



Chinese

bioinformatics
ZHANGroup.org

生物信息学与系统生物学

张世华

中国科学院数学与系统科学研究院

1



<http://zhangroup.aporc.org>
Chinese Academy of Sciences



课程信息

- 答疑&讨论: 课后或思源楼 1012/1003
- 对课程的意见和建议
- <http://www.aporc.org/doc/wiki/Course001>

邮件:

zsh@amss.ac.cn;

时间: 2012.2.22---4.27, 每周三、五下午13:30-16:10

地点: 中科院研究生院中关村教学楼N215教室



大纲

如何分析网络? (张世华)

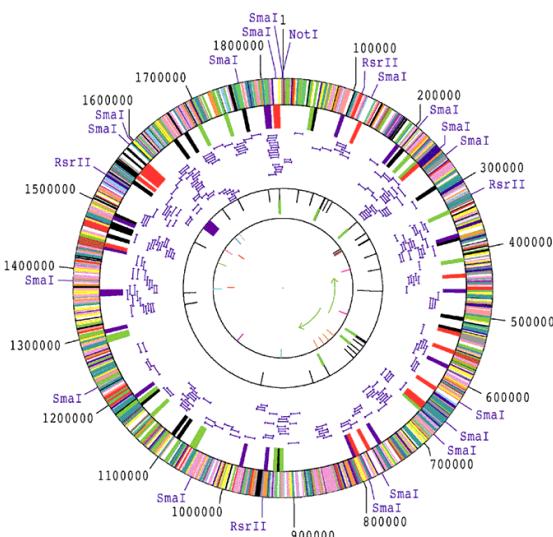
1. 生物分子网络分析
2. 生物分子网络motif, 模块分析
3. 生物分子网络比对
4. 生物活性通路与网络标记物识别
5. 拓展学习: 癌症基因组学

如何构建网络? (王勇)

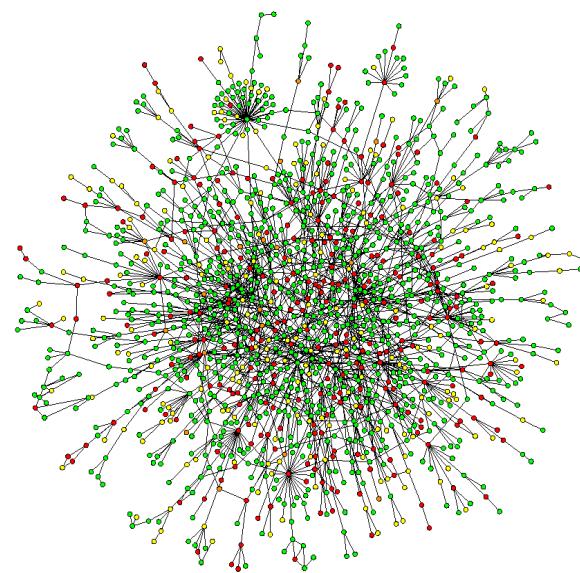
1. 基因调控网络重建
2. 转录调控网络重建
3. 转录因子合作网络预测
4. 蛋白质相互作用网络预测

生物分子网络

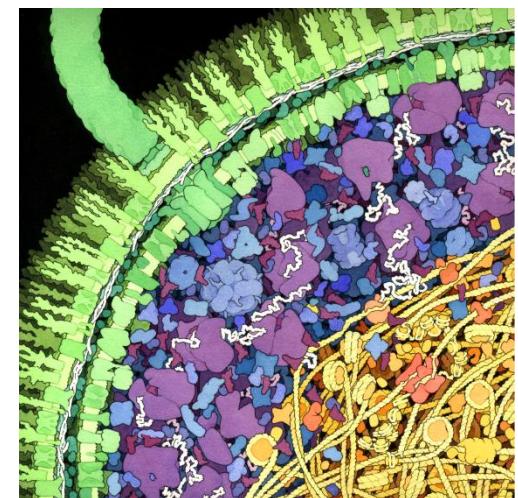
- 图作为基本工具用来强调相互作用并直观表示复杂的生物系统
- 节点代表生物分子，边代表他们之间在生命过程中的某种关系



1D: Complete
Genetic Partslist



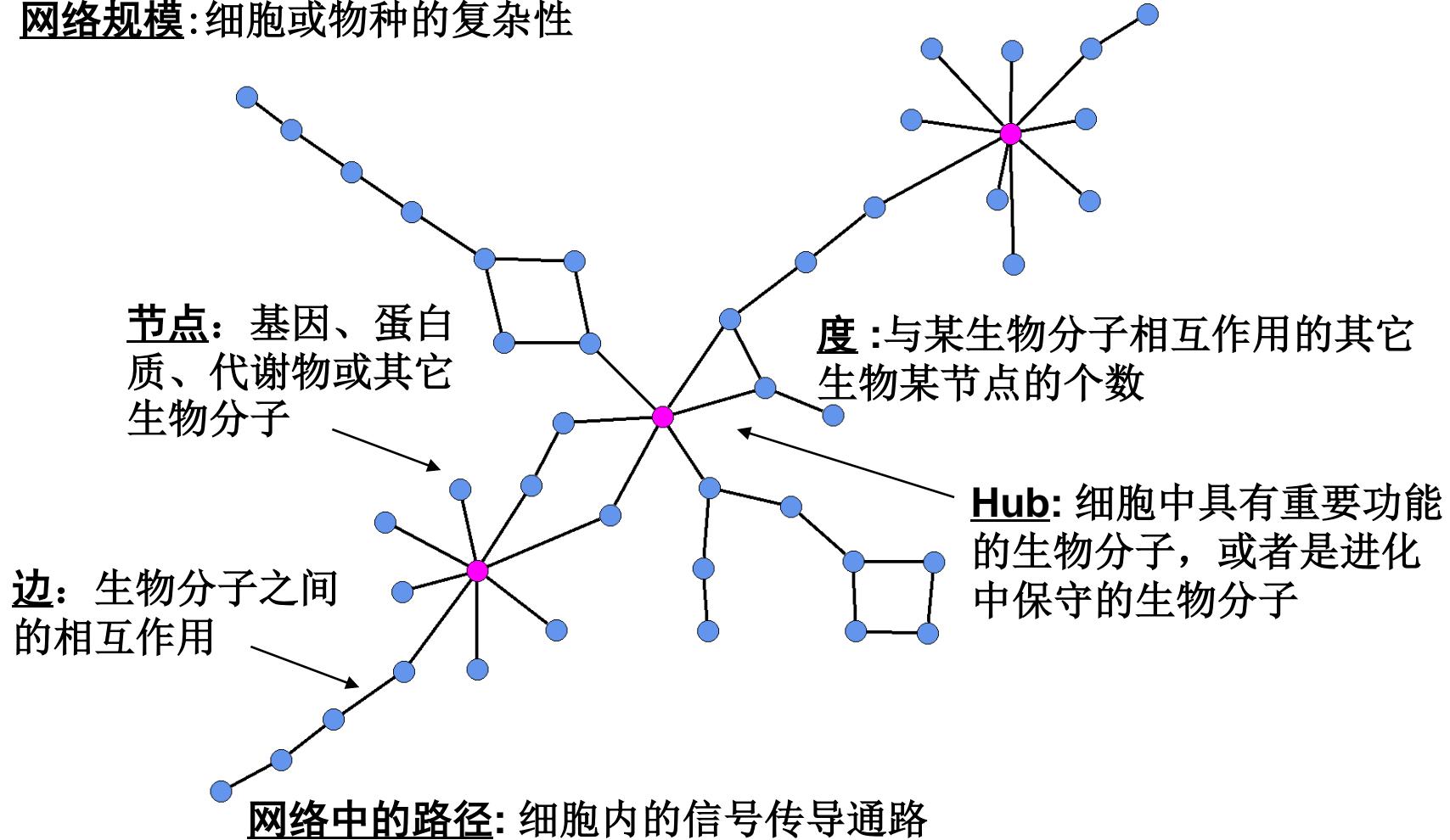
~2D: Bio-molecular
Network



3D: Detailed
structural
understanding of
cellular machinery

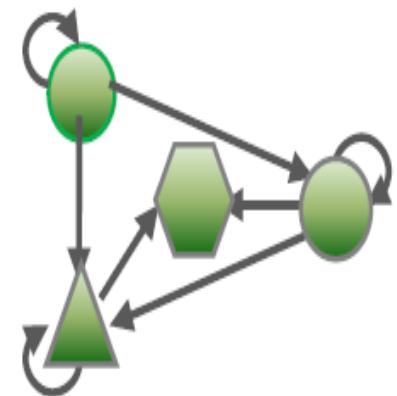
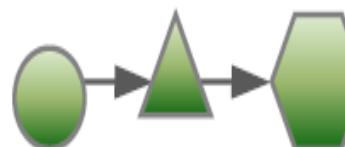
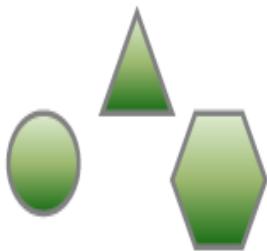
生物学语言下的网络

网络规模: 细胞或物种的复杂性



Main ingredients?

