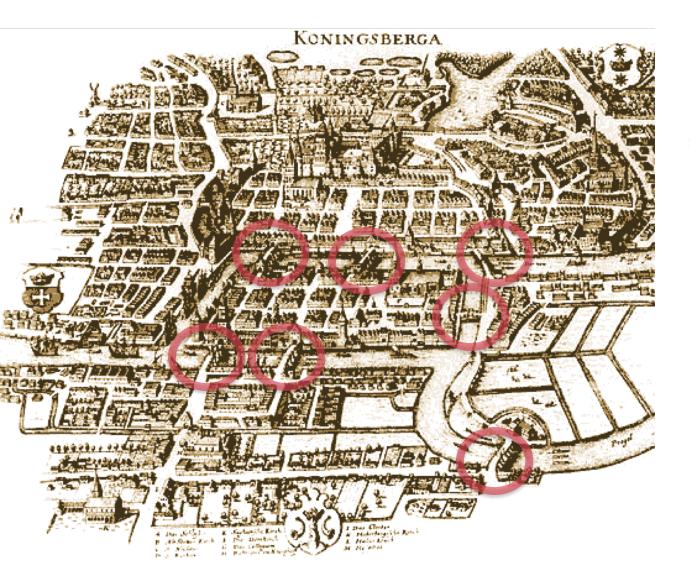
Introduction to network science

Sergio Baranzini, PhD Department of Neurology QB3 Program in Bioinformatics Institute for Human Genetics UCSF

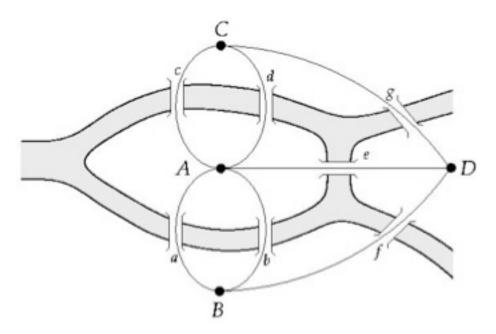
The Bridges of Konigsberg



Can one walk across the seven bridges and never cross the same bridge

twice?

The problem as a graph

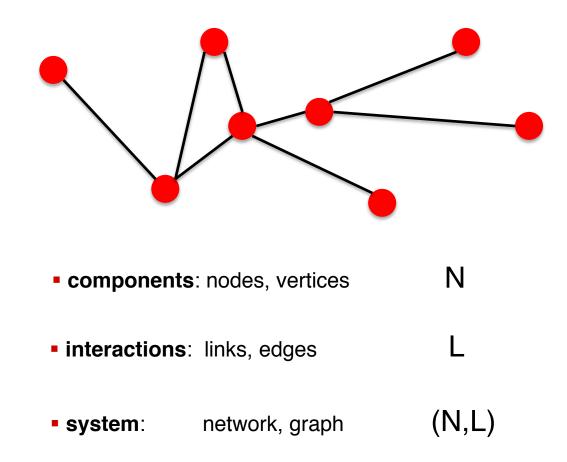


Can one walk across the seven bridges and never cross the same bridge twice?

1735: Euler's theorem:

- (a) If a graph has more than two nodes of odd degree, there is no path.
- (b) If a graph is connected and has no odd degree nodes, it has at least one path.

Networks as complex systems



Examples of real-life networks

Social networks

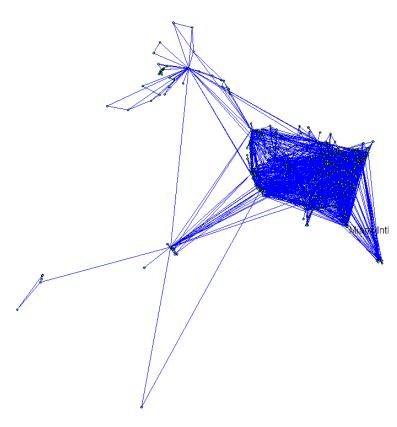
-connections among people
-trade among organizations, countries
-citation networks
-computer networks
-telephone calls

•Organic molecules in chemistry

•Genes and proteins in biology

Connections among words in text

•Transportation (airlines, streets, electric networks, etc)



Types of networks

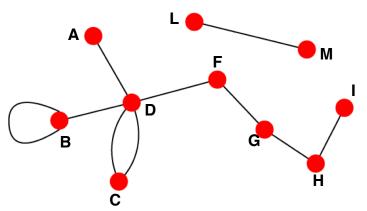
- Directed vs undirected
- Random vs scale-free
- Homogeneous vs bi-partite vs heterogeneous

Undirected vs directed networks

Undirected

Links: undirected (symmetrical)

Graph:



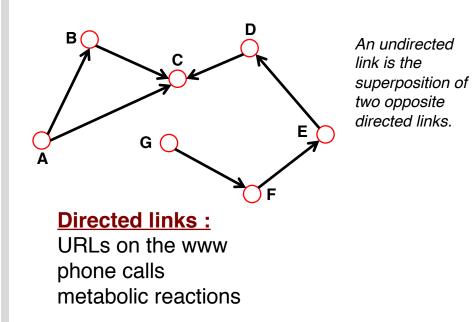
Undirected links :

coauthorship links Actor network protein interactions

Directed

Links: directed (arcs).

