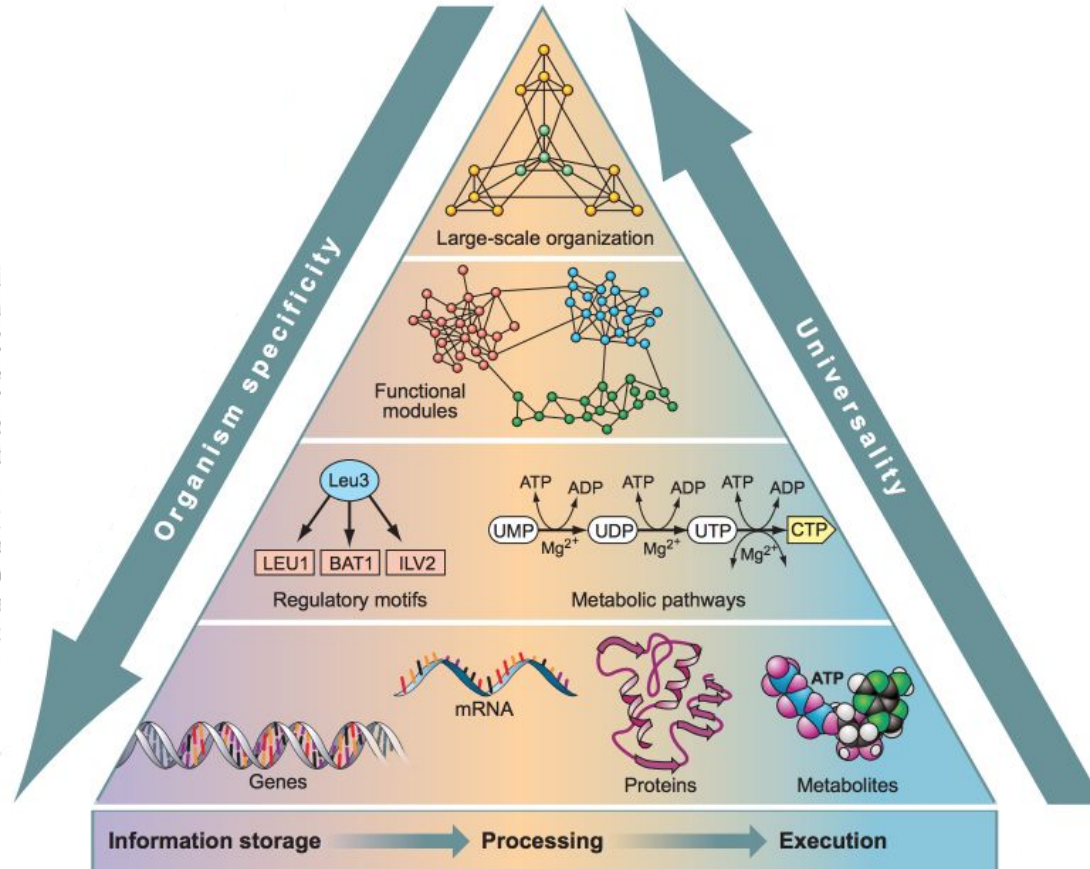


Lecture 14: Large-scale biological networks

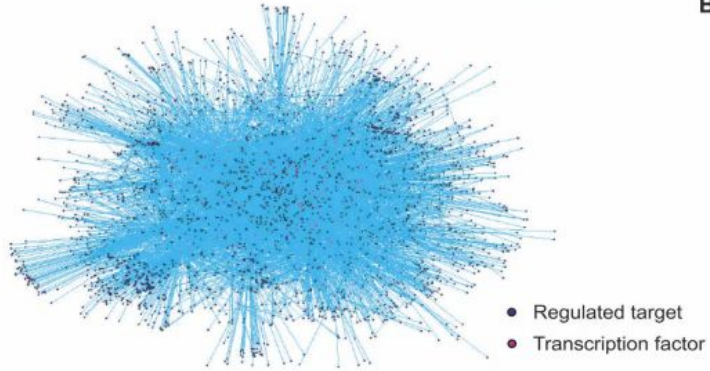
- Network topology
- Network motifs
- Condition-specific networks
- Network reconstruction

