Network Analysis

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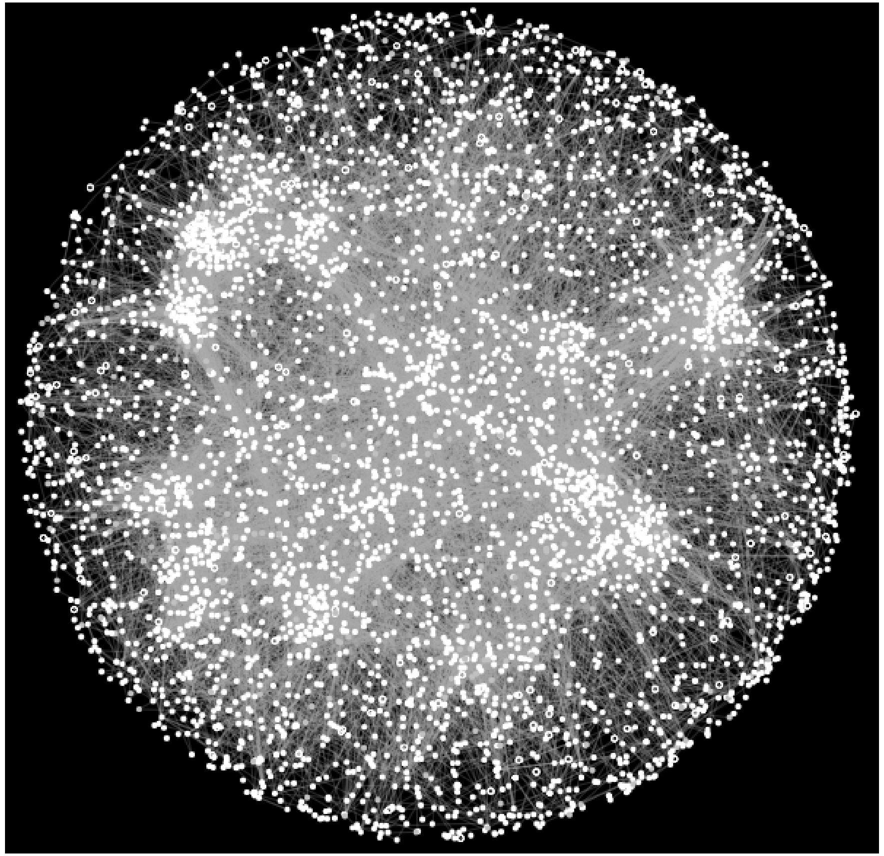
DATA606 2020-04-05

Genetic Interaction Network

- Yeast high-throuput double-knockdown assay
- ~5000 genes
- ~800k interactions

http://www.geneticinteractions.org/



Costanzo et al. (2016) Science. DOI: 10.1126/science.aaf1420

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Genetic Interaction Network

- Number of vertices: 2803
- Number of edges: 67,268

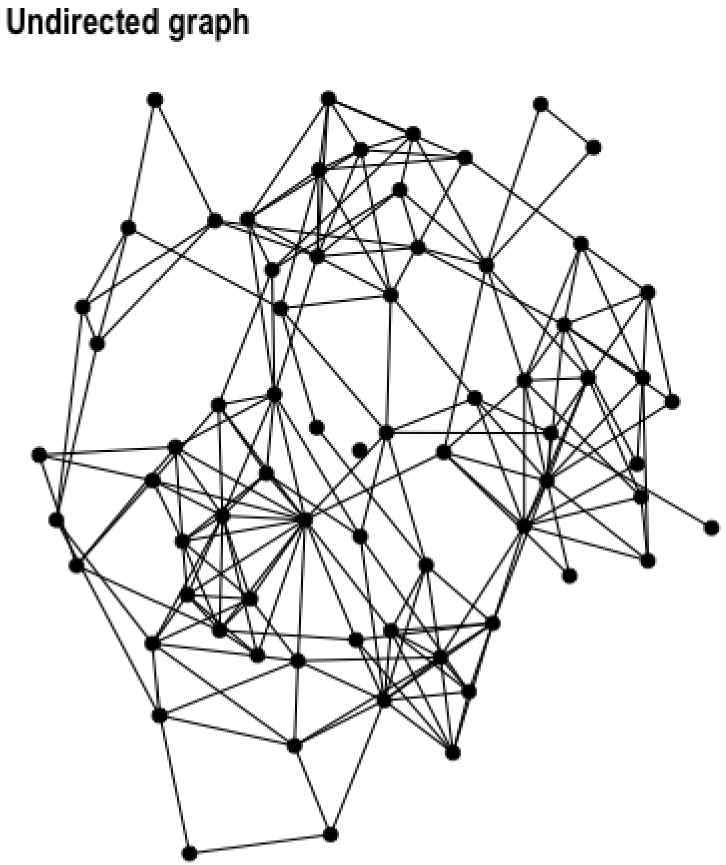
Preliminaries

Network: abstraction of *entities* and their interactions

Graph: mathematical representation

vertices: nodes

edges: links



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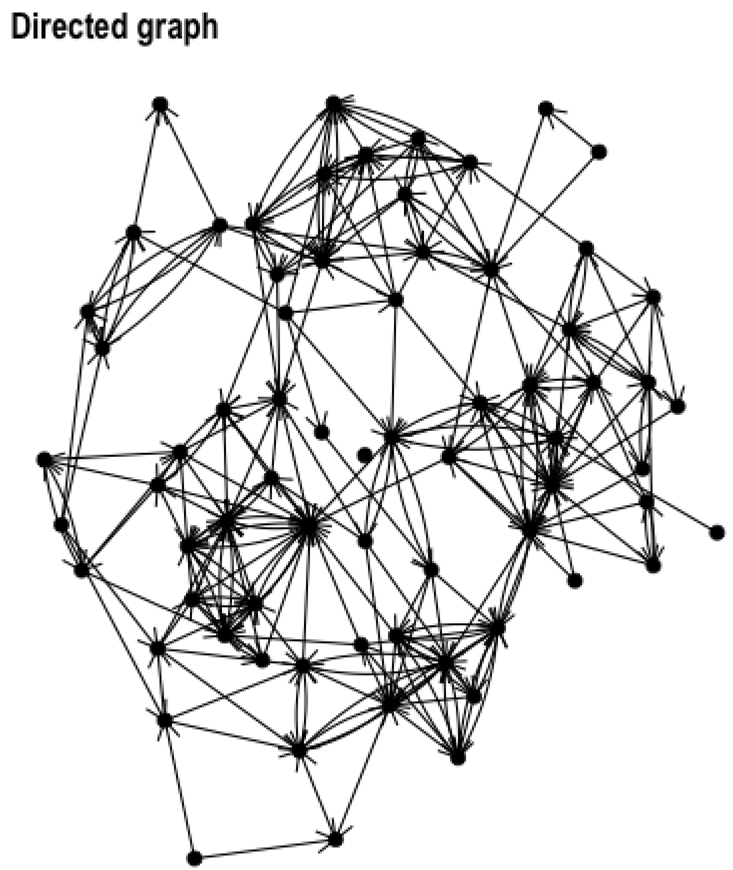

Network statistics: notation

Number of vertices: n

In our example: *number of genes*

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Number of edges: m

In our example: *number of genetic interactions*

Network statistics: notation

Number of vertices: n

In our example: *number of genes*

Number of edges: m

In our example: *number of genetic interactions*

Degree of vertex i: k_i

Number of genetic interactions for gene i

Network statistics: notation

On the board:

- Calculate number of edges m using degrees k_i (for both directed and undirected networks)
- Calculate *average degree* c
- Calculate *density* ρ

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- Calculate *density* ρ

In our example:

Average degree: 47.9971459
Density: 0.0171296

(On the board)