Digraph = directed graph:



Network topology metrics

- Degree (k) and distribution
- Path length
- Clustering Coefficient
- Eccentricity
- Radius
- Diameter
- Centrality
 - Closeness
 - betweenness

Setup in R

Install and load SNA package in R

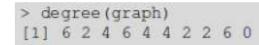
- Create a test graph (10 nodes, edges generated randomly)

```
> #Load the sna(social network analysis) library
> library(sna)
Parameters required for the graph
> #N(number of vertices in the graph)
> #plink(probability of a link between any 2 vertices)
> N=10
> plink=0.2
> #sna::rgraph() -- Generate Bernoulli Random Graphs
> #2nd argument(1) for one graph is to generated
> #4th argument ("graph") for the graph to be undirected
> #5th argument (FALSE) for the possibility of loops
> graph=rgraph(N,1,plink,"graph",FALSE)
> #generated graph in a matrix format
> graph
  [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8]
                                  [,9] [,10]
[1,] 0
       1
           1
                1
                    0
                        0
                             0
                                 0
                                     0
                                        0
          0
[2,] 1 0
             0 0 0
                            0 0
                                    0
                                        0
         0
             0 0 0 0 0 1
[3,] 1 0
                                       0
         0
             0 1 1 0 0 0
[4,] 1 0
                                        0
             1 0
                        0 1 0 0
      0
         0
[5,] 0
                                        0
             1 0 0 0 0 1
         0
[6,] 0 0
                                        0
             0 1 0 0 0 0
[7,] 0 0
         0
                                        0
             0 0 0 0 0
         0
[8,] 0 0
                                   1
                                        0
             0 0
          1
                        1
                                1
[9,] 0 0
                            0
                                    0
                                        0
[10,]0
      0 0
                0
                    0
                        0
                             0
                                0
                                    0
                                        0
```

gplot (graph) for visualization

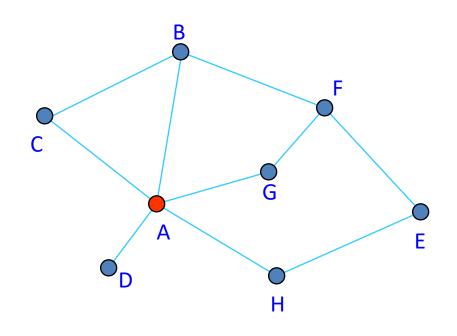
Degree

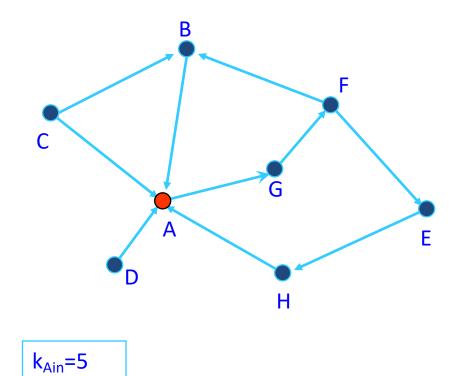
k_{Aout}=1



Undirected

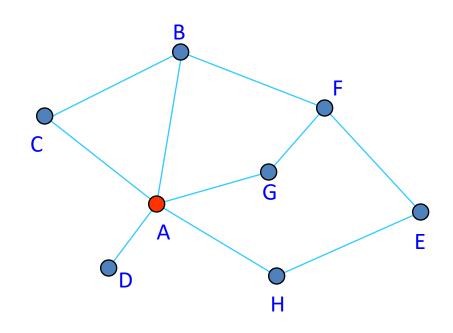
Directed

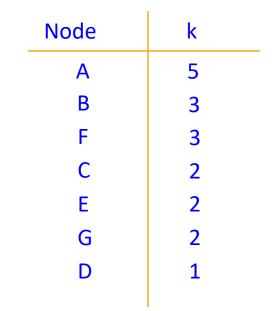




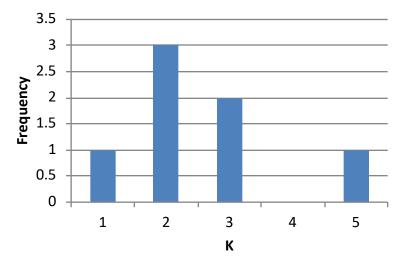
k_A=5

Degree Distribution



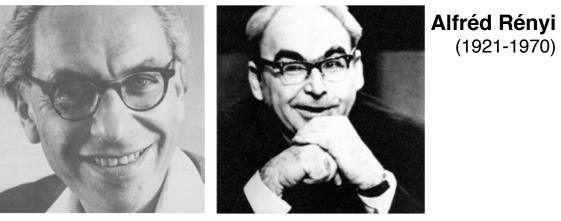


Connectivity (k) distribution



Random network model

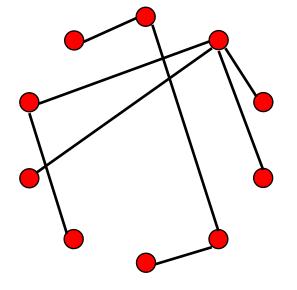
Pál Erdös (1913-1996)



Erdös-Rényi model (1960)

