

BIOLOGIA DE SISTEMAS

Hatylas Azevedo, hatylas@hotmail.com

Doutorando em Genômica e Biologia de Sistemas

Laboratório de Genômica Pediátrica (LIM36)

Departamento de Pediatria

Faculdade de Medicina da USP

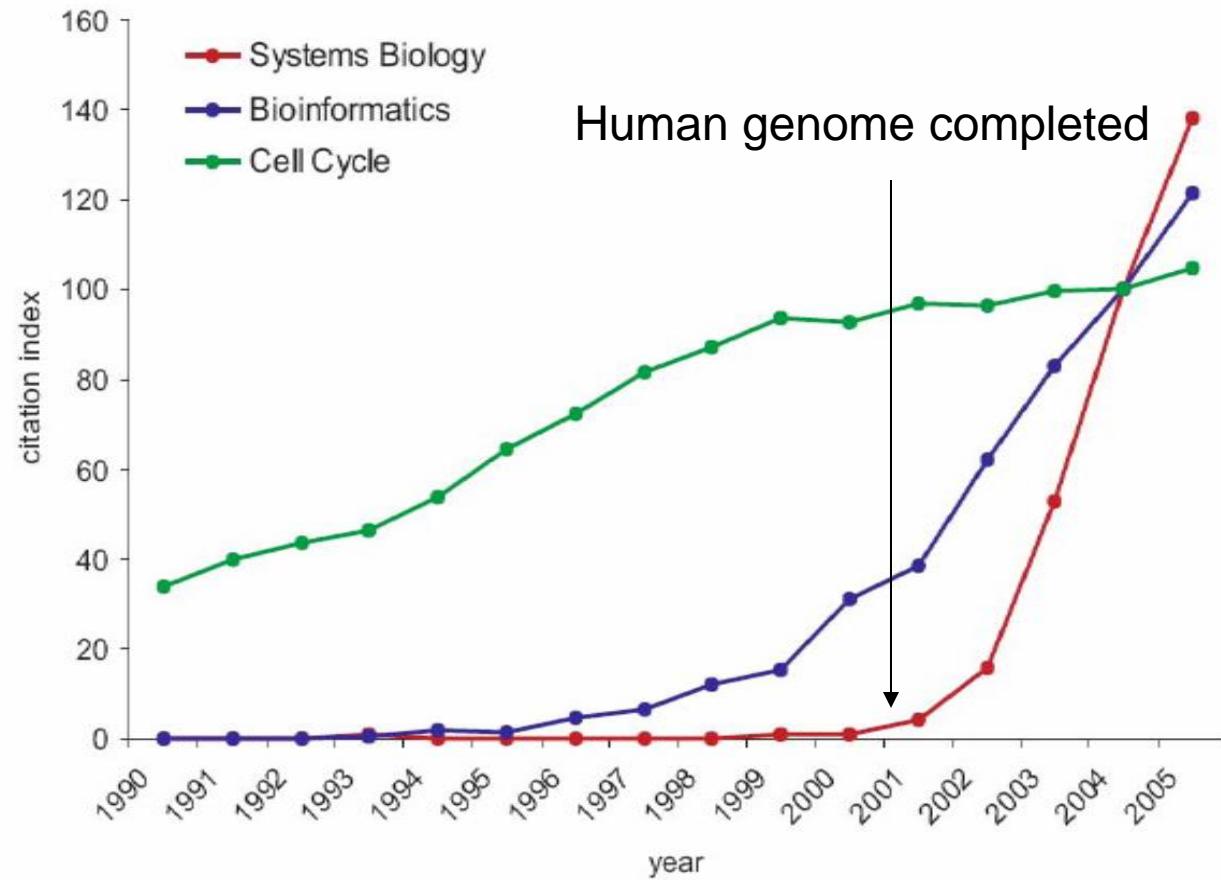
Agenda

1. Biologia de Sistemas
2. Análise de Redes Complexas
3. Exemplos de Estudos de Análises de Redes Biológicas
4. Experiências do Laboratório em Análises de Redes

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O que é Biologia de Sistemas?



O que é Biologia de Sistemas?

"Systems biology is just so general that it could apply to many things. When you're naming a category, the underlying principle is that if you make a statement like, 'I'm doing systems biology,' **do people know what you're talking about?**".....

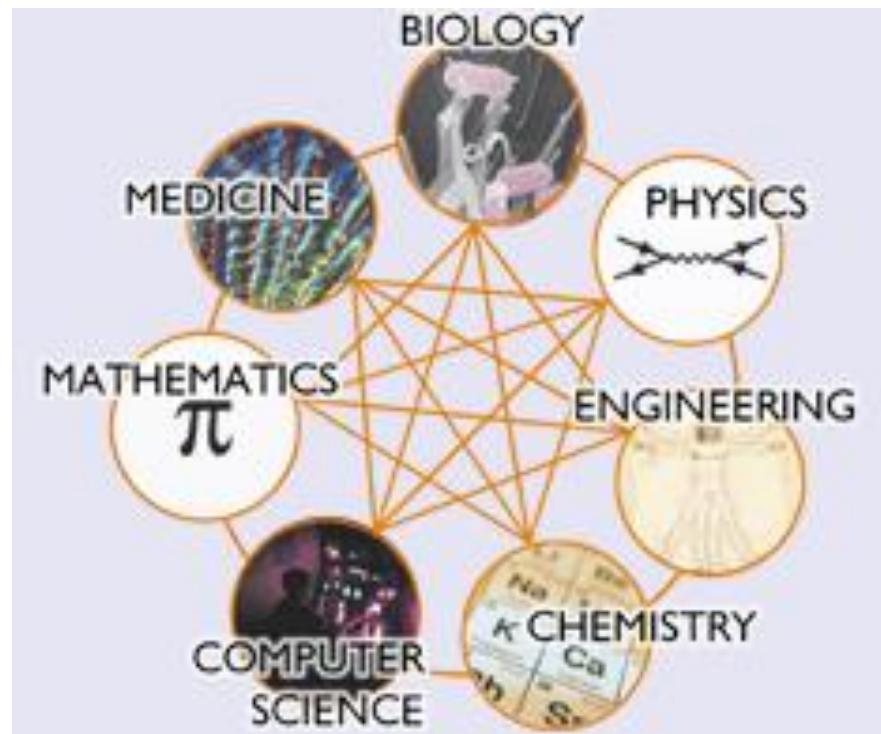
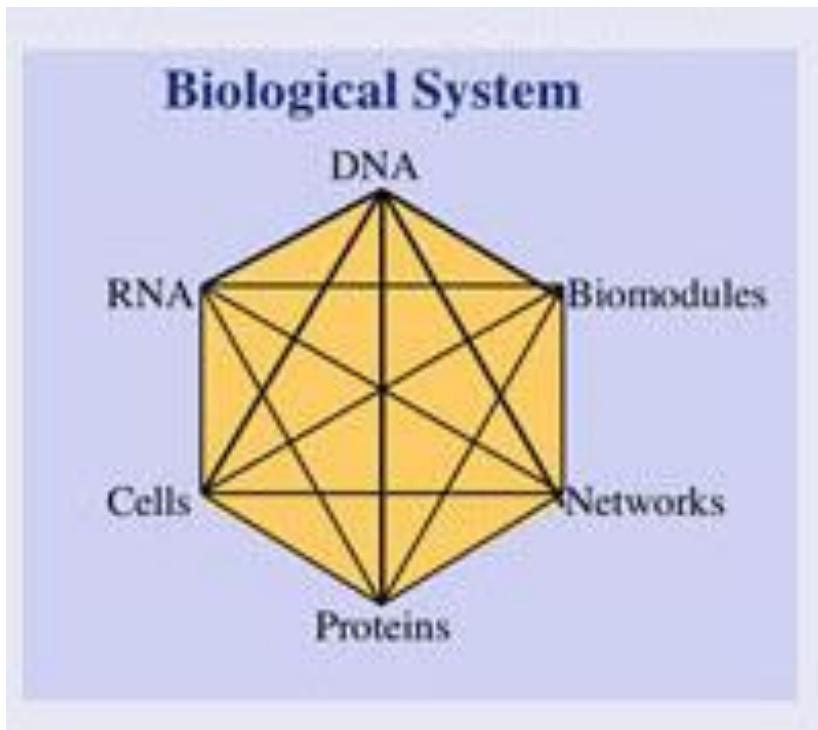
"a scientific **approach** that **combines** the principles of engineering, mathematics, physics, and computer science with extensive experimental data to develop **a quantitative as well as a deep conceptual understanding of biological phenomena**, permitting **prediction** and accurate simulation of **complex (emergent) biological behaviors**"

Ron Germain / Lab of Systems Biology - NIH

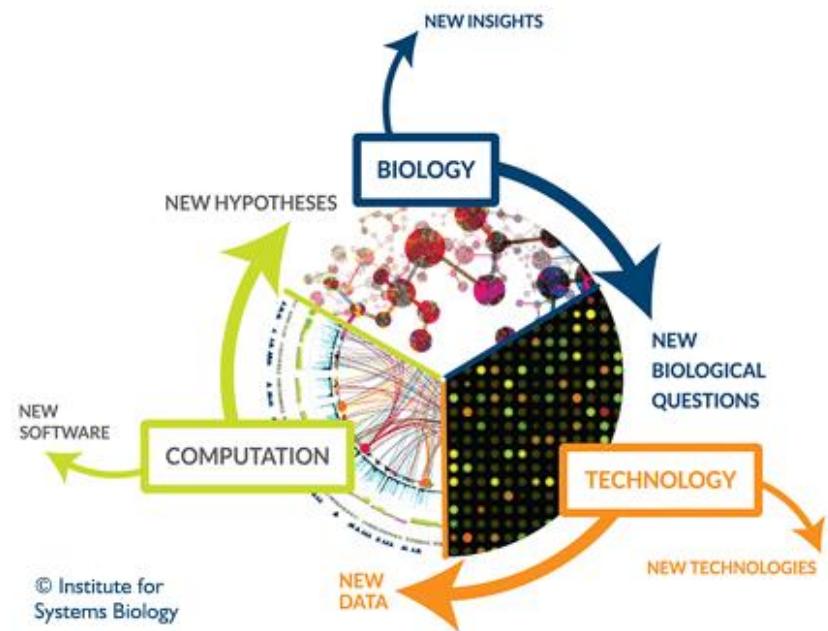
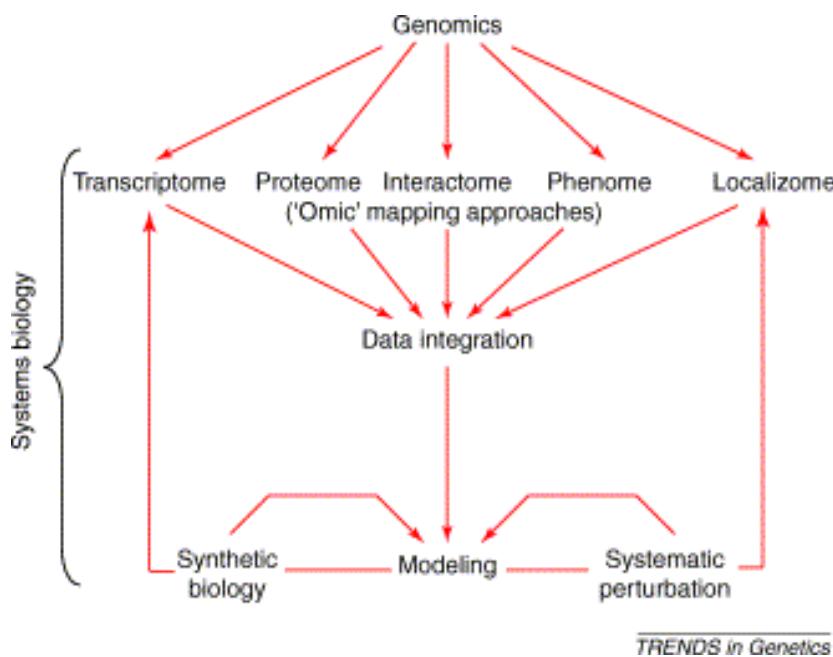


Volume 17 | Issue 19 | 27
Oct. 6, 2003, The Scientist

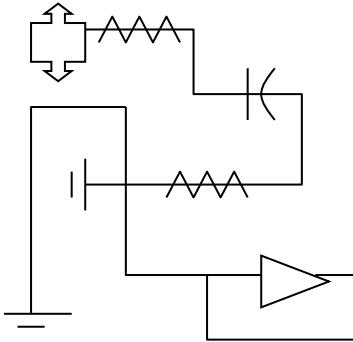
Biologia de Sistemas: integração de informações e abordagens múltiplas



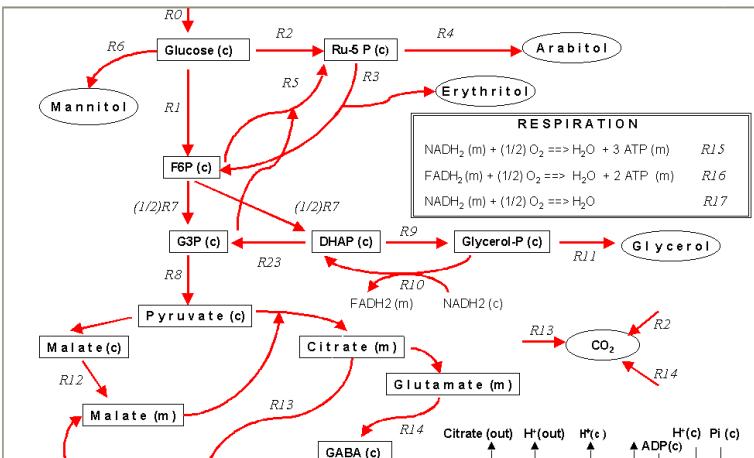
Integração, Modelagem, Simulação e Inferência



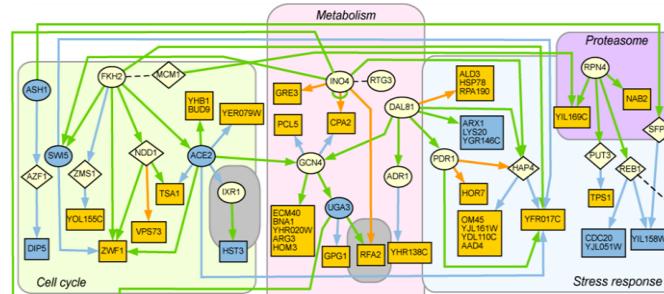
Each system has methods for modeling



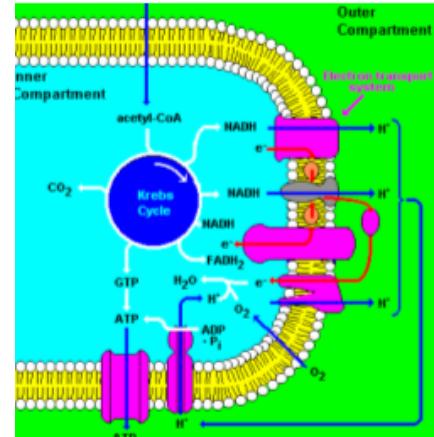
Electrical Circuit Model



Flux Balance Analysis



Networks



Differential Eqs

$$\frac{dx_1}{dt} = k_{11}x_1 + k_{21}x_2 + k_{31}x_3 + \dots$$

$$\frac{dx_2}{dt} = k_{12}x_1 + k_{22}x_2 + k_{32}x_3 + \dots$$

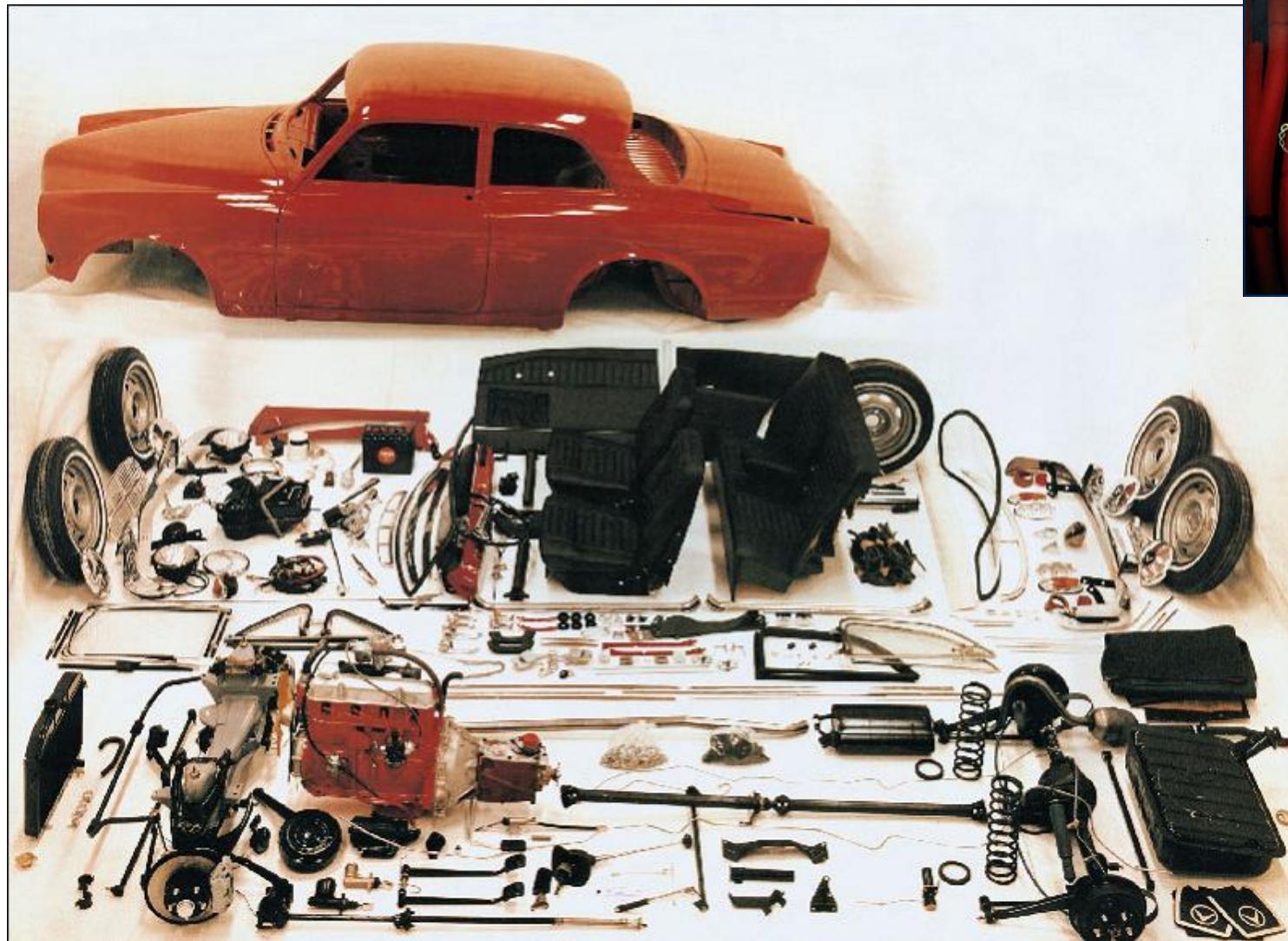
$$\frac{dx_3}{dt} = k_{13}x_1 + k_{23}x_2 + k_{33}x_3 + \dots$$

$$\frac{dx_4}{dt} = k_{14}x_1 + k_{24}x_2 + k_{34}x_3 + \dots$$

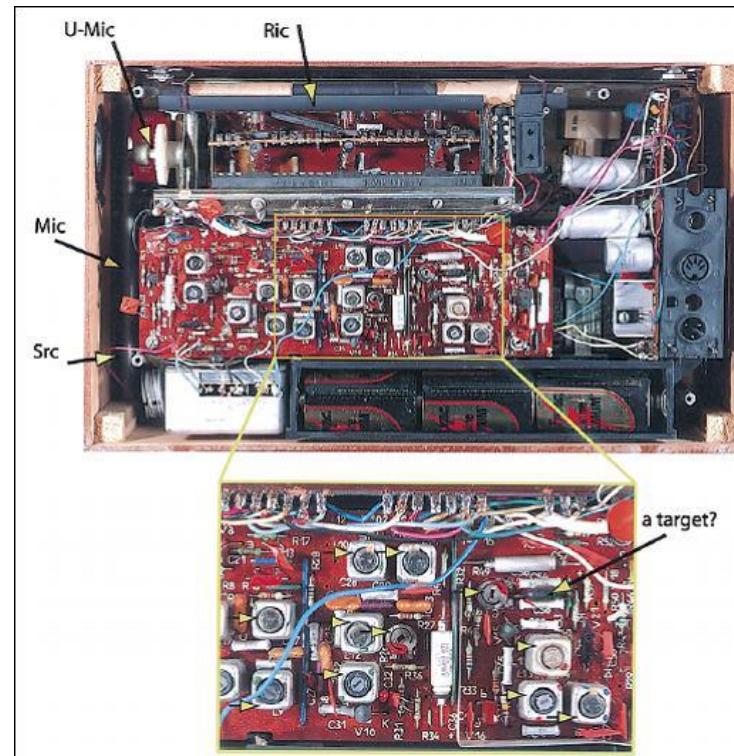
Por que Biología de Sistemas?

