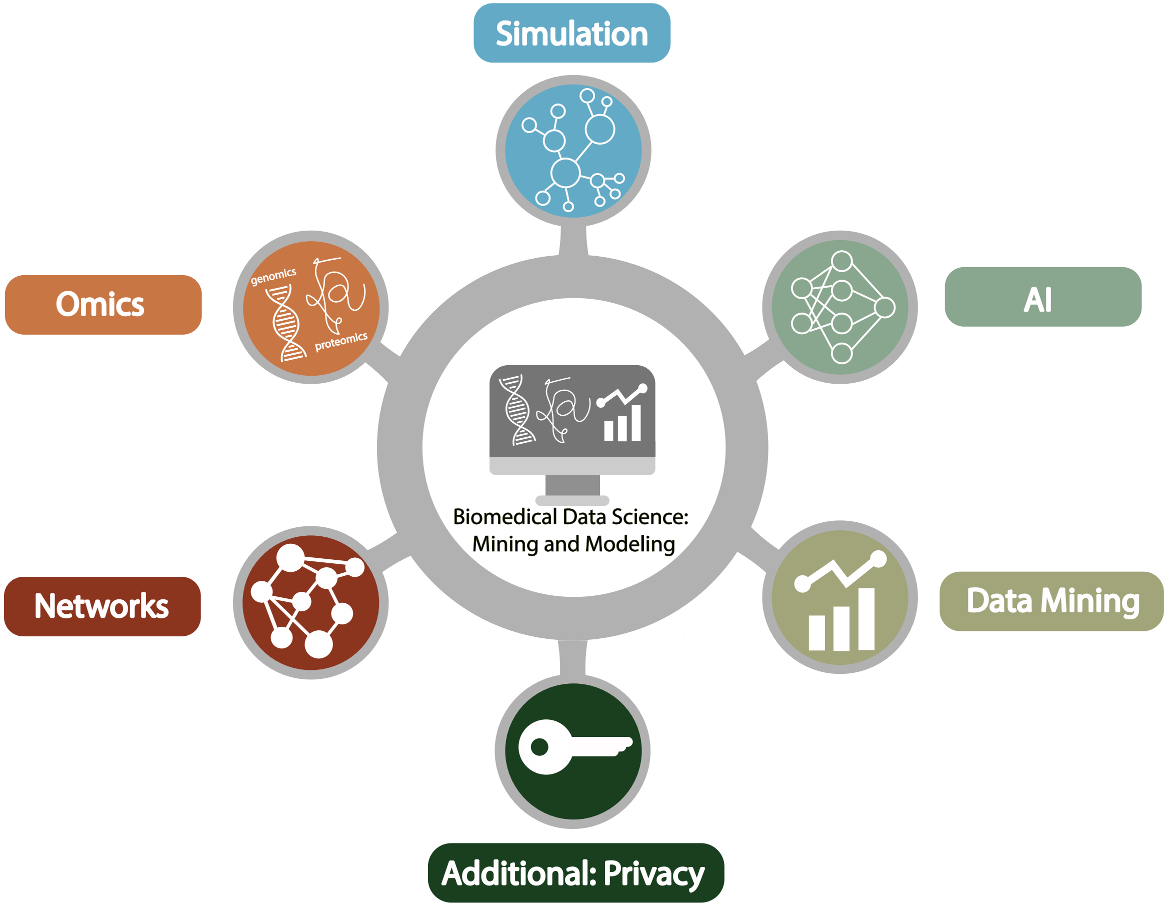
Biomedical Data Science (GersteinLab.org/courses/452)

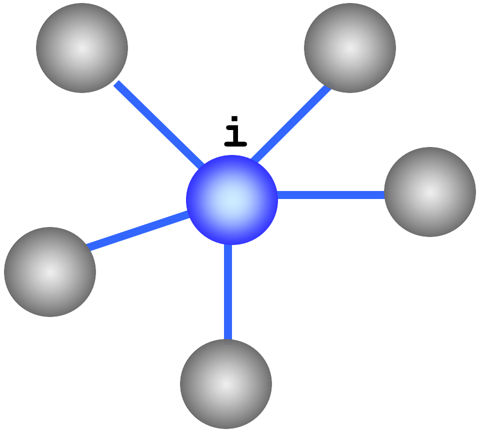
Network Topology – Network Quantities (25m10b)



Mark Gerstein
Yale U.