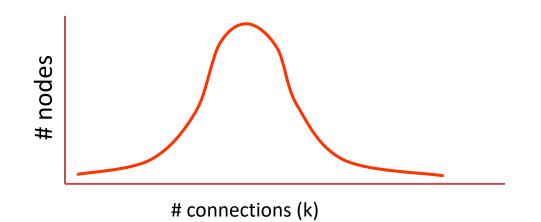
Connect with probability p

p=<mark>1/6</mark> N=10 <k>~1.5

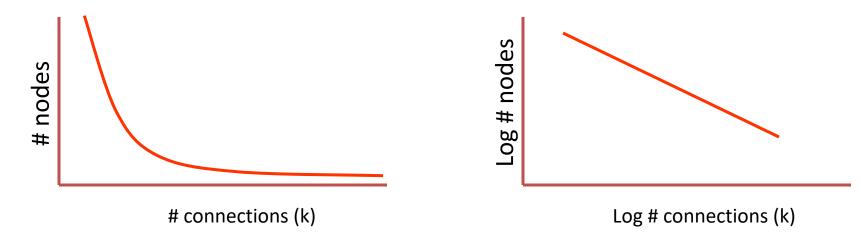


Random vs scale-free

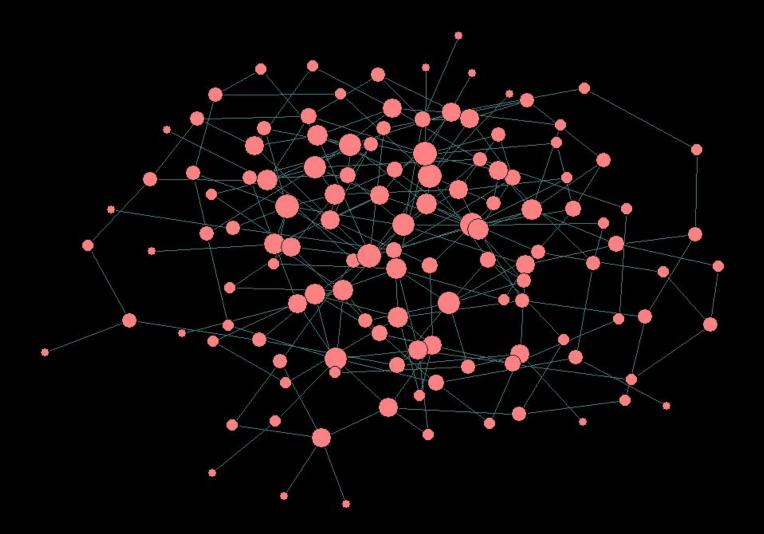
•E-R: connectivity per node follows normal distribution



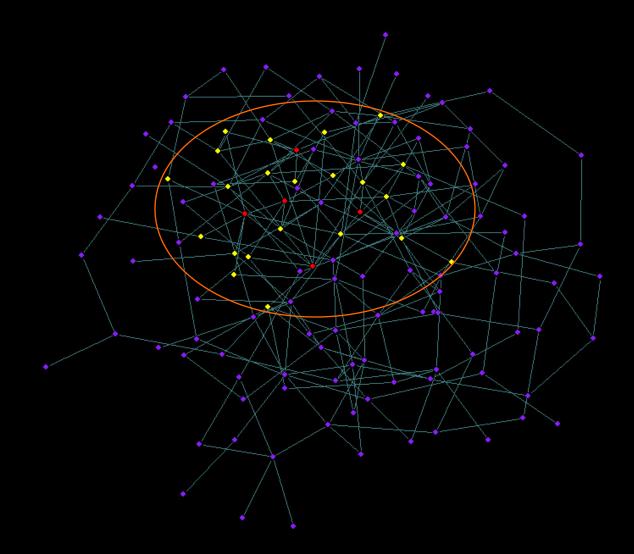
•Scale-free: Connectivity per node follows power law distribution