Number of edges using degrees (undirected)

$$m = \frac{1}{2}\sum_{i=1}^{n} k_i$$

Number of edges using degrees (directed)

$$m = \sum_{i=1}^{n} k_i^{\text{in}} = \sum_{i=1}^{n} k_i^{\text{out}}$$

(On the board)

Average degree

$$c = \frac{1}{n} \sum_{i=1}^{n} k_i$$

Density

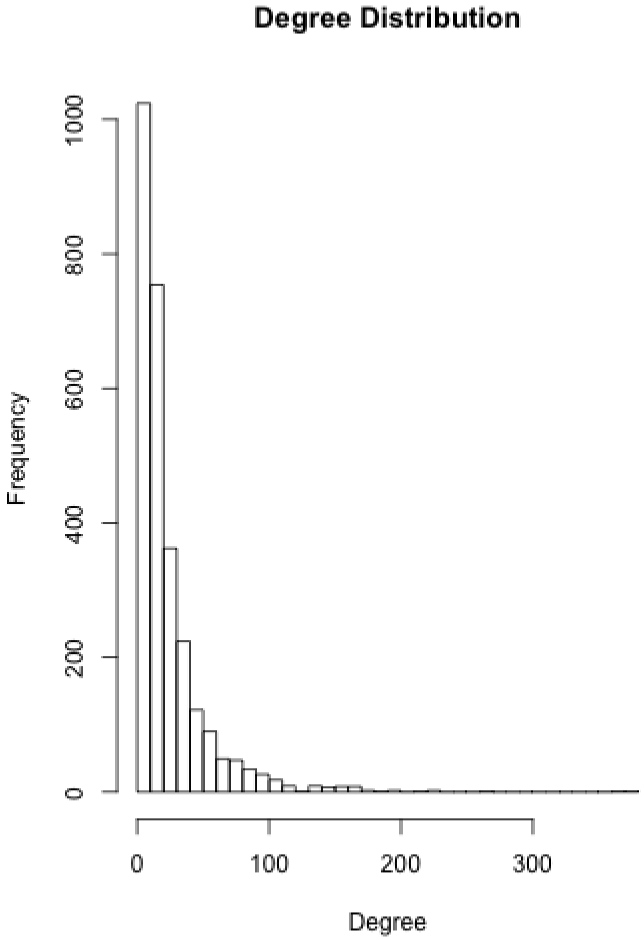
$$\rho = \frac{m}{\binom{n}{2}} = \frac{2m}{n(n-1)} = \frac{c}{n-1} \approx \frac{c}{n}$$

Degree distribution

Fundamental analytical tool to characterize networks

p_k: probability randomly chosen vertex has degree k

On the board: how to calculate p_k and how to calculate average degree c using degree distribution.



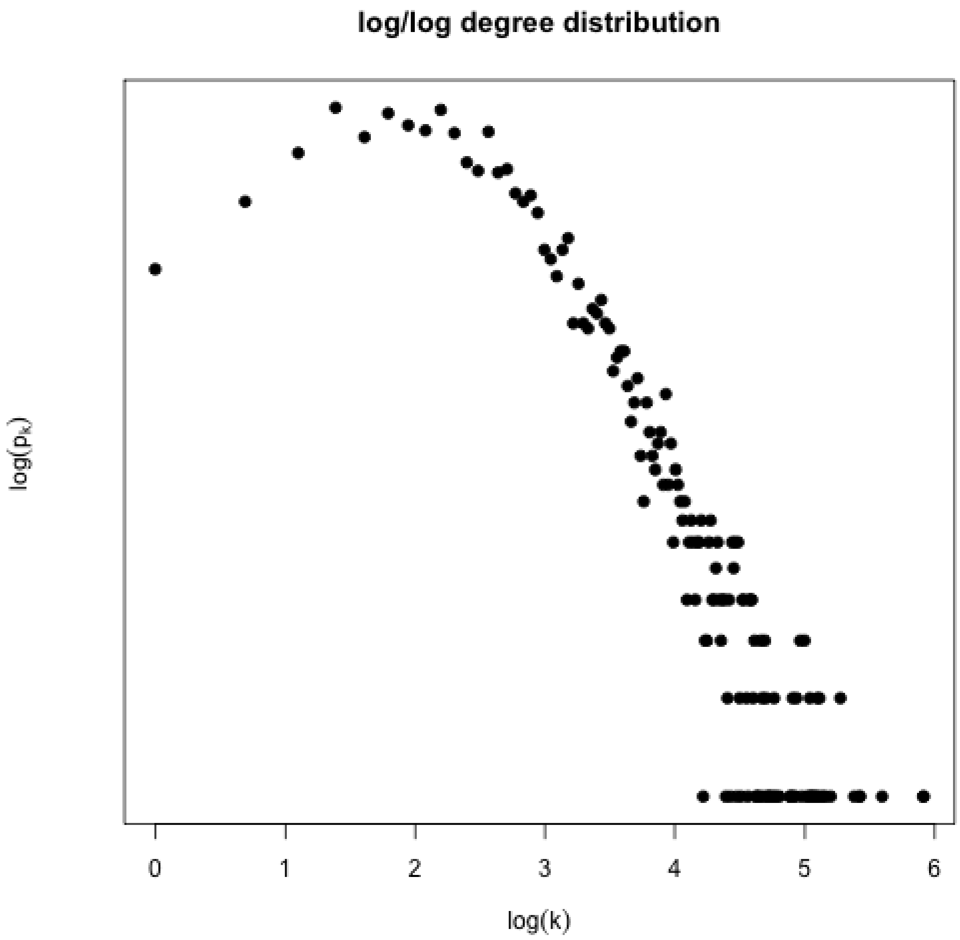
(On the board)

Degree distribution

$$p_k = \frac{n_k}{n}$$

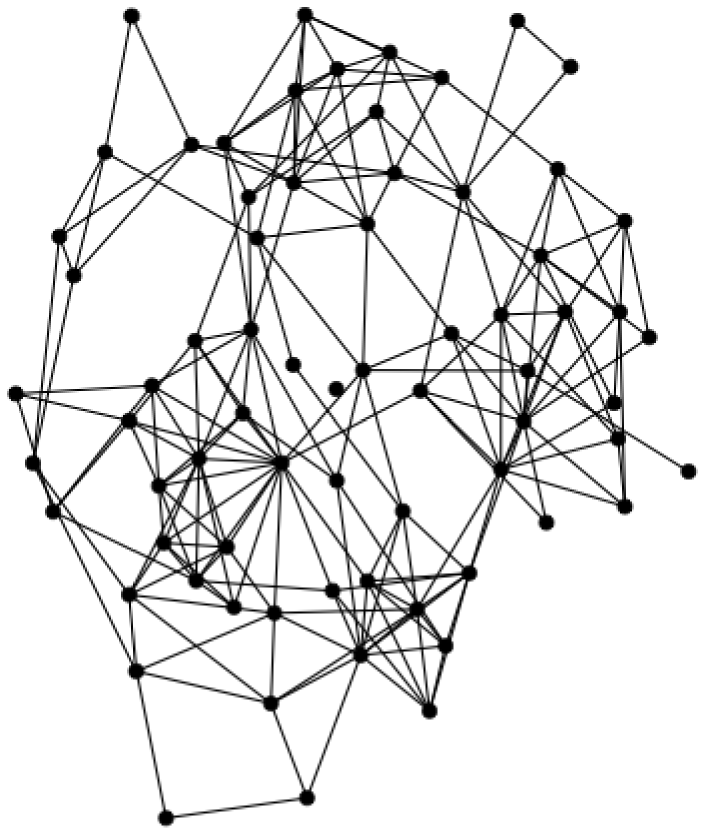
n_k: number of nodes in graph with degree k

