



*Visualisation en biologie cellulaire*

**Cytoscape, un nouveau microscope numérique pour la biologie cellulaire des systèmes**


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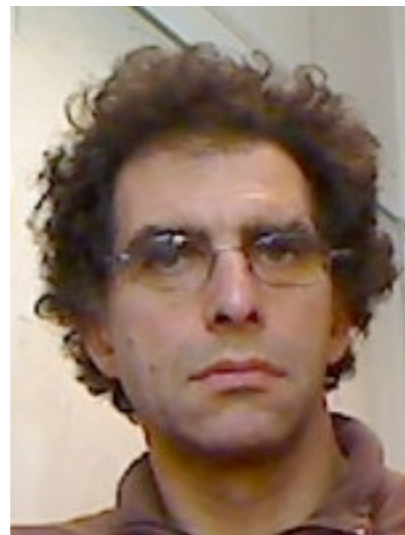



Frederik Gwinner 

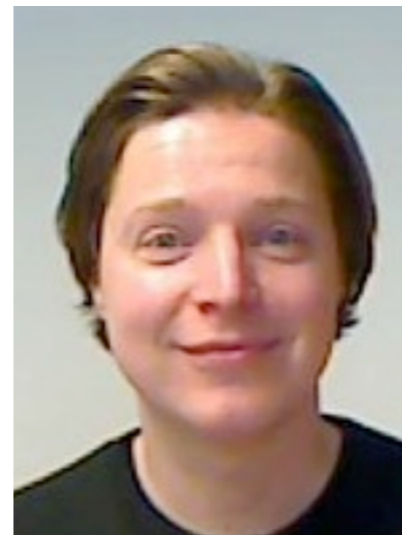



Xiaoyi Chen 

*Departing Ph.Ds*



Pascal Bochet 



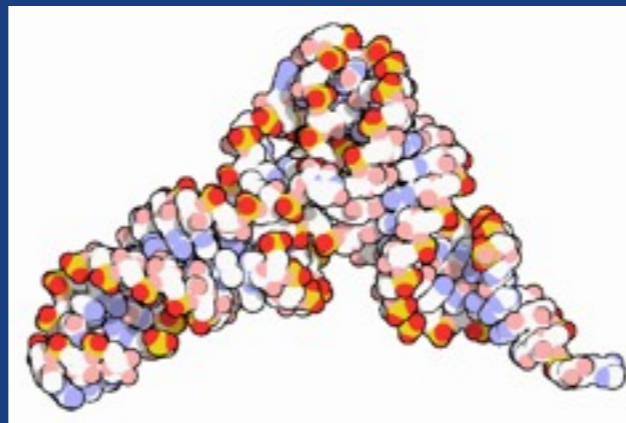
Tero Aittokallio 



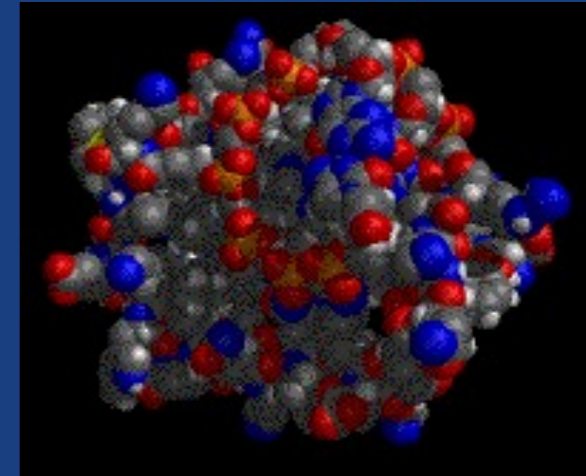
# Systems Biology: From molecules to networks



