



* Network dynamics

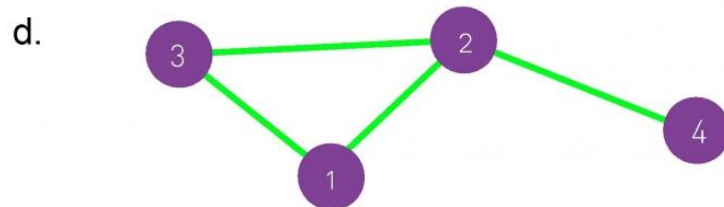
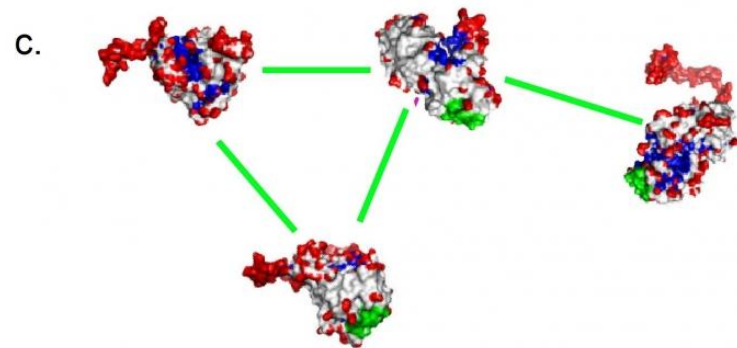
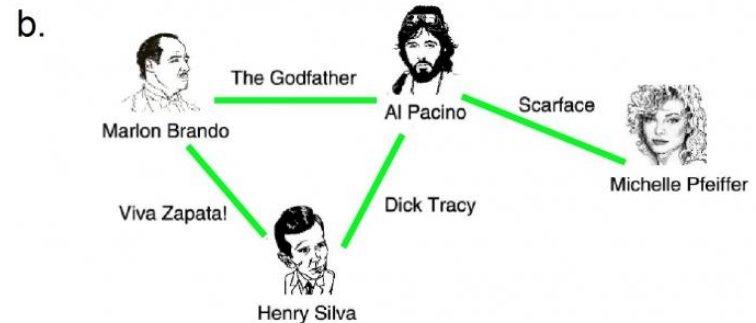
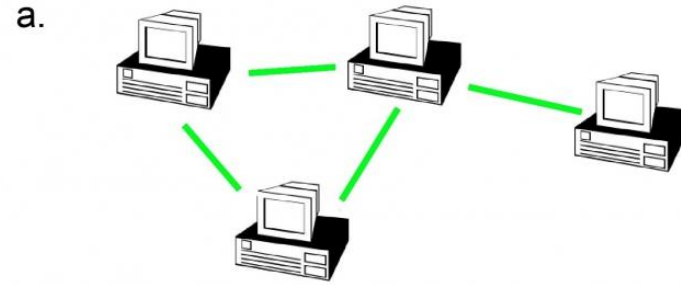
Networks

→ Graph:

- ◆ abstract mathematical representation, data structure

→ Network

- ◆ phenomenon modelled by graph



Network topology

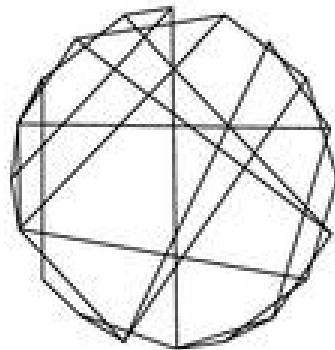
Regular



$$\rho = 0$$

(a)

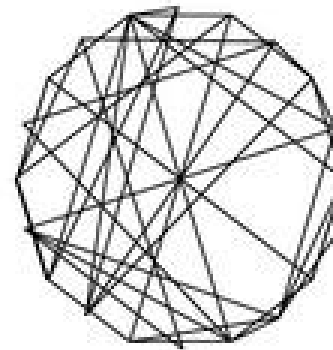
Small world



$$N = 20, k = 4$$

(b)

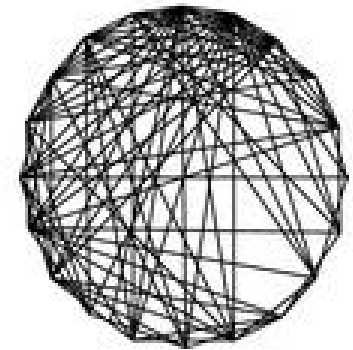
Random



$$\rho = 0$$

(c)

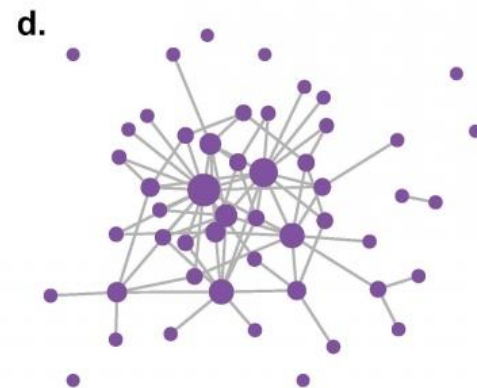
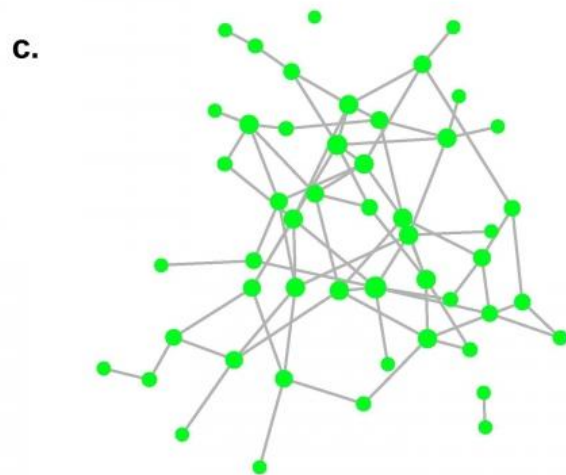
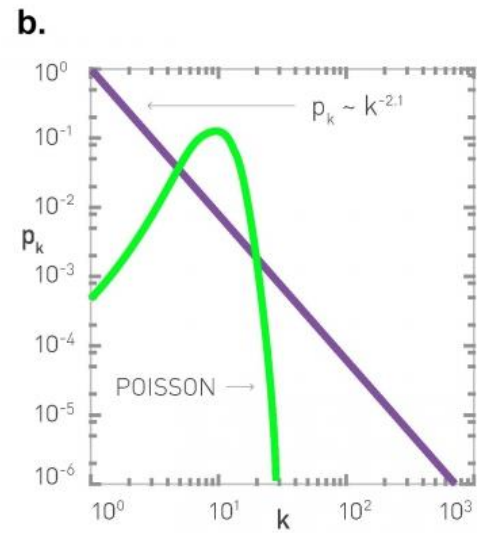
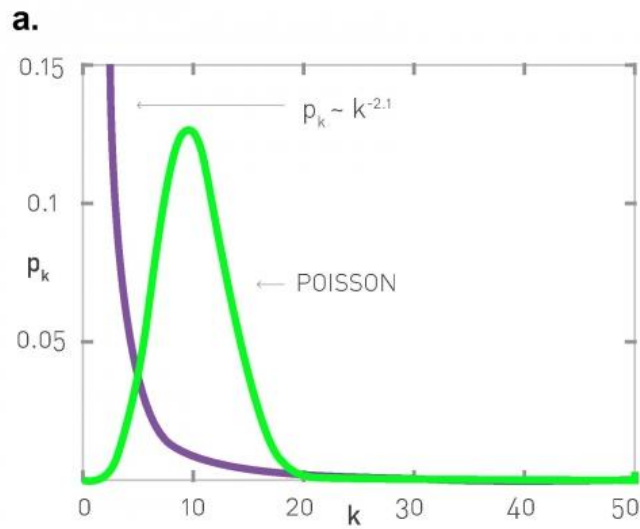
Free-scale



$$N = 30, m_0 = 6, k = 4$$

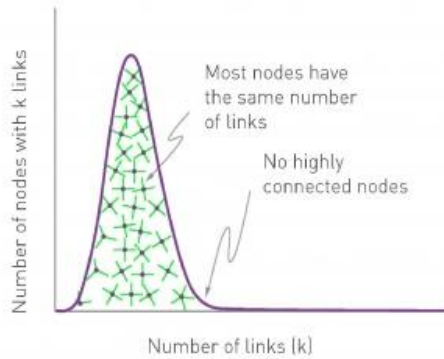
(d)

Scale-free topology

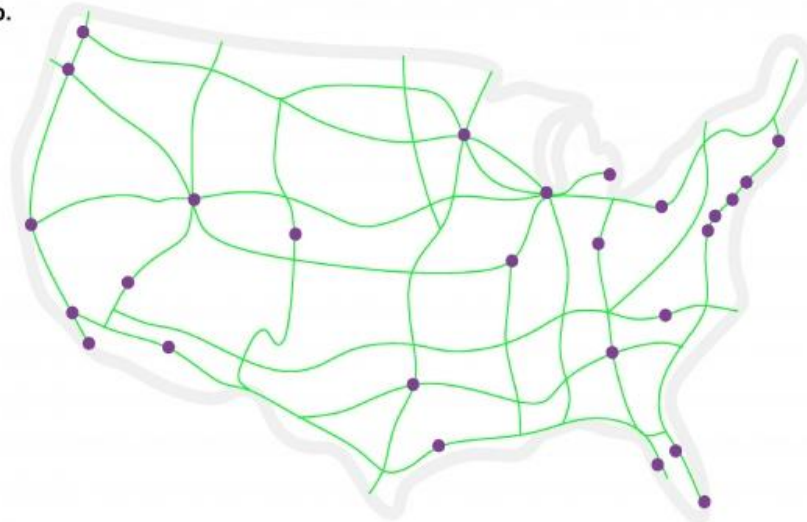


Scale-free topology

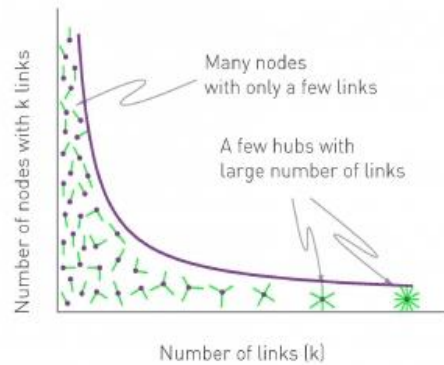
a. POISSON



b.