Life's complexity pyramid

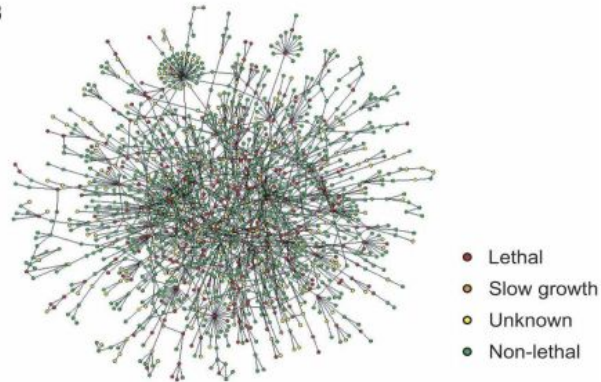


Biological networks

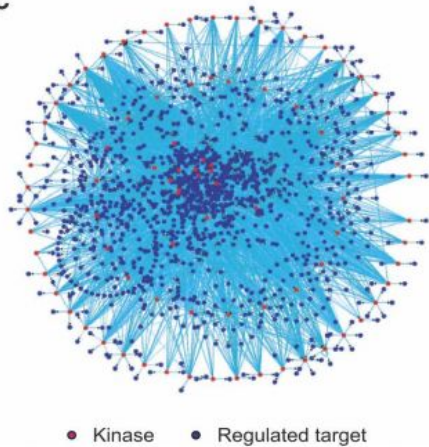
A



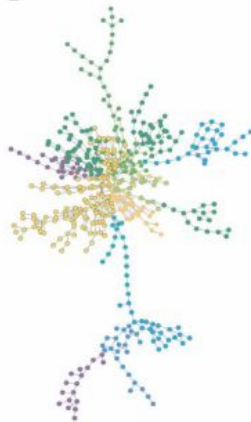
B



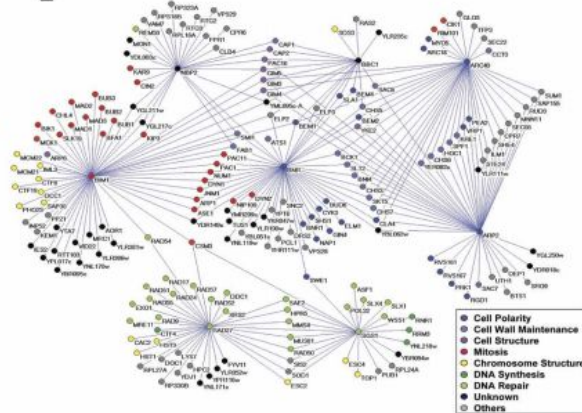
C



D

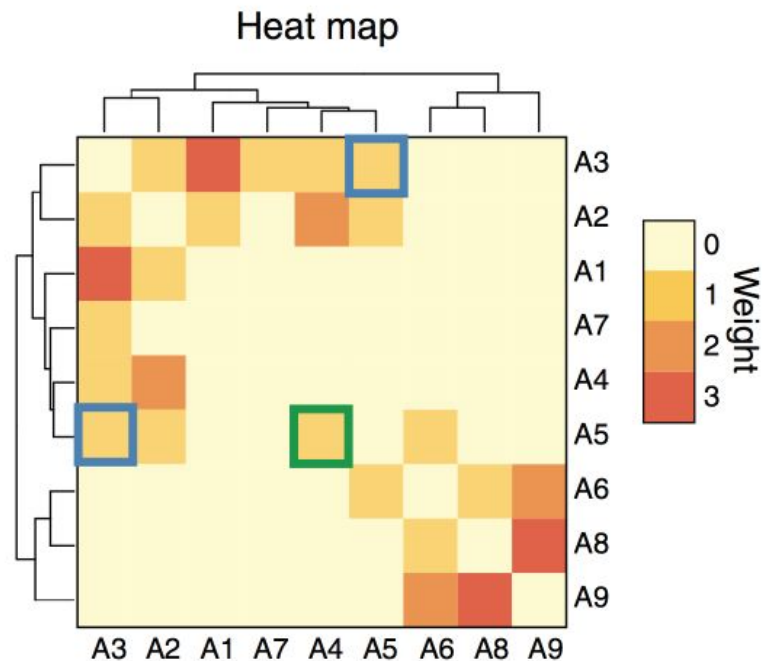
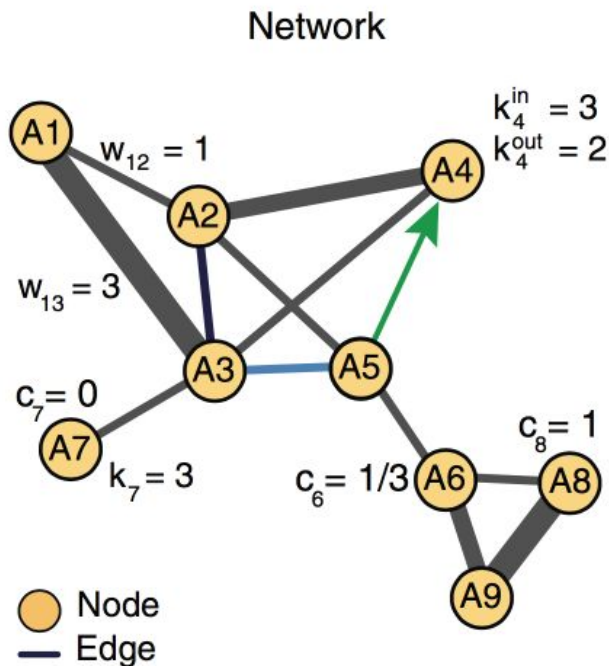


E



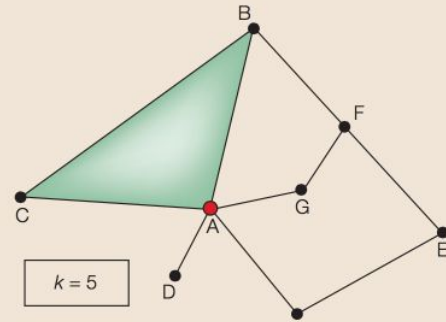
Network description and layout

Relationships	Optional weight
A1 ↔ A2	1
A1 ↔ A3	3
A2 ↔ A3	1
A2 ↔ A4	2
A2 ↔ A5	1
A3 ↔ A4	1
A3 ↔ A5	1
A3 ↔ A7	1
A5 → A4	1
A5 ↔ A6	1
A6 ↔ A8	1
A6 ↔ A9	2
A8 ↔ A9	3

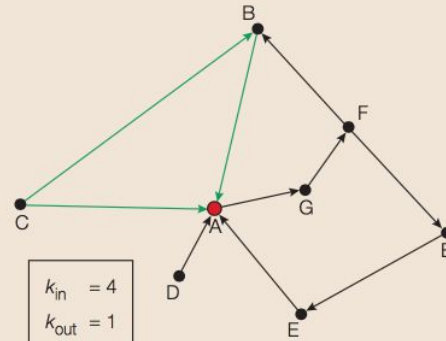


Network topology

a Undirected network

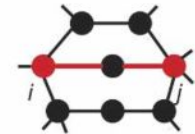


b Directed network



Degree

k_i = number of links connected to node i



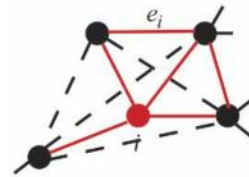
Distance

d_{ij} = shortest path length between node i and j



Diameter

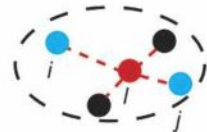
$D = \max \{ d_{ij} | i, j \in N \}$ N : all nodes in the network



Clustering Coefficient

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

e_i : number of existing links (labeled in red) among the k_i nodes that connect to node i



