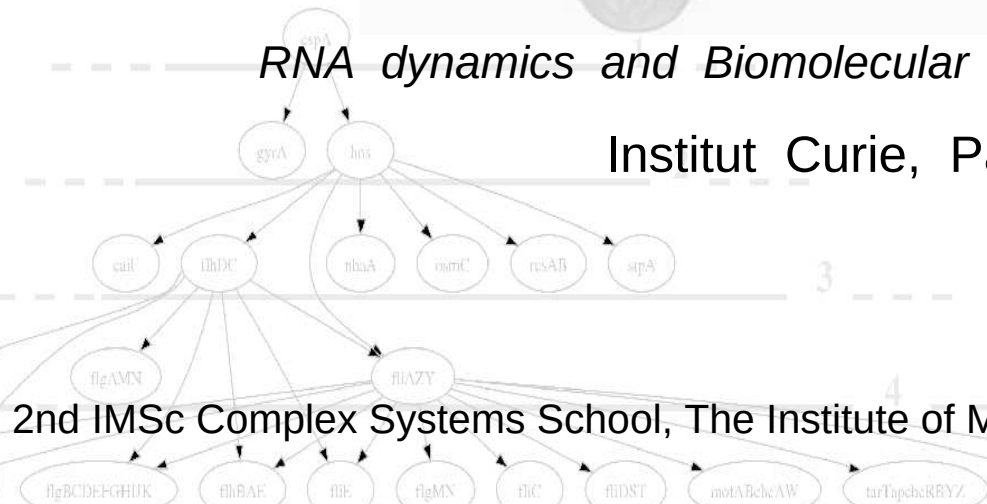


Biological Networks and their Evolution

Hervé ISAMBERT

RNA dynamics and Biomolecular Systems Lab, CNRS-UMR168

Institut Curie, Paris, France

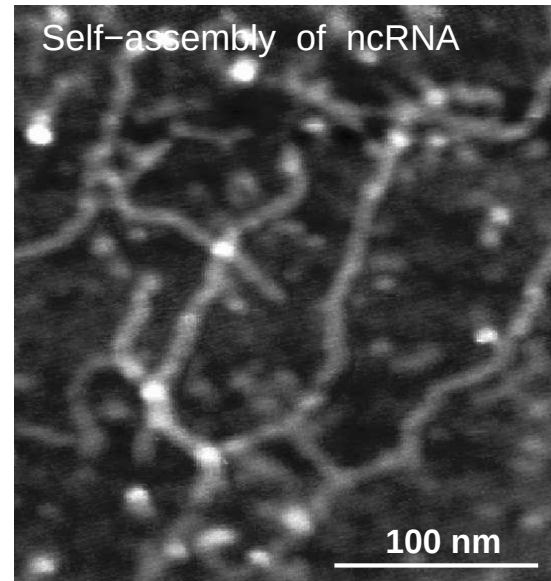
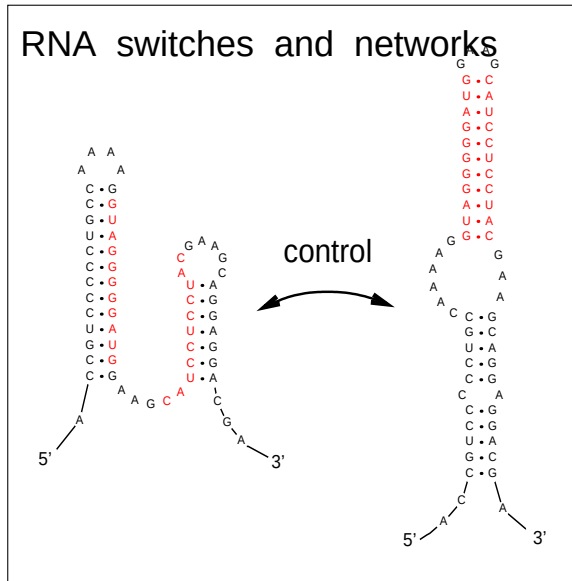


2nd IMSc Complex Systems School, The Institute of Mathematical Sciences, Jan 14 & 15, 2010

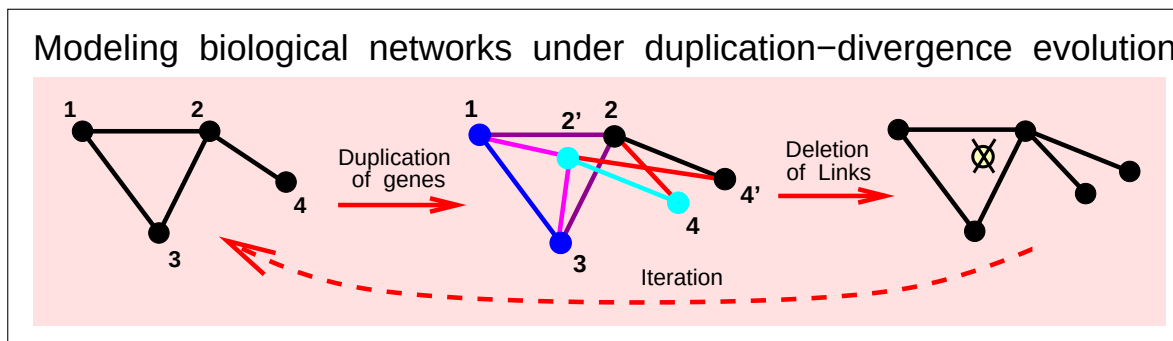
RNA Dynamics and Biomolecular Systems Lab

Institut Curie, CNRS, Paris

I. RNA Regulatory and Physical Networks



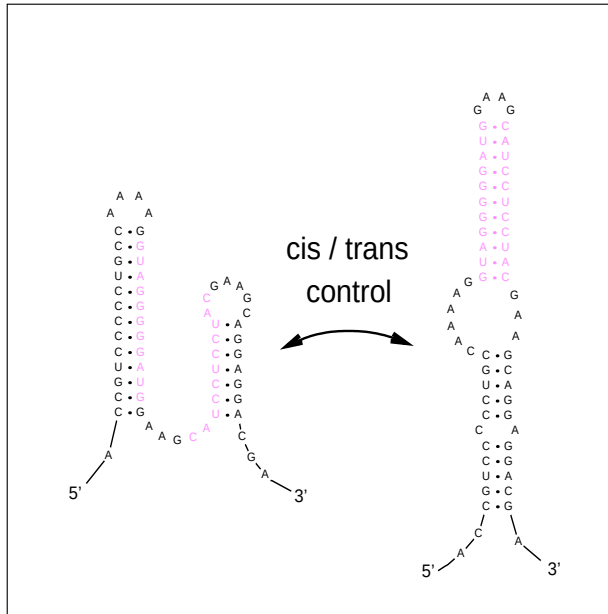
II. Evolution of Biological Networks



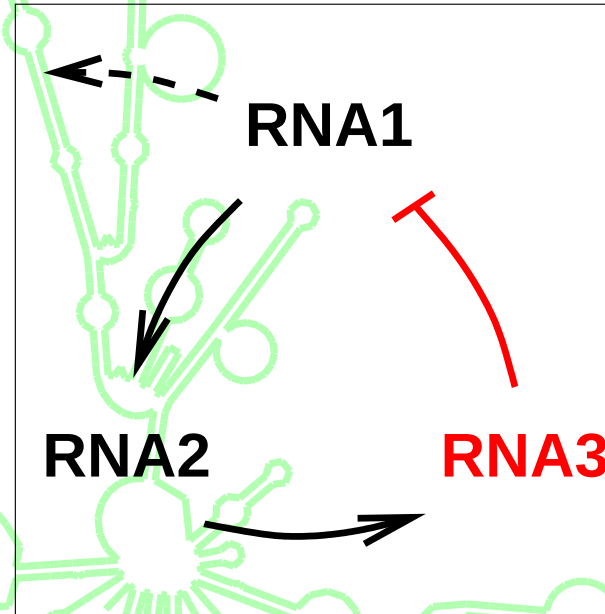
\$. Human Frontier, ANR, Ministère de la Recherche, Institut Curie, CNRS, Fondation PG de Gennes

RNA Switches and Networks

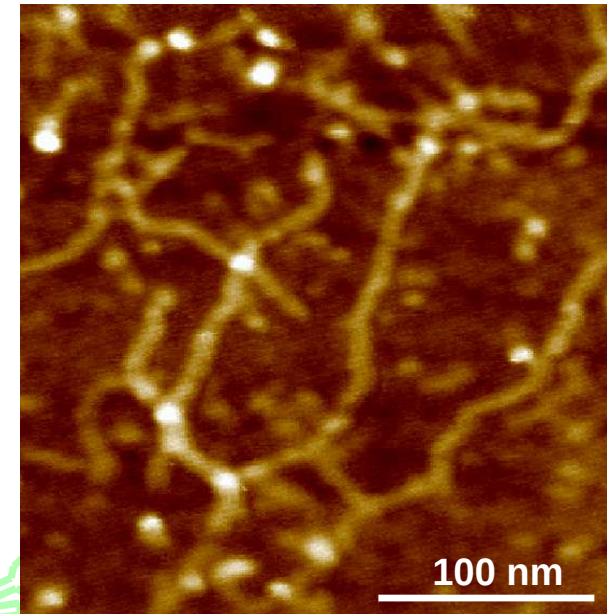
RNA switches



regulatory networks



physical networks



**Alain
Xayaphoummine**

PNAS 2003
NAR 2005



**Virgile
Viasnoff**

NanoLett 2006
NAR 2007



**Alexandre
Dawid**

Phys Biol 2009



**Bastien
Cayrol**

JACS 2009

Evolution and Topology of Large Biological Networks

Signaling Networks:

Richard Stein

Biol Direct, 4, 28 (2009)



Tree of Life
(from tolweb site)

Prot-Prot Interaction Networks:

Kirill Evlampiev

PNAS, 105, 9863–9868 (2008)

BMC Syst Biol 1:49 (2007)



Transcription Networks:

Marco Cosentino Lagomarsino

PNAS, 104, 5516–5520 (2007)

Mol BioSyst, 5, 170–179 (2009)



*Human Frontier, Ministere de la Recherche, ANR
Institut Curie, CNRS, Fondation PG de Gennes*

Biological Networks and their Evolution

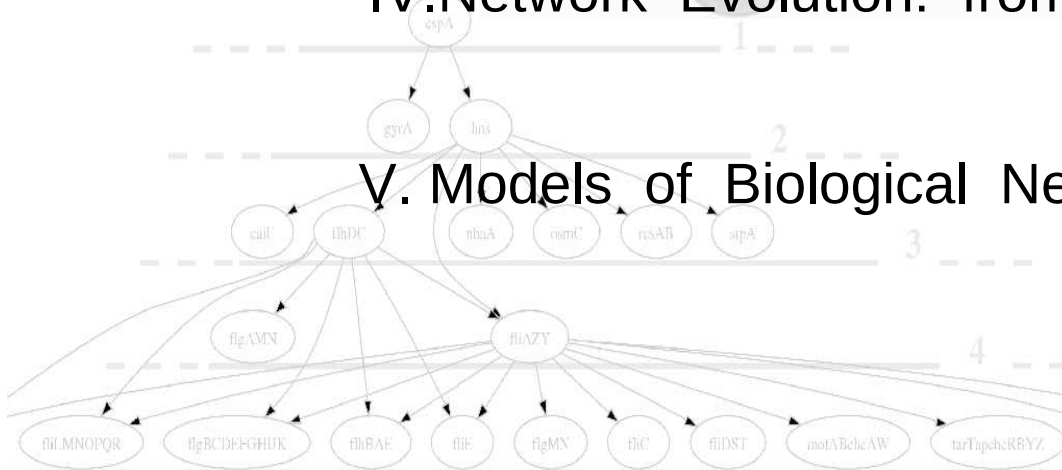
I. Introduction: from Genomes to Networks

II. Different Types of Biological Networks

III. Properties of Biological Networks

IV. Network Evolution: from Genes to Organisms

V. Models of Biological Network Evolution



Hervé ISAMBERT, Institut Curie, Paris

Biological Networks and their Evolution

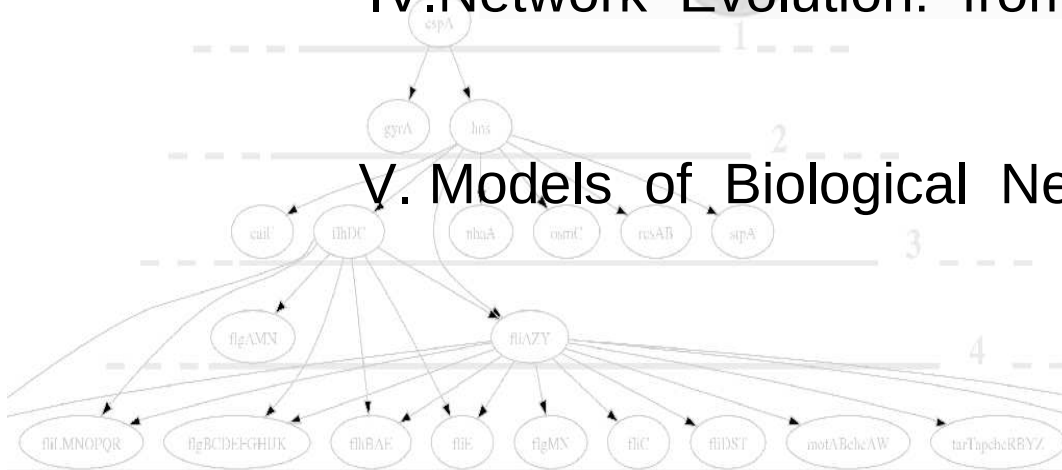
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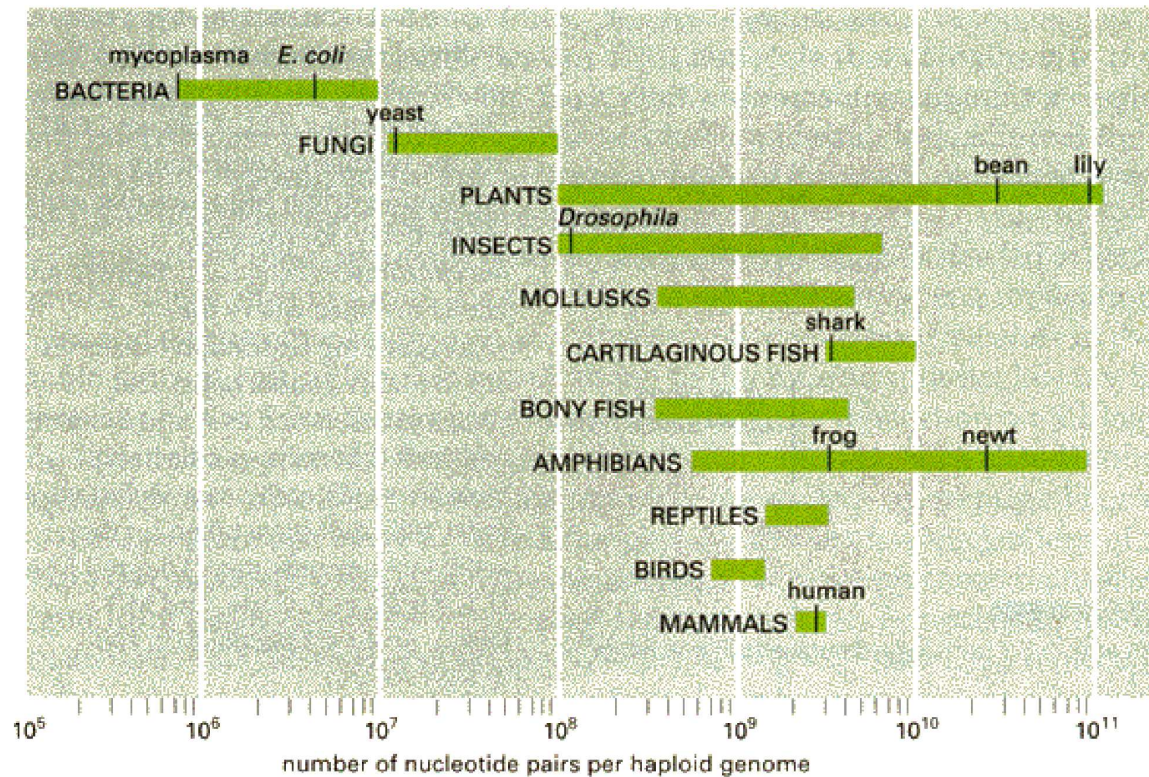
V. Models of Biological Network Evolution



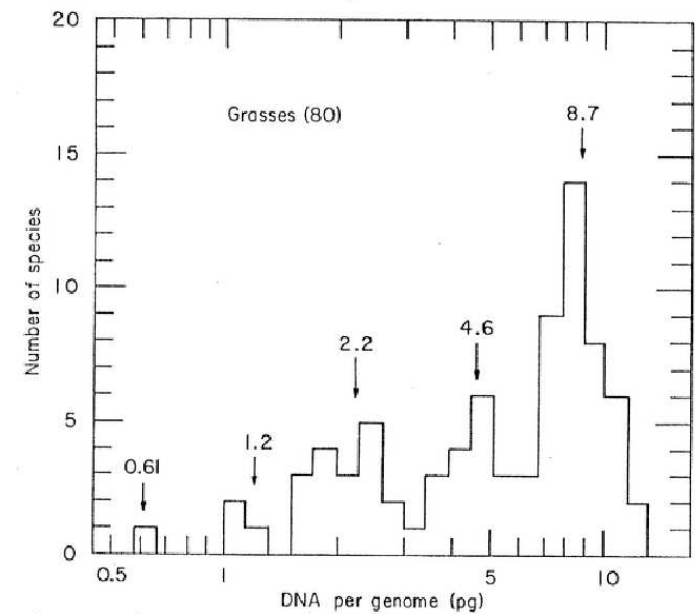
Genome size distribution

what was known before sequencing

5 decades (8 including viruses)

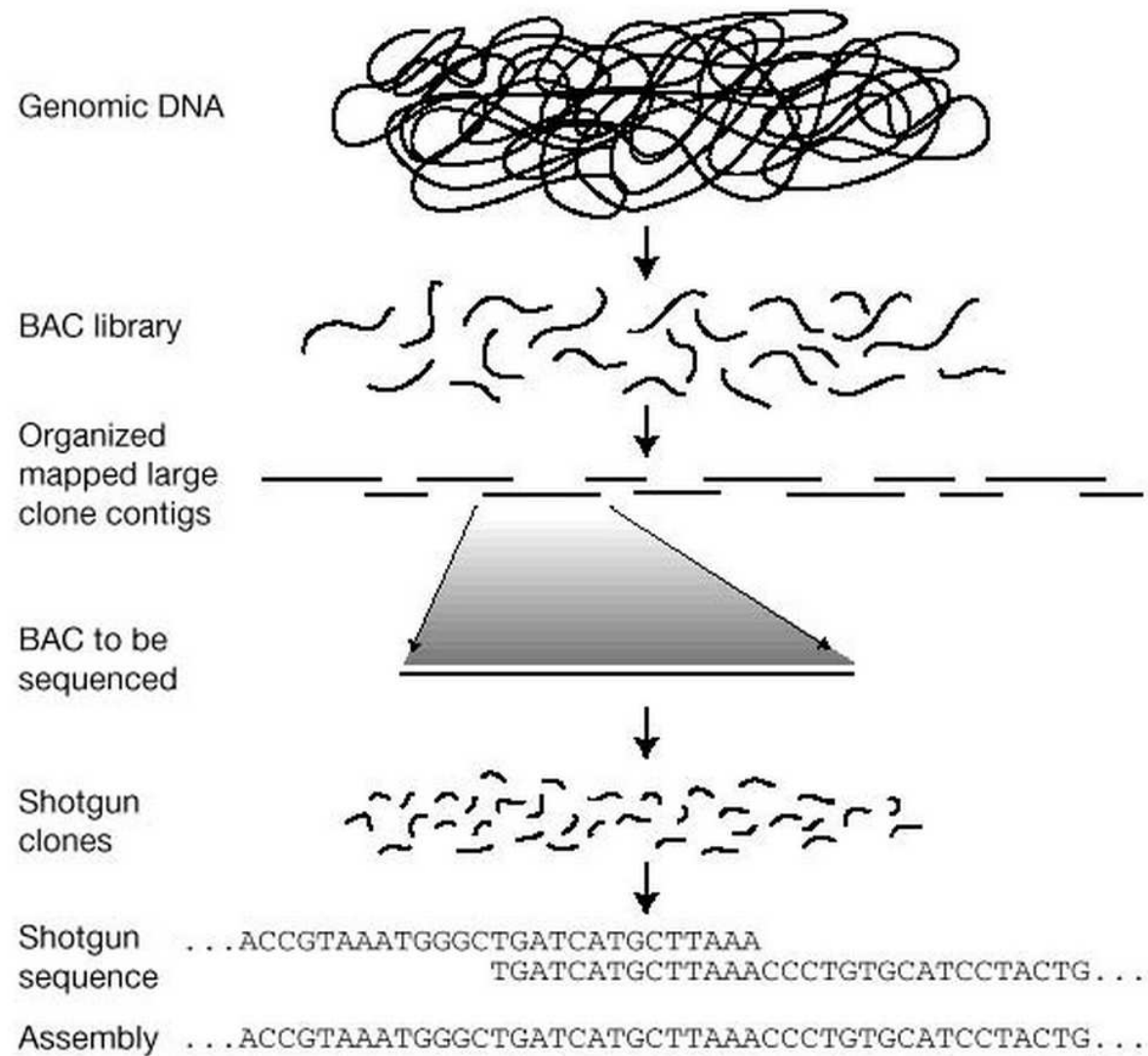


Even multimodal distribution within some species families



Sparrow 1976

Shotgun Genome Sequencing

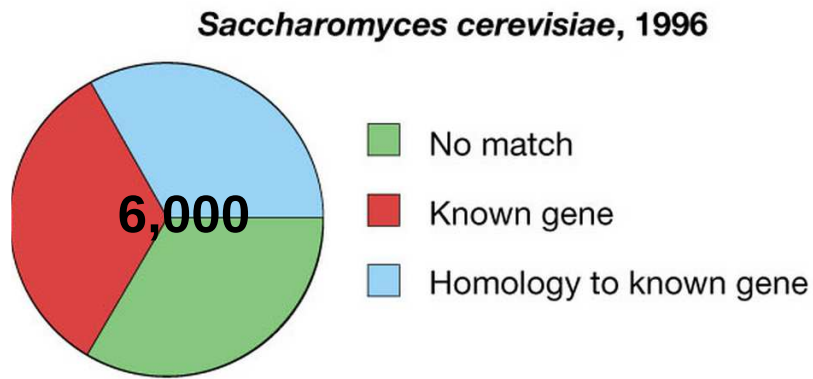
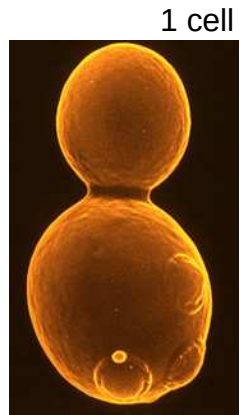


Genome Sequencing Statistics

Organism	Complete	Draft assembly	In progress	total
Prokaryotes	978	1044	980	3002
Archaea	67	13	36	116
Bacteria	911	1031	944	2886
Eukaryotes	22	187	172	381
Animals	4	75	60	139
Mammals	2	28	19	49
Birds		2	1	3
Fishes		3	6	9
Insects	1	21	7	29
Flatworms		2	2	4
Roundworms	1	9	11	21
Amphibians			1	1
Reptiles			1	1
Other animals		12	14	26
Plants	2	11	46	59
Land plants	2	8	40	50
Green Algae		3	6	9
Fungi	10	75	38	123
Ascomycetes	8	60	25	93
Basidiomycetes	1	10	8	19
Other fungi	1	5	5	11
Protists	6	24	24	54
Apicomplexans	1	11	7	19
Kinetoplasts	1	2	5	8
Other protists	4	10	12	26
total:	1000	1231	1152	3383

NCBI, 29 Sept 2009

Life great complexity and diversity despite *few genes... same genes...*



Tetraodon 22,000



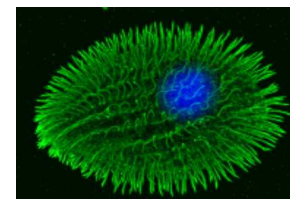
Human 20,000–25,000



Arabidopsis 29,000



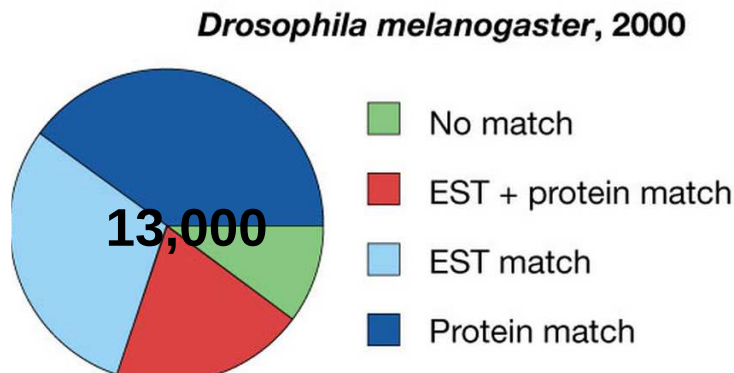
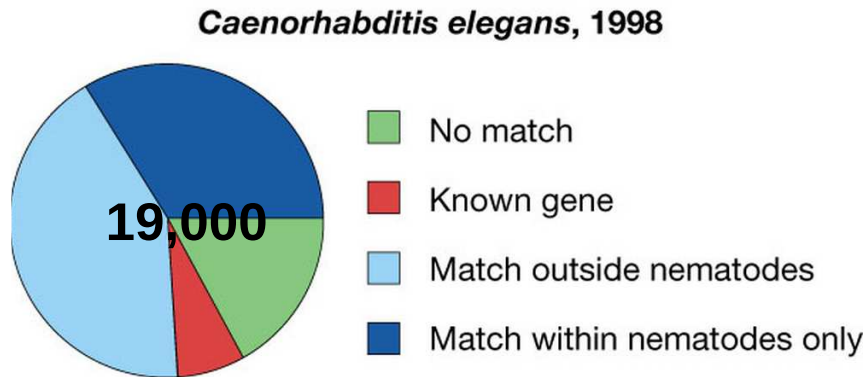
Gallus 20,000–23,000



Paramecium 39,000



Wheat 75,000 ?
(allohexaploid)



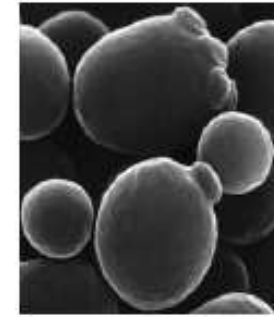
➔ Evolution through Duplication–Divergence of Genes and Genomes

Biological Networks

Project of Genome Sequencing

Number of genes

- Yeast 6000
- Tetraodon (fish) 22000
- Human ~ 25000
- Arabidopsis thaliana (plant) 29000



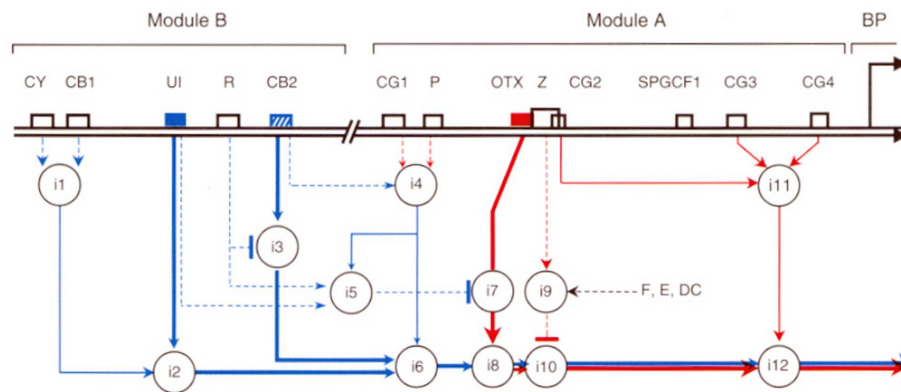
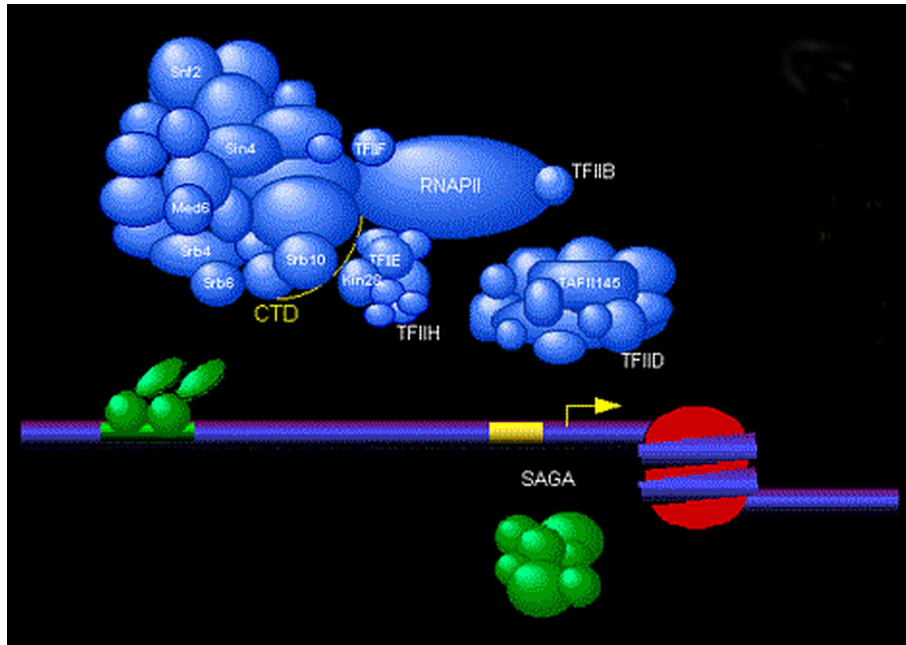
Few genes $\longleftrightarrow^{??}$ Complex processes

Same genes $\longleftrightarrow^{??}$ Great diversity of organisms

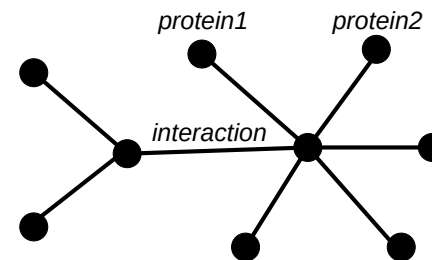
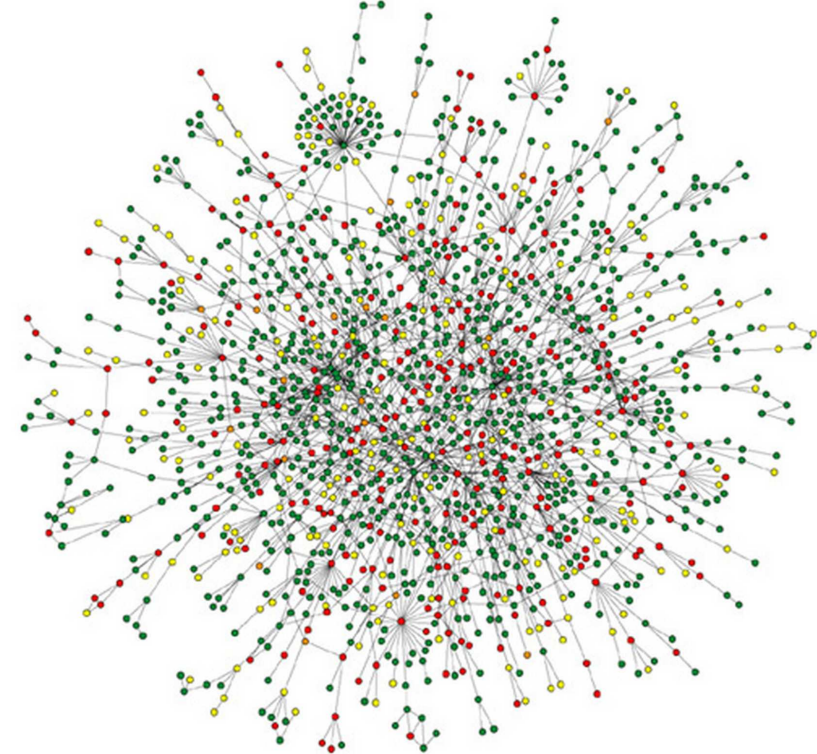
→ **Combinatorics of genes** = Complexity of interactions

Combinatorial Gene Expression

Detailed interaction logic (AND/OR/NOT)



Network-like schematic representations :



Combinatorics
without logic !!

Biological Networks and their Evolution

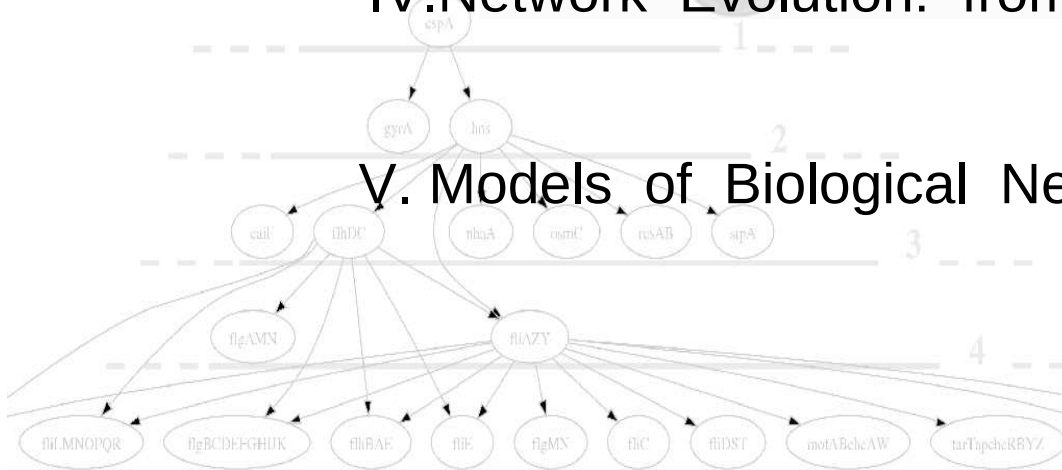
I. Introduction: from Genomes to Networks

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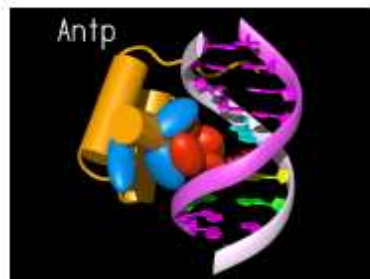
IV. Network Evolution: from Genes to Organisms

V. Models of Biological Network Evolution



Biological Networks

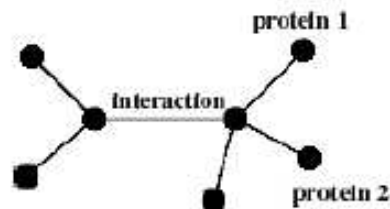
- a) Physical Protein-Protein Interactions
- b) Transcriptional Regulations
transcriptional stimulation/inhibition
- c) Enzymatic Reactions
catalysis of enzymatic reactions
- d) Signal Transduction
physical interactions, enzymatic reactions



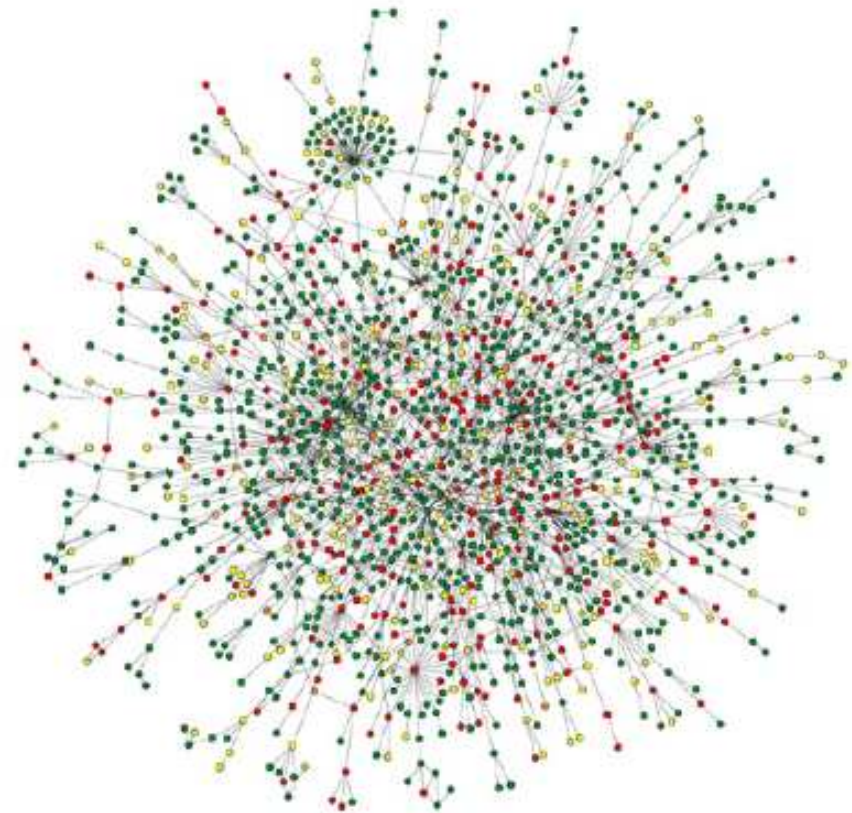
Protein-Protein Interaction Networks

This representation

- Contains direct pairwise interactions
- Does not contain indirect interactions
- is a **non oriented graph**



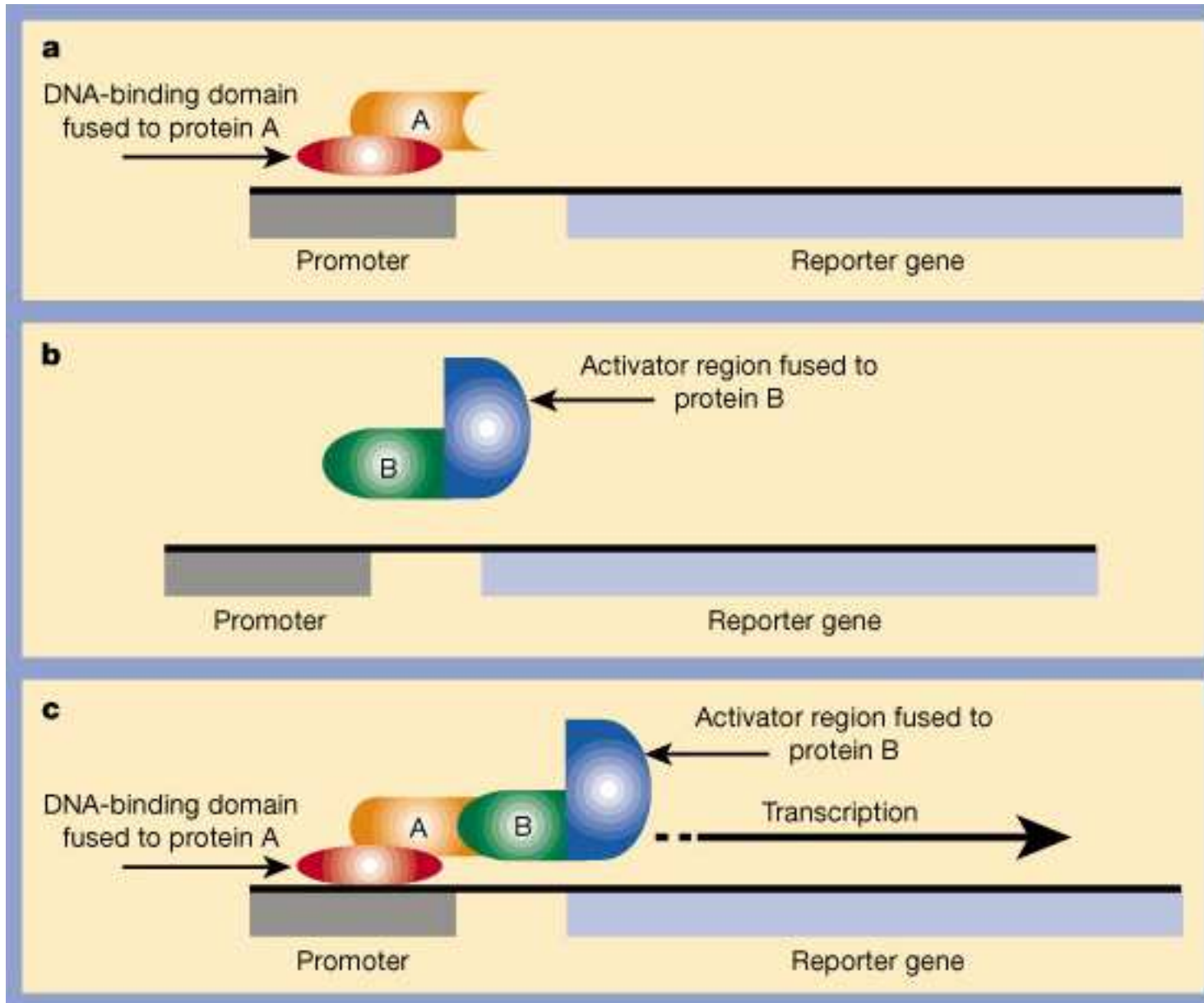
- Experimental methods
yeast two hybrids method
purified complexes