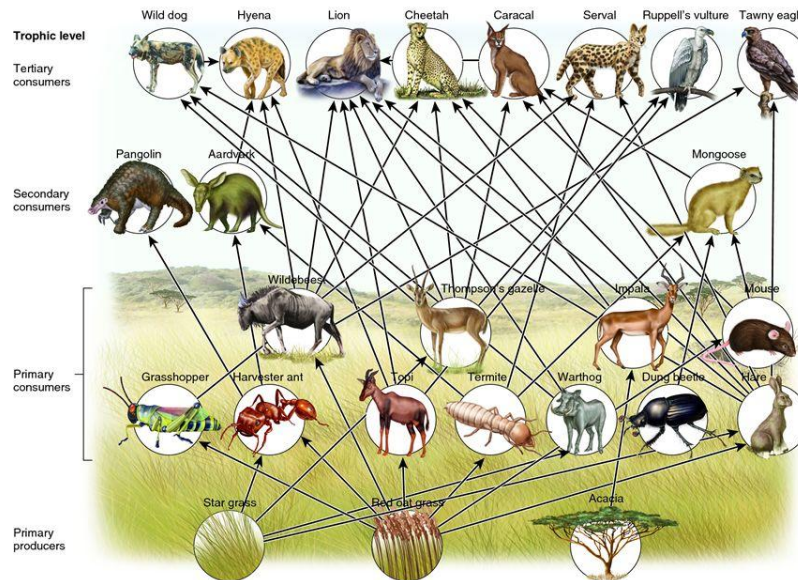
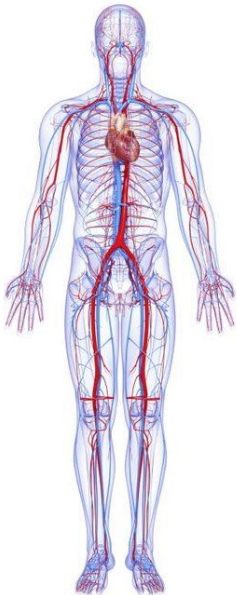
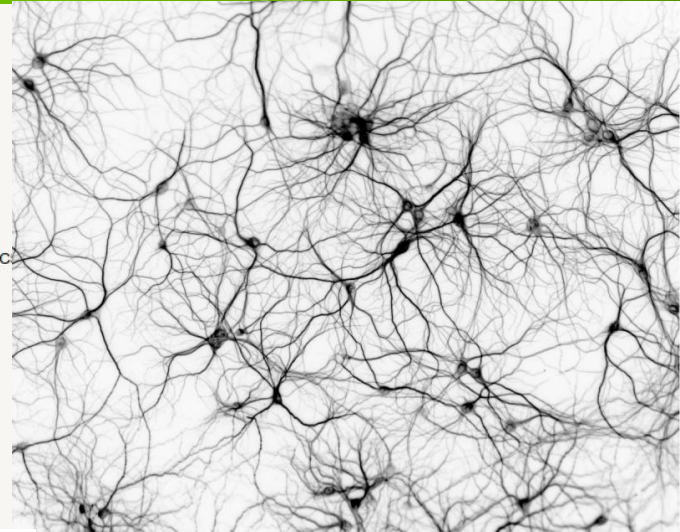
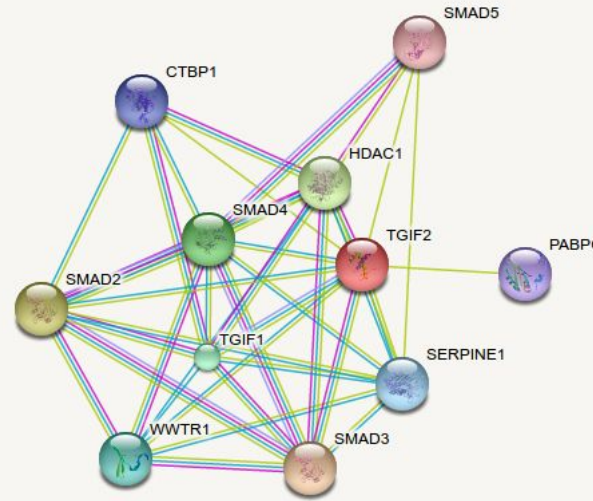
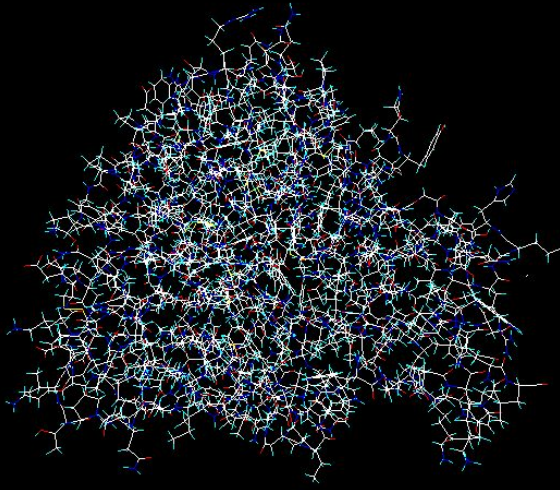
c. POWER LAW



d.



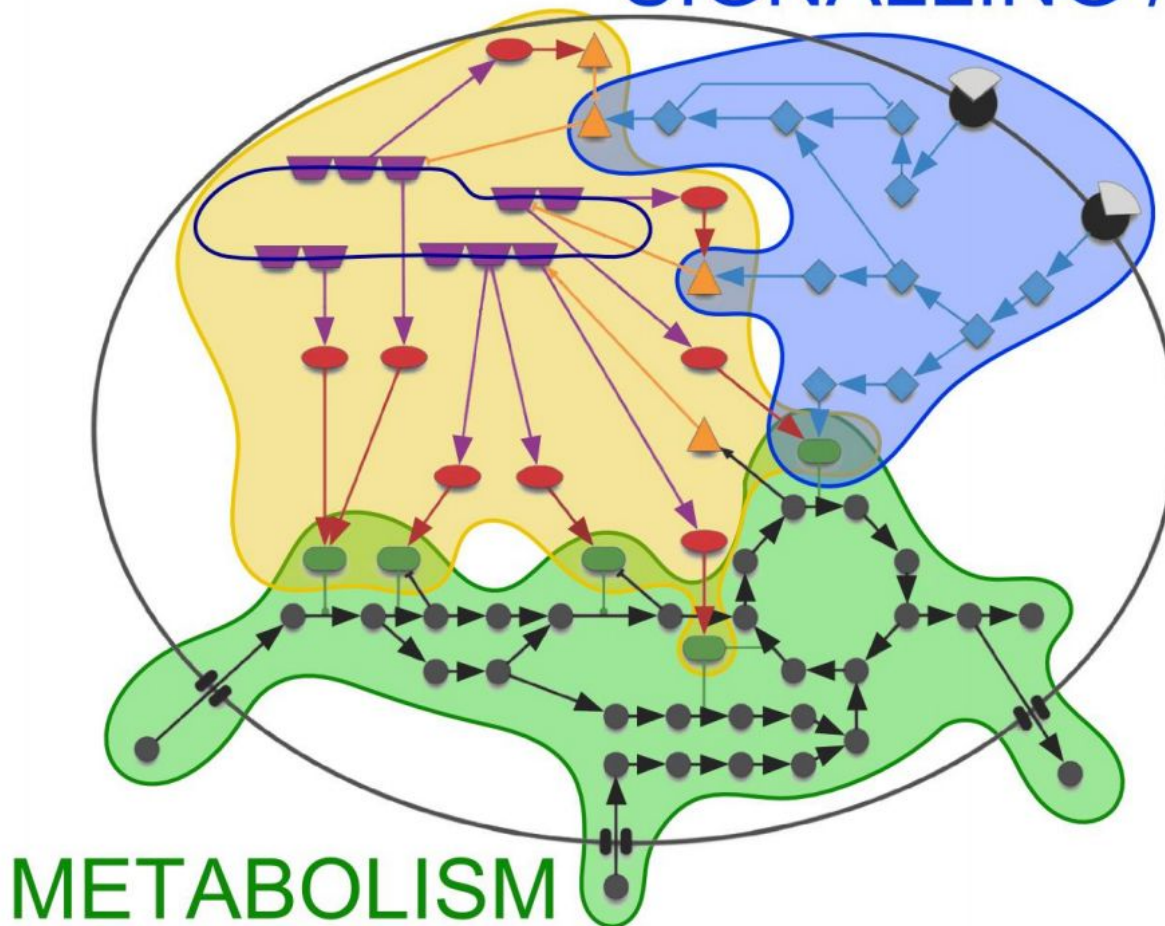
Nested networks



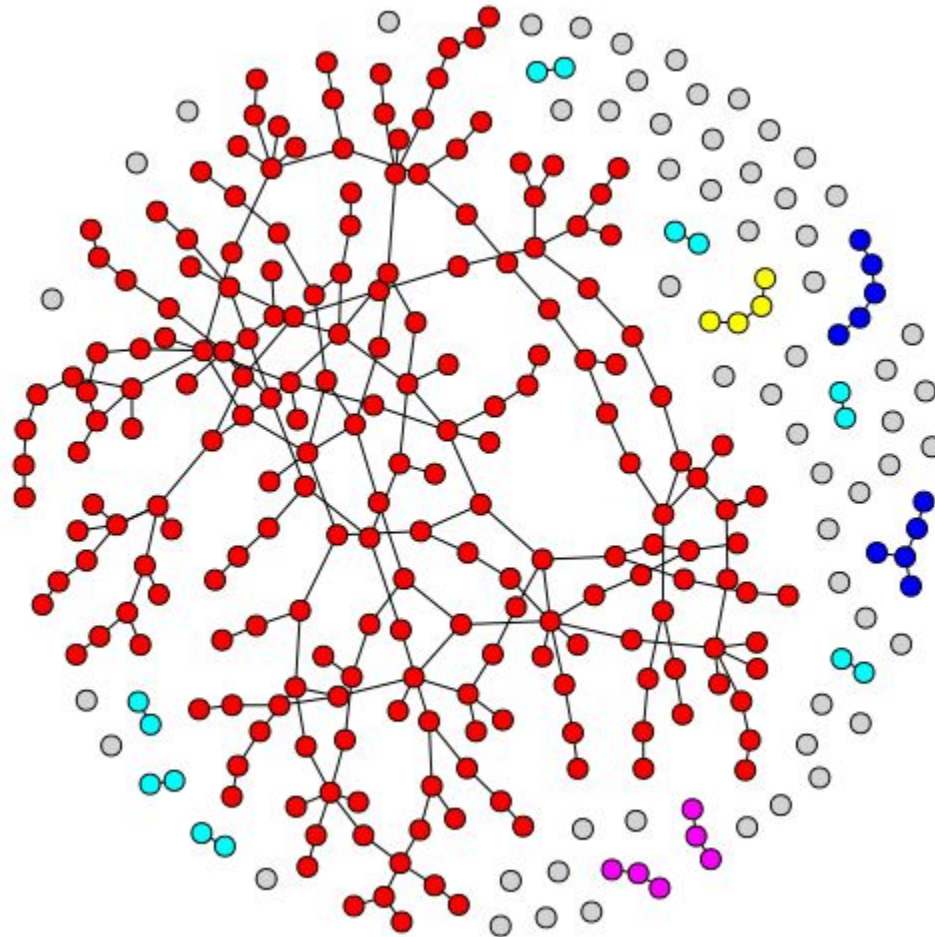
Molecular networks

REGULATION

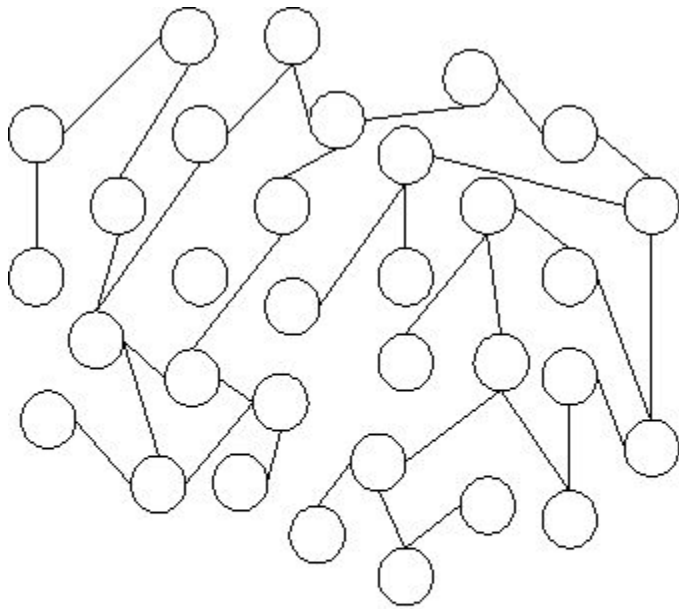
SIGNALLING / PPI



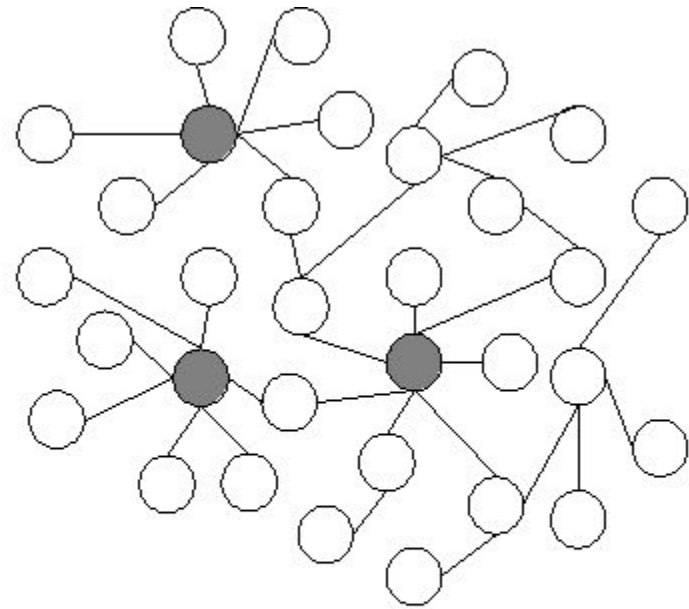
Giant component (sub-graphs)