Degree Distribution



Paths and Distances

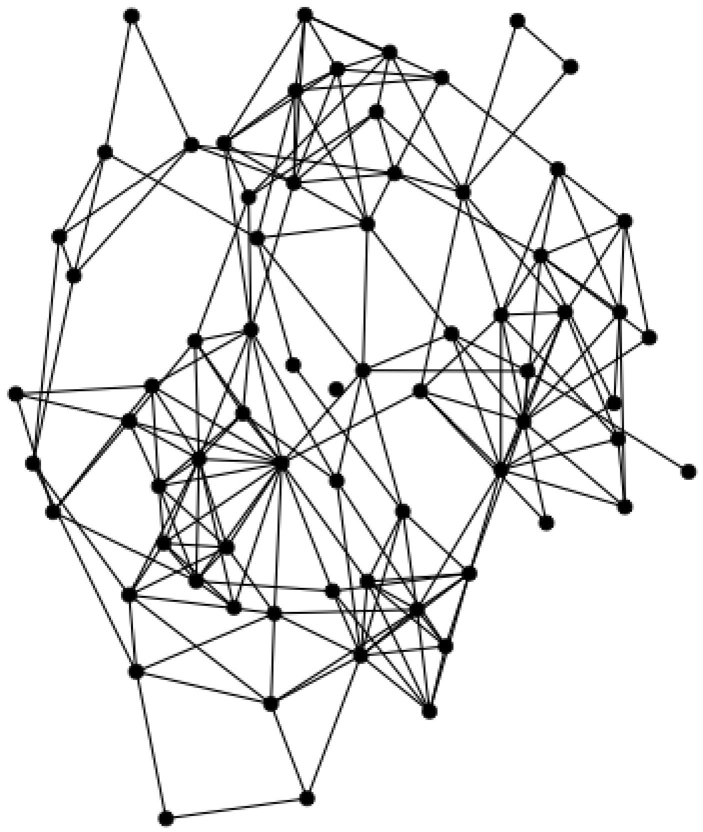
Distance d_{ij}: length of **shortest** path betwen vertices i and j.



Paths and Distances

Distance d_{ij}: length of **shortest** path betwen vertices i and j.

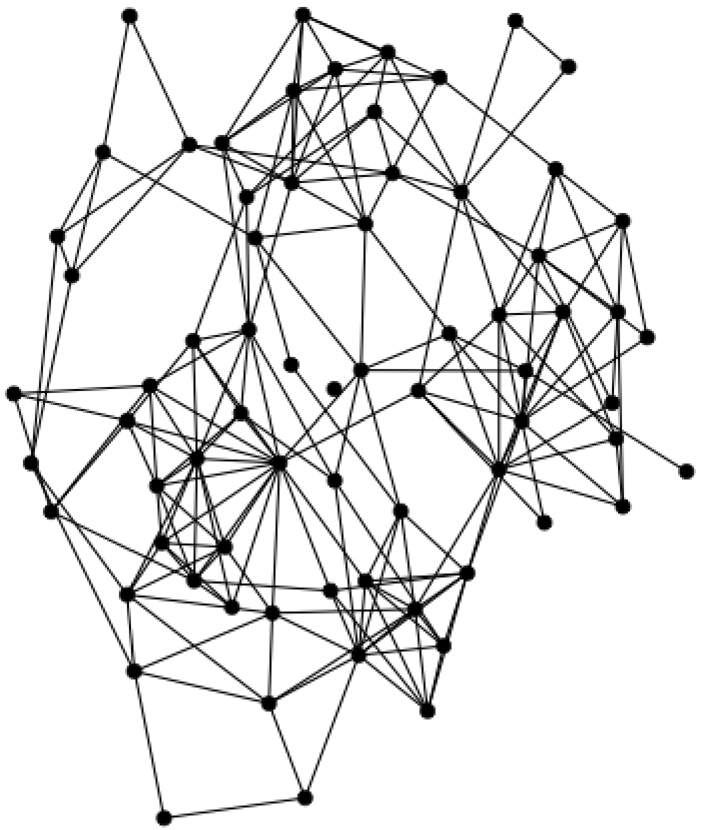
Diameter: longest shortest path $\max_{ij} d_{ij}$



Paths and Distances

Distance d_{ij}: length of **shortest** path betwen vertices i and j.

On the board: average path length

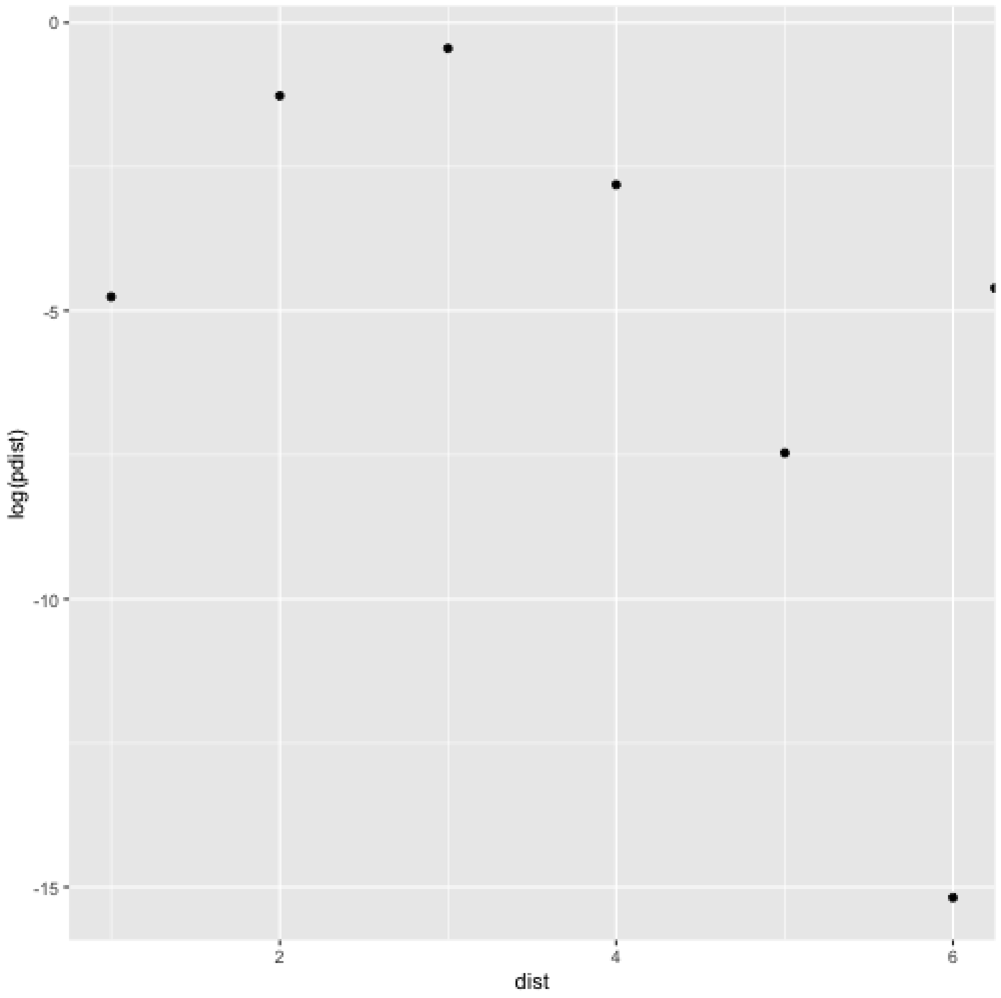


(On the board)

Average path length

$$\bar{d} = \frac{1}{n(n-1)} \sum_{i,j;i \neq j} d_{ij}$$

Distance Distribution



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By convention: if there is no path between vertices i and j then $d_{ij} = \infty$