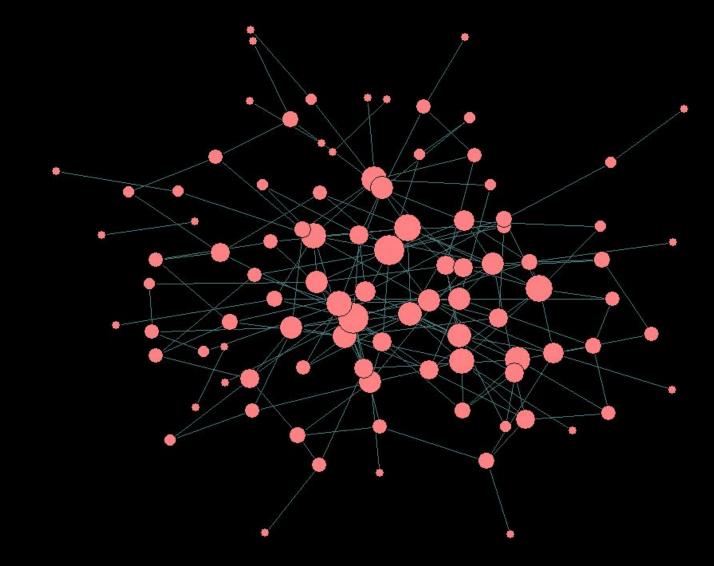
Random (E&R) network: An example



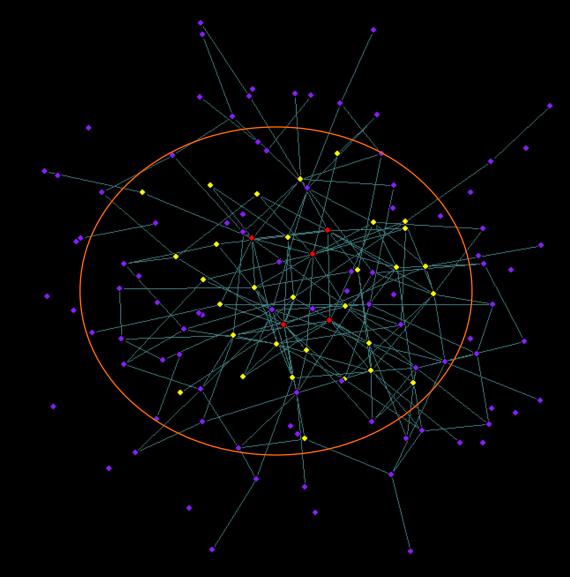
Random (E&R) network: limited reach



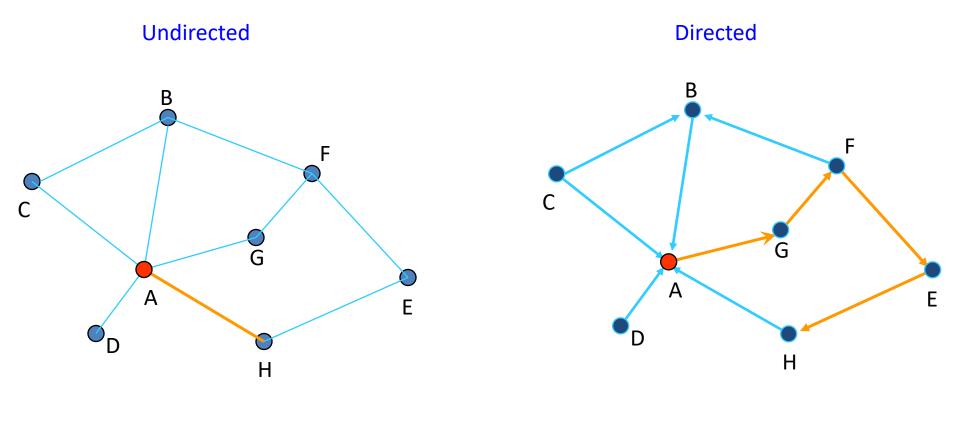
scale-free network: An example



scale-free network: wider reach



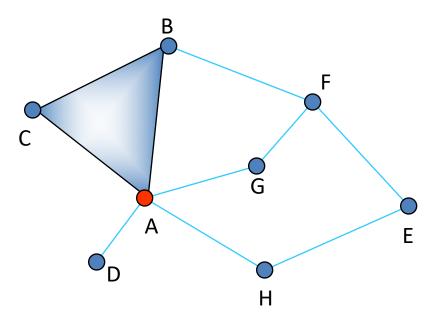
Shortest path



I_{AH}=1

I_{AH}=4

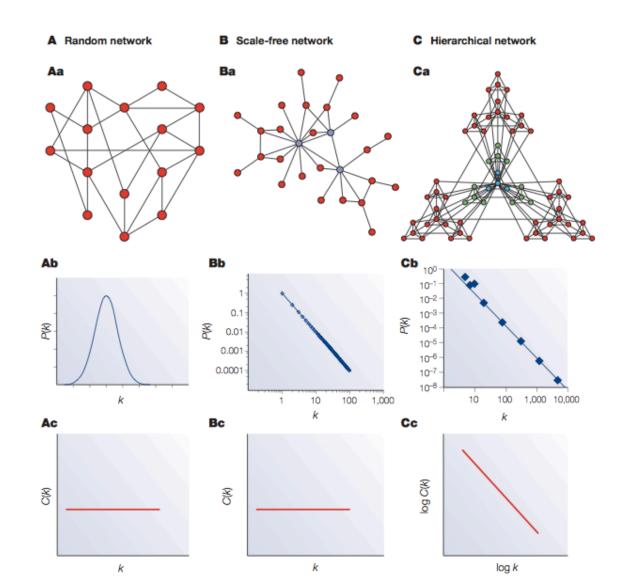
Clustering coefficient



 $C_{I}=2n_{I}/k(k-1)$

C_A=2*1/5(5-1)= 0.1

Network characterization by degree and clustering coefficient



Eccentricity

• The eccentricity of a vertex is the greatest geodesic distance between a given node and any other node. It can be thought of as how far a node is from the node most distant from it in the graph.

Diameter

- The diameter of a graph is the maximum eccentricity of any vertex in the graph. That is, it is the greatest distance between any pair of vertices.
- To find the diameter of a graph, first find the shortest path between each pair of vertices. The greatest length of any of these paths is the diameter of the graph.

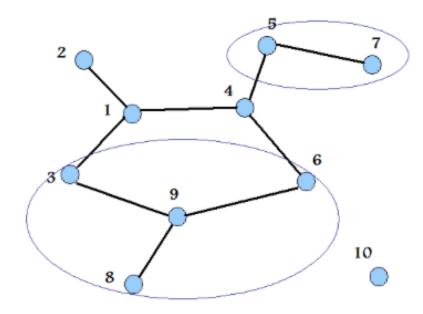
Radius

The radius of a graph is the **minimum eccentricity** of any vertex

Network Metrics in R: Egocentricity

Egocentric Network

- The egocentric network (or ego net) of vertex v in graph G is defined as the subgraph of G induced by v and its neighbors
- It can be used to compute metrics over a local neighborhood, especially useful when dealing with large networks

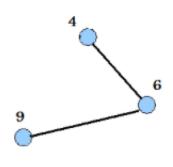


As depicted in this figure, the egocentric network of 9 has nodes 3, 6 and 8 (in addition to 9). Similarly, the ego net of 7 includes node 5.