- On the technology side (**PUSH**): Capabilities for high-throughput data gathering that have made us aware that **biological systems have many more components than we previously surmised**.
- On the biology side (**PULL**): The realization that to the extent that we don't **characterize biological systems quantitatively** in their full complexity, the scope and accuracy of our understanding of those systems will be compromised.

Systems biology and emerging properties

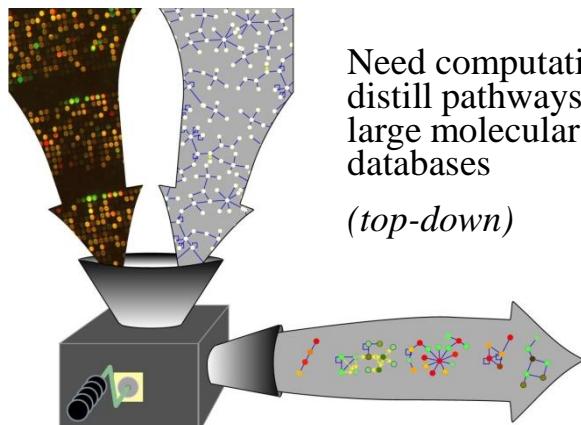
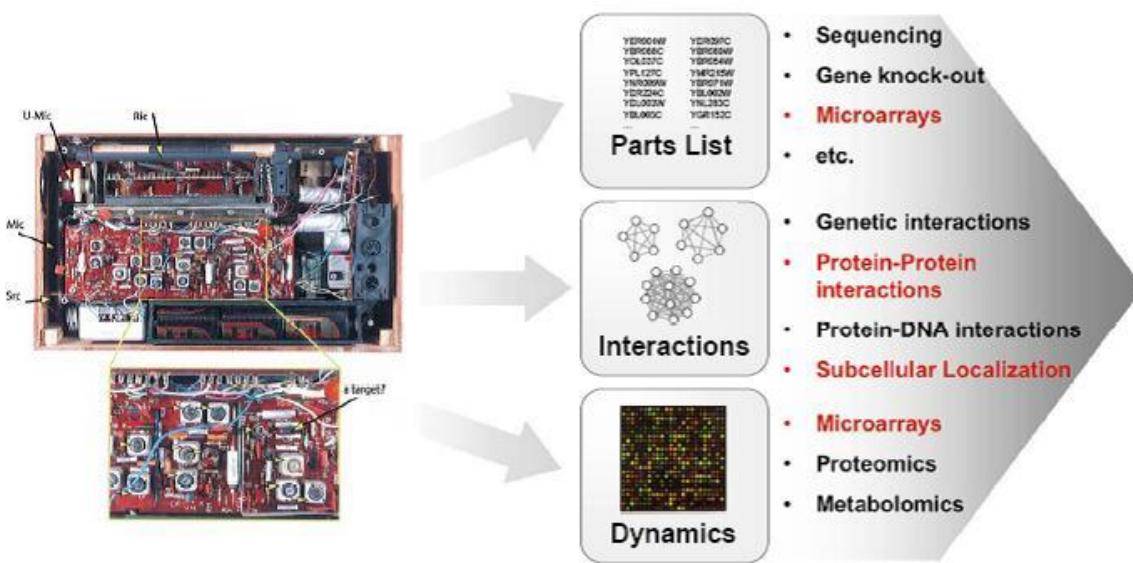


Can a biologist fix a radio?



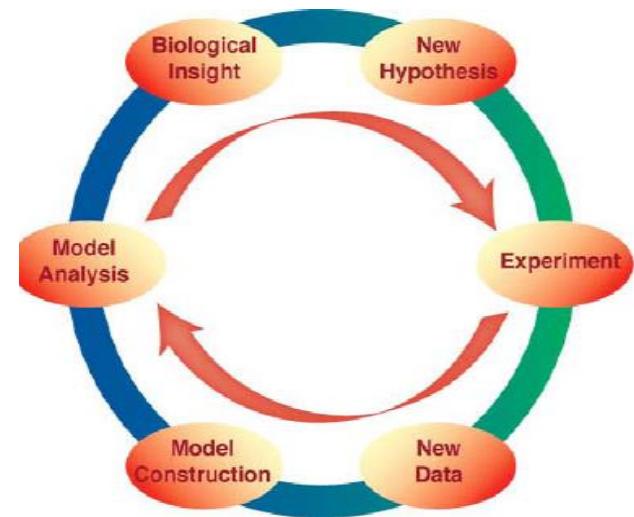
Lazebnik, Cancer Cell, 2002

Building models from parts lists

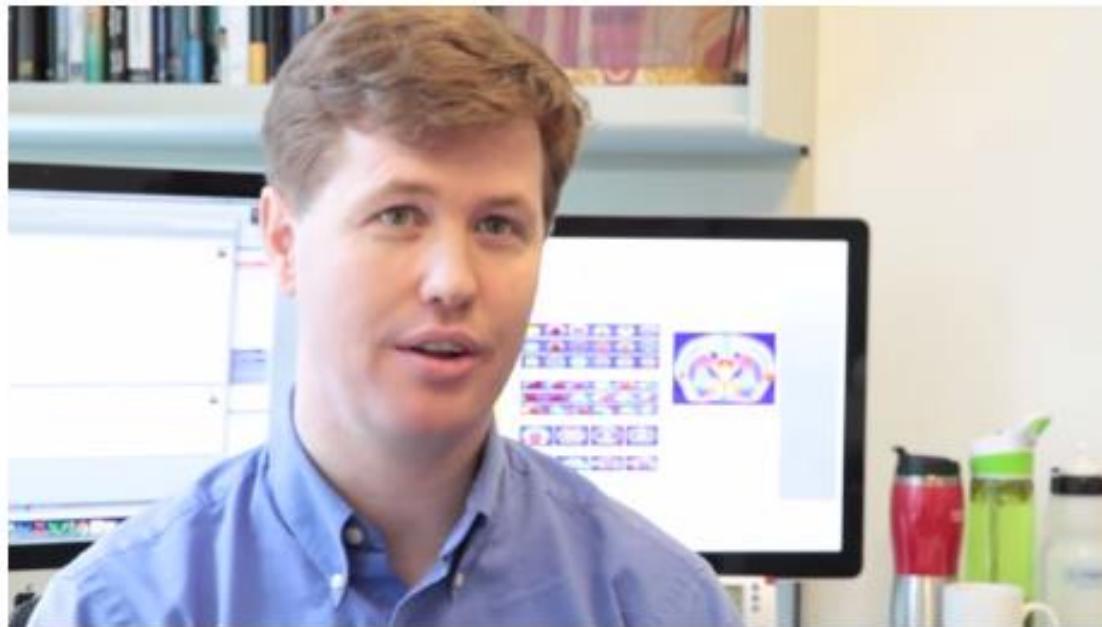


Need computational tools able to distill pathways of interest from large molecular interaction databases

(top-down)



Vídeo 1

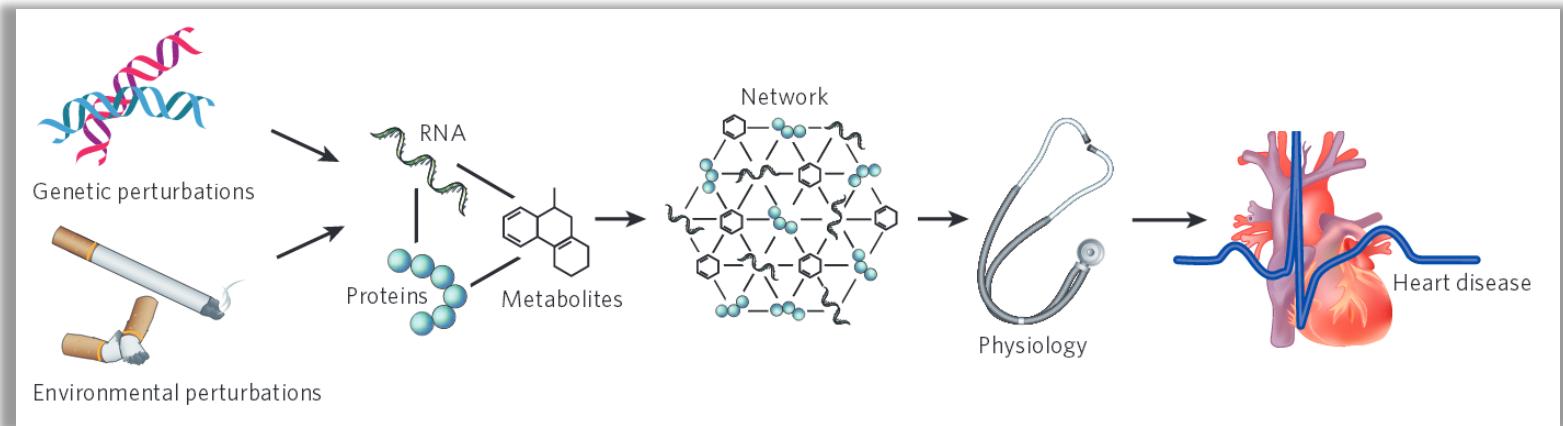


*Dr. Nathan Price, ISB Associate Director, explains systems biology. Watch on
[YouTube](#).*

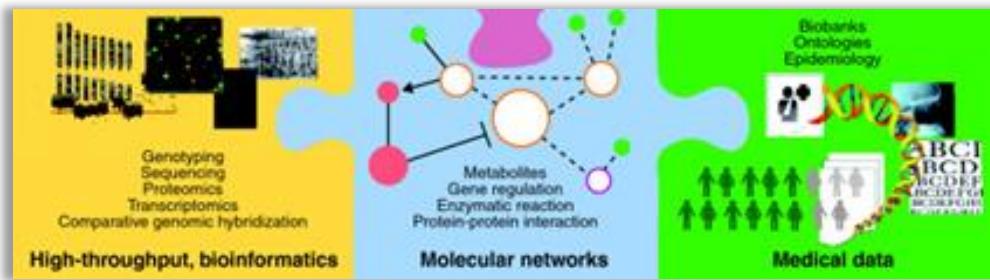
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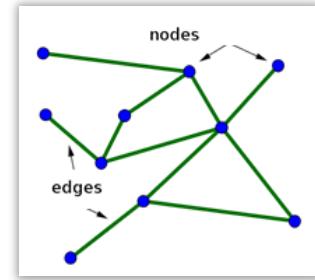
Molecular networks as sensors and drivers of human diseases



Data integration through molecular networks



Nodes and Edges



Barabási AL, et al. Network medicine: a network-based approach to human disease. *Nat Rev Genet*, 2011.

Baudot A et al. Translational disease interpretation with molecular networks. *Genome Biol*, 2009.

Schadt EE. Molecular networks as sensors and drivers of common human diseases. *Nature*, 2009.

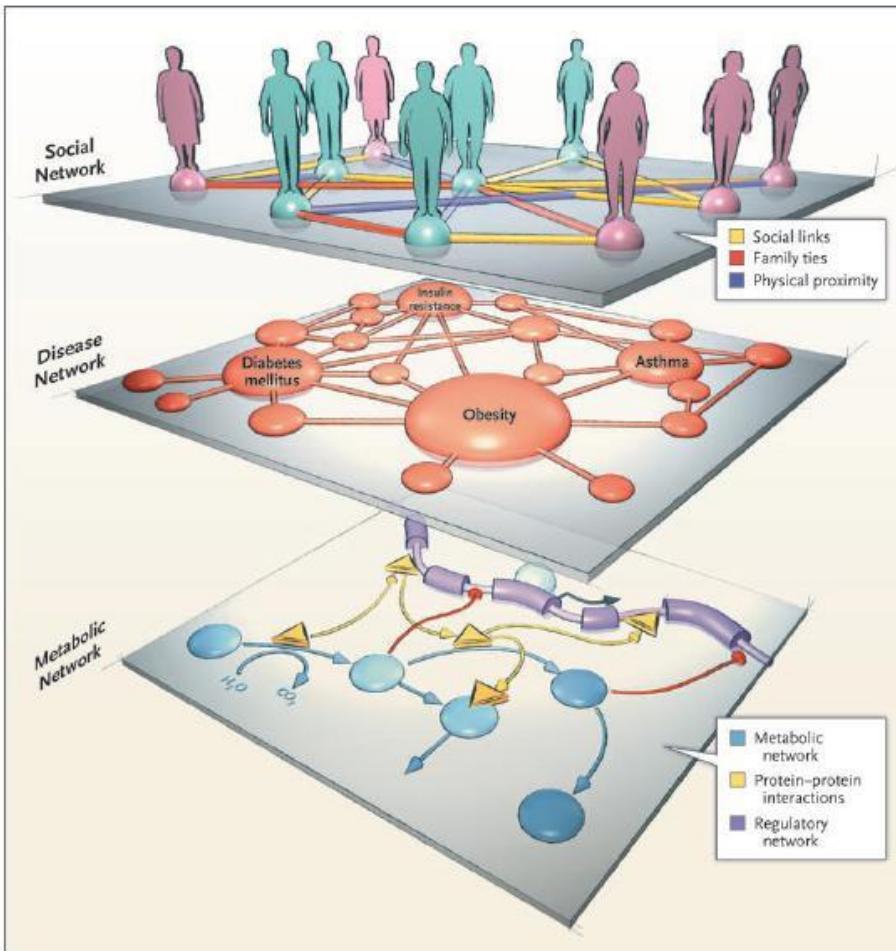
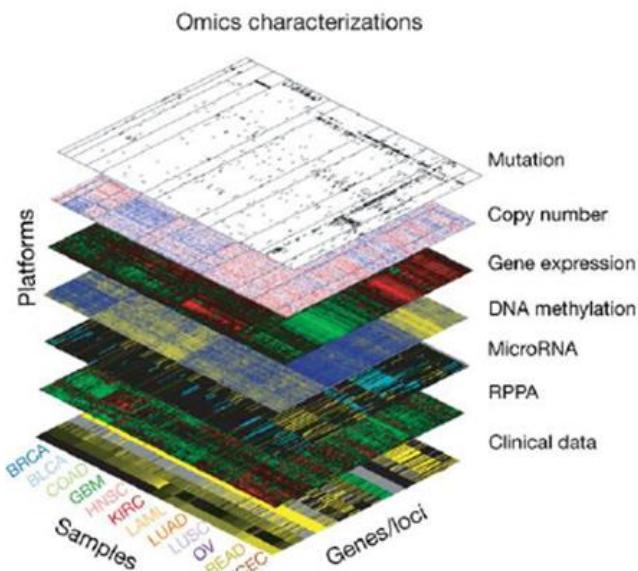
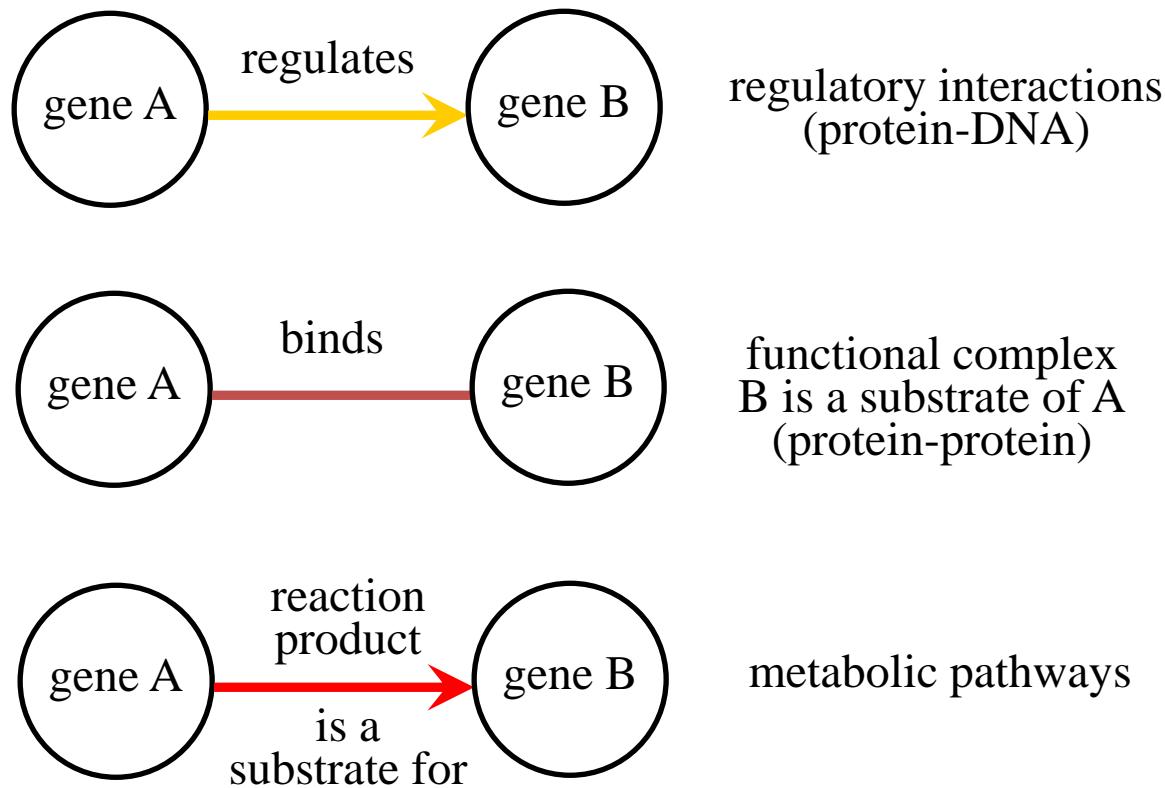


Figure 1. Complex Networks of Direct Relevance to Network Medicine.

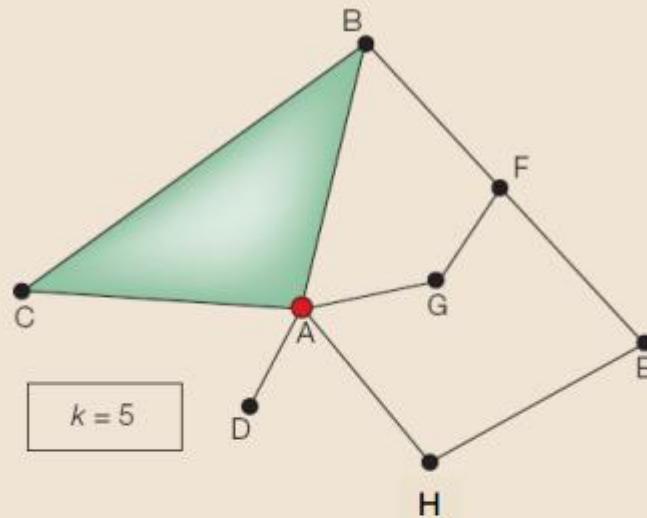
Although they are often treated separately, most human diseases are not independent of each other. Many diseases are associated with the breakdown of functional modules that are best described as subnetworks of a complex network connecting many cellular components. Therefore, an understanding of the functionally relevant genetic, regulatory, metabolic, and protein–protein interactions in a cellular network will play an important role in understanding the pathophysiology of human diseases (bottom layer). One way to visualize the ensuing potential interrelationships among human diseases is to construct a disease network (middle layer) in which two diseases are connected if they have a common genetic or functional origin. For example, on the basis of our current knowledge of disease genes, obesity is connected to at least seven other diseases such as diabetes, asthma, and insulin resistance, since genes associated with these diseases are known to affect obesity as well. The third network of key importance to human disease is the social network, which encompasses all human-to-human interactions (e.g., familial, friendship, sexual, and proximity-based contacts) that play a role in the spread of pathogens (top layer). These networks also have an important role in the spread of obesity. Efforts to understand the interactions between the cellular, disease, and social networks are part of network medicine, which aims to quantify the complex interlinked factors that may contribute to individual diseases.



