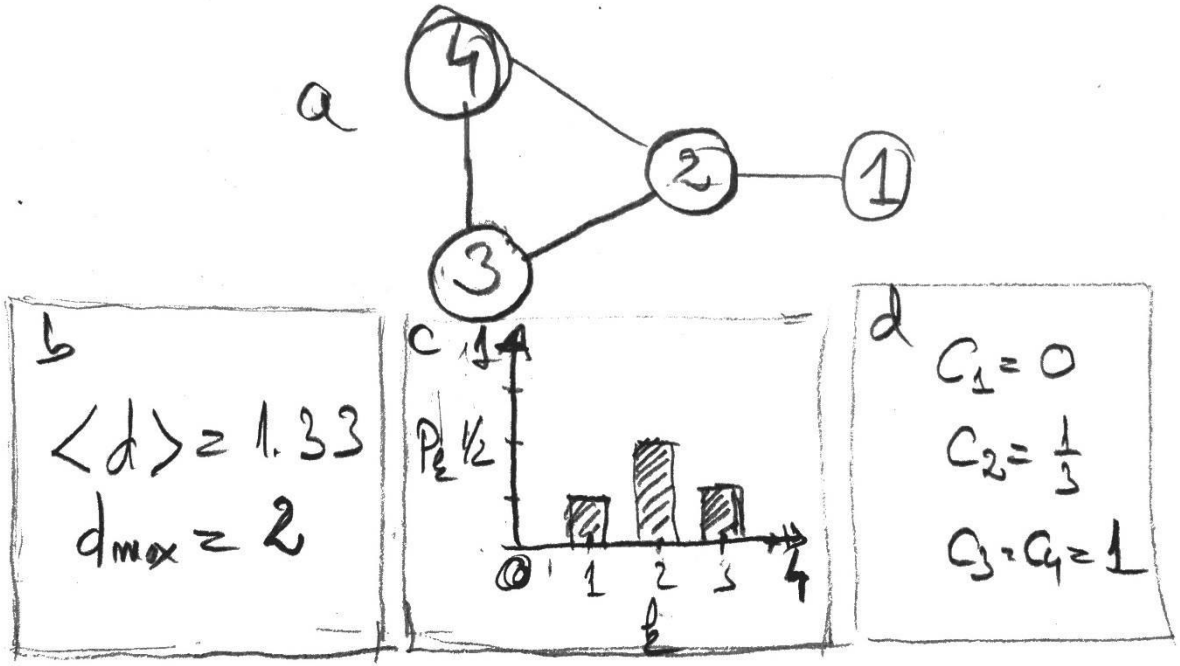
Average Path Length



$$(l_{1\to 2} + l_{1\to 3} + l_{1\to 4} + l_{1\to 5} + l_{2\to 3} + l_{2\to 4} + l_{2\to 5} + l_{3\to 4} + l_{3\to 5} + l_{4\to 5})/10 = 1.6$$

The average of the shortest paths for all pairs of nodes.

THREE CENTRAL QUANTITIES IN NETWORK SCIENCE



A. Degree distribution: p_k

B. Path length: $\langle d \rangle$

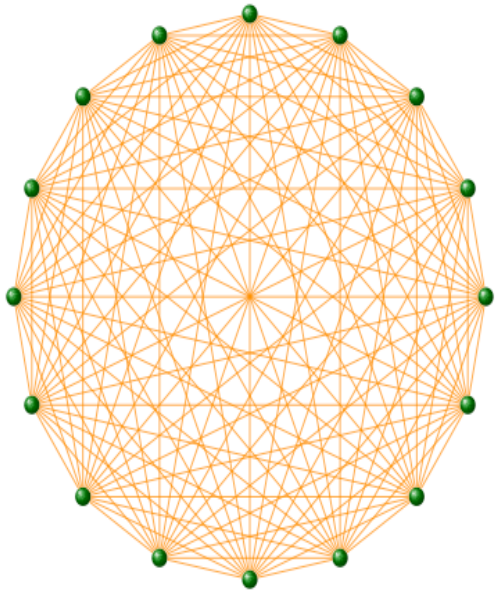
C. Clustering coefficient:

$$C_i = \frac{2e_i}{k_i(k_i - 1)}$$

COMPLETE GRAPH

The maximum number of links a network of N nodes can have is:

$$L_{\max} = \binom{N}{2} = \frac{N(N-1)}{2}$$



A graph with degree $L=L_{max}$ is called a complete graph, and its average degree is **<k>=N-1**

REAL NETWORKS ARE SPARSE

Most networks observed in real systems are sparse:

$$L \ll L_{max}$$

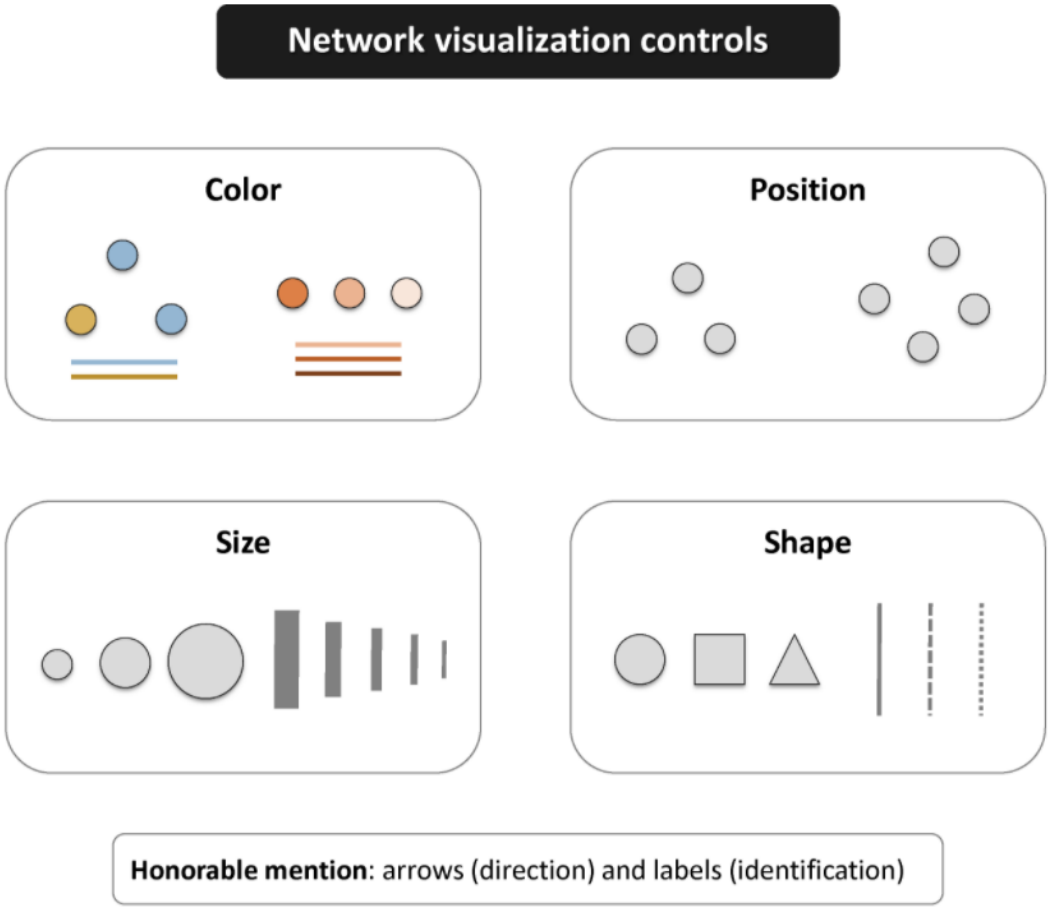
or

$$\langle k \rangle \ll N-1.$$

(Source: Albert, Barabasi, RMP2002)

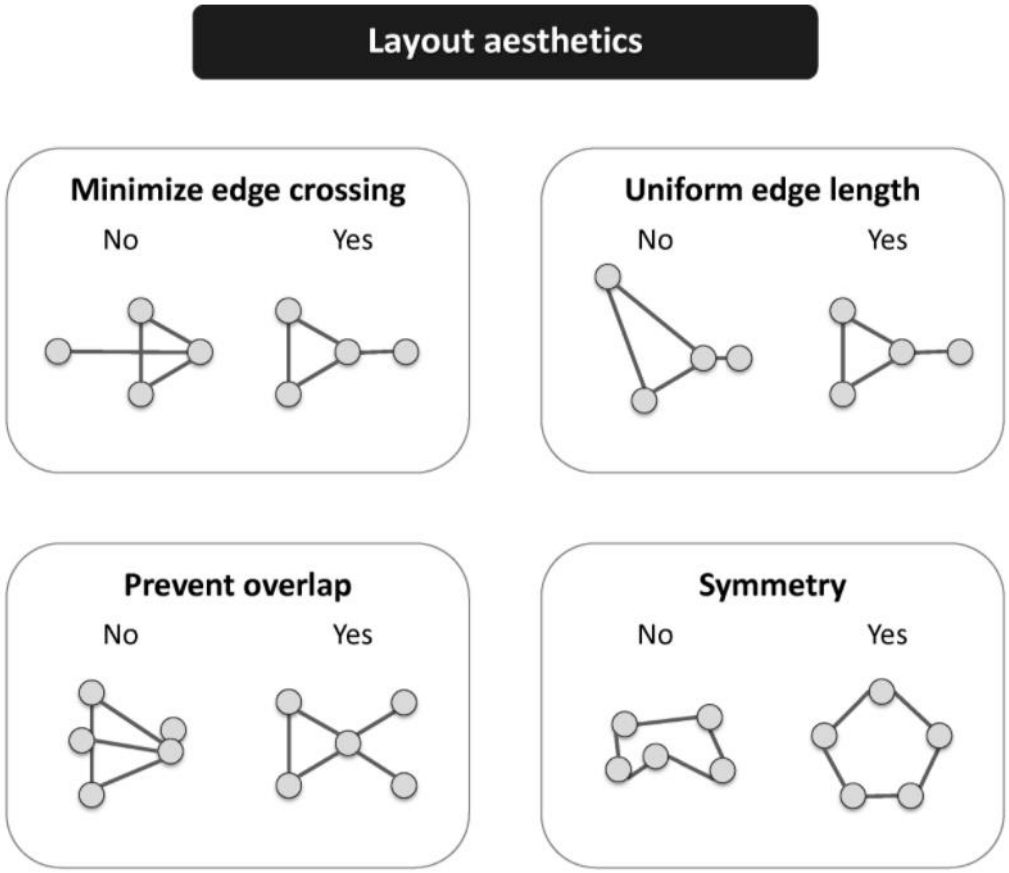
Elements controlling the outcome

In network maps, as in other visualization formats, we have several key elements that control the outcome. The major ones are color, size, shape, and position.



Network Layouts

Modern graph layouts are optimized for speed and aesthetics. In particular, they seek to minimize overlaps and edge crossing, and ensure similar edge length across the graph.

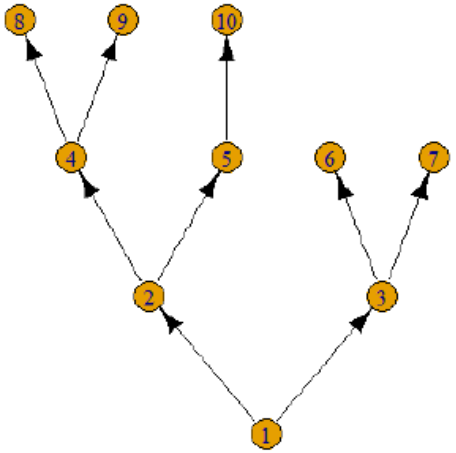


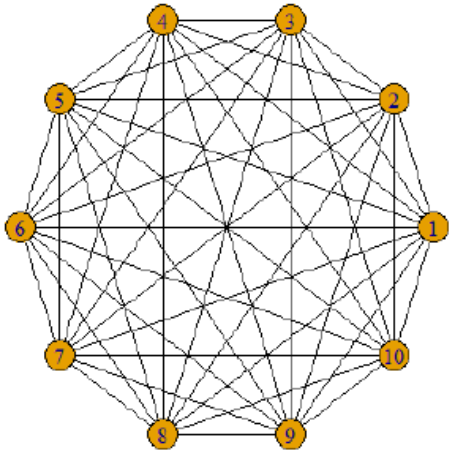
Diagrams: Trees and Graphs

A number of R packages are specialized to draw particular types of diagrams.
igraph is designed for network diagrams of nodes and edges

```
library(igraph)
tree <- graph.tree(10)
tree <- set.edge.attribute(tree, "color", value="black")
plot(treeIgraph,
   layout=layout.reingold.tilford(tree,
   root=1, flip.y=FALSE))
```

```
full <- graph.full(10)
fullIgraph <- set.edge.attribute(full, "color",
value="black")
plot(full, layout=layout.circle)
```