Molecules Interactions Pathways Networks



Individual molecules \Rightarrow Pairwise interactions \Rightarrow Local structures \Rightarrow Global networks

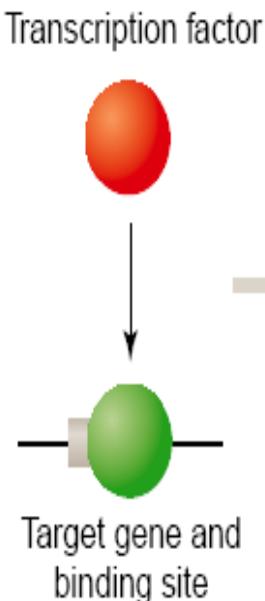
Local

Global

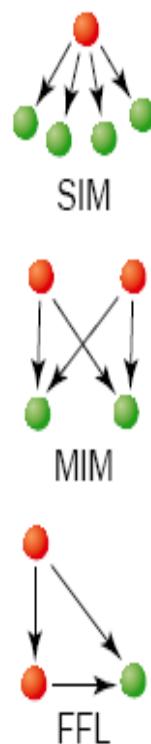
Hierarchical Relations

Transcriptional regulatory network

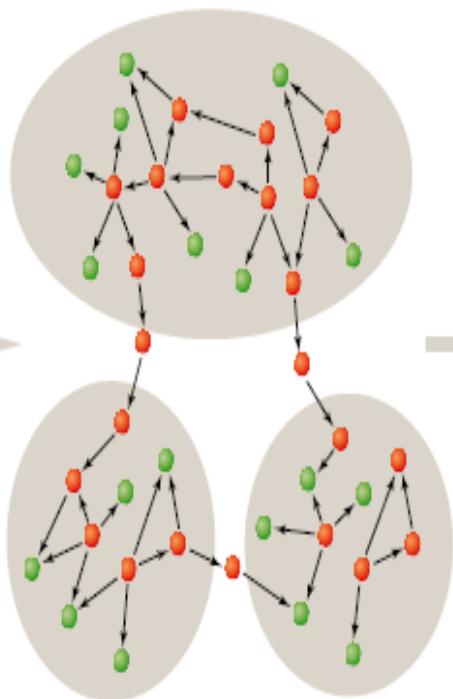
(a) Basic unit



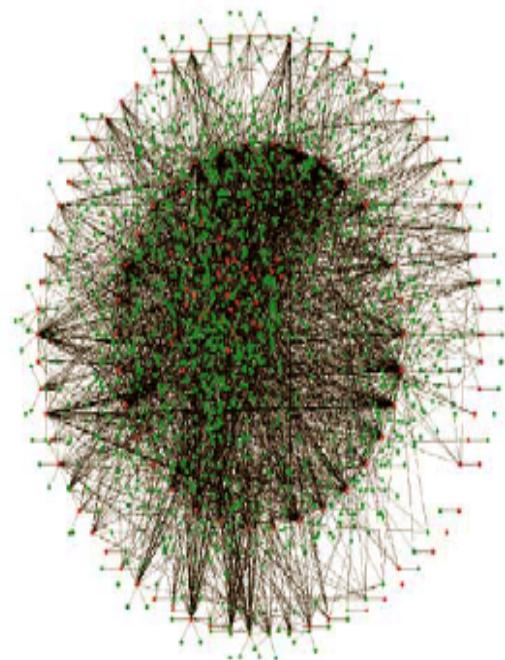
(b) Motifs



(c) Modules



(d) Transcriptional regulatory network



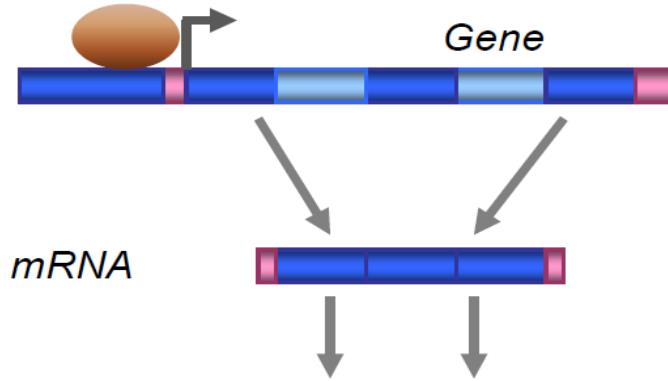
Current Opinion in Structural Biology

Subset of genetic network

Node: TF and genes, Edge: regulation relationships
Directed, Edge weighted

Biological networks

Transcription factor



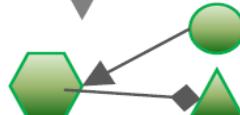
mRNA

Protein

Metabolite



Heterogeneous components



Transcription regulatory network
(DNA-TF interactions)

Gene regulatory network
(gene-gene interactions)

Protein interaction network
(protein-protein interactions)

Metabolic network
(enzyme-substrate interactions)

Signaling network
(molecule-molecule interactions)

Molecules

vs.

Networks

Central Dogma of Biology



网络分析

- 拓扑分析 (Topology)

Hub and bottleneck

Hierarchy structure

Network motif

- 网络动态分析 (Dynamics)

Hubs in different conditions

Subnetworks in different conditions

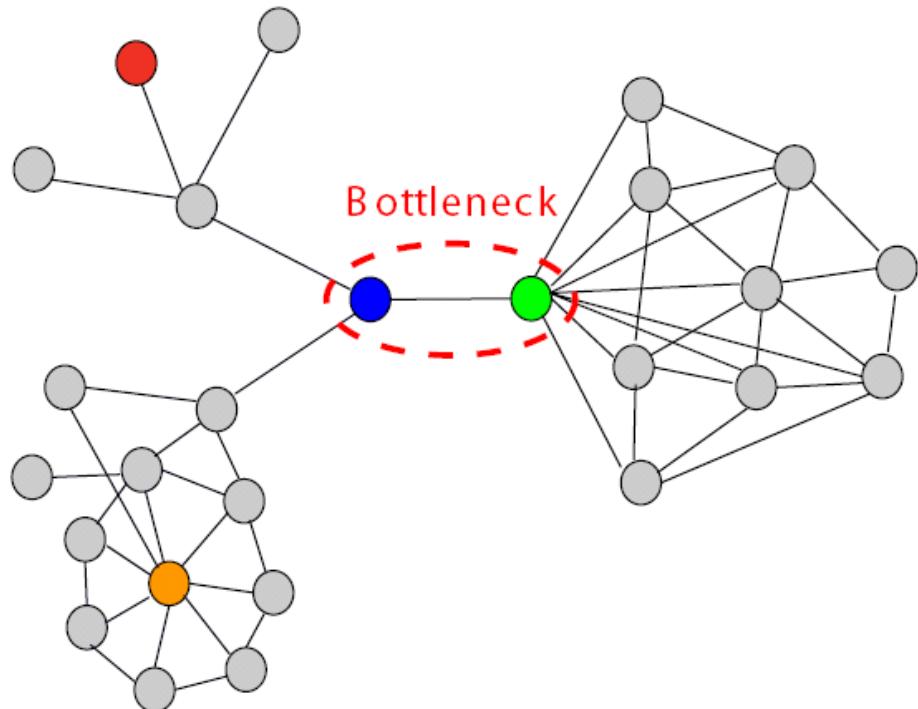
- 子网络分析 (Subnetworks)