Betweenness

$b_l = \sum_{ij} p_{ij}(l) / p_{ij}$

p_{ij} : number of shortest paths between i and j

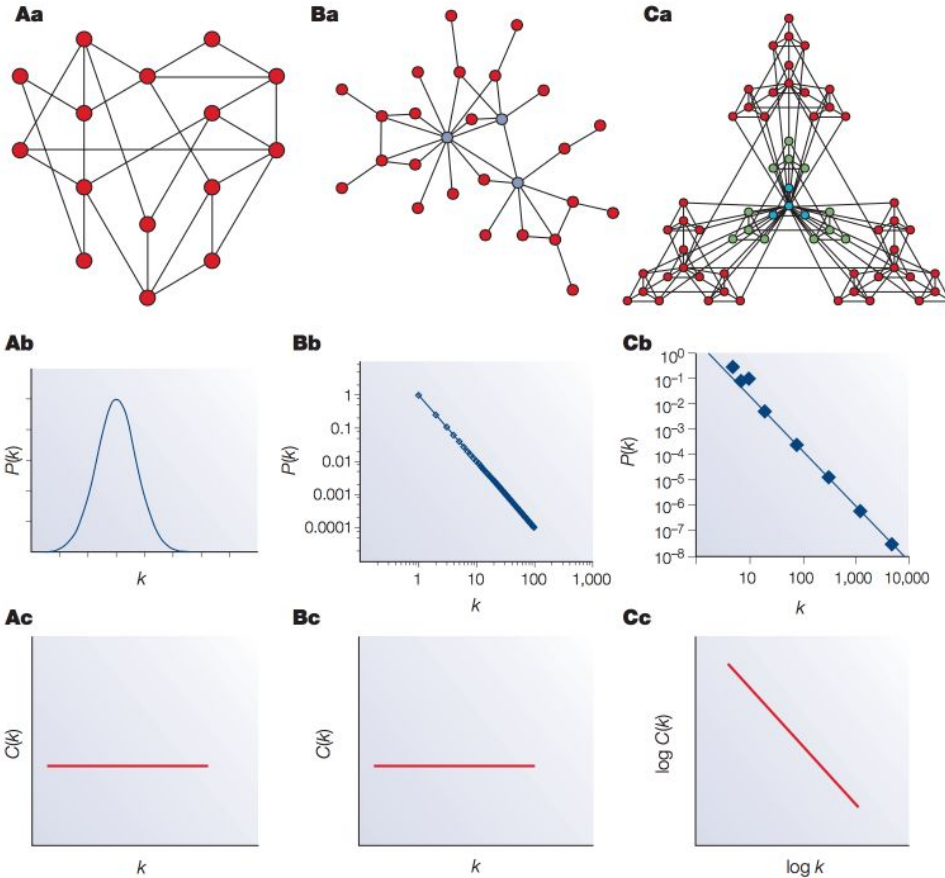
$p_{ij}(l)$: number of shortest paths between i and j going through node l

Barabasi, Oltvai (2004) Nat.

Rev. Genet.

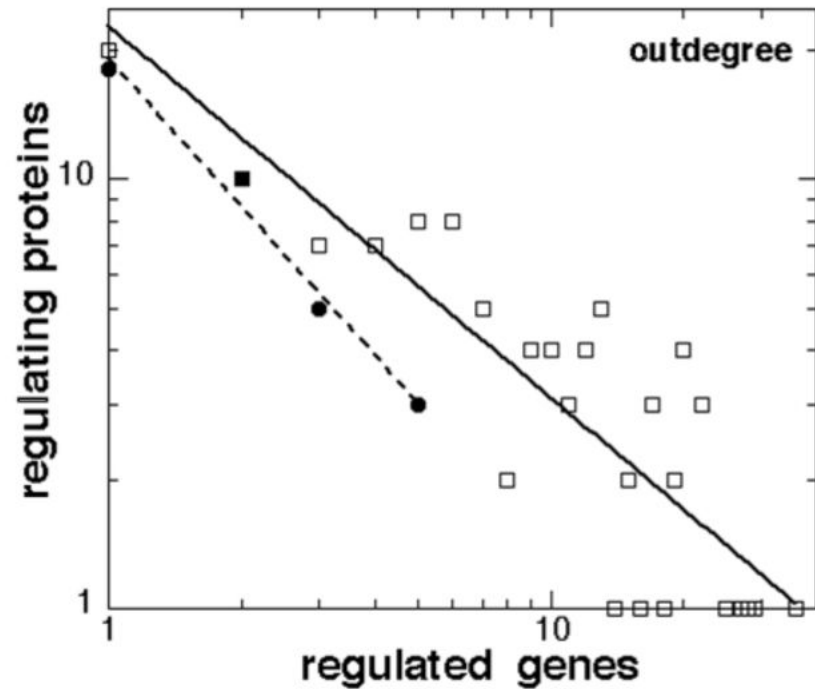
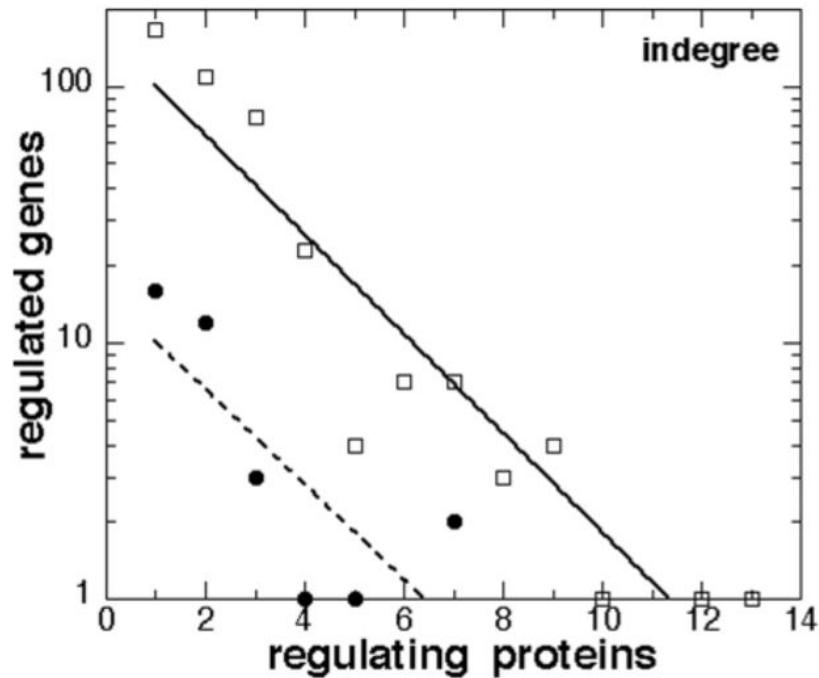
Zhu (2007) Genes & Dev.