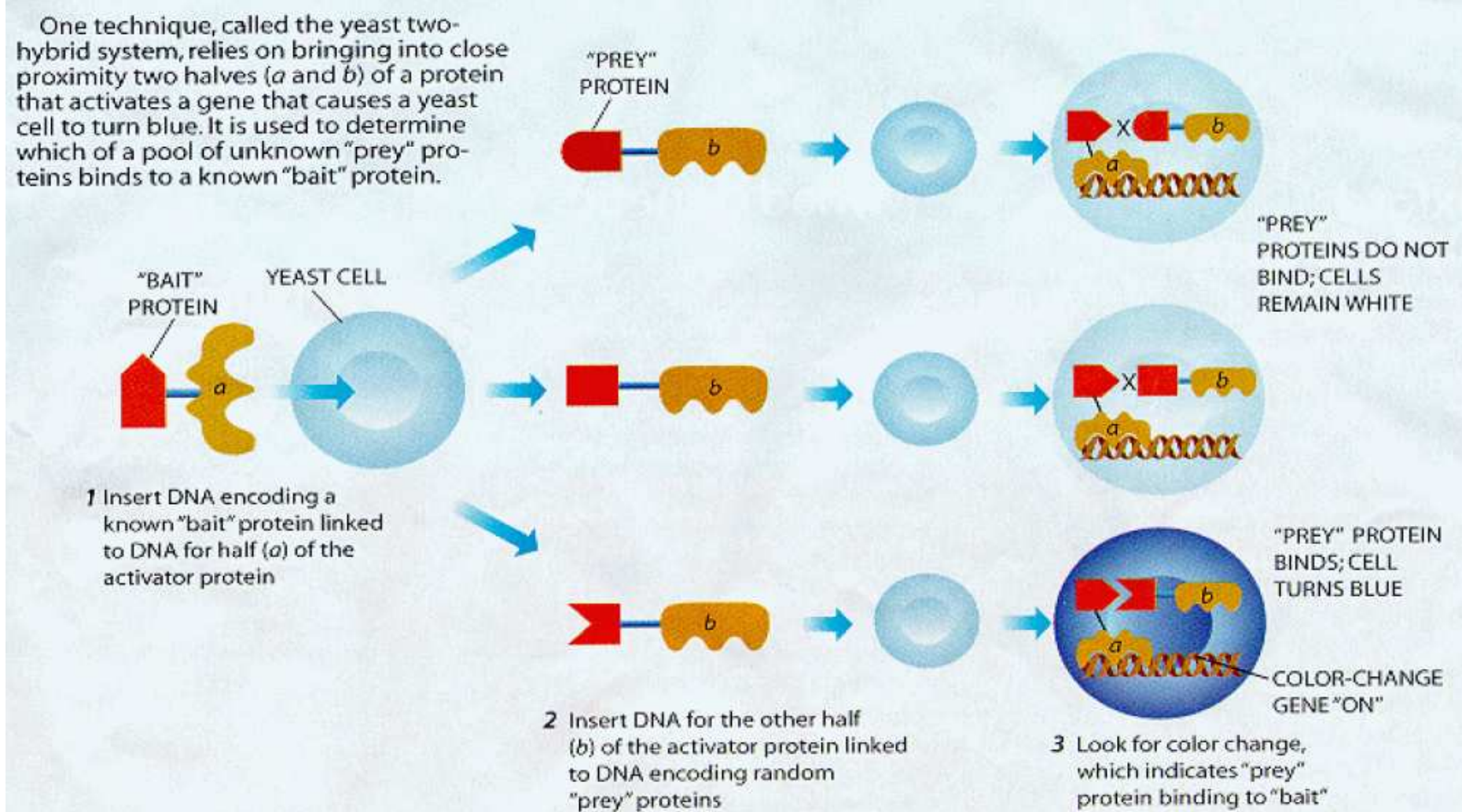
Nature Reviews | Genetics

Protein-protein interaction network
of the Yeast *S. Cerevisiae*
from H. Jeong et al., Nature 411 (2001)

Double hybrid method



Double hybrid method



Other method: Tandem Affinity Purification (TAP) +
Mass spectroscopy of purified protein complexes

Protein-Protein Interaction Networks

Databases

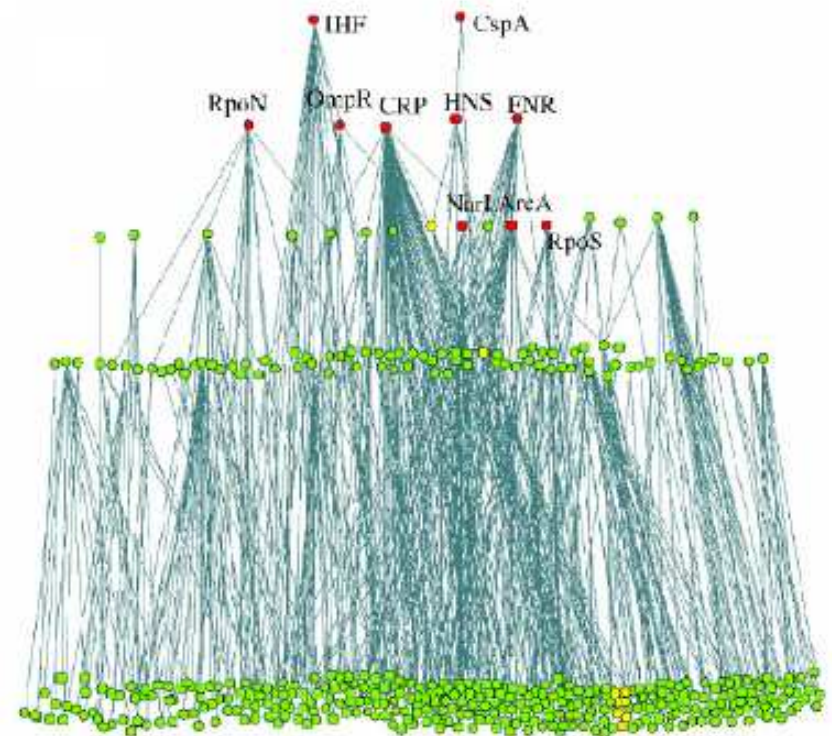
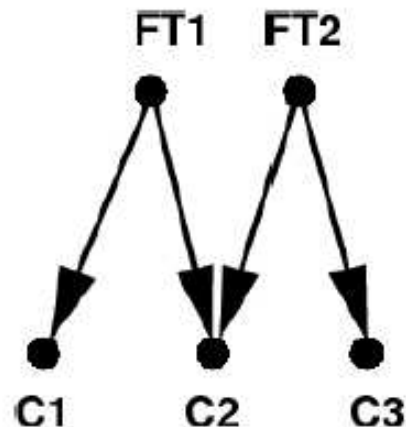
- **BIND** (Biomolecular Interaction Network Database)
various methods, many taxons <http://bind.ca>
- **MPact** of MIPS (Munich Information Center for Protein Sequences)
various methods, yeast *S. Cerevisiae* <http://mips.gsf.de/genre/proj/mpact>
- **DIP** (Database of Interacting Proteins)
various methods, many taxons <http://dip.doe-mbi.ucla.edu>

and many others....

Transcriptional Regulation Networks

This representation

- Contains direct regulational relationships
Transcription Factors → Regulated targets
- Different regulations are independent
- Is an **oriented** graph



Transcriptional regulation
network of *E. Coli*

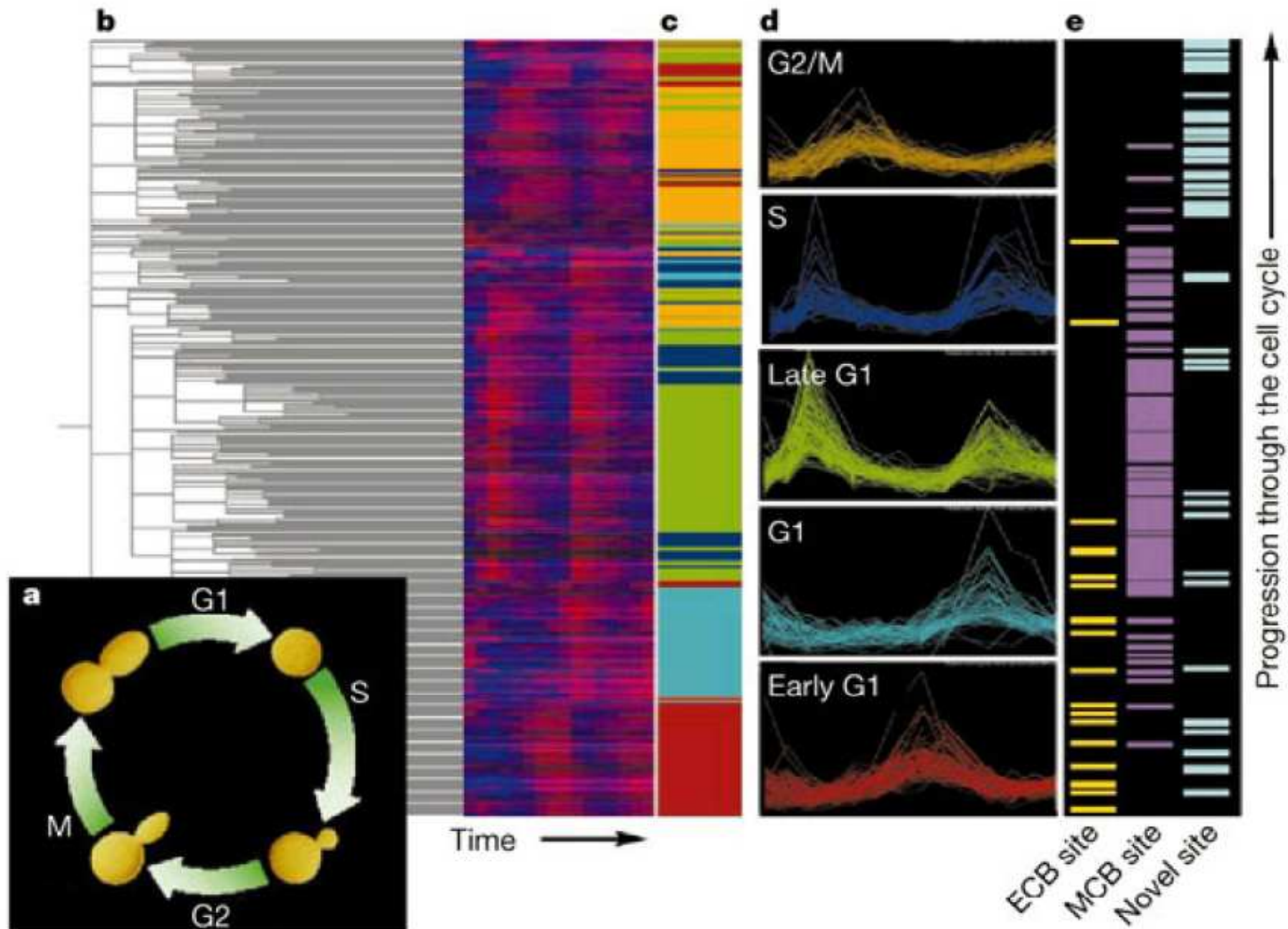
Transcriptional Regulation Networks

Experimental methods: *Chormatin Immunoprecipitation*
Genome-Wide Location analysis

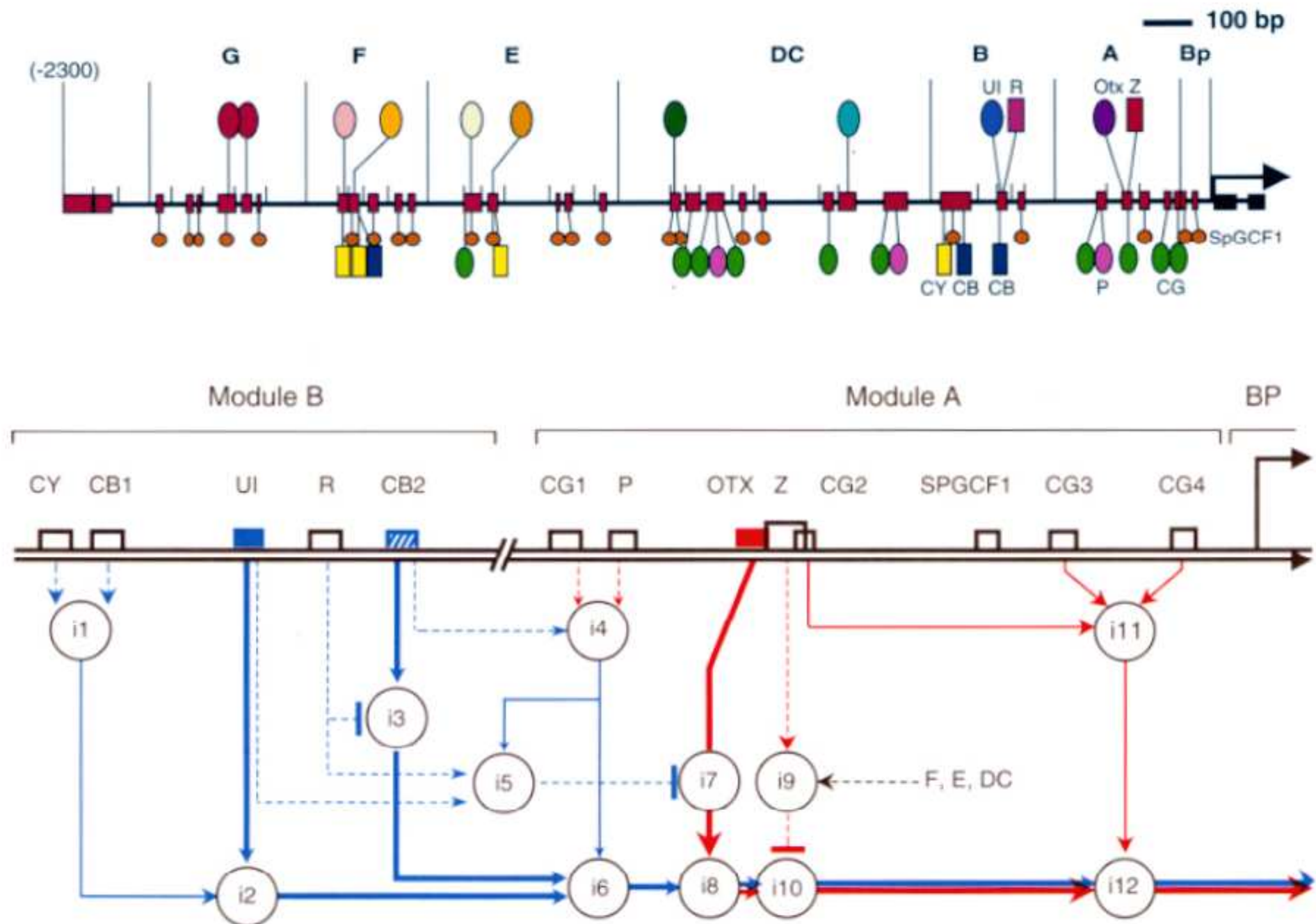
Databases

- **Regulon DB** <http://regulondb.ccg.unam.mx/>
transcriptional regulation of the bacterium *E. Coli*
- **EcoCyc Database** <http://ecocyc.org/>
transcriptional regulation of the bacterium *E. Coli*
- **Data of publications**
Uri Alon's group (*E. Coli* & *S.Cerevisiae*)
Data of Lee *et al.*(2002) (GWLA for *S.Cerevisiae*)
Data of Balaji *et al* (2006) (*S.Cerevisiae*)

Exemple: analyse du cycle cellulaire de la levure



Exemple : développement de l'oursin de mer



A1



A2



A3



A4



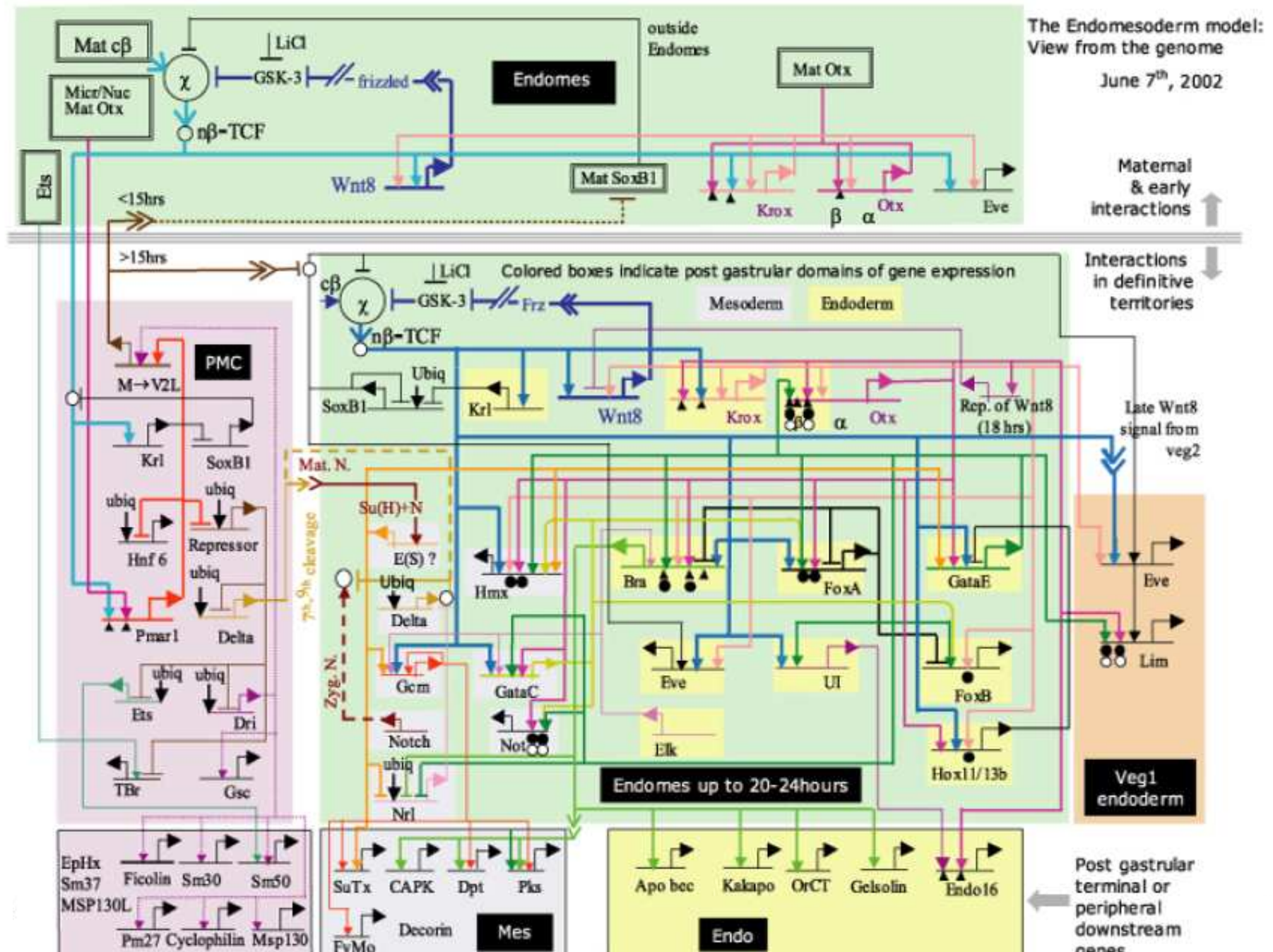
A5



A6

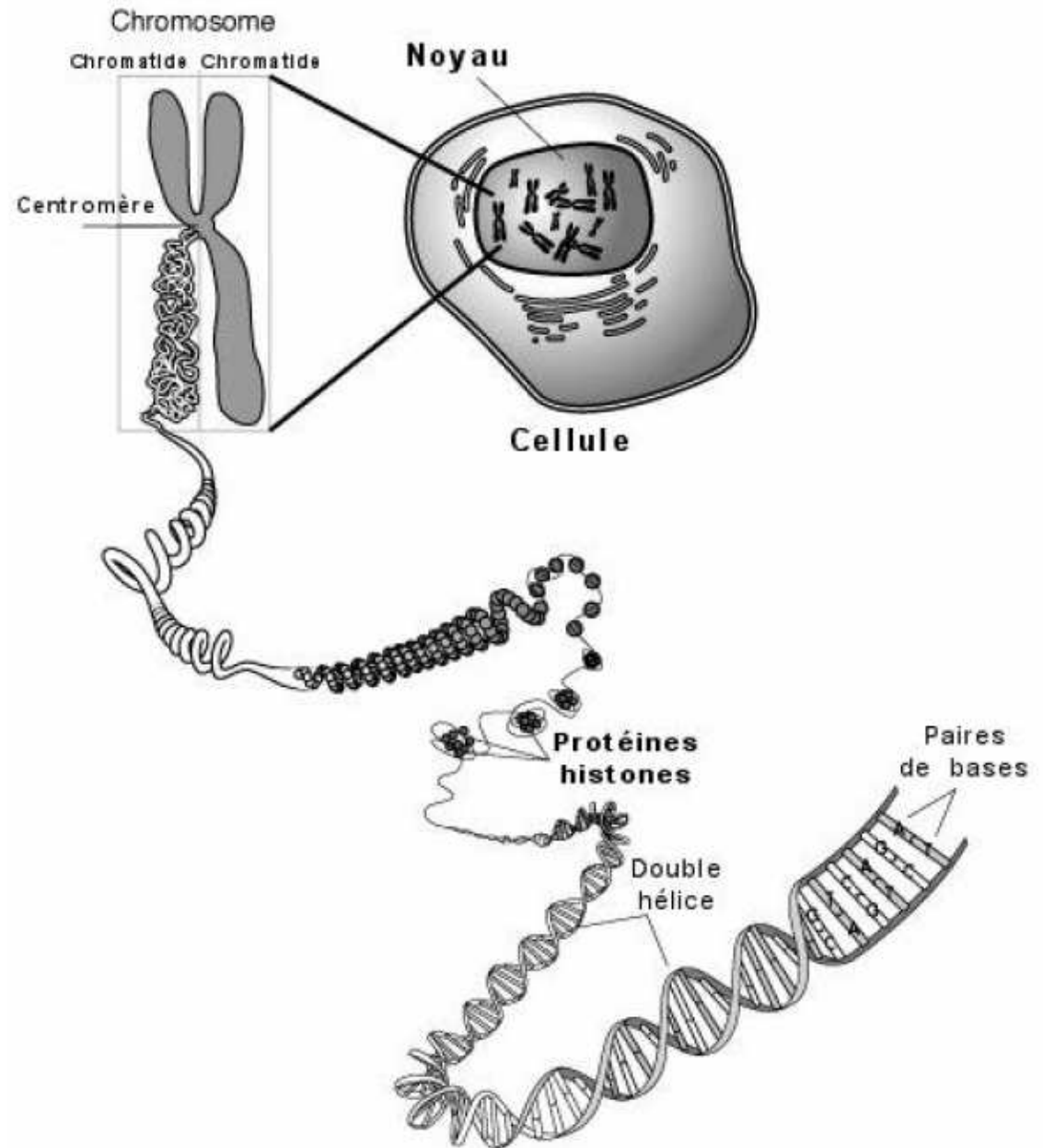


Circuit de gènes dans le développement de l'oursin de mer

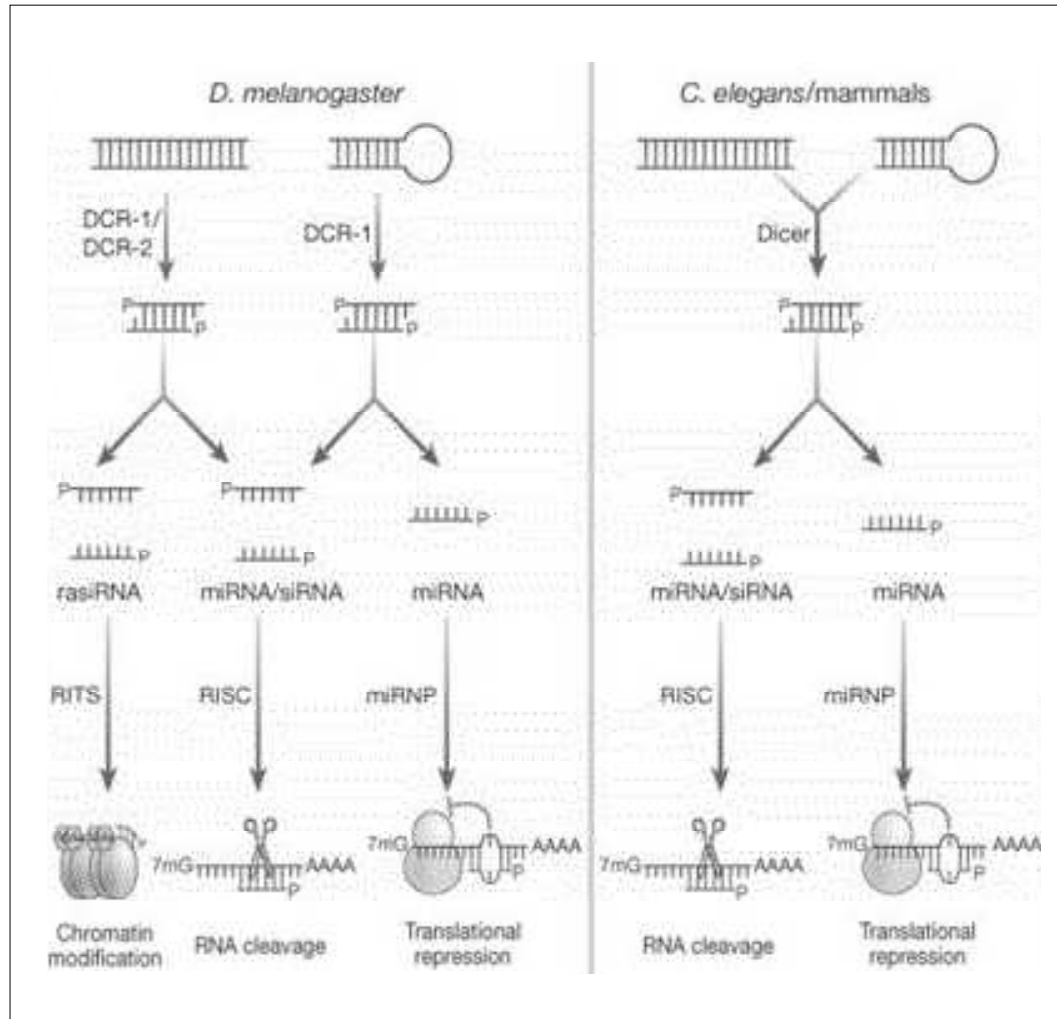


Silencing and Epigenetics Regulation

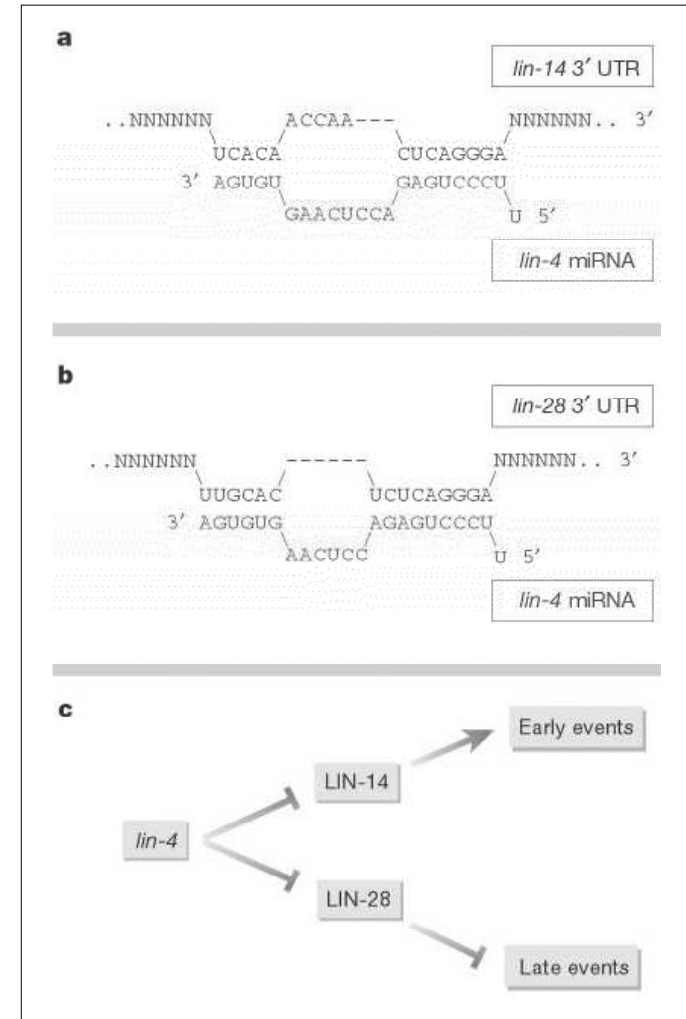
Chromatine Structure



Post-transcriptional regulation through RNA Interference

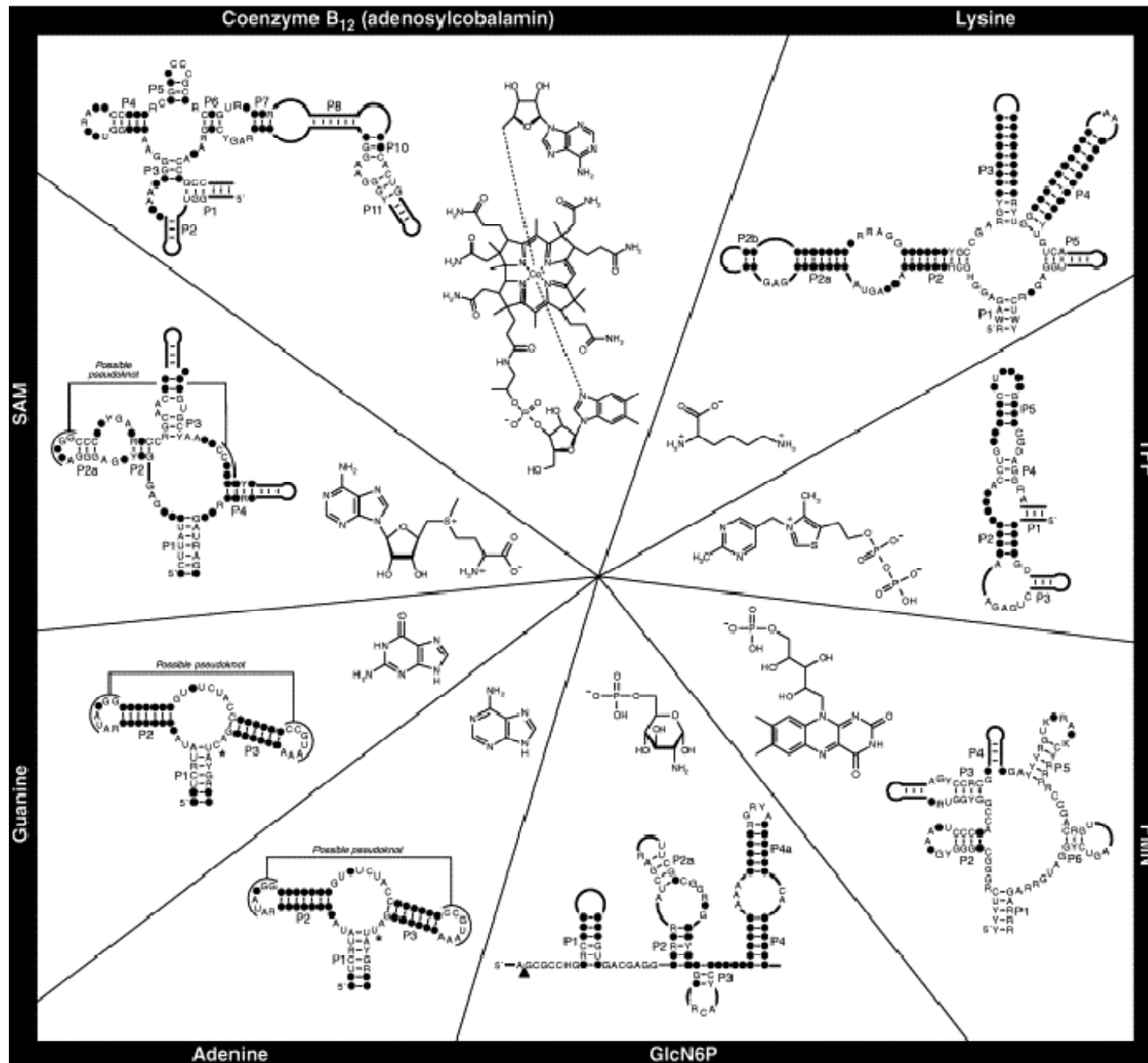


RNA silencing pathways in different organisms
(Meister & Tuschl, Nature, sept 2004)



miRNAs (*lin-4/let-7*) in developmental timing
of *C. elegans* (Cell, 1993; Nature, 2000)

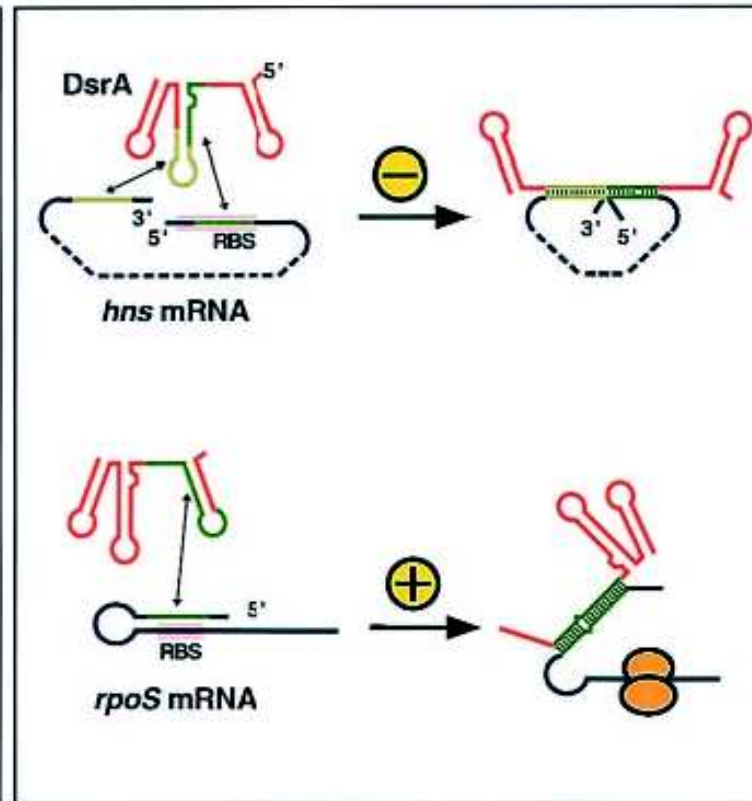
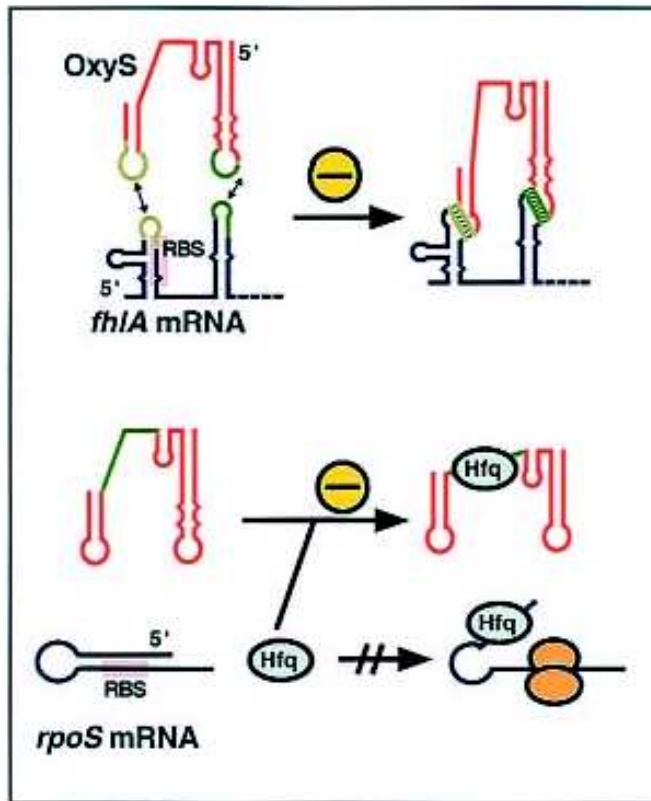
Riboswitches (metabolite-induced conformational change)



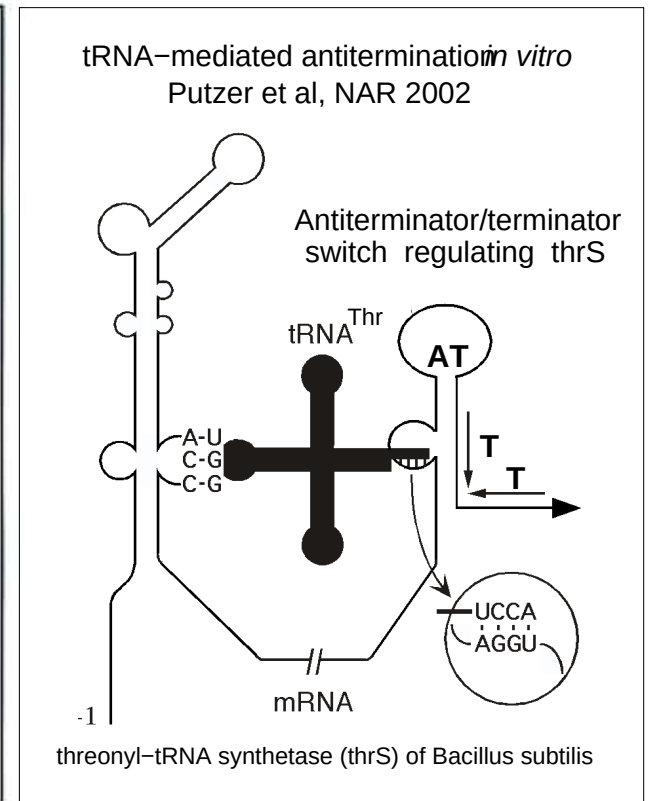
Breaker et al.
2002–2004

RNA-based regulation through RNA switch control

Escherichia coli



Bacillus subtilis



→ combine : antisense interaction + structural switching

Switches and Networks

regulatory networks

physical networks

RNA1

RNA2

RNA3

100 nm

Alexandre Dawid

The image is a composite. On the left, a schematic diagram of a 'regulatory network' shows three RNA molecules: RNA1 (black), RNA2 (black), and RNA3 (red). RNA1 has a dashed arrow pointing to RNA2, and RNA2 has a solid black arrow pointing to RNA3. RNA3 has a red T-bar arrow pointing to RNA1. On the right, a micrograph of a 'physical network' shows a complex, interconnected network of yellowish-brown filaments with bright spots at the nodes. A scale bar in the bottom right corner indicates '100 nm'. At the bottom center, there is a small portrait of a man with grey hair, identified as Alexandre Dawid.

The diagram illustrates the concept of cis/trans control in RNA folding. It shows two alternative secondary structures for an RNA sequence, connected by a double-headed arrow labeled "cis / trans control".