Special nodes in scale-free networks

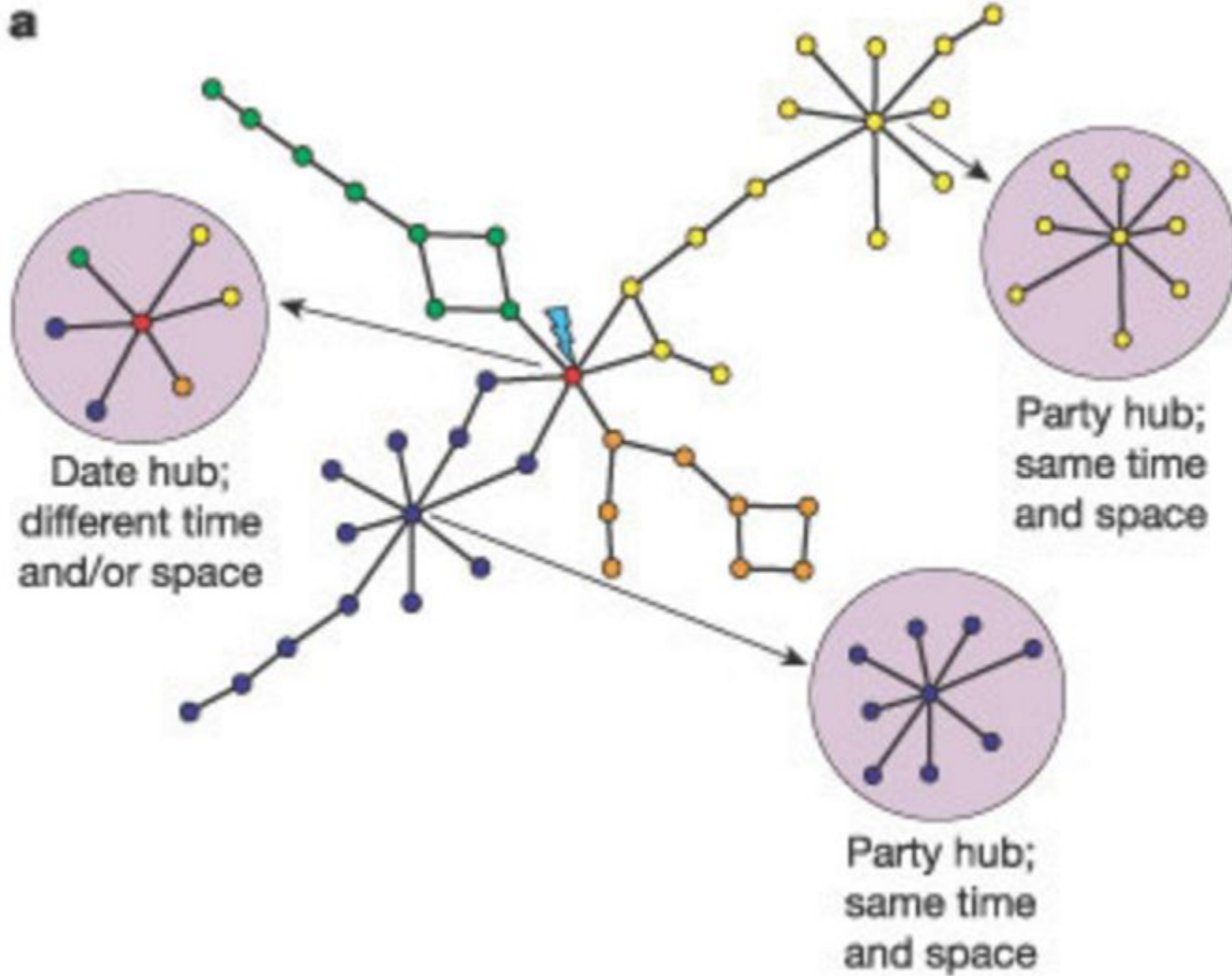


(a) Random network

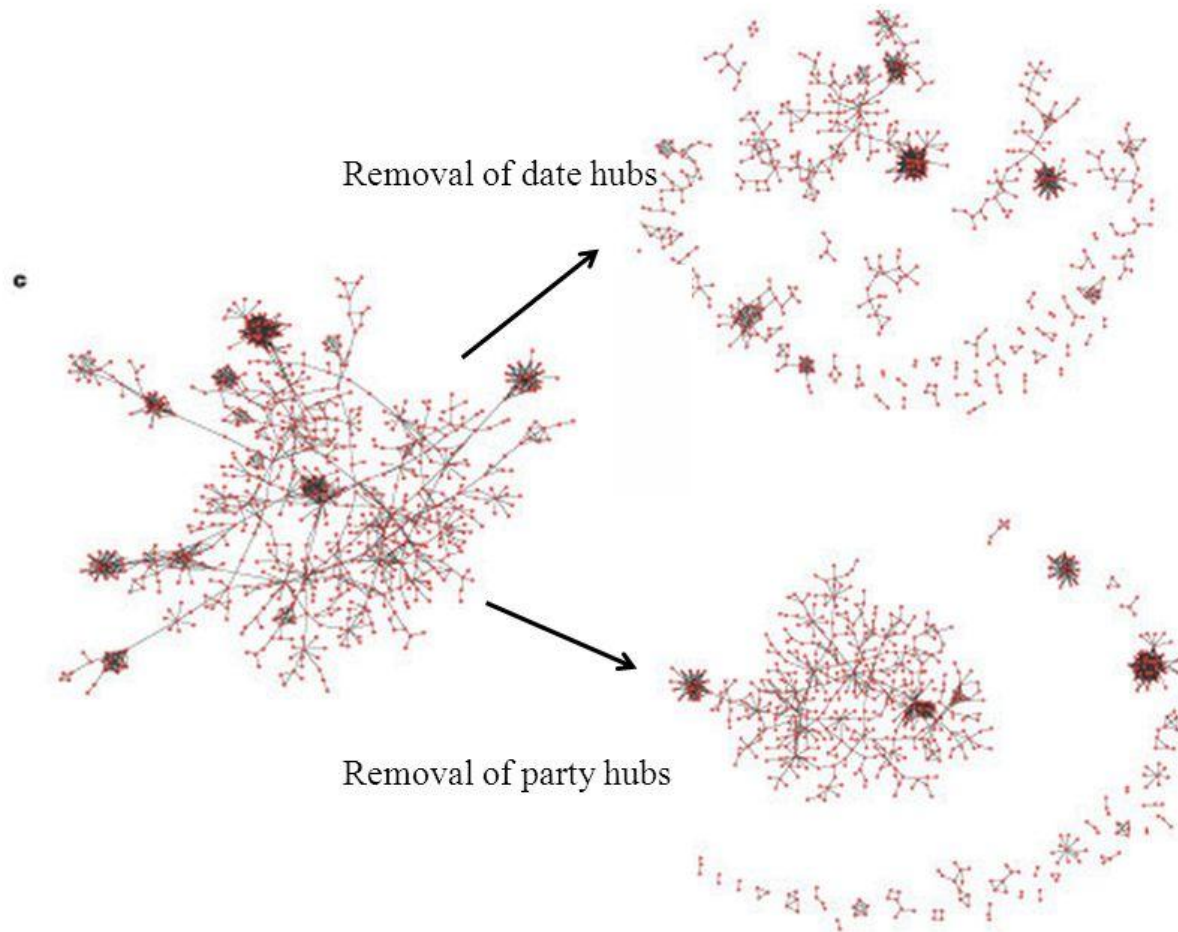


(b) Scale-free network

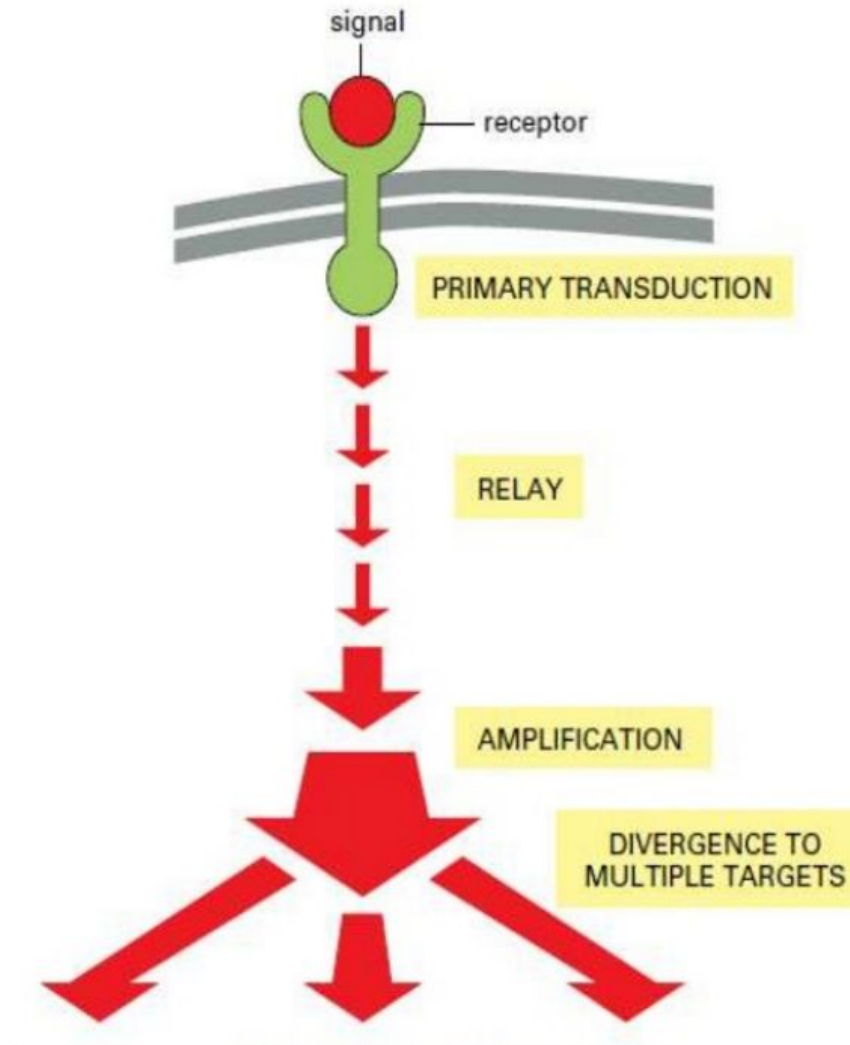
Party hub, date hub



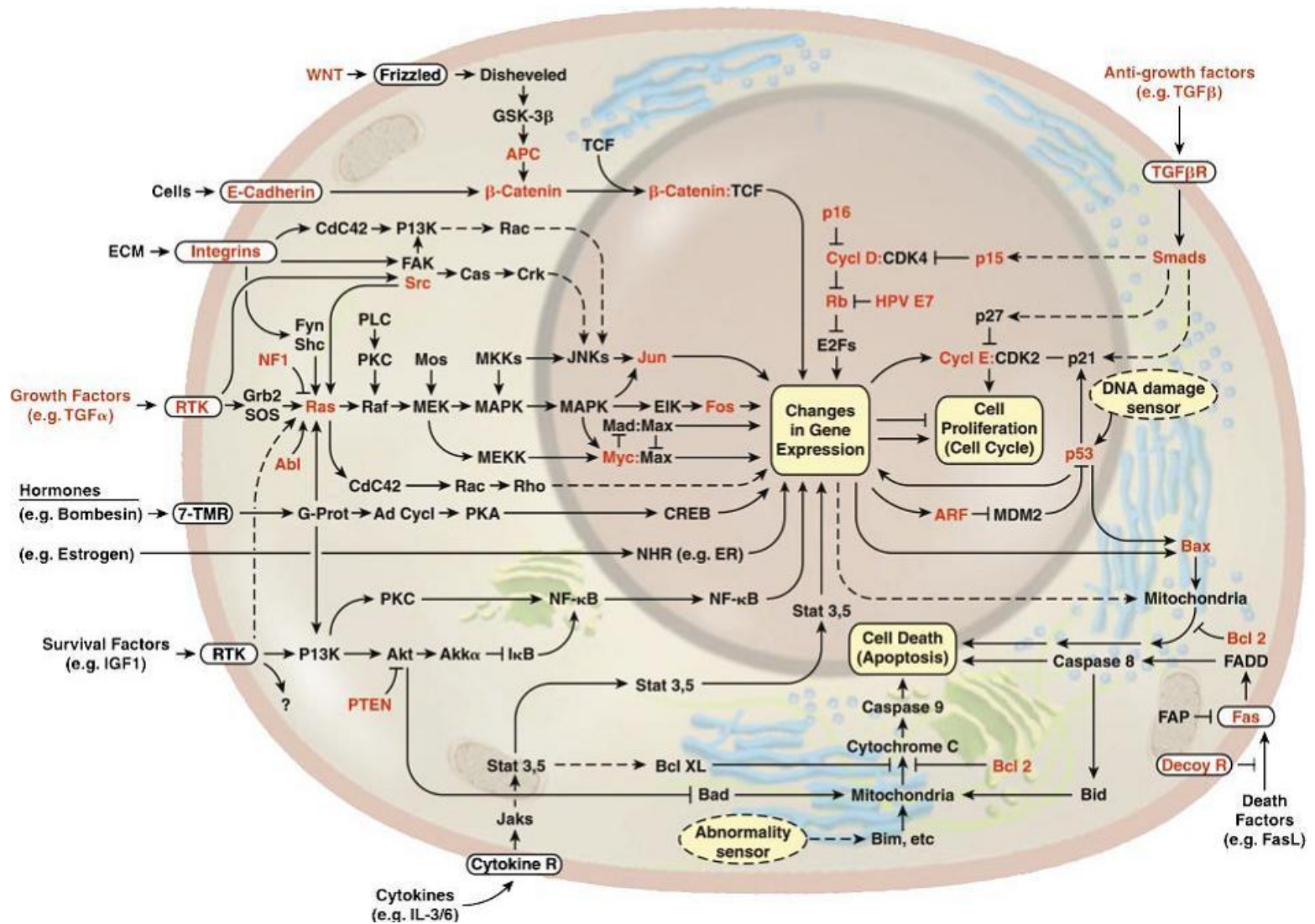
Party hub, date hub



Singnal flow

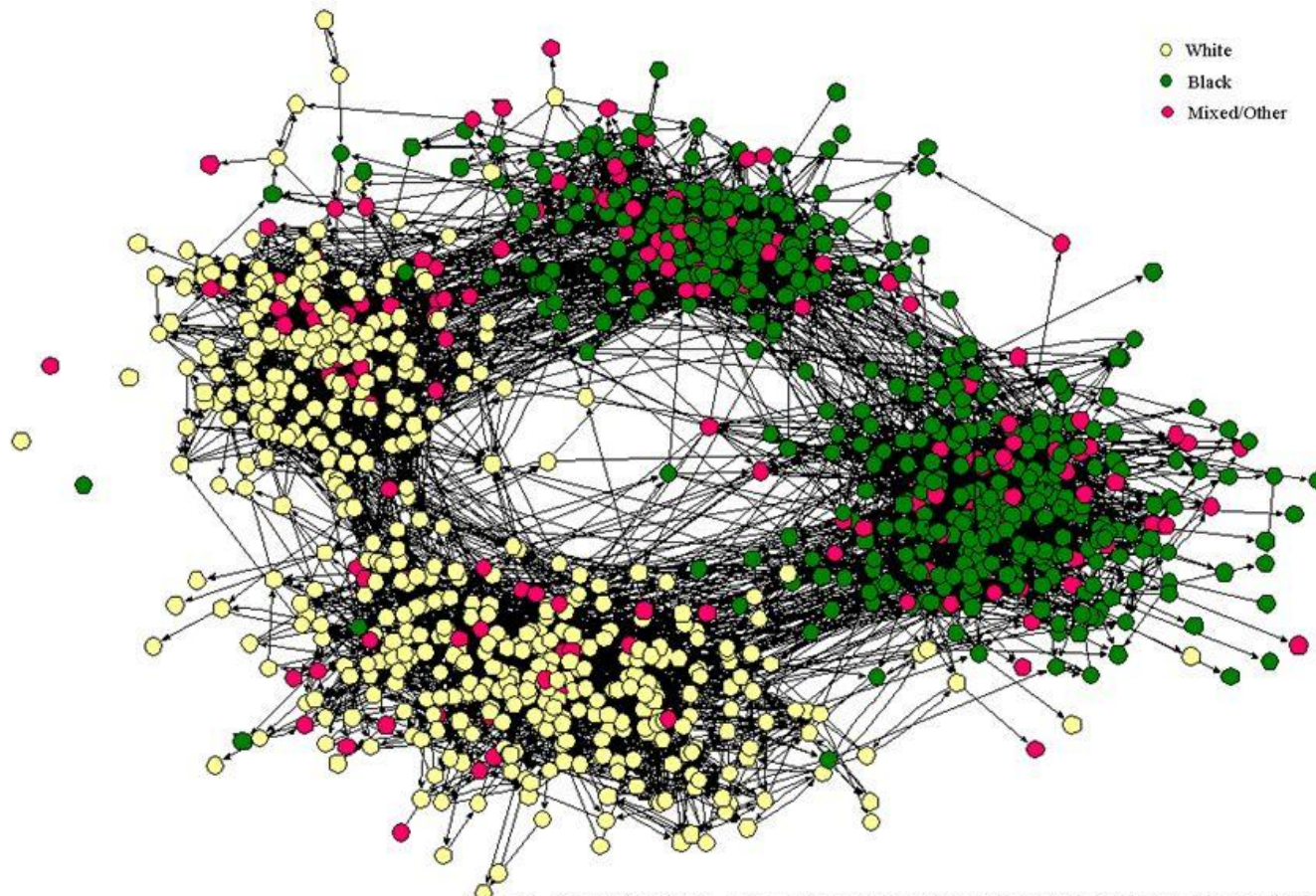


Singnal flow



Modules, communities, clusters

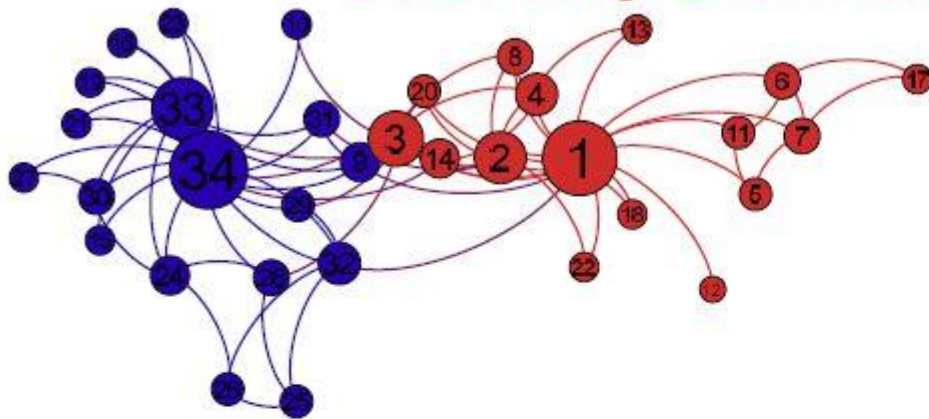
Race & school friendships