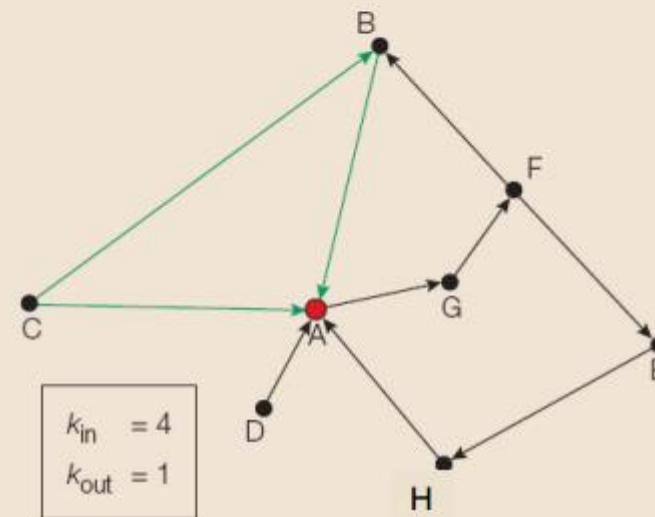
Relações entre nós



a Undirected network



b Directed network



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Topology of molecular interaction networks

BMC Systems Biology 2013, 7:90 doi:10.1186/1752-0509-7-90

Wynand Winterbach (w.winterbach@tudelft.nl)
Piet Van Mieghem (p.f.a.vanmieghem@tudelft.nl)
Marcel Reinders (m.j.t.reinders@tudelft.nl)
Huijuan Wang (h.wang@tudelft.nl)
Dick de Ridder (d.deridder@tudelft.nl)

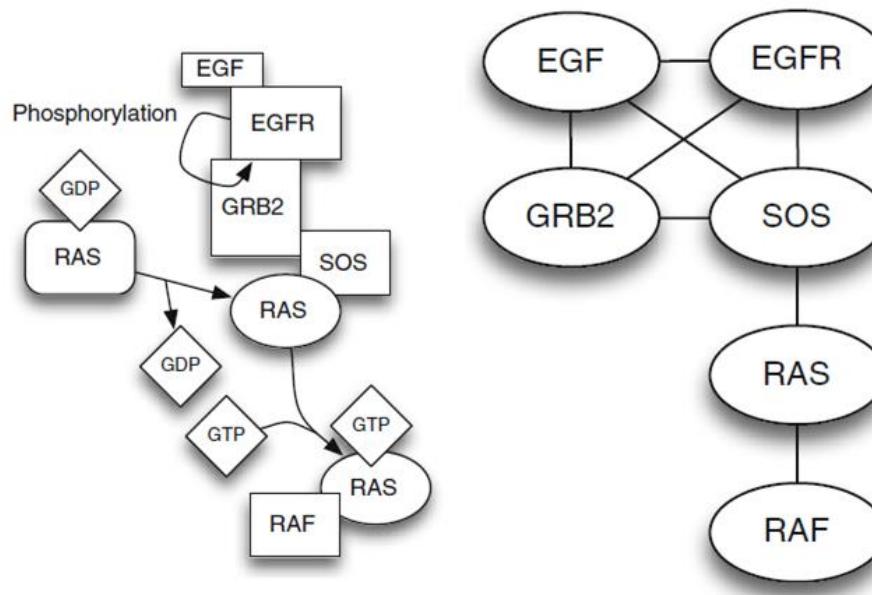


Figure 2 From biological models to networks. (a) Simple overview of molecular interactions in the cell. (b) Part of the MAPK/ERK pathway modeled as a network. (c) Homogenous protein interaction graph representation of part of the MAPK/ERK pathway.

Tipos de Redes

Cell

Leading Edge
Review

Interactome Networks and Human Disease

Marc Vidal,^{1,2,*} Michael E. Cusick,^{1,2} and Albert-László Barabási^{1,3,4,*}

¹Center for Cancer Systems Biology (CCSB) and Department of Cancer Biology, Dana-Farber Cancer Institute, Boston, MA 02215, USA

²Department of Genetics, Harvard Medical School, Boston, MA 02115, USA

³Center for Complex Network Research (CCNR) and Departments of Physics, Biology and Computer Science, Northeastern University, Boston, MA 02115, USA

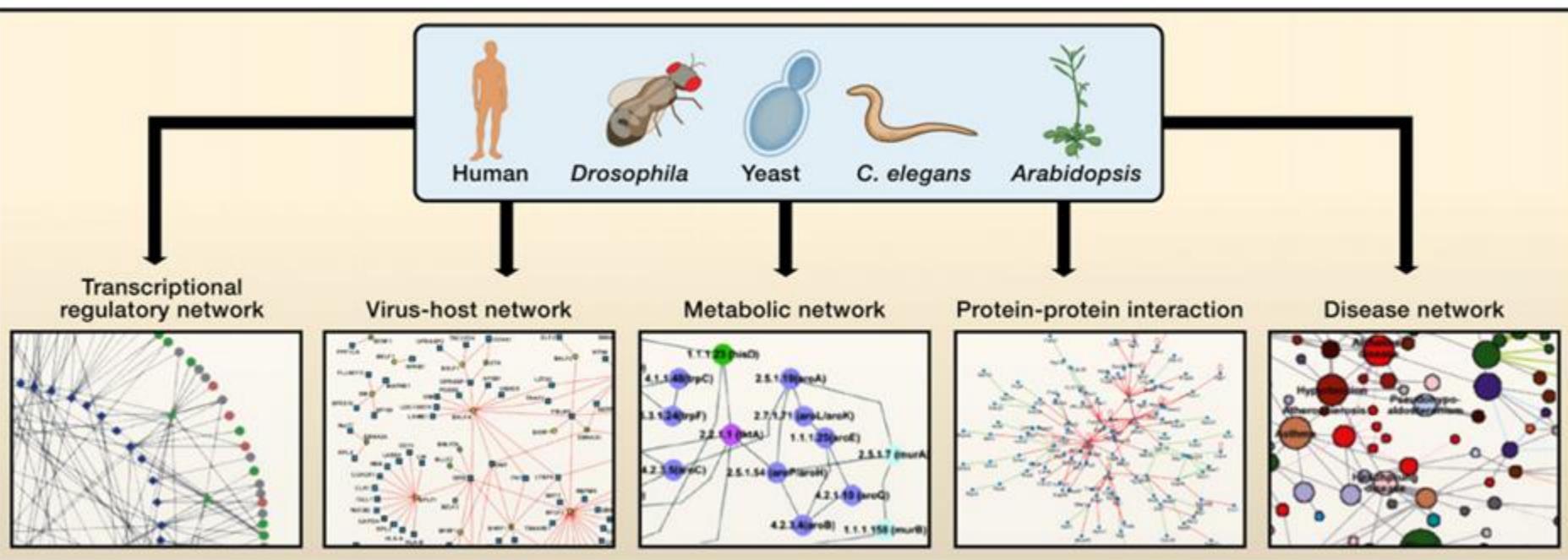
⁴Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA

*Correspondence: marc_vidal@dfci.harvard.edu (M.V.), alb@neu.edu (A.-L.B.)

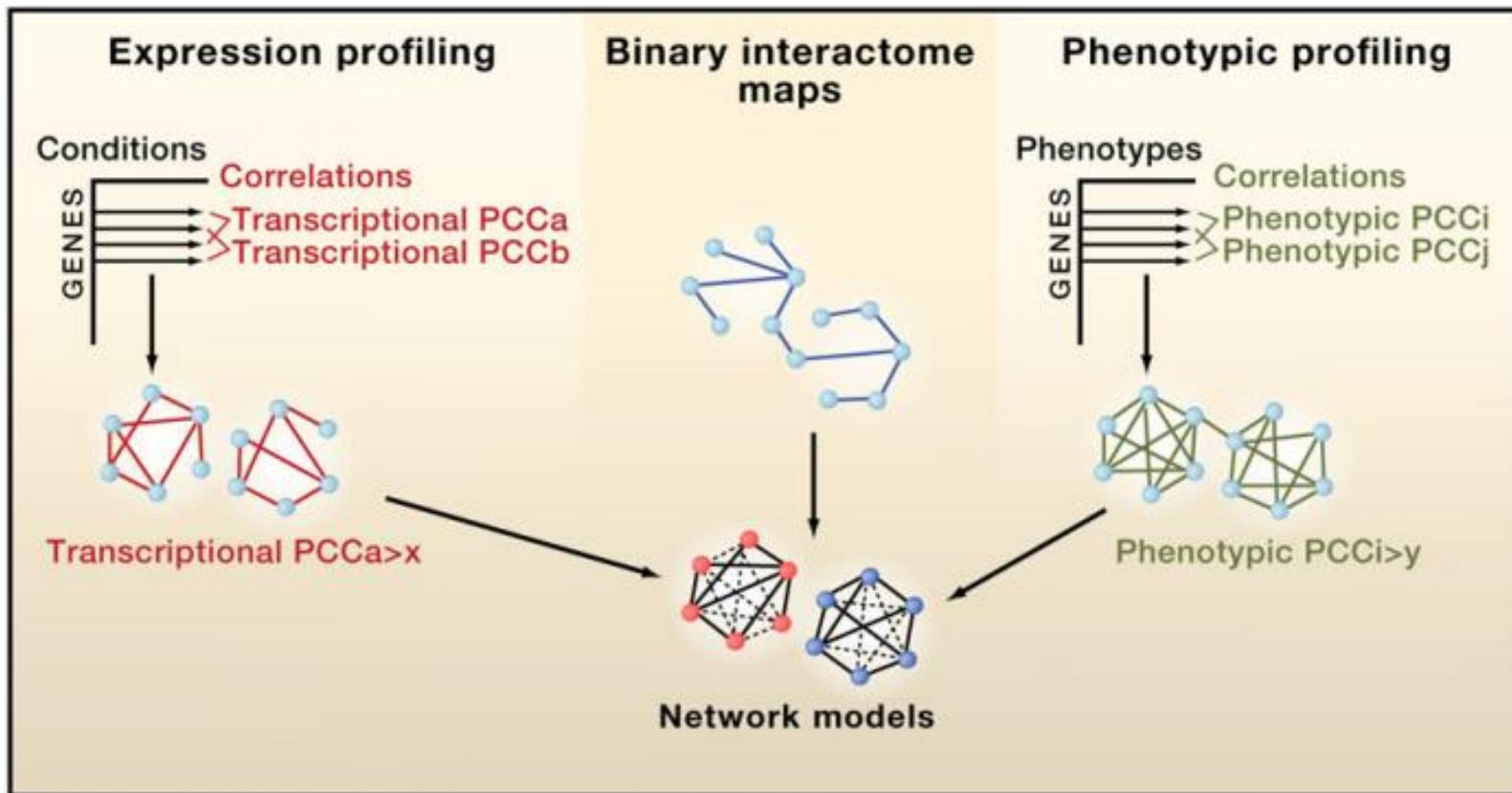
DOI 10.1016/j.cell.2011.02.016

Complex biological systems and cellular networks may underlie most genotype to phenotype relationships. Here, we review basic concepts in network biology, discussing different types of interactome networks and the insights that can come from analyzing them. We elaborate on why interactome networks are important to consider in biology, how they can be mapped and integrated with each other, what global properties are starting to emerge from interactome network models, and how these properties may relate to human disease.

Tipos de Redes



Tipos de Redes



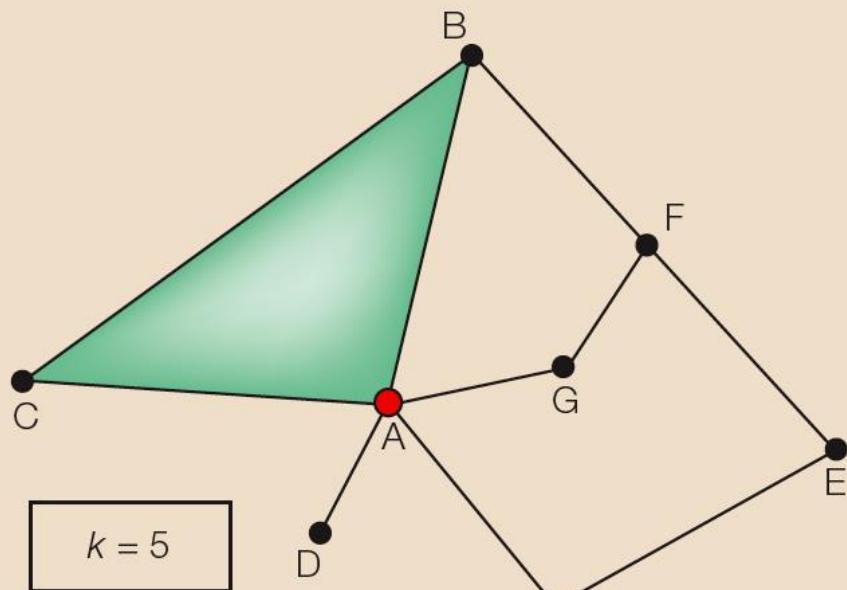
MEDIDAS EM REDES BIOLÓGICAS

Medidas em redes

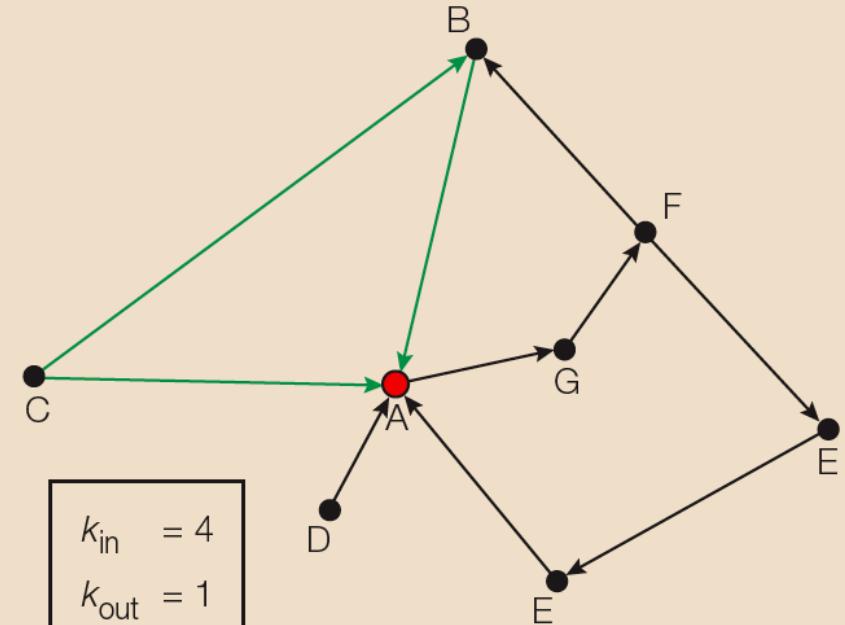
- Degree k_i
- Shortest or Average path length
- Betweenness
- Network Diameter
- Clustering Coefficient

Network Measures: Degree

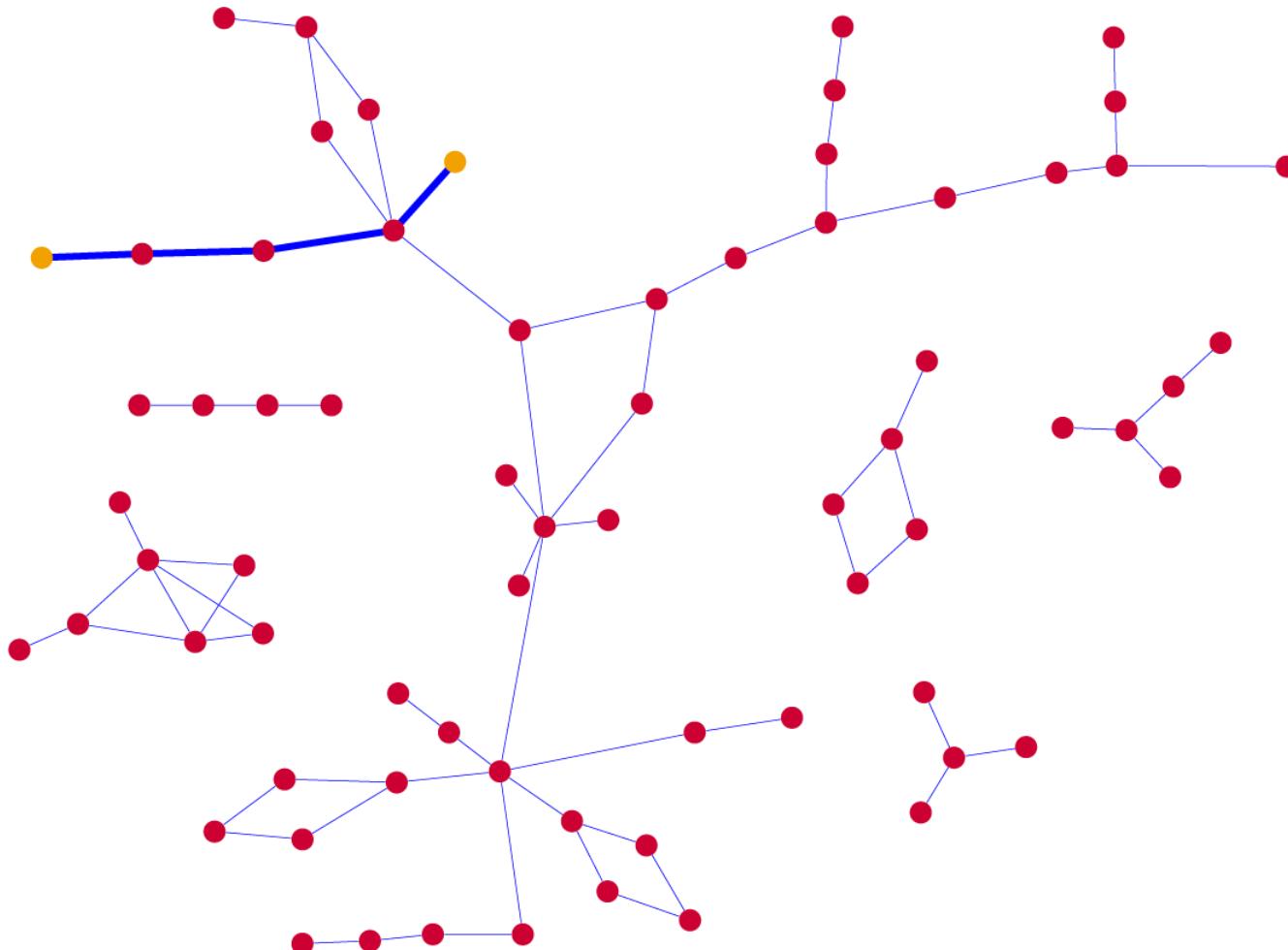
a Undirected network



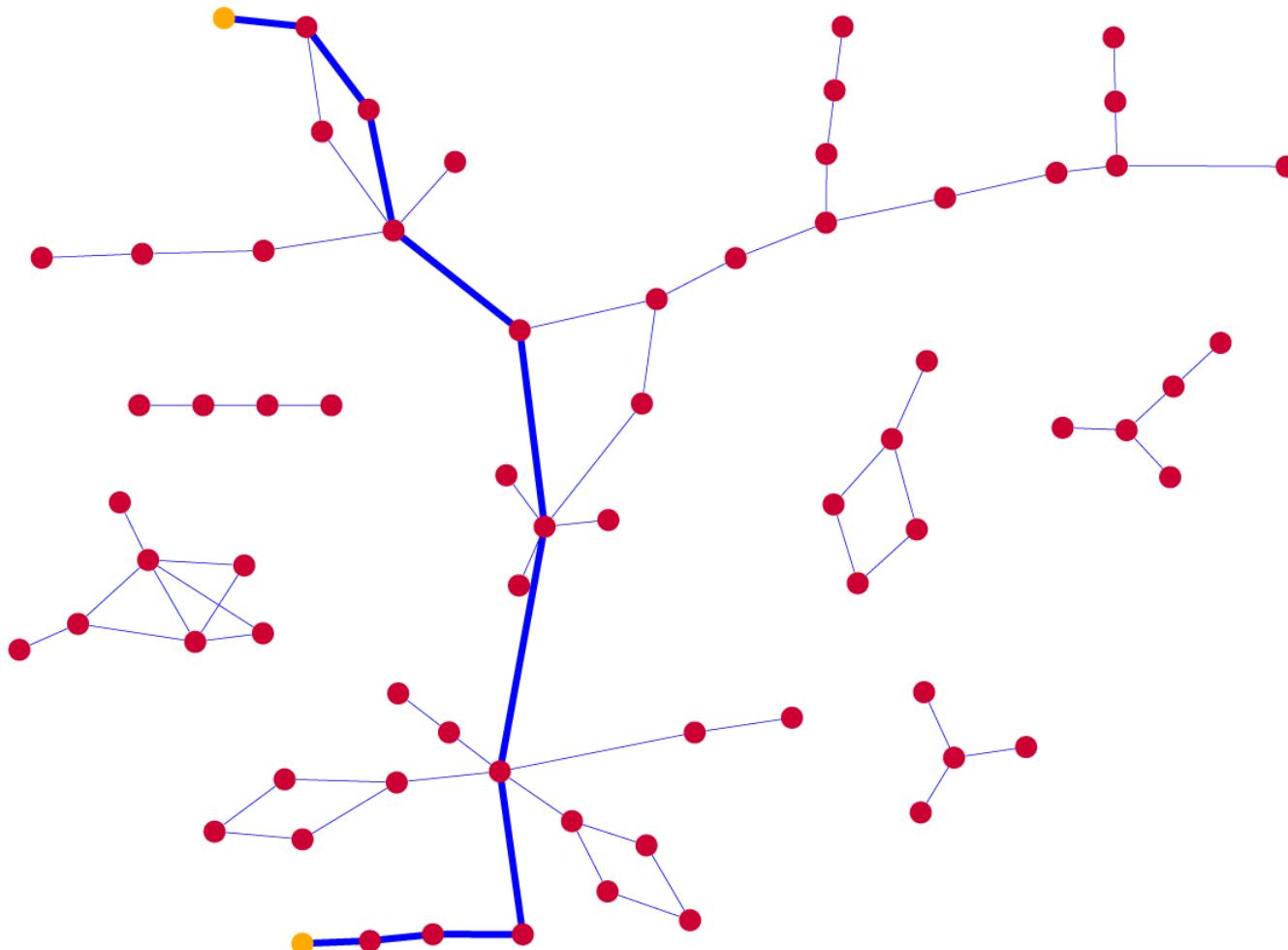
b Directed network



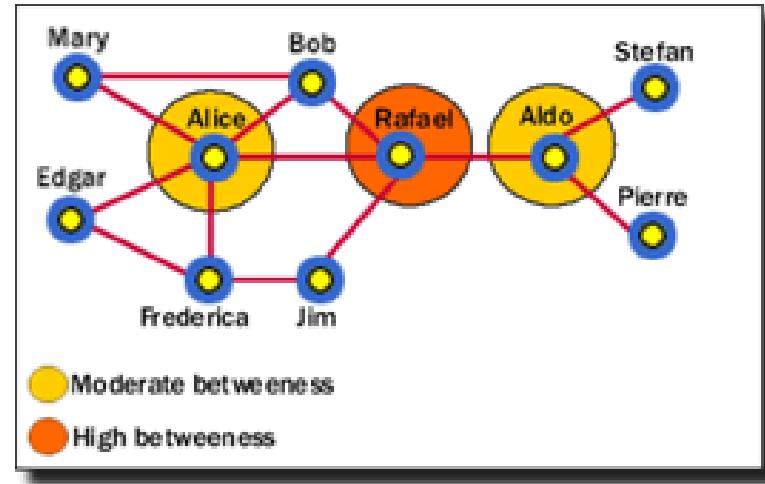
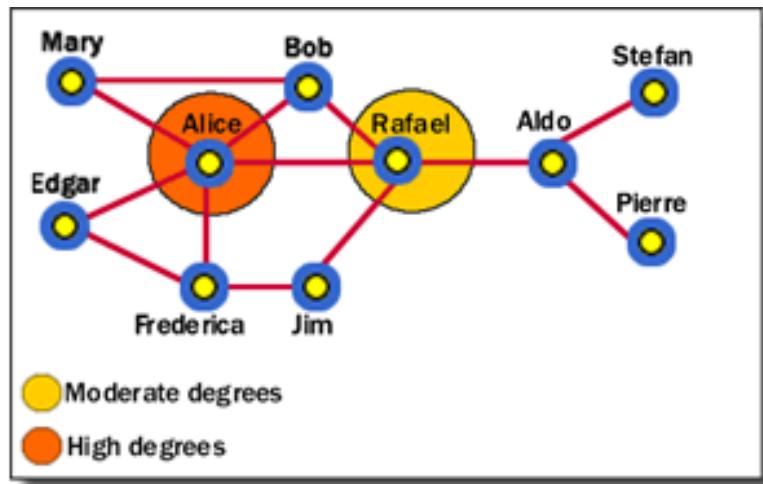
Shortest-Path between nodes