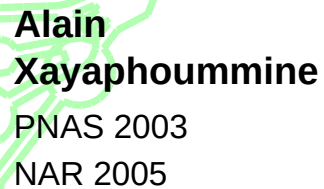
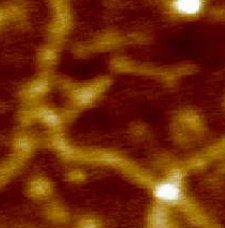
Left Structure (Compact Fold):

- Top: A A
- Stem 1 (left): C • G, C • G, G • U, U • A, C • G, C • G, C • G, C • G, U • A, G • U, C • G, C • G
- Stem 2 (right): G A A G, C, U • A, C • G, C • G, U • A, C • G, U • A, C • A, C • G
- Bottom: 5' A A A G C A 3'

Right Structure (Extended Fold):

- Top: A A A G
- Stem 1 (left): G • C, U • A, A • U, G • C, G • U, G • C, G • C, U • A, U • A, U • A, G • C
- Stem 2 (right): G A A G, A A A, C • G, G • C, U • A, C • G, C • G, C • G, C • G, U • A, G • C, C • G
- Bottom: 5' A C A 3'

Diagram illustrating the interaction of three RNA molecules (RNA1, RNA2, and RNA3) with a green protein structure. RNA1 is shown as a black dashed line with an arrow pointing to the protein. RNA2 is shown as a black solid line with an arrow pointing to the protein. RNA3 is shown as a red solid line with an arrow pointing away from the protein.



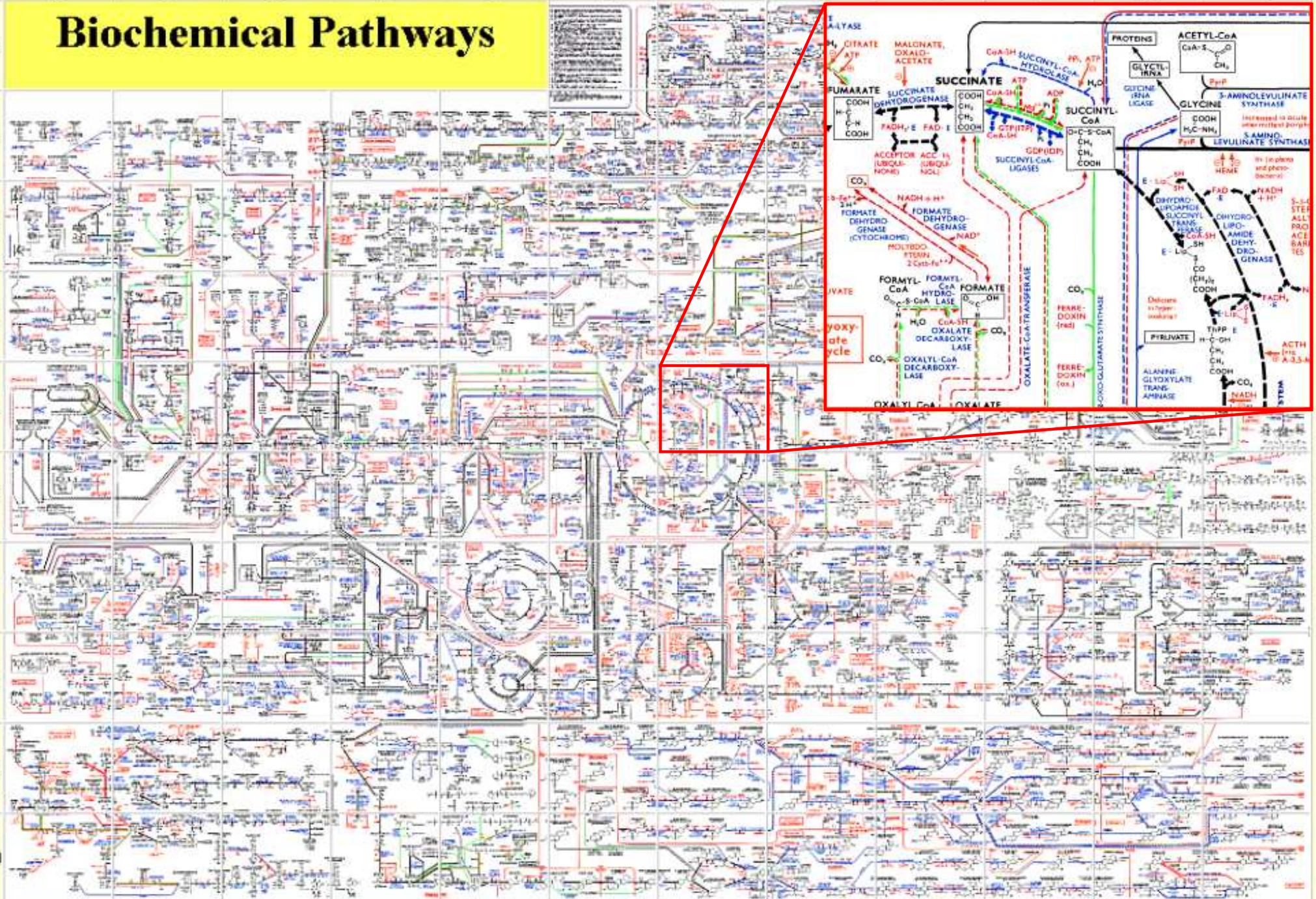
**Alexandre
Dawid**
Phys Biol 2009



JACS 2009

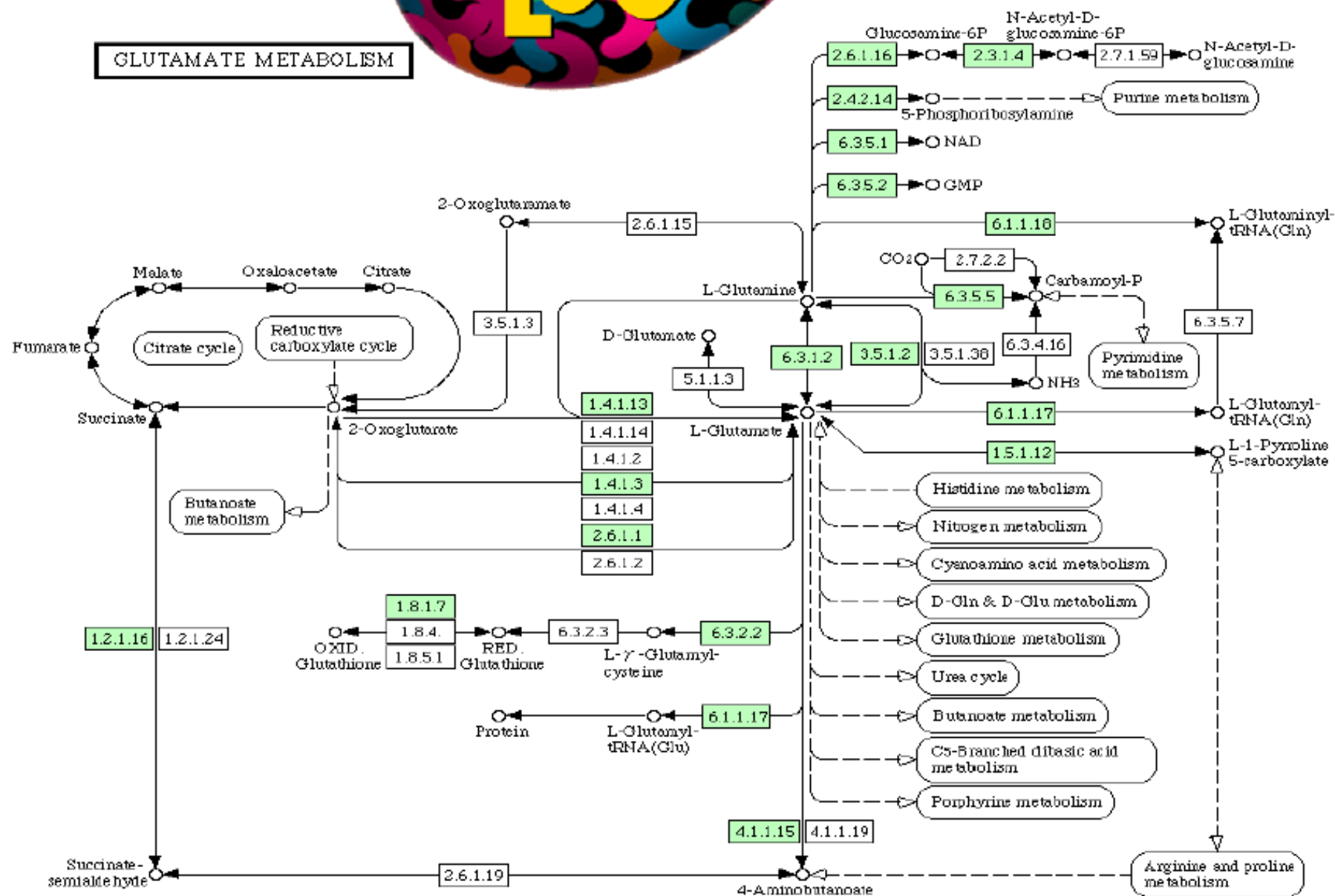
Biochemical Pathways

2
3
4
5
6
7
8
9
10



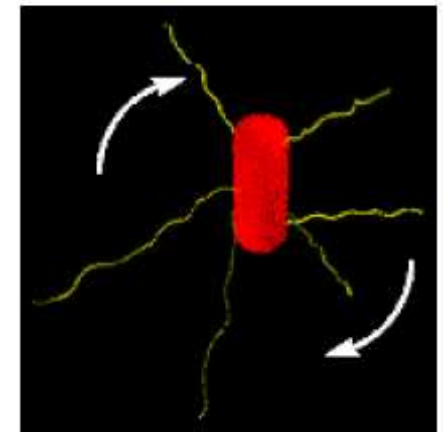
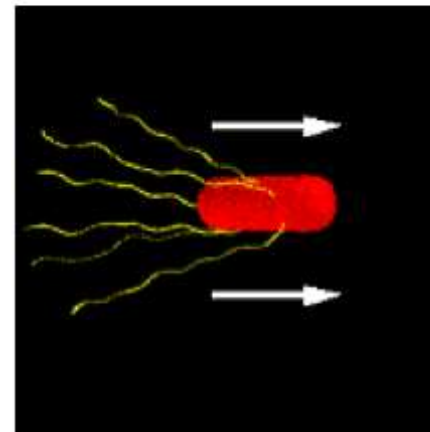
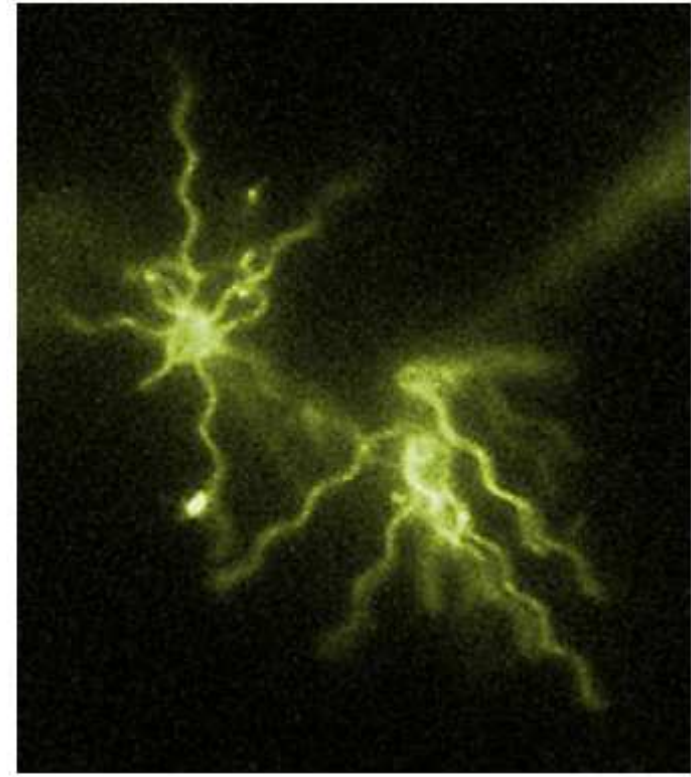
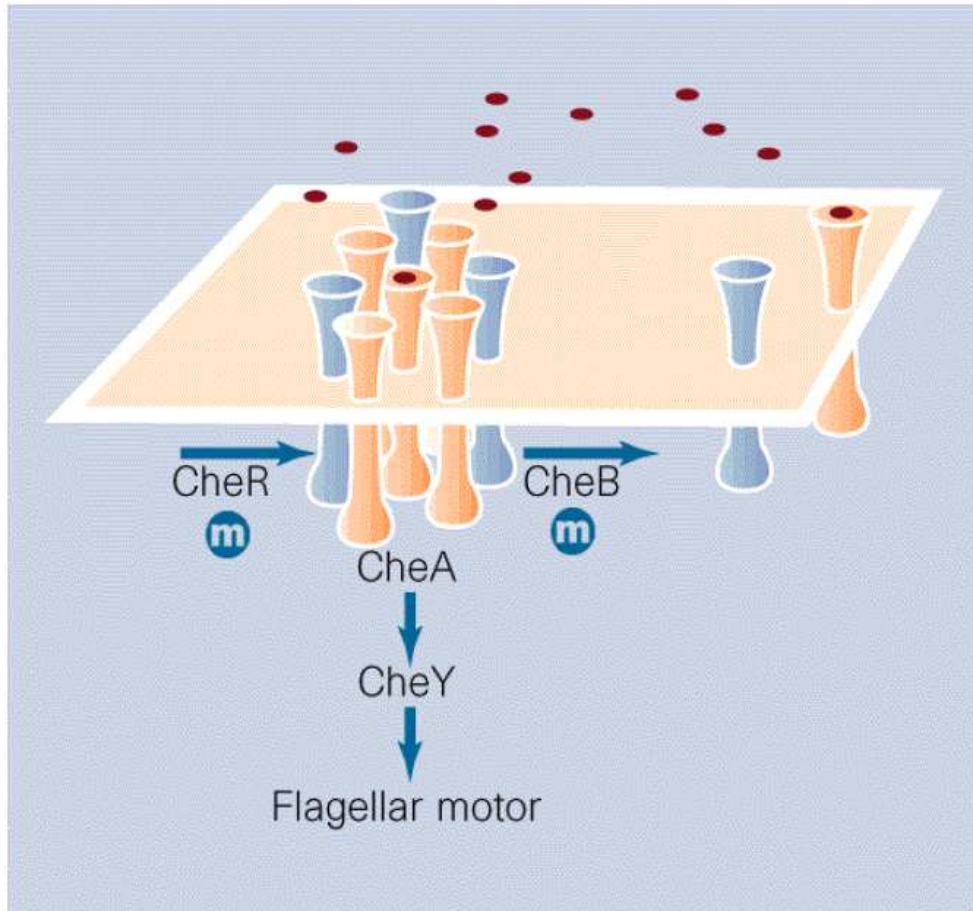


GLUTAMATE METABOLISM

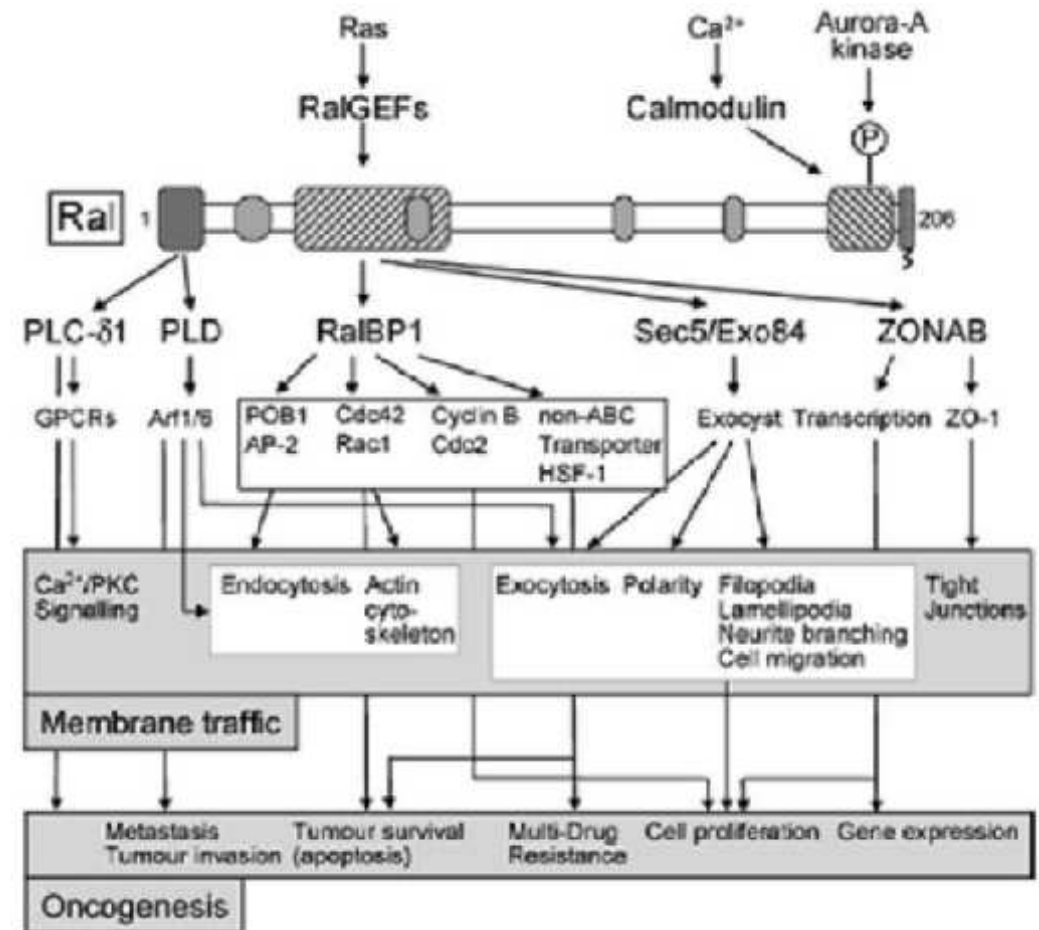
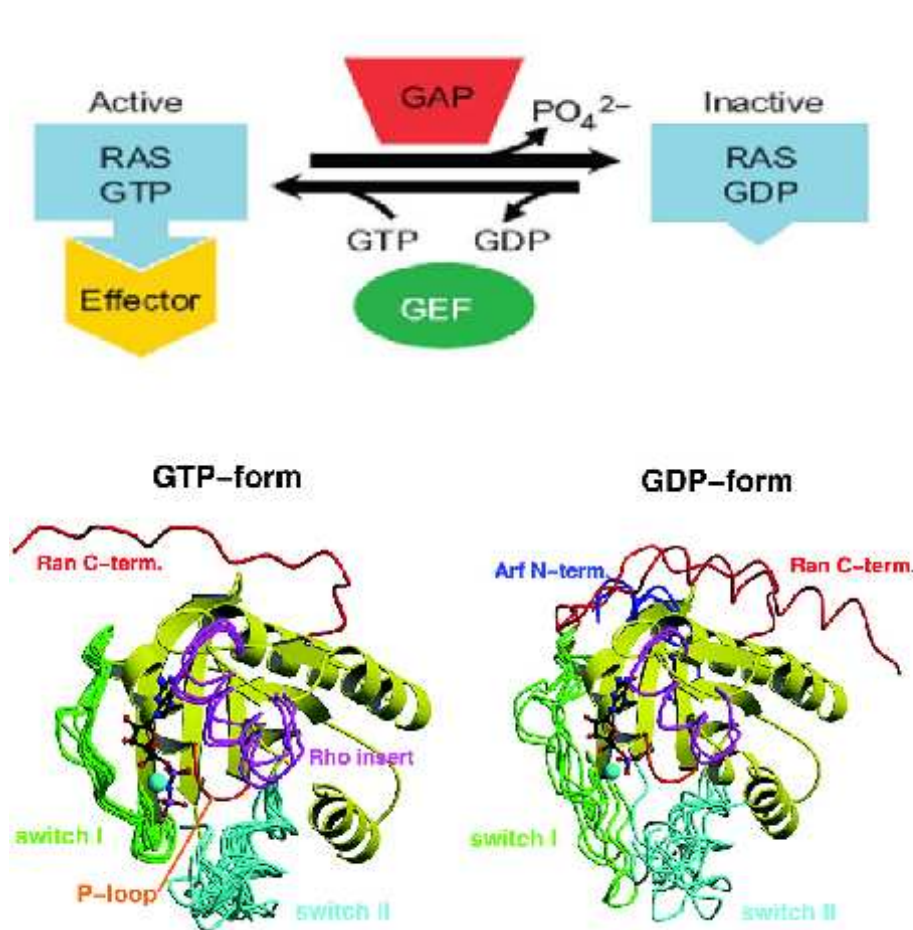


Signal Transduction Networks

Example : chemotaxis



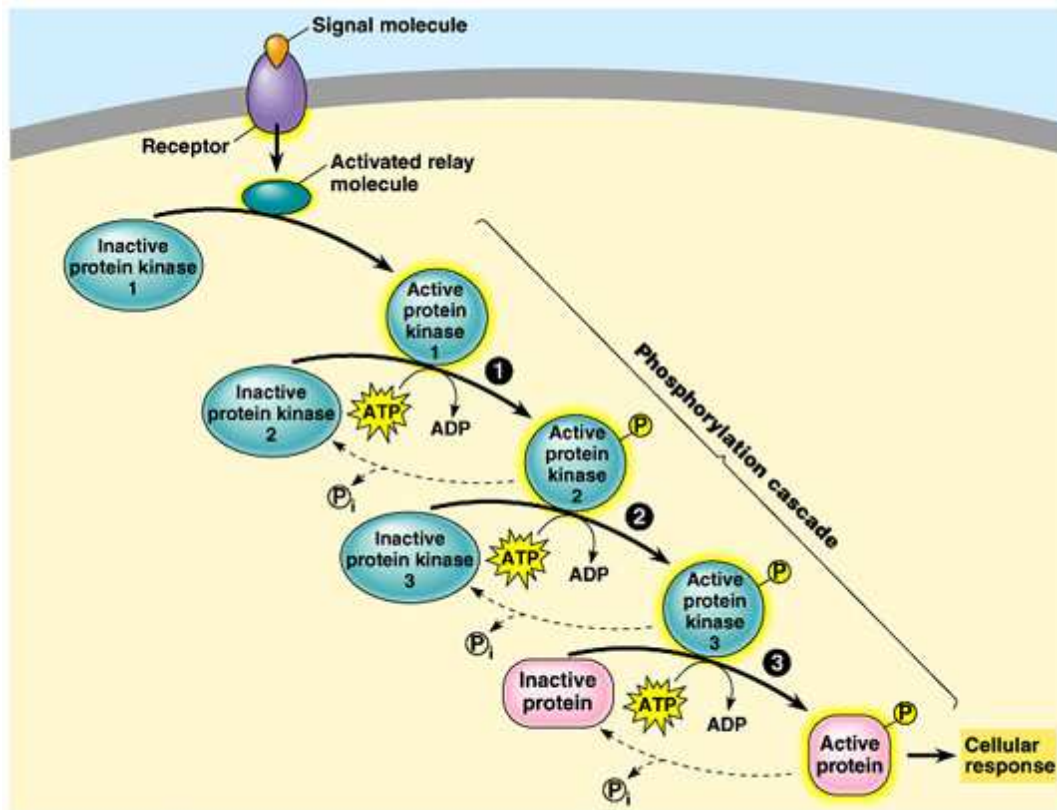
RAS Signaling Pathways



→ cytokinesis / adhesion / mobility → cancer

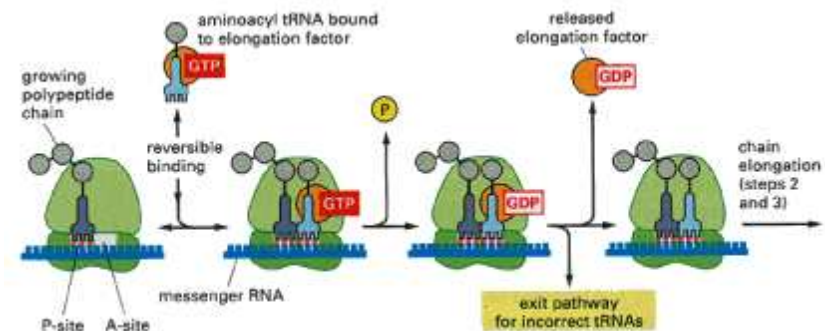
Kinetic Proof Reading behind Irreversible Steps

Phosphorylation cascades



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Translation Error Corrections



Biological Networks and their Evolution

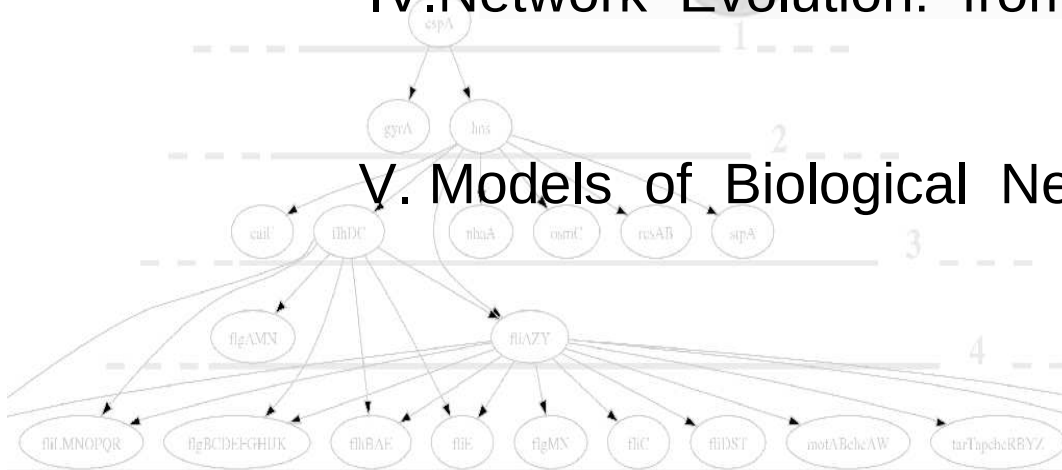
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Topology of Biological Networks

Numbers of links, nodes, nodes of a given degree k

$$L, N, N_k$$

(global quantities)

Degree distribution p_k

$$p_k = \frac{N_k}{N}, \quad \langle k \rangle = \sum_{k \geq 1} k p_k = \frac{2L}{N}$$

Mean degree $\langle k \rangle$

(local quantities, 1st neighbours only)

Average connectivity of neighbours g_k

$$g_k = \frac{\sum_{i: n. of (k)} d_i}{k N_k}$$

(2nd neighbours)

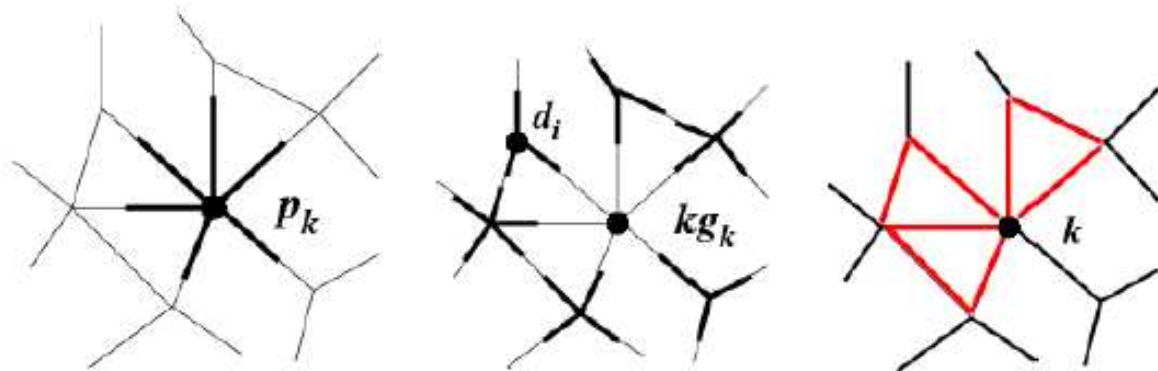
Clustering coefficient C_k

$$C_k = \frac{2N_{\Delta, k}}{k(k-1)N_k}$$

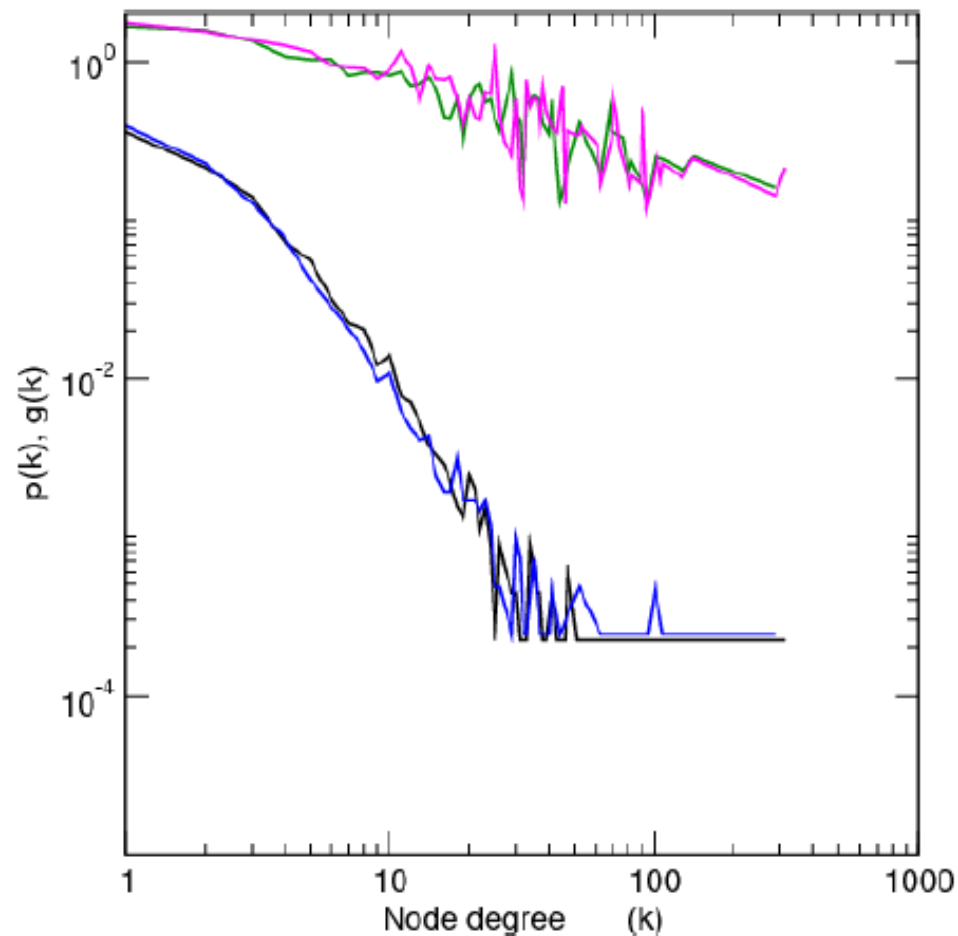
(local topology)

Motifs

*(topology at
a greater scale)*



Yeast Protein-Protein Interaction Network



BIND (version 11/08/2005)

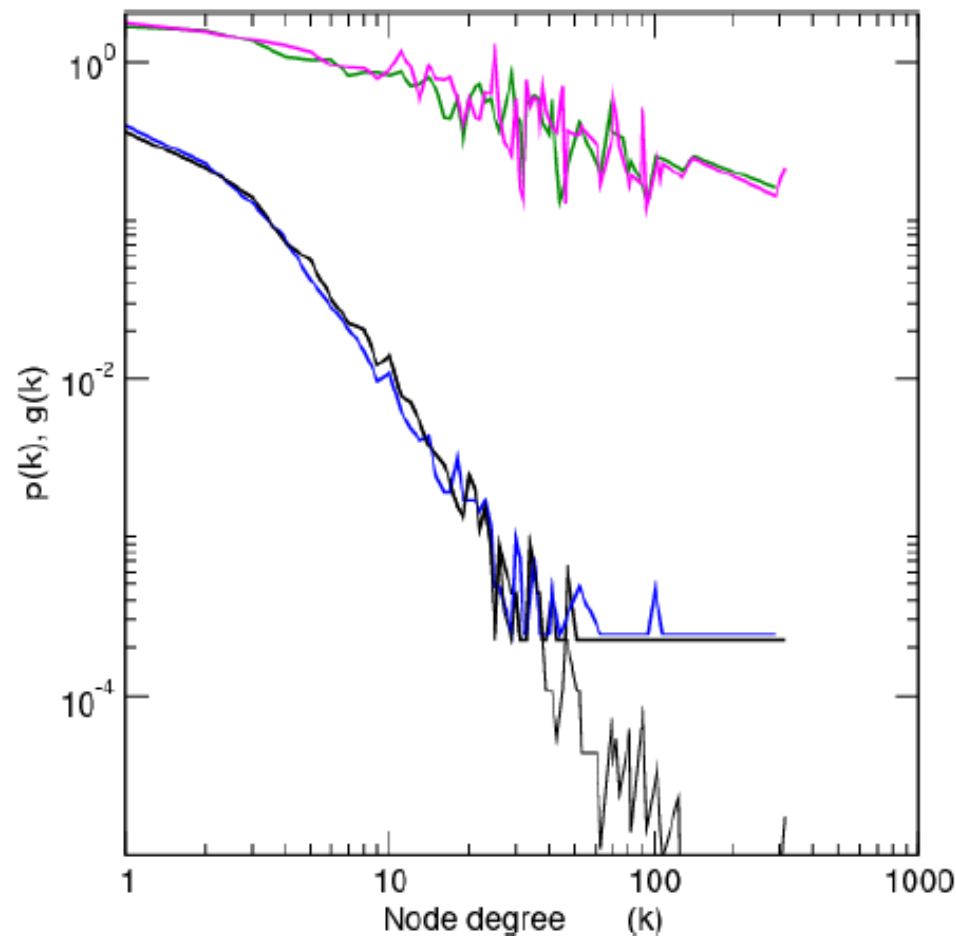
$N=4576$, $L=9395$, $N_{\Delta}=4228$, $\langle k \rangle=4.03$

Mpact

$N=4153$, $L=7417$, $N_{\Delta}=1799$, $\langle k \rangle=3.57$

Comparison MPact/BIND
PPI Network of Yeast *S. Cerevisiae*

Yeast Protein-Protein Interaction Network



BIND (version 11/08/2005)

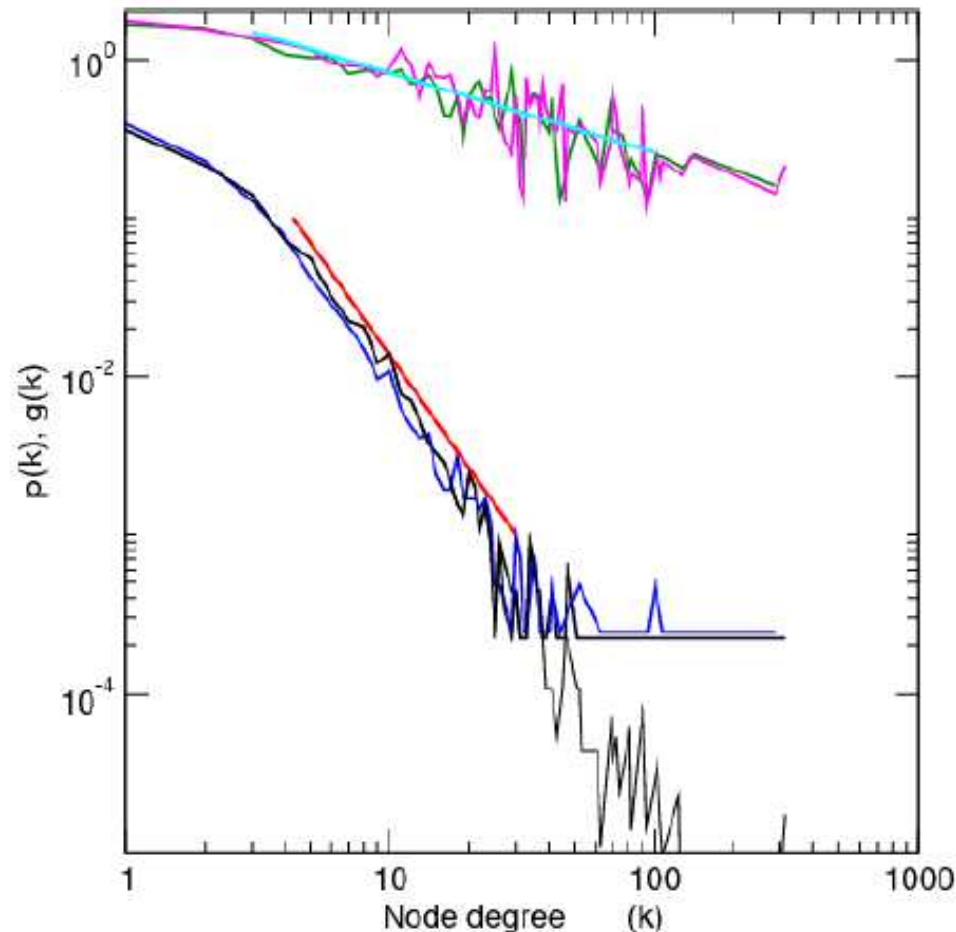
$N=4576$, $L=9395$, $N_{\Delta}=4228$, $\langle k \rangle=4.03$

Mpact

$N=4153$, $L=7417$, $N_{\Delta}=1799$, $\langle k \rangle=3.57$

Comparison MPact/BIND
PPI Network of Yeast *S. Cerevisiae*

Yeast Protein-Protein Interaction Network



Comparison MPact/BIND
PPI Network of Yeast *S. Cerevisiae*

BIND (version 11/08/2005)

$N=4576$, $L=9395$, $N_{\Delta}=4228$, $\langle k \rangle=4.03$

MPact

$N=4153$, $L=7417$, $N_{\Delta}=1799$, $\langle k \rangle=3.57$

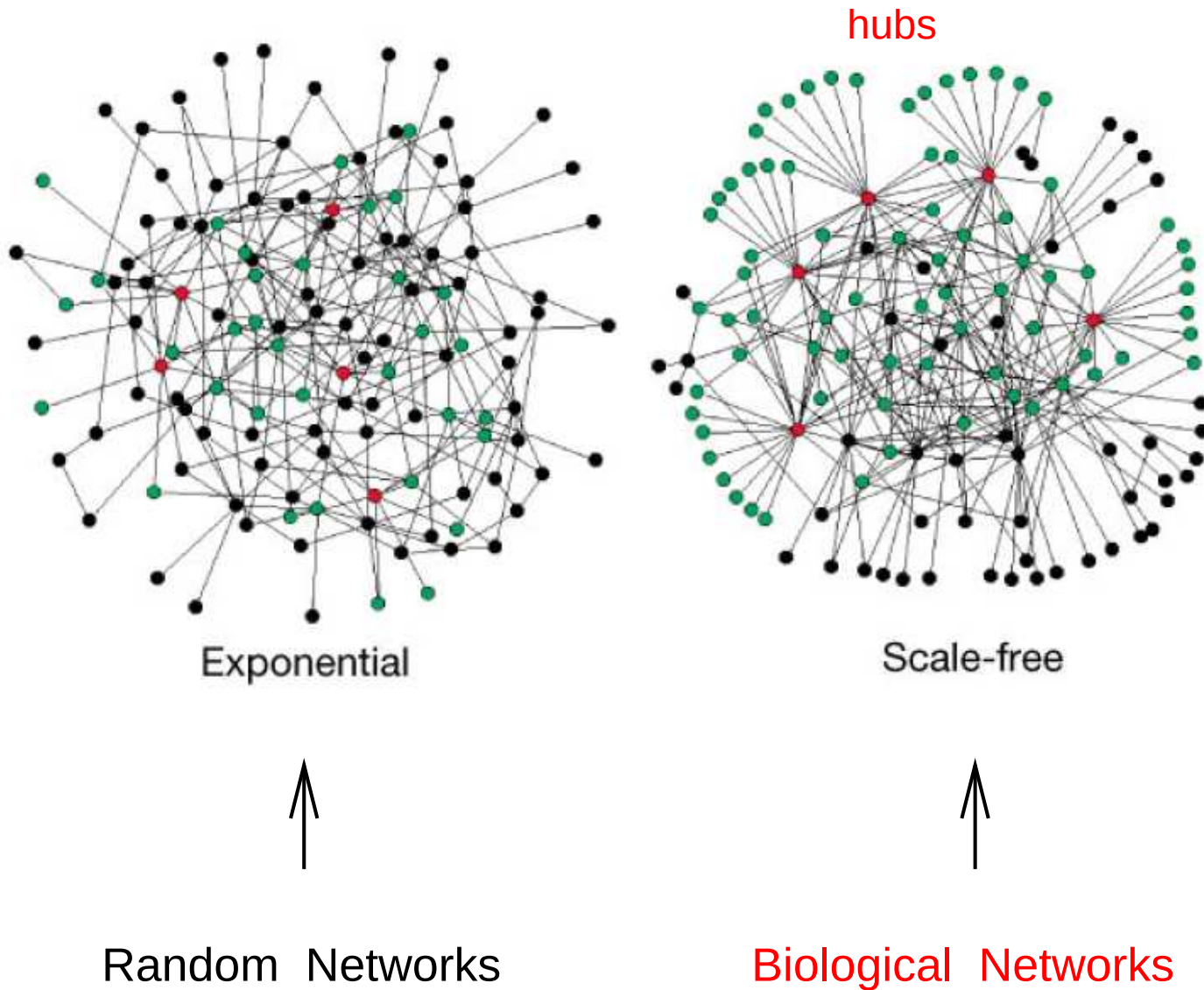
Approximative power law

$$p_k \propto k^{-\alpha-1}, \quad \alpha \sim 2.5$$

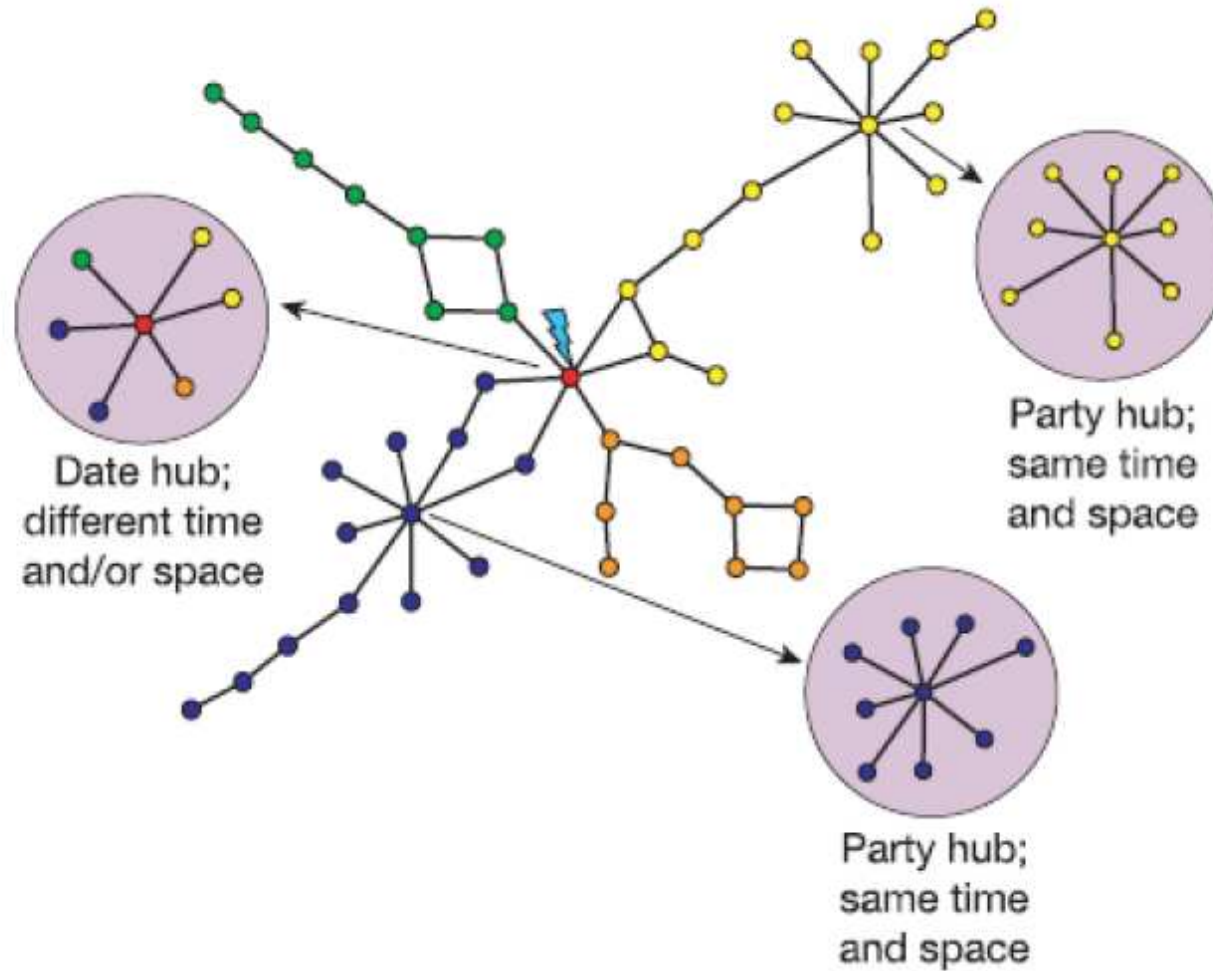
$$g_k \propto k^{-\delta-1}, \quad \delta \simeq -0.2$$

These networks are
not random!!!!