Aging and disease subnetwork

Evolution in TF subnetwork

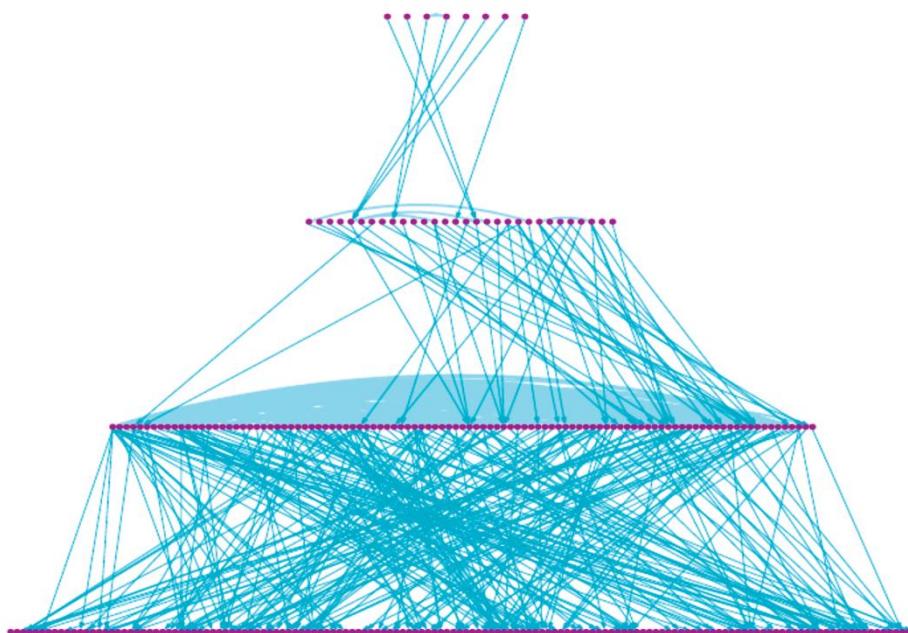
Q1: Finding Central Nodes in Networks: Hubs & Bottlenecks

Which are key nodes in networks ? How do we locate them ?

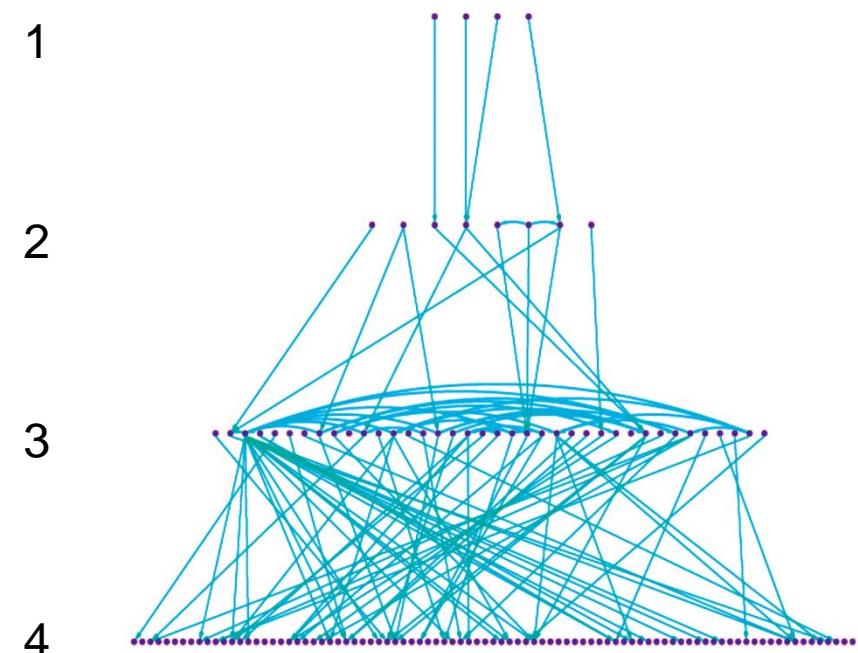


Q2: Does the Bio-molecular networks posses hierarchy structure

Does the network has the hierarchy structure? How do we identify them? What does it mean?



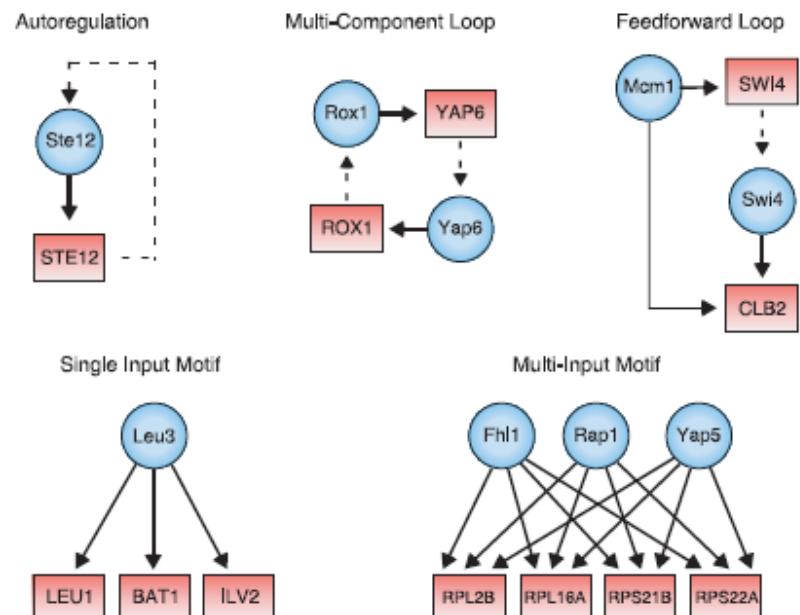
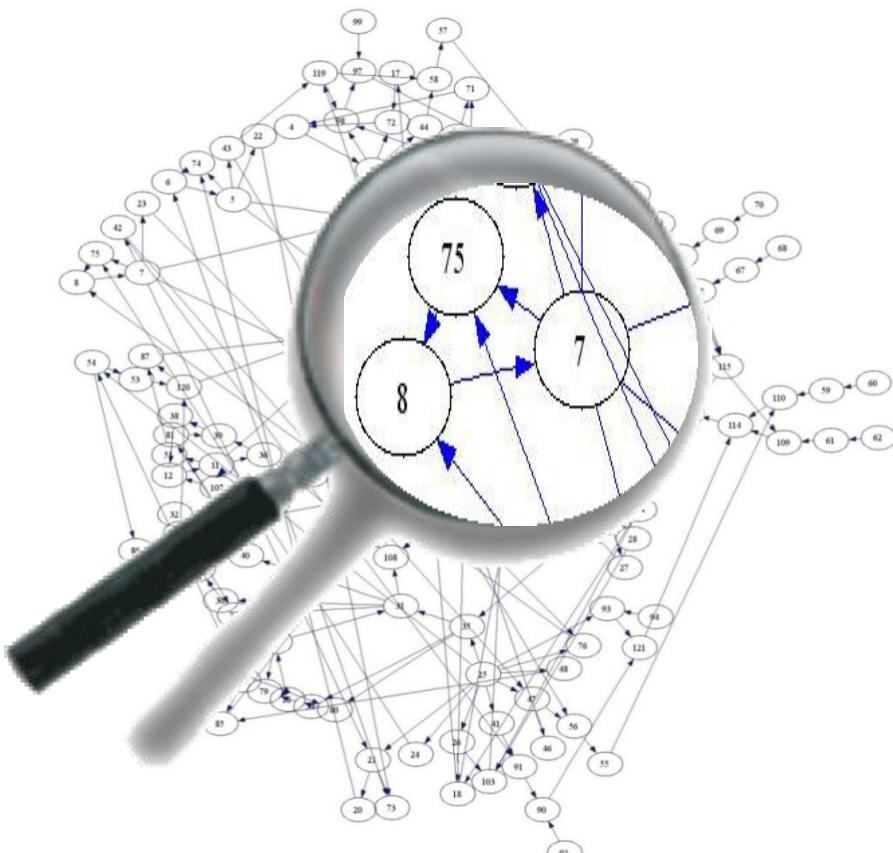
S. cerevisiae



E. coli

Q3: Are there some building blocks in the Bio-molecular networks?