Last edit in spring '25. Very similar to 2022's 22m10b & 2021's M10b [which has a video].

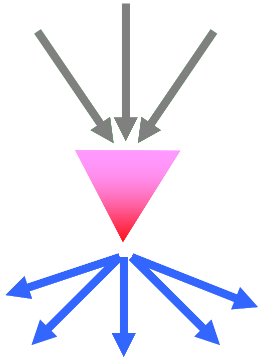
- Degree of a node: the number of edges incident on the node



Degree of node i = 5

Network parameters

Number of incoming and outgoing connections



Connectivity

Incoming connections = 2.2

→each gene is regulated by ~2 TFs

In-degree

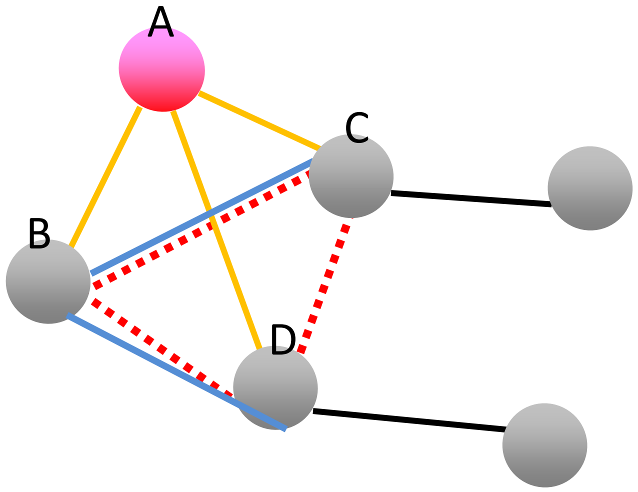
Outgoing connections = 20.2

→each TF regulates ~20 genes

Out-degree

Clustering coefficient

- Clustering Coefficient:
  - Ratio of existing links to maximum number of links for neighbouring nodes
  - Example:
    - For A:
      - 3 neighbours
      - 2 existing link
      - 3 possible links
    - Clustering coefficient
      - $C_A=2/3$



Example from: http://www.learner.org/courses/mathilluminated/units/11/textbook/04.php

Clustering coefficient

- Average Coefficient:
  - Average of clustering coefficients of all nodes n

$$\overline{C} = \frac{1}{n}\sum_{i=1}^{n} C_i$$

  - Measure of inter-connectedness of the network
  - Global property

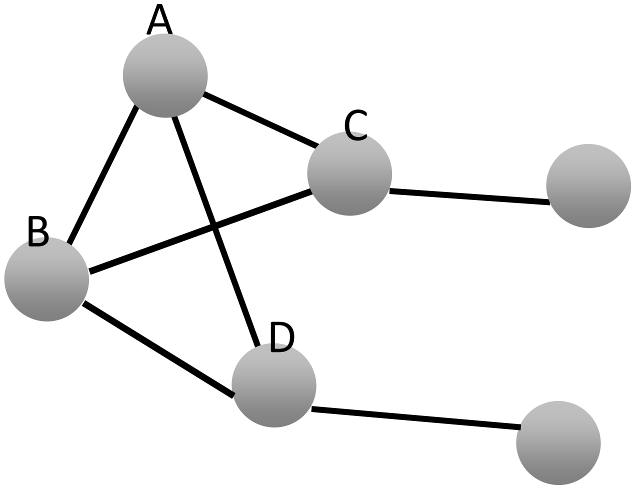
- Example:
  - Clustering coefficient:

$C_A=2/3$ $C_B=2/3$

$C_C=1/3$ $C_D=1/3$

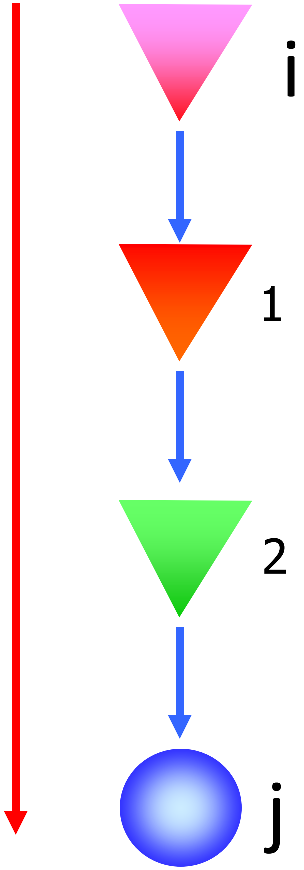
  - Average coefficient =

1/4(2/3+2/3+1/3+1/3)= 0.5



Example from: http://www.learner.org/courses/mathilluminated/units/11/textbook/04.php

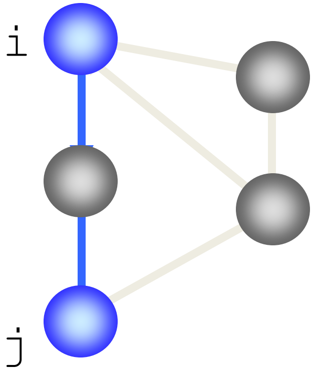
Path length



- Number of edges along a path
- Path length = 3
- Meaning:
  - Number of intermediate TFs to reach final target
  - Indication of how immediate a response is

Path length

- Shortest path length:
  - $L_{(i,j)}$ is the minimum number of edges that must be traversed to travel from a vertex i to another vertex j of a graph G



$$L_{(i,j)} = 2$$

Graph Theory Terminology (Batten, pp. 92-105)

- Characteristic path length (Average path length)
  - The characteristic path length *L* of a graph is the average of the $L_{(i,j)}$ for every possible pair (i,j)

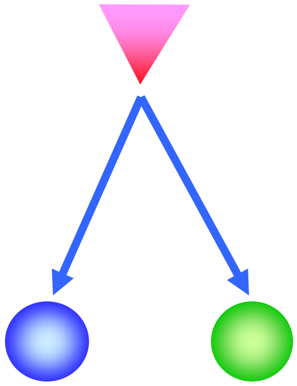
$$L = \frac{1}{n(n-1)} \sum_{i,j} L_{(i,j)}$$

  - Networks with small values of L are said to have the “small world property”

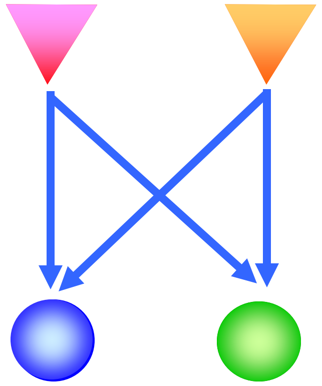
http://en.wikipedia.org/wiki/Average_path_length