Exponential versus Scale-free Network Topology

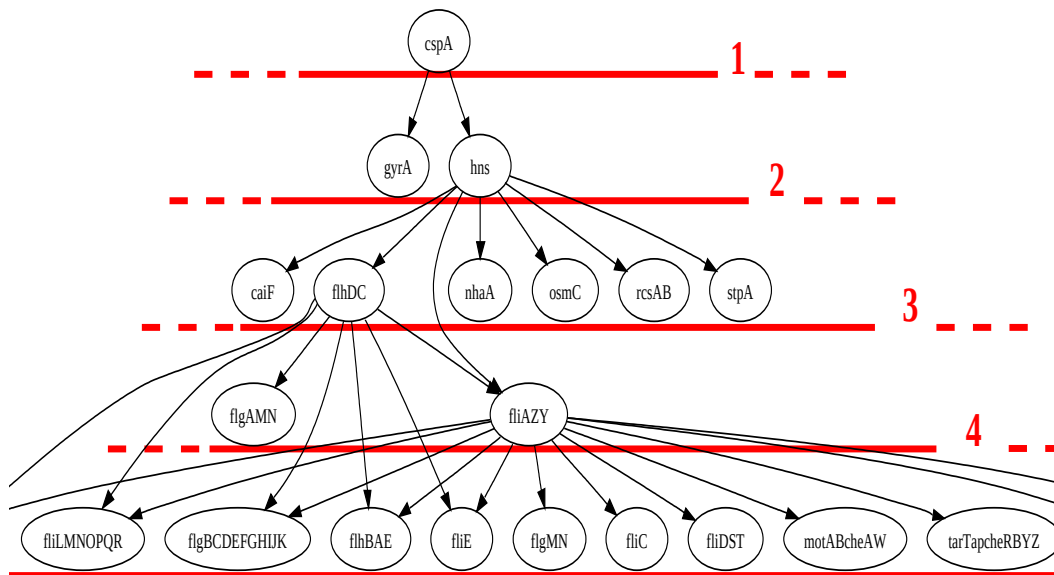


Modularity of Protein Interaction Networks

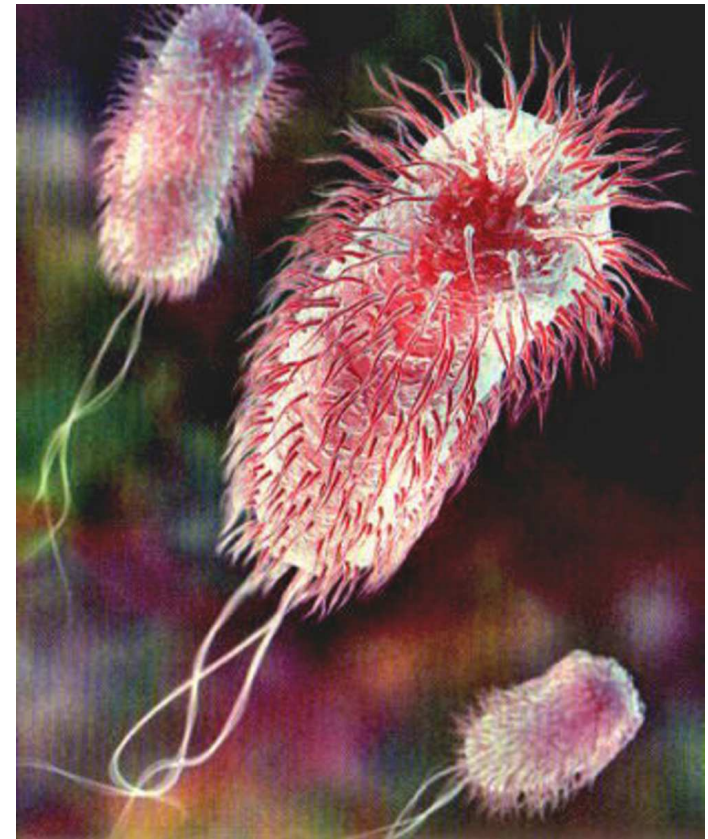


Topology of Bacterial Transcription Networks

E.coli shallow Transcription Network



No large scale feedbacks
but 60% autoregulators (AR)

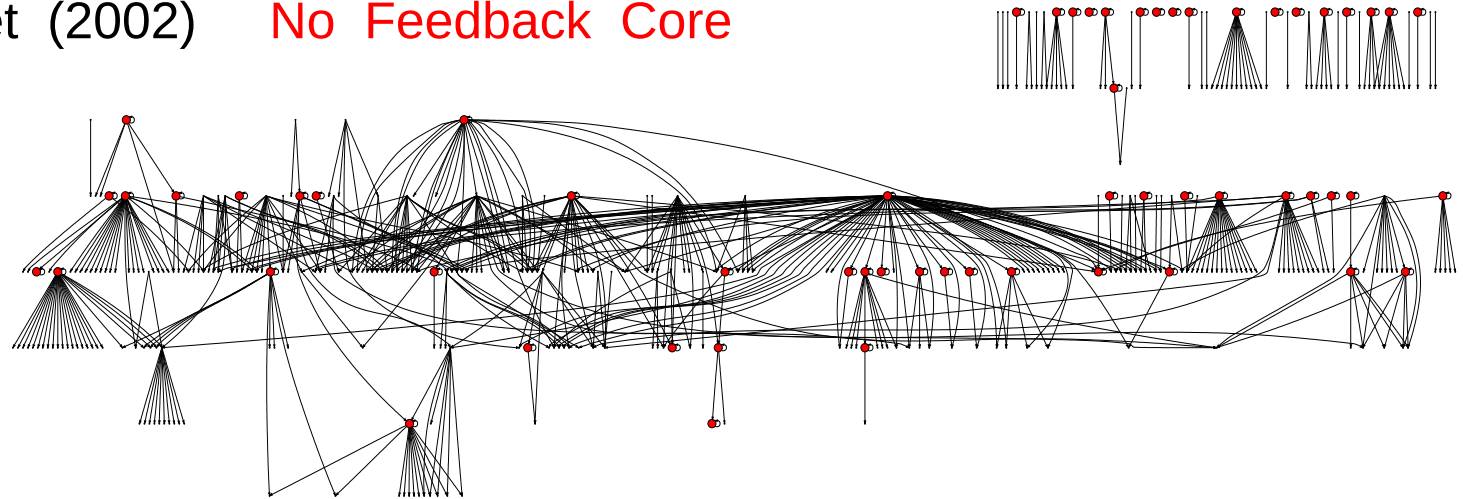


Hierarchy with Mostly Self-Regulatory Feedback

Shen-Orr Dataset (2002)

No Feedback Core

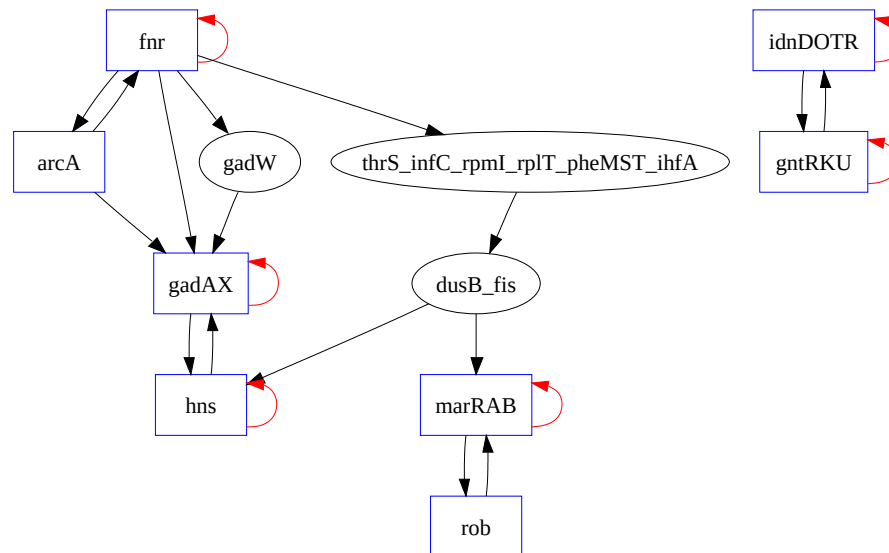
Operons : 423
TFs : 117
ARs : 59 (50% TFs)
Reg Int : 578



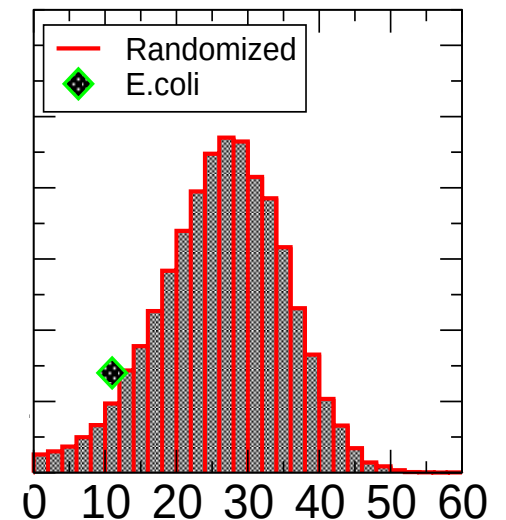
RegulonDB 5.5 (2006)

Small Feedback Core

Operons : 648
TFs : 147
ARs : 85 (58% TFs)
Reg Int : 1170



Feedback Core Sizes



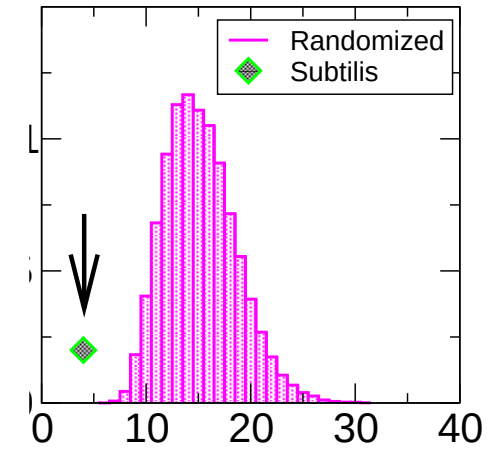
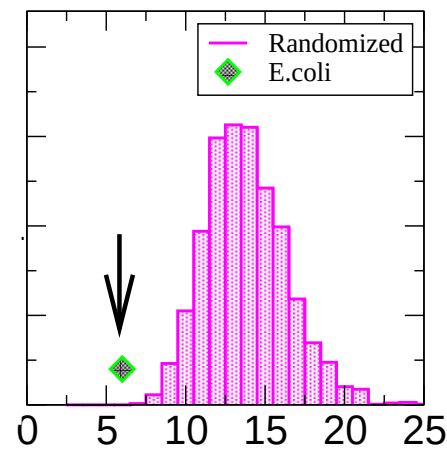
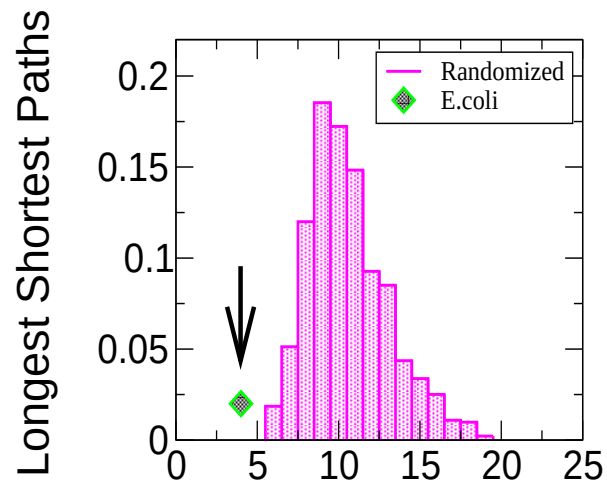
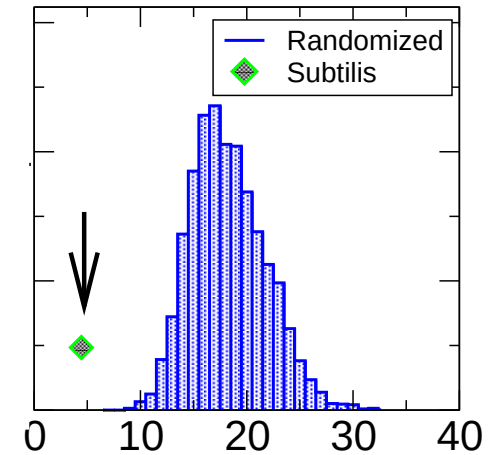
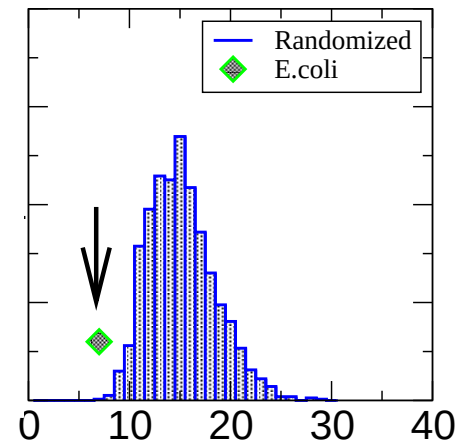
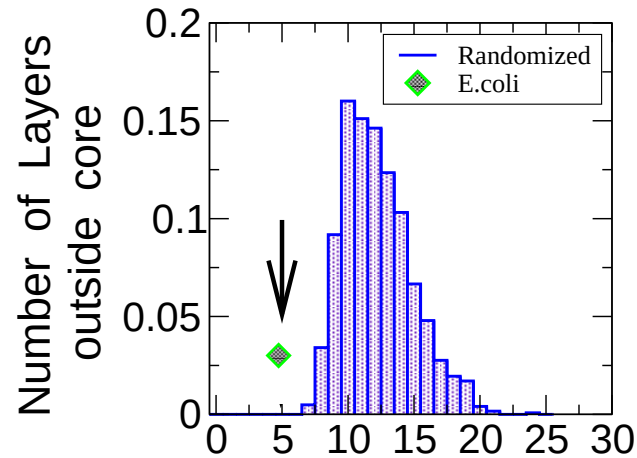
Hierarchy with few Transcriptional Layers

Escherichia coli

Bacillus subtilis

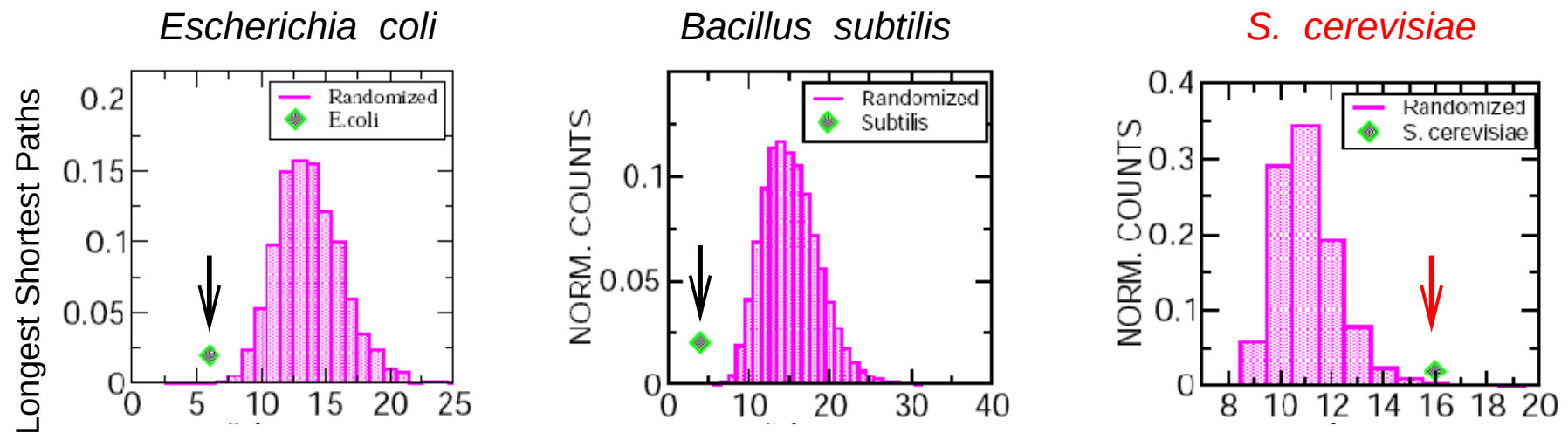
Shen Orr et al (2002)

RegulonDB 5.5 (2006)



Bacteria versus Eukaryote Transcriptional Hierarchy

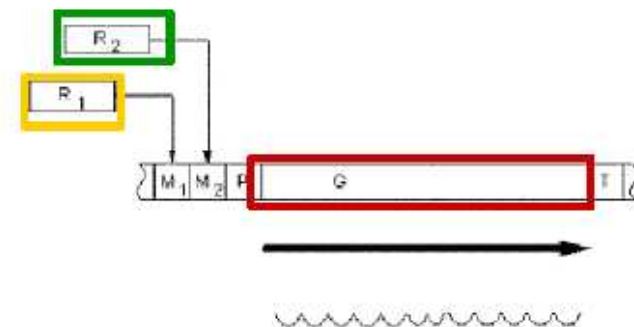
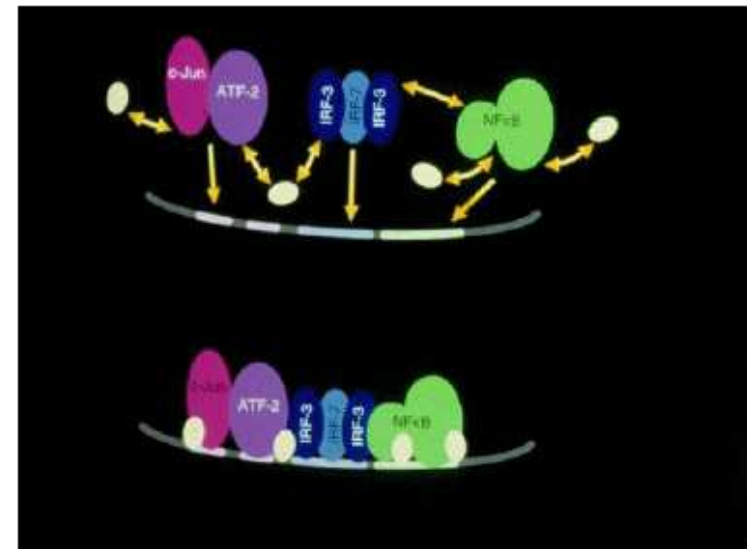
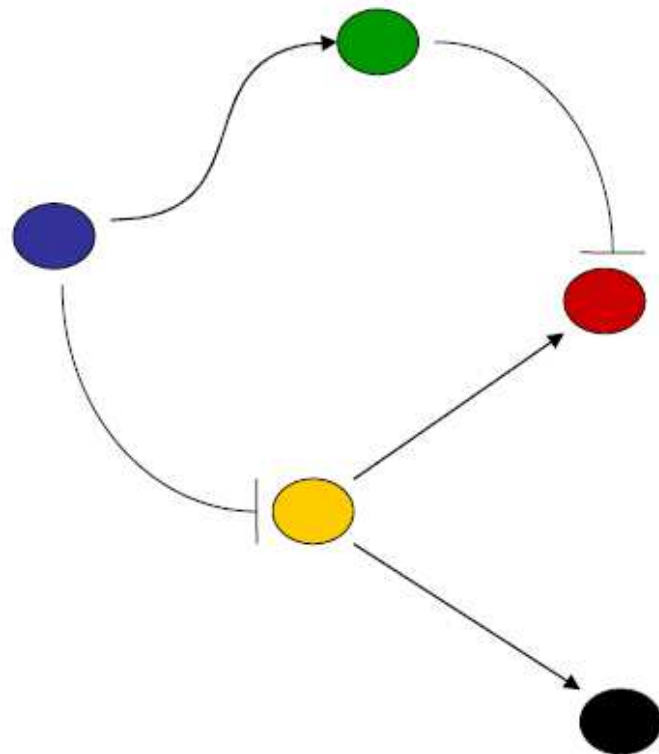
S. cerevisiae has long transcriptional cascades
while bacteria have short ones



Cosentino-Lagomarsino, Jona, Bassetti & Isambert, PNAS 2007

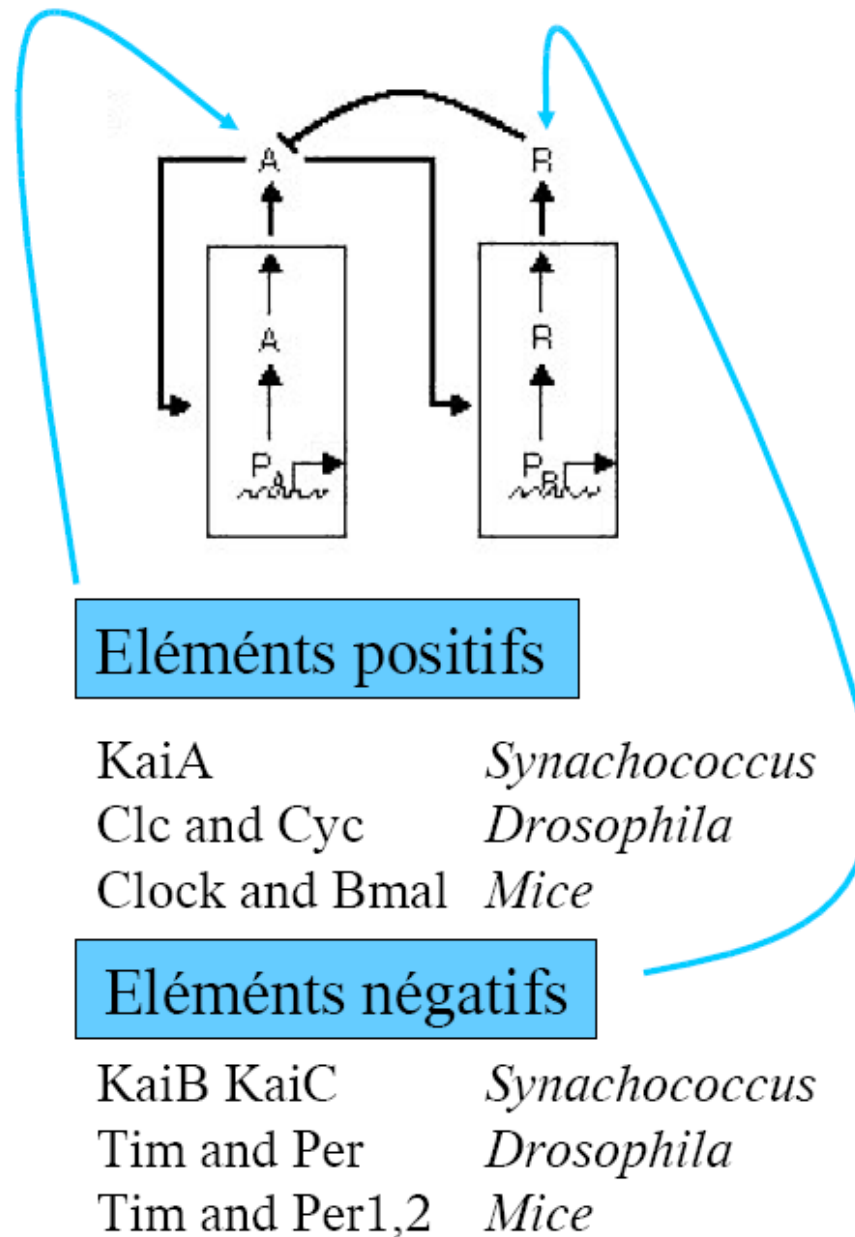
Sellerio et al., Mol BioSyst 2009

Eléments positifs et négatifs

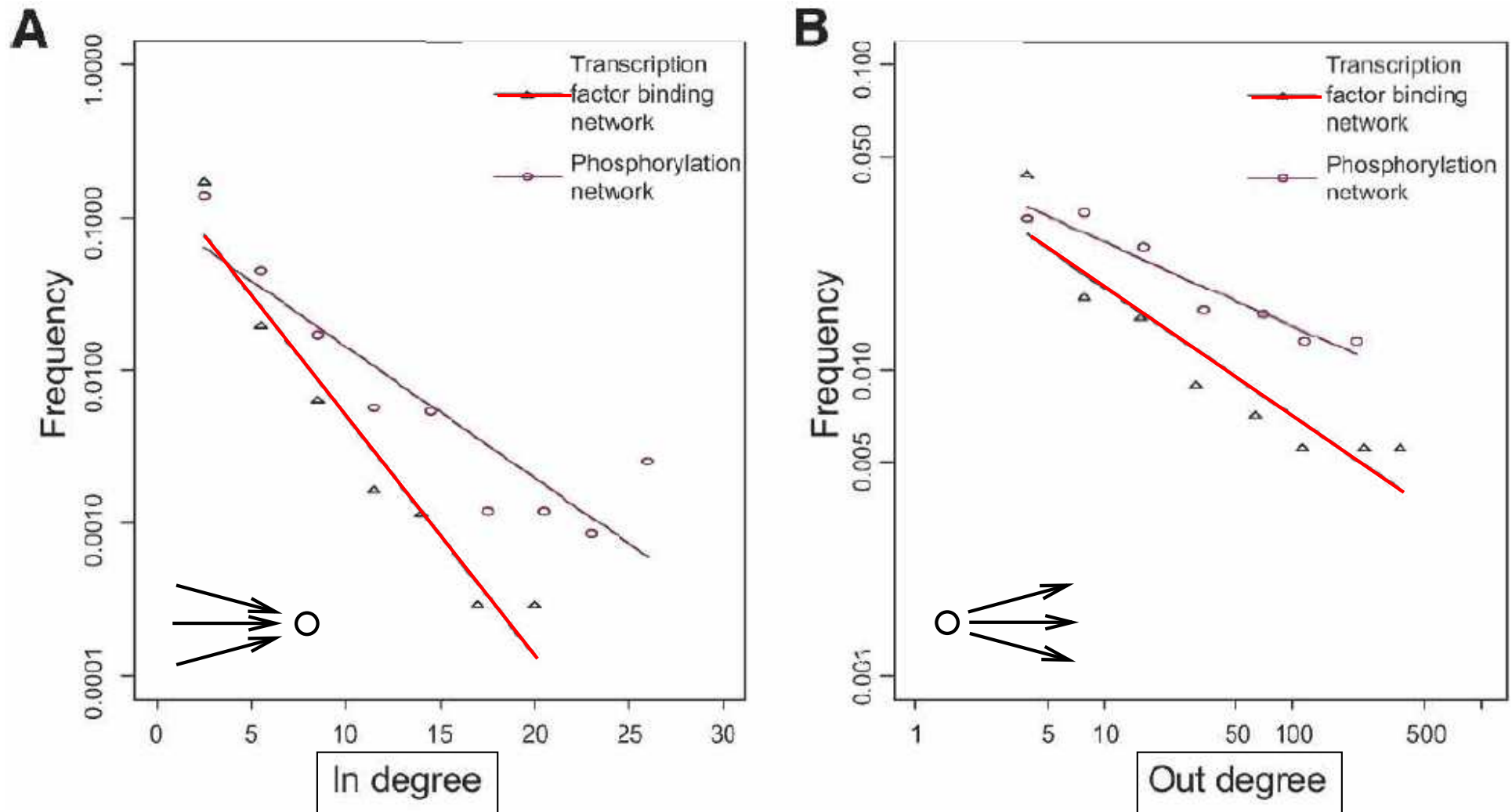


Presence		Expression
R ₁	R ₂	AND
Yes	Yes	OFF
Yes	No	ON
No	Yes	OFF
No	No	OFF

Horloges Circadiens : homologie des circuits



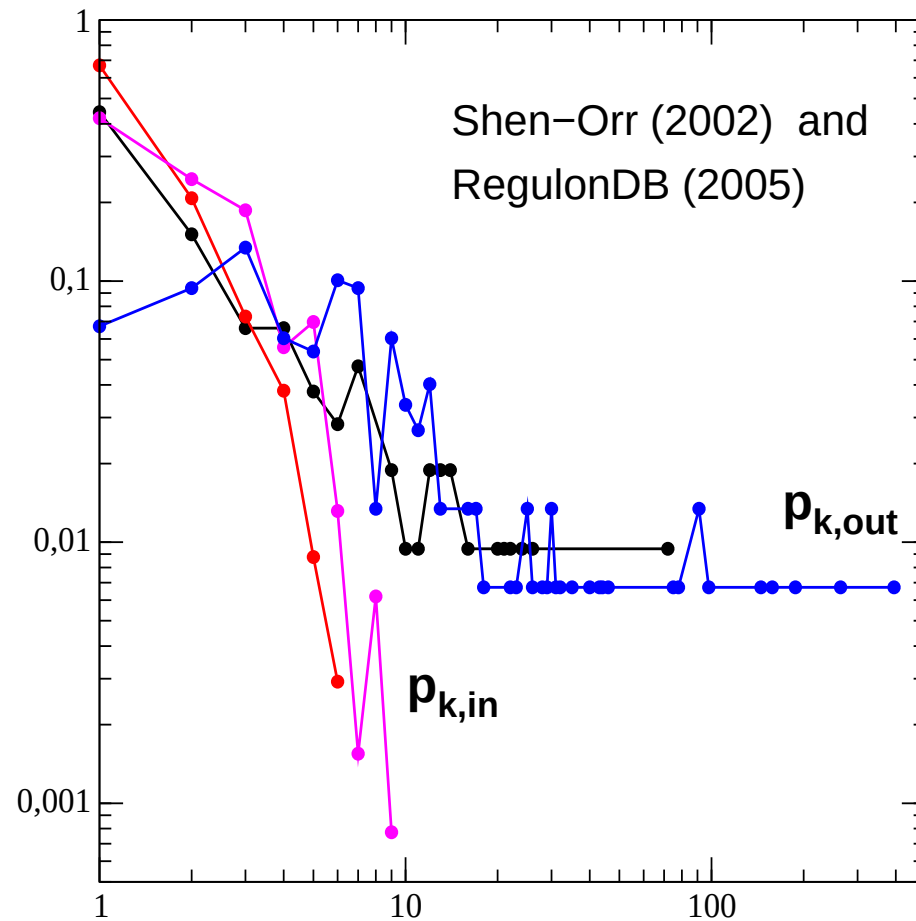
Topology of Oriented Biological Networks



Zhu et al. Genes Dev (2007)

Structures of Regulatory Networks

IN and OUT Degree distributions

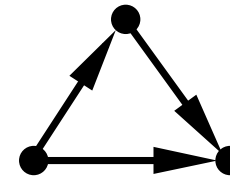


"Over-represented" Motifs

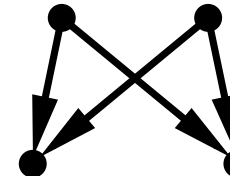
A Autoregulatory Loop



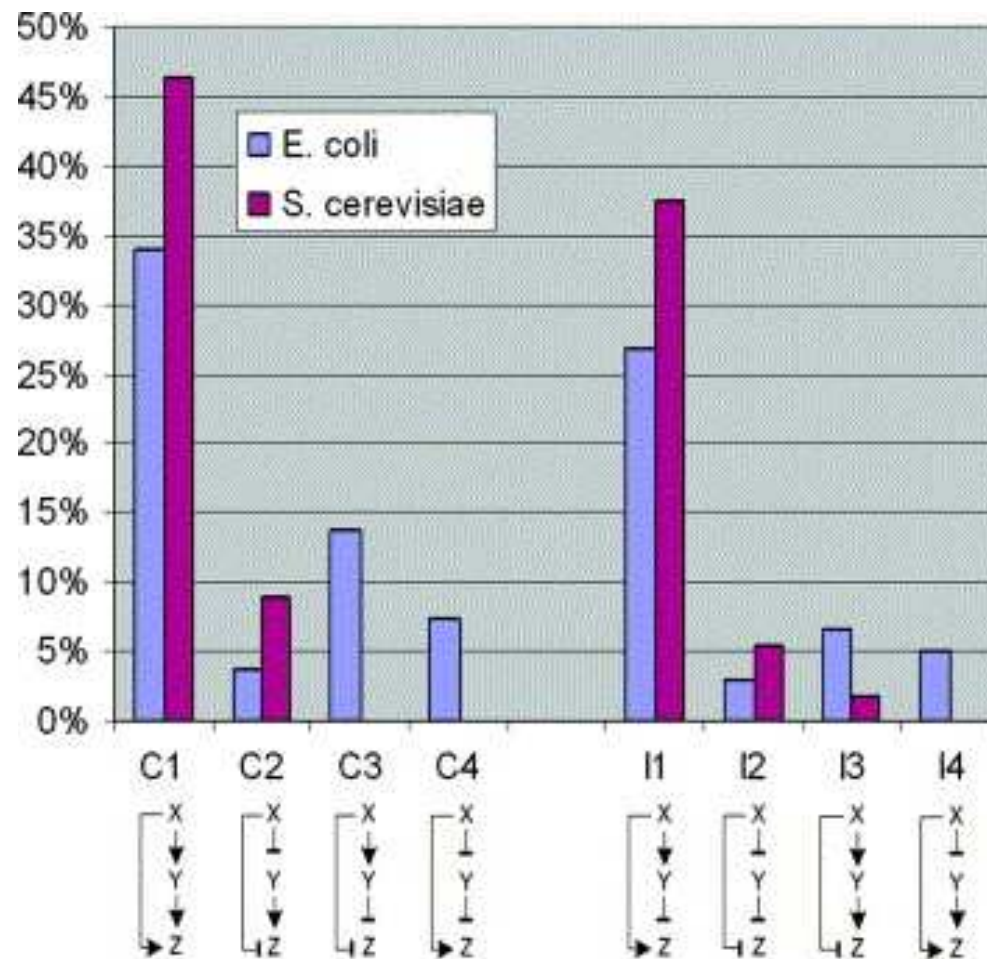
B Feed Forward Loop



C Bi-Fan

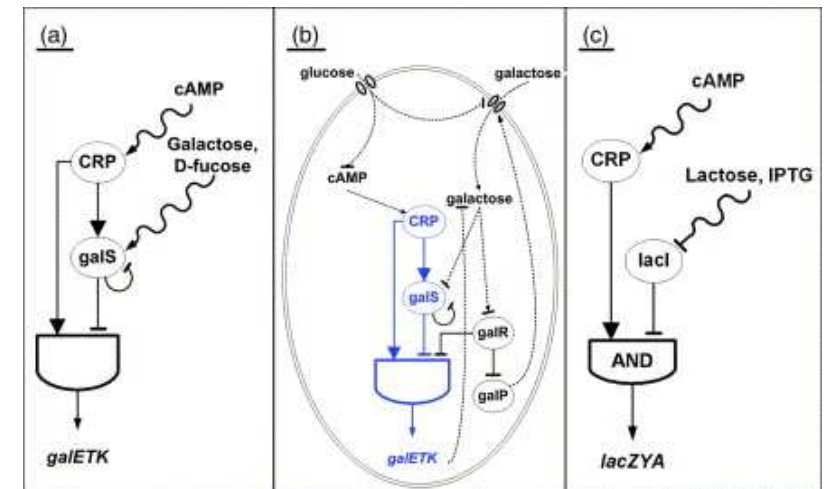


Coherent and Incoherent Feedforward Loops

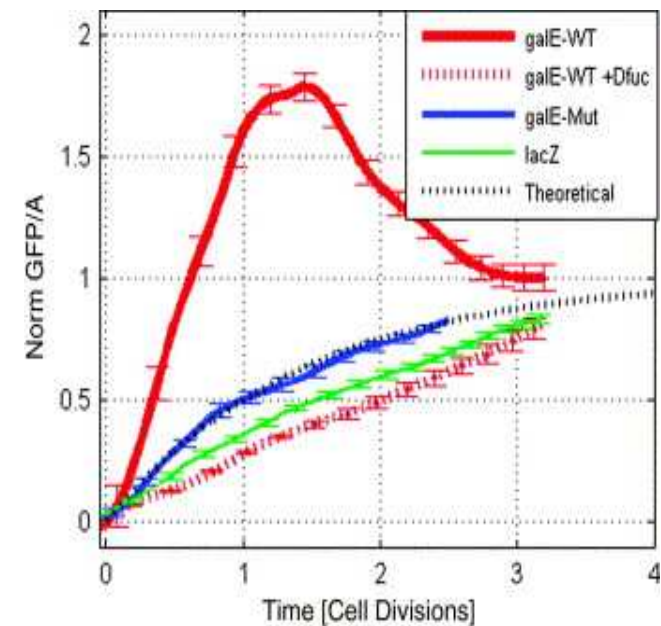


Mangan et al, JMB 2006

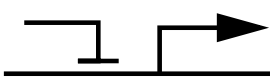
BUT... such motifs are NOT conserved!