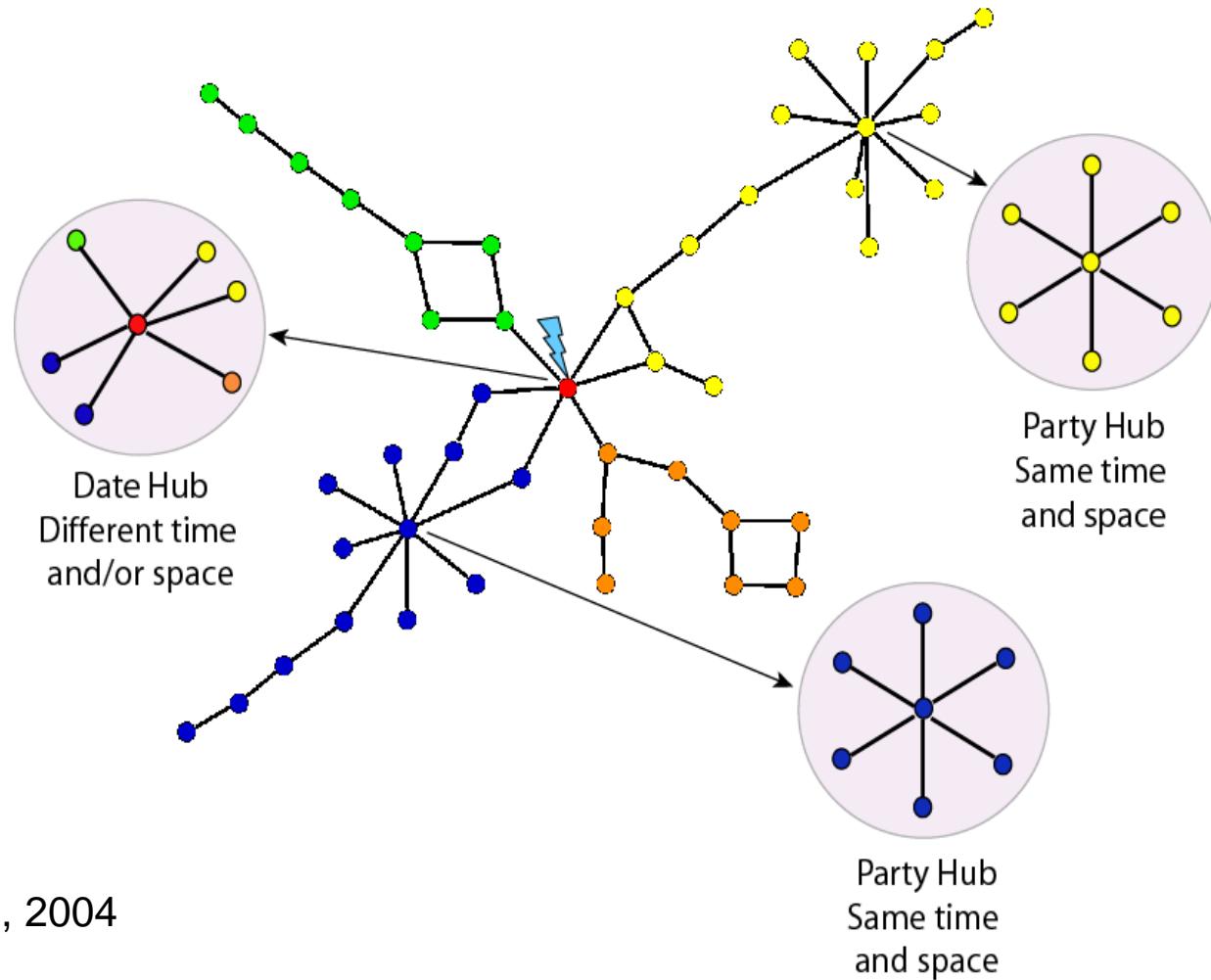
Where are they? How do we identify them? What does it mean?



Science, 298:799-804, 2002

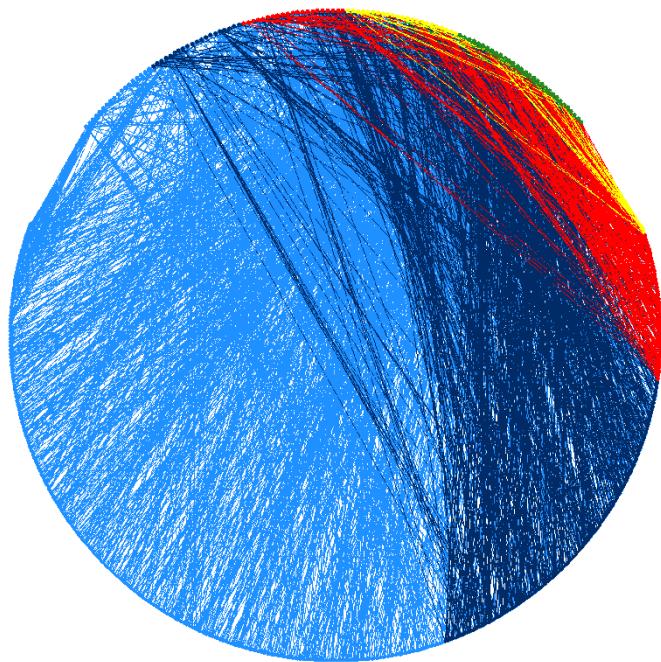
- The design principles of this network
- “Evolution preserves modules that define specific function.”
- Motifs are those subgraphs which occur in higher frequencies than in random graphs.

Q4: Are all hubs equal? From the temporal aspect!!



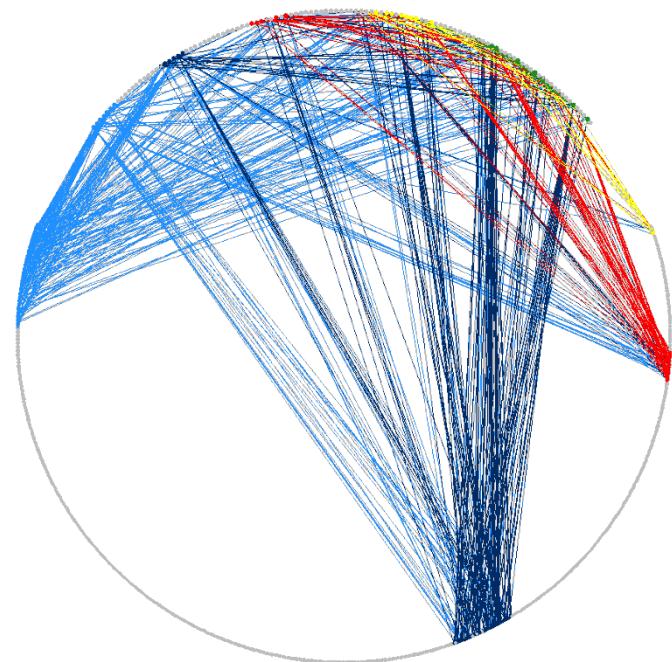
Q5: Substructure in the interactome network are known to be very important to the network topology and function.