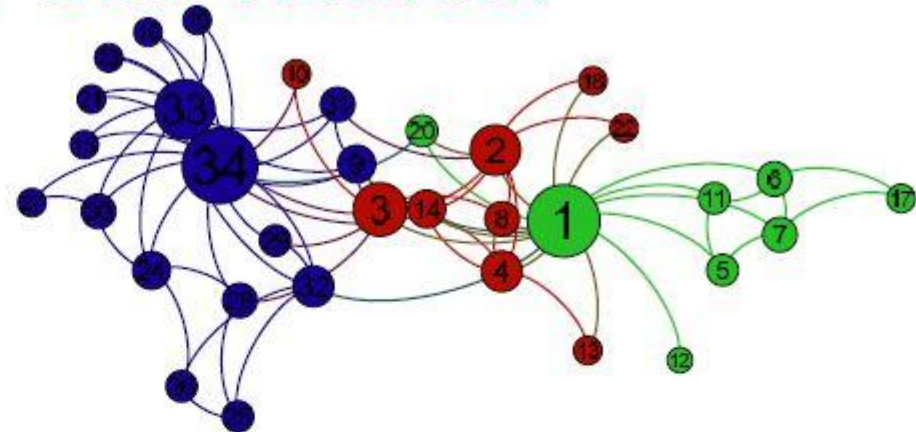
Moody, Jame (2002) Race, School Integration, and Friendship Segregation in America. The American journal of sociology [0002-9602] Moody yr:2002 vol:107 iss:3 pg:679

Modules, communities, clusters

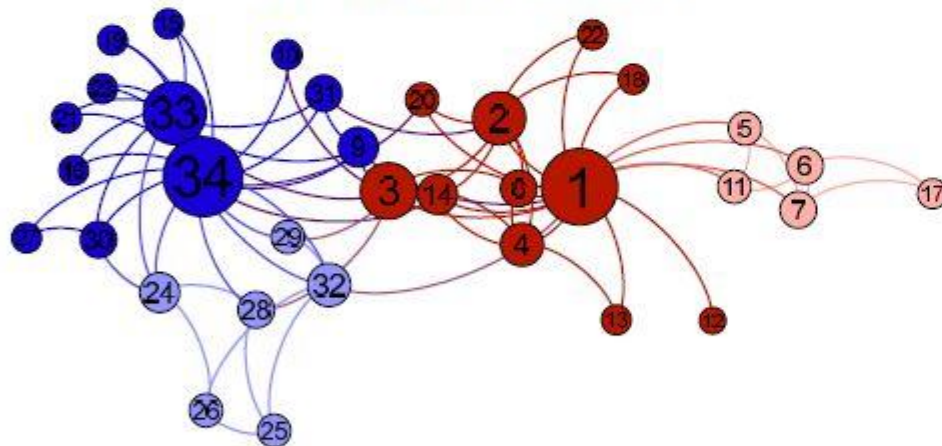
Zachary's Karate Club Network



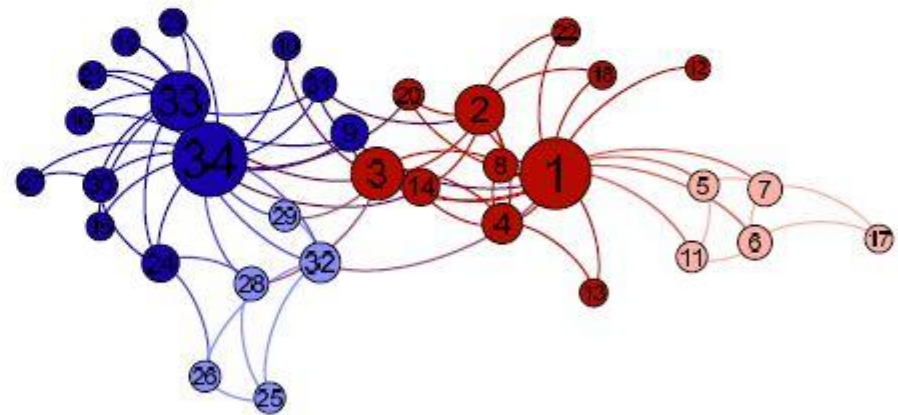
(a) Ground truth communities.



(b) Communities detected with *Greedy Q*.



(c) Communities detected with *Fine-tuned Q*.