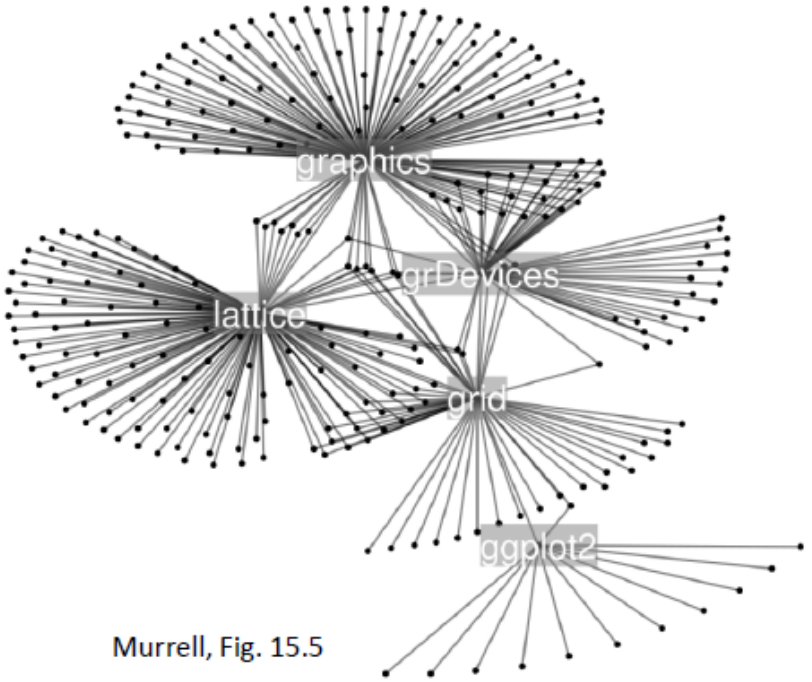


Diagrams: Network diagrams

graphvis (http://www.graphviz.org/) is a comprehensive program for drawing network diagrams and abstract graphs. It uses a simple notation to describe nodes and edges.
The Rgraphviz package (from Bioconductor) provides an R interface

This example, from Murrell's *R Graphics* book, shows a node for each package that directly depends on the main R graphics packages.

An interactive version could provide "tool tips", allowing exploring the relationships among packages



Murrell, Fig. 15.5


THE END

LET’S TRY TO CREATE A NETWORK USING CYTOSCAPE !

Data for the network representation

ncbi.nlm.nih.gov/pmc/articles/PMC4223495/

Mol Cell Proteomics. 2014 Nov; 13(11): 3114–3125.
Published online 2014 Jul 29. doi: 10.1074/mcp.M113.037127
PMCID: PMC4223495
PMID: 25073741

Suberoylanilide Hydroxamic Acid (SAHA)-Induced Dynamics of a Human Histone Deacetylase Protein Interaction Network

Mihaela E. Sardiu,[‡§] Karen T. Smith,[‡§] Brad D. Groppe,[‡] Joshua M. Gilmore,[‡] Anita Saraf,[‡] Rhonda Egidy,[‡] Allison Peak,[‡] Chris W. Seidel,[‡] Laurence Florens,[‡] Jerry L. Workman,[‡] and Michael P. Washburn[‡¶‖]

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Associated Data

Supplementary Materials

Abstract

Histone deacetylases (HDACs) are targets for cancer therapy. Suberoylanilide hydroxamic acid (SAHA) is an HDAC inhibitor approved by the U.S. Food and Drug Administration for the treatment of cutaneous T-cell lymphoma. To obtain a better mechanistic understanding of the Sin3/HDAC complex in cancer, we extended its protein–protein interaction network and identified a mutually exclusive pair within the complex. We then assessed the effects of SAHA on the disruption of the complex network through six homologous baits. SAHA perturbs multiple protein interactions and therefore compromises the composition of large parts of the Sin3/HDAC network. A comparison of the effect of SAHA treatment on gene expression in breast cancer cells to a knockdown of the ING2 subunit indicated that a portion of the

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Deacetylase inhibitors dissociate the histone-targeting ING2 subunit from the Sin3 complex. [Chem Biol. 2010]

Histone deacetylase inhibitor, suberoylanilide hydroxamic acid (SAHA), enhances anti-tumor effects of [Breast Cancer Res. 2015]

Structural Requirements of Histone Deacetylase Inhibitors: SAHA Analogs Modified on the Hydroxar [Arch Pharm (Weinheim). 2016]

Zn(II)-dependent histone deacetylase inhibitors: suberoylanilide hydroxamic acid and trichostatin A. [Int J Biochem Cell Biol. 2009]

The safety profile of vorinostat (suberoylanilide hydroxamic acid) in hematologic malignancies: A review of [Cancer Treat Rev. 2016]

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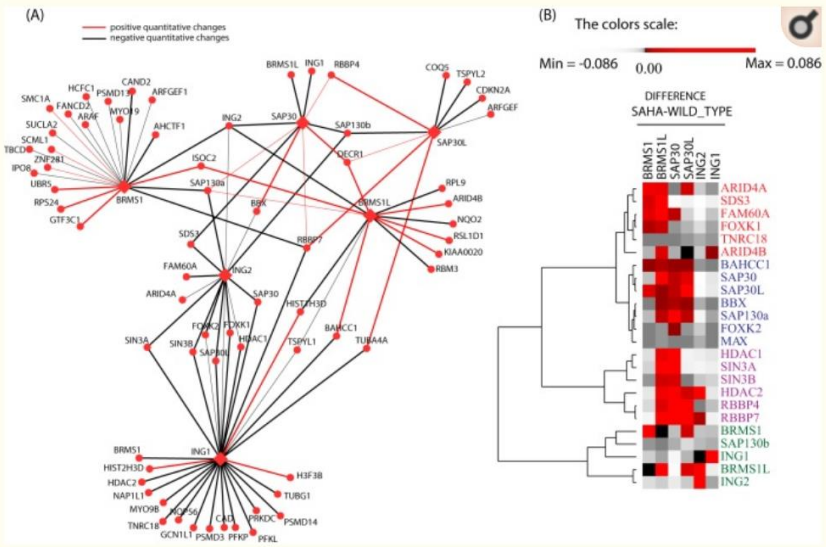
ncbi.nlm.nih.gov/pmc/articles/PMC4223495/