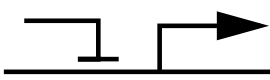


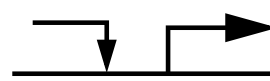
Speed up genetic response

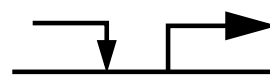


Demand Rule in Gene Regulation

Repressor  *Low*

Repressor  *High*

Activator  *Low*

Activator  *High*

Savageau PNAS (1977)

Demand Rule in Gene Regulation

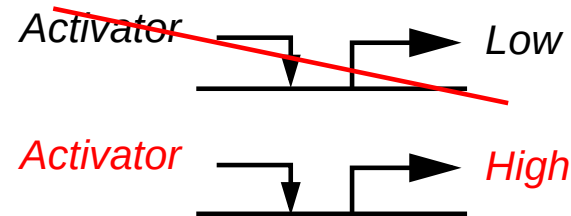
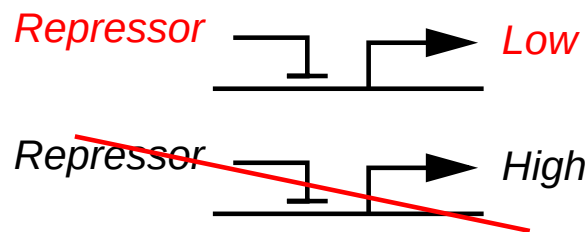


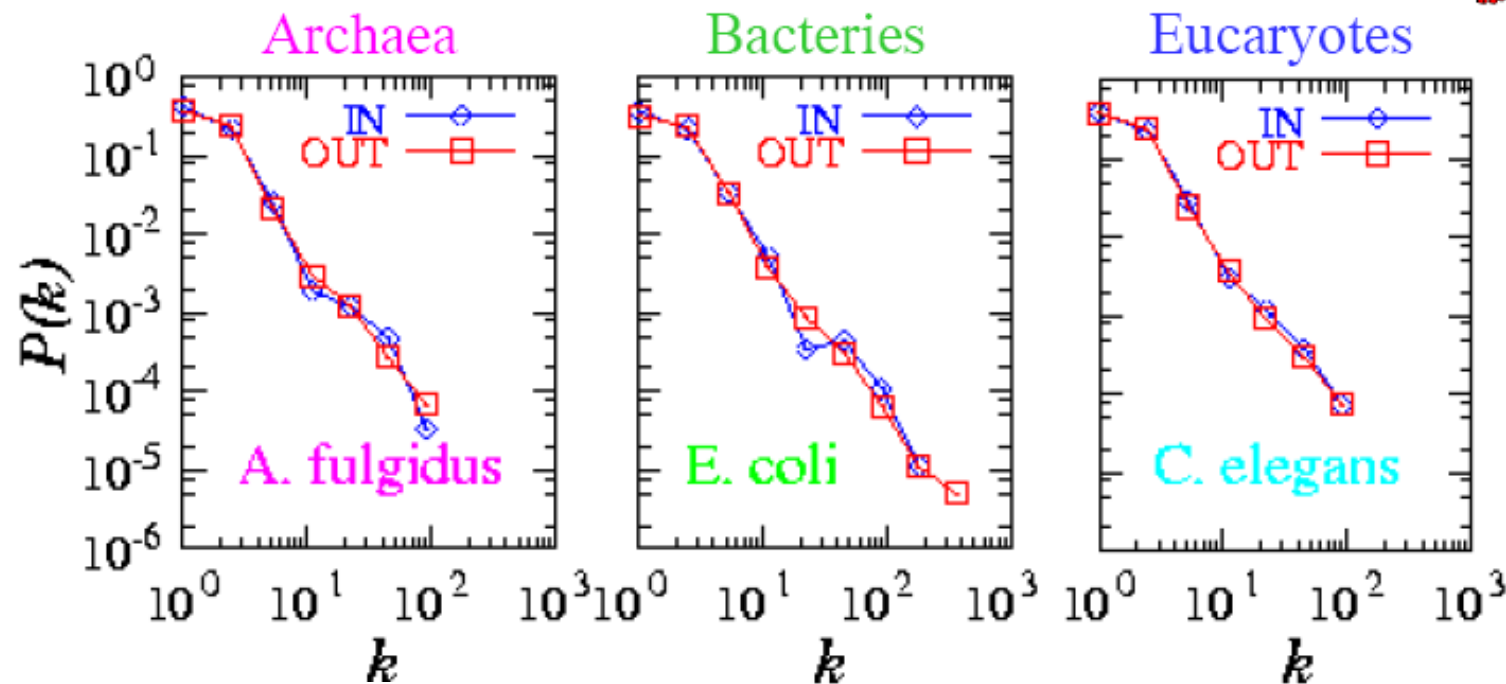
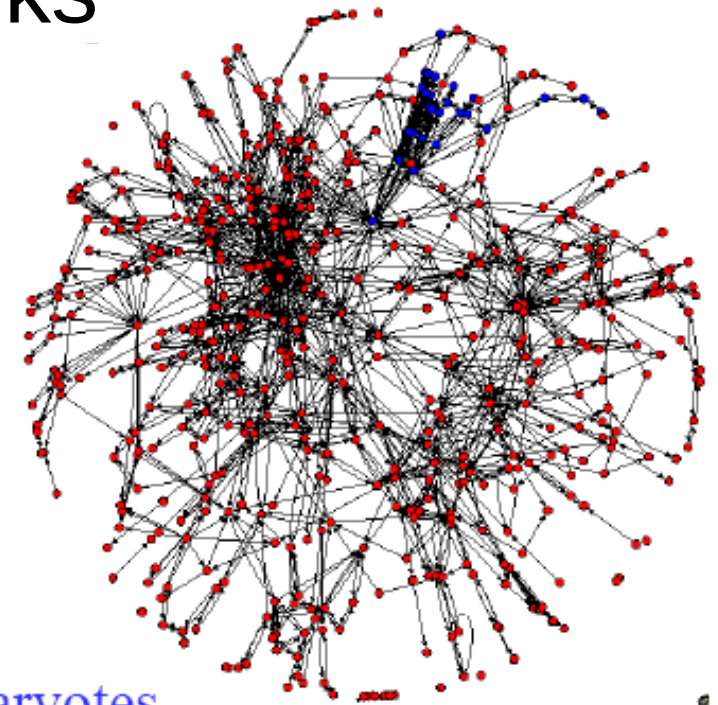
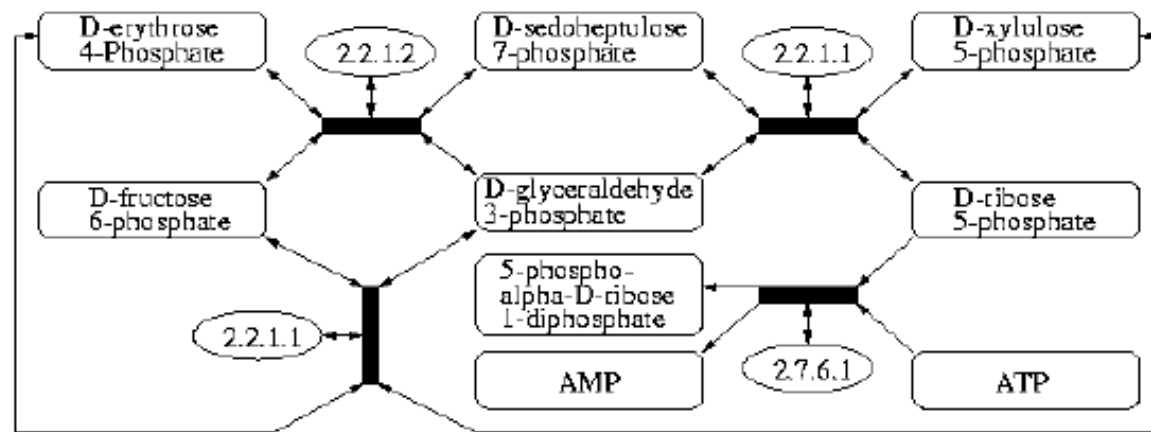
Table 2. Nature of regulator correlates with demand for expression of regulated genes

System ^a	Nature of regulator		Demand for expression	
	Observed ^f	Predicted	Predicted	Observed ^f
Inducible catabolic pathways				
Arabinose	Activator	→	High	High
Galactose	Repressor	→	Low	Low
Glycerol	Repressor	→	Low	Low
Histidine	Repressor	→	Low	Low
Lactose	Repressor	→	Low	Low
Maltose	Activator	→	High	High
Rhamnose	Activator	→	High	High
Mannose	?	Activator ←	High	High
Tryptophan	?	Activator ←	High	High
Xylose	?	Activator ←	High	High
Repressible biosynthetic pathways				
Arginine	Repressor	→	Low	Low
Cysteine	Activator	→	High	High
Isoleucine-valine ^b	Activator	→	High	High

Savageau PNAS (1977)

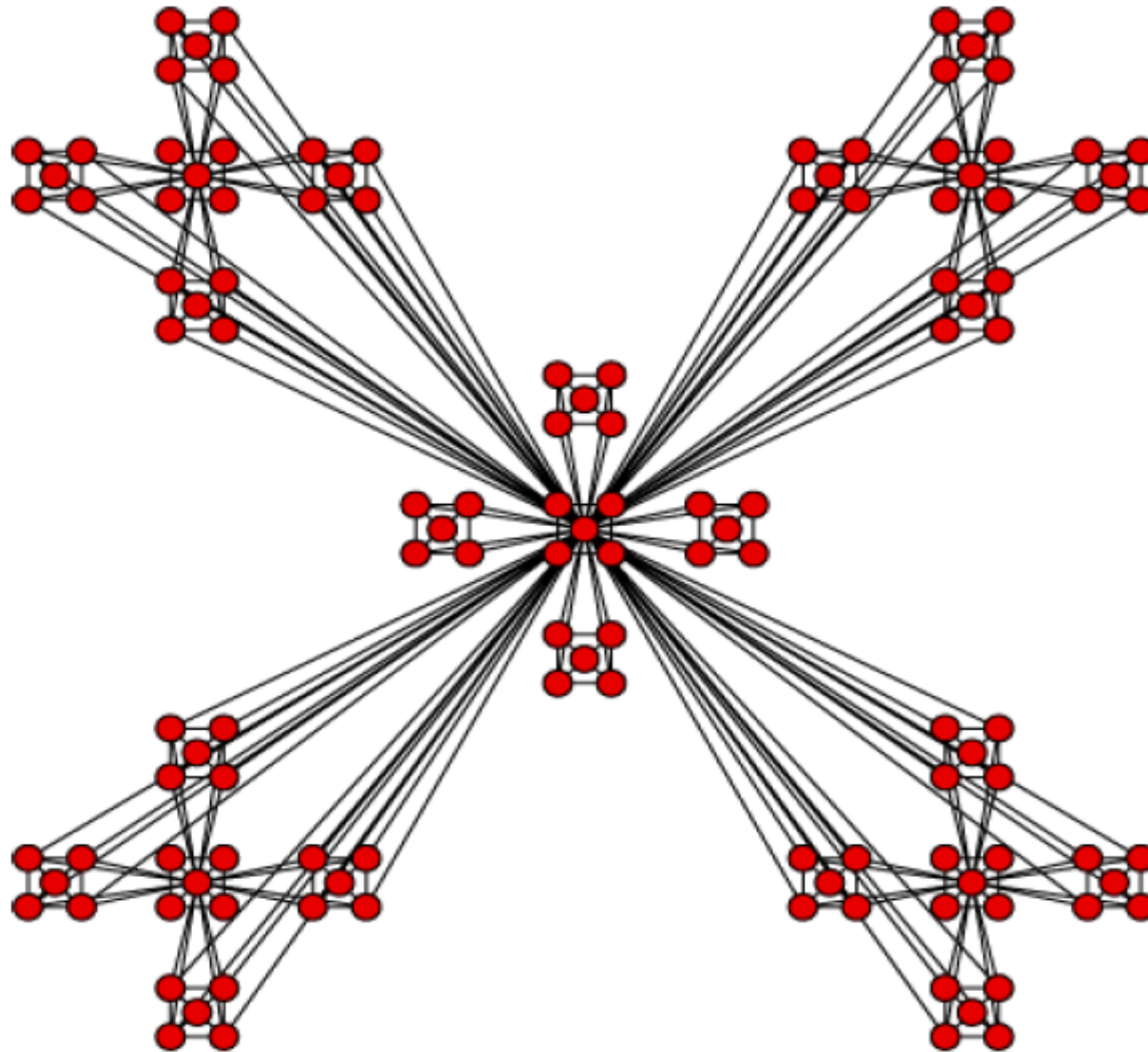
Lysine	Repressor	→	Low	Low
Tryptophan	Repressor	→	Low	Low
Histidine	?	Activator ←	High	High
Isoleucine-valine	?	Activator ←	High	High
Inducible biosynthetic enzymes (within repressible biosynthetic pathways)				
Isoleucine-valine	Activator	→	High	High
Tryptophan ^c	Repressor	→	Low	?
Inducible drug resistance				
Penicillin ^{d,e}	Repressor	→	Low	Low
Tetracycline	Repressor	→	Low	Low
Chloramphenicol ^d	?	Repressor ←	Low	Low
Erythromycin ^d	?	Repressor ←	Low	Low
Inducible prophages				
λ	Repressor	→	Low	Low
P1	Repressor	→	Low	Low
P2	Repressor	→	Low	Low
P22	Repressor	→	Low	Low

Metabolic Networks



H. Jeong, B. Tombor, R. Albert, Z.N. Oltvai, and A.L. Barabasi, **Nature**, 2000

Hierarchical Networks ??!



Very Preliminary Conclusion

Biological Networks are NOT Random Graphs !

but is it for FUNCTIONAL reason ??

*or is it because they CANNOT be random
by CONSTRUCTION ??*

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Then what sense does it make to compare them to randomized graphs ??

Very Preliminary Conclusion

Biological Networks are NOT Random Graphs !

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by CONSTRUCTION ??*

Then what sense does it make to compare them to randomized graphs ??

*"Nothing in biology makes sense...
... except in the light of evolution"*

Theodosius Dobzhansky (1973)

Biological Networks and their Evolution

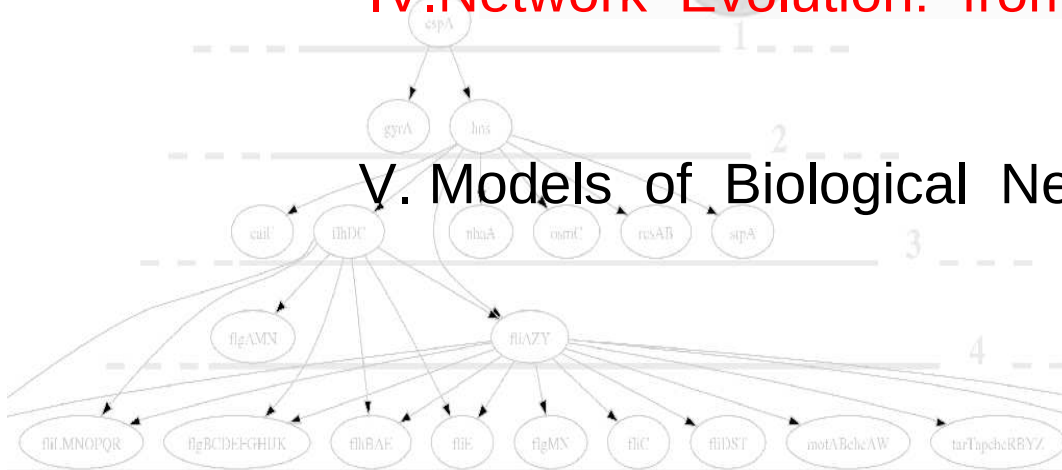
I. Introduction: from Genomes to Networks

II. Different Types of Biological Networks

III. Properties of Biological Networks

IV. Network Evolution: from Genes to Organisms

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Biological Networks and their Evolution

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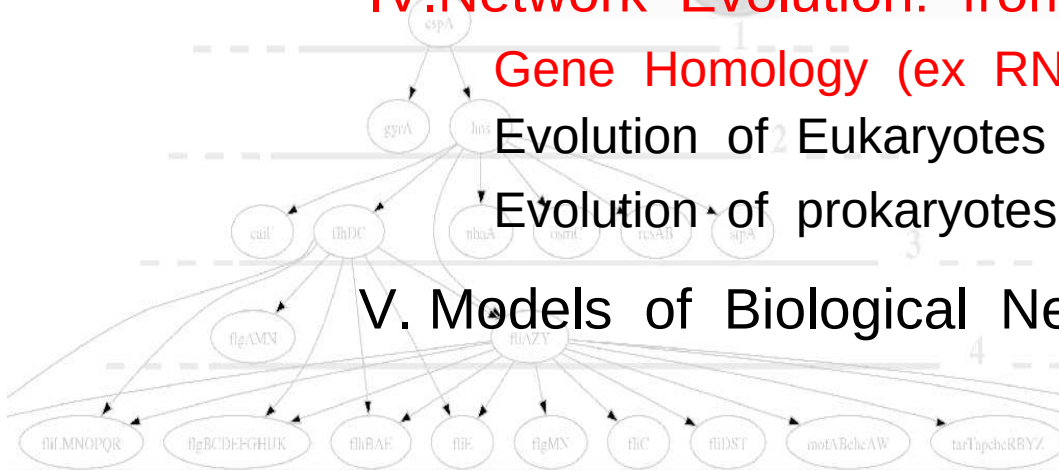
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Gene Homology (ex RNA pol and Ribosome)

Evolution of Eukaryotes

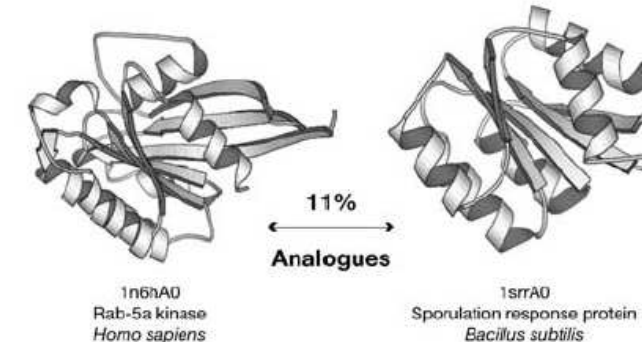
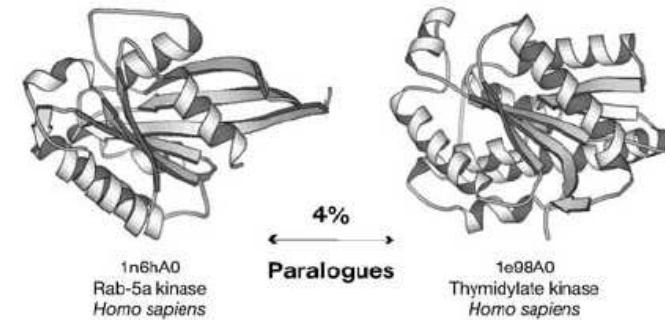
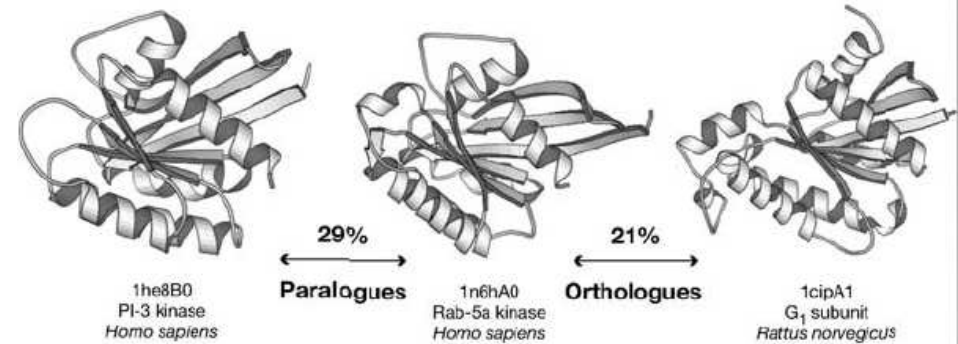
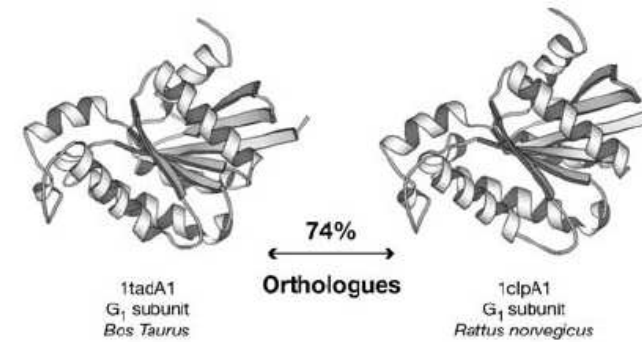
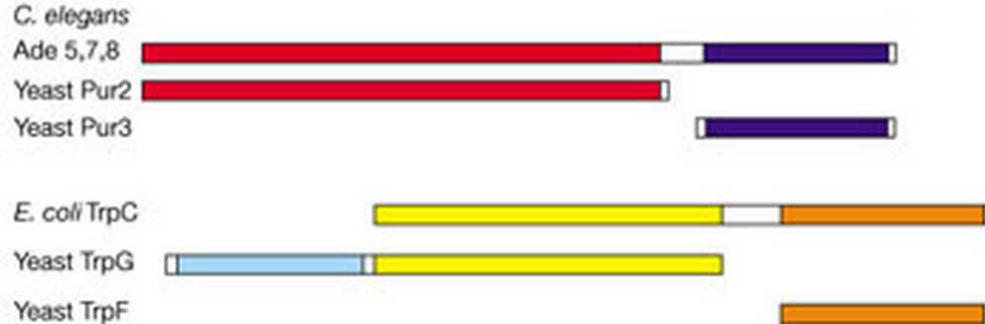
Evolution of prokaryotes

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Protein Homology at the level of Domains

General concept



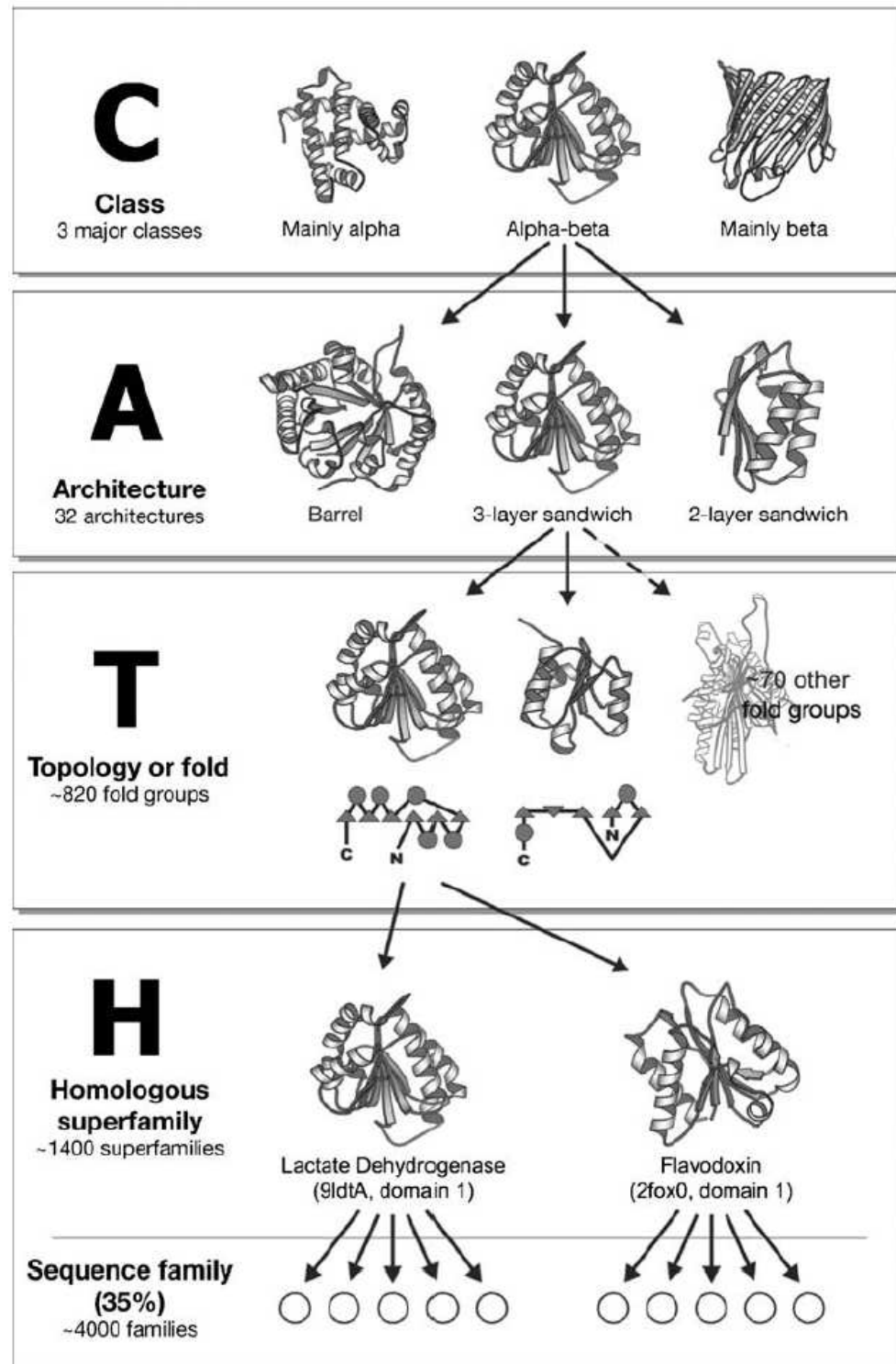
Close Homologues

Remote Homologues

Distant Homologues

Analogues

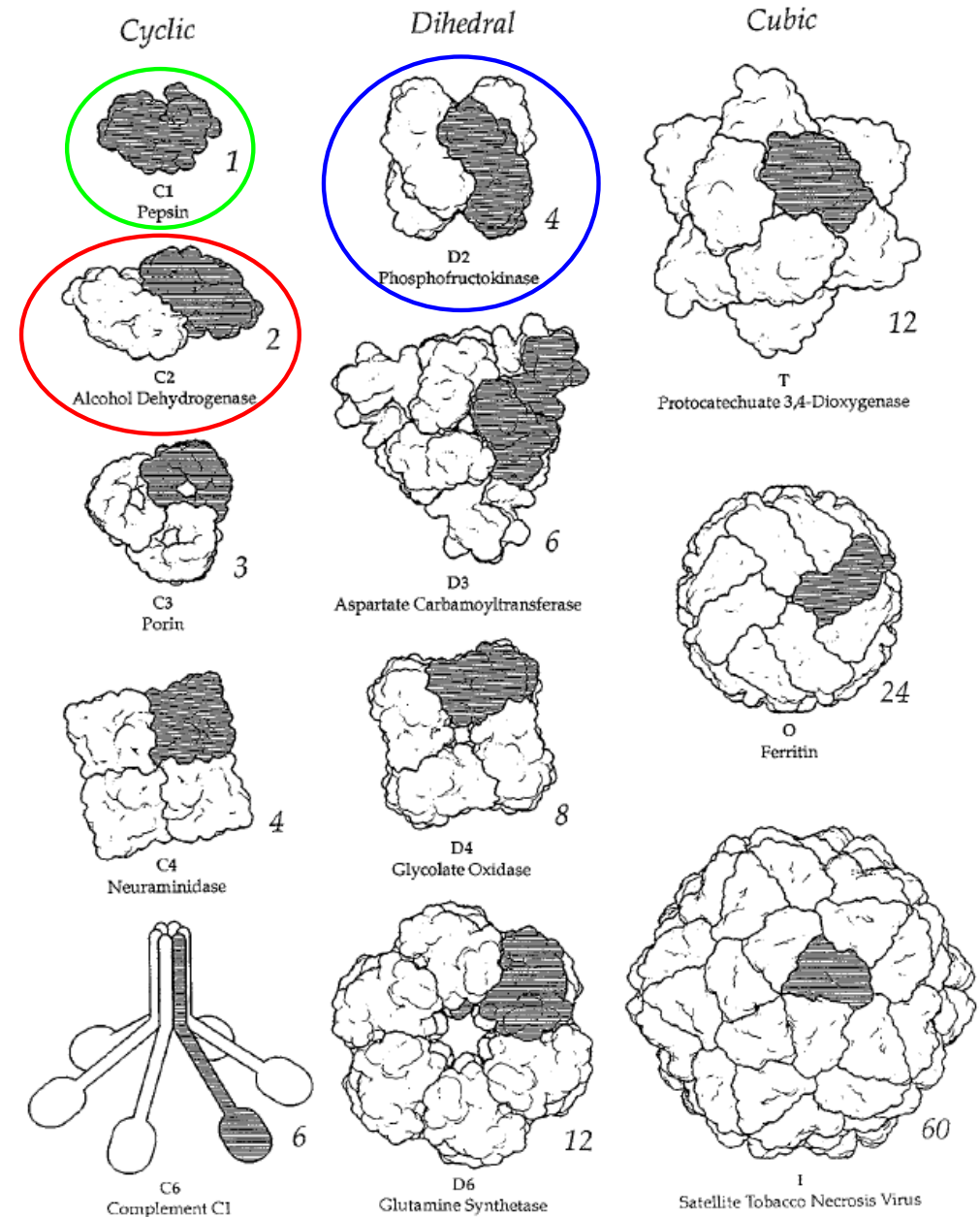
Domain Folds



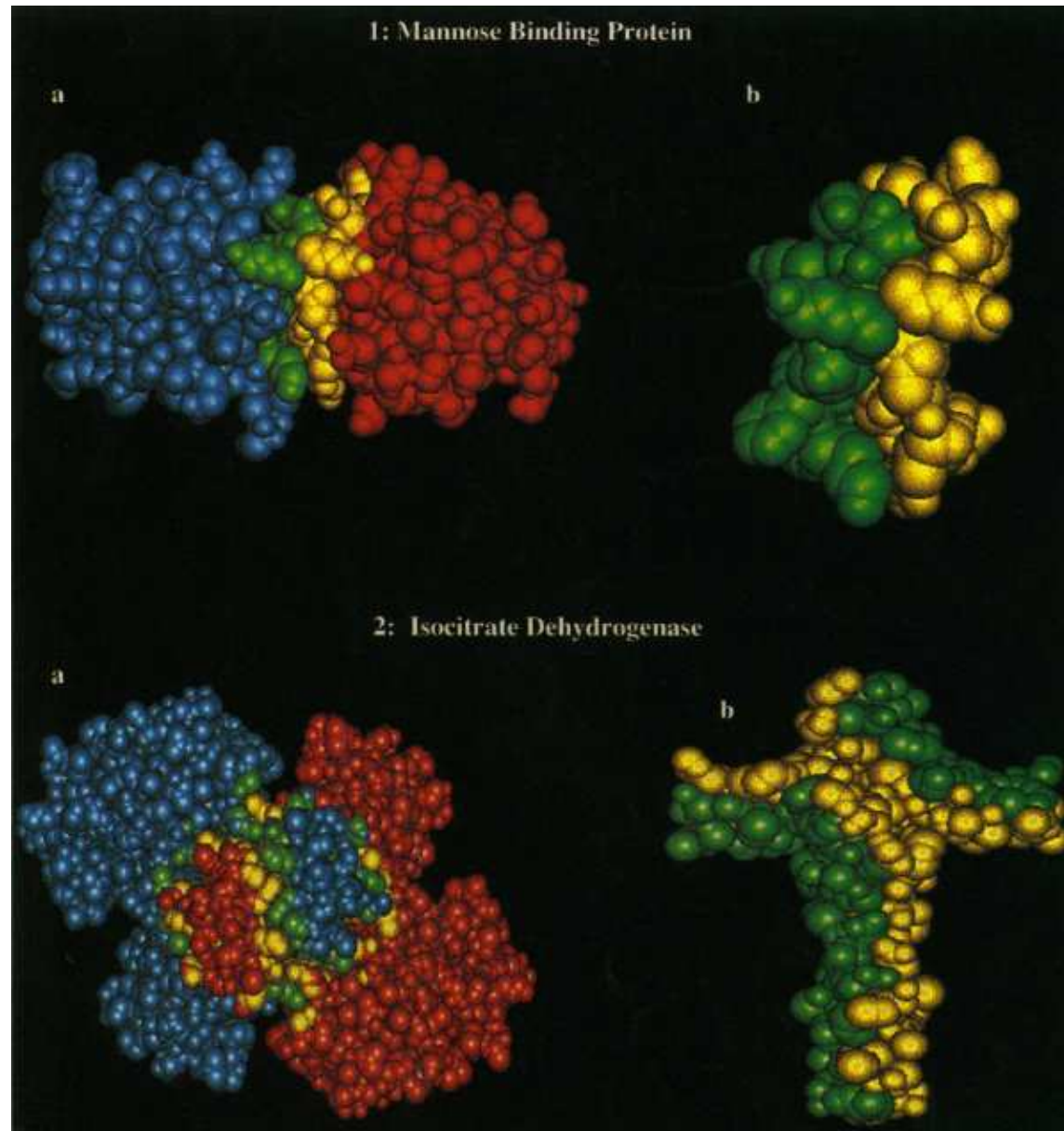
Protein Oligomers and Group Symmetry

TABLE 1 Natural occurrence of oligomeric proteins in *Escherichia coli*^a

Oligomeric state	Number of homooligomers	Number of heterooligomers	Percent
<u>Monomer</u>	72		19.4
<u>Dimer</u>	115	27	38.2
Trimer	15	5	5.4
<u>Tetramer</u>	62	16	21.0
Pentamer	1	1	0.1
Hexamer	20	1	5.6
Heptamer	1	1	0.1
Octamer	3	6	2.4
Nonamer	0	0	0.0
Decamer	1	0	0.0
Undecamer	0	1	0.0
Dodecamer	4	2	1.6
Higher oligomers	8		2.2
Polymers	10		2.7



Homodimers Interaction Surface Symmetry



Information Content and Interaction Symmetry

Xayaphoummine, Viasnoff, Harlepp & Isambert, NAR, 35, 614 (2007)

Sequence alphabet $D=20$ (protein) $D=4$ (nucleic acid) letters

Number of sequences of N letters D^N

Information Content and Interaction Symmetry

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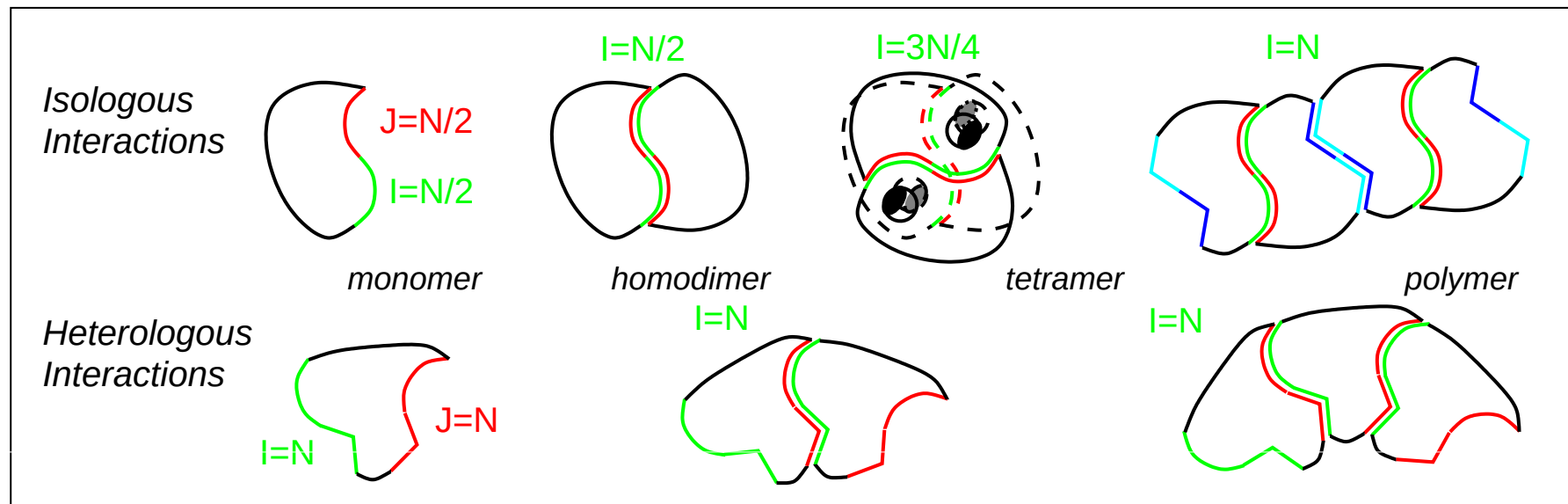
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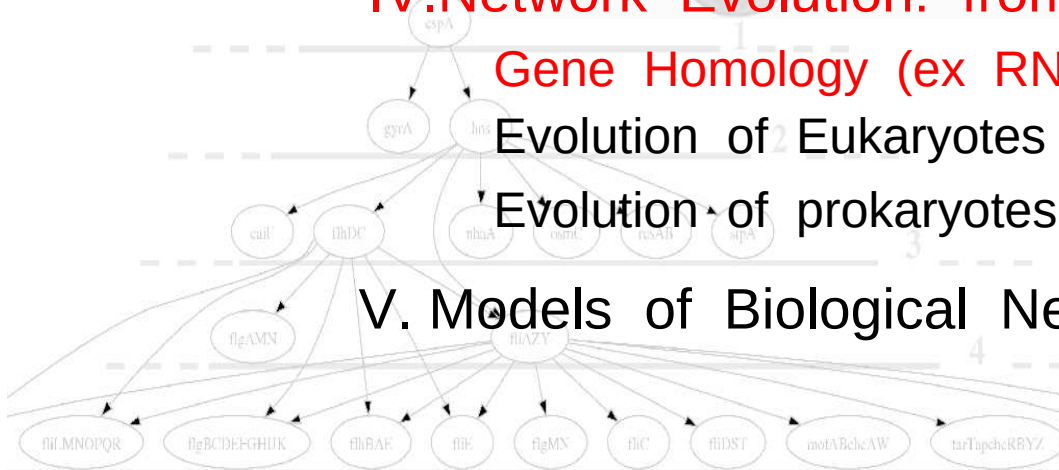
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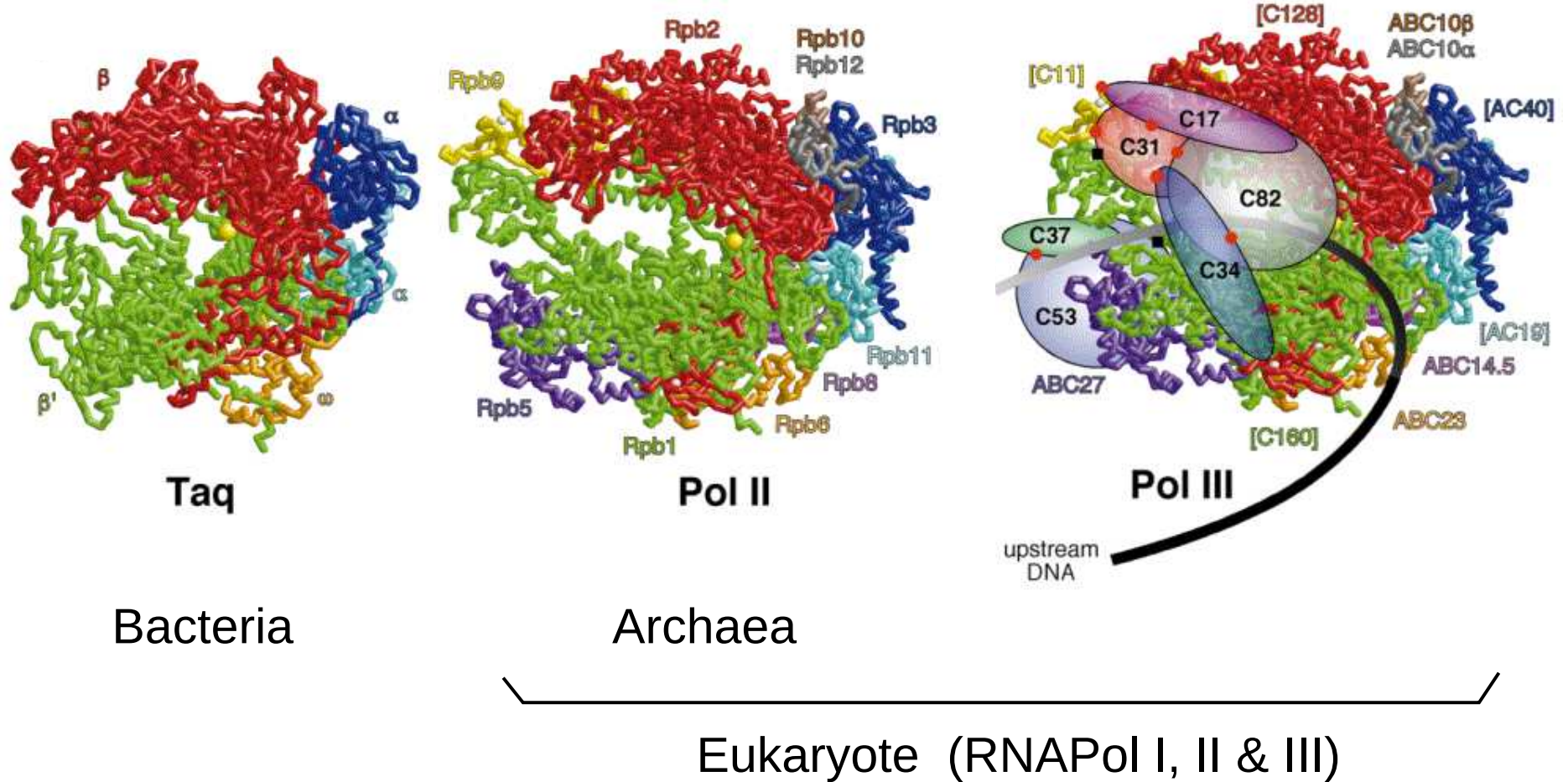
Evolution of Eukaryotes