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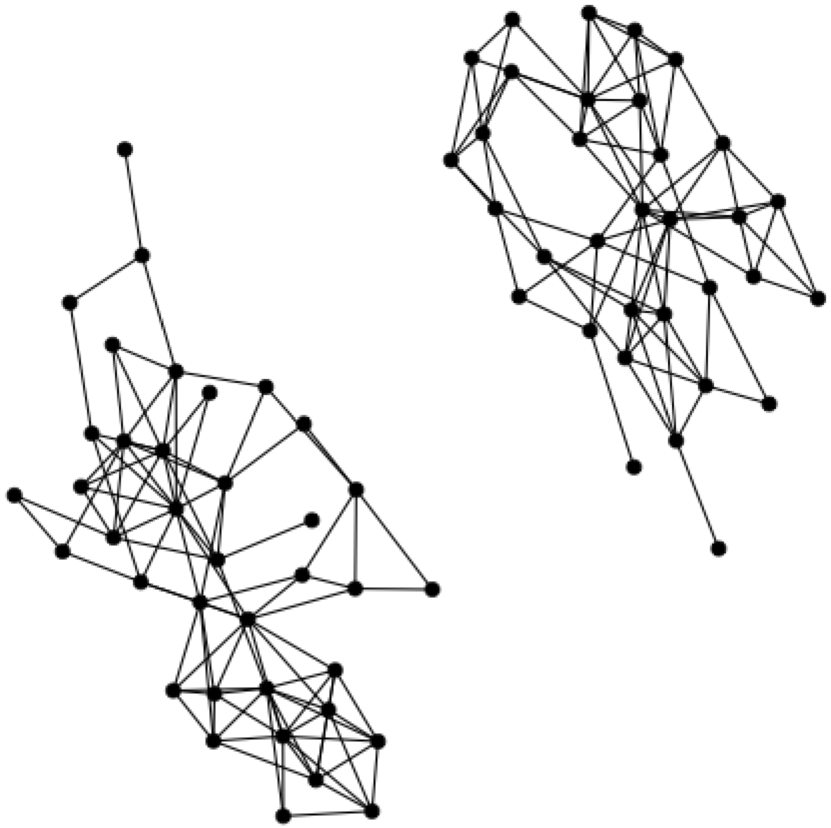
Components maximal subset of connected components

Components



Clustering Coefficient

Another quantity of interest: how dense is the neighborhood around vertex i?

Do the genes that interact with me also interact with each other?

Related to the *locality* property.

Definition on the board

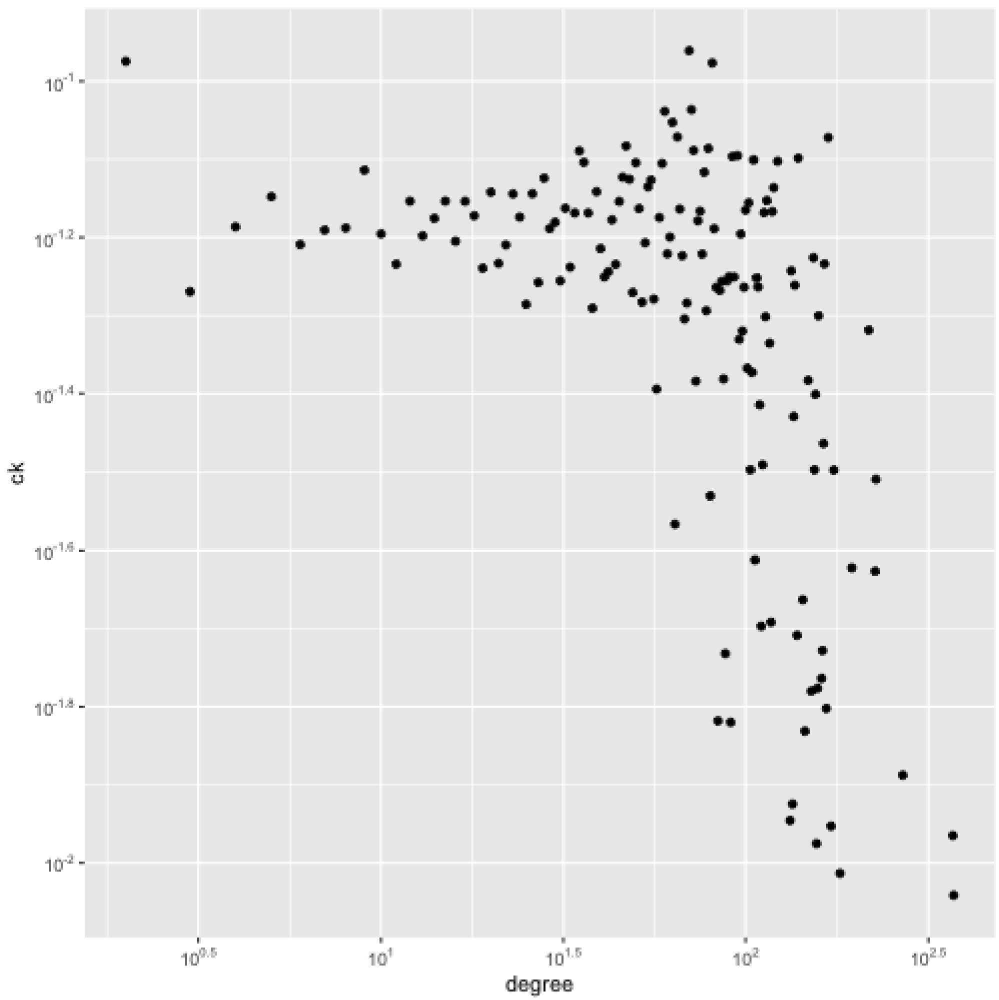
(On the board)