complete network



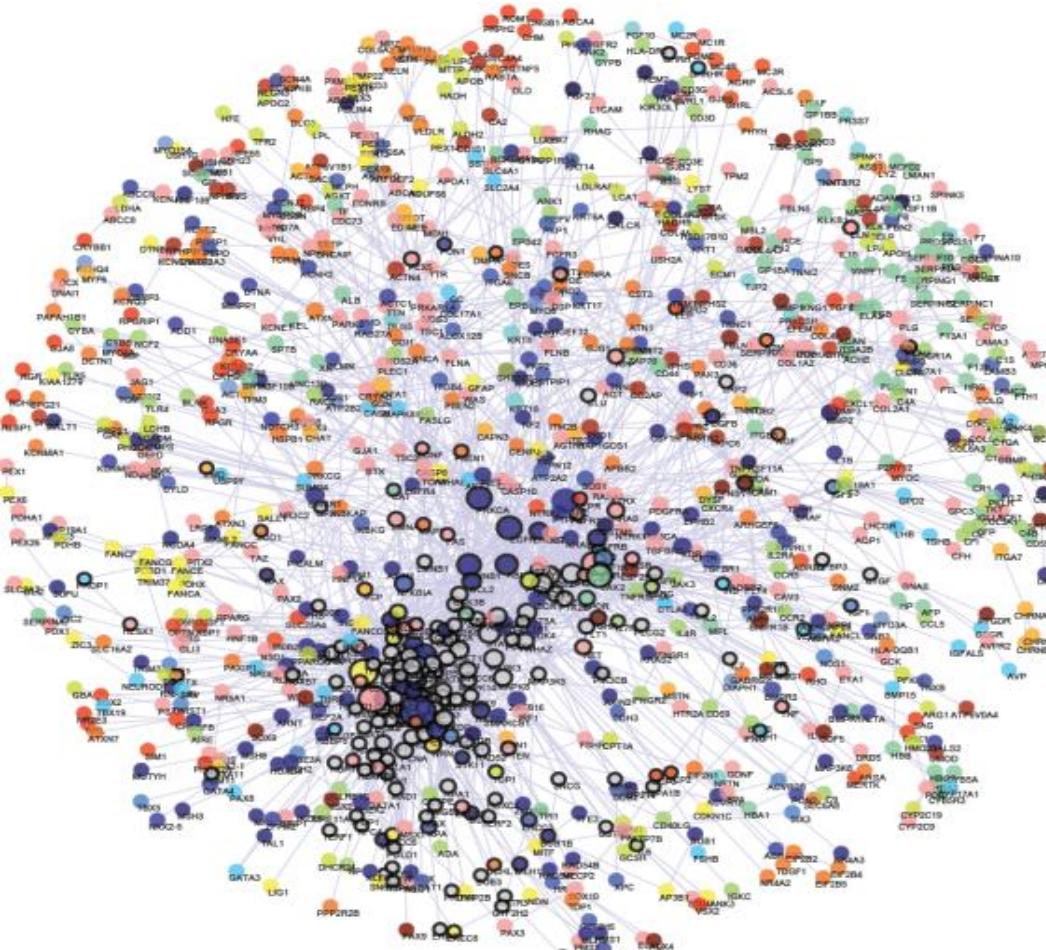
- 142 TFs
- 3,420 genes
- 7,074 interactions

cell cycle sub-network



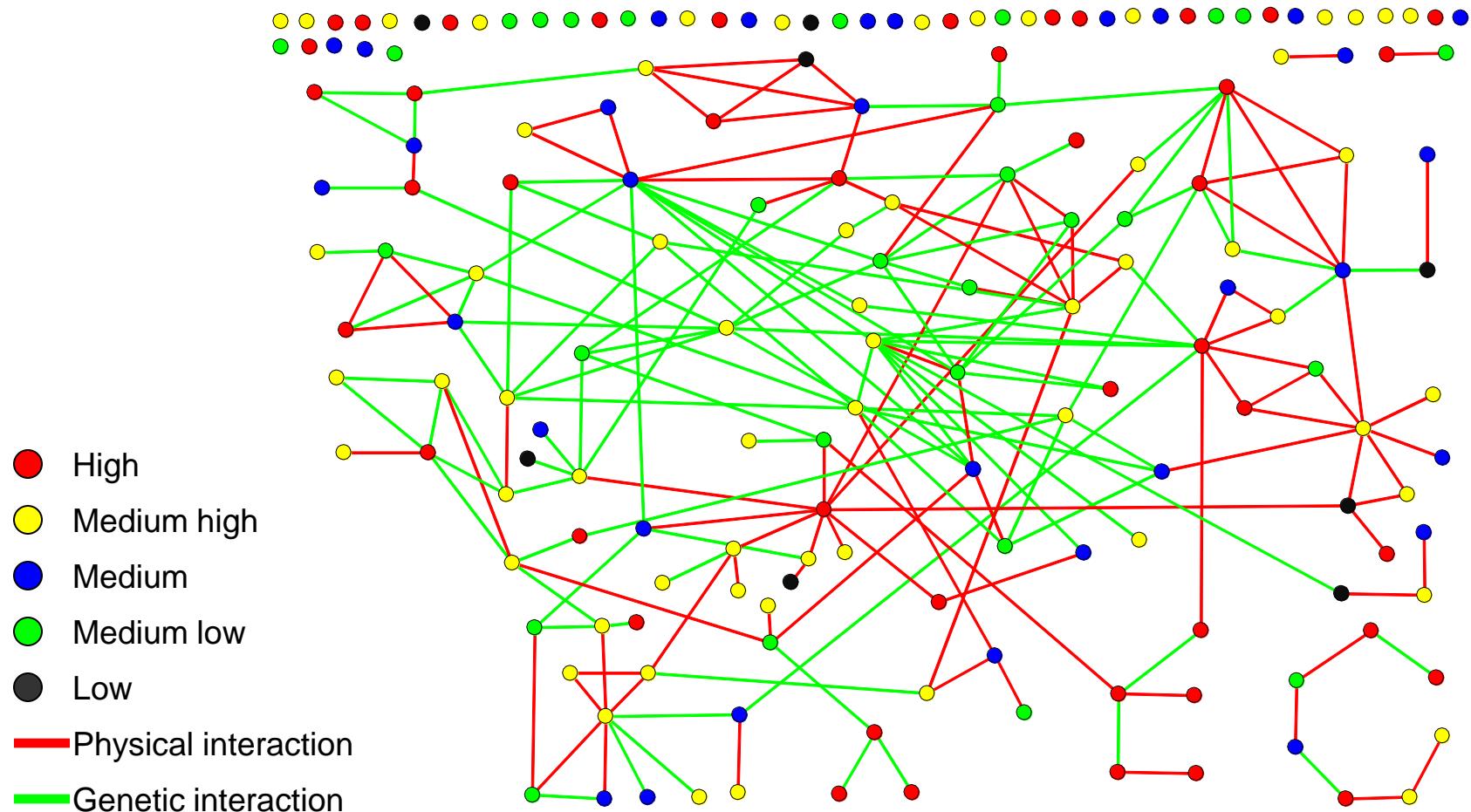
- 70 TFs
- 280 genes
- 550 interactions

Q6: Aging and disease are known to be closely related. Can we see this relationship in the interactome?

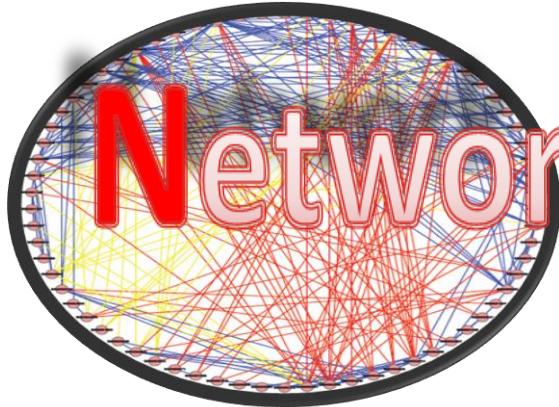


[PloS CB, 2009]

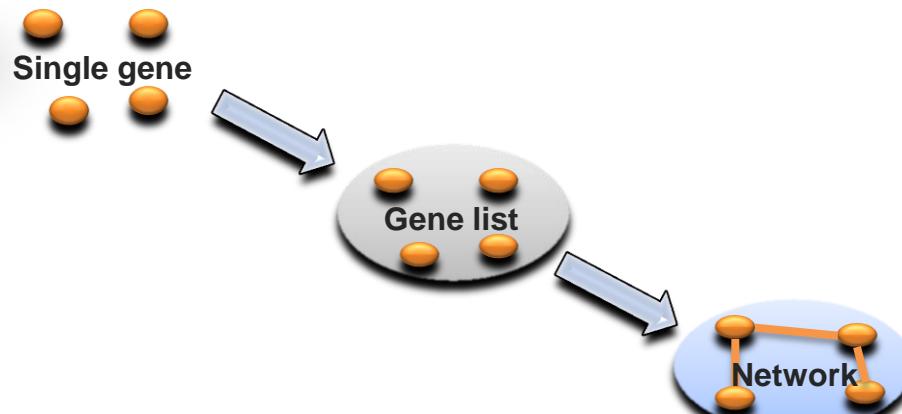
Q7: Regarding to **evolution principles**, is the subnetwork and the whole interactome the same?