Network topology

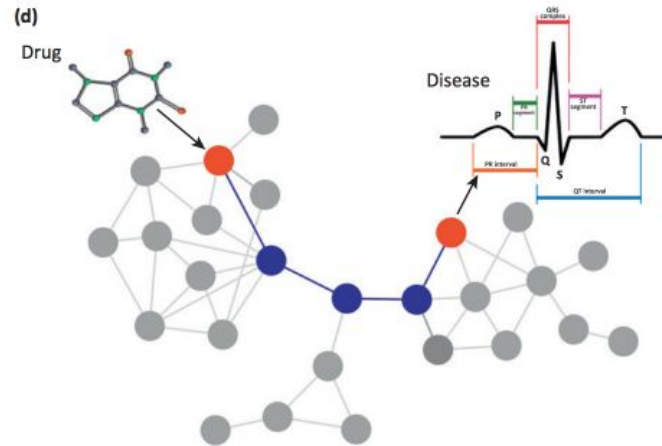
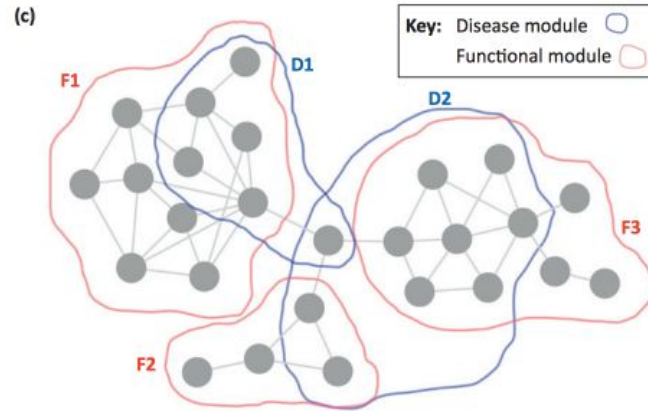
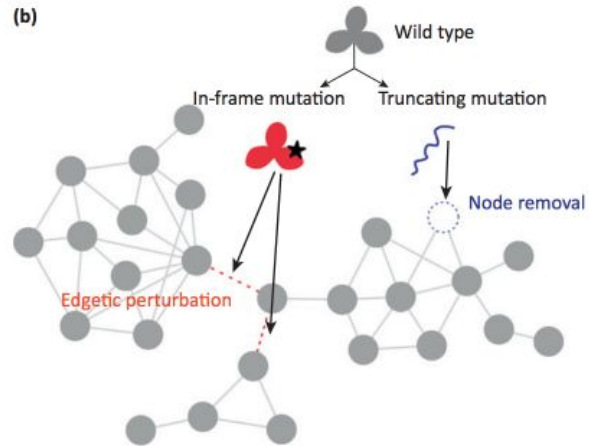
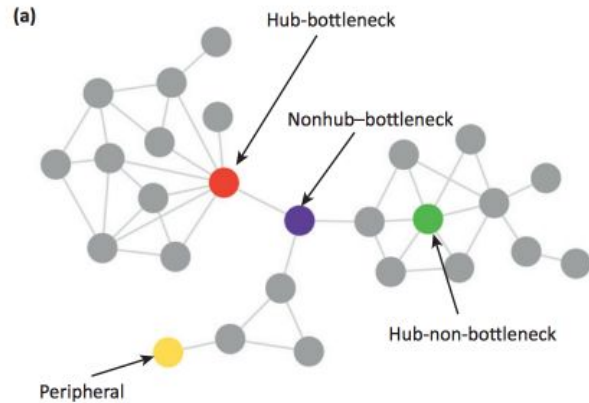