Shortest-Path between nodes



Degree x Betweenness



PROPRIEDADES DAS REDES BIOLÓGICAS

1. Redes biológicas apresentam organização topológica

NETWORK BIOLOGY: UNDERSTANDING THE CELL'S FUNCTIONAL ORGANIZATION

*Albert-László Barabási** & *Zoltán N. Oltvai[†]*

A key aim of postgenomic biomedical research is to systematically catalogue all molecules and their interactions within a living cell. There is a clear need to understand how these molecules and the interactions between them determine the function of this enormously complex machinery, both in isolation and when surrounded by other cells. Rapid advances in network biology indicate that cellular networks are governed by universal laws and offer a new conceptual framework that could potentially revolutionize our view of biology and disease pathologies in the twenty-first century.

Konigsberg Bridge Problem

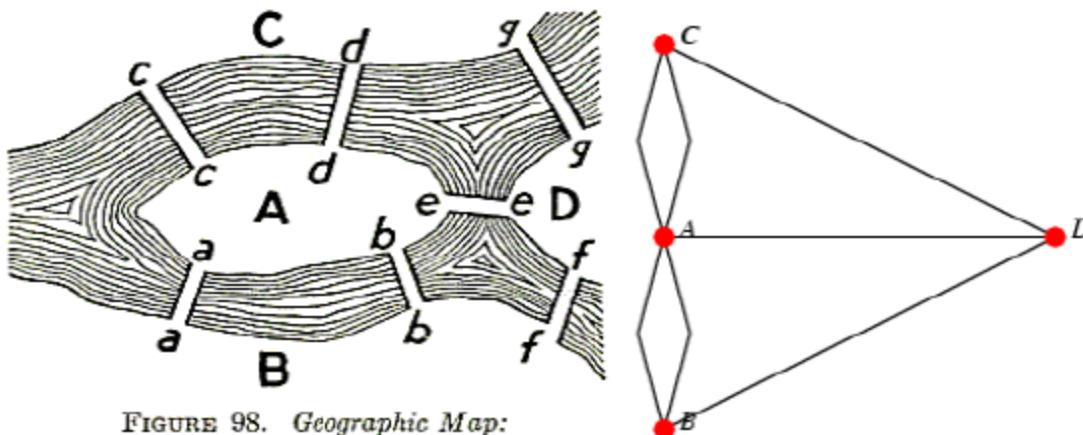


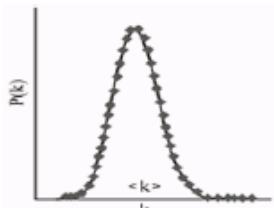
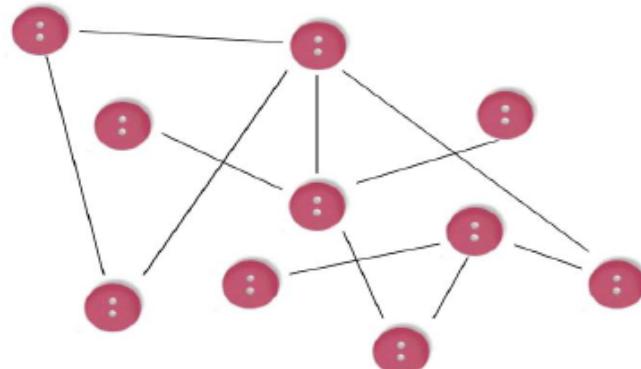
FIGURE 98. *Geographic Map:
The Königsberg Bridges.*

The Königsberg bridge problem asks if the seven bridges of the city of Königsberg (left figure; Kraitchik 1942), formerly in Germany but now known as Kaliningrad and part of Russia, over the river Preger can all be traversed in a single trip without doubling back, with the additional requirement that the trip ends in the same place it began. This is equivalent to asking if the [multigraph](#) on four nodes and seven edges (right figure) has an [Eulerian circuit](#). This problem was answered in the negative by Euler (1736), and represented the beginning of [graph theory](#).



<http://mathworld.wolfram.com/KoenigsbergBridgeProblem.html>

Erdos-Renyi Random Networks



P. Erdos A. Rényi. Publ. Math.
(Debrecen) 6, 290-297 (1959)



In the 1960's Paul Erdos and Alfred Renyi studied the properties of random graphs.

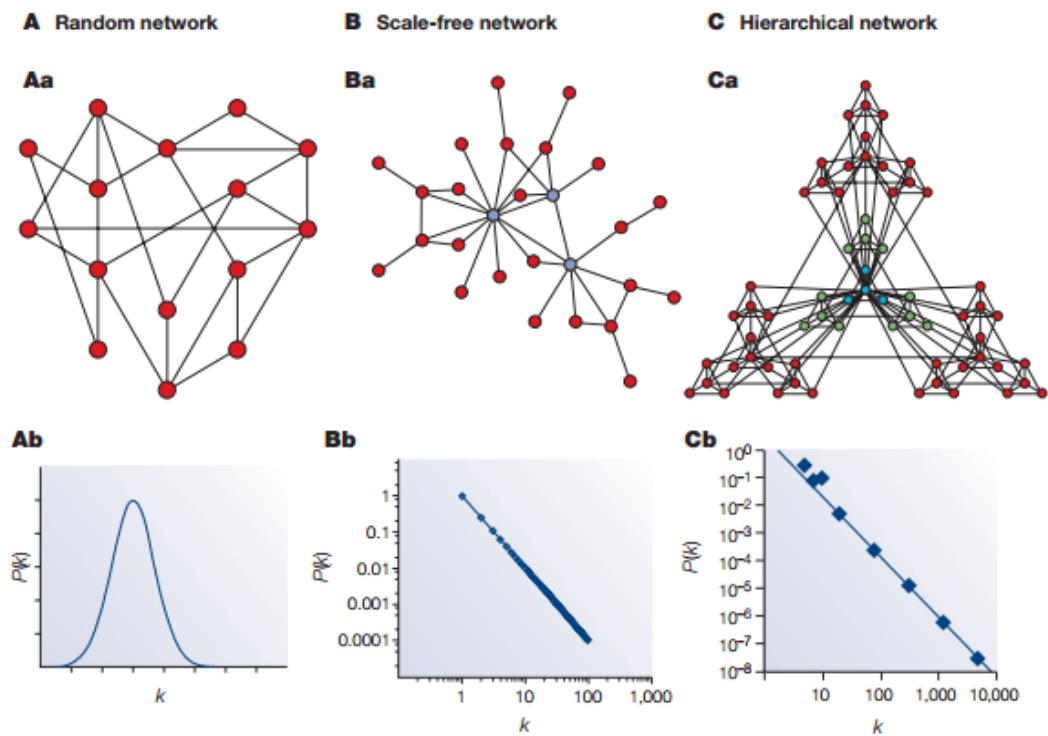
What are the mathematical consequences of throwing on the floor a random number of buttons and randomly connecting them with a random number of links?

Modelos de Evolução de Redes

**Lei de potência¹ x
Distribuição gaussiana²**

1. Eventos raros de grande magnitude ocorrem em paralelo a eventos frequentes de baixa magnitude

2. A partir da média, a causa é exponencialmente declinante, mantendo os valores em um intervalo determinado e relativamente pequeno



For real networks the distribution is often a power-law: $\mathbf{P(k) \sim k^{-\gamma}}$
Such networks are said to be **scale-free**

Princípios que geram a lei de potência em redes livre de escala

- Crescimento (duplication-divergence) e conexão preferencial (*rich get richer*)



chevy



mazda



toyota



nissan



browser wars



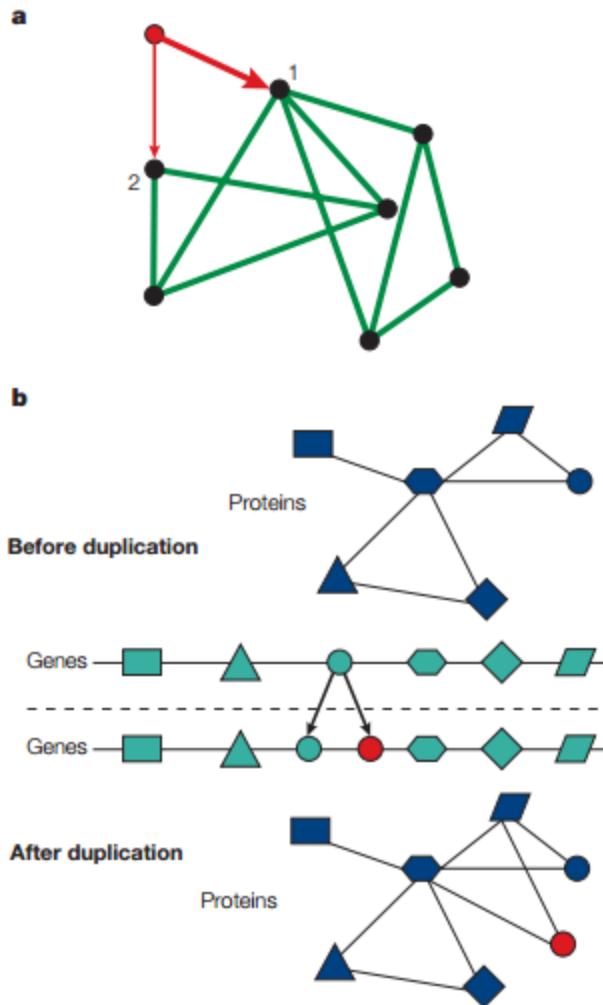
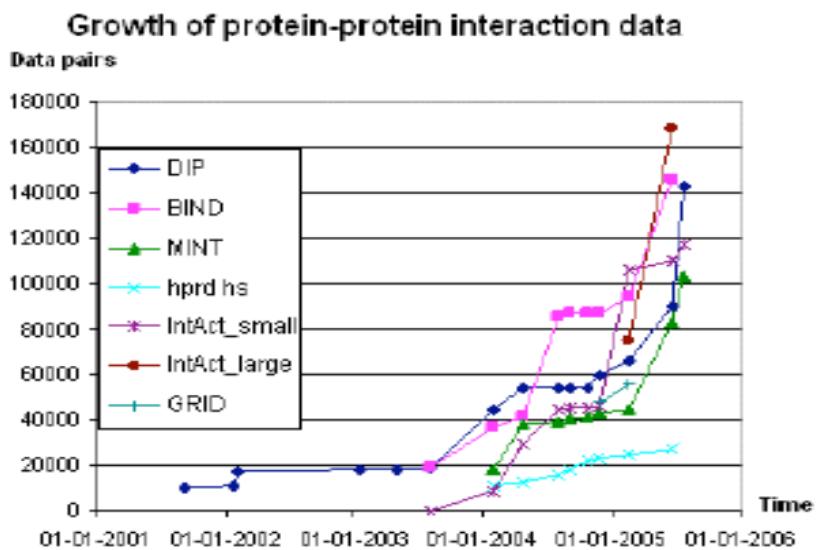
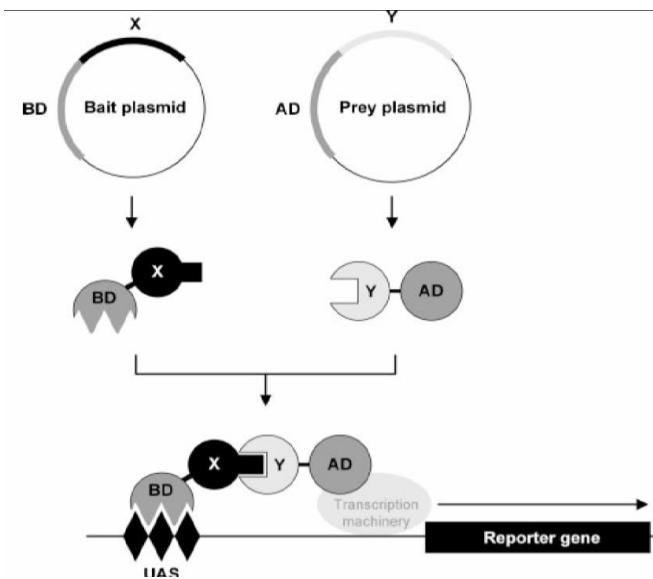


Figure 3 | The origin of the scale-free topology and hubs in biological networks.

2. Redes possuem nós que são mais relevantes para sua organização

Yeast Protein Interaction Network

Yeast two-hybrid method



HUBS: The most highly connected proteins in the cell are the most important for its survival



In yeast, only ~20% of proteins are lethal when deleted, and are 5 times more likely to have degree $k>15$ than $k<5$.

The largest cluster, which contains ~78% of all proteins, is shown.

The colour of a node indicates the phenotypic effect of removing the corresponding protein

(red = lethal, green = non-lethal, orange = slow growth, yellow = unknown).

Jeong et al. *Lethality and centrality in protein networks*. Nature 411, 41-42 (2001)

Barabasi & Oltvai, Nature Reviews, 2004

Date and Party Hubs

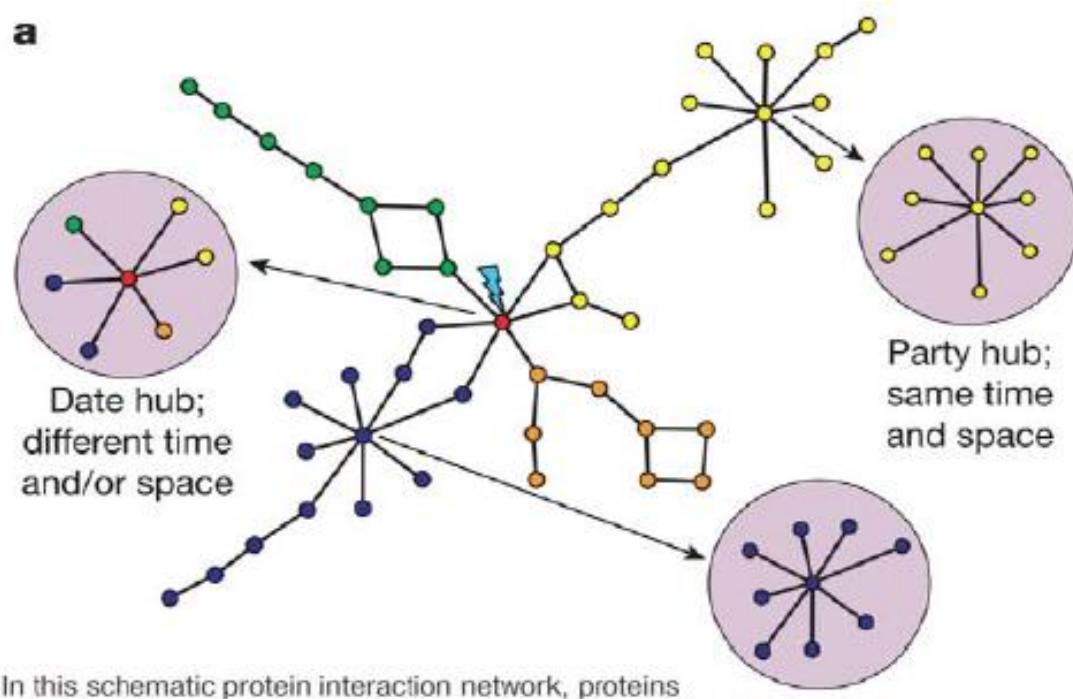
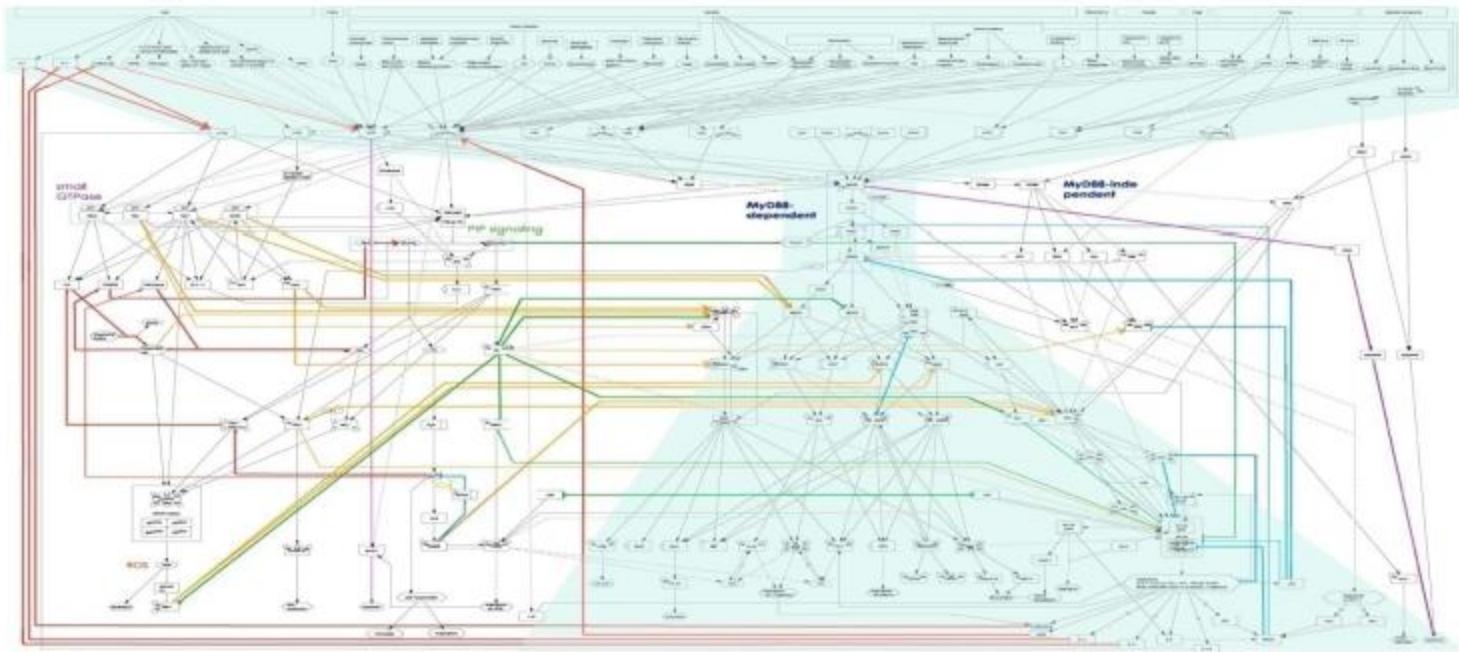


Figure 1 Date and party hubs. **a**, In this schematic protein interaction network, proteins are coloured according to mutual similarity in their mRNA expression patterns. 'Party' hubs are highly correlated in expression with their partners, and presumably interact with them at similar times. The partners of 'date' hubs exhibit more limited co-expression, and presumably the corresponding physical interactions occur at different times and/or different locations.