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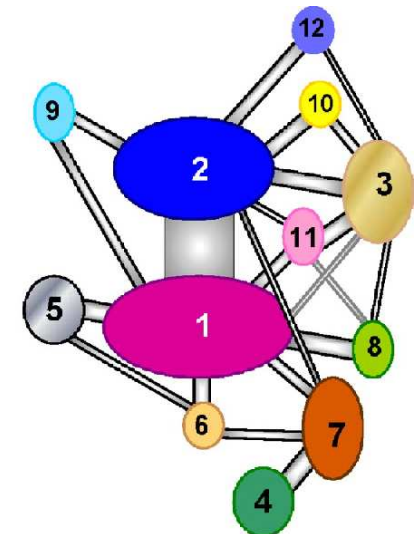
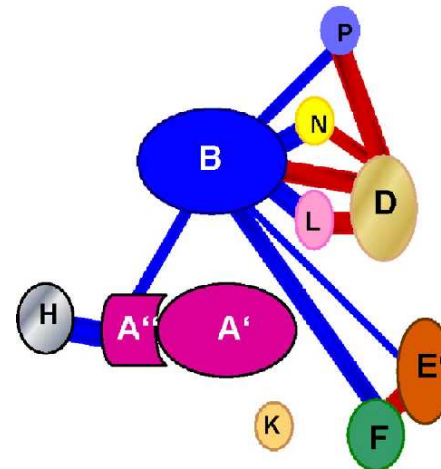


Homologies between RNA Polymerases



Homologies between RNA Polymerases

	Archaea	Eukarya	Bacteria
	<i>P. furiosus</i> RNAP	<i>S. cerevisiae</i> RNAPII	<i>E. coli</i> RNAP
		Rpb1	
		Rpb2	β' β
127.0	B		
103.5	A'		
44.4	A''	Rpb3	
29.8	D	Rpb4 Rpb5	α_2
21.7	E'	Rpb6 Rpb7	
14.1	F	Rpb8 Rpb9	
11.1	L	Rpb11	
9.3	H	Rpb10	
8.2	N	Rpb12	
6.2	K		ω
5.8	P		



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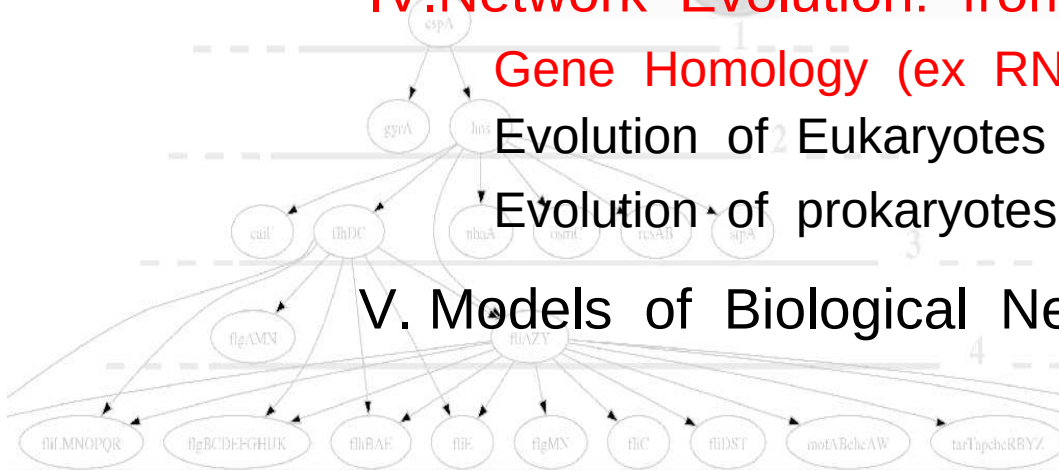
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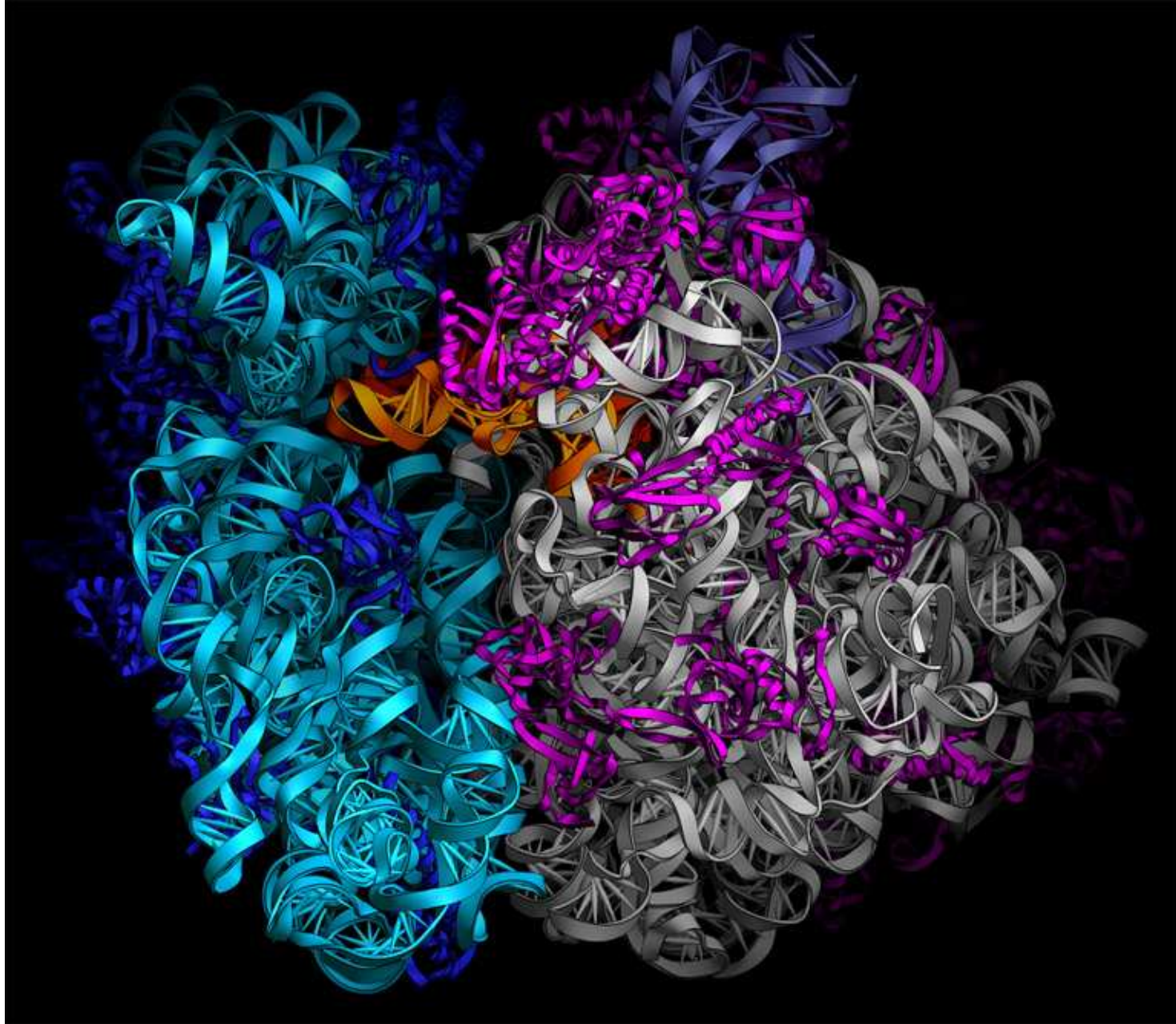
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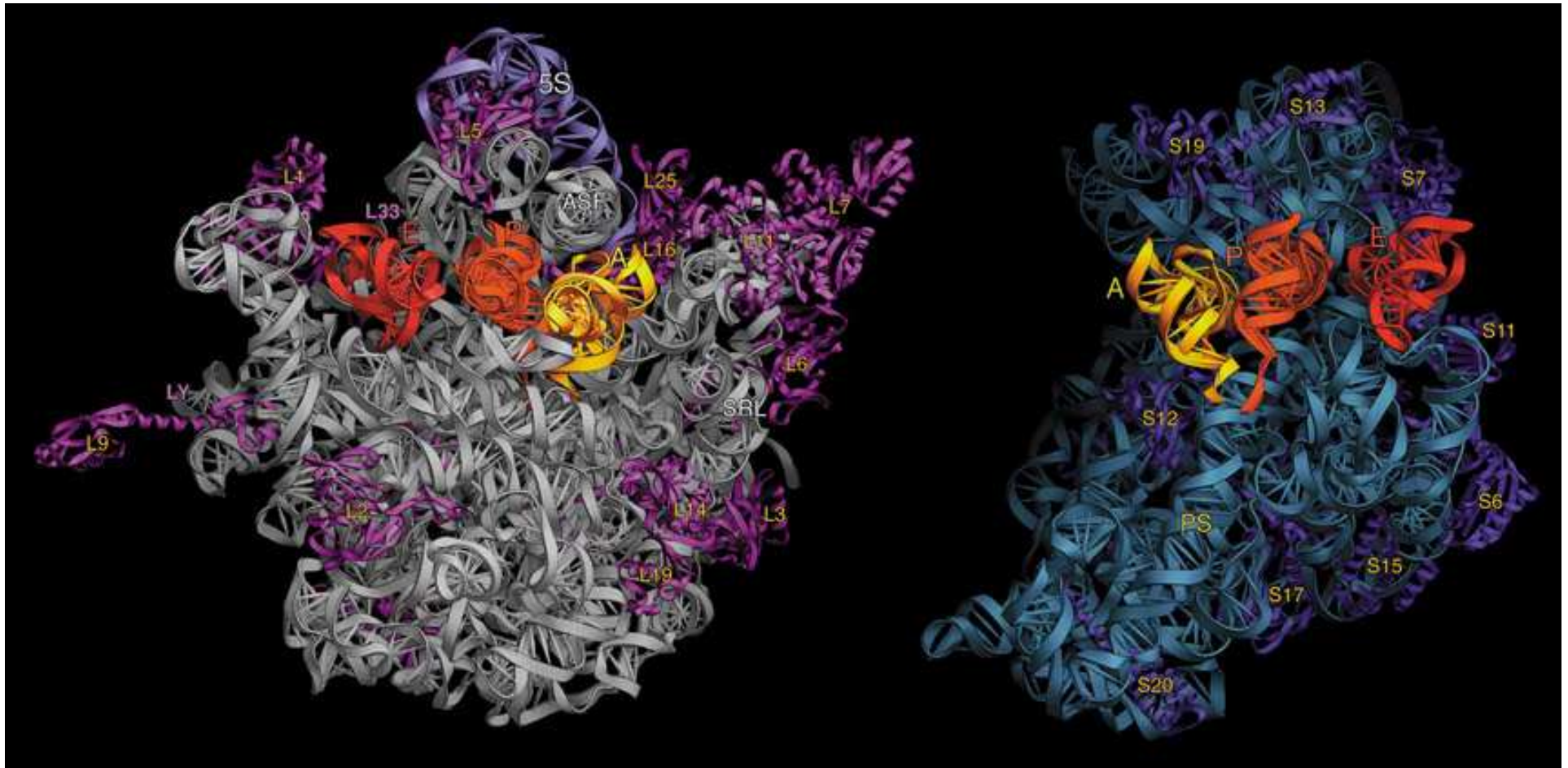
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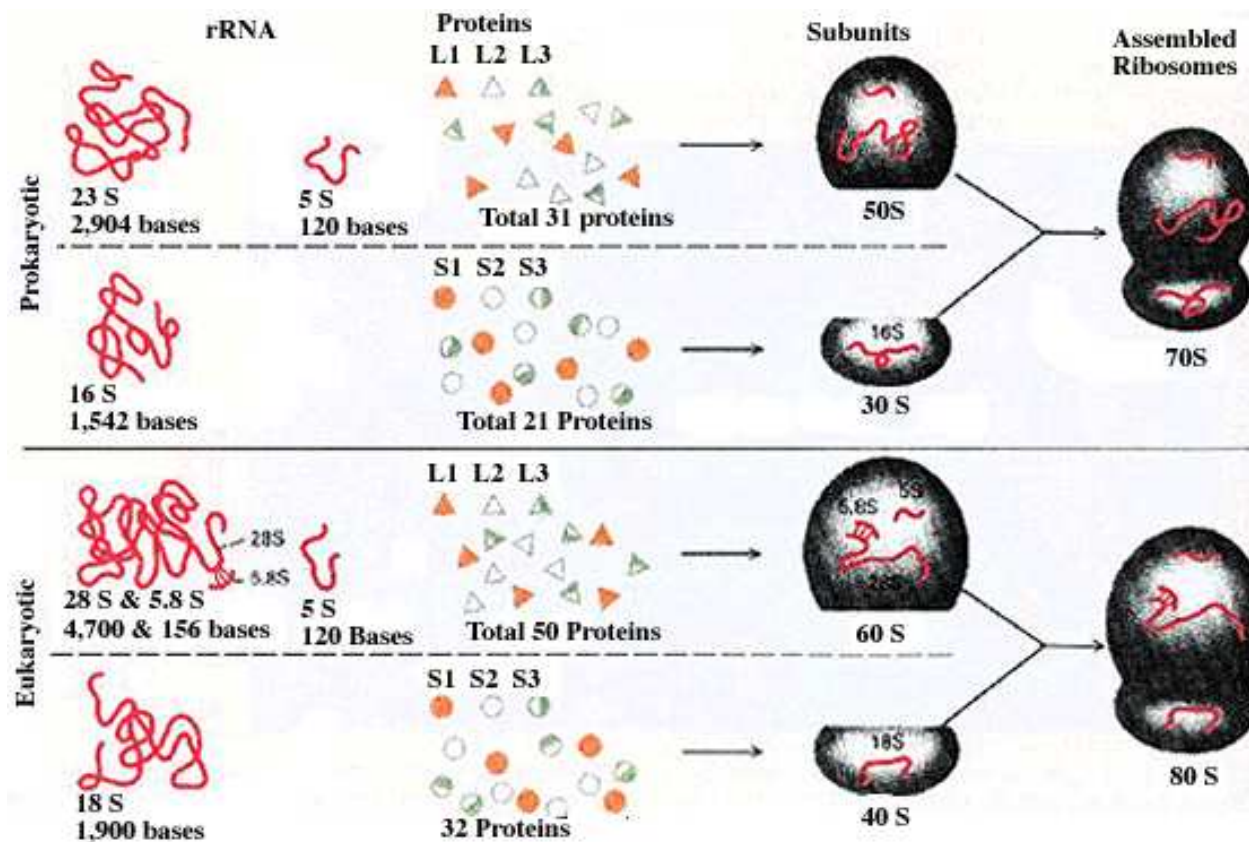
The Ribosome



The Ribosome



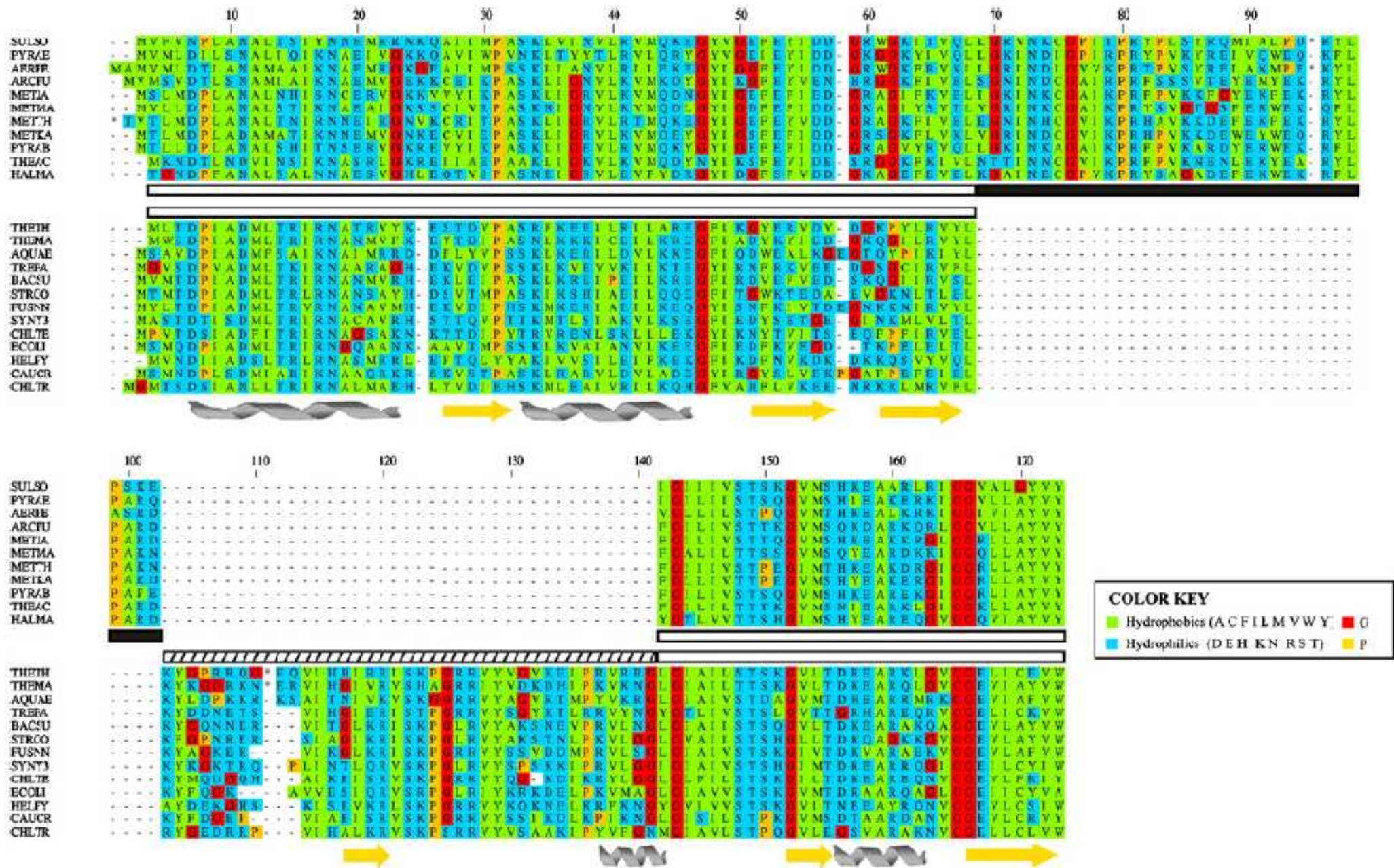
The Ribosome



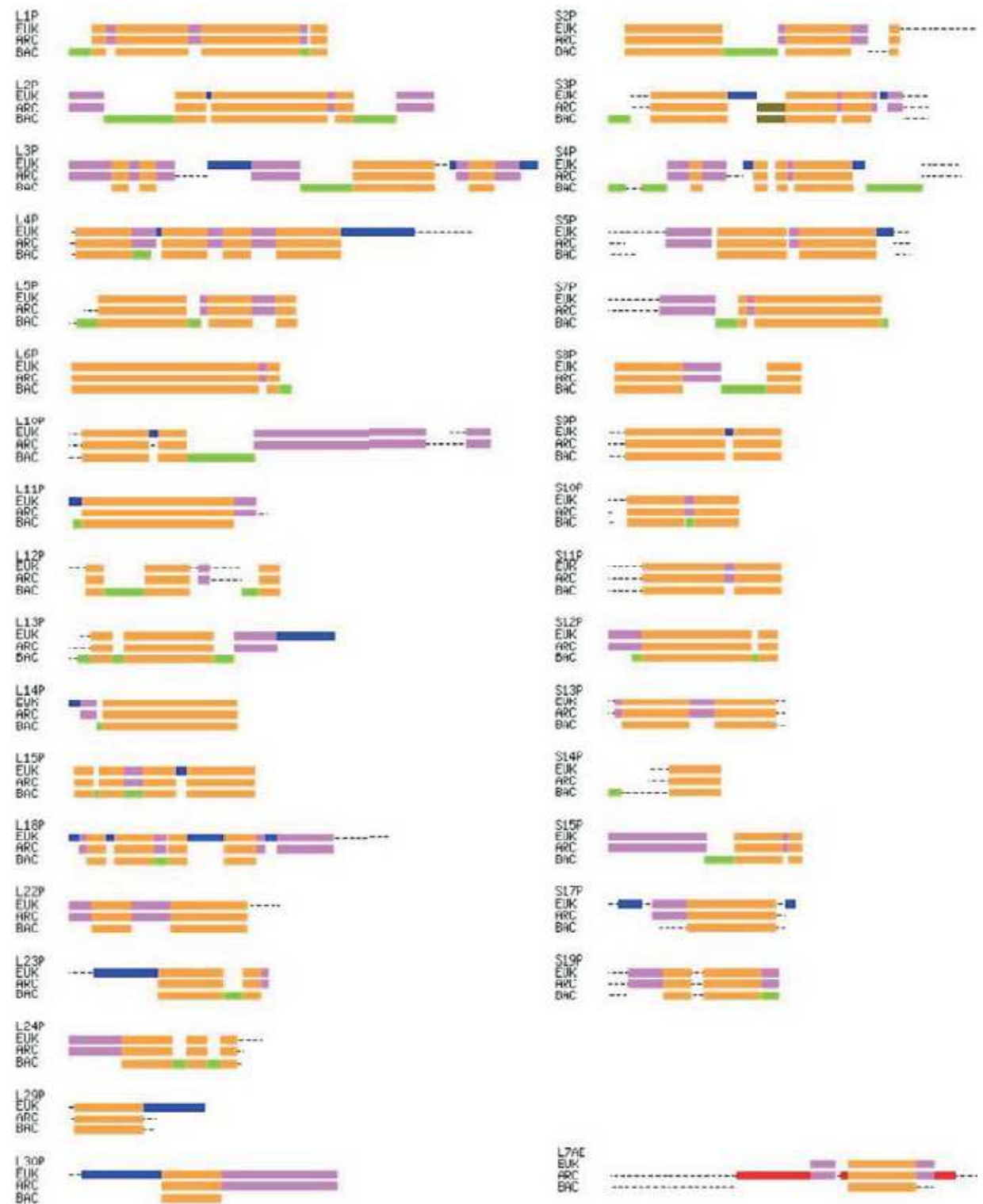
33 Euk – Arc – Bac Universal Ribosomal Proteins

34 Euk – Arc only Homologous Ribosomal Proteins

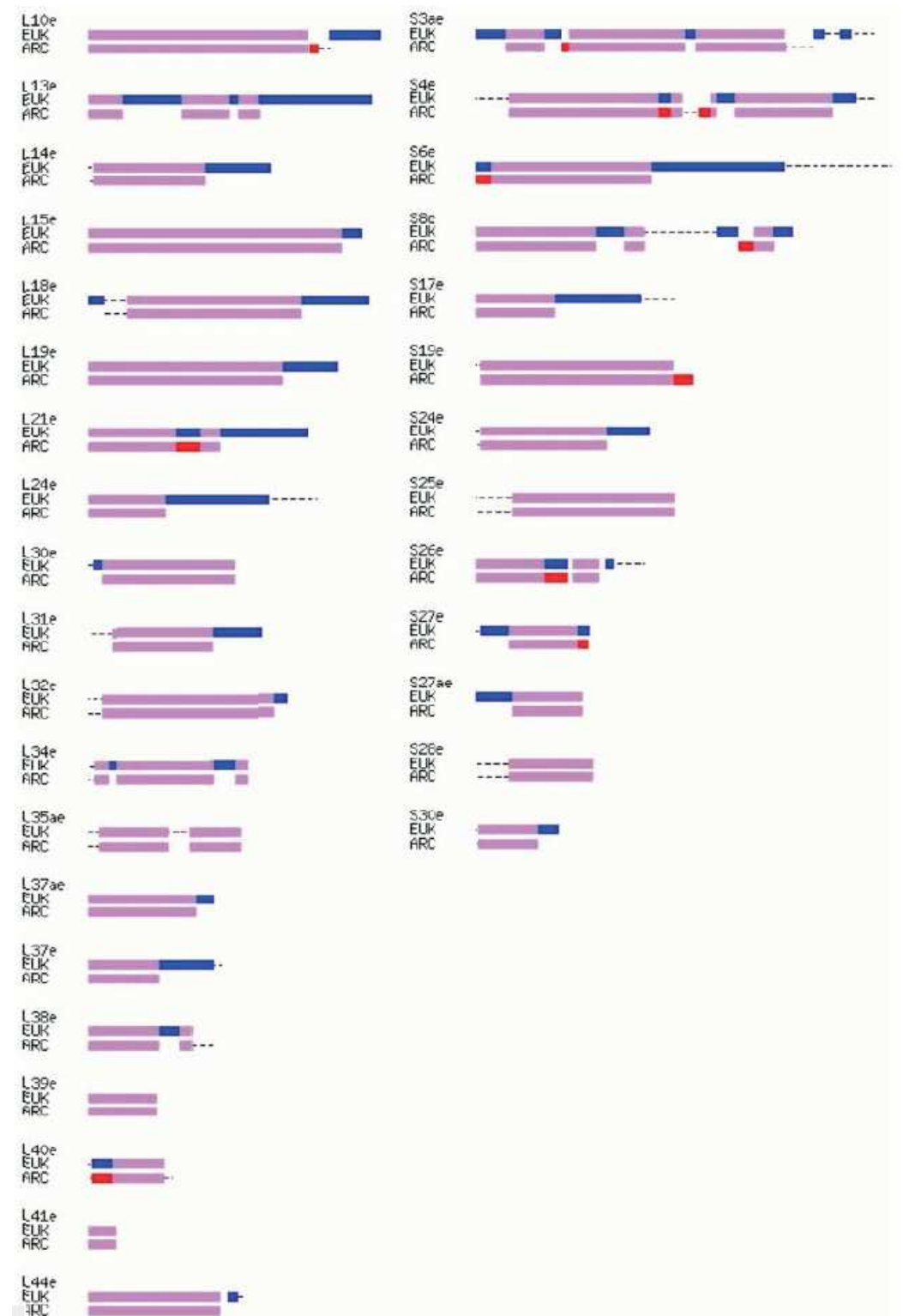
Ribosomal Protein S8 in Archaea and Bacteria



Universal Ribosomal Proteins bwn Eukaryotes, Archaea and Bacteria



Remaining Homologous Proteins bwn Eukaryotes and Archaea



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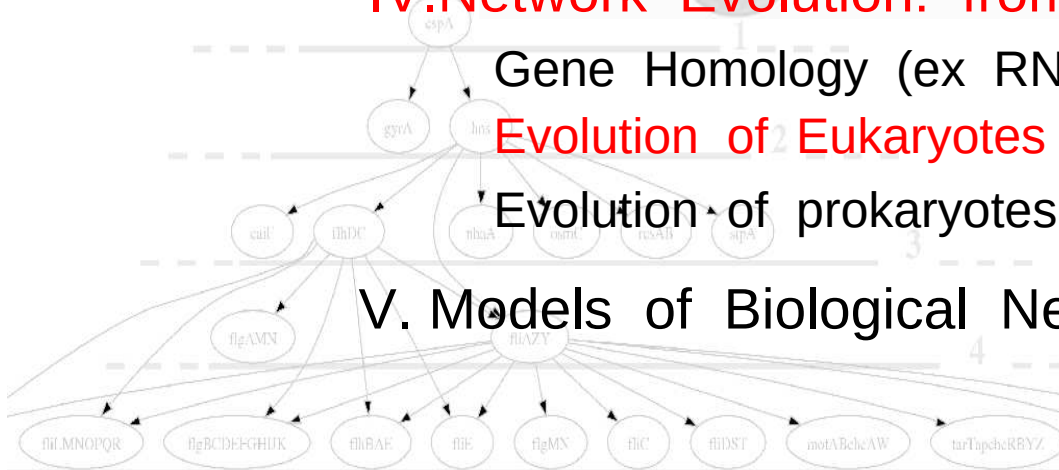
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Mechanisms of Genome Evolution

- Random mutations (nucleotide substitutions)
 - synonymous (the same aminoacid)
 - nonsynonymous (a different aminoacid)
 - nonsense codon modifications (Stop)
- Recombinations – crossing over/gene conversion
 - exchange of homologous sequences between homologous chromosomes
 - non reciprocal exchange (loss of one of the variant sequences)
- Deletions and Insertions – unequal crossing over
 - gene deletion and local gene duplication → *shuffling of protein domains*
- Global gene duplication – whole genome duplication
 - replication of chromosomes without segregation

Long suspected... recently proved!

Mechanisms of Genome Evolution

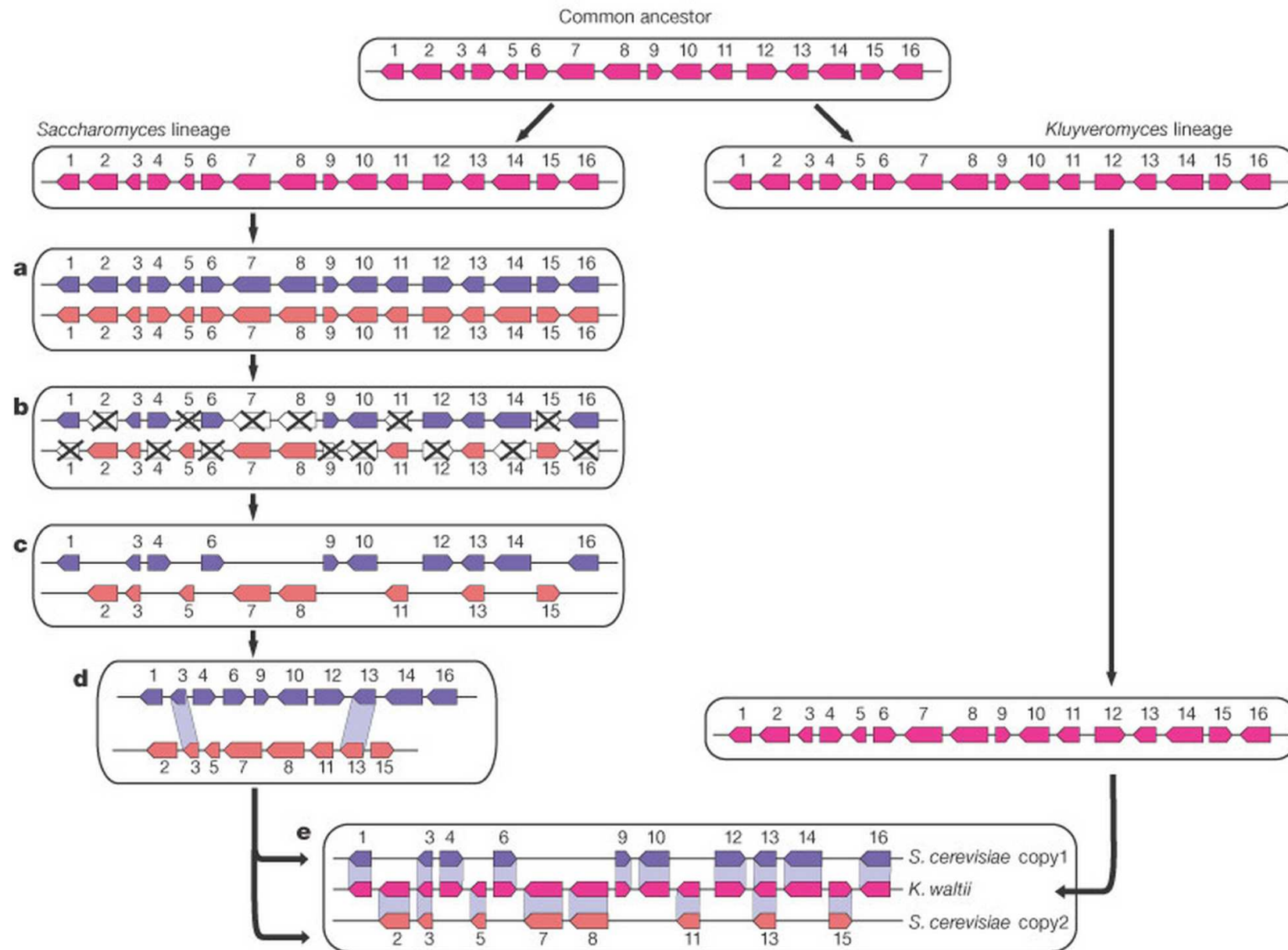
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Recently proved!!!

Implies important genetic modifications!!