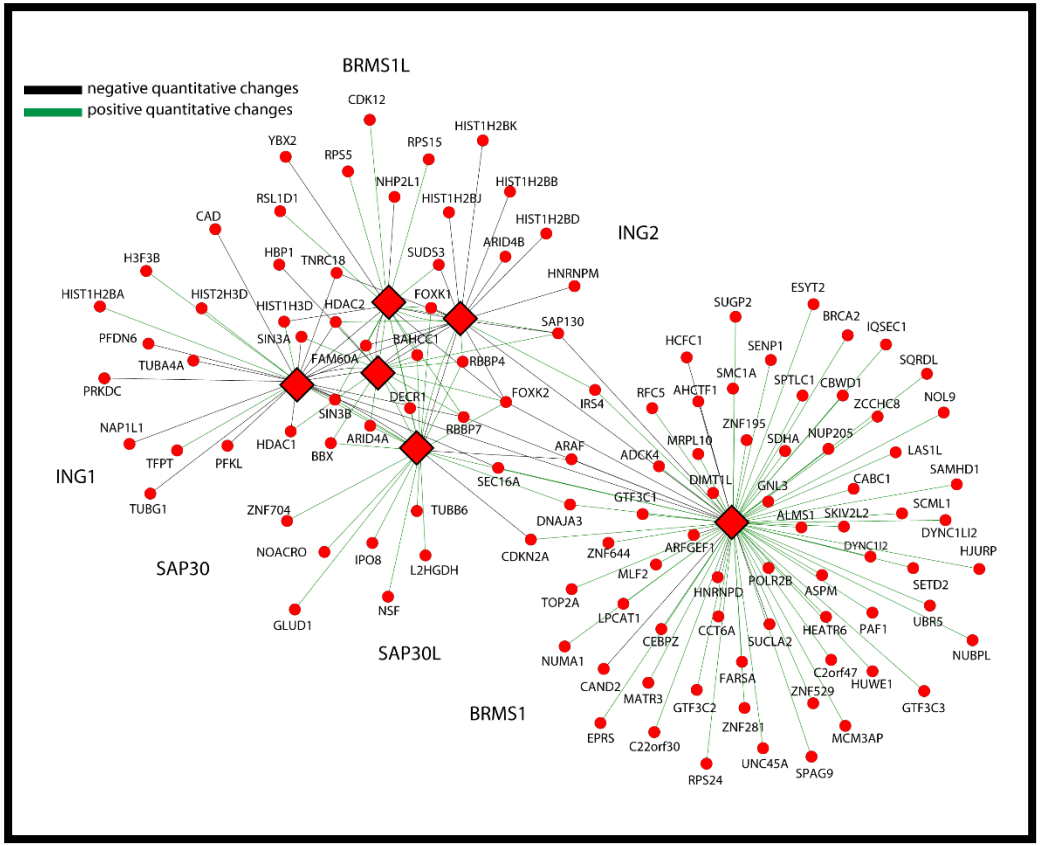
Open in a separate window

Fig. 3.

SAHA-induced differential network analysis. *A*, the SAHA interaction network of Sin3/HDAC-centered complexes. The SAHA drug-interaction differential network was generated from six purifications (BRMS1,

INPUT FILE FOR CREATING PPI INTERACTION NETWORKS

PREY	INTERACTION_MEASURE	BAIT	EDGE
NHP2L1	-1.134172	BRMS1L	black
ING2	-1.039711	BRMS1L	black
YBX2	-0.636206	BRMS1L	black
HIST1H3D	-0.549784	BRMS1L	black
FOXK2	-0.44092	BRMS1L	black
SAP30	0.616034	BRMS1L	green
FOXK1	0.678633	BRMS1L	green
CDK12	0.684784	BRMS1L	green
FAM60A	0.708989	BRMS1L	green
ARID4A	0.741885	BRMS1L	green
SIN3B	0.774813	BRMS1L	green
SUDS3	0.88933	BRMS1L	green
RPS5	0.924608	BRMS1L	green
BAHCC1	1.022857	BRMS1L	green
RBBP7	1.355856	BRMS1L	green
SAP130	1.37844	BRMS1L	green
RSL1D1	2.179295	BRMS1L	green
DECR1	2.562922	BRMS1L	green
RPS15	2.571938	BRMS1L	green
FOXK2	-5.061072	ING2	black
FOXK1	-2.592065	ING2	black
SAP30L	-2.097223	ING2	black
SAP30	-2.010512	ING2	black
SAP130	-1.71355	ING2	black
HNRNPM	-1.690127	ING2	black
FAM60A	-1.603063	ING2	black
HIST1H2B	-1.516204	ING2	black
HIST1H2B	-1.516204	ING2	black
HIST1H2B	-1.491035	ING2	black
HIST1H2B	-1.491035	ING2	black
SUDS3	-1.436816	ING2	black
ARID4B	-1.191539	ING2	black
TNRC18	-0.589795	ING2	black
ING2	0.781019	ING2	green
IRS4	0.963255	ING2	green
BRMS1L	2.049276	ING2	green