Egocentric networks for nodes 9 and 7

Network Metrics in R: Egocentricity

- Example: ego.extract()
 - > #ego.extract takes one or more input graphs and returns a list containing the egocentric networks centered on vertices named in ego, using adjacency rule neighborhood to define inclusion. > ego.extract(graph,6) \$`6` [,1] [,2] [,3] [1,] 0 1 1 [2,] 1 0 0 [3,] 1 0 0



- The ego-centric network of node 6 has nodes 6, 4 and 9
- Note that the sub-graph extracted in this example has the original nodes 6, 4, 9 renamed to 1, 2, 3, respectively
- Looking at the adjacency matrix, it can be inferred that node 6 is connected to both nodes 4 and 9, whereas nodes 4 and 9 are not directly connected to each other

Network Metrics in R: Betweenness

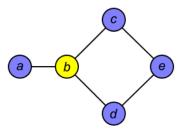
Betweenness Centrality

- A measure of the degree to which a given node lies on the shortest paths (geodesics) between other nodes in the graph
- For node v in graph G, betweenness centrality (C_b) is defined as:

$$C_b(v) = \sum_{s,t \neq v} \frac{\Omega_v(s,t)}{\Omega(s,t)}$$

where $\Omega(s,t)$ is the number of distinct geodesics from s to t and $\Omega_{\nu}(s,t)$ is the number of geodesics from s to t that pass through v.

- A node has high betweenness if the shortest paths (geodesics) between many pairs of other nodes in the graph pass through it
- Thus, when a node with high betweenness fails, it has a greater influence on the information flow in the network



Network Metrics in R: Betweenness

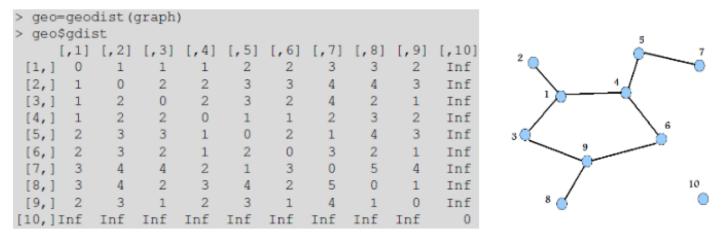
Example: betweenness()

> #Here node 4 has the highest betweenness

> betweenness(graph)

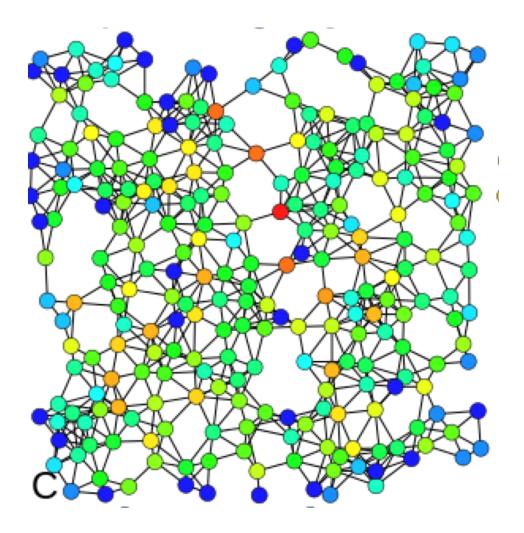
[1] 20 0 8 28 14 12 0 0 16 0

Path lengths/geodesic distances can be calculated using geodist()



 It could be inferred that node 5 requires two hops to reach node 1 and node 10 is not reachable by any other node

Betweenness centrality



Network Metrics in R: Closeness

Closeness Centrality

- Closeness Centrality (CLC) is a category of measures that rate the centrality of a node by its closeness (distance) to other nodes
- CLC of a node v is defined as:

$$CLC(v) = \frac{|V| - 1}{\sum_{i, v \neq v_i} dist ance(v, v_i)}$$

where |V| is the number of nodes in the given graph and v_i is the node *i* of the given graph.

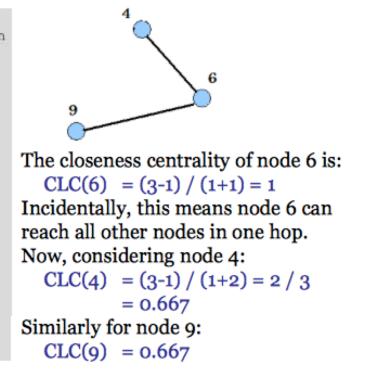
 Closeness Centrality decreases if either the number of nodes reachable from the node in question decreases, or the distances between the nodes increases

Network Metrics in R: Closeness

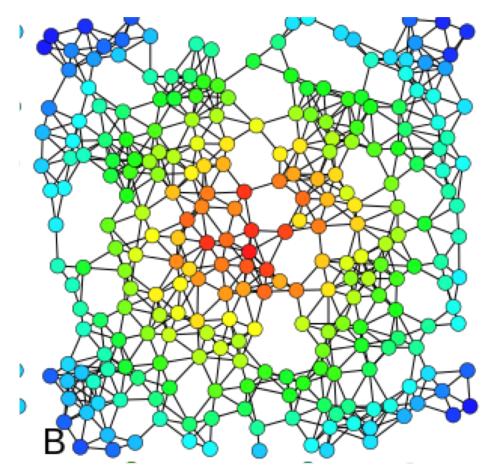
Example: closeness()