Bow-Tie Structure of Signaling Networks



Oda and Kitano. Molecular Systems Biology 2:2006.0015 (2006)

3. Redes biológicas possuem organização modular

BMC Systems Biology



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Topology of molecular interaction networks

BMC Systems Biology 2013, **7**:90 doi:10.1186/1752-0509-7-90

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Marcel Reinders (m.j.t.reinders@tudelft.nl)

Huijuan Wang (h.wang@tudelft.nl)

Dick de Ridder (d.deridder@tudelft.nl)

Redes e Módulos Funcionais

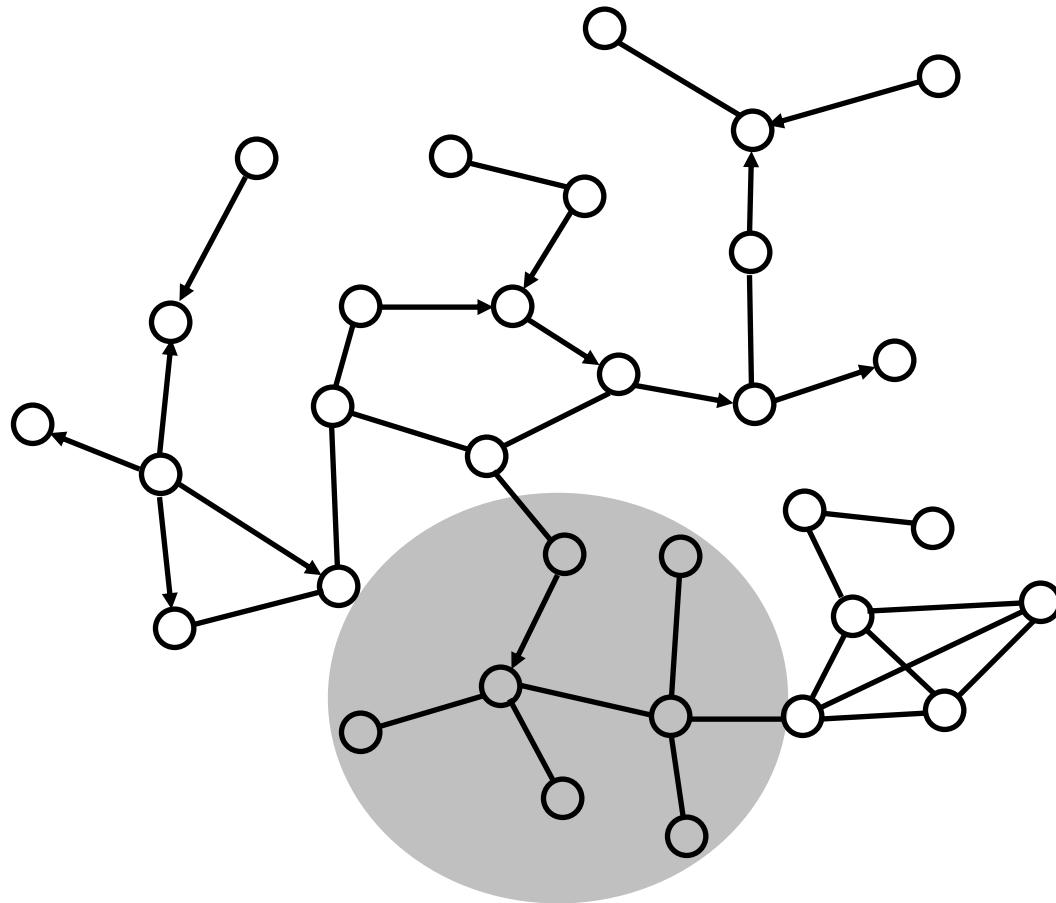


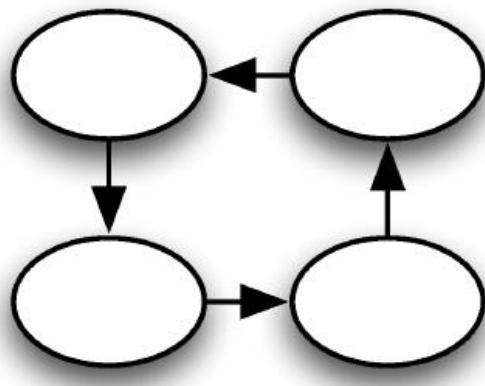
Table 4 Modules, motifs and graphlets: concepts for decomposing networks into smaller units

Network decomposition	Decomposition description
Modules	are induced subgraphs whose link density is high in comparison to the rest of the graph. This definition is deliberately vague, as what constitutes a module depends on the context and the algorithm used to discover modules.
Motifs	are small subgraphs, usually of 3 or 4 nodes, whose over- or underrepresentation may indicate that their structures are important or detrimental to the system [21]. Usually, all distinct motifs in a network are counted, yielding a motif signature for the network that may then be compared to signatures obtained by sampling from an appropriate random network null model (see Table 3) to determine over- or underrepresentation. A signature for all motifs on 3 nodes is shown in Figure 1d. Motif signatures can be used to characterize networks.
Graphlets	are similar to motifs but always fully connected. As with motifs, graphlets are used to construct signatures that capture the local characteristics of a network [56].

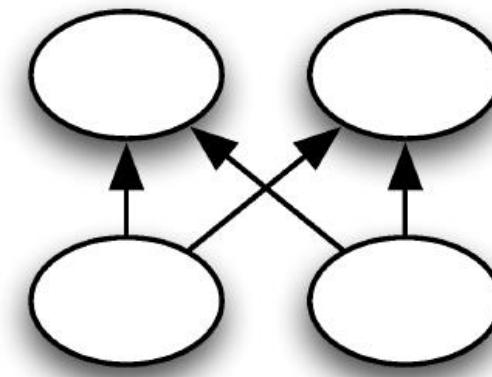
Graphlets: motifs in undirected networks

Principais motivos

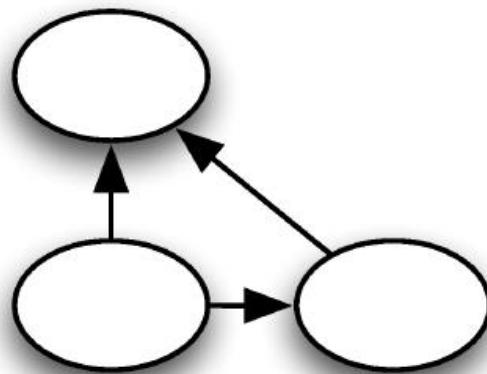
Feed-back loops



Bi-fan



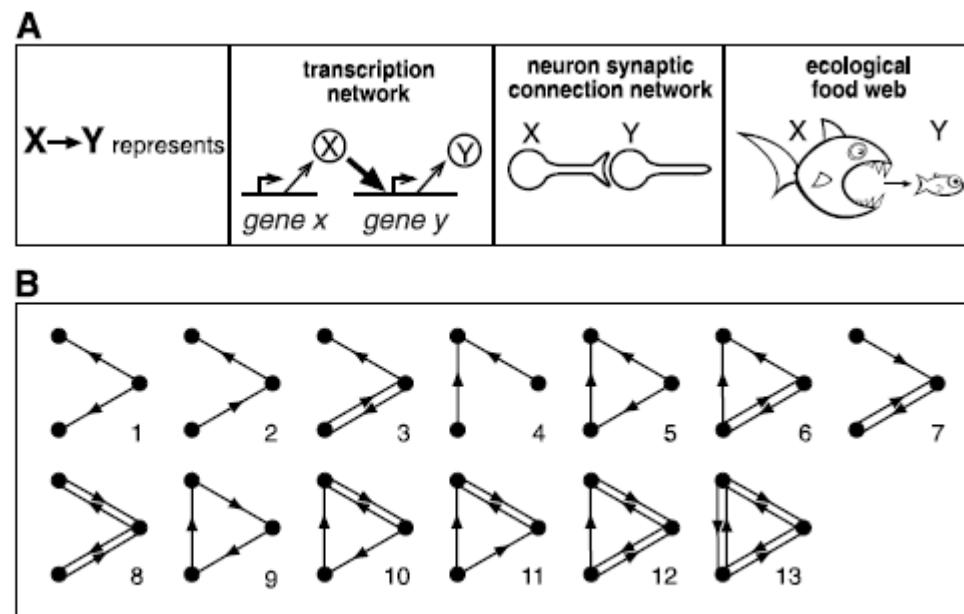
Feed-forward loops



Network Motifs: Simple Building Blocks of Complex Networks

R. Milo,¹ S. Shen-Orr,¹ S. Itzkovitz,¹ N. Kashtan,¹ D. Chklovskii,²
U. Alon^{1*}

Fig. 1. (A) Examples of interactions represented by directed edges between nodes in some of the networks used for the present study. These networks go from the scale of biomolecules (transcription factor protein X binds regulatory DNA regions of a gene to regulate the production rate of protein Y), through cells (neuron X is synaptically connected to neuron Y), to organisms (X feeds on Y). (B) All 13 types of three-node connected subgraphs.



Motivos mais frequentes em redes biológicas: Bifans e Feed-forward

Network	Nodes	Edges	N_{real}	$N_{\text{rand}} \pm \text{SD}$	Z score	N_{real}	$N_{\text{rand}} \pm \text{SD}$	Z score	N_{real}	$N_{\text{rand}} \pm \text{SD}$	Z score
Gene regulation (transcription)				Feed-forward loop			Bi-fan				
<i>E. coli</i>	424	519	40	7 ± 3	10	203	47 ± 12	13			
<i>S. cerevisiae*</i>	685	1,052	70	11 ± 4	14	1812	300 ± 40	41			
Neurons				Feed-forward loop			Bi-fan		Bi-parallel		
<i>C. elegans†</i>	252	509	125	90 ± 10	3.7	127	55 ± 13	5.3	227	35 ± 10	20
Food webs				Three chain			Bi-parallel				
Little Rock	92	984	3219	3120 ± 50	2.1	7295	2220 ± 210	25			
Ythan	83	391	1182	1020 ± 20	7.2	1357	230 ± 50	23			
St. Martin	42	205	469	450 ± 10	NS	382	130 ± 20	12			
Chesapeake	31	67	80	82 ± 4	NS	26	5 ± 2	8			
Coachella	29	243	279	235 ± 12	3.6	181	80 ± 20	5			
Skipwith	25	189	184	150 ± 7	5.5	397	80 ± 25	13			
B. Brook	25	104	181	130 ± 7	7.4	267	30 ± 7	32			

4. Os nós em redes biológicas estão próximos (*small-worldness*)

Watts and Strogatz model

Random graph model with small-world properties, including short average path lengths and high clustering

Collective dynamics of ‘small-world’ networks

Duncan J. Watts* & Steven H. Strogatz

Department of Theoretical and Applied Mechanics, Kimball Hall,
Cornell University, Ithaca, New York 14853, USA

Nature ,1998

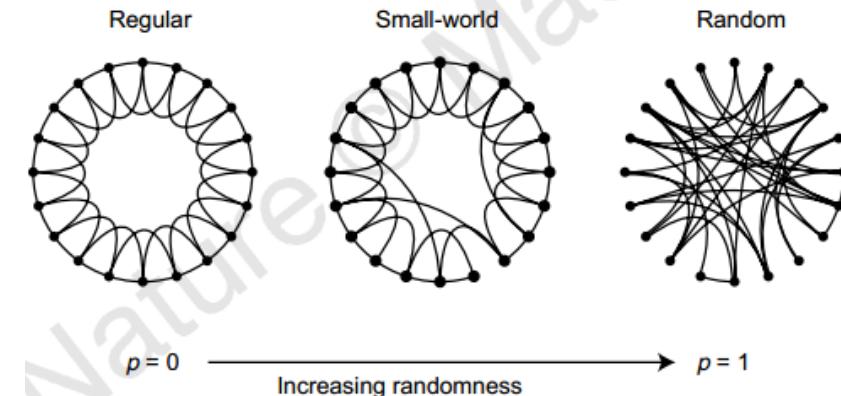
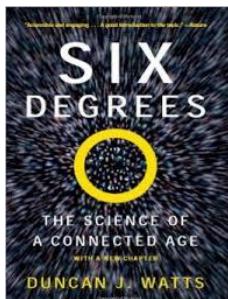


Table 1 Empirical examples of small-world networks

	L_{actual}	L_{random}	C_{actual}	C_{random}
Film actors	3.65	2.99	0.79	0.00027
Power grid	18.7	12.4	0.080	0.005
<i>C. elegans</i>	2.65	2.25	0.28	0.05

Characteristic path length L and clustering coefficient C for three real networks, compared to random graphs with the same number of vertices (n) and average number of edges per vertex (k). (Actors: $n = 225,226, k = 61$. Power grid: $n = 4,941, k = 2.67$. *C. elegans*: $n = 282, k = 14$.) The graphs are defined as follows. Two actors are joined by an edge if they have acted in a film together. We restrict attention to the giant connected component¹⁶ of this graph, which includes ~90% of all actors listed in the Internet Movie Database (available at

Agenda

1. Biologia de Sistemas
2. Análise de Redes Complexas
- 3. Exemplos de Estudos de Análises de Redes Biológicas**
4. Experiências do Laboratório em Análises de Redes

Hubs of brain functional networks are radically reorganized in comatose patients

Sophie Achard^{a,1}, Chantal Delon-Martin^{b,c}, Petra E. Vértes^d, Félix Renard^a, Maleka Schenck^e, Francis Schneider^e, Christian Heinrich^f, Stéphane Kremer^g, and Edward T. Bullmore^{d,h,i}

^aCentre National de la Recherche Scientifique, Grenoble Image Parole Signal Automatique, 38402 Grenoble, France; ^bInstitut National de la Santé et de la Recherche Médicale, U836, BP 170, F-38042 Grenoble Cedex 9, France; ^cUniversité Joseph Fourier, Grenoble Institut des Neurosciences, BP 170, F-38042 Grenoble Cedex 9, France; ^dBehavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge CB2 0SZ, United Kingdom; ^eService de Réanimation Médicale, Hôpital de Hautepierre, Centre Hospitalier Universitaire de Strasbourg, Université de Strasbourg, 67098 Strasbourg, France; ^fLaboratoire des Sciences et de l'Image, de l'Informatique et de la Télédétection, Université de Strasbourg, 67412 Illkirch, France; ^gService de Radiologie 2, Hôpital de Hautepierre, Centre Hospitalier Universitaire de Strasbourg, Université de Strasbourg, 67098 Strasbourg, France; ^hCambridgeshire and

RMN funcional

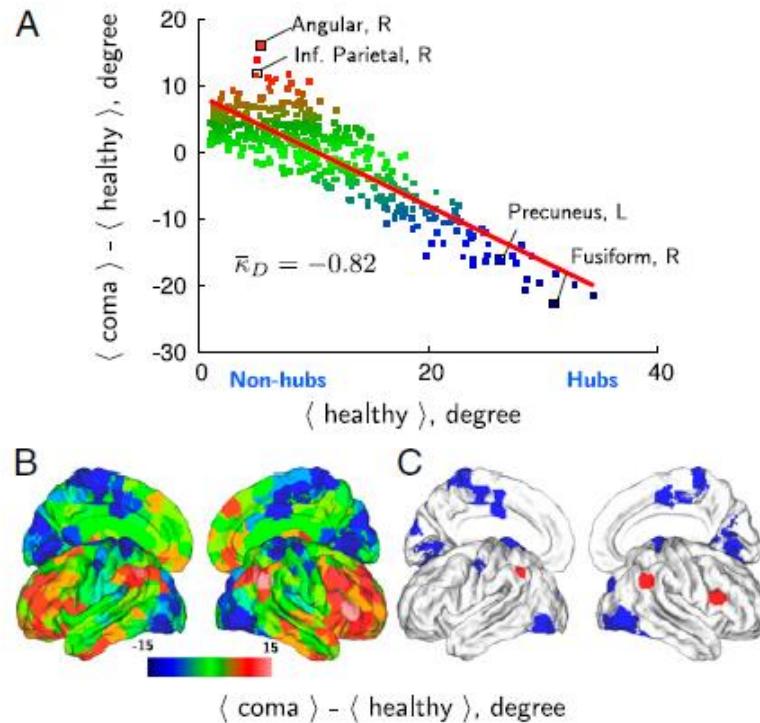


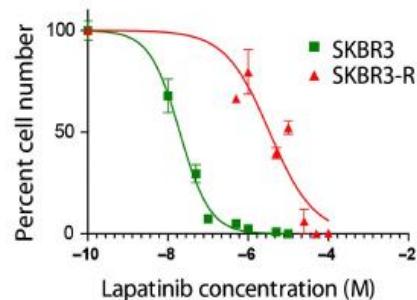
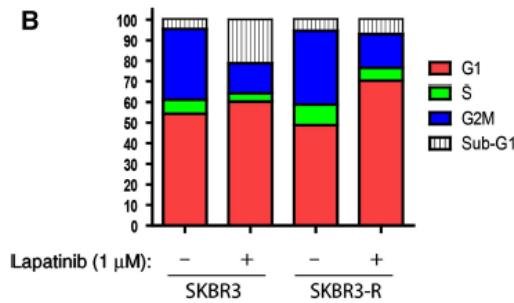
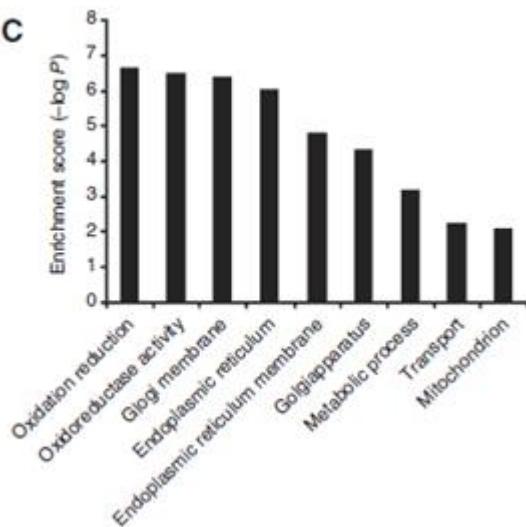
Fig. 2. Hub disruption of functional networks in comatose patients.