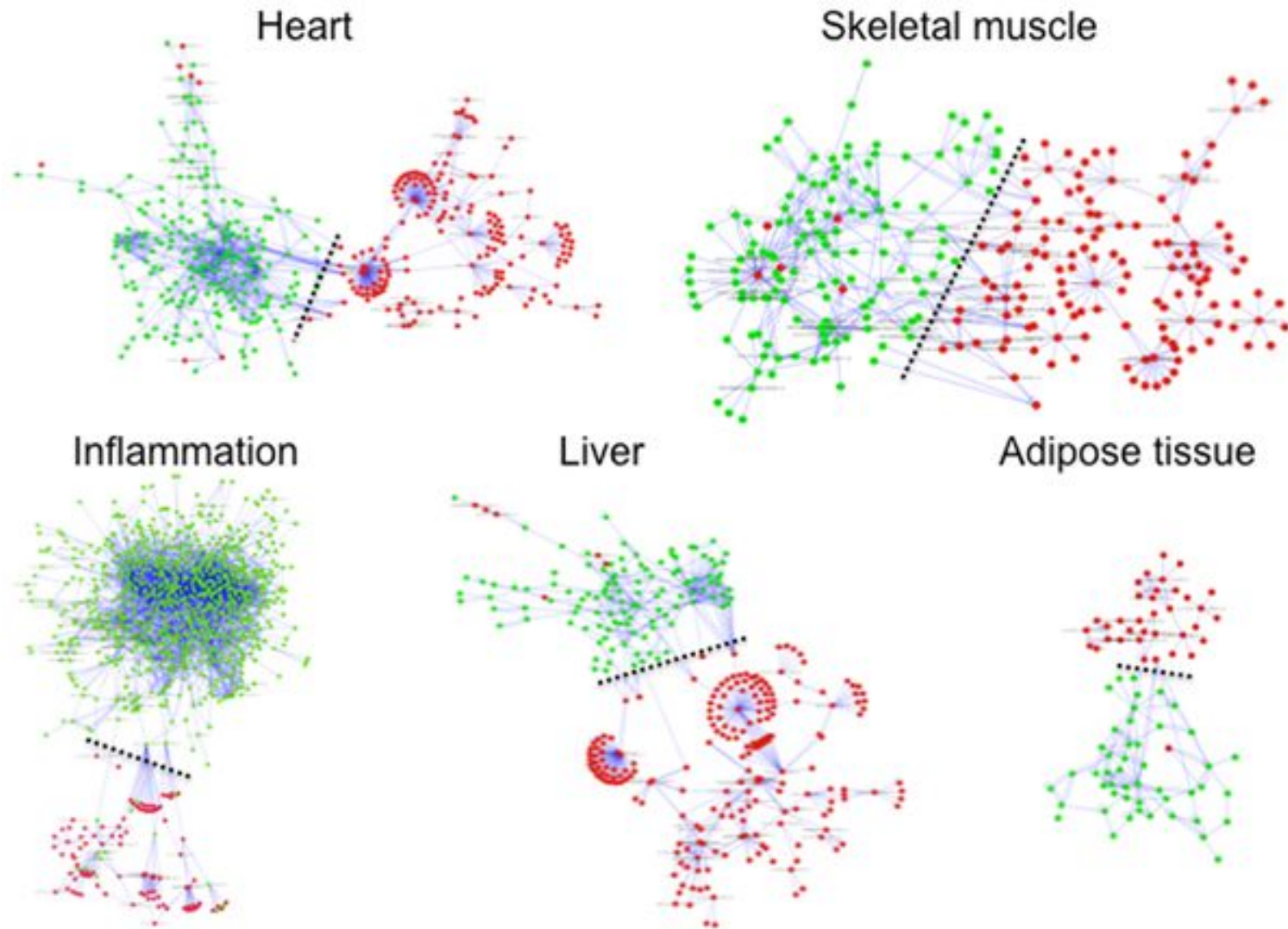


(d) Communities detected with *Fine-tuned Q_{ds}* .

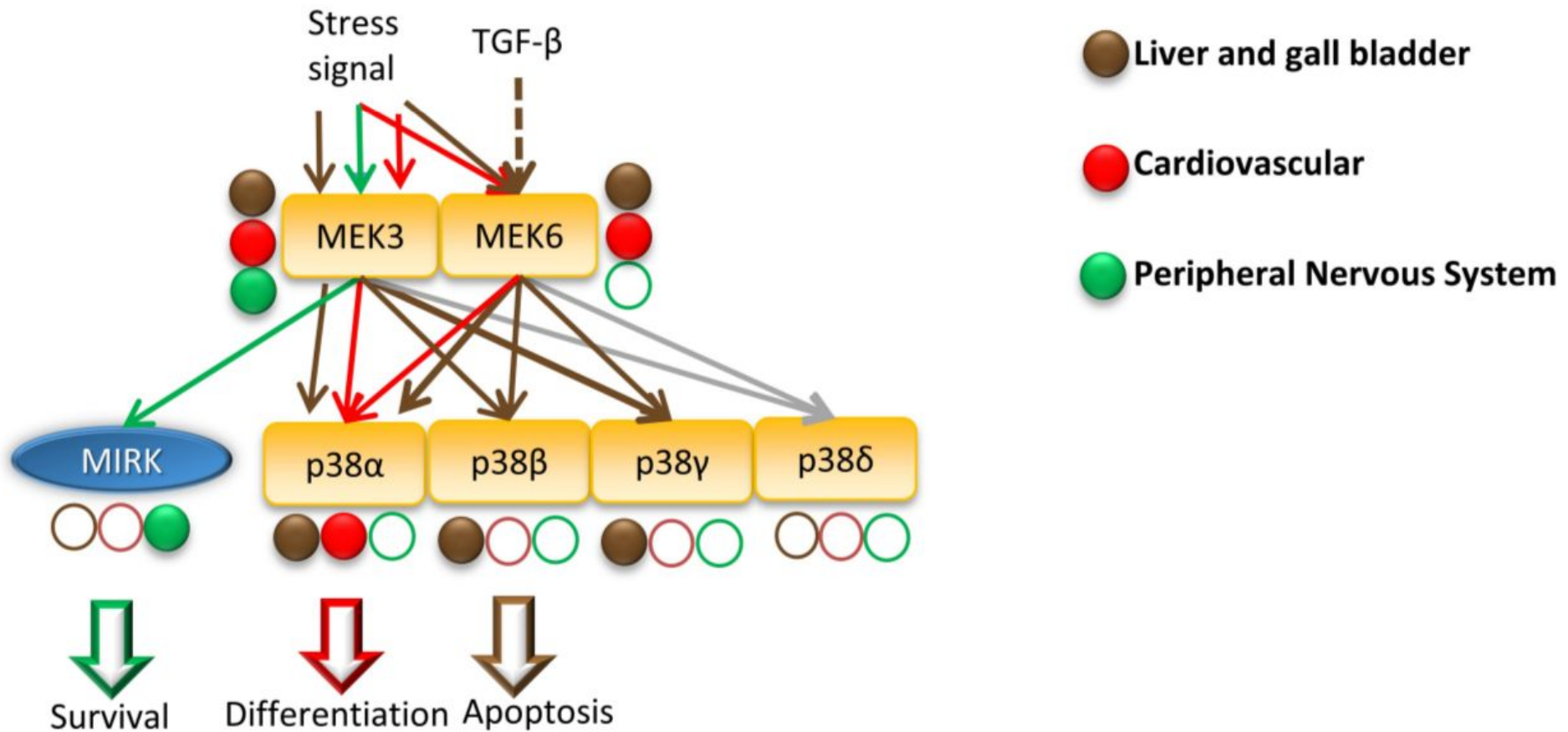
Probabilistic networks

- By the present methods, we can study all possible molecular interactions
- Many interactions
- High false-positive rate
- All connections can not be concurrent at the same time:
 - ◆ common binding surface
 - ◆ different expression
 - ◆ different localization

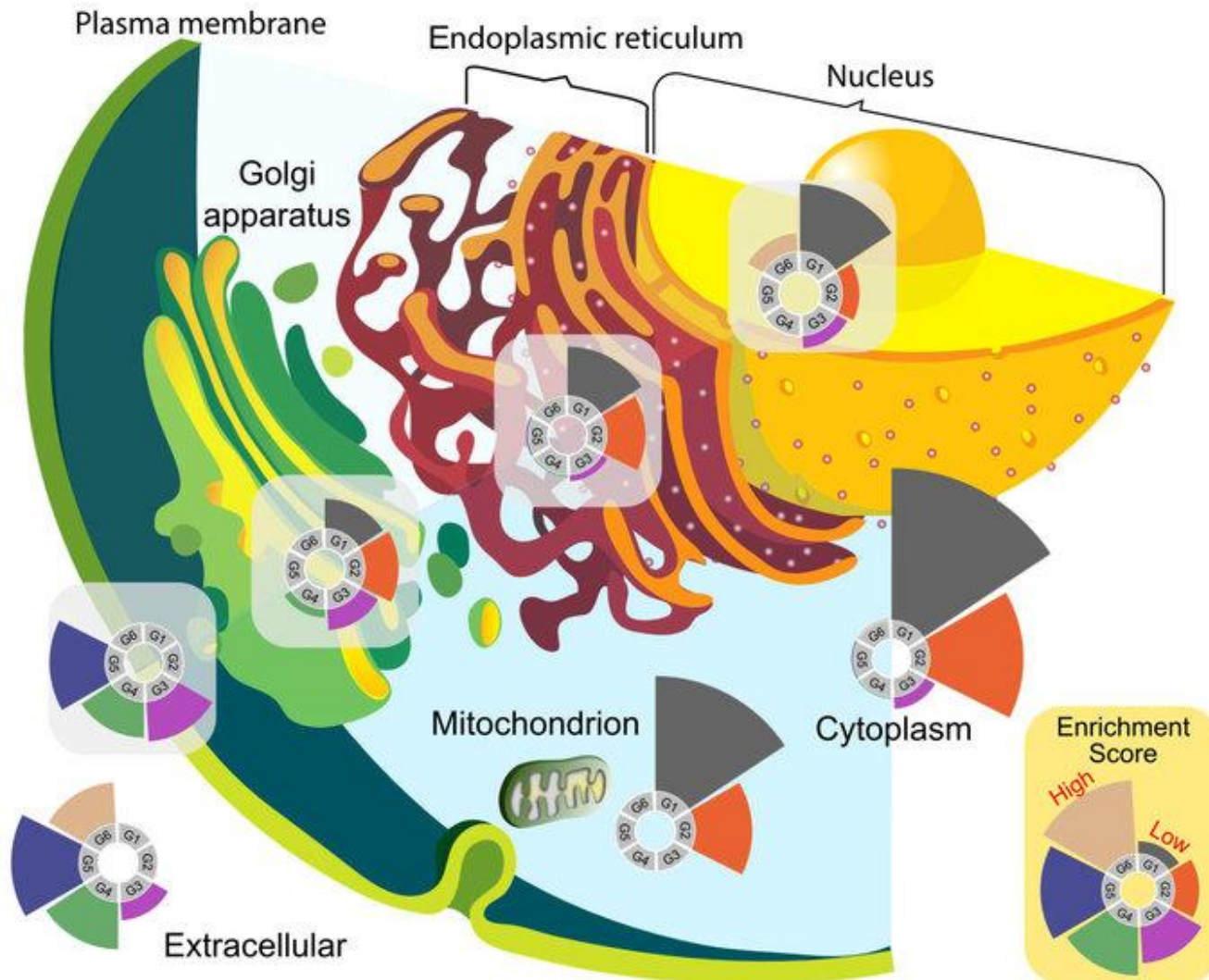
Context specific via different expression