Network topology

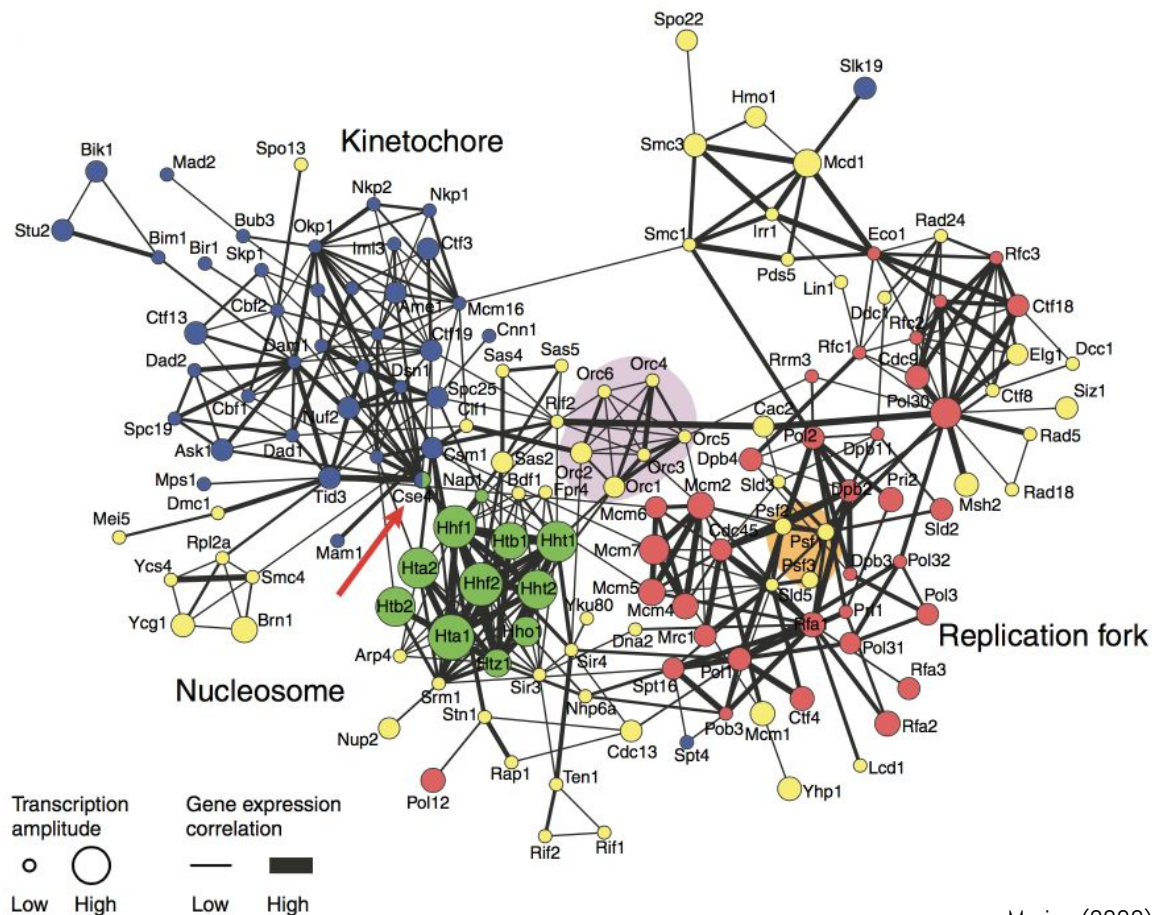
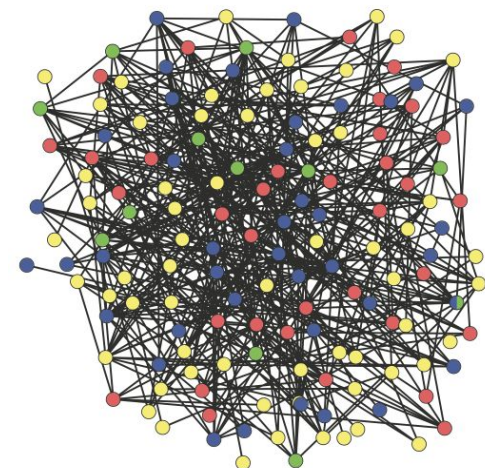
Yeast TF-target network