Clustering coefficient

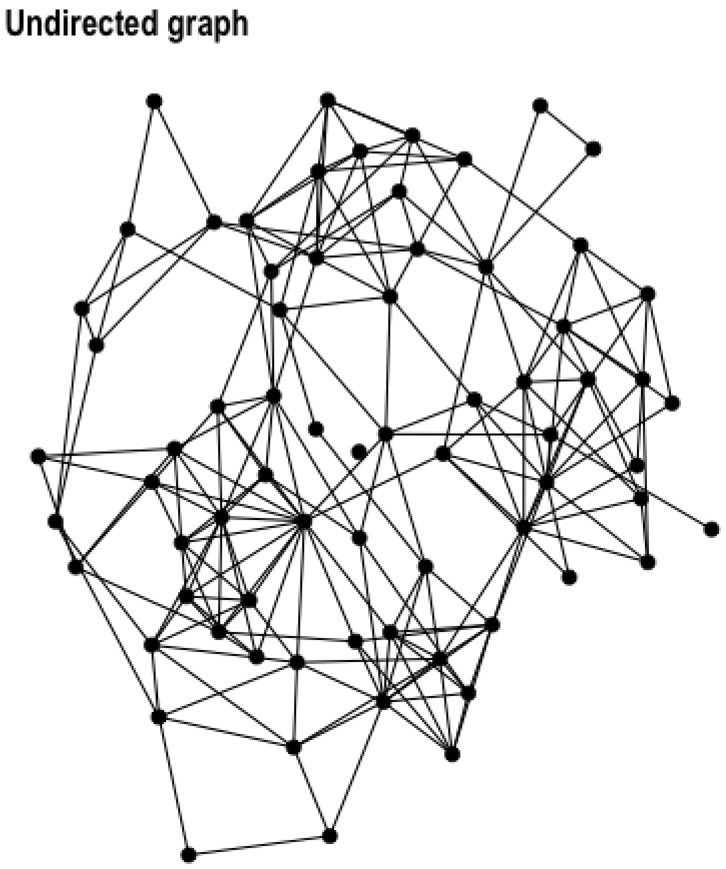
$$c_i = \frac{2m_i}{k_i(k_i - 1)}$$

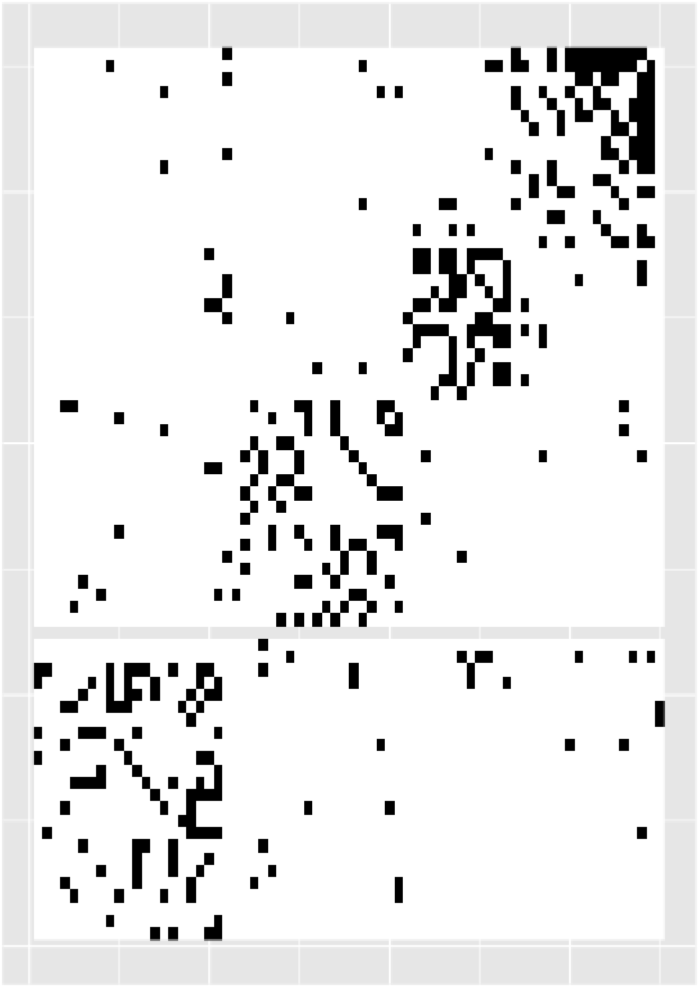
m_i: number of edges between neighbors of vertex i

Clustering coefficient



Adjacency Matrix

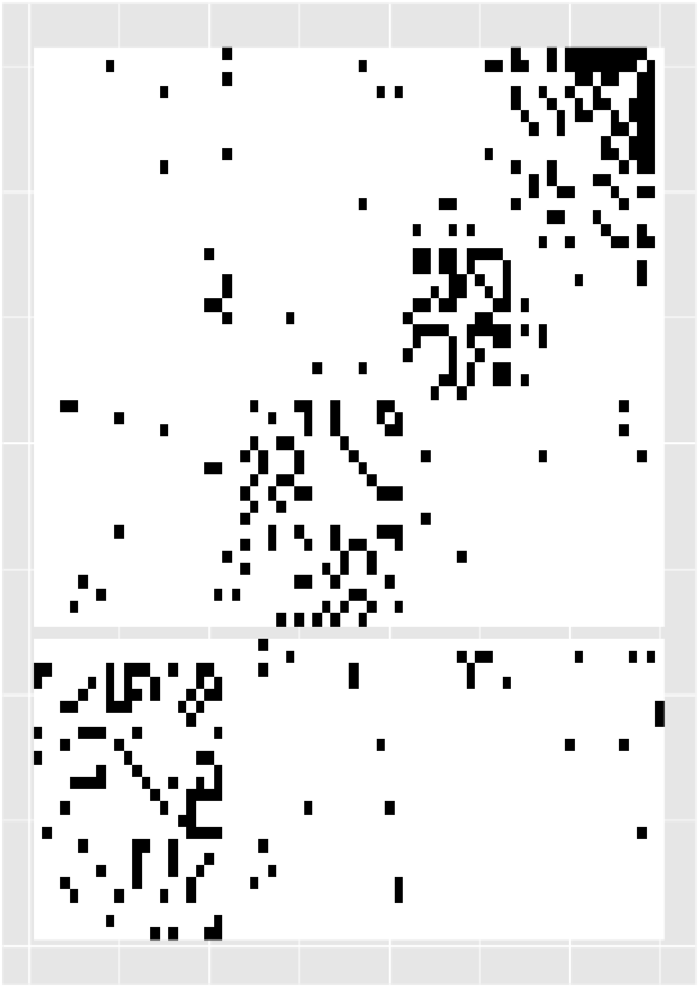




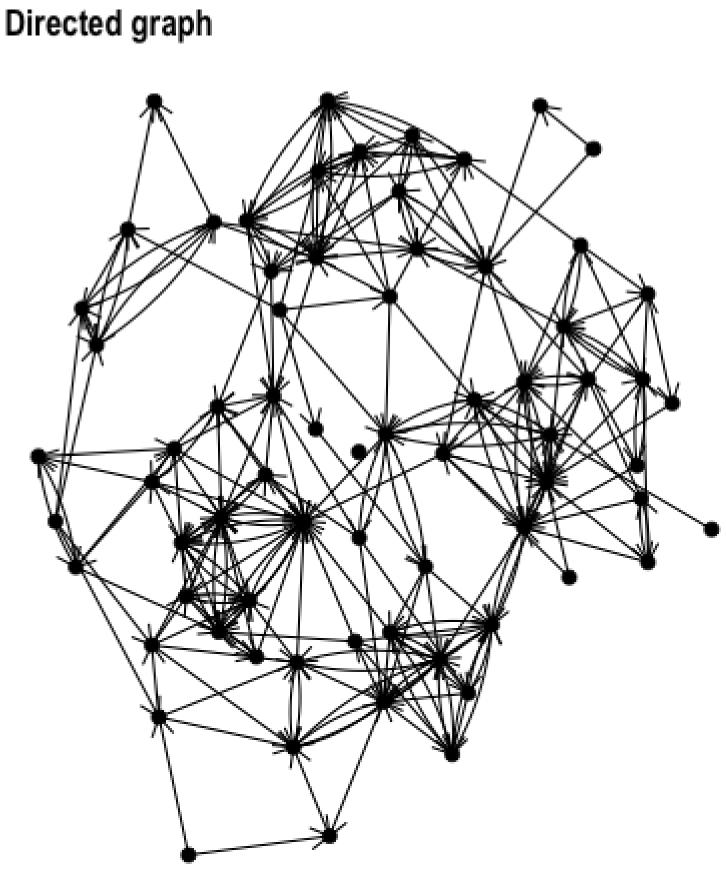
Adjacency Matrix

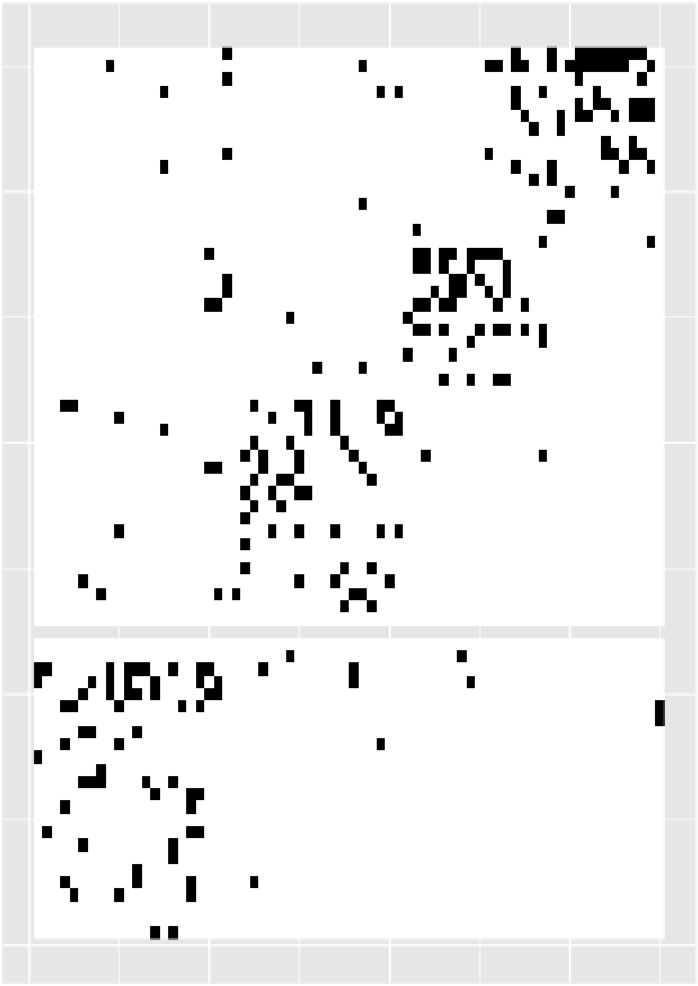
On the board:

- Definition
- Computing degree with adj. matrix
- Computing num. edges m with adj. matrix
- Computing paths with adj. matrix



Adjacency Matrix





Weighted networks

Edges are assigned a weight indicating quantitative property of interaction

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- Strength of genetic interaction (evidence from experiment)
- Rates in a metabolic network
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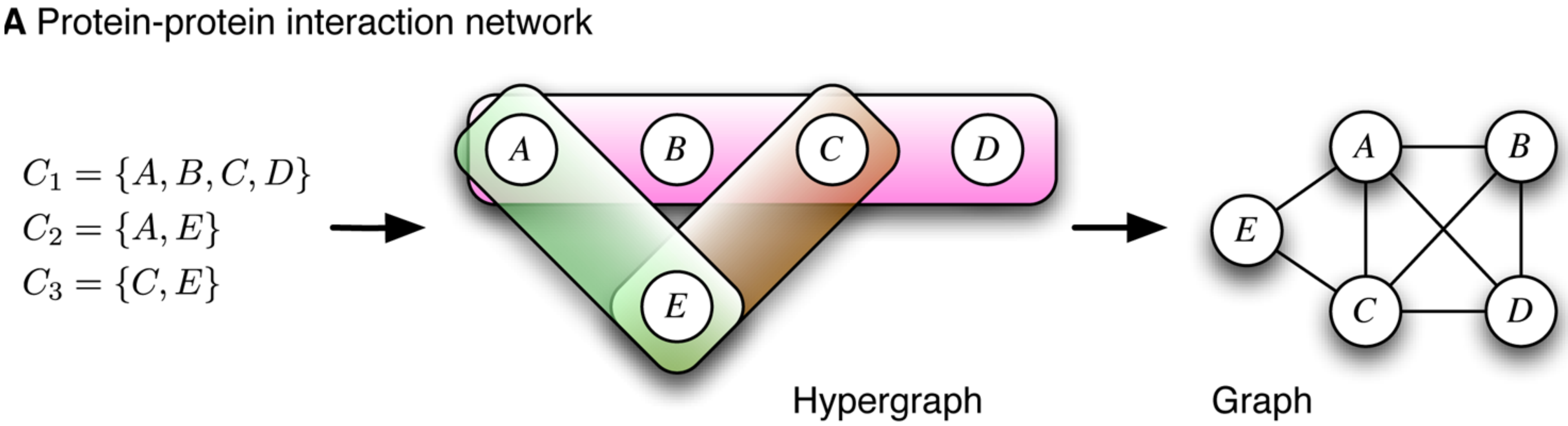
Adjacency matrix contains weights instead of 0/1 entries