- The 10-node graph we have been using has one disconnected node; the resulting infinite distances thus created invalidate any aggregate measure over all nodes such as Closeness Centrality
- So, we choose a sub-graph the egocentric network of node 6

```
> #closeness centrality measures how many steps are
  required to access every other vertex from a given
  vertex
> closeness (graph)
 [1] 0 0 0 0 0 0 0 0 0 0
> #We now consider a sub-graph of the graph
 generated for easy understanding of closeness
> graph1=ego.extract(graph, 6)
> graph1
5'6'
     [,1] [,2] [,3]
[1, ]
         0
     1
[2,]
                  0
[3,1
     1
                  0
> closeness(graph1)
             6
[1,] 1.0000000
[2,] 0.66666667
[3,] 0.6666667
```



Closeness Centrality



Six degrees of separation

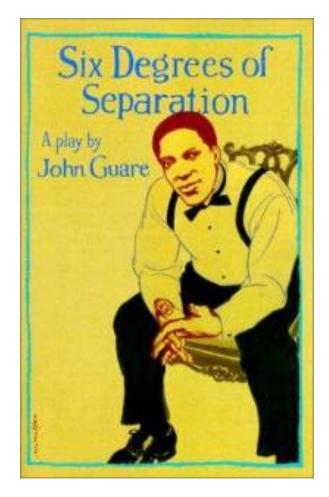
1. ADD YOUR NAME TO THE ROSTER AT THE BOTTOM OF THE SHEET. So that the next person who receives the letter will know where it came from

- 2. DETACH ONE POSTCARD. FILL IT OUT AND RETURN IT TO HARVARD UNIVERSITY. To allow us to keep track of the folder as it moves toward the target person
- 3. IF YOU KNOW THE TARGET PERSON ON PERSONAL BASIS, MAIL THIS FOLDER DIRECTLY TO HIS/HER.
- 4. IF YOU DO NOT KNOW THE TARGET PERSON, MAIL THIS FOLDER TO A PERSONAL ACQUAINTANCE WHO IS MORE LIKELY THAN YOU TO KNOW THE TARGET PERSON

Milgram, S (1967). Psychol. Today, 2, 60-67)

Milgram' s experiment

SIX DEGREES 1991: John Guare



"Everybody on this planet is separated by only six other people. Six degrees of separation. Between us and everybody else on this planet. The president of the United States. A gondolier in Venice.... It's not just the big names. It's anyone. A native in a rain forest. A Tierra del Fuegan. An Eskimo. I am bound to everyone on this planet by a trail of six people. It's a profound thought. How every person is a new door, opening up into other worlds."

Network Science: Random Graphs January 31, 2011

WWW: 19 DEGREES OF SEPARATION

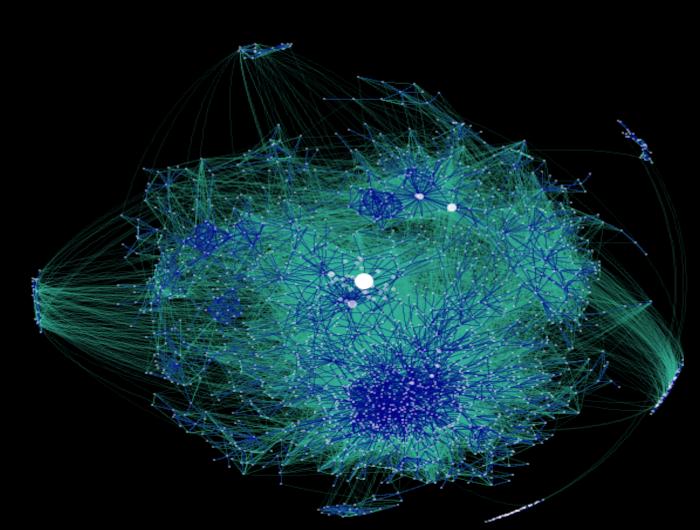
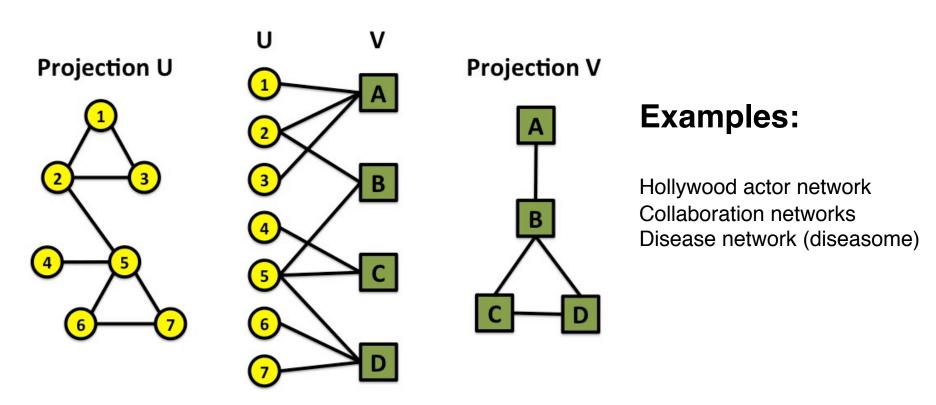


Image by **Matthew Hurst** *Blogosphere*

Network Science: Random Graphs January 31, 2011

Bi-partite networks

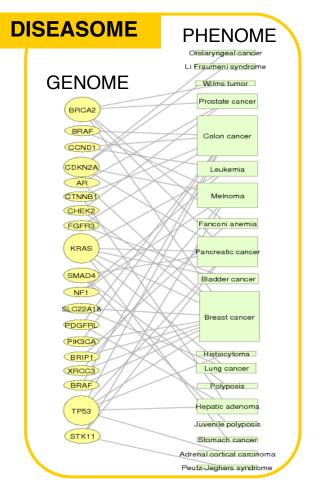
bipartite graph (or bigraph) is a graph whose nodes can be divided into two disjoint sets U and V such that every link connects a node in U to one in V; that is, U and V are independent sets.