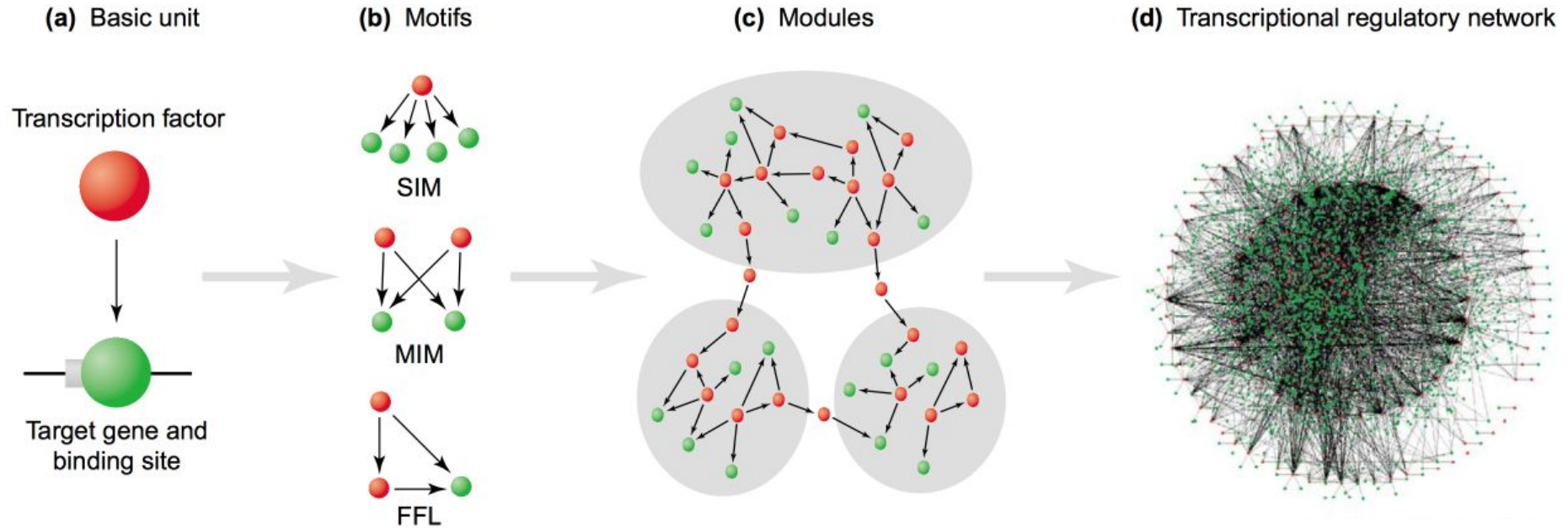
Network topology



Network description and layout

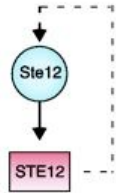


Network motifs

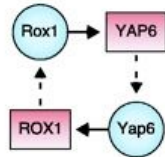


Network motifs

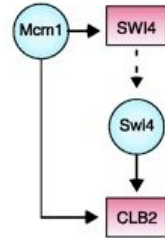
Autoregulation



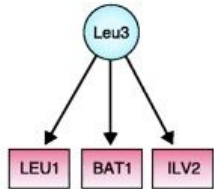
Multi-Component Loop



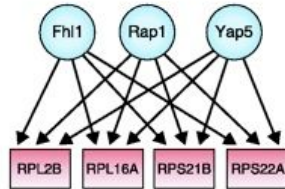
Feedforward Loop



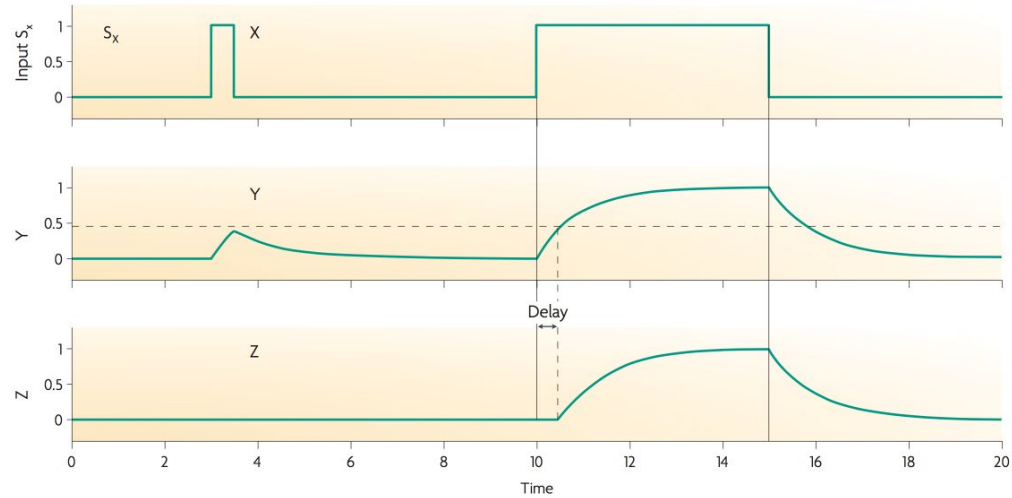
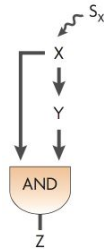
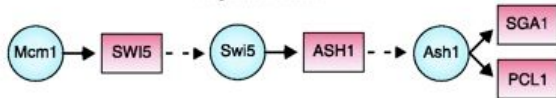
Single Input Motif