Network Ontology Analysis

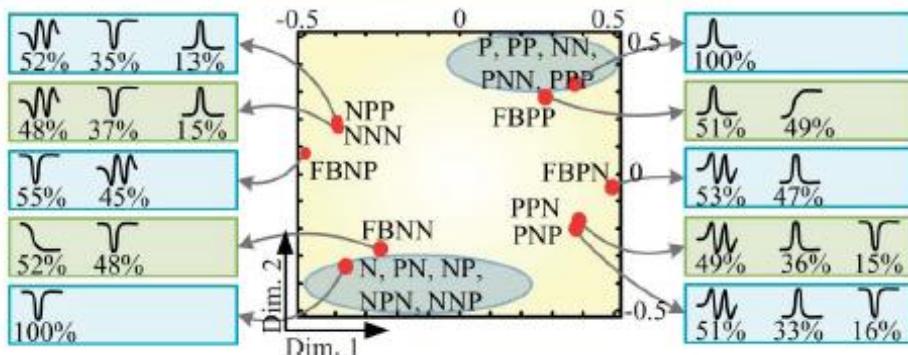
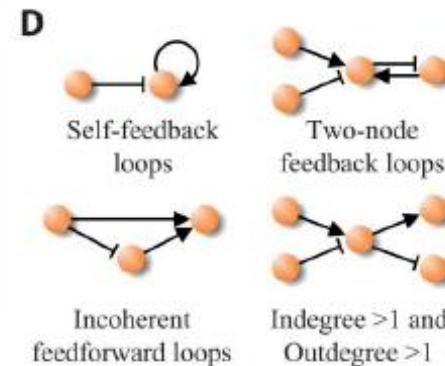
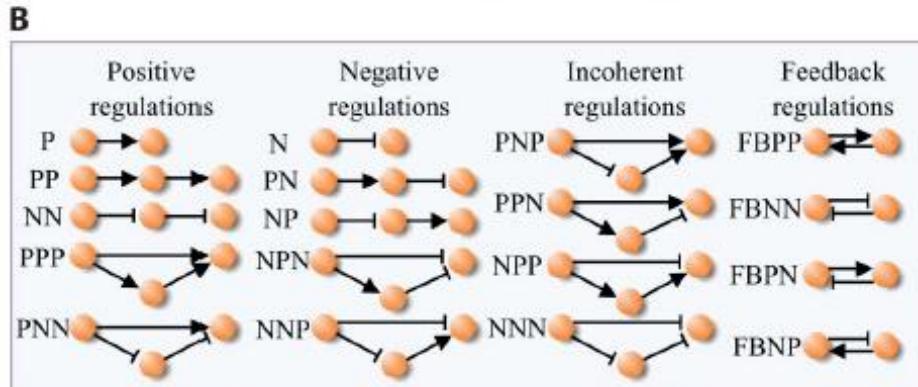
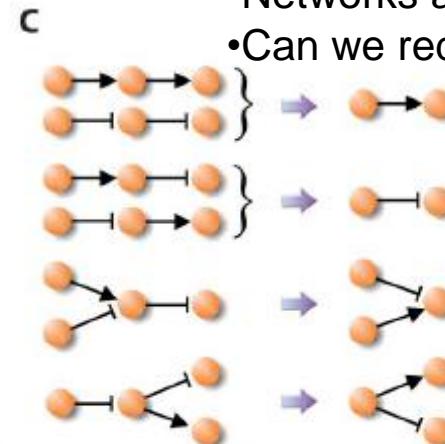
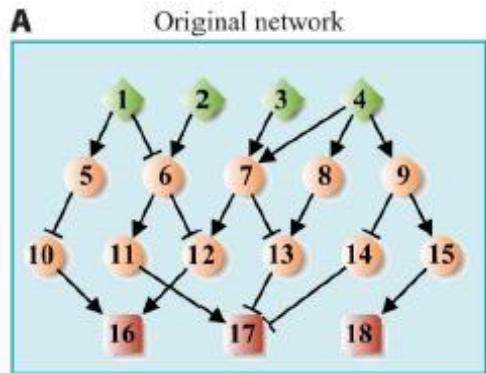


Network Ontology Analysis



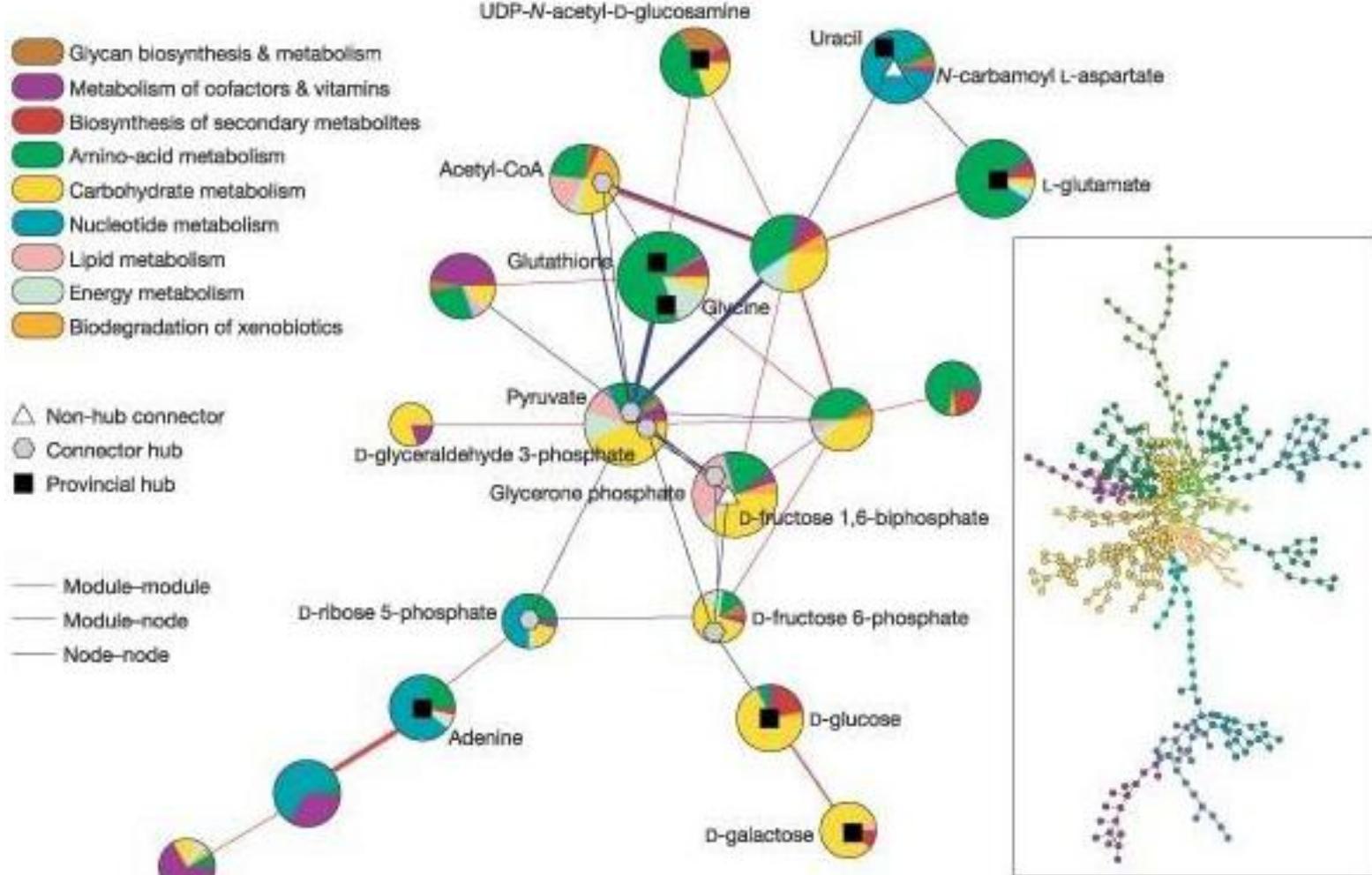
NAR, 2011.