Córtex fusiforme e Precúneo



Atividade está relacionada com:

- Função cerebral após dano cerebral
- nível de consciência

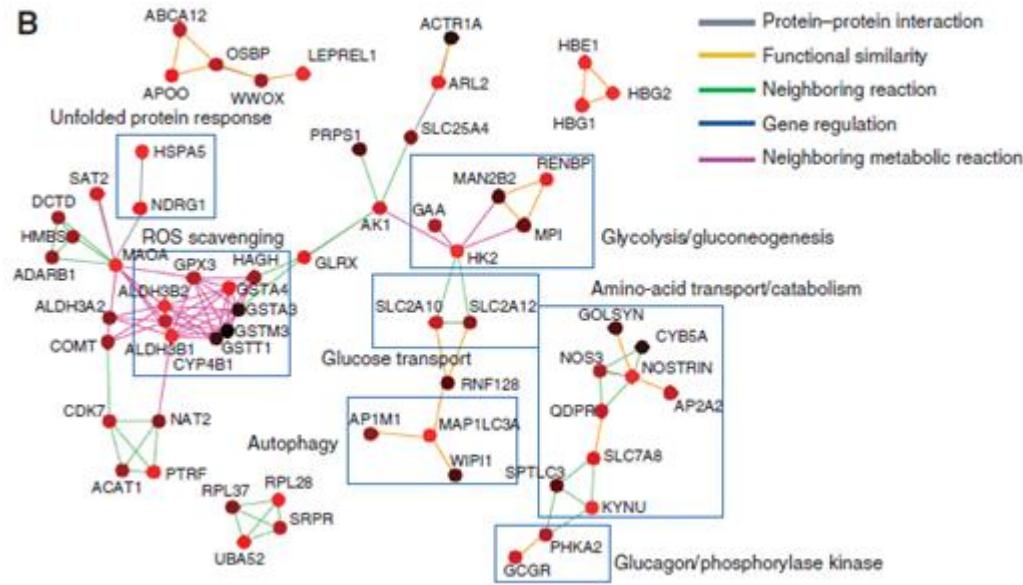
A**B****C**

Molecular Systems Biology 8; Article number 596; doi:10.1038/msb.2012.25
Citation: *Molecular Systems Biology* 8:596
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www.molecularsystemsbiology.com

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systems
biology

The glucose-deprivation network counteracts lapatinib-induced toxicity in resistant ErbB2-positive breast cancer cells

Kakajan Komurov¹, Jen-Te Tseng¹, Melissa Muller¹, Elena G Seviour¹, Tyler J Moss¹, Lifeng Yang², Deepak Nagrath² and Prahlad T Ram^{1,*}



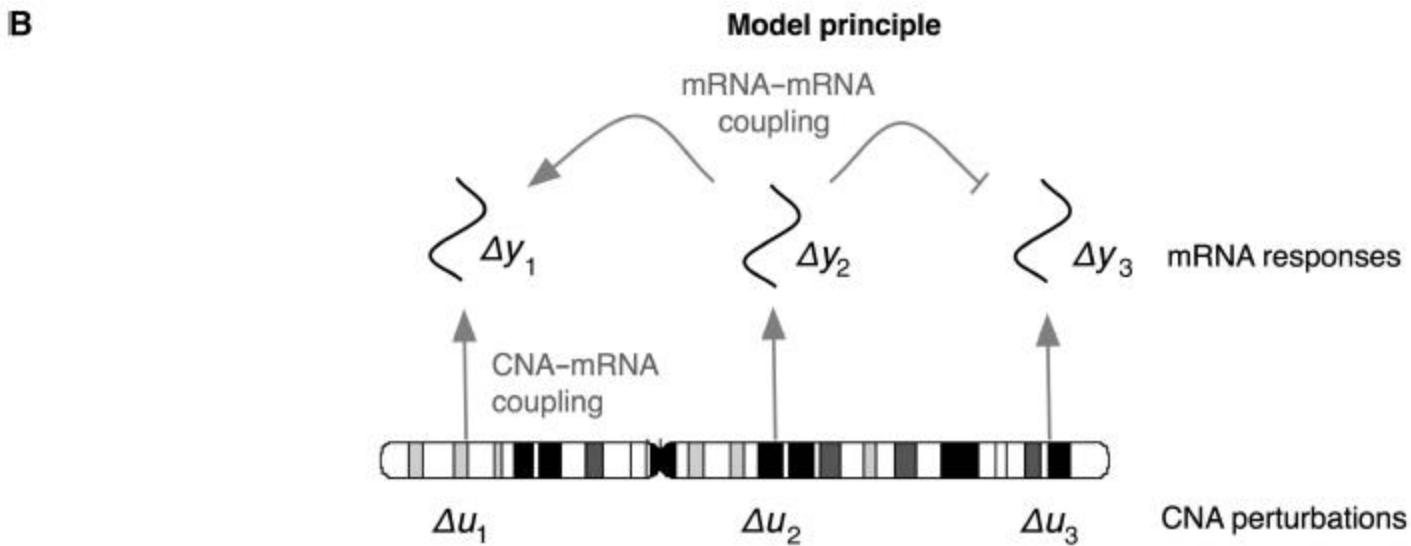
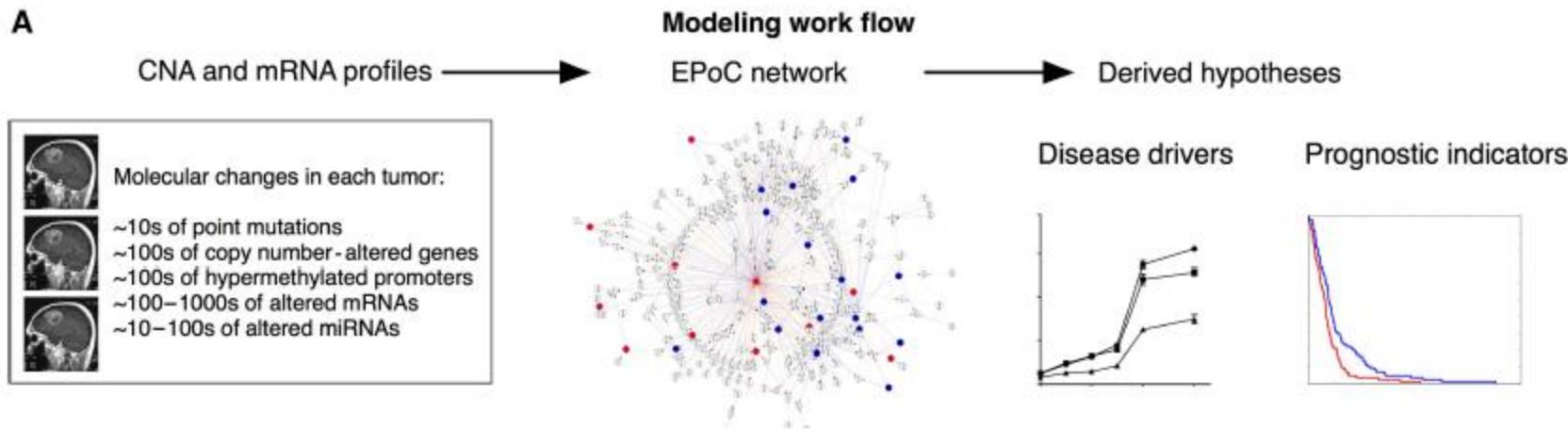
Network modeling of the transcriptional effects of copy number aberrations in glioblastoma

Rebecka Jörnsten¹, Tobias Abenius^{1,2}, Teresia Kling², Linnéa Schmidt², Erik Johansson^{2,3}, Torbjörn EM Nordling⁴, Bodil Nordlander², Chris Sander⁵, Peter Gennemark^{1,6}, Keiko Funa^{2,3}, Björn Nilsson⁷, Linda Lindahl² and Sven Nelander^{2,*}

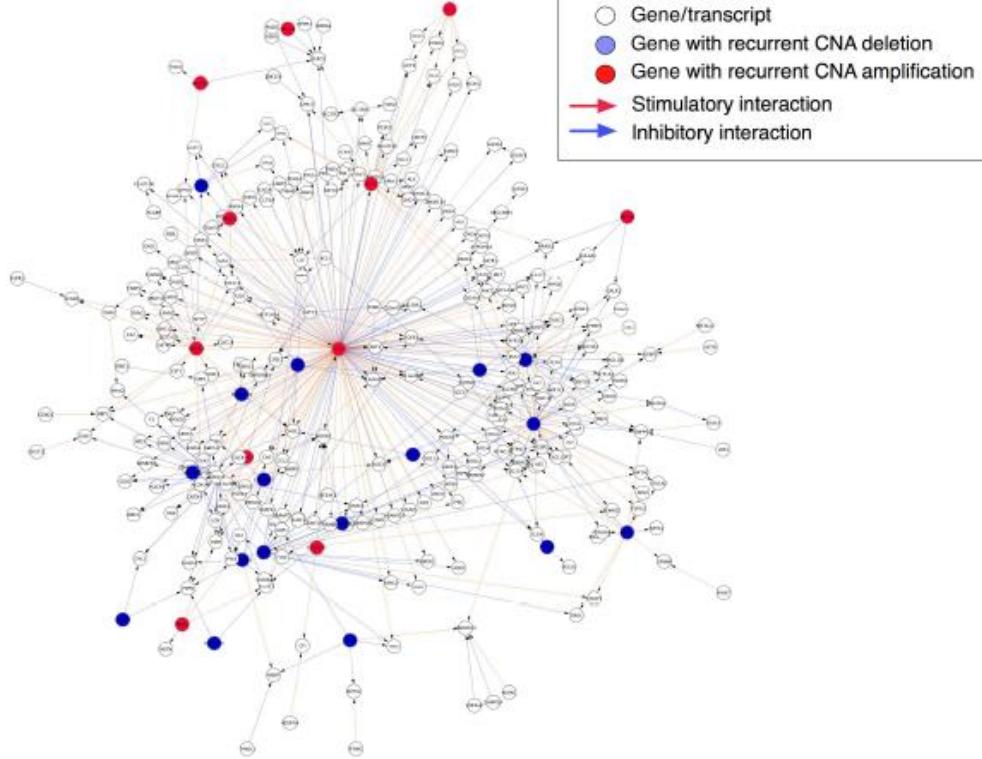
¹ Mathematical Sciences, University of Gothenburg and Chalmers University of Technology, Gothenburg, Sweden. ² Sahlgrenska Cancer Center, Institute of Medicine, Gothenburg, Sweden. ³ Medical Biochemistry, Institute of Biomedicine, Gothenburg, Sweden. ⁴ Automatic Control, School of Electrical Engineering, KTH Royal Institute of Technology, Stockholm, Sweden. ⁵ Memorial Sloan-Kettering Cancer Center, Computational Biology Center, New York, NY, USA.

⁶ Department of Mathematics, Uppsala University, Uppsala, Sweden and ⁷ Department of Laboratory Medicine, Lund University, Lund, Sweden

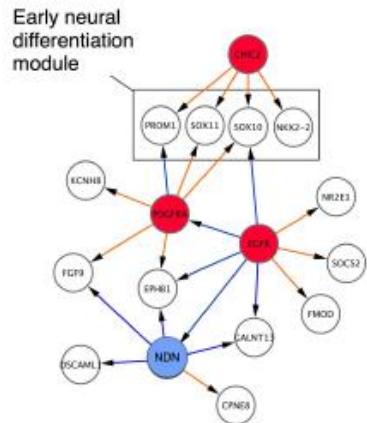
* Corresponding author. Sahlgrenska Cancer Center, University of Gothenburg, Institute of Medicine, Box 425, Gothenburg 41530, Sweden. Tel.: + 46 76 138 0123; Fax: + 46 46 422 0717; E-mail: sven.nelander@gu.se



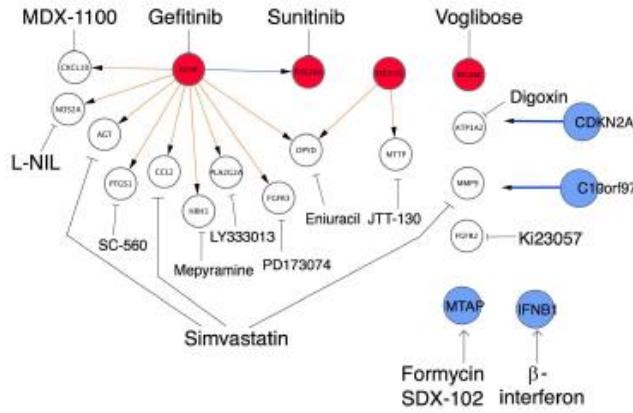
A CNA-driven network of glioblastoma

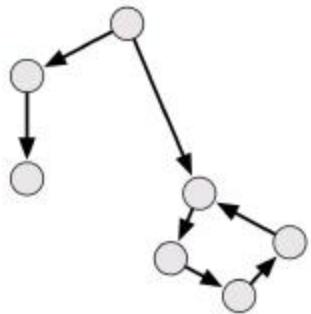
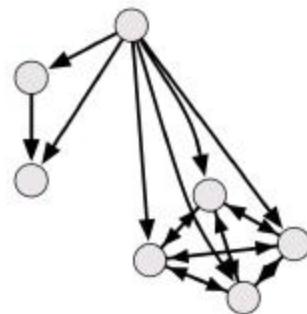
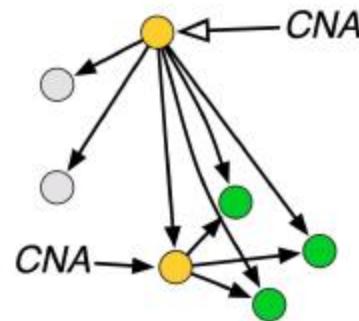


B Differentiation markers



C Overlap with compound-target databases



C**Transcriptional (A) and CNA-driven (G) networks**Transcriptional network (A)CNA-driven network (G)Axes of signal amplification
(singular value decomposition of G)

Key:

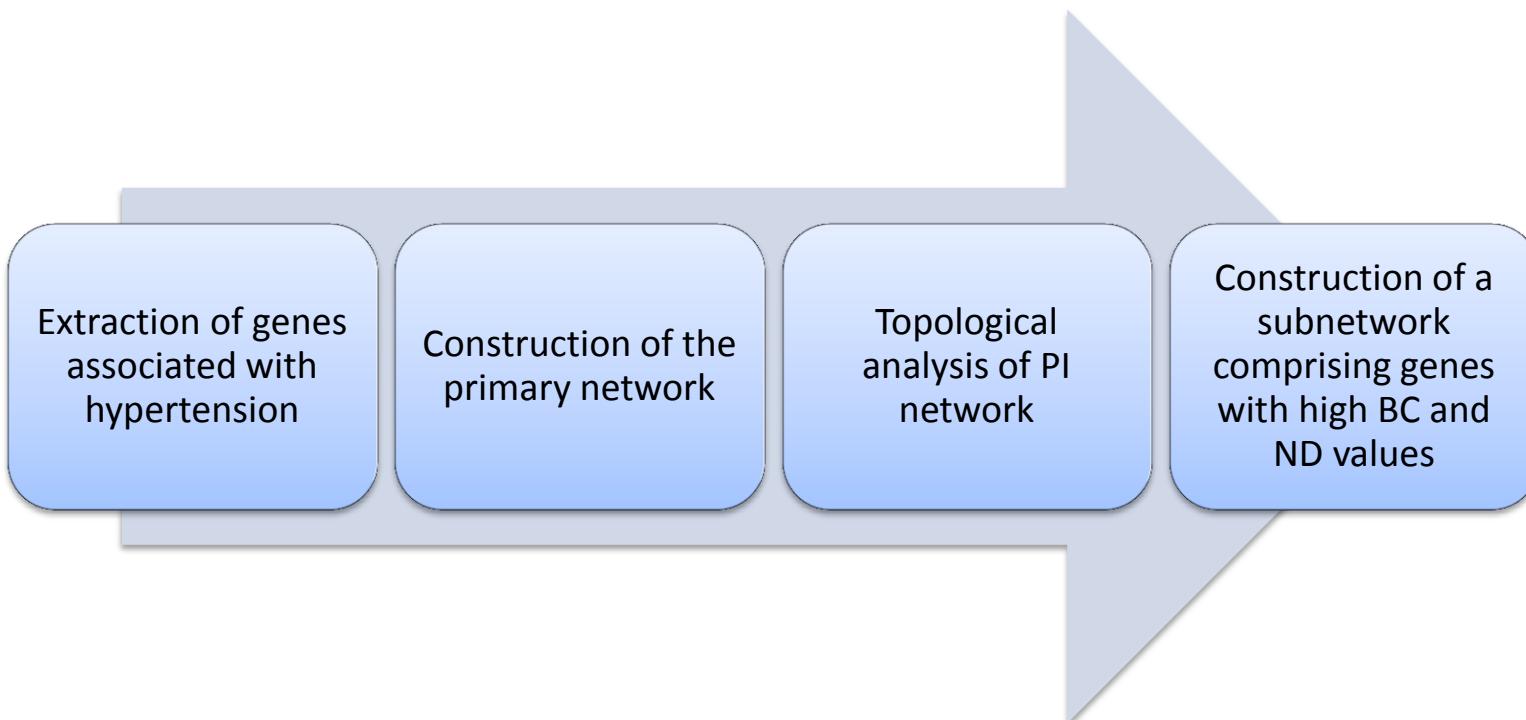
● Gene/transcript	● Highly amplified CNA perturbations
→ Interaction	● mRNAs with high response level

RESEARCH ARTICLE

Open Access

Construction and analysis of the protein-protein interaction network related to essential hypertension

Jihua Ran^{1,2†}, Hui Li^{1†}, Jianfeng Fu², Ling Liu¹, Yanchao Xing², Xiumei Li¹, Hongming Shen¹, Yan Chen¹, Xiaofang Jiang¹, Yan Li¹ and Huiwu Li^{1,3*}



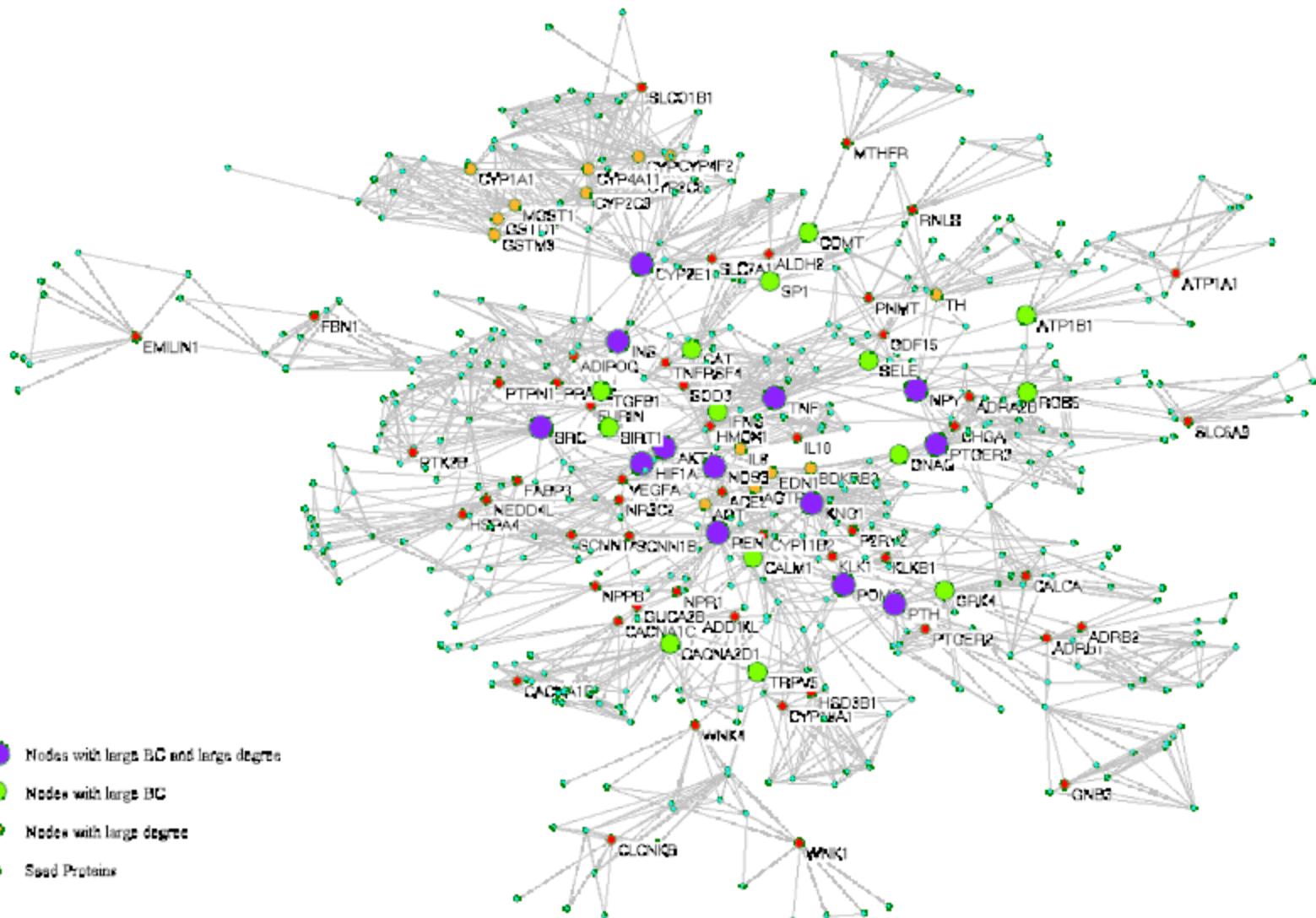


Figure 2 The topology of the giant network. The giant network extracted from the extended network is the biggest component in the extended network. The size of nodes corresponds to their BC values.

Topological analysis of PI network

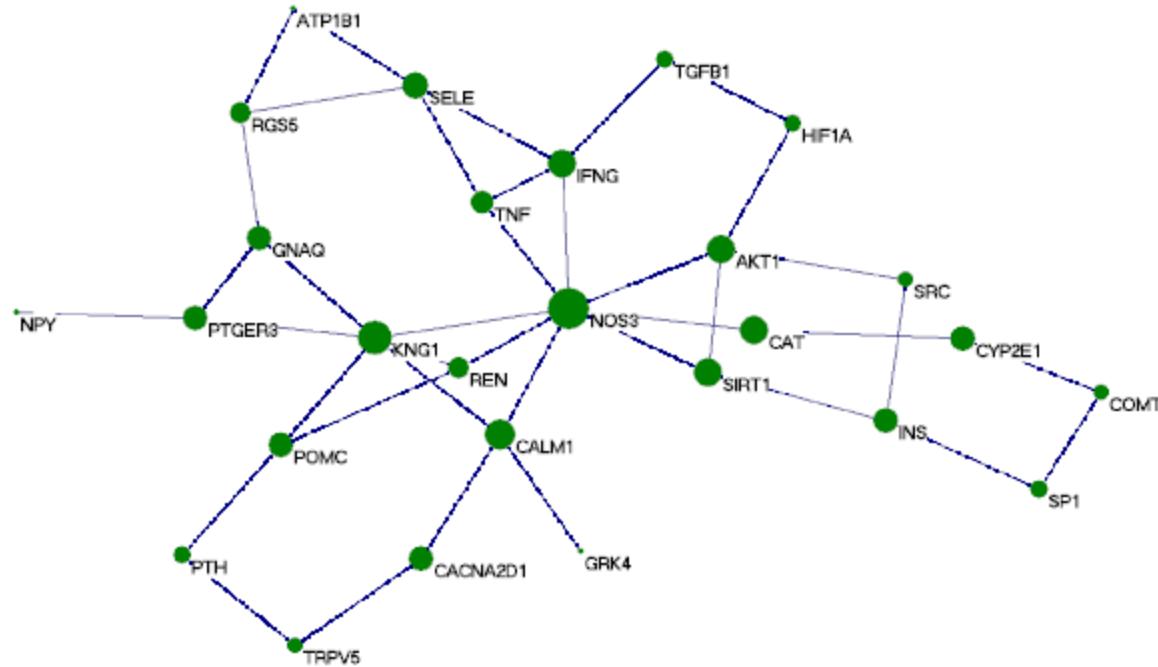


Figure 3 The topology of the backbone network. The backbone network consists from 27 nodes with high BC value. The size of nodes corresponds to their BC values.