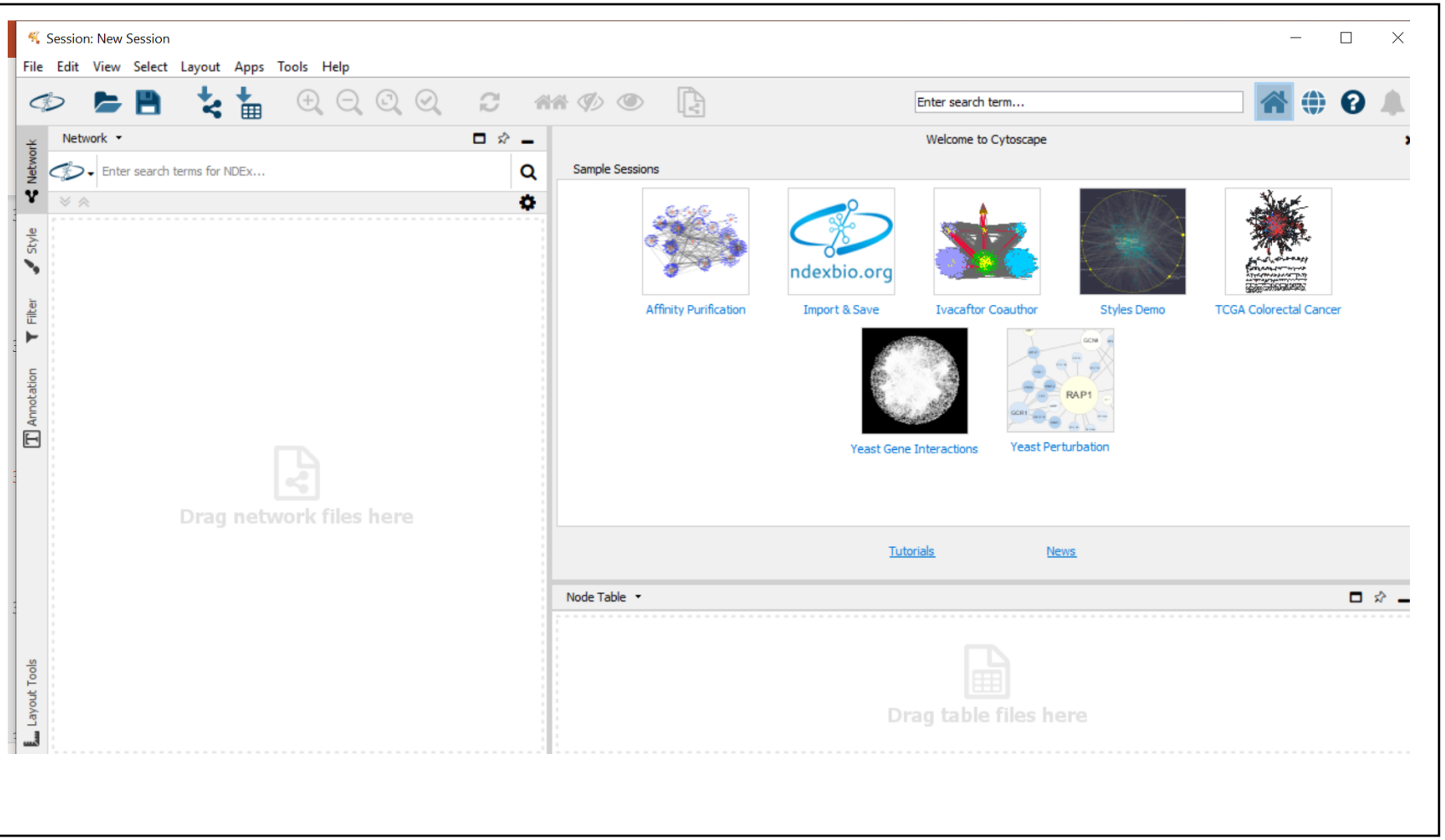
CREATING PPI INTERACTION NETWORKS

CYTOSCAPE

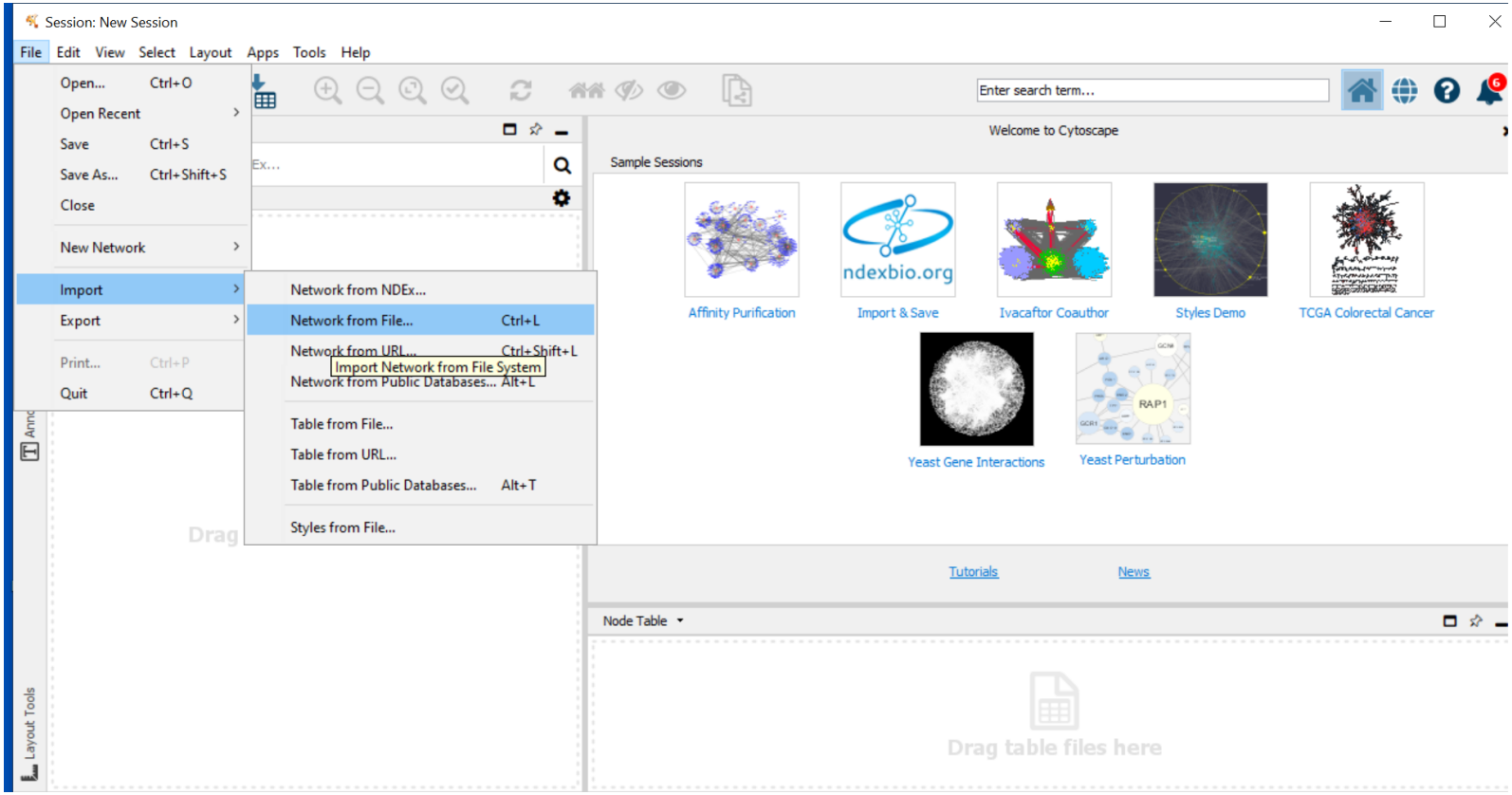
An Open Source Platform for Complex Network Analysis and Visualization