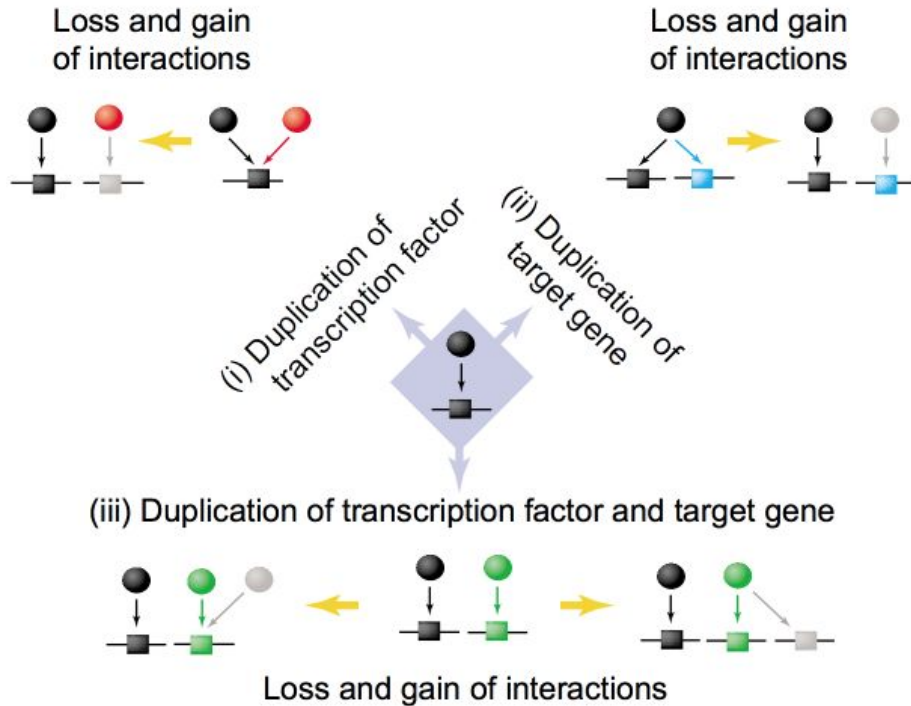
Multi-Input Motif



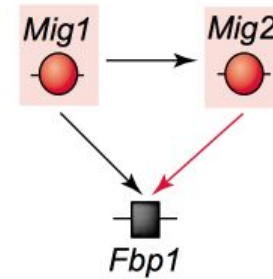
Regulator Chain



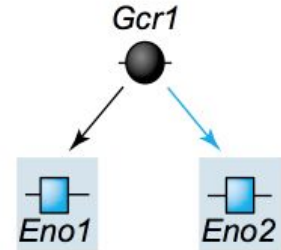
Network evolution



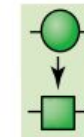
(i) Duplication of transcription factor



(ii) Duplication of target gene

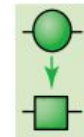


Aro80



Aro9

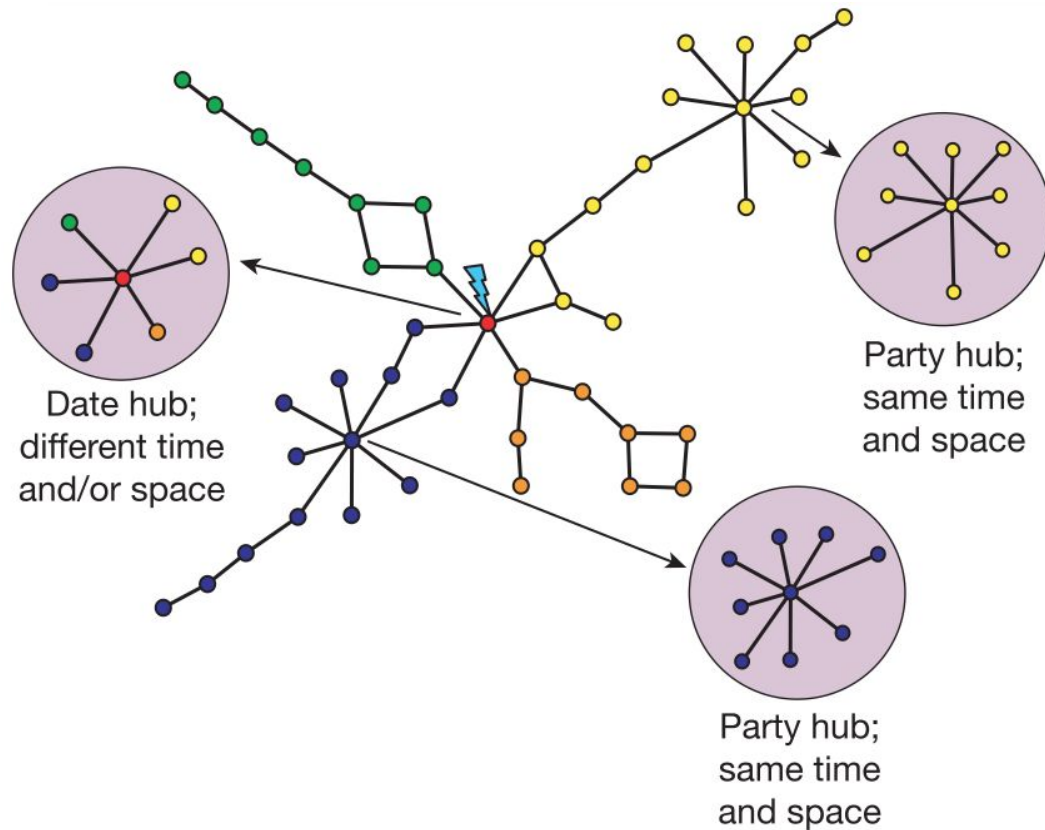
Dal81



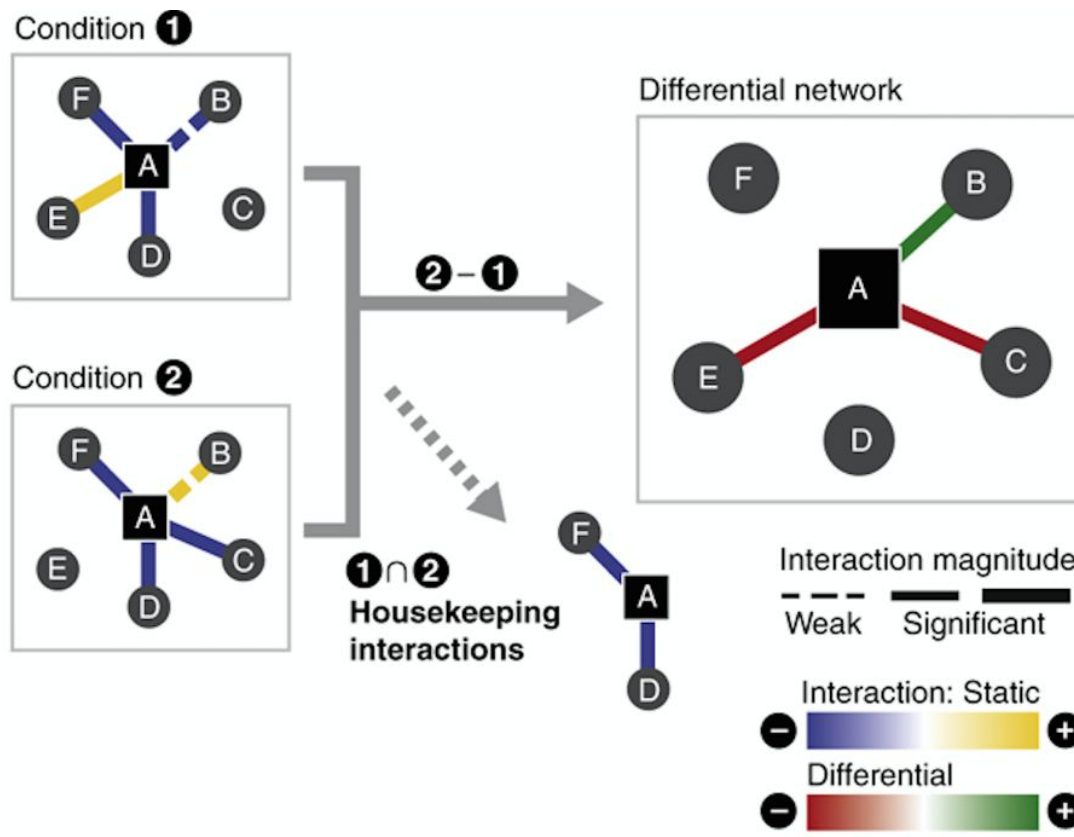
Uga1

(iii) Duplication of transcription factor and target gene

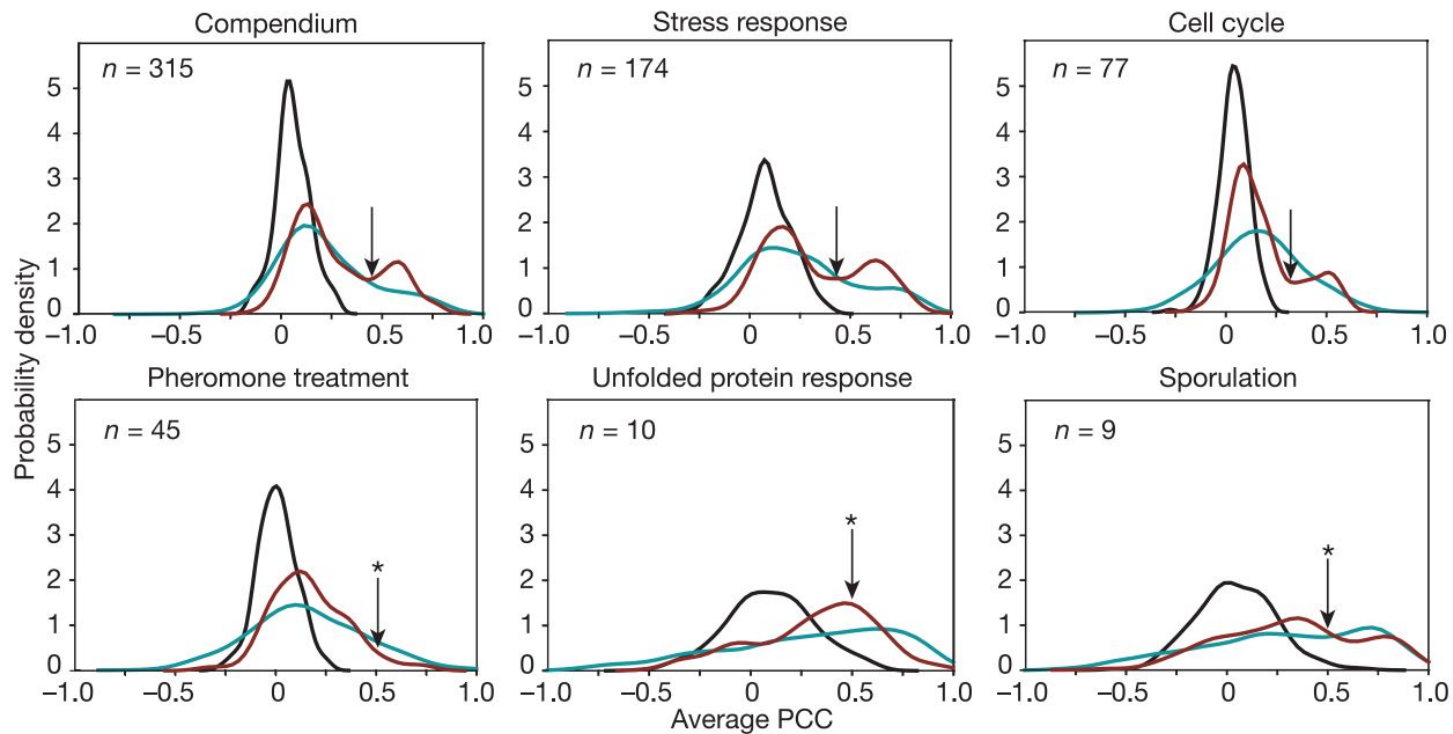
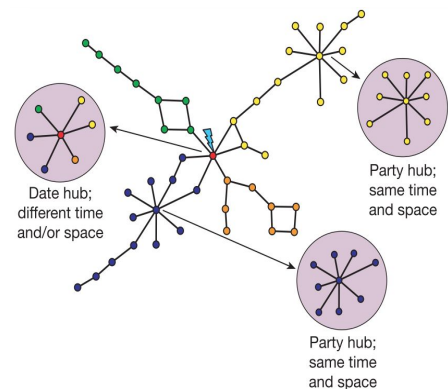
Network interactions are condition-specific



Network interactions are condition-specific

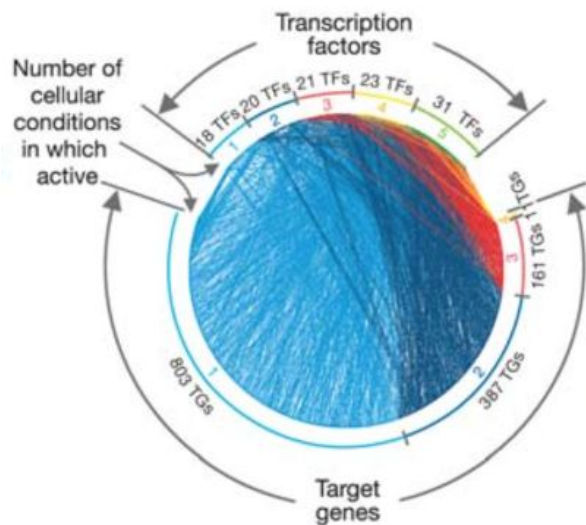


Network interactions are condition-specific



Network interactions are condition-specific

Static



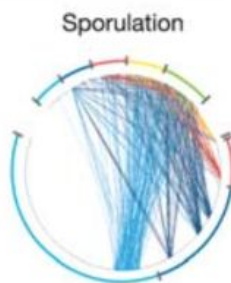