Table 5 The list of proteins with both high BC and large degree and their functions

Symbol	Function description
NOS3	Produces nitric oxide which is implicated in vascular smooth muscle relaxation.
CYP2E1	An effective producer of reactive oxygen species.
KNG1	Precursor of vasoactive kinins.
NPY	A peptide with direct and potential effects on vasoconstriction.
HIF1A	Functions as a master transcriptional regulator of the adaptive response to hypoxia.
POMC	Controls energy homeostasis.
REN	Generates angiotensin I from angiotensinogen in the plasma.
TNF	A proinflammatory cytokine which induces endothelial dysfunction.
PTH	Elevates calcium level by dissolving the salts in bone and preventing their renal excretion.
SRC	Involves in cell maintenance and communication.
AKT1	Phosphorylates NOS3.
PTGER3	Receptor for prostaglandin E2.
INS	Decreases blood glucose concentration.

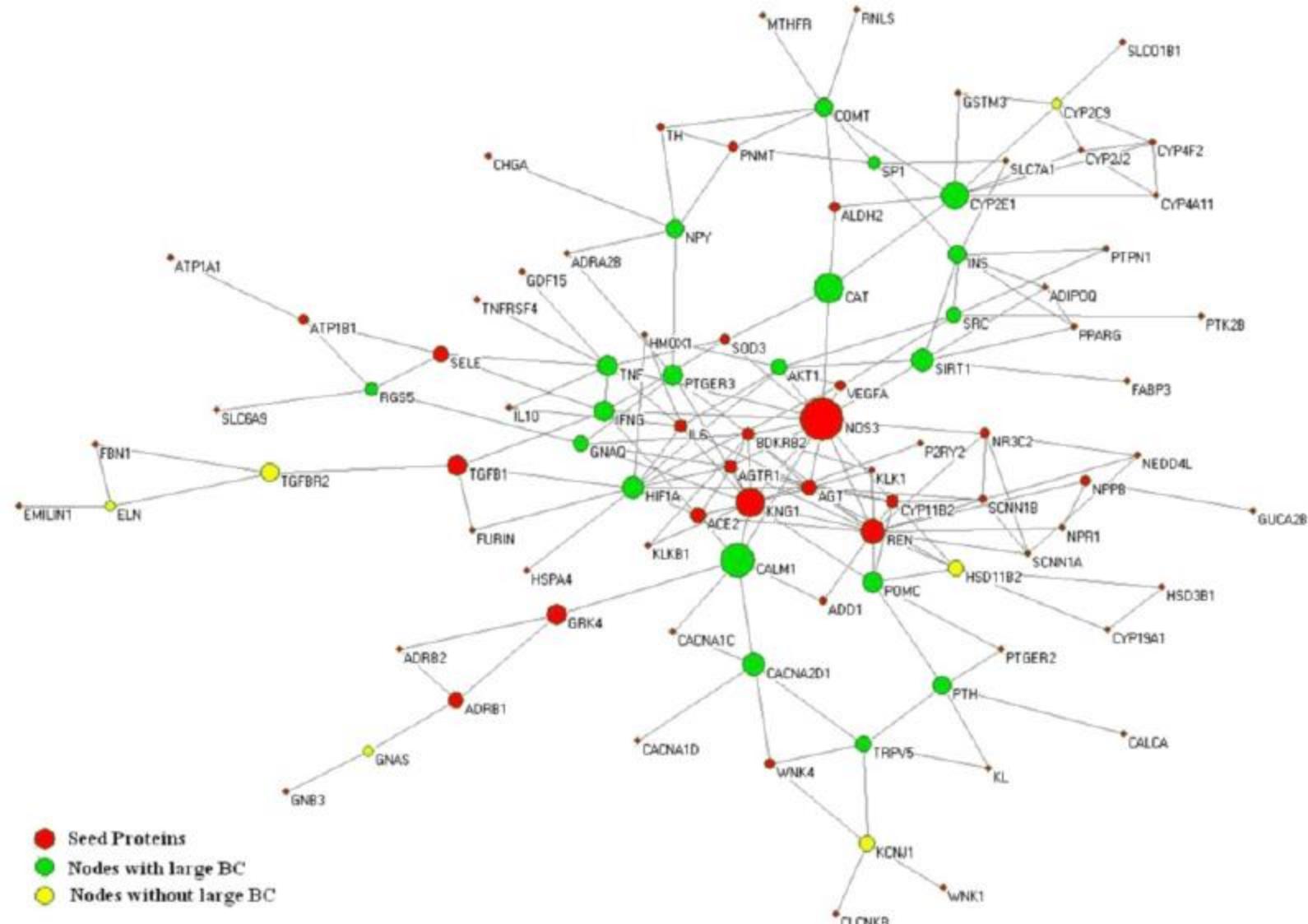
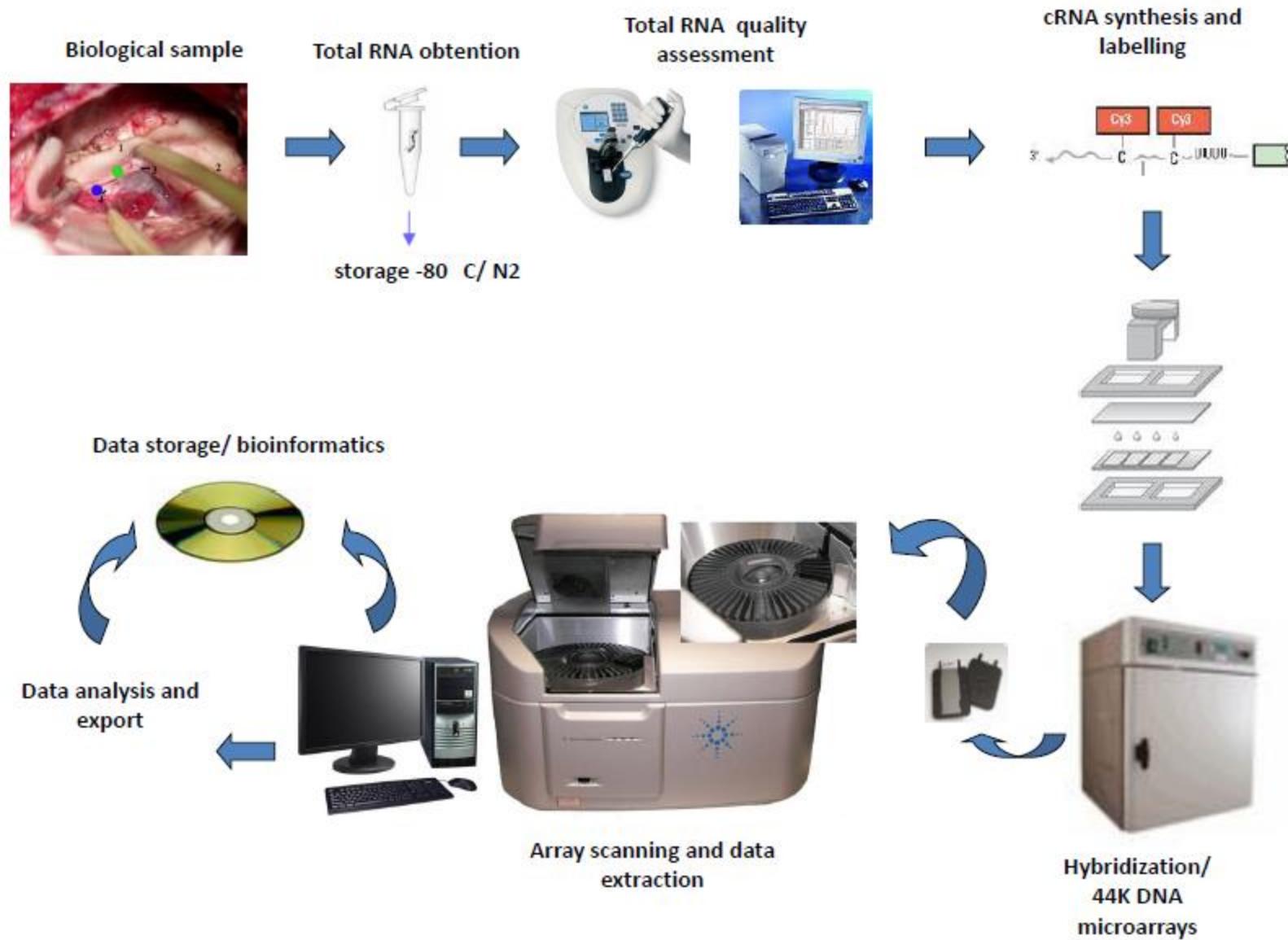


Figure 4 The subnetwork consisting of all shortest paths between the genes associated with essential hypertension. The candidate genes are connected by all shortest paths in the giant network. The size of nodes corresponds to their BC values and there are 6 yellow nodes without large BC (6 outside 27).

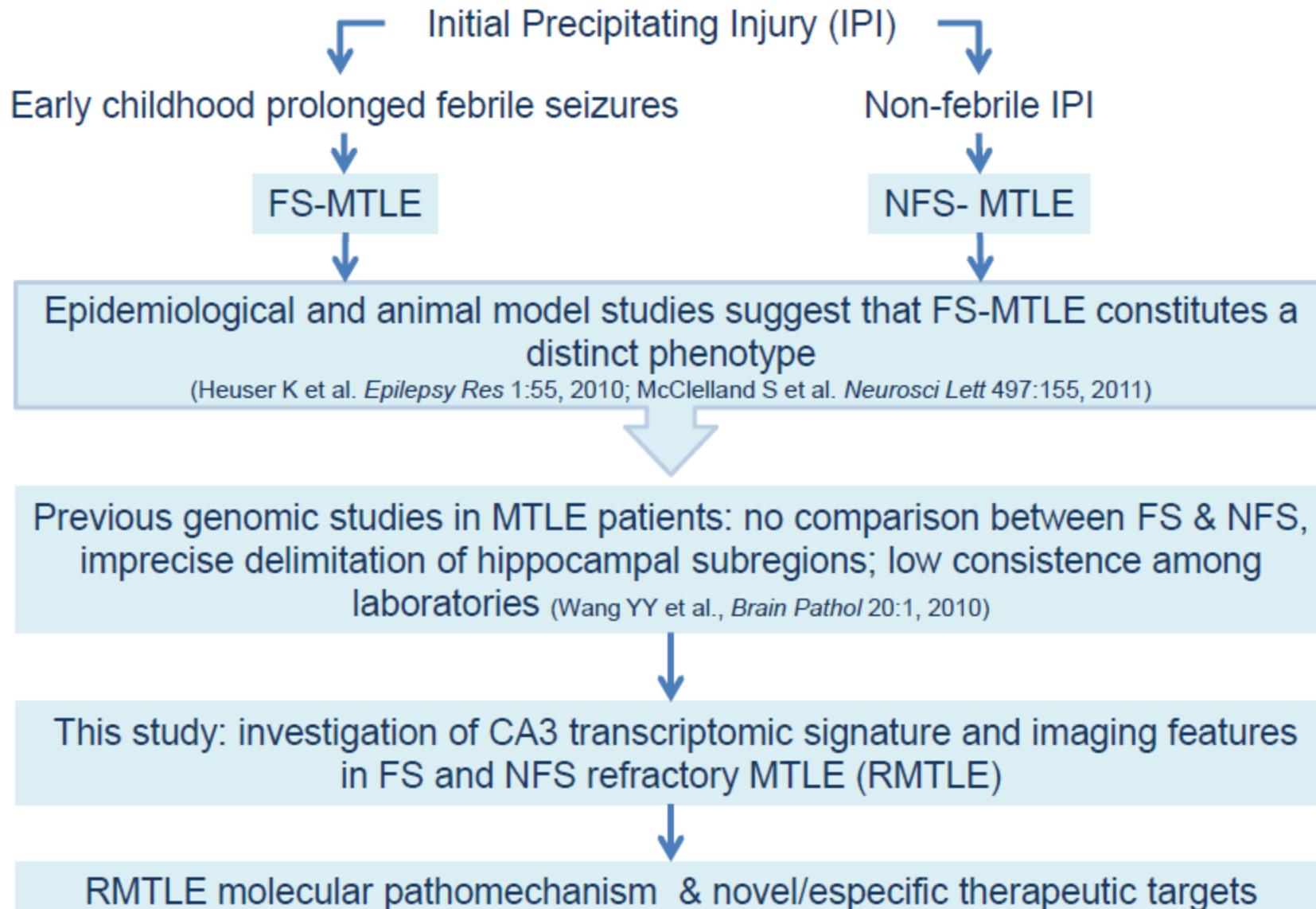
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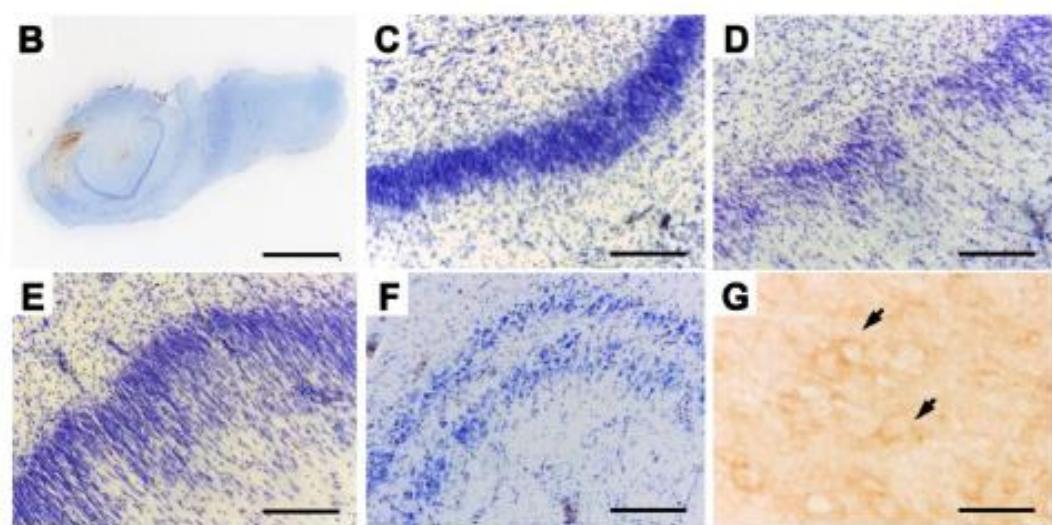
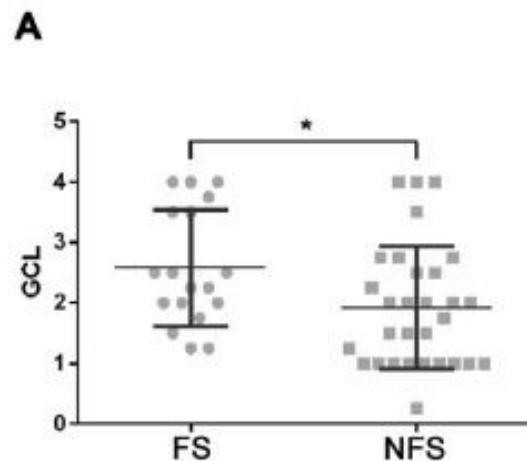
Análise Global da Expressão Gênica



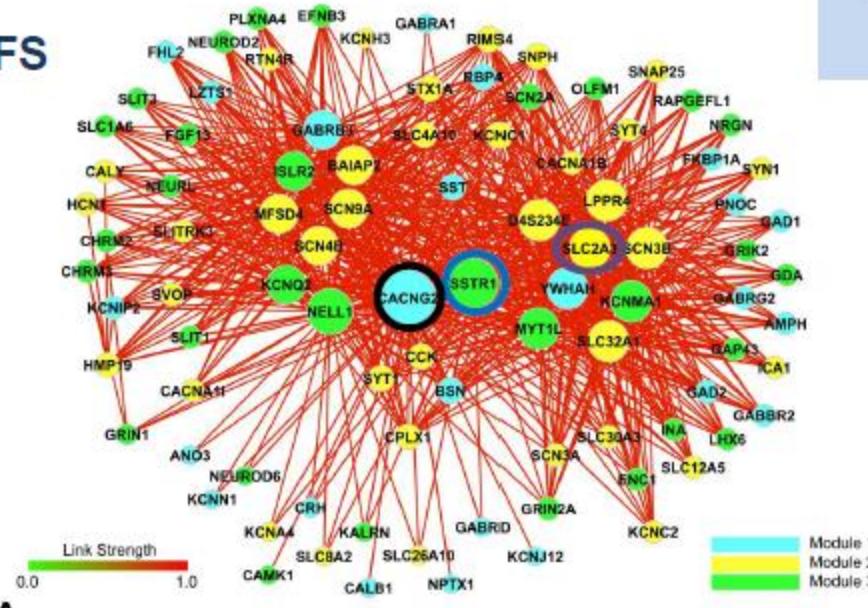
Febrile (FS) and non-febrile (NFS) IPI in Mesial Temporal Lobe Epilepsy (MTLE): a systems biology approach



A perda de células granulares é mais pronunciada em pacientes com epilepsia desenvolvida a partir de insulto febril...

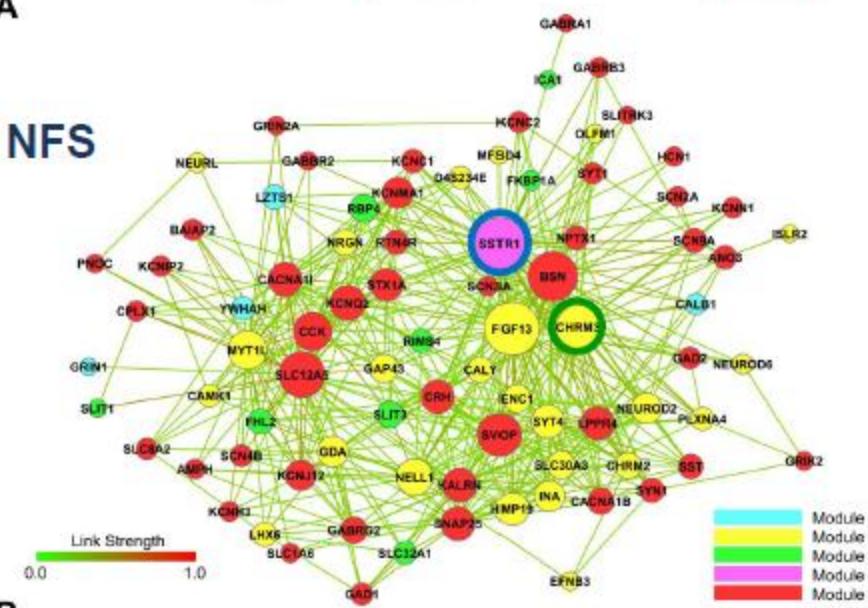


Systems Biology: GO Biological Process transcriptional interaction network



Exclusive hubs

○ glutamatergic synaptic transmission
○ glucose transporter



Potential therapeutic targets

Major distinctive hub

○ synaptic transmission

Broker genes: genes involved in complex diseases usually have a high number of gene-gene connections and a low clustering coefficient (number of connections among neighbors).

Cai JJ et al. *Genome Biol. Evol.* 2:815, 2010

Complex Network Analysis of CA3 Transcriptome Reveals Pathogenic and Compensatory Pathways in Refractory Temporal Lobe Epilepsy

Short Title: Complex Transcriptional Networks in Epilepsy

¹Silvia Yumi Bando; ²Filipi Nascimento Silva; ²Luciano da Fontoura Costa; ³Alexandre V. Silva; ³Luciana R. Pimentel-Silva, ⁴Luiz H.M. Castro; ⁵Hung-Tzu Wen, ⁶Edson Amaro Jr; ¹Carlos Alberto Moreira-Filho*

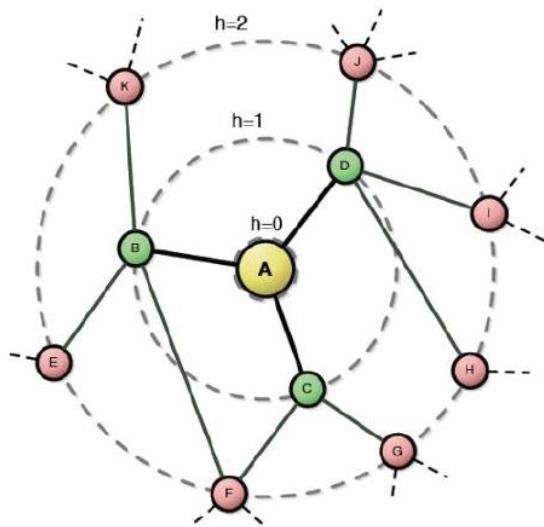


Figure 1: Example of concentric levels of a network for node A as reference (i.e. centered at node A). Each concentric level is represented by rings $R_h(A)$, namely $R_0(A) = \{A\}$, $R_1(A) = \{B, C, D\}$ and $R_2(A) = \{E, F, G, H, I, J, K\}$, with concentric node degrees $k_0(A) = 3$ and $k_1(A) = 8$.