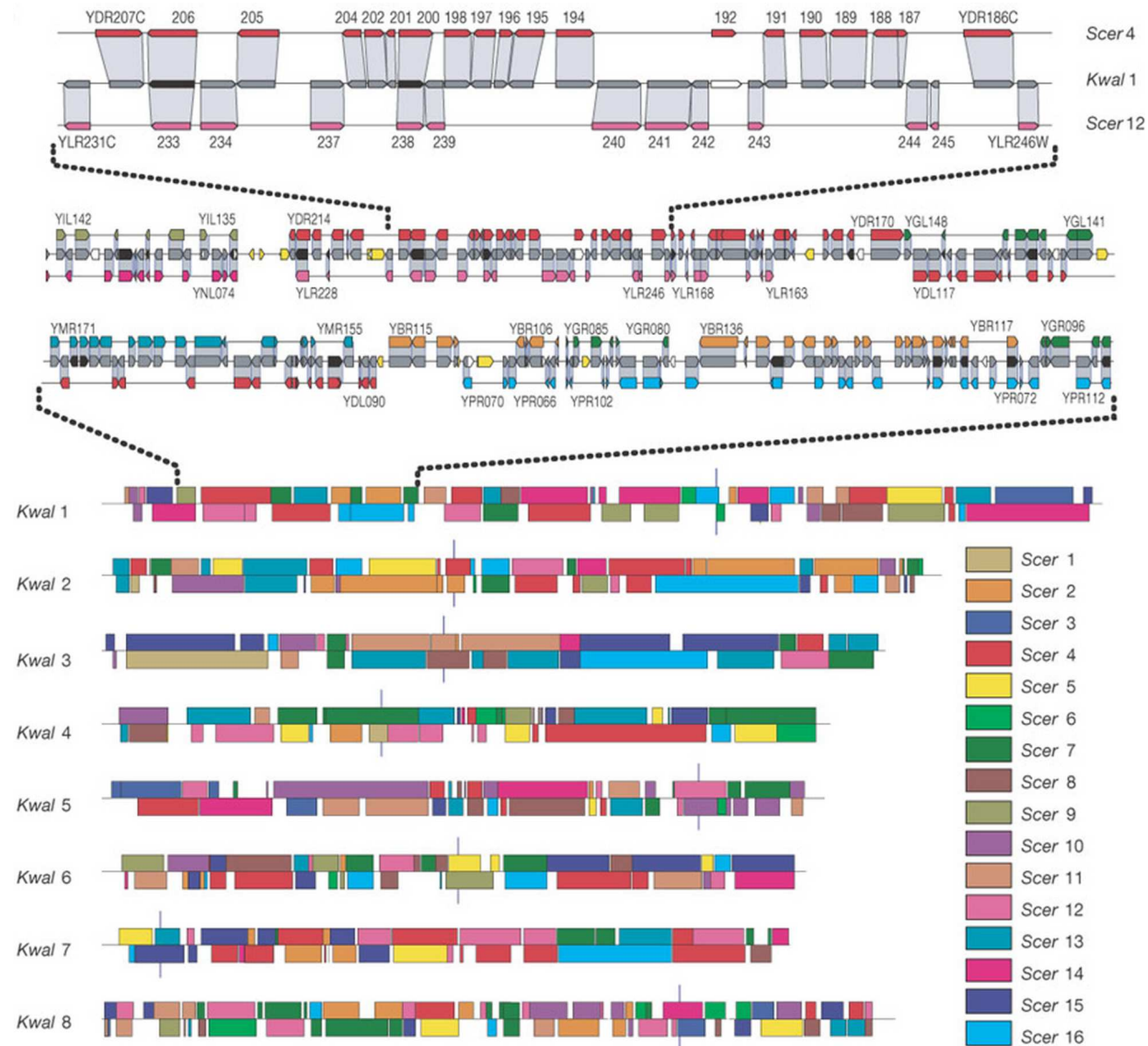
Whole Genome Duplication in Yeast Genome

Kellis et al. 2004

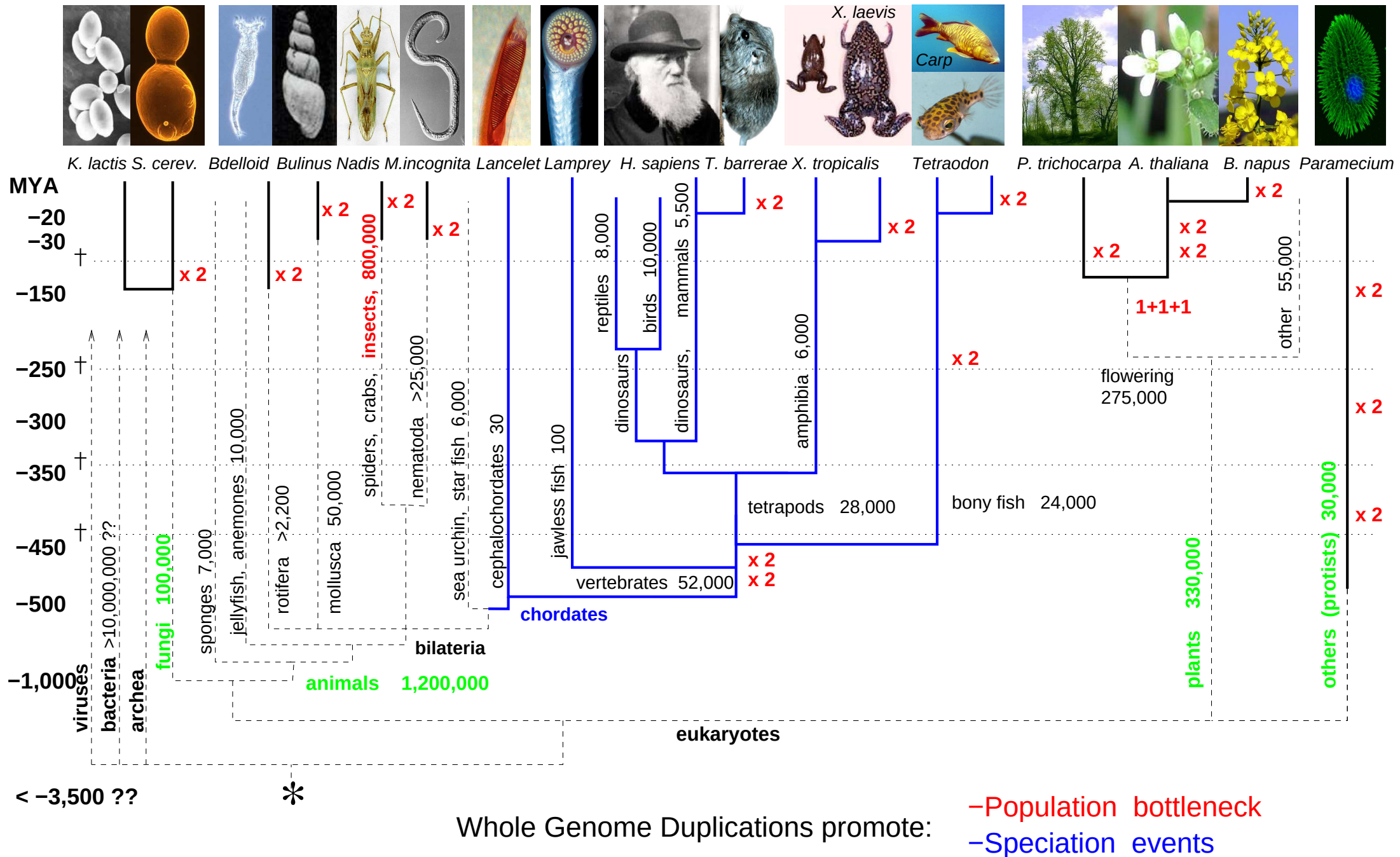


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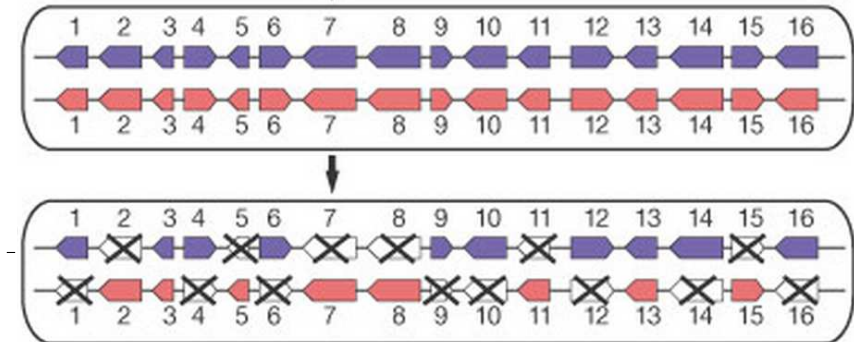
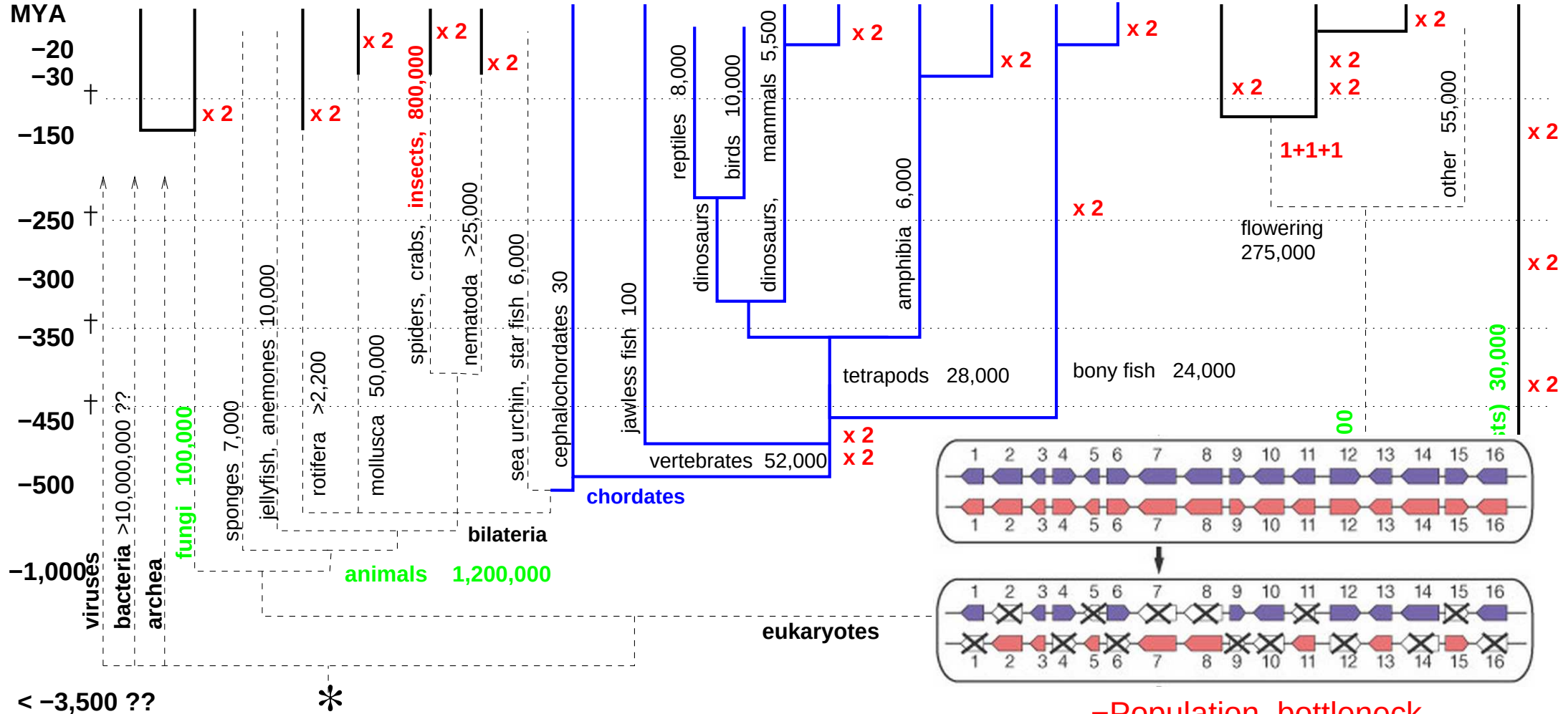
Whole Genome Duplications in Evolution



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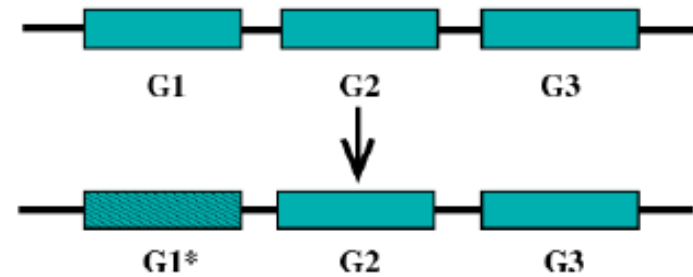


K. lactis *S. cerev.* *Bdelloid* *Bulinus* *Nadis* *M. incognita* *Lancelet* *Lamprey* *H. sapiens* *T. barrerae* *X. tropicalis* *Tetraodon* *P. trichocarpa* *A. thaliana* *B. napus* *Paramecium*

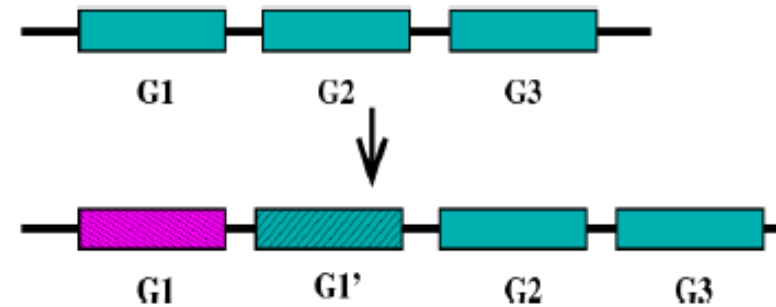


Evolution by Duplication Divergence

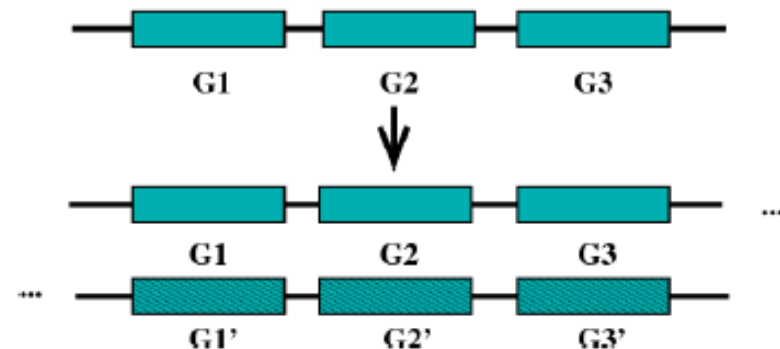
- Point mutations (substitutions)
continuously occurring
 10^{-3} fixed events/ nucleotide / MY



- Duplication of single genes
and groups of genes
high frequency at evolutionary timescale
 10^{-3} fixed events/ gene /MY

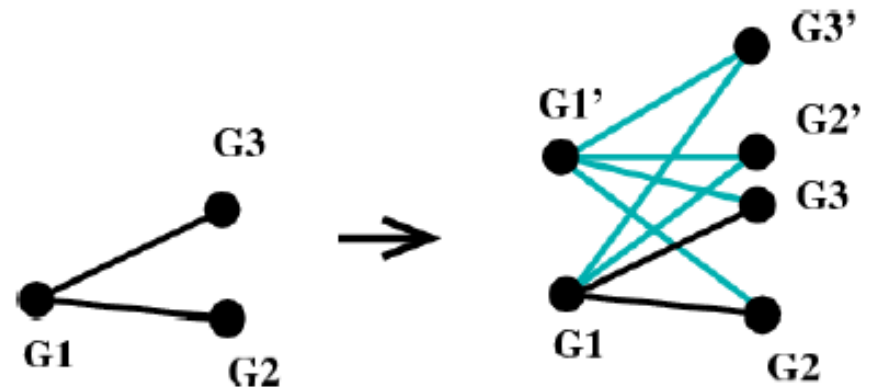
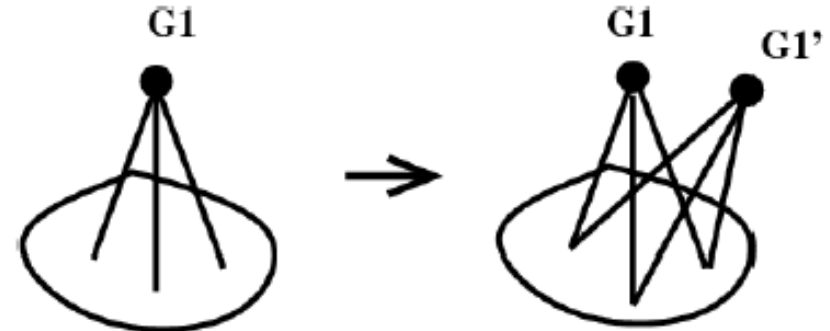
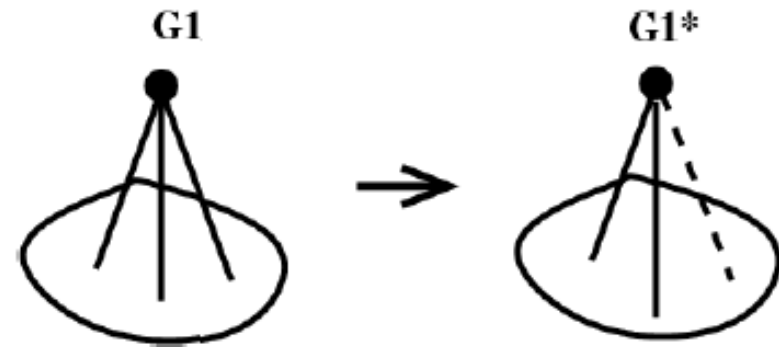
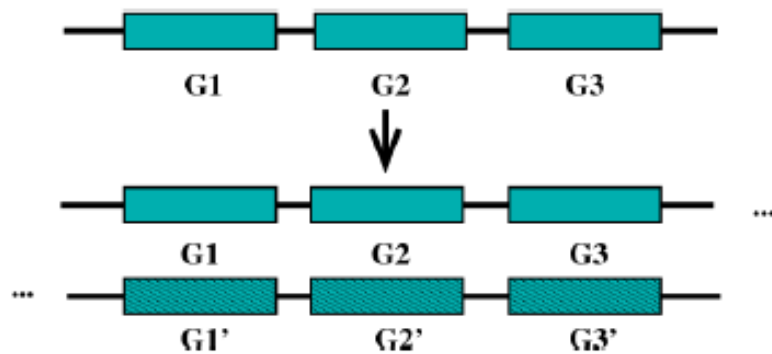
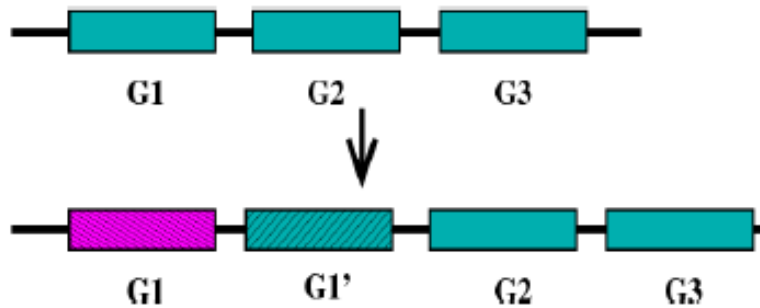
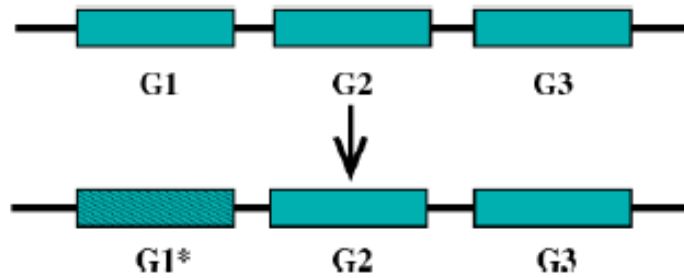


- Duplication of chromosomes
and of whole genome
rare events



1 fixed event / 100-200 MY = 10^{-3} events/ gene /MY

Evolution by Duplication Divergence

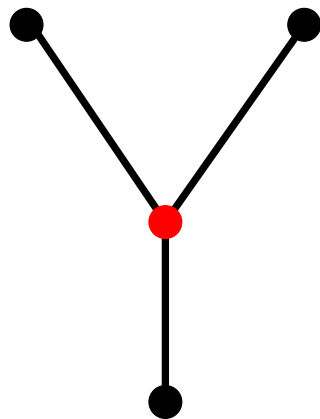


Evidence of Genome Duplication on PPI network

Yeast 6000 genes : 4000 in PPI network

500 duplicates from WGD : 250 with both duplicates in available PPI network

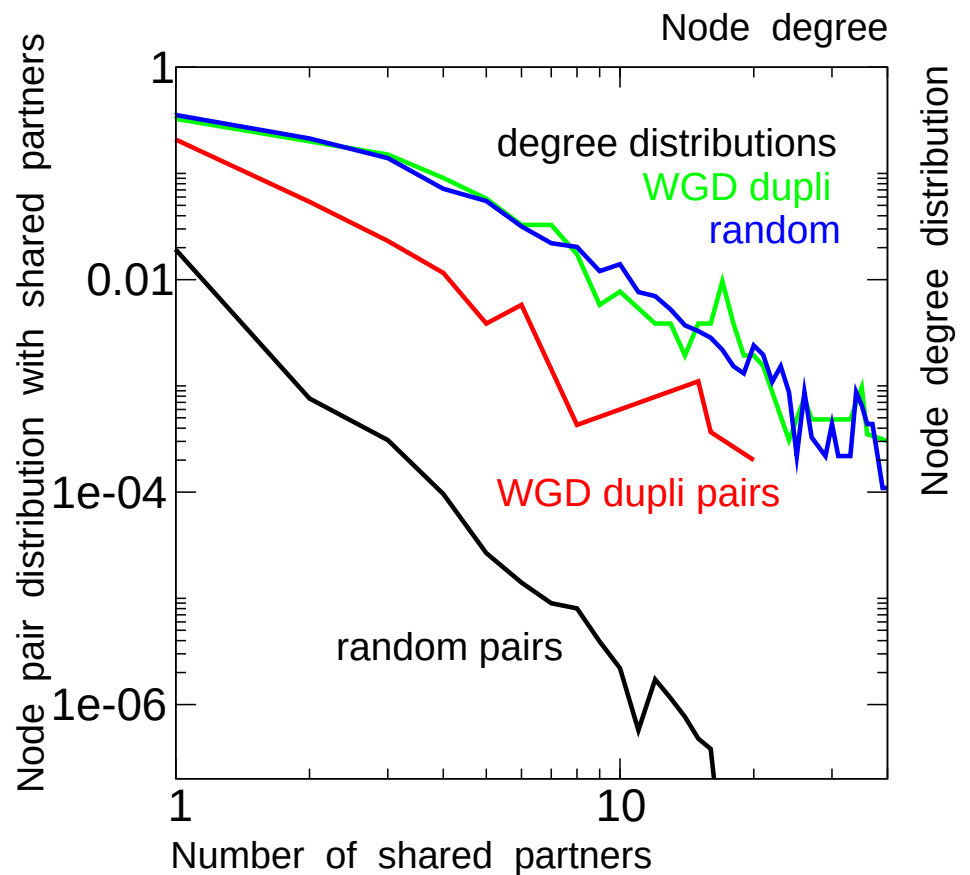
PPI network



Proba to share $k+$ partners :

$k=1$ WGD dupli > 20 x random pairs

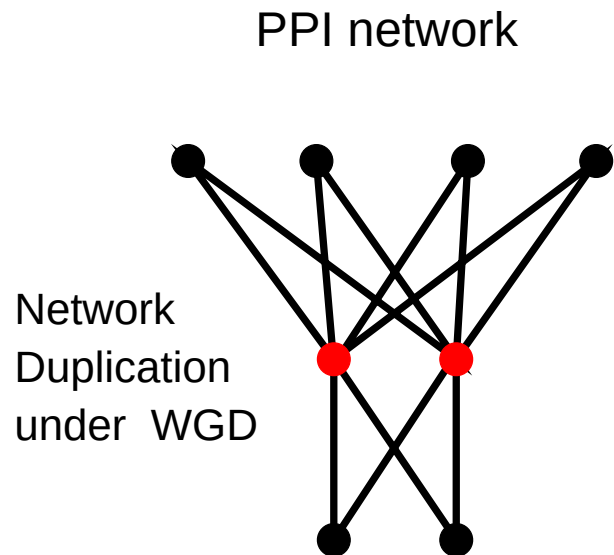
$k=10$ WGD dupli > 1,000 x random pairs



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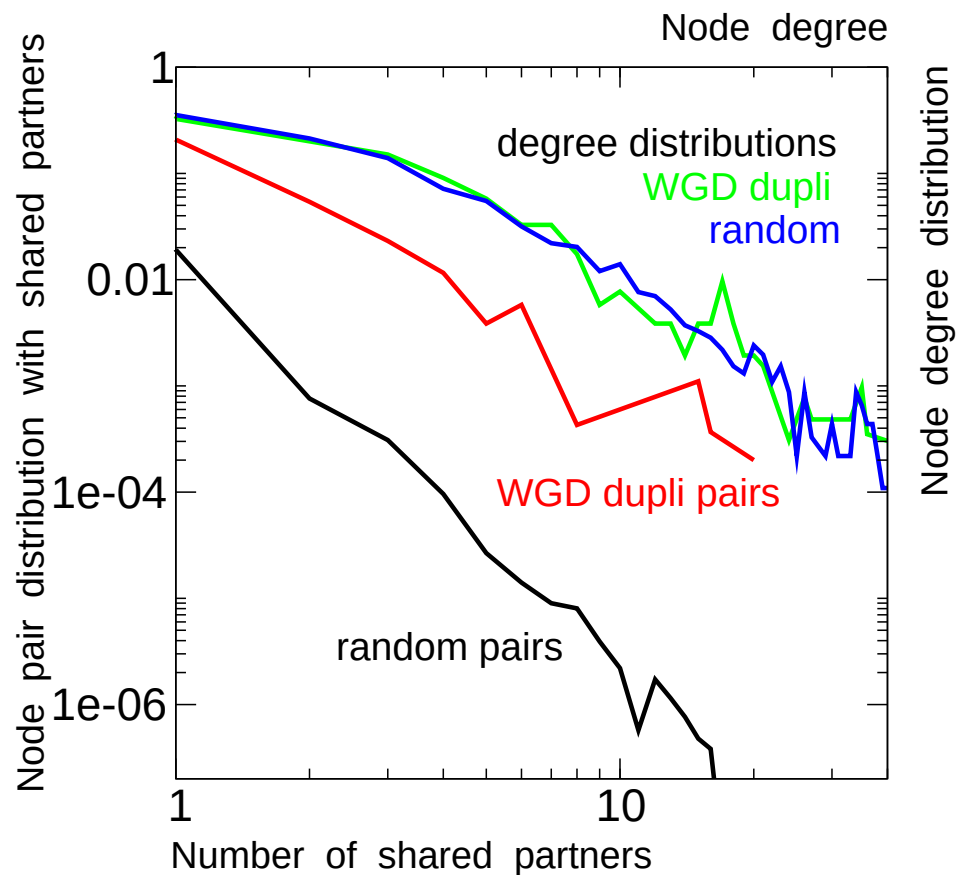
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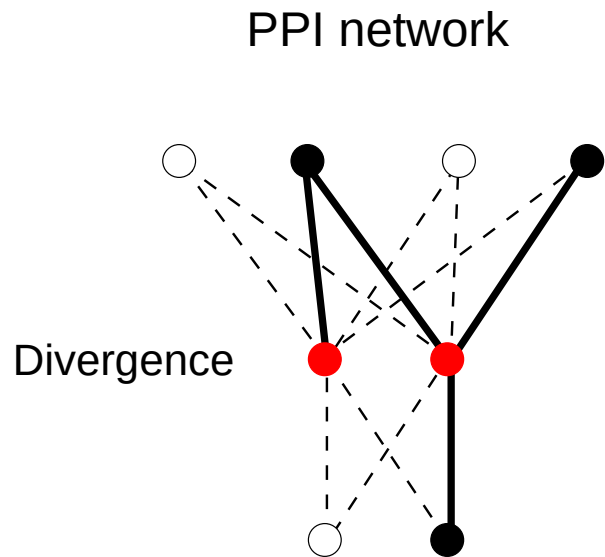
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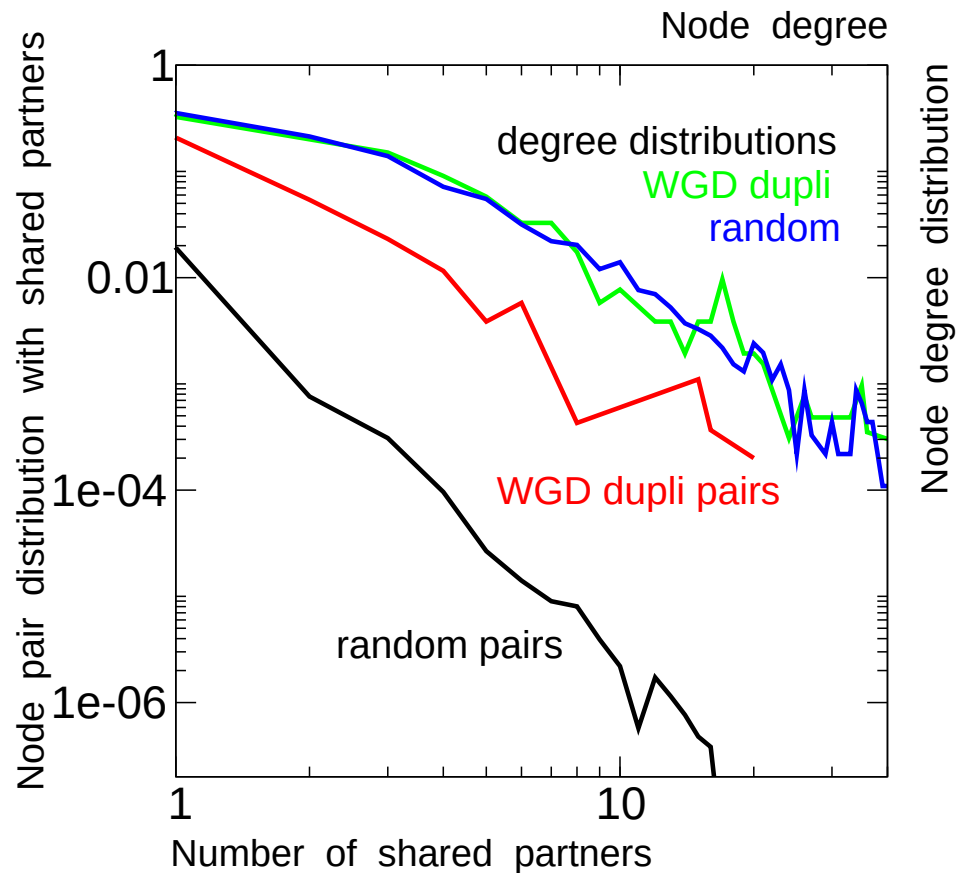
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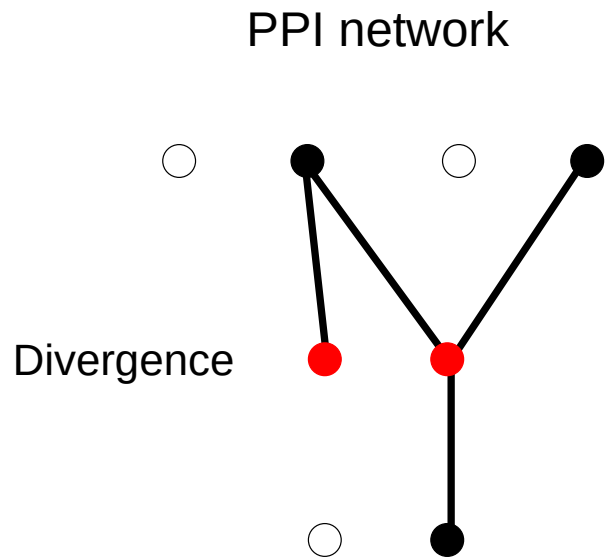
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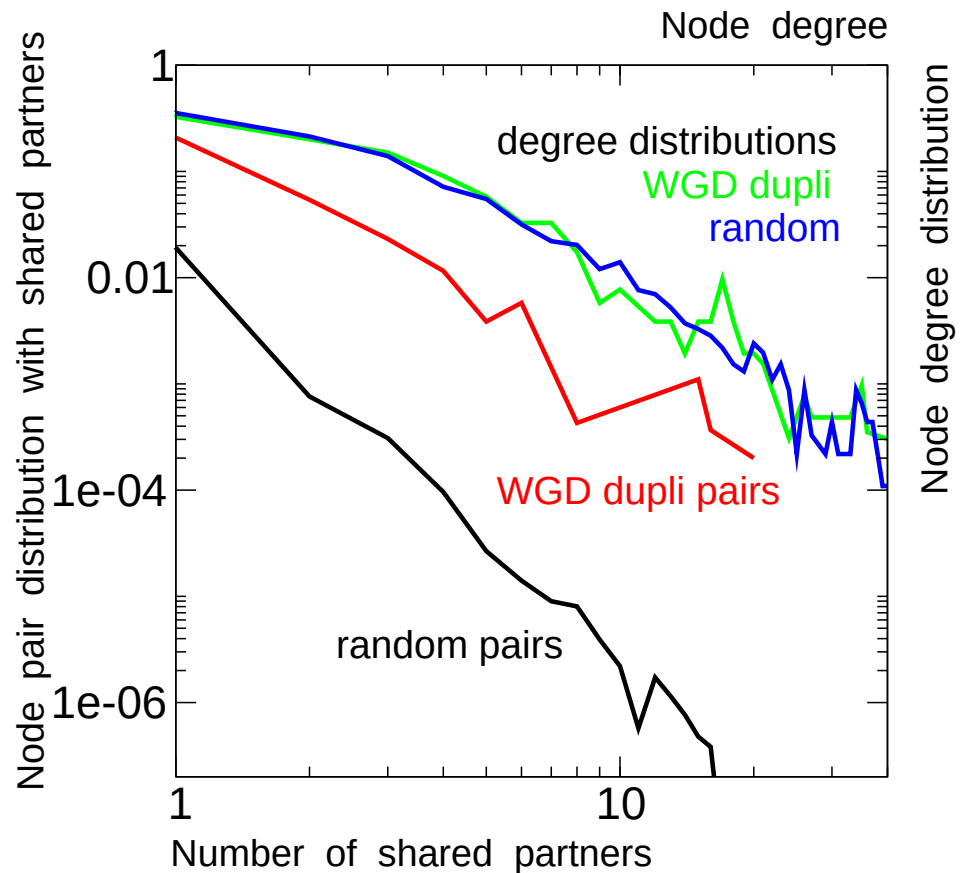
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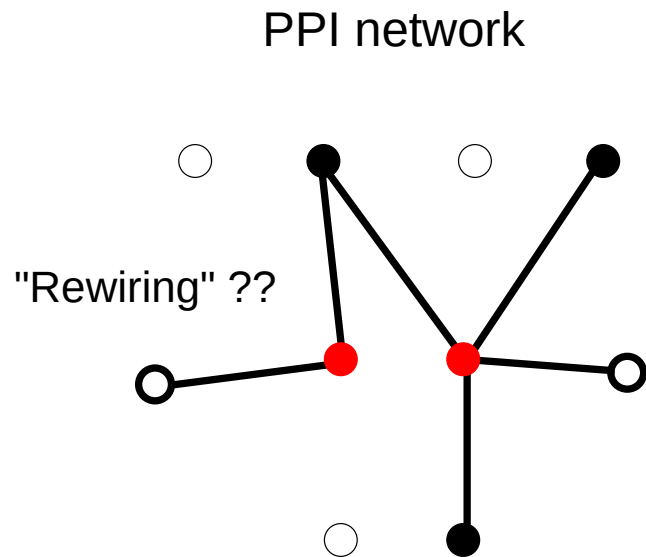
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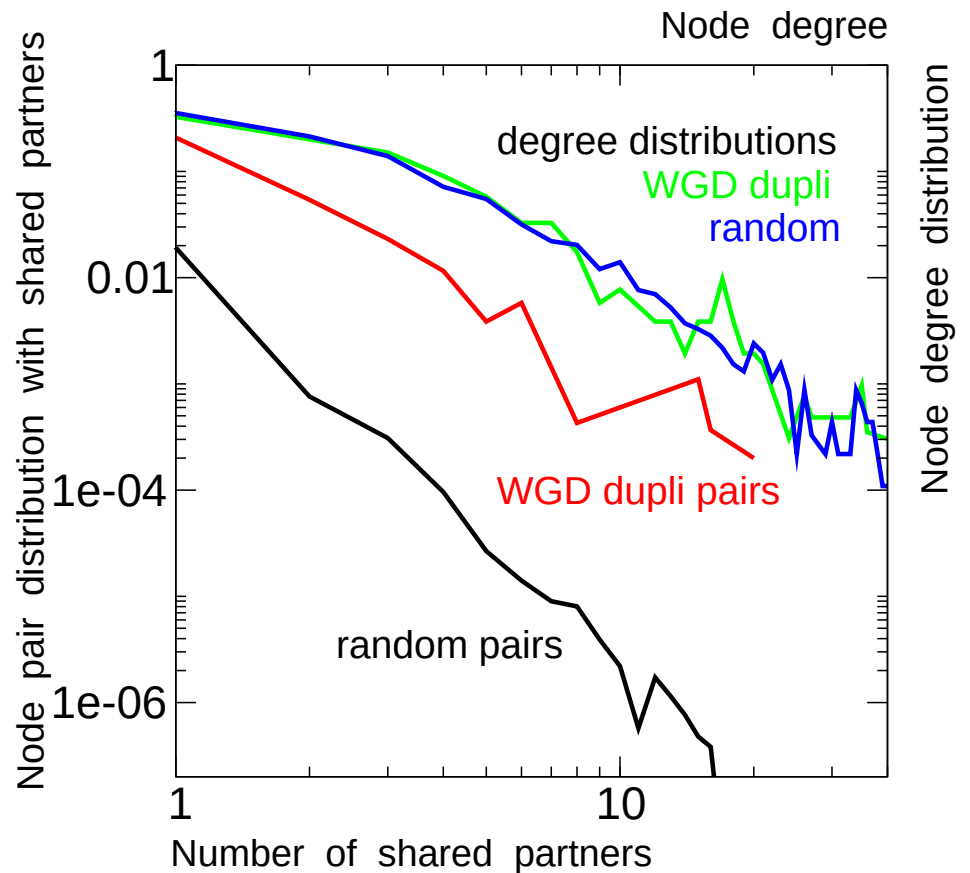
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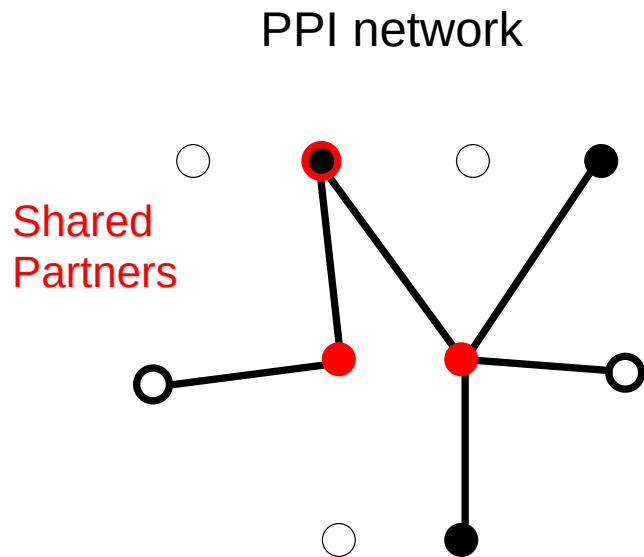
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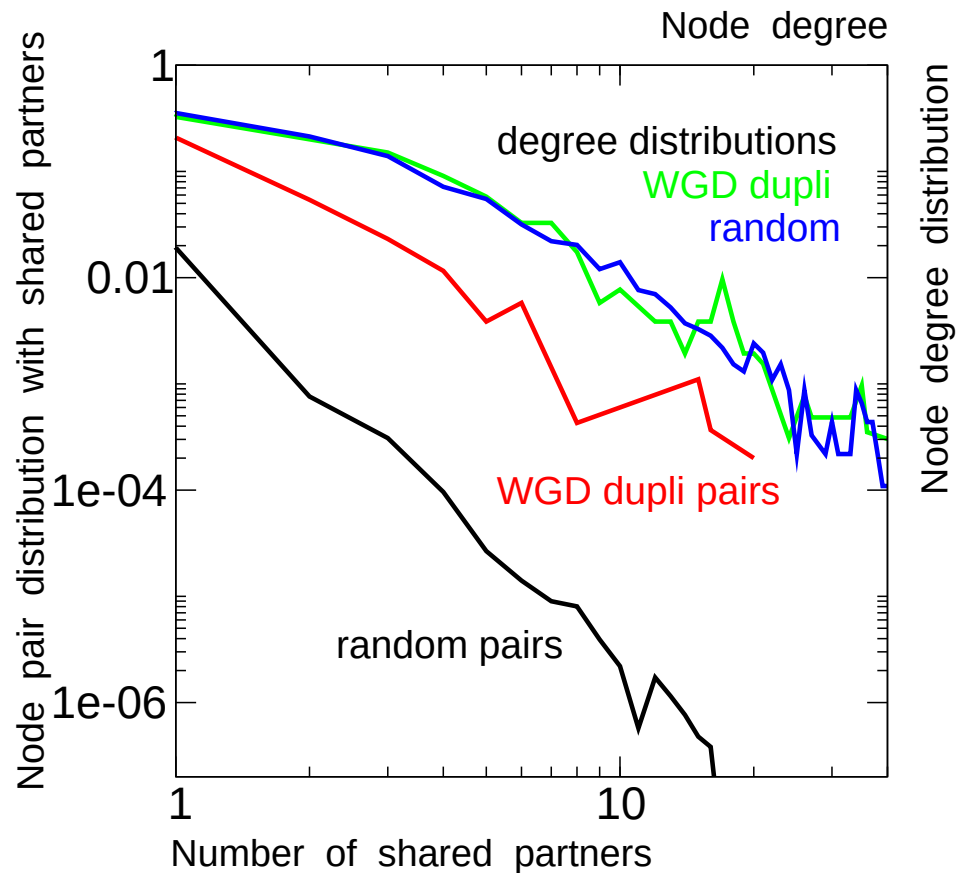
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Biological Networks and their Evolution

I. Introduction: from Genomes to Networks

II. Different Types of Biological Networks

III. Properties of Biological Networks

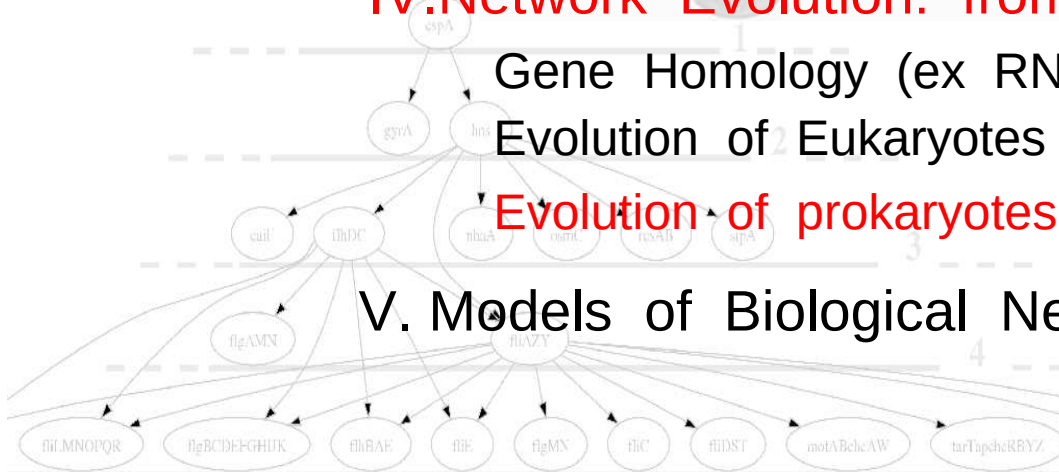
IV. Network Evolution: from Genes to Organisms

Gene Homology (ex RNA pol and Ribosome)