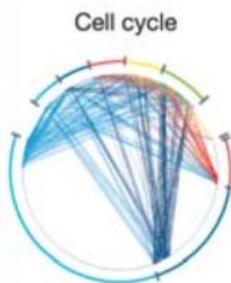
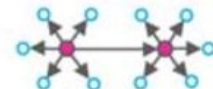
Endogenous

- Complex transcription factor combinations
- Few targets per transcription factor
- Long path lengths
- Highly inter-connected transcription factors
- Many feed-forward loops



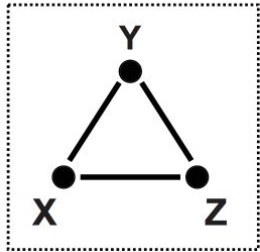
Exogenous

- Simple transcription factor combinations
- Many targets per transcription factor
- Short path lengths
- Few inter-connected transcription factors
- Many single input motifs

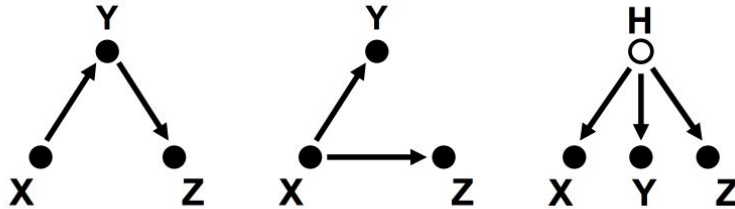


Reconstructing networks from observational data

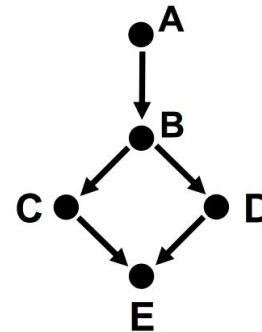
Coexpression



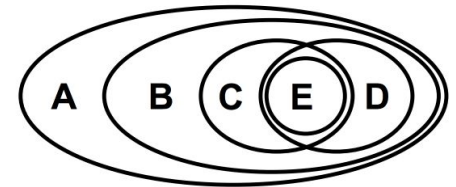
Regulatory network



Pathway structure



Downstream effects of interventions



Reconstructing networks from observational data

Context likelihood relatedness