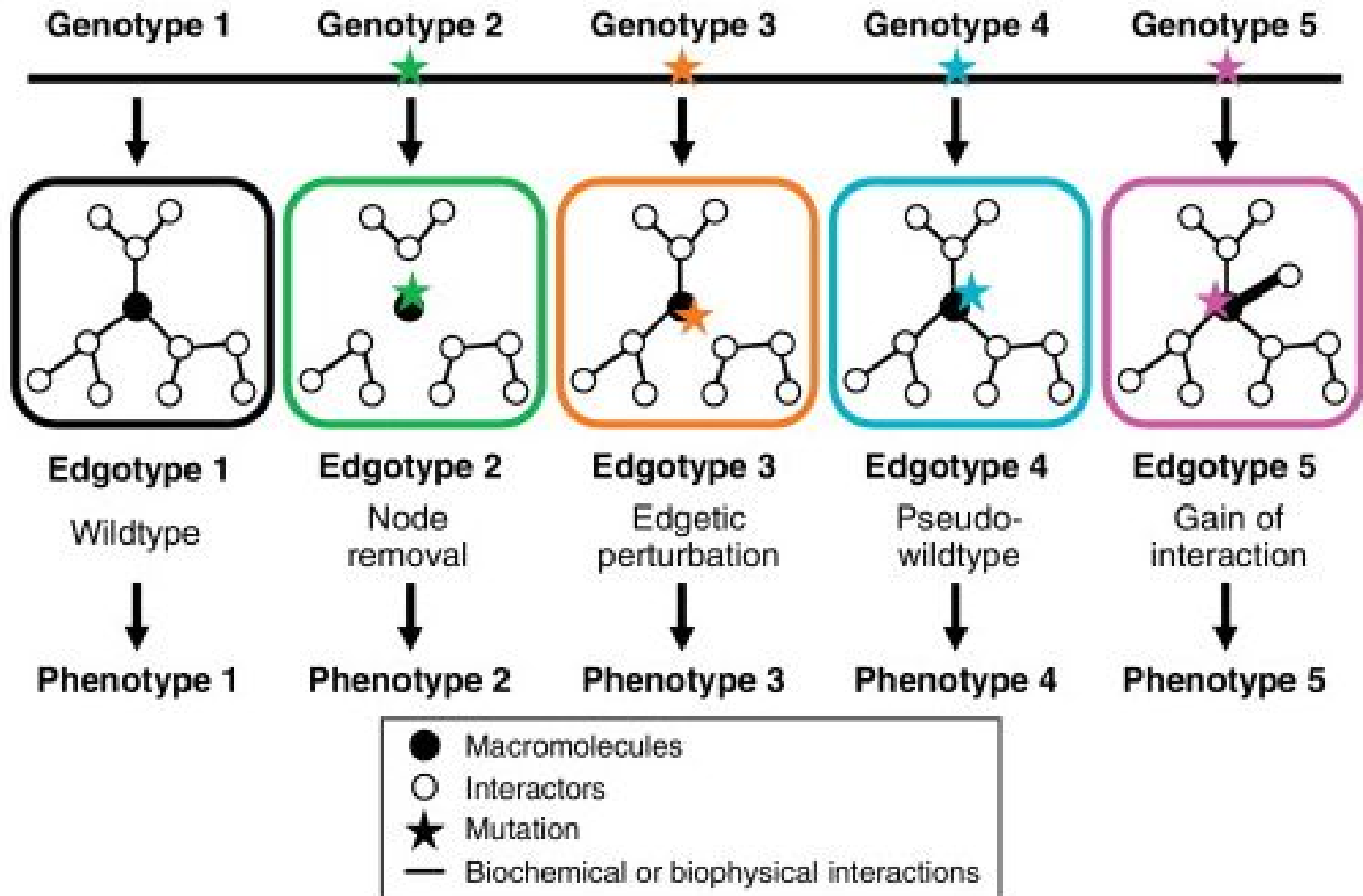
Context specific via different expression



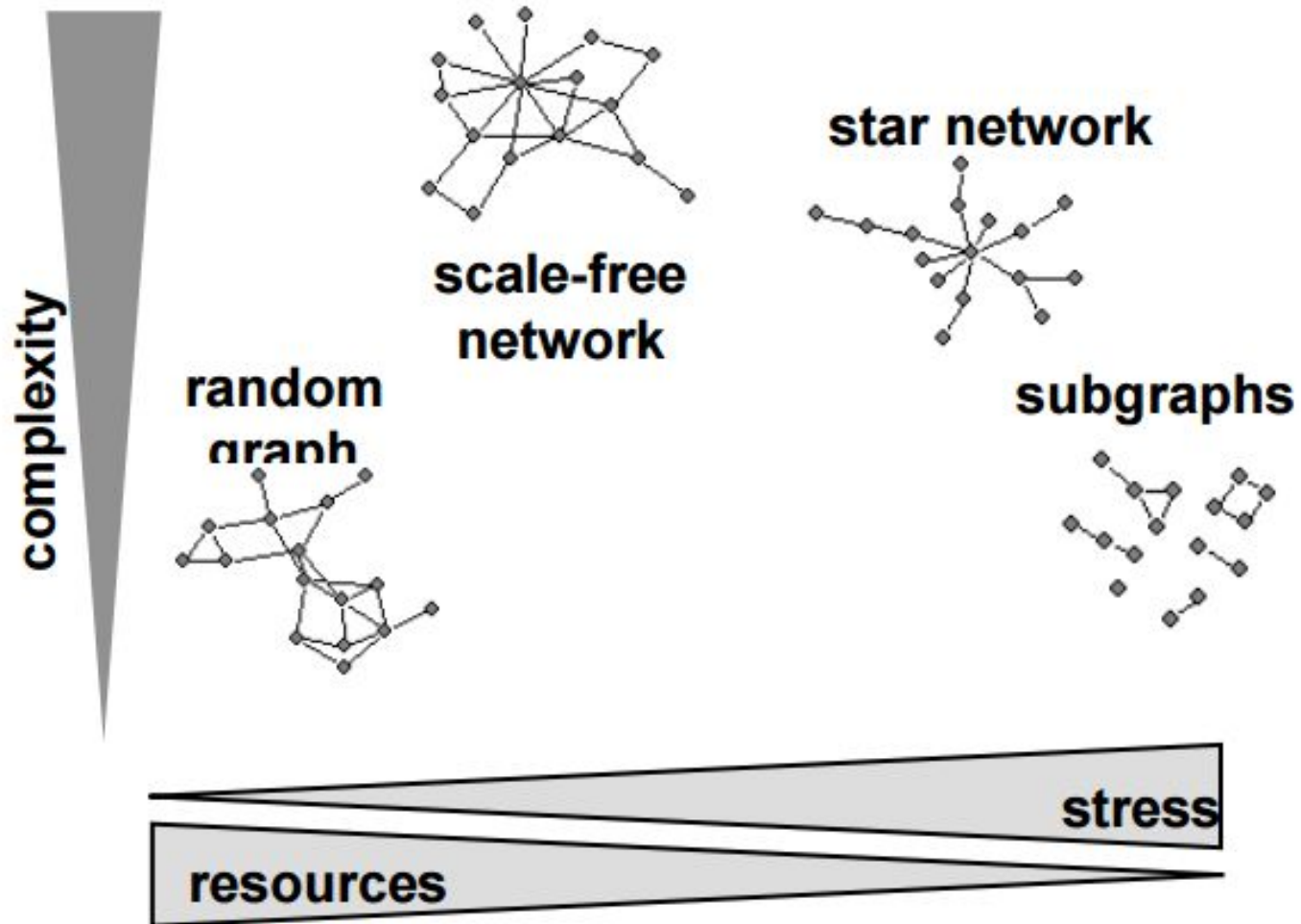
Context specific via subcellular localization



Edgetics - ???



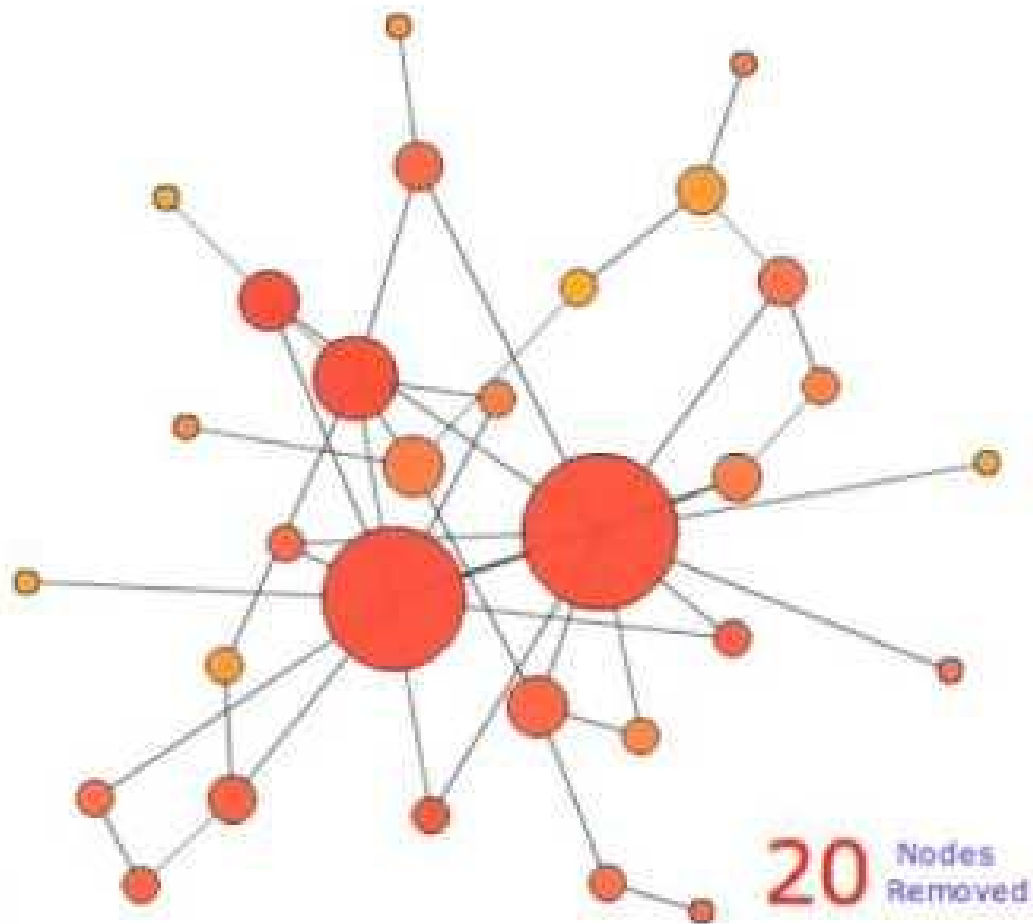
Topological phase transformations



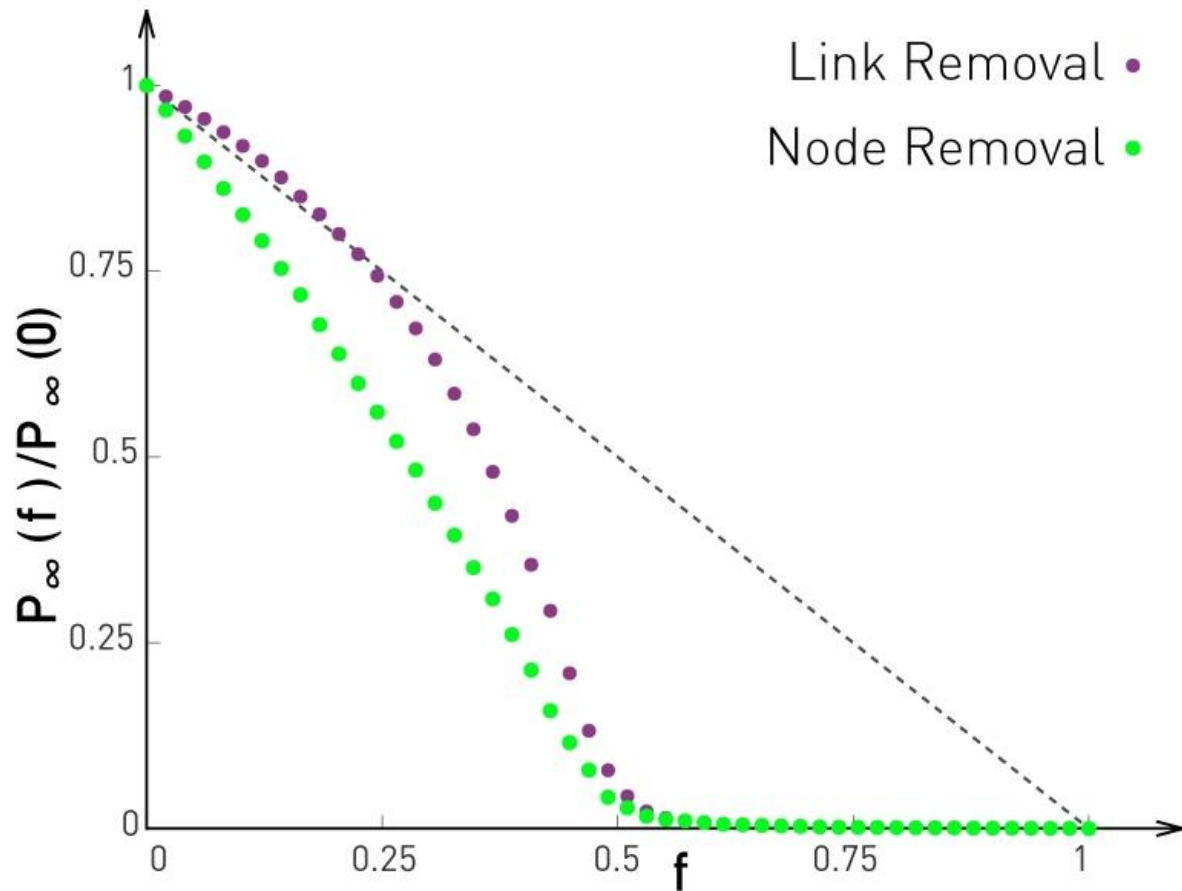
Network stability

- Network stability indicates that a given network responds to external influences
- External impact: Termination of point or connection
- Attack strategy:
 - ◆ random
 - ◆ planned