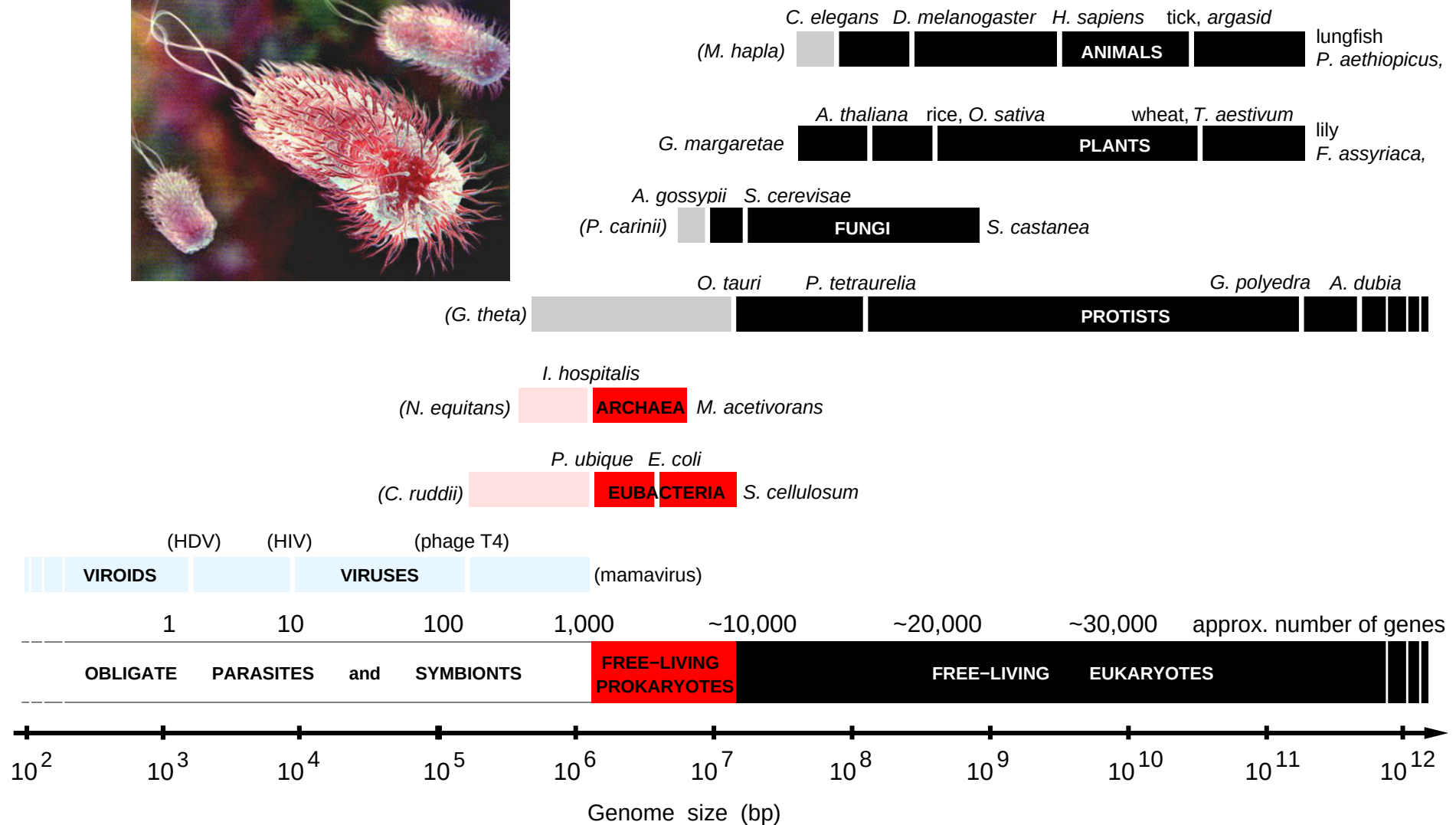
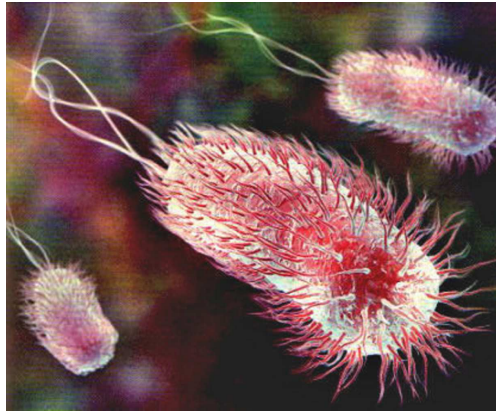
Evolution of Eukaryotes

Evolution of prokaryotes

V. Models of Biological Network Evolution

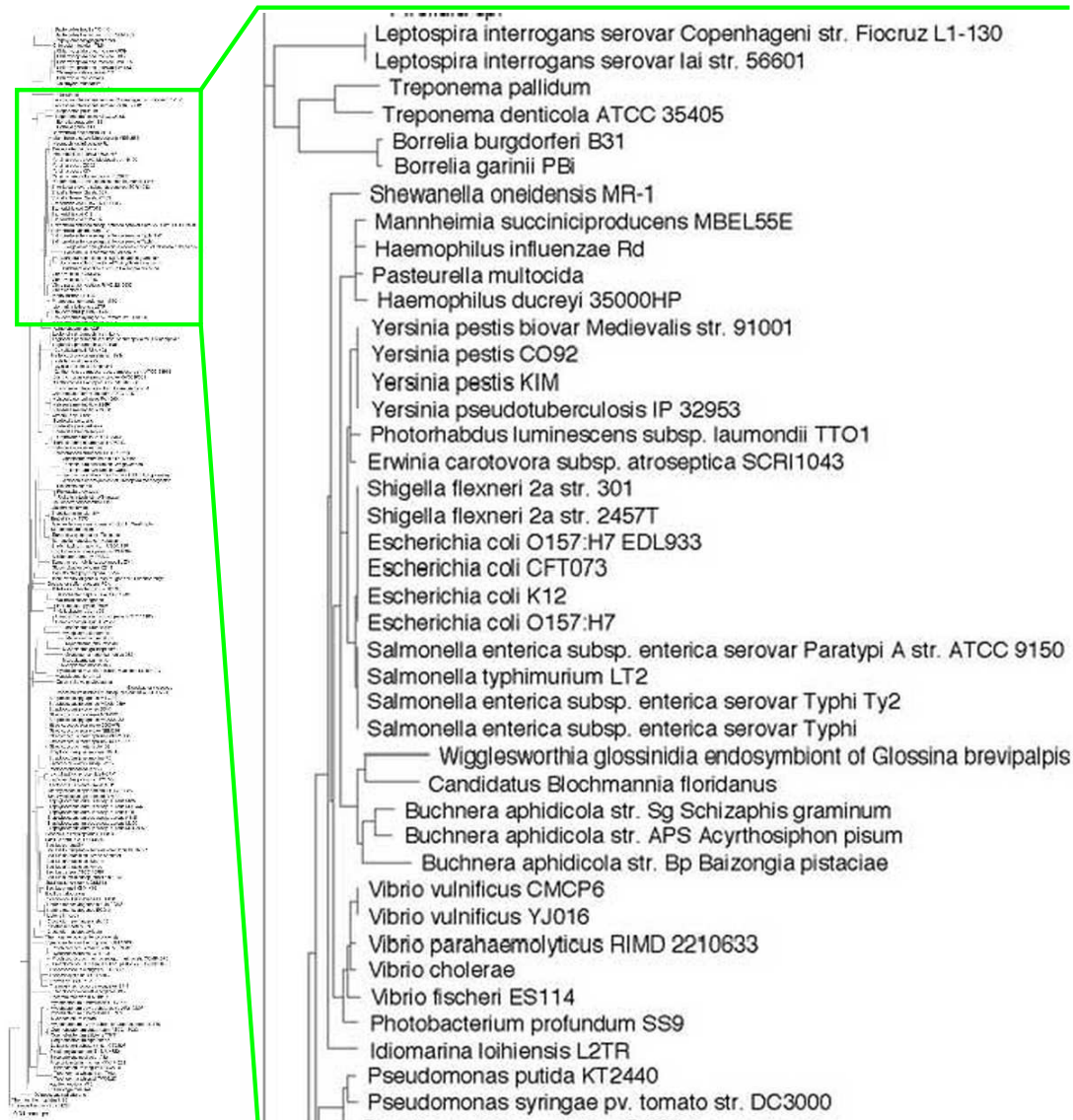


Genome Size Restriction of Free-living Prokaryotes



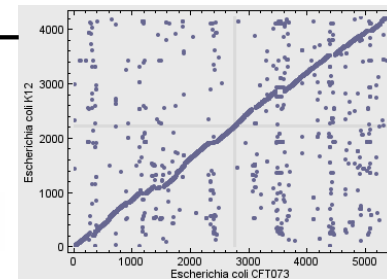
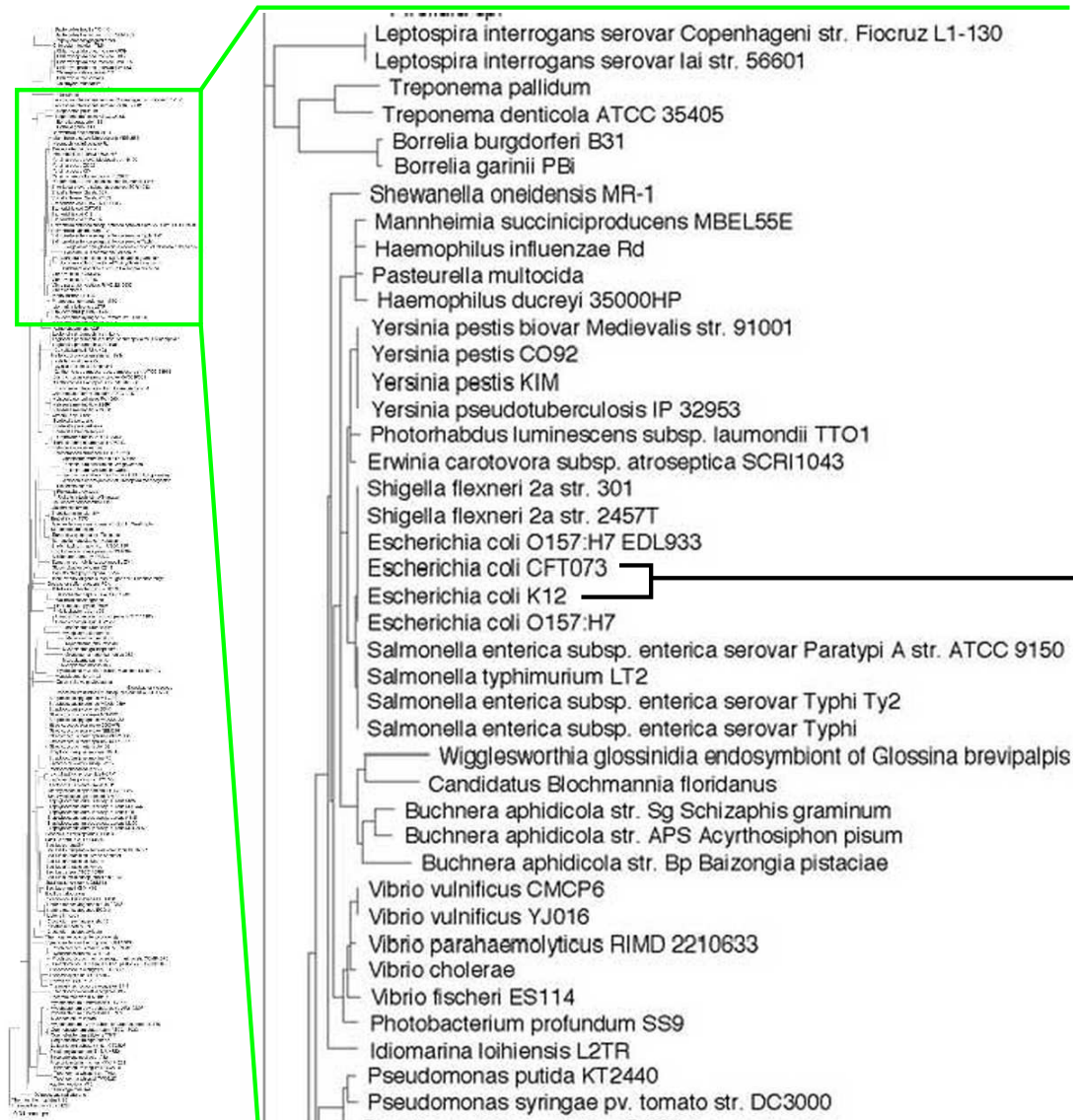
Homology bwn Prokaryote Genomes

+500 sequenced genomes



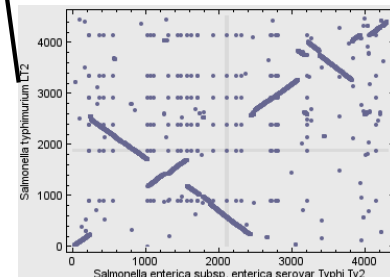
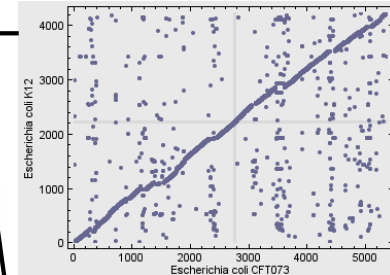
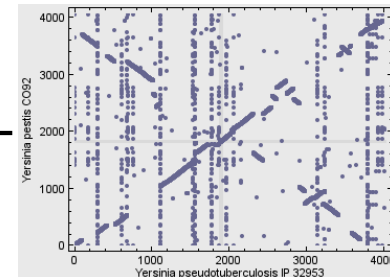
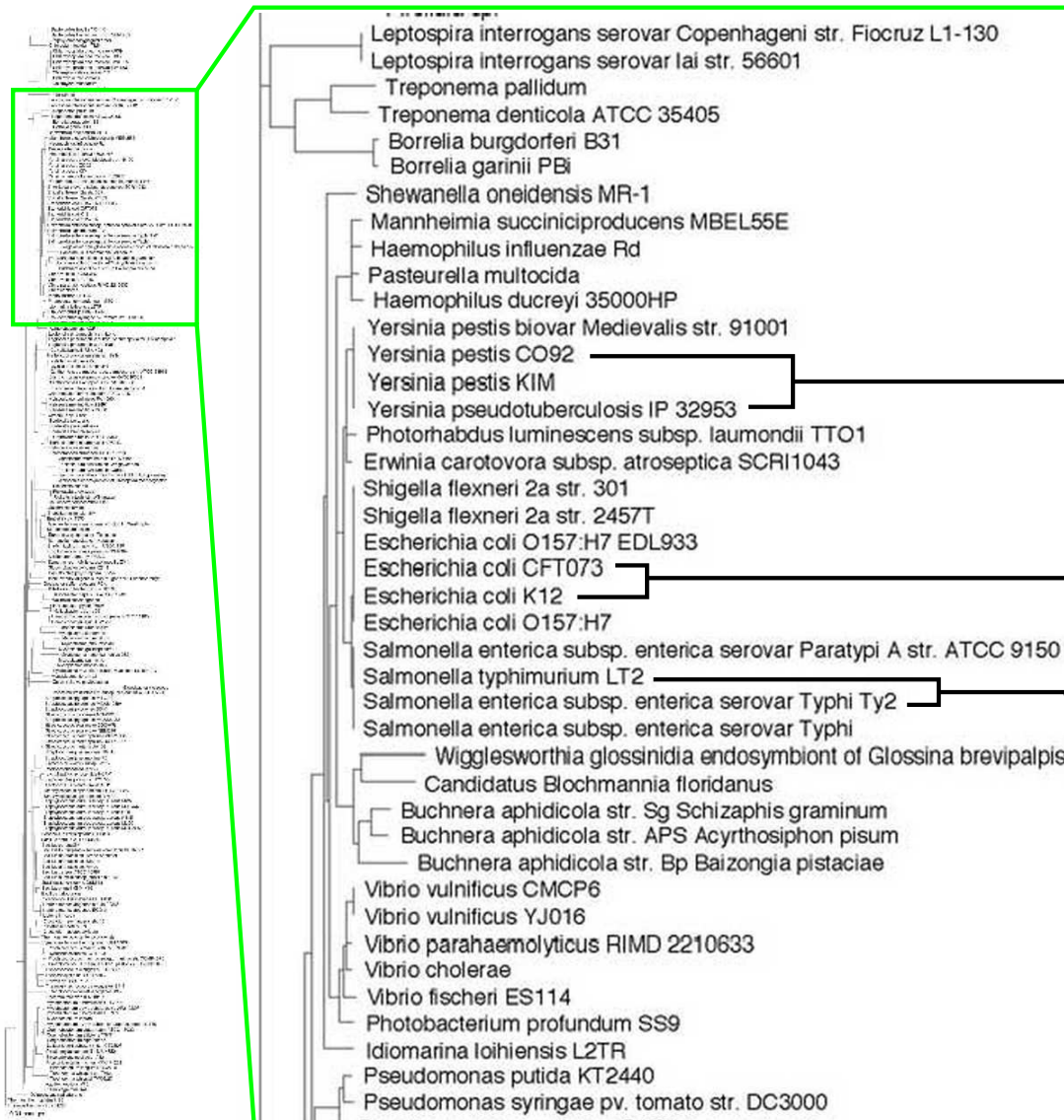
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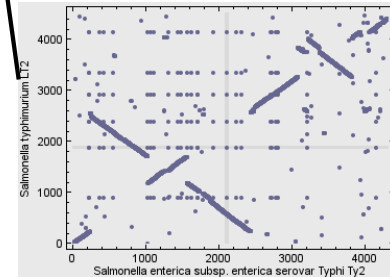
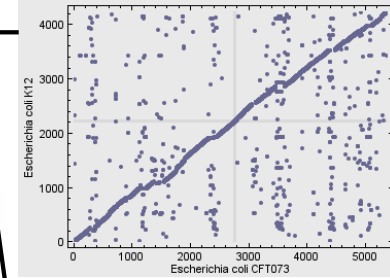
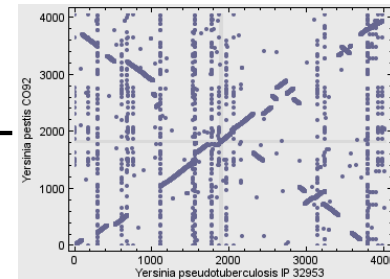
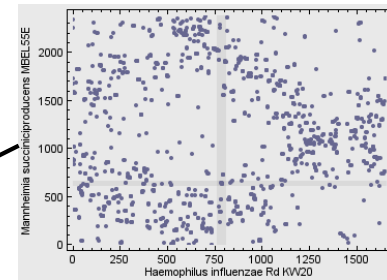
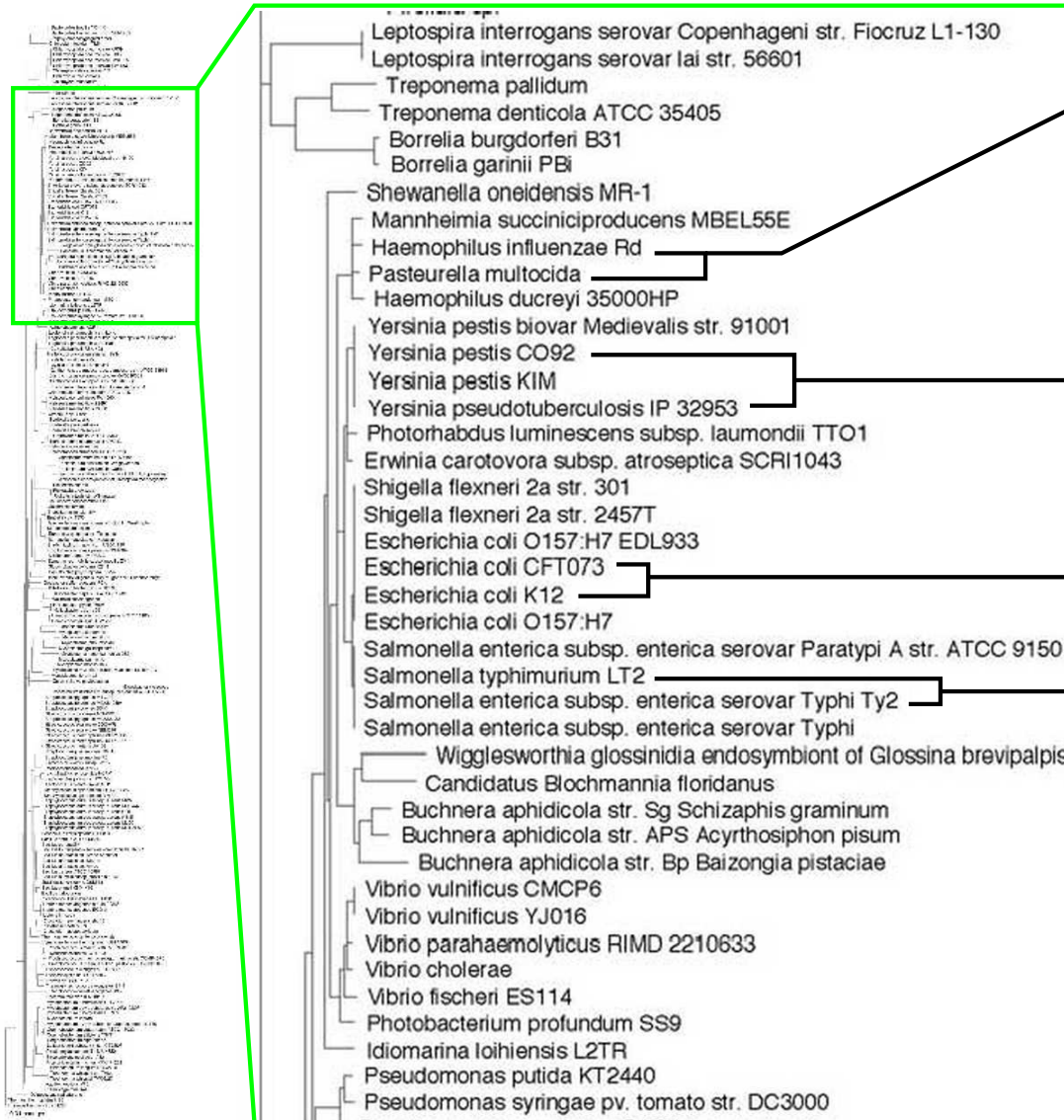
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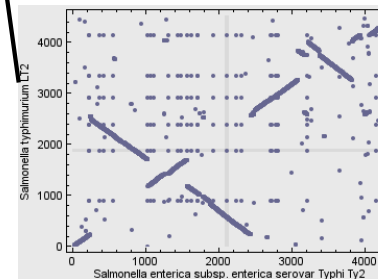
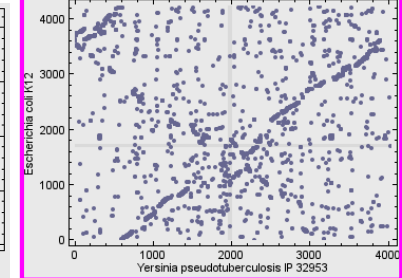
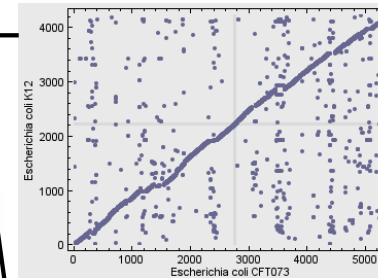
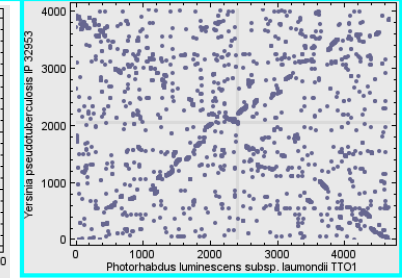
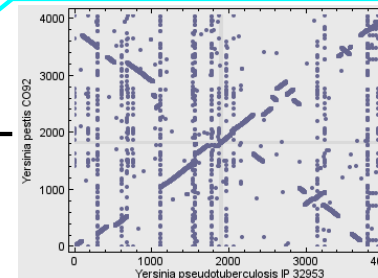
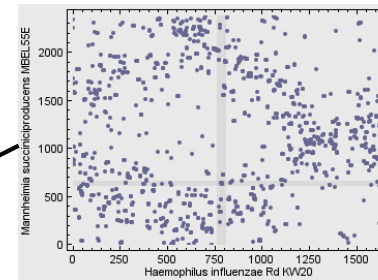
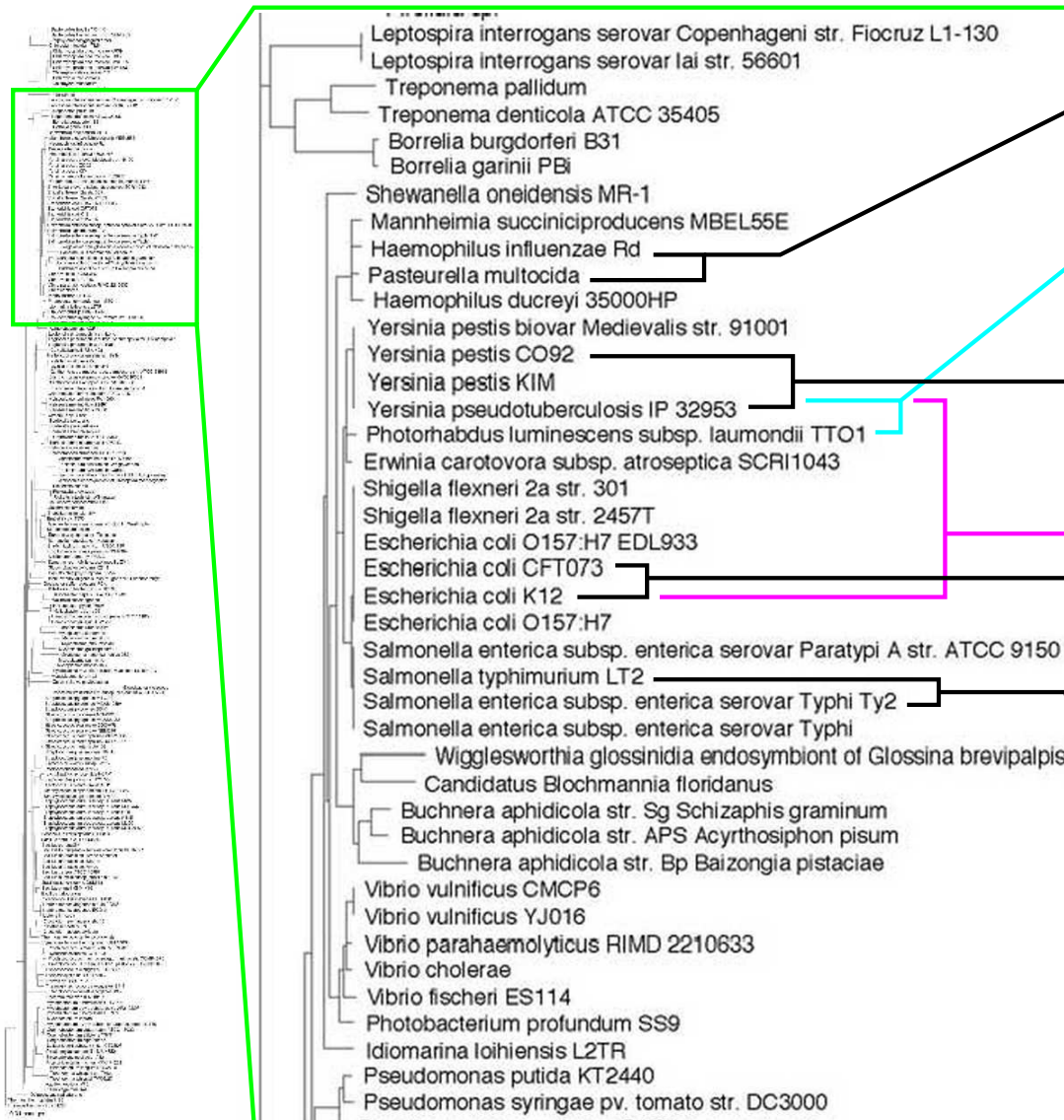
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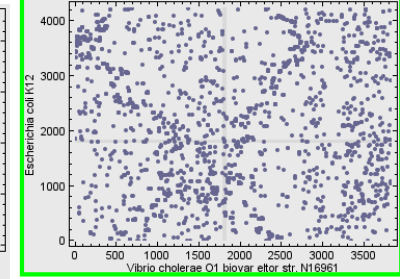
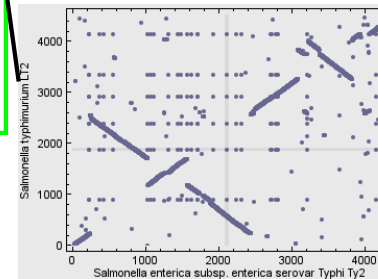
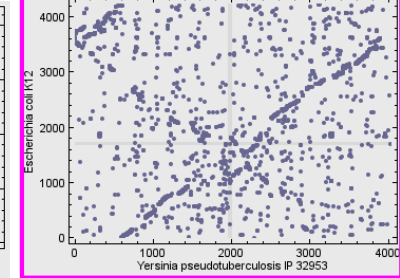
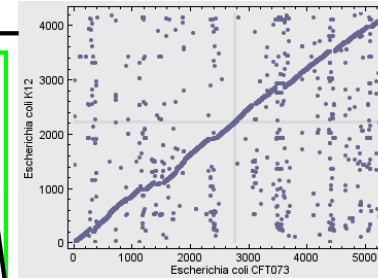
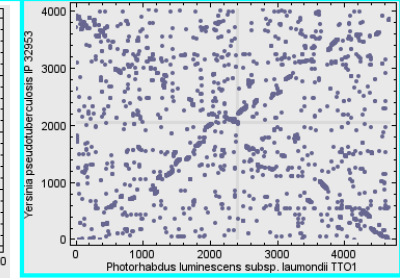
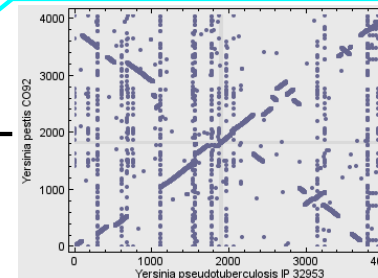
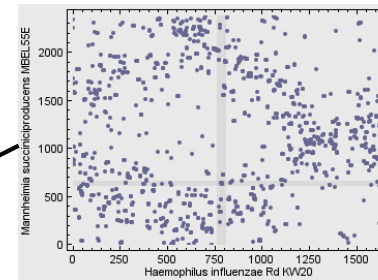
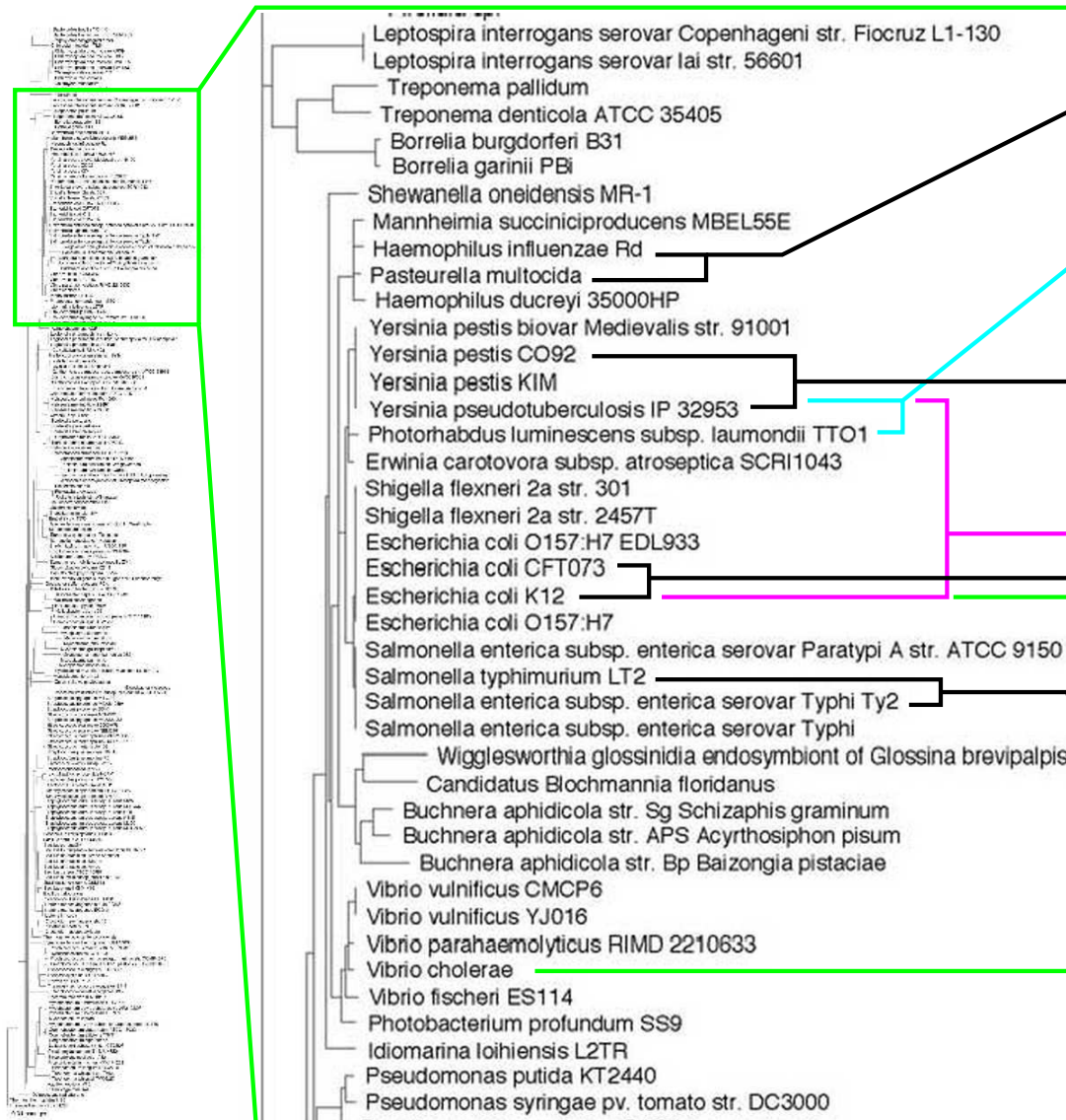
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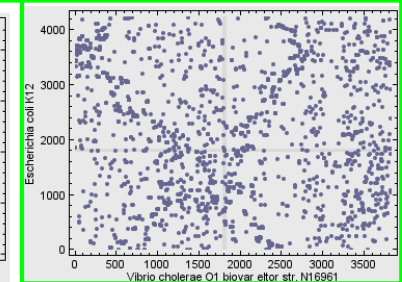
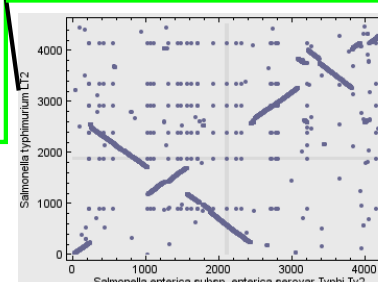
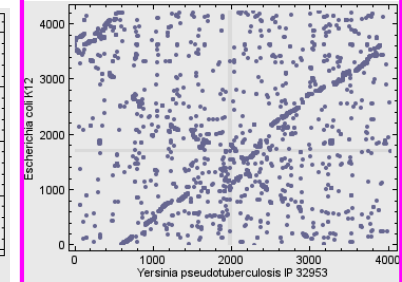
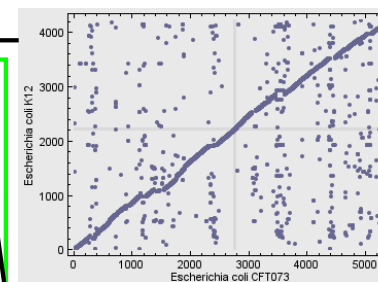
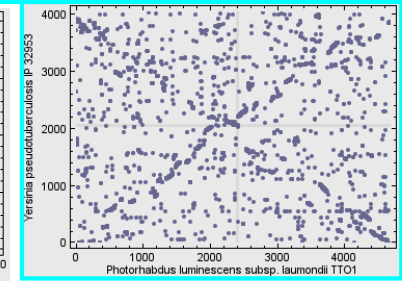
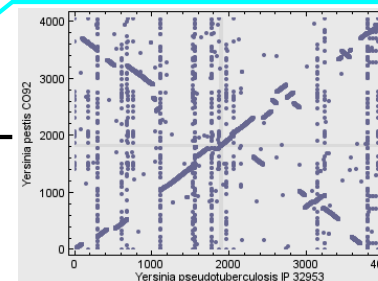
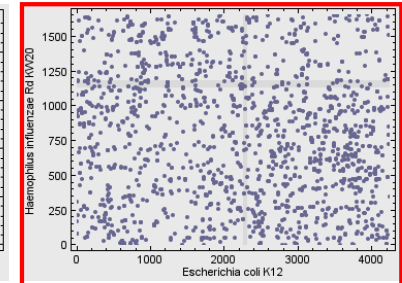
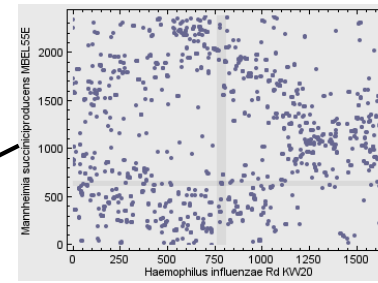
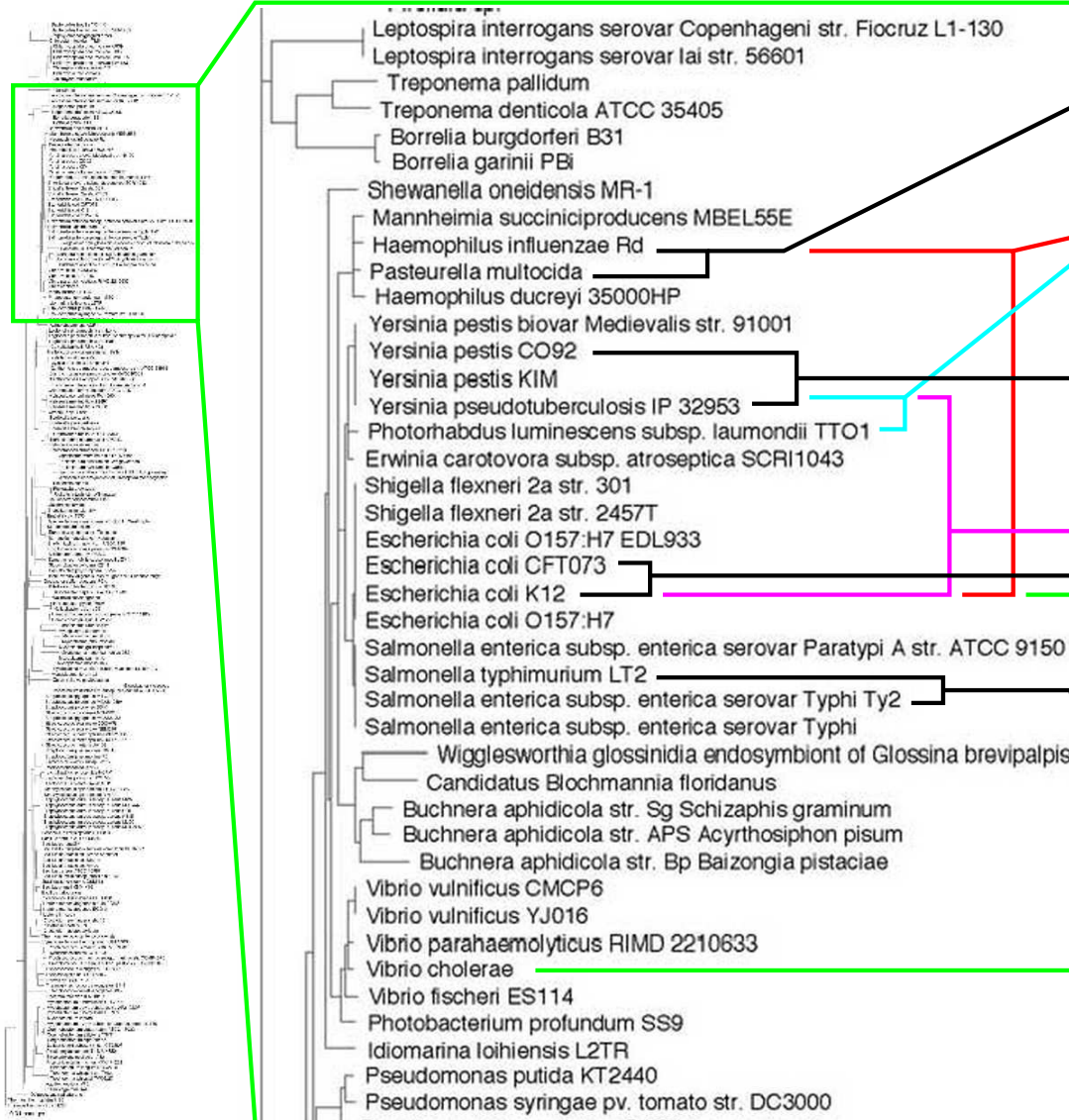
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