http://opentutorials.cgl.ucsf.edu/index.php/Tutorial:Introduction_to_Cytoscape

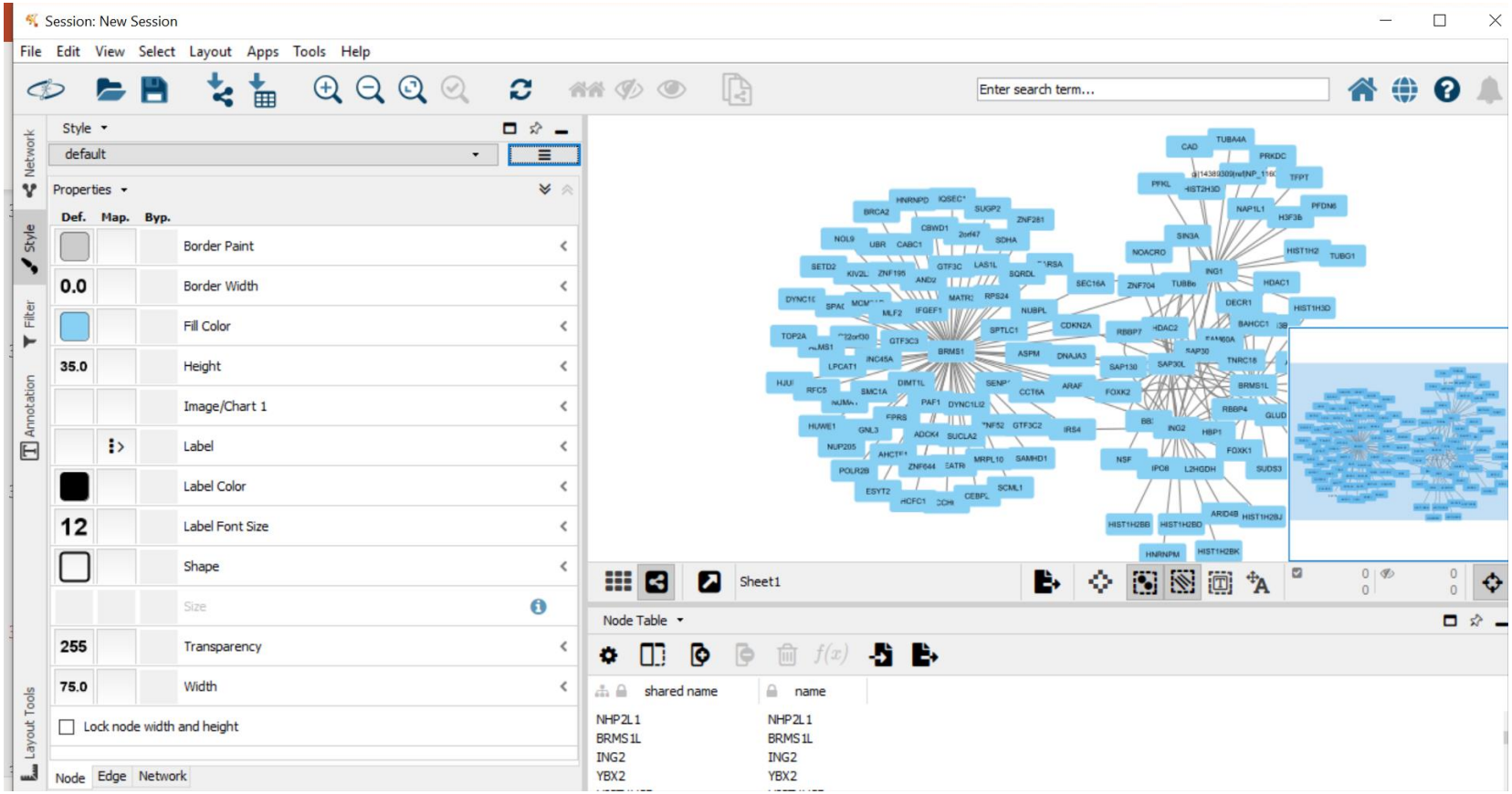
Cytoscape interface



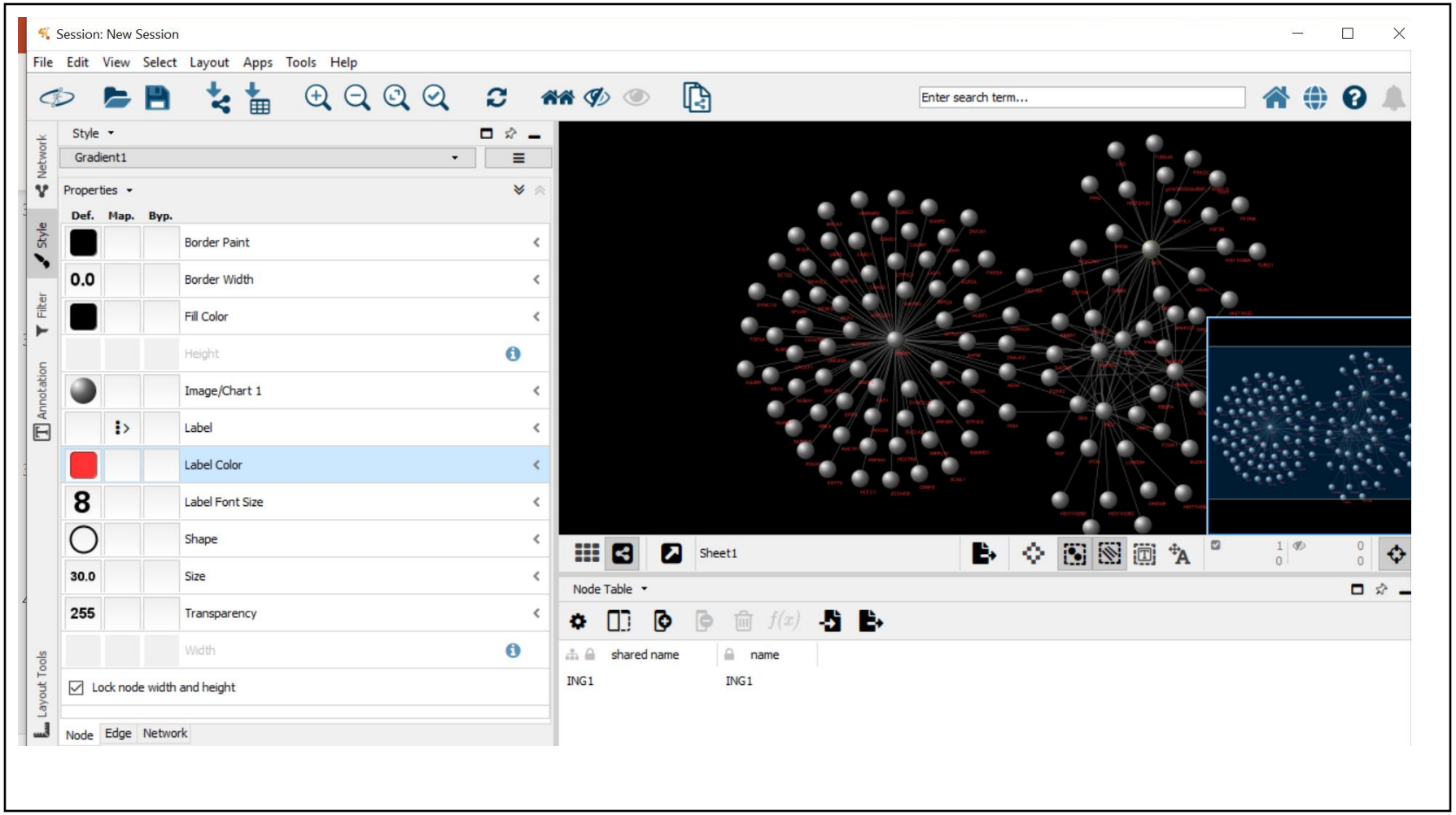
Open the file in cytoscape



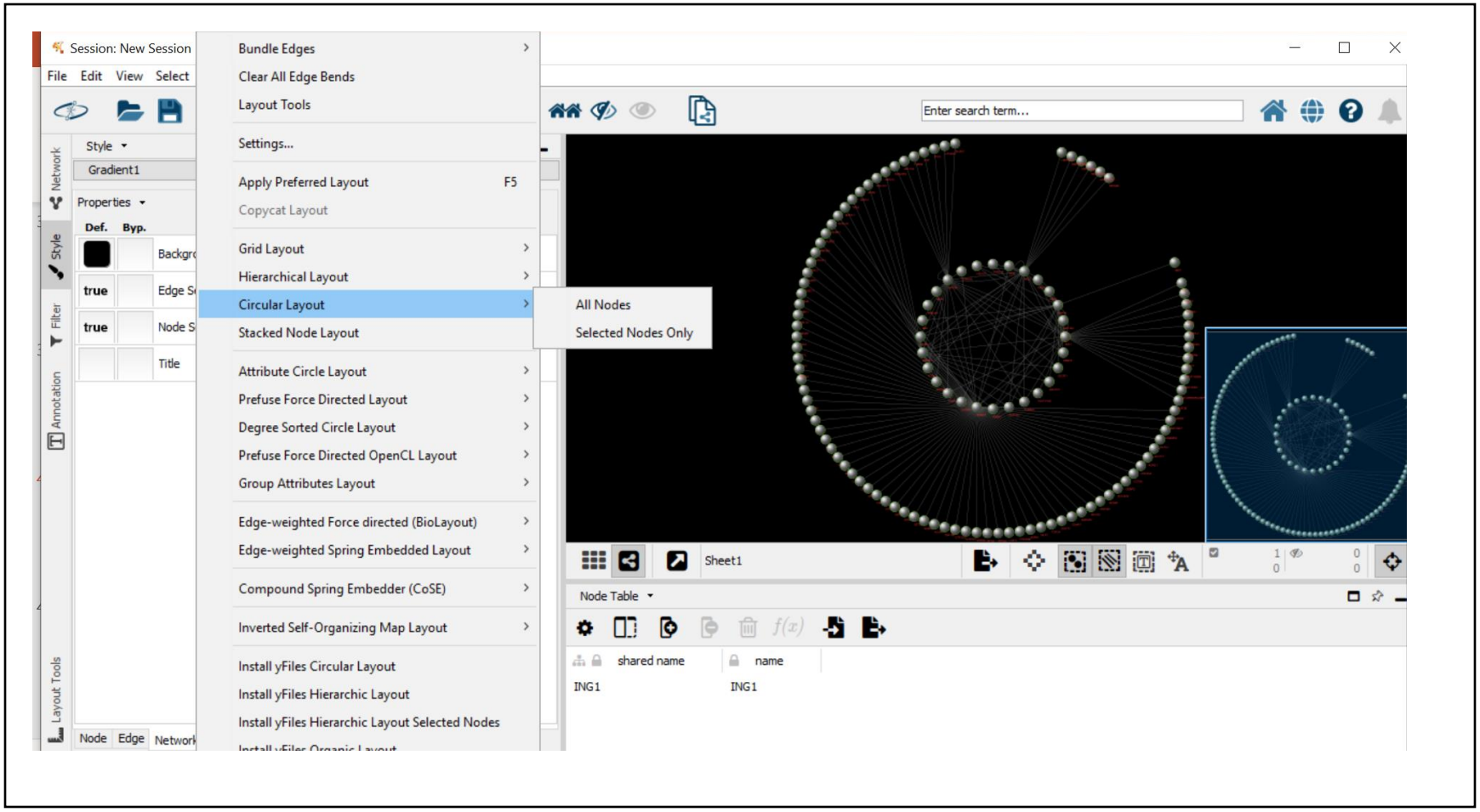
Network visualization



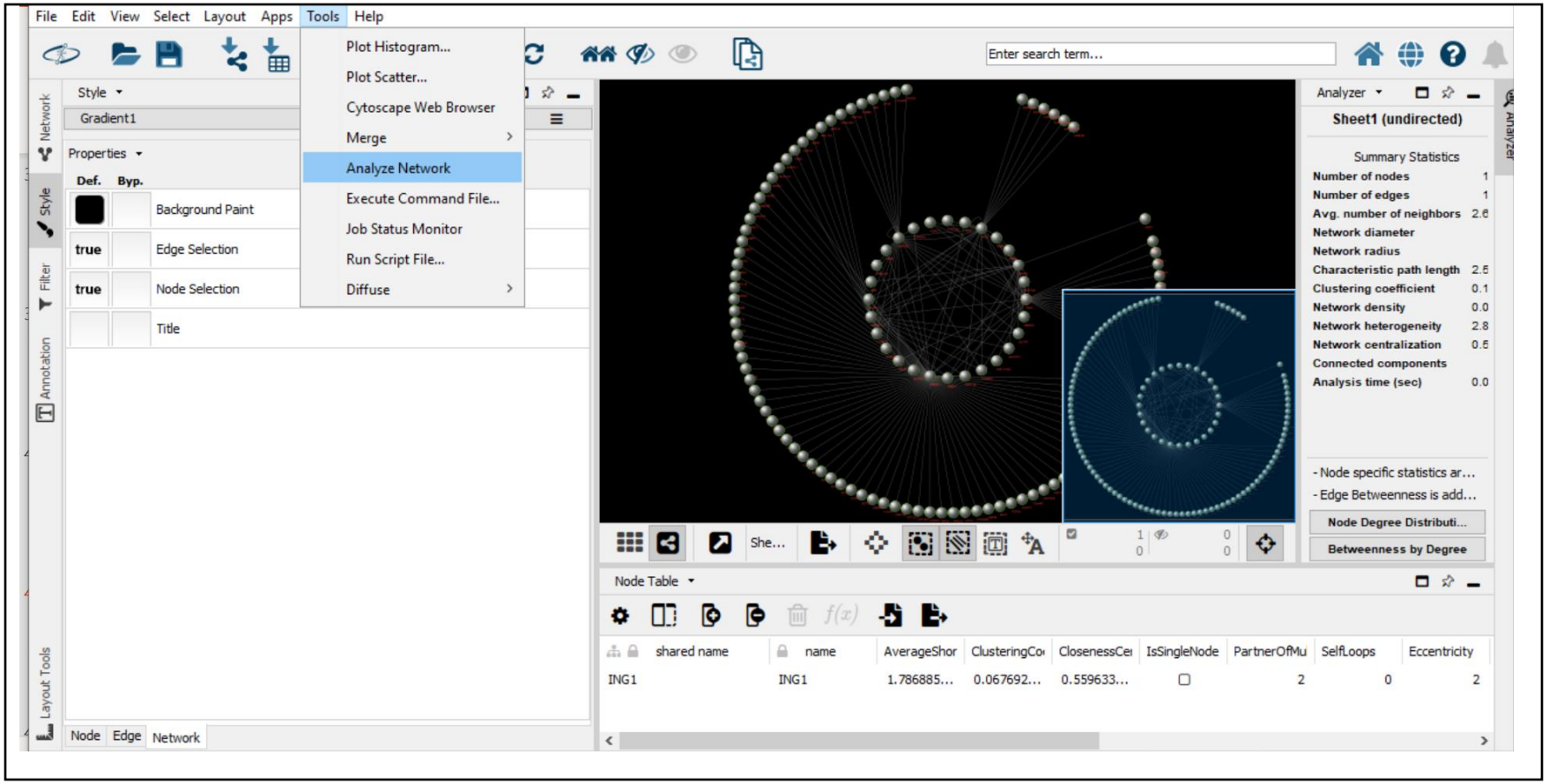