Network motifs

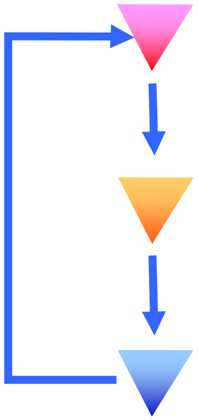
Regulatory modules within the network



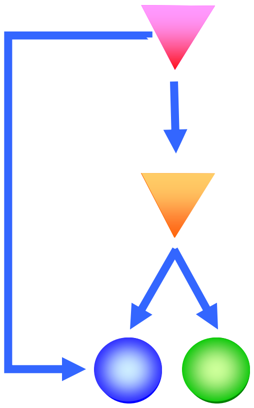
SIM



MIM



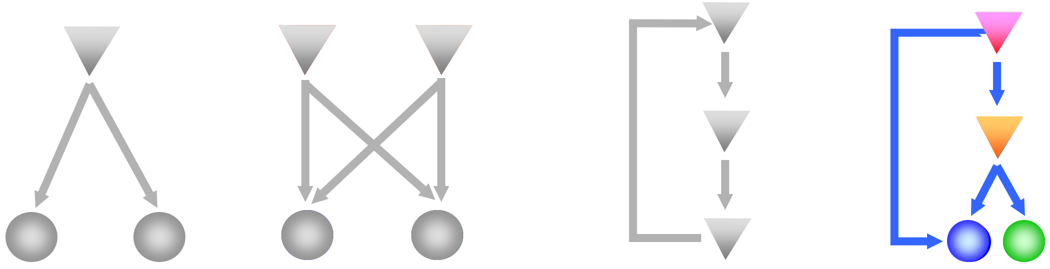
FBL

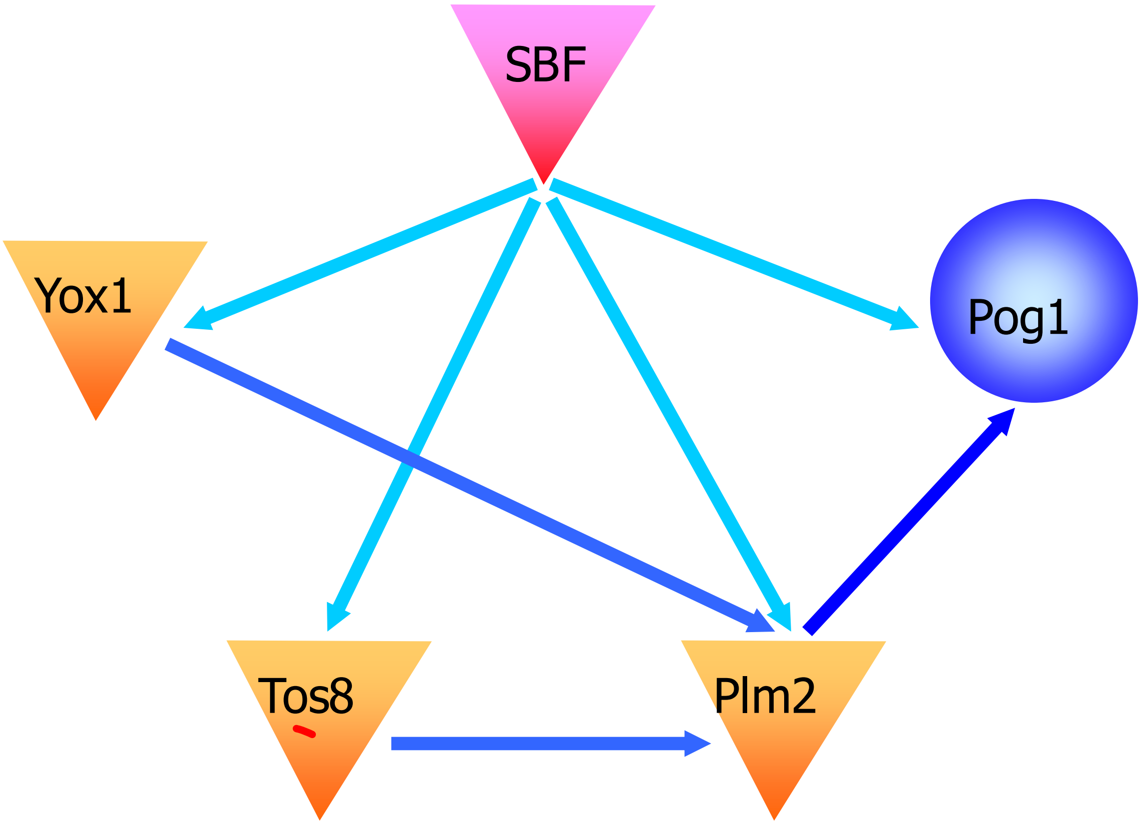


FFL

[Alon U, 2007, Nature Reviews Genetics, Network motifs: theory and experimental approaches]