Path lengths are the sum of edge weights in a path

Hypergraphs

Edges connect more than two vertices

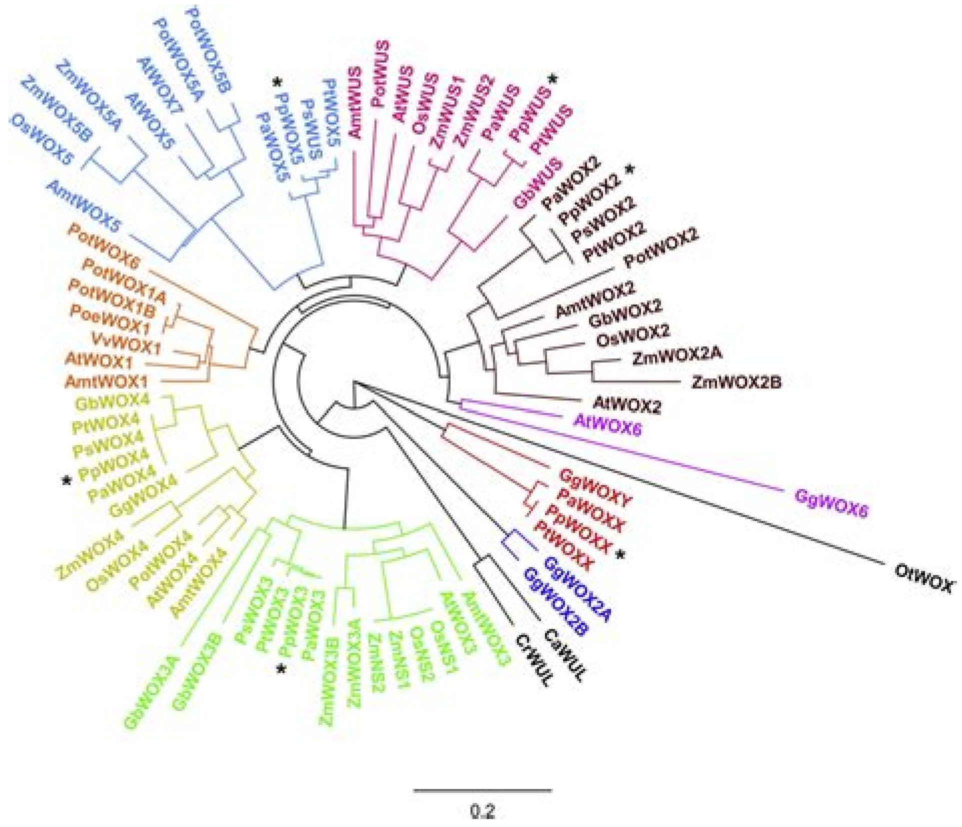


https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1000385

Trees

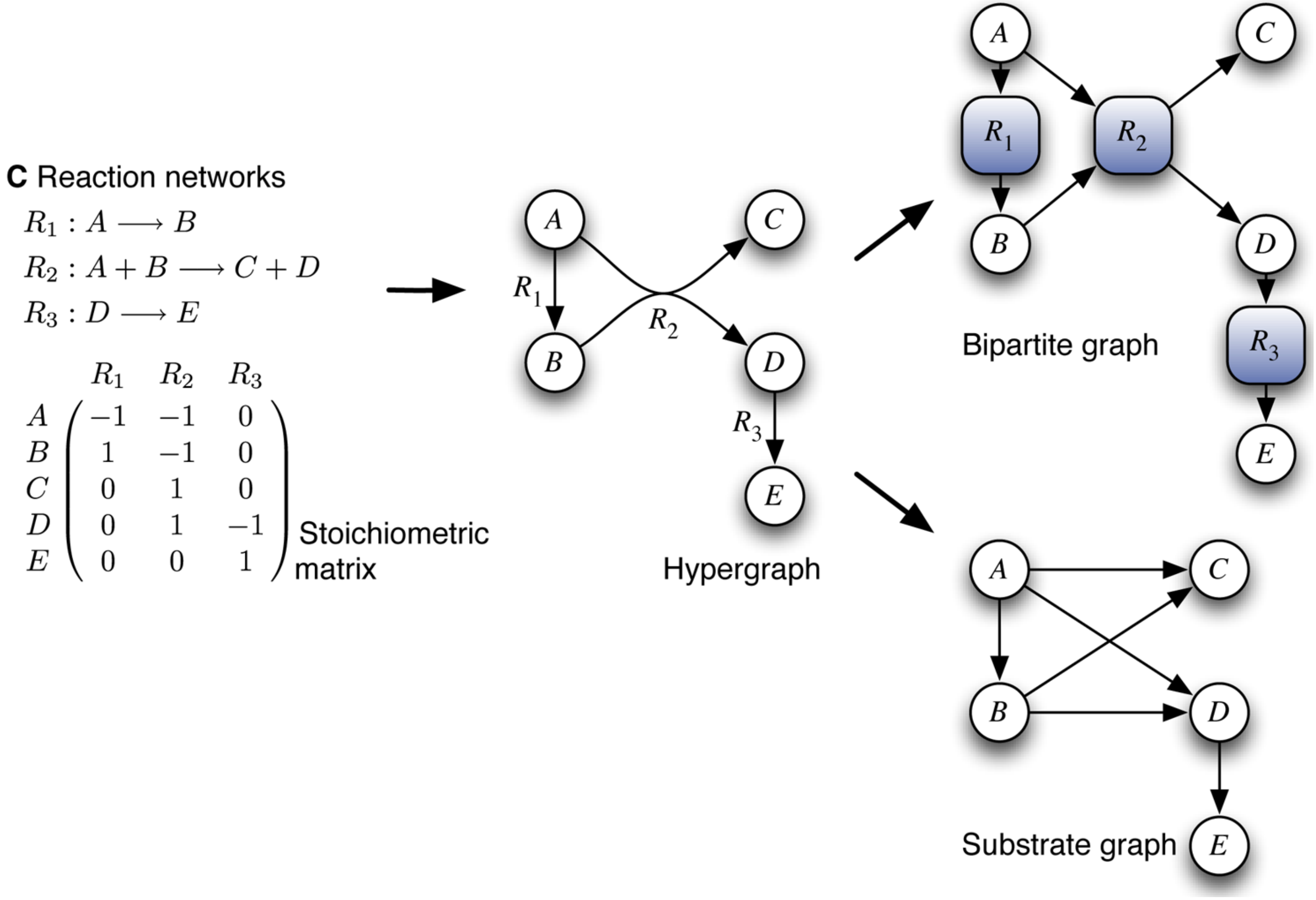
Acyclic graphs

Single path between any pair of vertices



https://www.sciencedirect.com/science/article/pii/S0981942817304321

Bipartite Networks



Bipartite Networks

We use an *Incidence Matrix* B instead of *Adjacency Matrix*

(On the board): definition

Bipartite Networks

Projections

vertex projection: P_{ij}, num. of groups in which vertices i and j co-occur

group projection: P'_{ij}, num. of members groups i and j share

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(On the board)

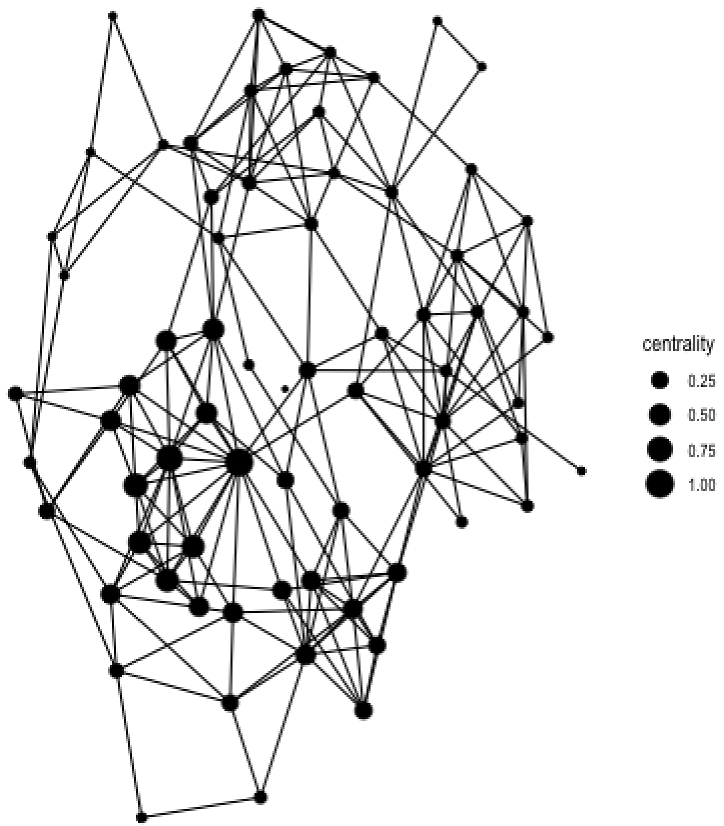
$$P = B^T B$$

$$P' = BB^T$$

Centrality

What are the *important* nodes in the network?

What are *central* nodes in the network?