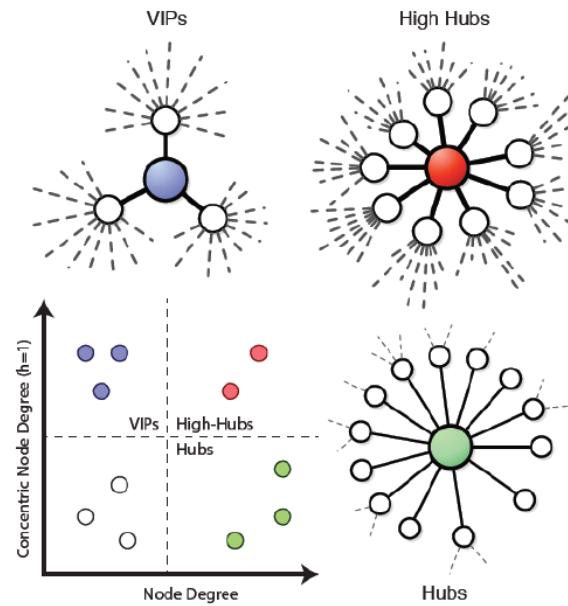
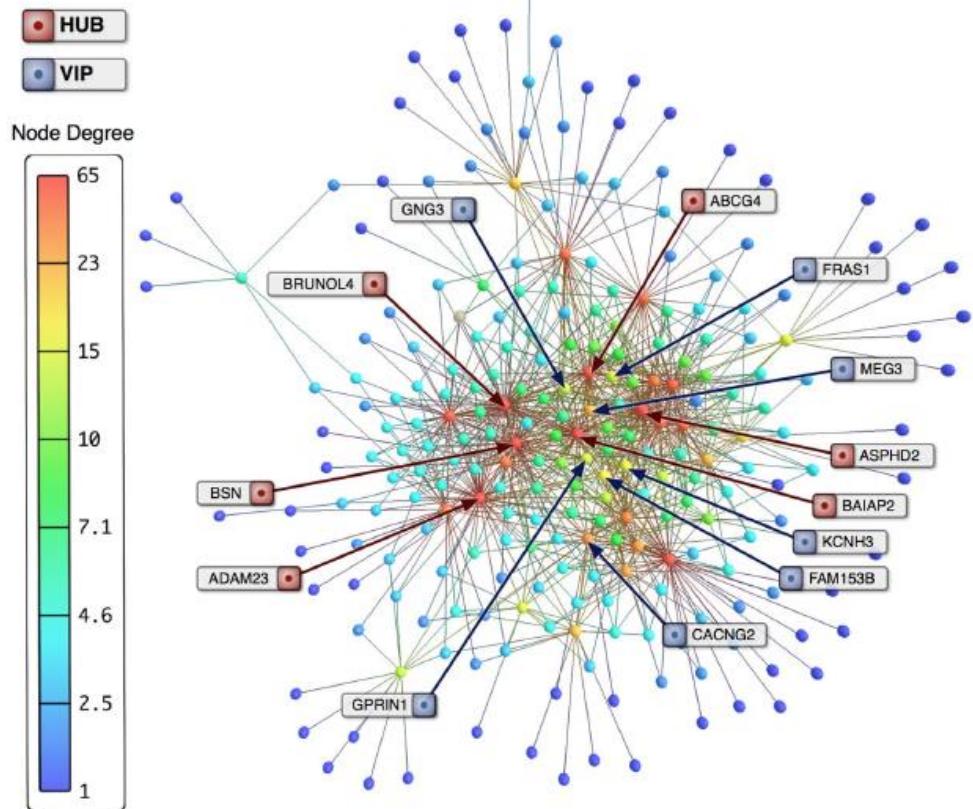
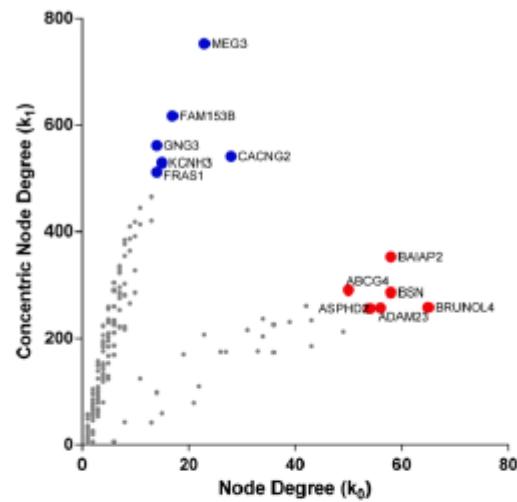
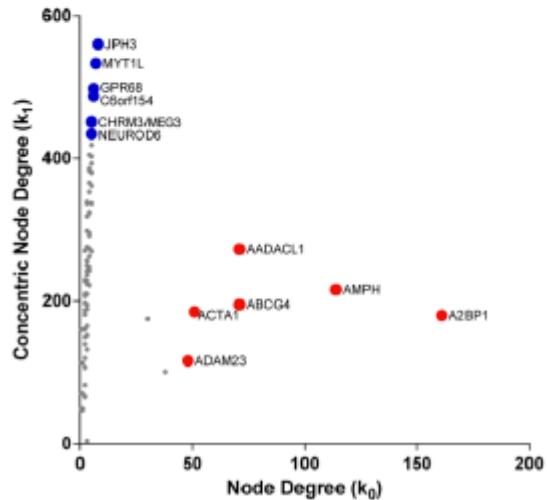
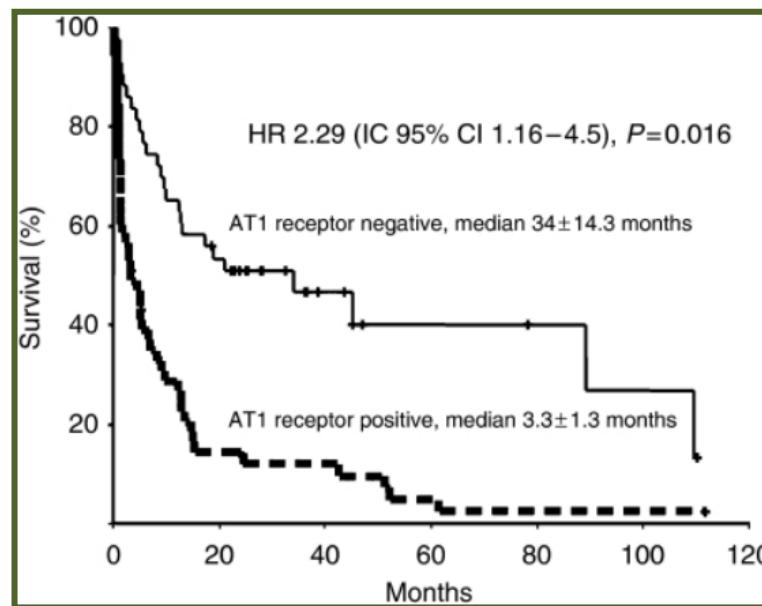


Figure 2: Networks illustrating the three proposed categories of nodes with VIPs presenting low node degree but high concentric node degree at first level, hubs with lower concentric node degree and higher node degree and high-hubs presenting high values of both properties.

**B****C**

"Expression of AT1 and AT2 angiotensin receptors in astrocytomas is associated with poor prognosis"

Tumour grade	AT1*		AT2**	
	Negative (%)	Positive (%)	Negative (%)	Positive (%)
Grade 1	12 (86)	2 (14)	12 (86)	2 (14)
Grade 2	14 (93)	1 (7)	12 (80)	3 (20)
Grade 3	5 (28)	13 (72)	7 (39)	11 (61)
Grade 4	21 (34)	40 (66)	30 (49)	31 (51)
Total	52 (48)	56 (52)	61 (56.5)	47(43.5)

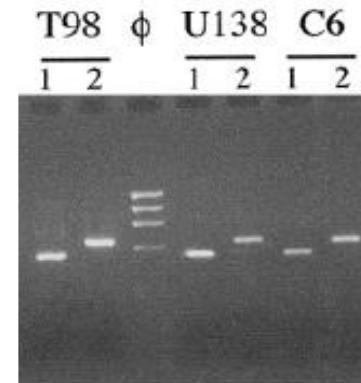
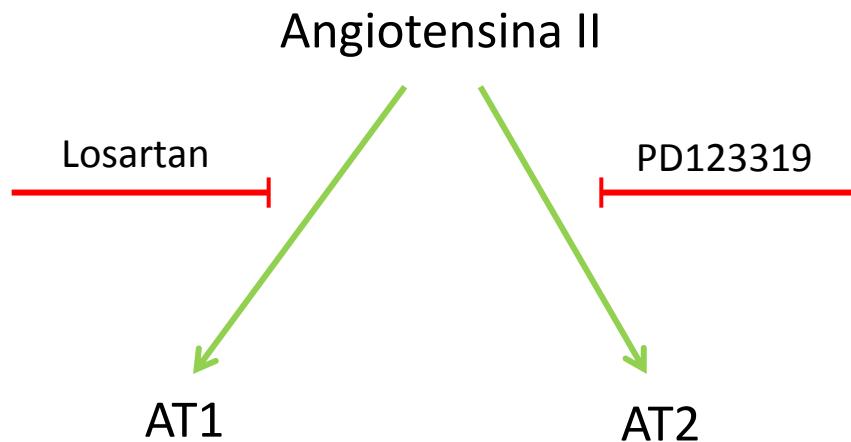


Arrieta et al, 2008

Transcriptional Network Analysis Reveals that AT1 and AT2 Angiotensin II Receptors Are Both Involved in the Regulation of Genes Essential for Glioma Progression

Hátylas Azevedo¹, André Fujita², Silvia Yumi Bando¹, Priscila Iamashita¹, Carlos Alberto Moreira-Filho^{1*}

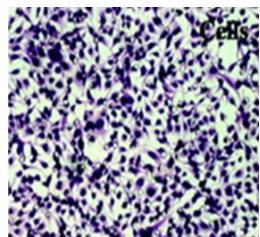
1 Department of Pediatrics, Faculdade de Medicina da Universidade de São Paulo (FMUSP), São Paulo, SP, Brazil, **2** Department of Computer Science, Instituto de Matemática e Estatística, Universidade de São Paulo, São Paulo, SP, Brazil



Fogarty, 2002

AT1 AT2

Desenho Experimental



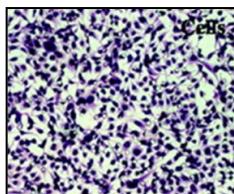
C6

Cultura



4 grupos (3 e 6h)

- I. Controle
- II. AngII
- III. AngII + Antagonista AT1 (Losartan)
- IV. AngII + Antagonista AT2 (PD123319)



Amostra



Extração RNA

-Quantidade

-Qualidade

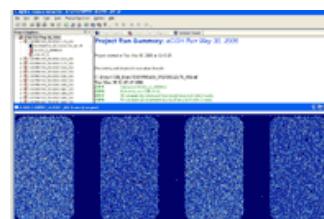


Síntese e marcação (Cy3) do cRNA

Hibridização e Escaneamento

Análise dos dados

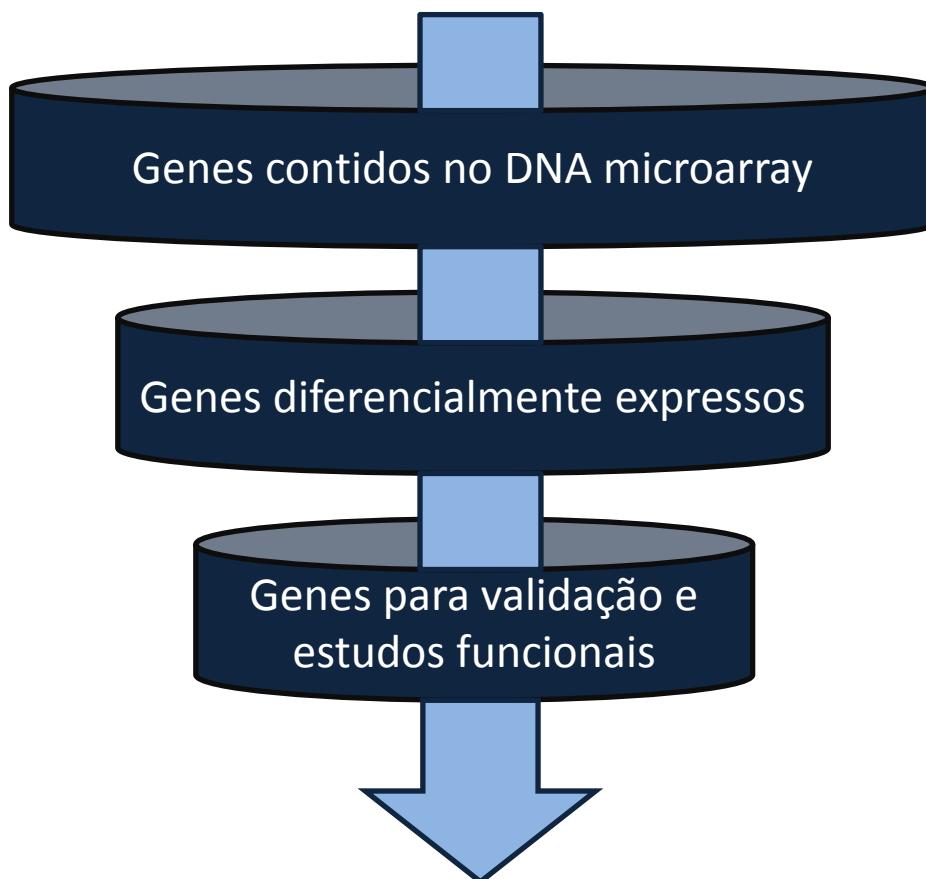
← Conversão da imagem em dados e CQ



1. Up and Down
2. Transcriptômica Funcional
3. Redes de interatoma

ANÁLISE DE DADOS DE MICROARRAY

Mineração dos dados



Genes diferencialmente expressos



**Enriquecimento Funcional →
GO / KEGG**



**Sobreposição de Resultados
(Diagramas de Venn)**



Análise das Redes de Proteínas

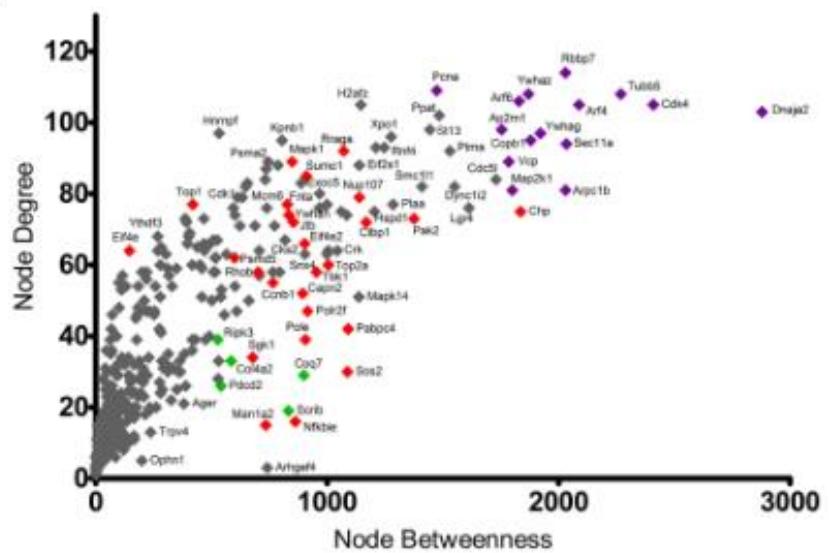


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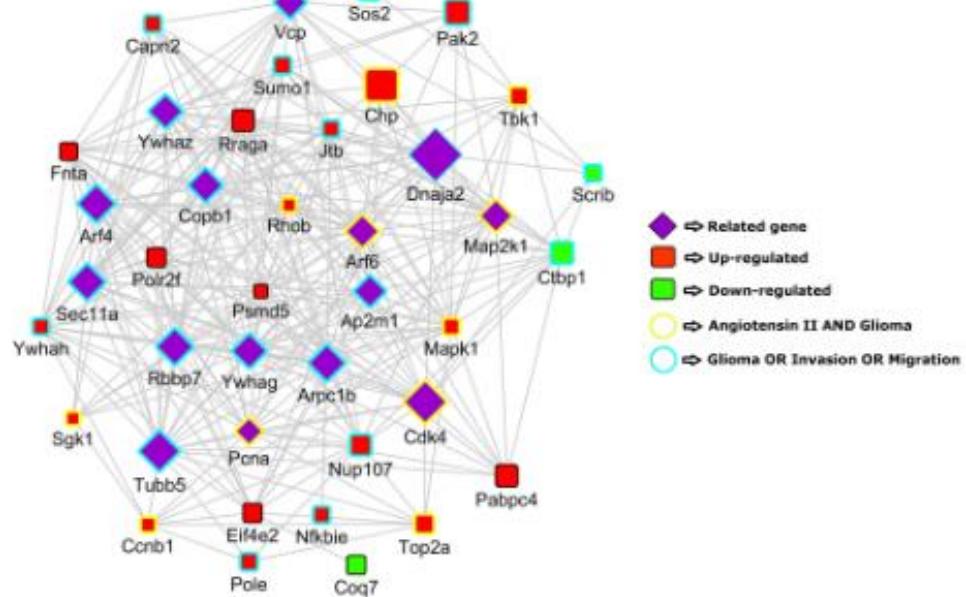
3

A

Ang II x Control 6h

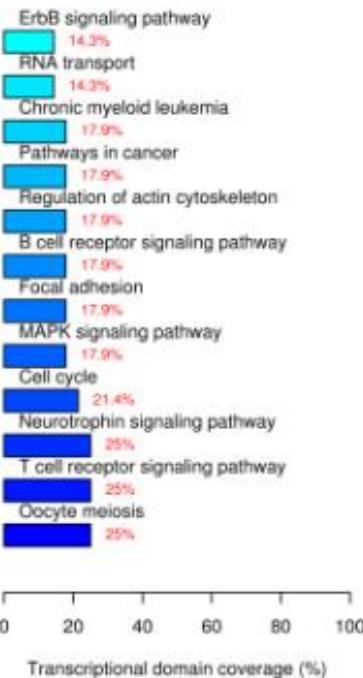


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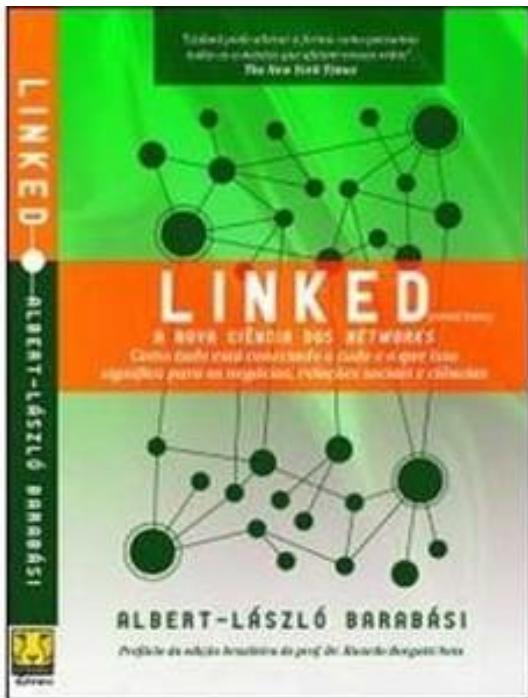


C

KEGG



Vídeo 2



Albert-László Barabási at TEDMED 2012

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- 2 Experimental Methods in Systems Biology
- 3 Network Analysis in Systems Biology
- 4 Dynamical Modeling Methods for Systems Biology
- 5 Integrated Analysis in Systems Biology
-  Capstone Project

Course 1

Introduction to Systems Biology

Upcoming Session: TBA

Duration: TBA

Estimated Workload: 6-8 hours/week

Topics covered include:

- Systems Level Reasoning: Bottom-Up and Top-Down Approaches for Complex Systems
- Cell Signaling Pathways: Molecules to Pathways, cAMP and MAP-kinase Pathways
- Signal Flow: Pathways to Networks
- The Actin Cytoskeleton: The Cell Motility Machine
- Mathematical Representations of Cell Biological Systems Time and Space
- Gathering Large Data Sets in Genomics and Proteomics
- Inferring Modules: Computational Analysis of Large Data Sets; Building Networks
- Small Scale Systems Biology Experiments