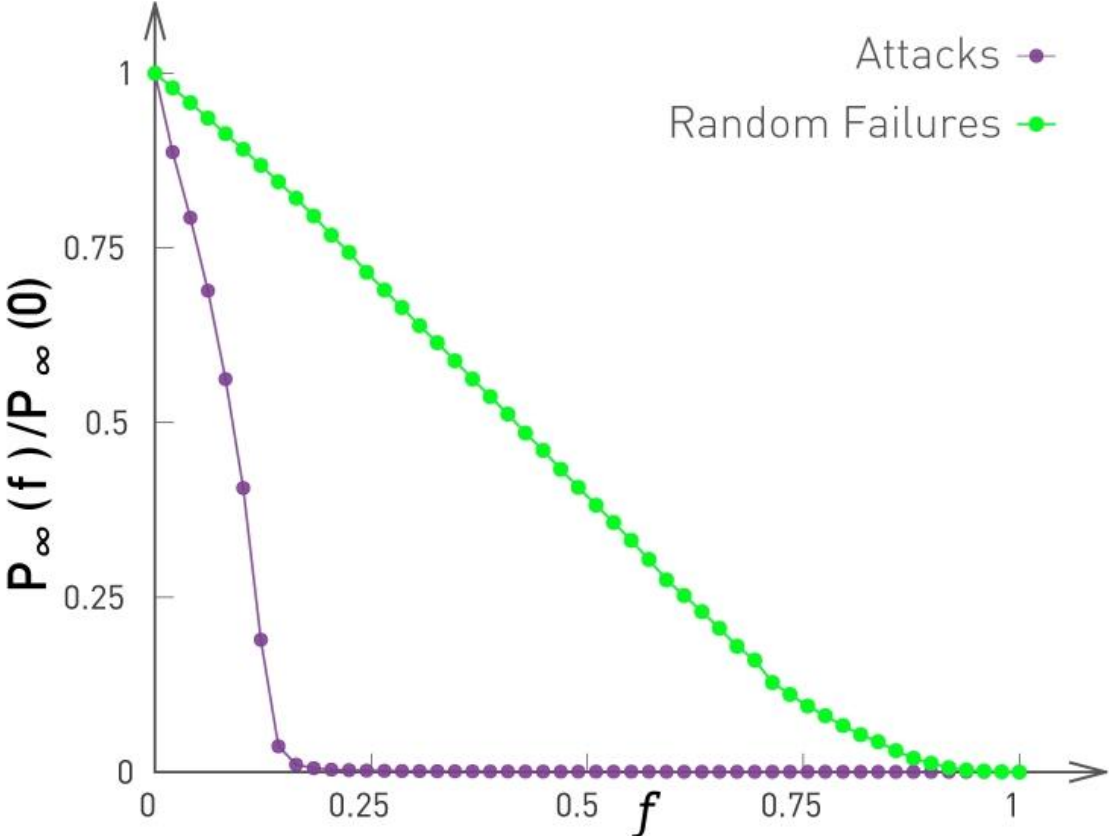
Network stability



Network stability - scale-free networks



Network stability - scale-free networks



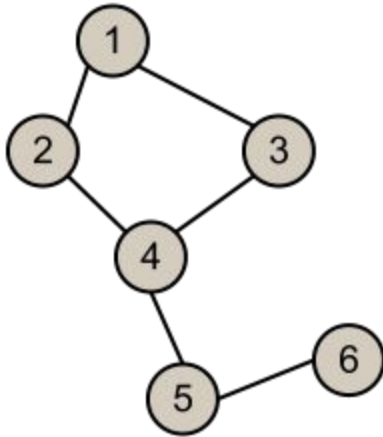
Storing network data - datastructure

→ Adjacency list

→ Adjacency matrix

Adjacency matrix

Undirected Graph & Adjacency Matrix



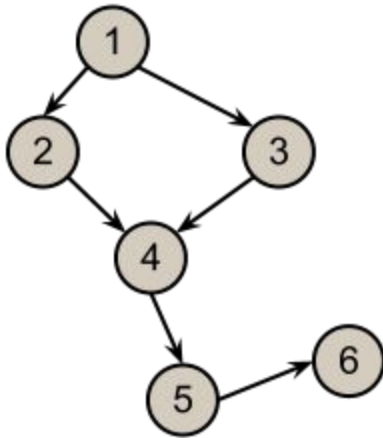
Undirected Graph

	①	②	③	④	⑤	⑥
①	0	1	1	0	0	0
②	1	0	0	1	0	0
③	1	0	0	1	0	0
④	0	1	1	0	1	0
⑤	0	0	0	1	0	1
⑥	0	0	0	0	1	0

Adjacency Matrix

Adjacency matrix

Directed Graph & Adjacency Matrix



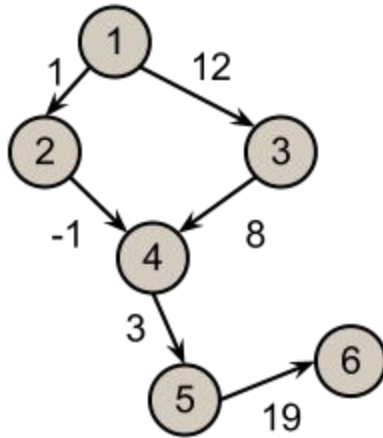
Undirected Graph

	①	②	③	④	⑤	⑥
①	0	1	1	0	0	0
②	-1	0	0	1	0	0
③	-1	0	0	1	0	0
④	0	-1	-1	0	1	0
⑤	0	0	0	-1	0	1
⑥	0	0	0	0	-1	0

Adjacency Matrix

Adjacency matrix

Weighted Directed Graph & Adjacency Matrix



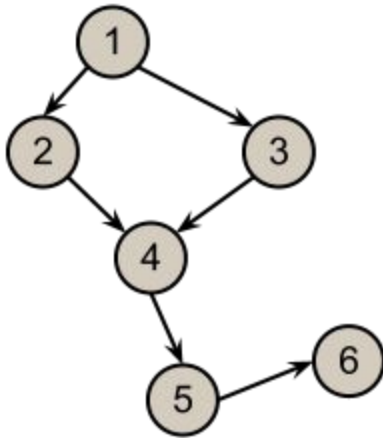
Weighted Directed Graph

	①	②	③	④	⑤	⑥
①	0	1	12	0	0	0
②	-1	0	0	-1	0	0
③	-12	0	0	8	0	0
④	0	1	-8	0	3	0
⑤	0	0	0	-3	0	19
⑥	0	0	0	0	-19	0

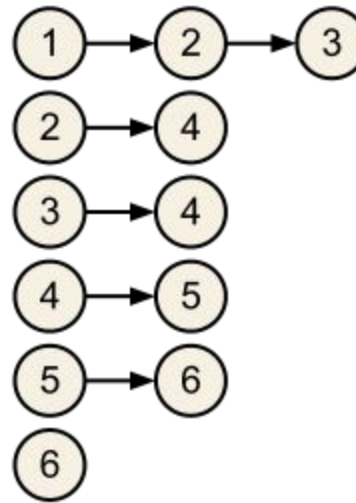
Adjacency Matrix

Adjacency list

Directed Graph & Adjacency List



Undirected Graph



Adjacency Matrix

Adjacency list - file formats

- CSV, TSV
 - ◆ table
- SQL
 - ◆ relational database
- XML
 - ◆ table like
- SBML
 - ◆ special XML
- BioPax
 - ◆ special XML
- PSI-MI
 - ◆ complex format syntax and ontology

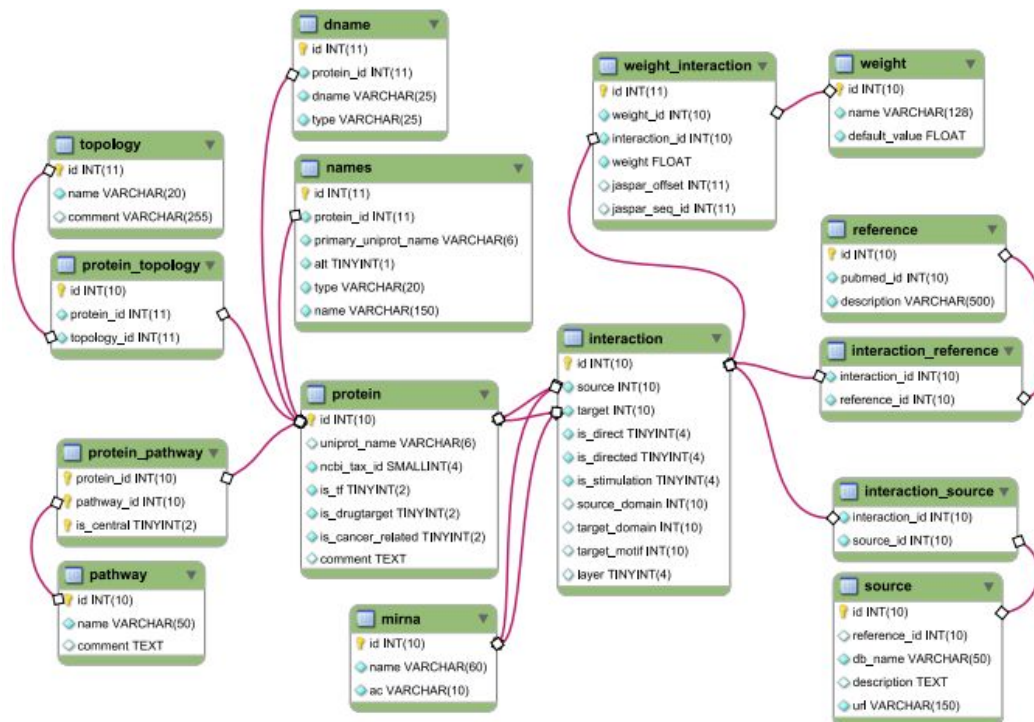
Storing network data - file formats - CSV, TSV