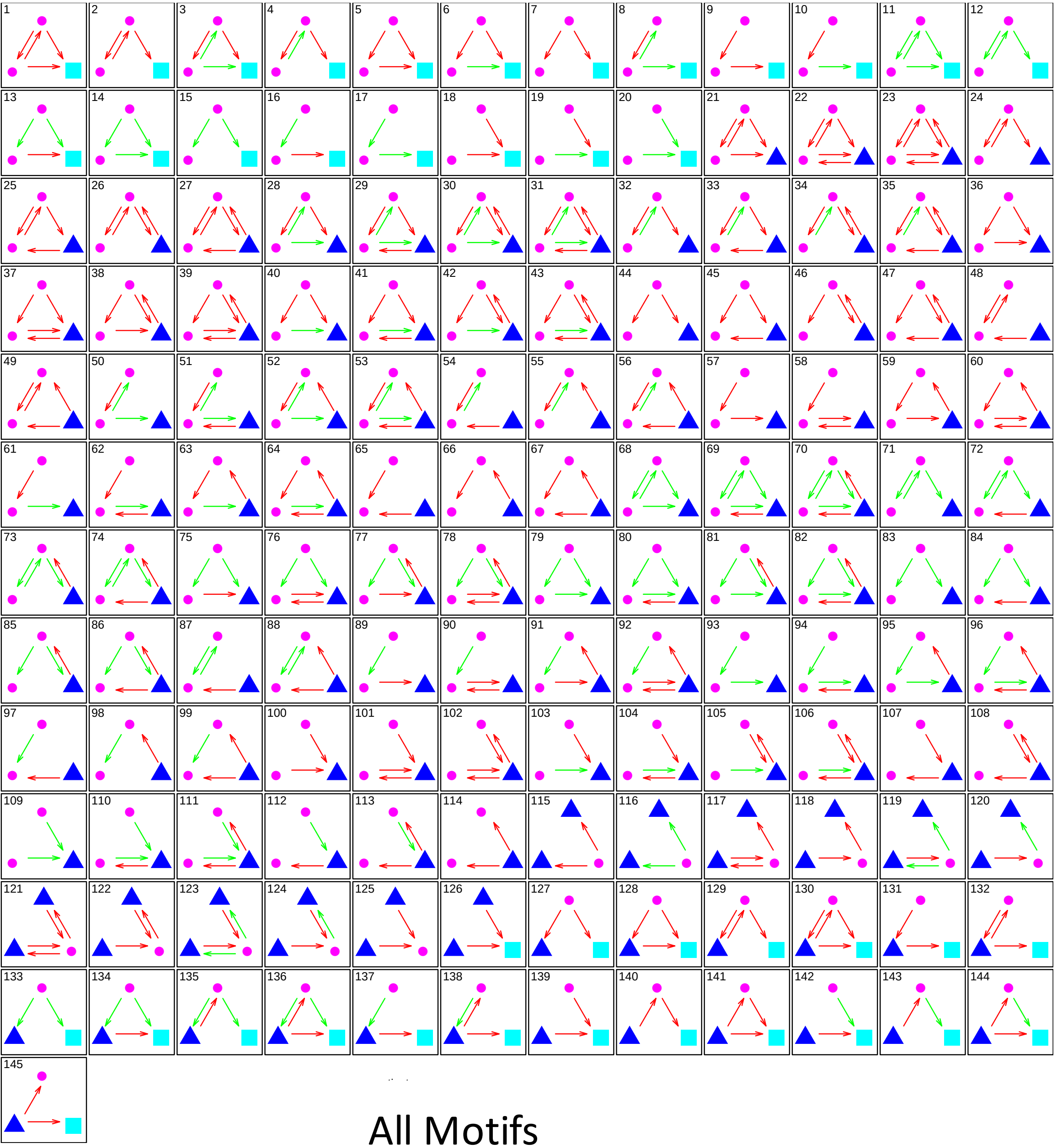
FFL = Feed-forward loops





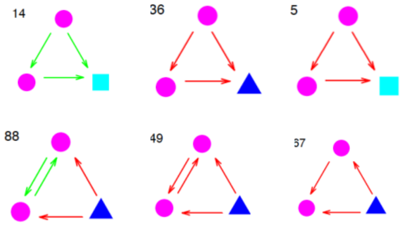
[Alon U, 2007, Nature Reviews Genetics]