Style and Colors



NETWORK LAYOUT



Network properties



VizMapper

EDGE(COLOR) INTERACTION
PASSTHROUGH
EDGE(STROKE COLOR) INTERACTION
PASSTHROUGH

NODE (LABEL) ID
PASSTHROUGH

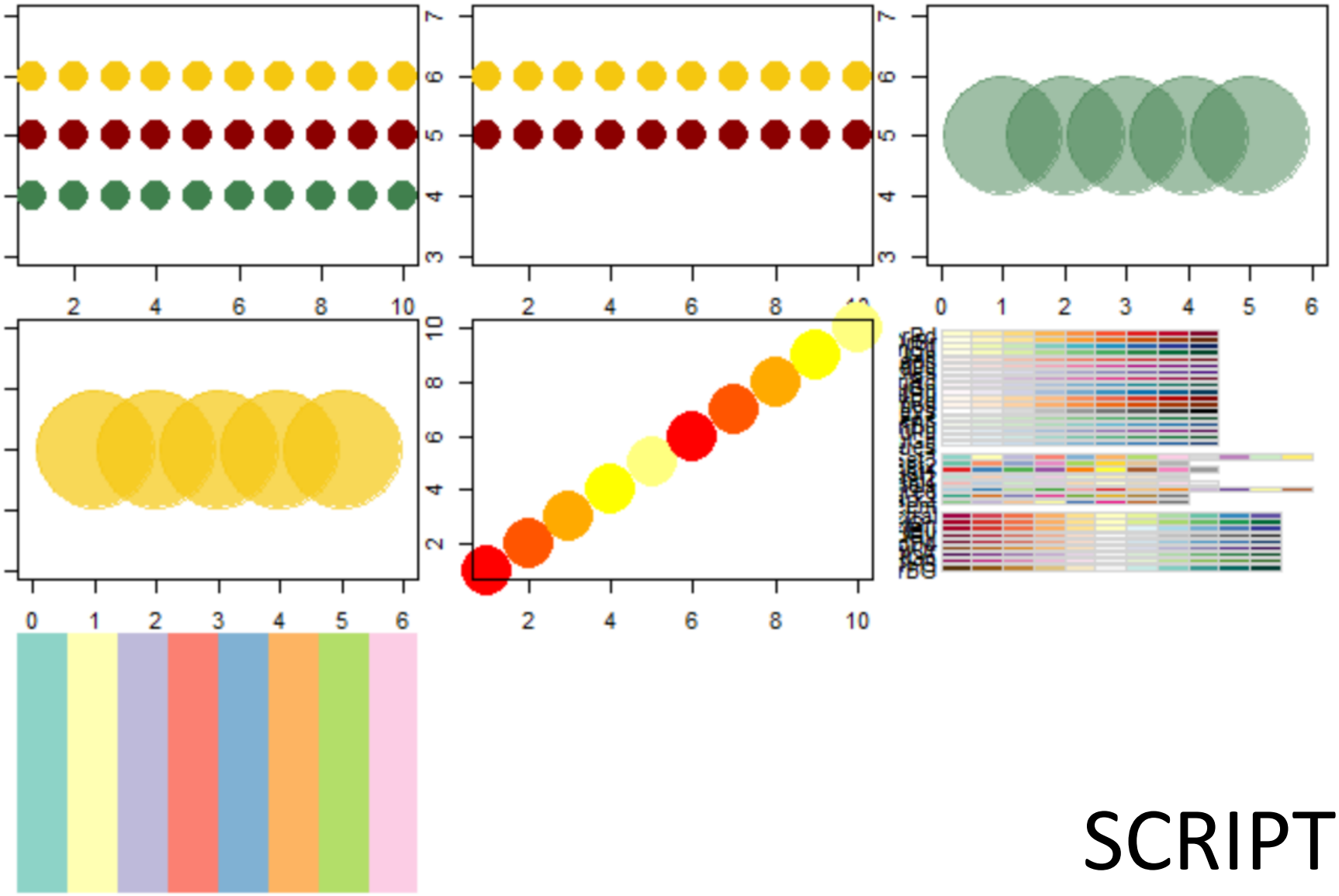
EDGE(LABEL) INTERACTION
DISCRETE MAPPING

Network visualization with R

Install packages in R to create networks

```
install.packages("igraph")
install.packages("network")
install.packages("sna")
install.packages("ggraph")
install.packages("visNetwork")
install.packages("threejs")
install.packages("networkD3")
install.packages("ndtv")
```

Colors in R recap



SCRIPT