- Semicolon or Tabbed Text Format
- Can be edited with MS Excel
- It is easy to read with the program and manually

```
1 source_name;source_uniprotAC;source_speciesID;source_species;source_topology;source_pathways;target_name;ta
2 JAK2;060674;ENSG00000096968;H. sapiens;Mediator;JAK/STAT(core);PTPN11;Q06124;ENSG00000179295;H. sapiens;Co-
3 PTPN11;Q06124;ENSG00000179295;H. sapiens;Co-factor,Scaffold;RTK(non-core),JAK/STAT(non-core);JAK2;060674;ENS
4 IRS1;P35568;ENSG00000169047;H. sapiens;Mediator,Scaffold;RTK(core),JAK/STAT(core);JAK1;P23458;ENSG0000016243
5 JAK1;P23458;ENSG00000162434;H. sapiens;Mediator;RTK(core),JAK/STAT(core);IRS1;P35568;ENSG00000169047;H. sapi
6 GSK3B;P49841;ENSG00000082701;H. sapiens;Mediator,Co-factor;RTK(non-core),RTK(core),Hedgehog(core),TGF(core)
7 AXIN1;015169;ENSG00000103126;H. sapiens;Mediator,Scaffold;RTK(non-core),TGF(non-core),TGF(core),WNT/Wingless
8 MAP2K1;Q02750;ENSG00000169032;H. sapiens;;RTK(core),Hedgehog(core);MAPK3;P27361;ENSG00000102882;H. sapiens;T
9 MAPK3;P27361;ENSG00000102882;H. sapiens;Mediator;RTK(core),JAK/STAT(core),TGF(core);MAP2K1;Q02750;ENSG000001
10 SMAD3;P84022;ENSG00000166949;H. sapiens;Mediator,Transcription factor;RTK(core),NHR(core),TGF(core),WNT/Wing
11 ESR1;P03372;ENSG00000091831;H. sapiens;Receptor,Transcription factor;NHR(core),TGF(non-core);SMAD3;P84022;EN
12 PEA15;Q15121;ENSG00000162734;H. sapiens;Co-factor;RTK(non-core);MAPK3;P27361;ENSG00000102882;H. sapiens;Medi
13 MAPK3;P27361;ENSG00000102882;H. sapiens;Mediator;RTK(core),JAK/STAT(core),TGF(core);PEA15;Q15121;ENSG0000010
14 IL10RB;Q08334;ENSG00000243646;H. sapiens;Ligand ;JAK/STAT(core);IL28RA;Q8IU57;ENSG00000185436;H. sapiens;Re
15 IL10RB;Q08334;ENSG00000243646;H. sapiens;Ligand ;JAK/STAT(core);IL28RA;Q8IU57;ENSG00000185436;H. sapiens;Re
16 SMURF2;Q9HAU4;ENSG00000108854;H. sapiens;Co-factor,Endocytosis related ,Scaffold;TGF(non-core),WNT/Wingless
17 SMAD2;Q15796;ENSG00000175387;H. sapiens;Mediator,Transcription factor;RTK(core),TGF(core),WNT/Wingless(core)
18 SMAD3;P84022;ENSG00000166949;H. sapiens;Mediator,Transcription factor;RTK(core),NHR(core),TGF(core),WNT/Wing
19 NOTCH1;P46531;ENSG00000148400;H. sapiens;Receptor,Endocytosis related ;Notch(core),WNT/Wingless(core);SMAD3
20 MAP2K2;P36507;ENSG00000126934;H. sapiens;Mediator;RTK(core);MAPK1;P28482;ENSG00000100030;H. sapiens;Mediato
```


Storing network data - file formats - SQL

- Database management language
- It can be used remotely for a database server
- Can be edited manually and programmatically



Storing network data - file formats - XML

- "Incomplete" tables are practical
- "Tag" format
- It is difficult to read, hand-handy

```
1 <?xml version="1.0" encoding="UTF-8"?>
2 <sbml xmlns="http://www.sbml.org/sbml/level2" level="2" version="1">
3   <model id="Salmonella_consensus_build_1">
4     <listOfUnitDefinitions>
5       <unitDefinition id="mmol_per_gDW_per_hr">
6         <listOfUnits>
7           <unit kind="mole" scale="-3"/>
8           <unit kind="gram" exponent="-1"/>
9           <unit kind="second" exponent="-1" multiplier="0.000277777777777778"/>
10        </listOfUnits>
11      </unitDefinition>
12    </listOfUnitDefinitions>
13    <listOfCompartments>
14      <compartment id="p" name="periplasm" size="1"/>
15      <compartment id="c" name="cytosol" size="1"/>
16      <compartment id="e" name="extracellular" size="1"/>
17    </listOfCompartments>
18    <listOfSpecies>
19      <species id="M_12dgr120_c" name="1-2-Diacyl-sn-glycerol-didodecanoyl-n-C120" compartment="c" charge="1">
20        <notes>
21          <html xmlns="http://www.w3.org/1999/xhtml">
22            <p>FORMULA: C27H52O5</p>
23            <p>KEGG ID: C00641</p>
24            <p>PubChem ID: 3914</p>
25            <p>ChEBI ID: 17815</p>

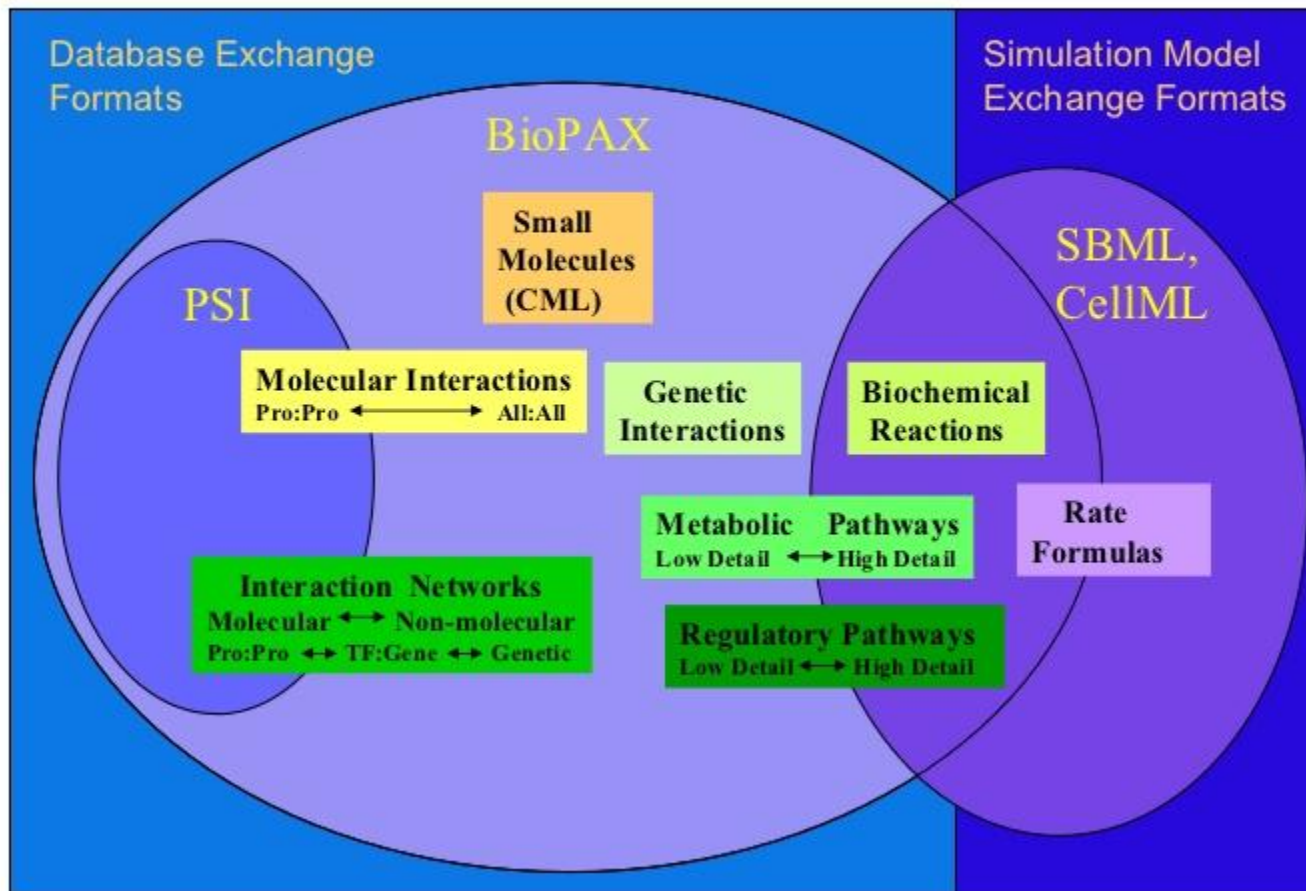
```

Storing network data - file formats - PSI-MI

- Proteomics Standards Initiative - Molecular Interaction
- Standard format for expressing molecular contact data
- Two format:
 - ◆ XML
 - ◆ TSV
- MI ontology

Storing network data - file formats

Exchange Formats in the Pathway Data Space

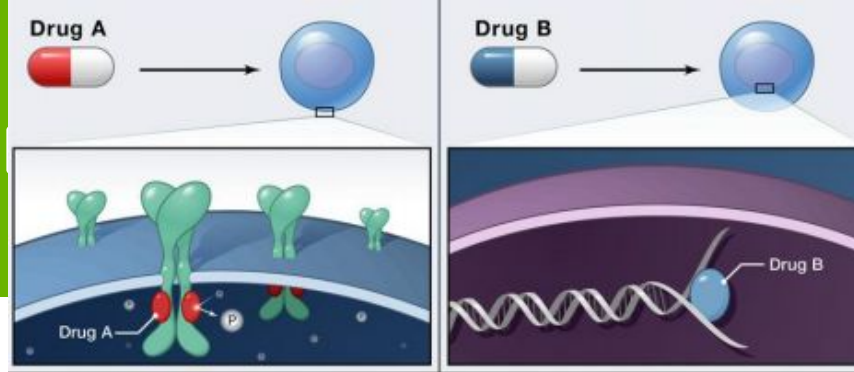


Application of network biology

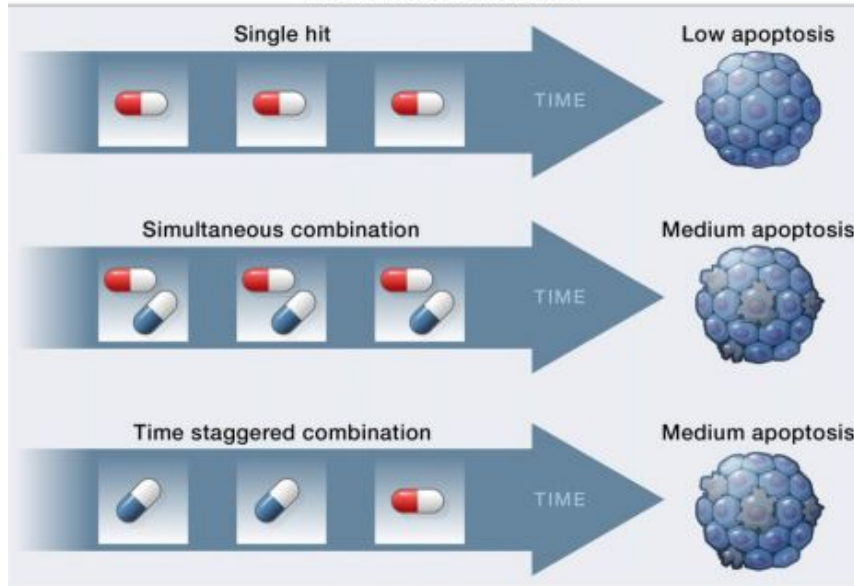
Papers (optional):

Michael J. Lee, Albert S. Ye, Alexandra K. Gardino, Anne Margriet Heijink, Peter K. Sorger, Gavin MacBeath, Michael B. Yaffe Sequential Application of Anticancer Drugs Enhances Cell Death by Rewiring Apoptotic Signaling Networks *Cell*, Volume 149, Issue 4, 11 May 2012, Pages 780-794

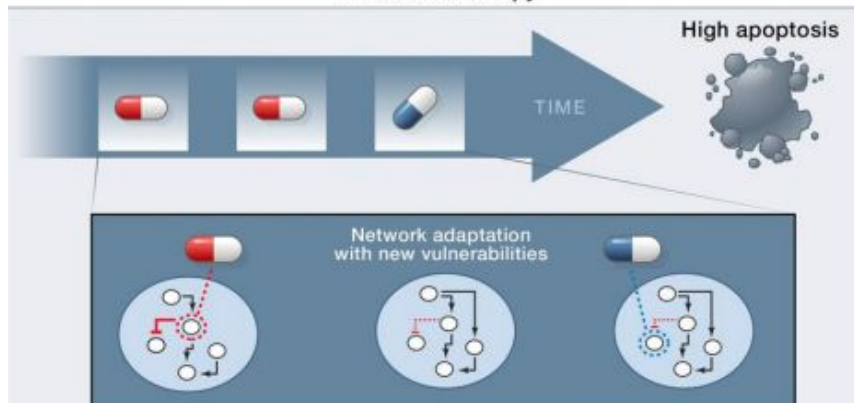
Preview: Janine T. Erler, Rune Linding Network Medicine Strikes a Blow against Breast Cancer *Cell*, Volume 149, Issue 4, 11 May 2012, Pages 731–733



Less Effective Therapies



Effective Therapy



Application of network biology

Combination Erl-Dox Nanoparticles in vivo