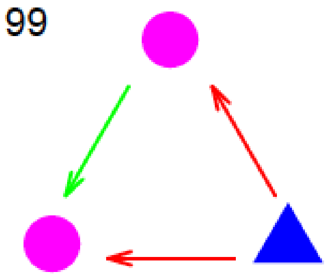
Network Motifs



All Motifs

7 Motifs
Over-represented





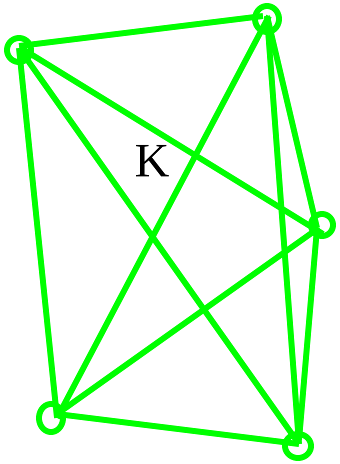
FFL involving
miRNA & 2 TFs

[*Science* 330:6012; Cheng et al. *PLOS CB* '11]

Cliques

- Fully connected sub-components
- Related measures

  k-cores : For all vertices in a graph G have degree at least k

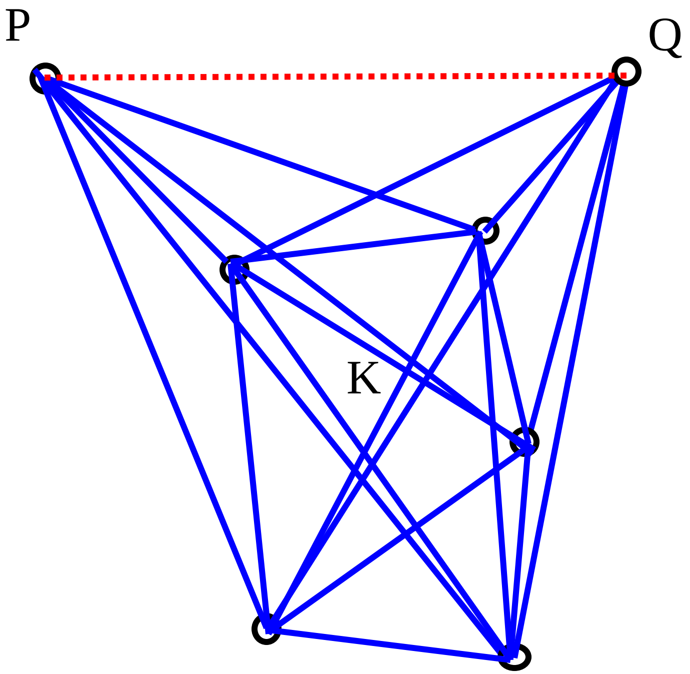


[Hogue et al, BMC BIOINFORMATICS, 2003]

Problem: High-throughput experiments are prone to missing interactions

One solution—defective cliques

- If proteins P and Q interact with a clique K of proteins which all interact with each other, then P and Q are more likely to interact with each other
- P, Q, and K form a defective clique



Predicting protein interactions by completing defective cliques

[Yu et al. Bioinformatics (2006)]

References

- McGillivray, P., Clarke, D., Meyerson, W., Zhang, J., Lee, D., Gu, M., Kumar, S., Zhou, H., & Gerstein, M. (2018). Annual Review of Biomedical Data Science, 1(1), 153–180.
  Network analysis as a grand unifier in biomedical data science.
  https://doi.org/10.1146/annurev-biodatasci-080917-013444
  (Section 2.)