Reduction of Networks



- Networks are powerful!
- Networks are complicated!
- Can we reduce the network?

Community structure of Networks



Guimera and Amaral, *Nature*, 2005

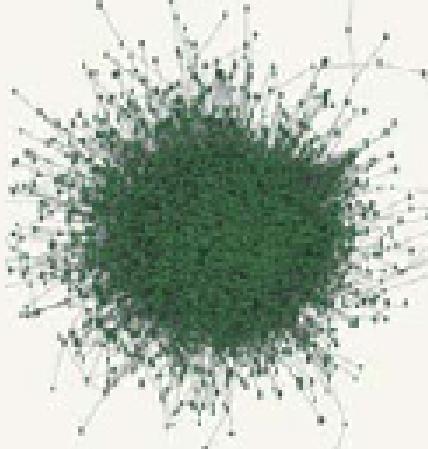
Network Alignment of Networks

Biological networks

Species 1
(Condition/type 1)



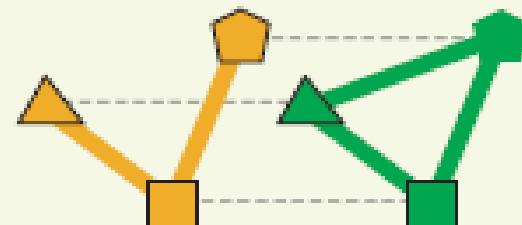
Species 2
(Condition/type 2)



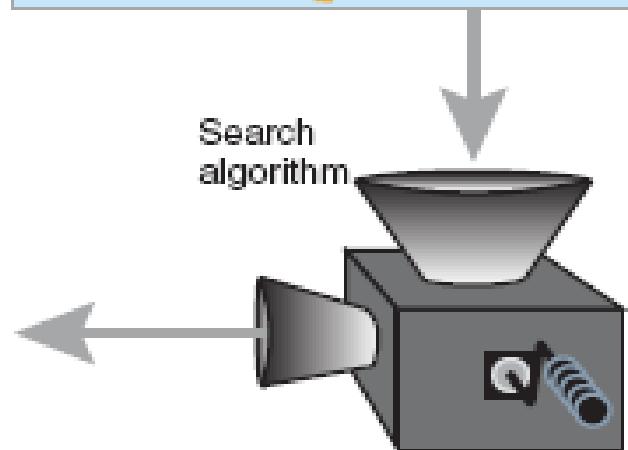
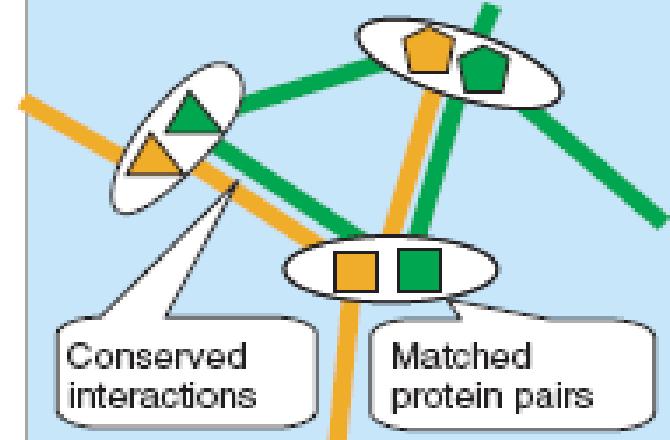
Matched proteins
Match protein pairs that are
sequence-similar

PRSDIDVDLCLCSELMAKACSE - GV
PKS +D+DLCSEL+ KAC++ +
PKSSLDIDLCSELIIKACTDKI

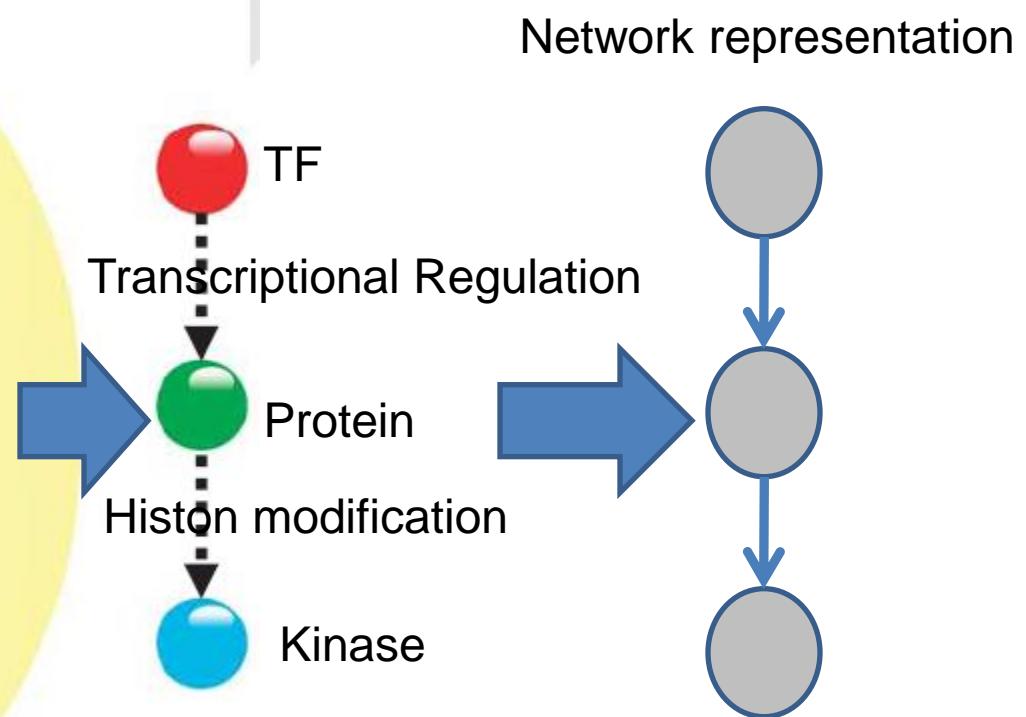
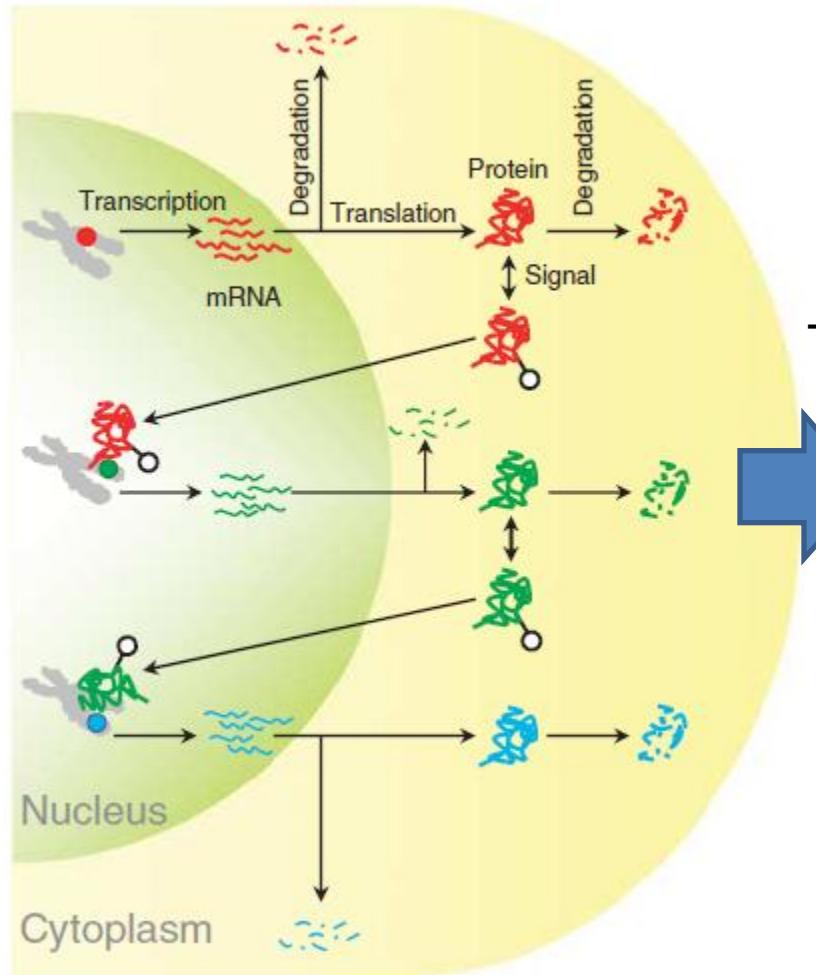
High-scoring
conserved subnetworks