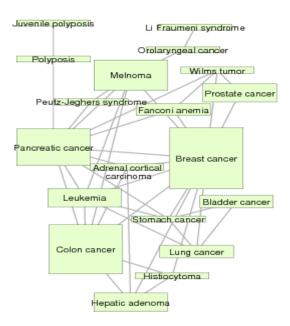


GENE NETWORK – DISEASE NETWORK

FGFR3 NF1 TP53 BRCA2 BRIP1 PDGFRD PIK3CA BRAF CTNNB1 SMAD4 SLC22A18 CHEK2 BRAF XRCC3 CCND1 STK11 CDKN2A) KRAS AB

Gene network

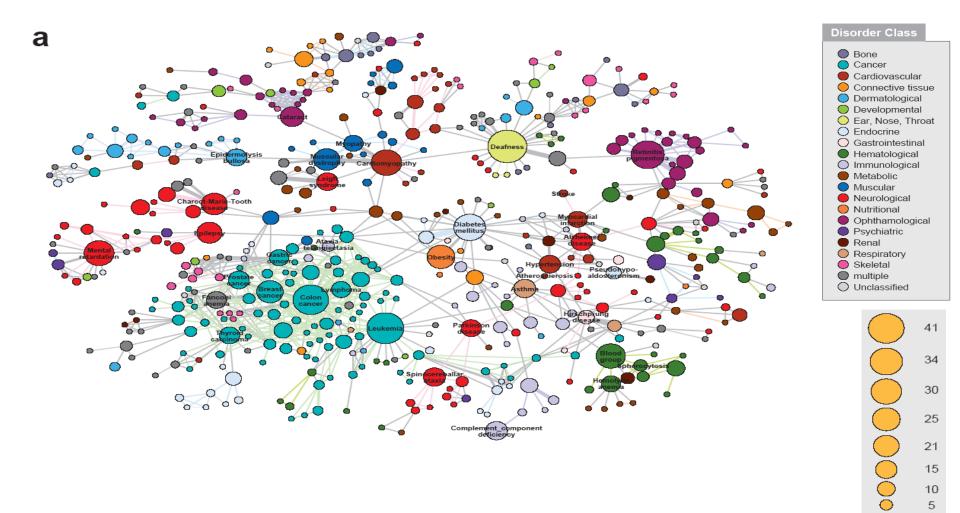


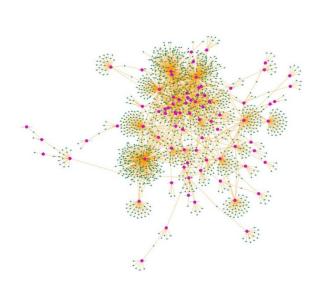


Disease network

Goh, Cusick, Valle, Childs, Vidal & Barabási, PNAS (2007)

The diseasome





GWAS

OMIM

1547 nodes 2010 edges Ratio N/E= 0.77 2265 nodes 2228 edges Ratio N/E= 1.01

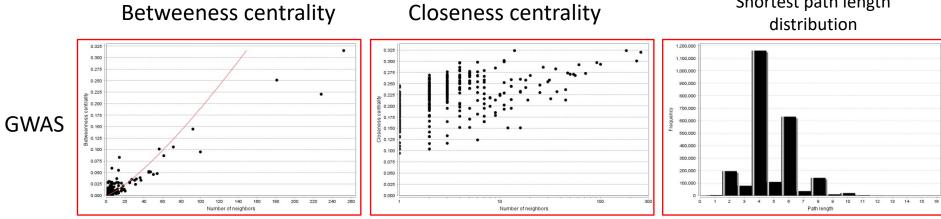
Summary network statistics

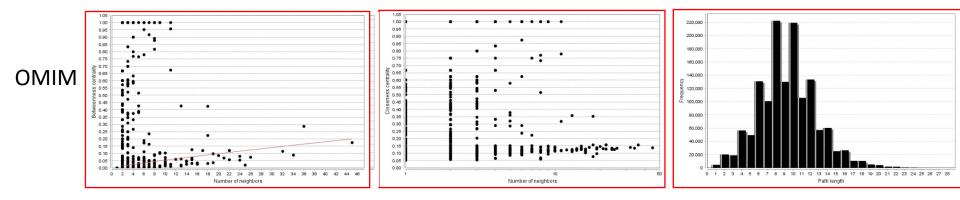
Results Panel				
Network Statistics of all_diseases_genes_gia	ant_component (MEDIC) (undir	ected) Ne	etwork Statistics of all_	diseases_genes_giant \langle \langle
Connected comp Network d Networ Network centra	efficient : 0.0 ponents : 1 Jiameter : 15 k radius : 8 alization : 0.162 st paths : 2391662 (100%) h length : 4.739	ing Coeffi Netwo Num Multi	T	02 42

GWAS

s_genes_giant_component (MEDIC) (undire	ected) Network Statistics of a	all_diseases_genes_giant_compo	nent (OMIM) (undirected)	
Betweenness Centrality	Closeness Centralit	y Stress Ce	Stress Centrality Distribution	
Shortest Path Length Distribution	Shared Neighbors Distri	oution Neighborhood	Neighborhood Connectivity Distribution	
Simple Parameters Node Degree Di	Distribution Avg. Cluste	ering Coefficient Distribution	Topological Coefficient	
Network o Networ Network centr Shorte Characteristic pat	nponents : 321 diameter : 27 yrk radius : 1 ralization : 0.019 est paths : 1394242 (27%) th length : 9.315 neighbors : 1.967	Number of nodes : 2265 Network density : 0.001 Network heterogeneity : 1.436 Isolated nodes : 0 Number of self-loops : 0 Multi-edge node pairs : 0 Analysis time (sec) : 12.896		

OMIM





Shortest path length

Complex systems maintain their basic functions even under errors and failures

Cell \rightarrow mutations

There are uncountable number of mutations and other errors in our cells, yet, we do not notice their consequences.