Centrality

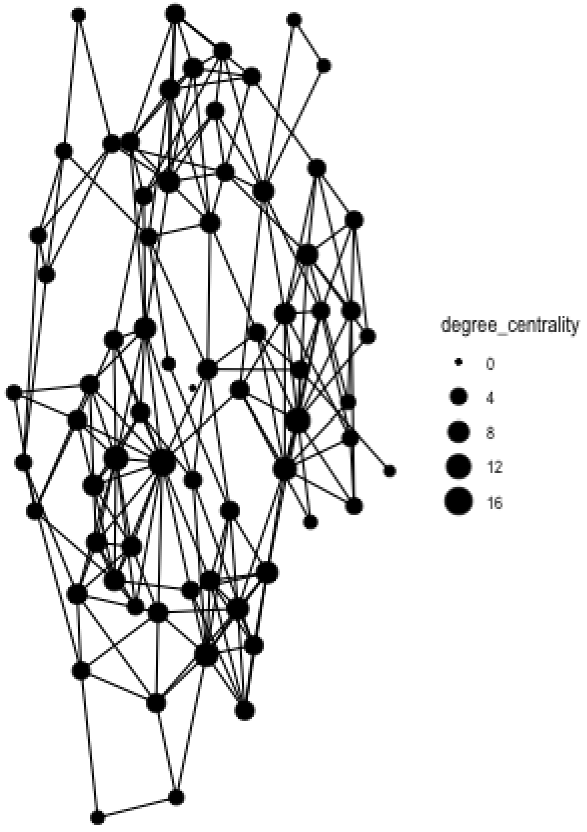
Undirected Graphs

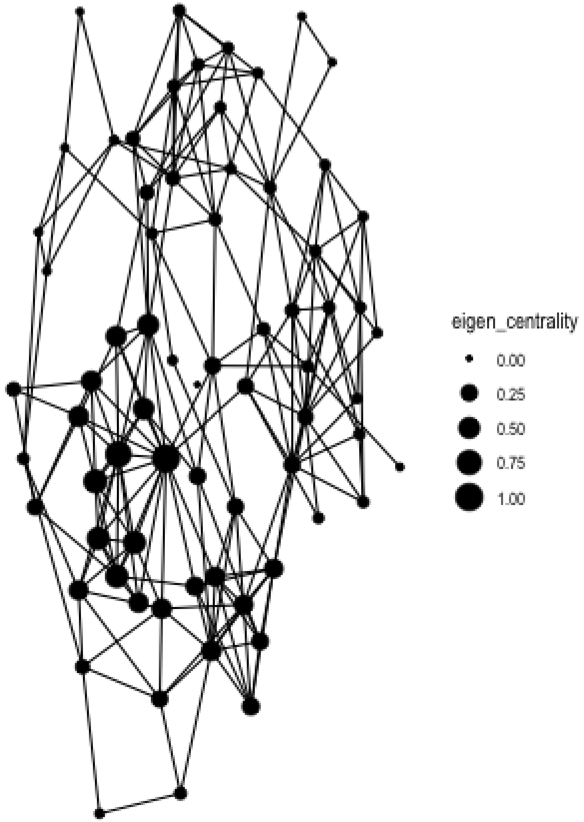
- Eigenvalue Centrality

Directed Graphs

- Katz Centrality
- Pagerank

Centrality

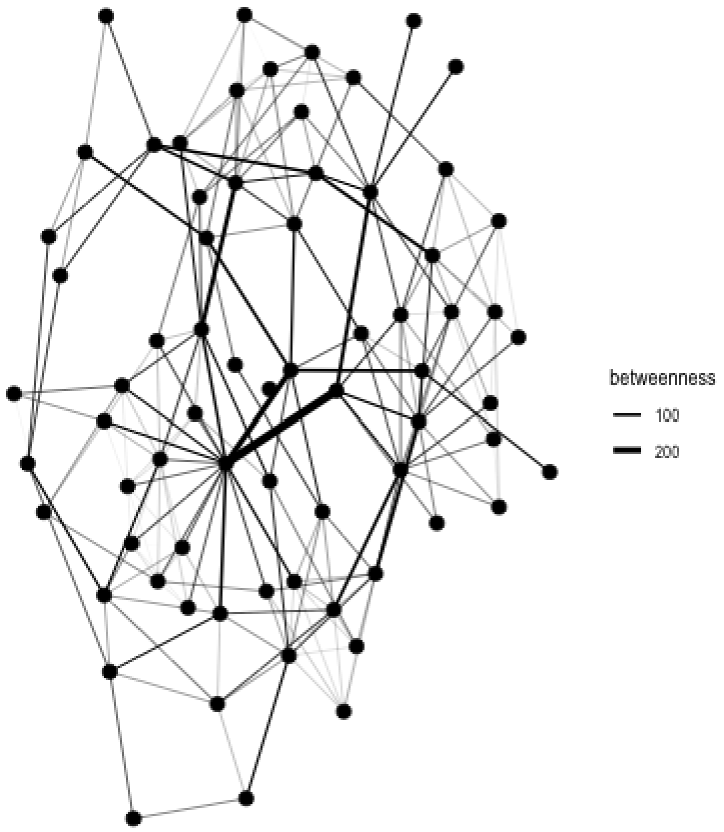

degree_centrality
0
4
8
12
16


eigen_centrality
0.00
0.25
0.50
0.75
1.00

Betweenness

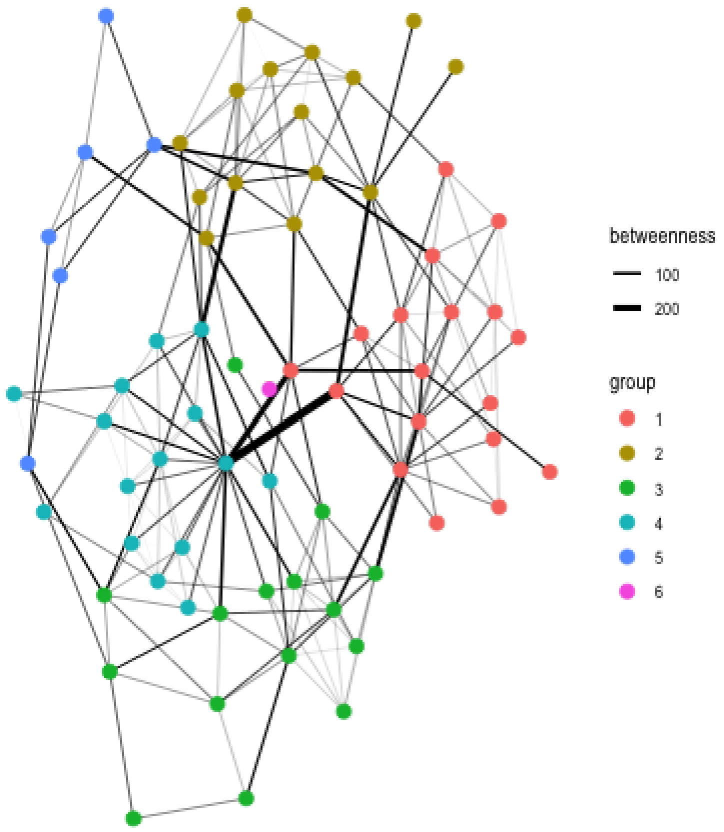
What are the *important* edges in the network?

What are edges that may connect clusters of nodes in the network?



Betweenness

Girvan-Newman Algorithm - hierarchical method to partition nodes into communities using edge betweenness



Girvan-Newman Algorithm

Two phases:

Phase One: Compute betweenness for every edge

Phase Two: Discover communities by removing *high* betweenness edges (similar to hierarchical clustering)

Girvan-Newman Algorithm

Calculating Betweenness

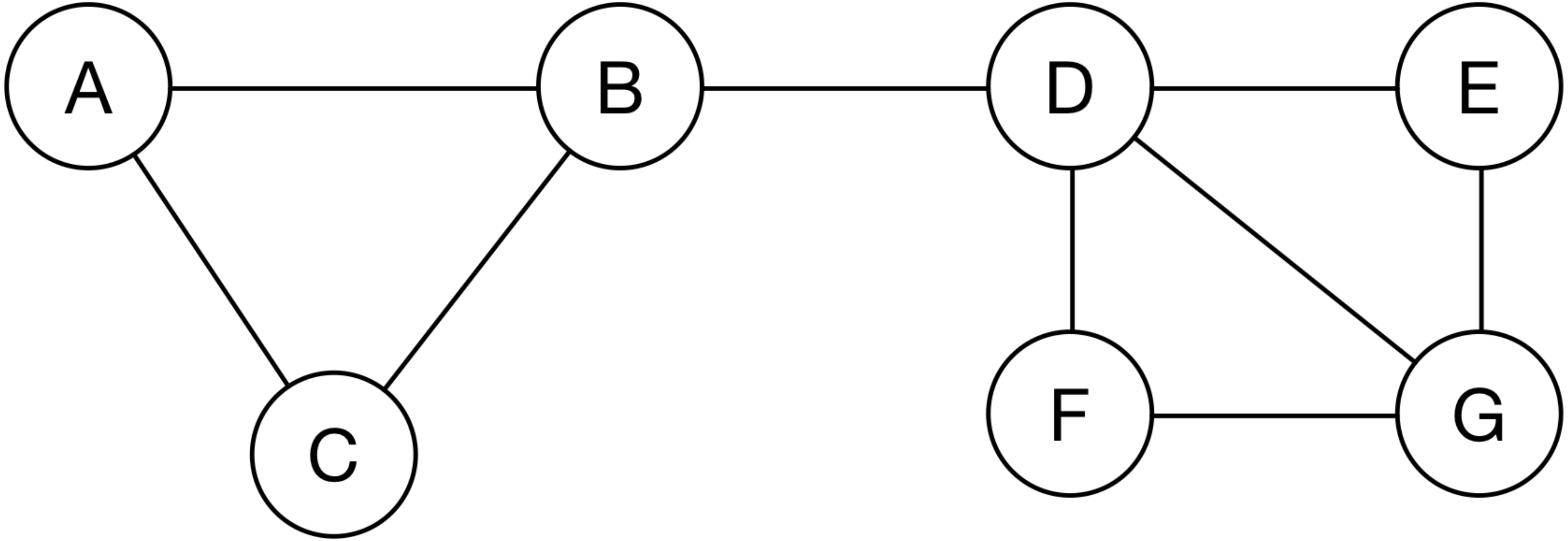
Formally, $\mathrm{betweenness}(e)$: fraction of node pairs (x, y) where shortest path crosses edge e

For each node x, use breadth-first-search to count number of shortest paths through each edge in graph

Sum result across nodes, and divide by two

Girvan-Newman Algorithm

Example



Resources

Cross-language

igraph: http://igraph.org/

Resources

R

Workhorses:

- `igraph`
- `Rgraphviz`

Tidyverse (https://tidyverse.org):

- `tidygraph`
- `ggraph`

Resources

Python

- `igraph`
- `networkx`