Network alignment

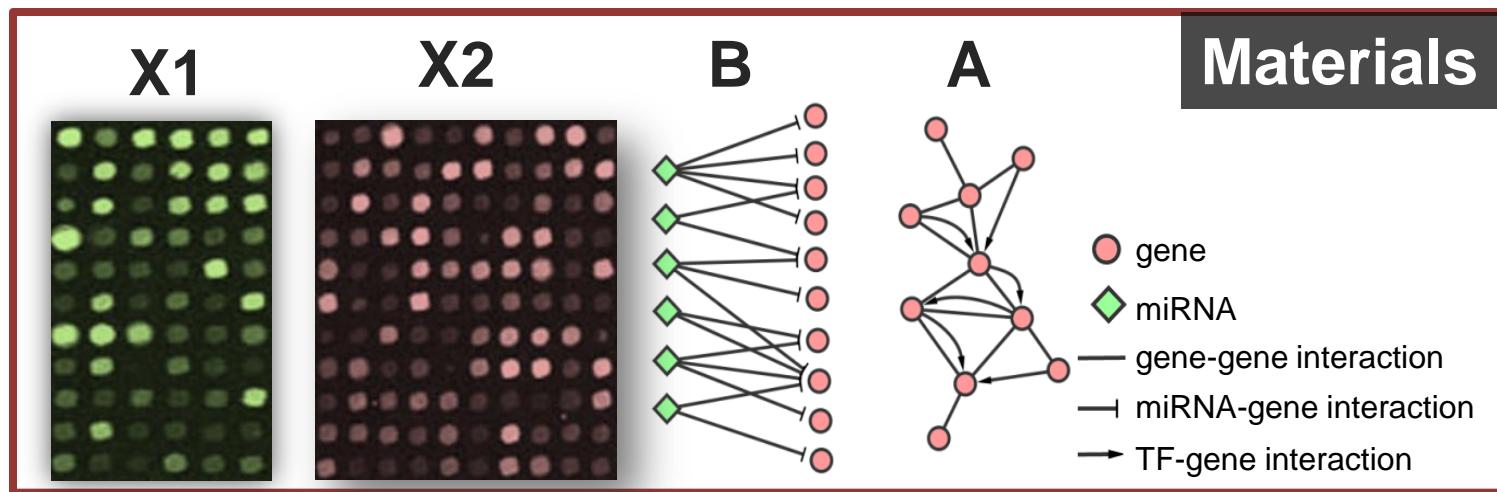


Conditional specific pathway or subnetwork identification

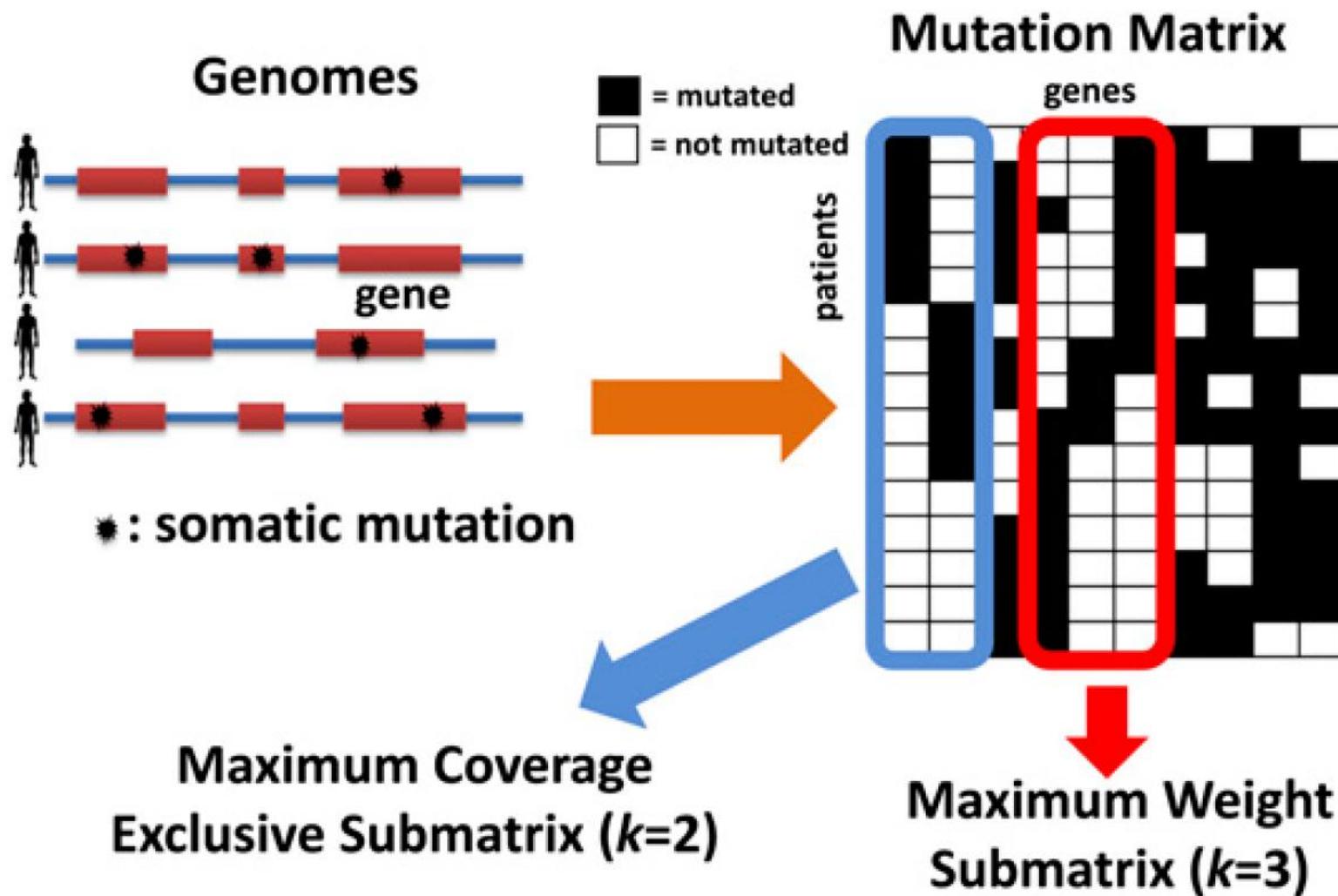


Although a series of regulatory events can be conveniently represented as a node in the network, **the dynamics of the entities and the biological processes that make up the node are not captured.**

Data integration: microRNA-gene co-module identification



Cancer genomics: driver genes and pathways identification







致谢！

该PPT课件的制作基于2010、2011版本，并有适当增删。

感谢章祥荪研究员、吴凌云和王勇博士以及整个课题组！

感谢许多工作的原始作者，限于时间和篇幅文献和作者未能及时标注。

谢谢大家！