Internet \rightarrow router breakdowns

At any moment hundreds of routers on the internet are broken, yet, the internet as a whole does not loose its functionality.

Where does robustness come from?

There are feedback loops in most complex systems that keep tab on the component's and the system's 'health'.

Could the network structure affect a system's robustness?

Attack threshold for arbitrary P(k)

Attack problem: we remove a fraction f of the hubs.

At what threshold f_c will the network fall apart (no giant component)?

Hub removal changes

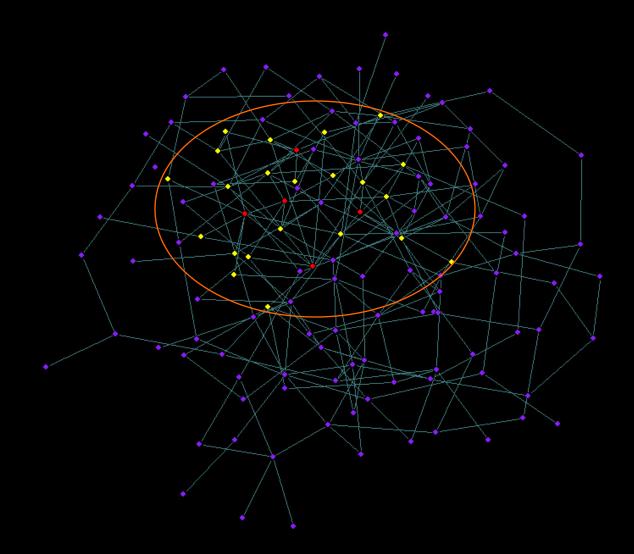
the maximum degree of the network [$K_{max} \rightarrow K'_{max} \leq K_{max}$)

the degree distribution $[P(k) \rightarrow P'(k')]$

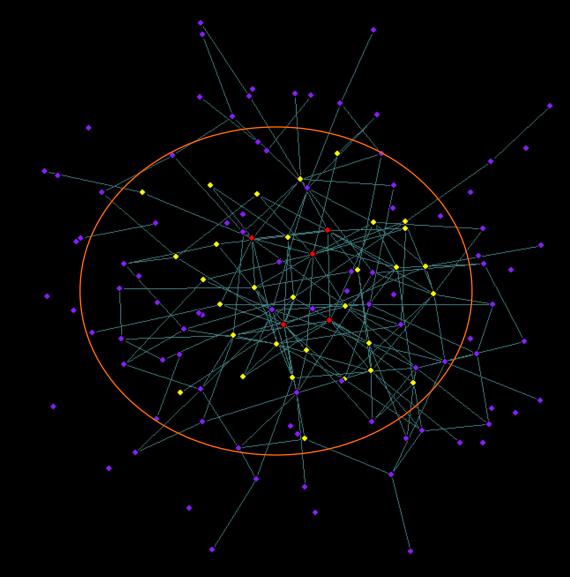
A node with degree k will loose some links because some of its neighbors will vanish.

Cohen et al., Phys. Rev. Lett. 85, 4626 (2000).

Random (E&R) network: limited reach



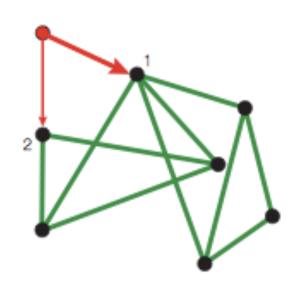
scale-free network: wider reach

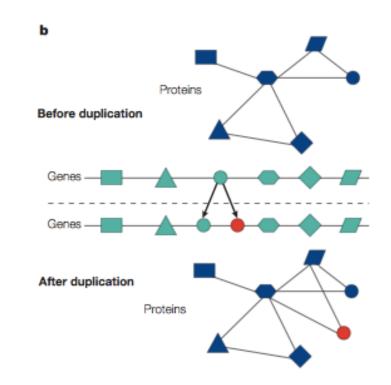


Evolution of scale-free networks

- 1. duplication
- 2. Preferential attachment

а





Google page rank: an example of preferential attachment

- Preferential attachment will favor older nodes (e.g. journal article citations). Early journal articles on a given topic more likely to be cited.
 Once cited, this material is more likely to be cited again in new articles, so original articles in a field have a higher likelihood of becoming hubs in a network of references.
- The Google search engine (PageRank) interprets a link from page A to page B as a vote, by page A, for page B. It also analyzes the page that casts the vote. Votes cast by pages that are themselves "important" weigh more heavily and help to make other pages "important".

Useful links on networks

- http://barabasilab.neu.edu/courses/phys5116/
- http://math.nist.gov/~RPozo/complex_datasets.html
- http://www2.econ.iastate.edu/tesfatsi/netgroup.htm
- http://www.visualcomplexity.com/vc/about.cfm
- http://necsi.edu/publications/dcs/
- http://cnets.indiana.edu