DNA / genes



RNA

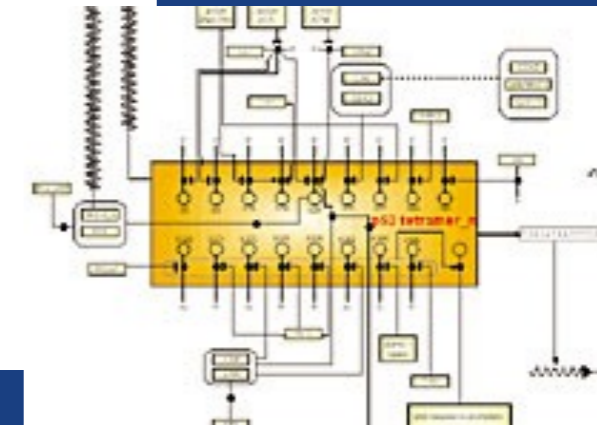
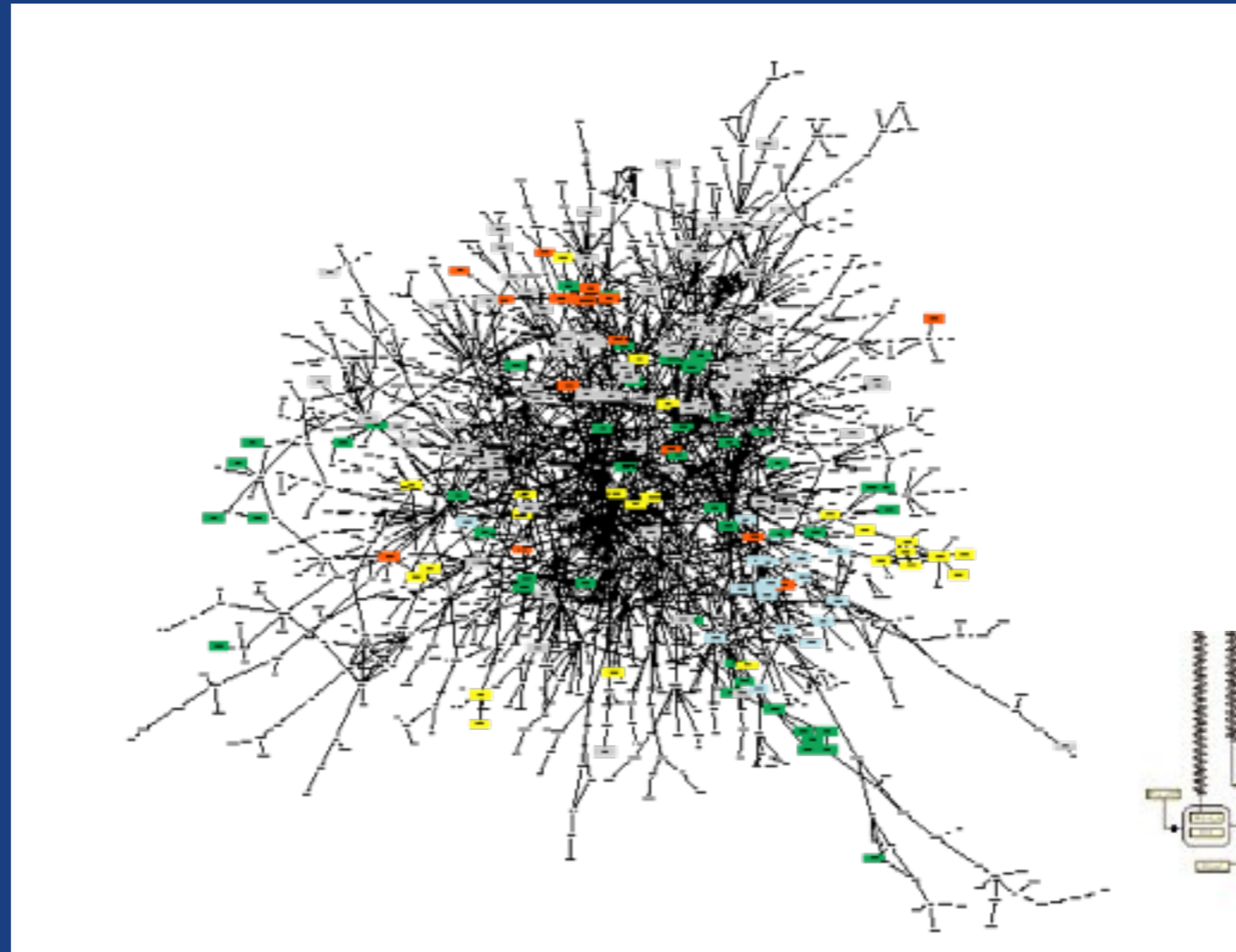


Protein

- Experimental observation
- Computational models



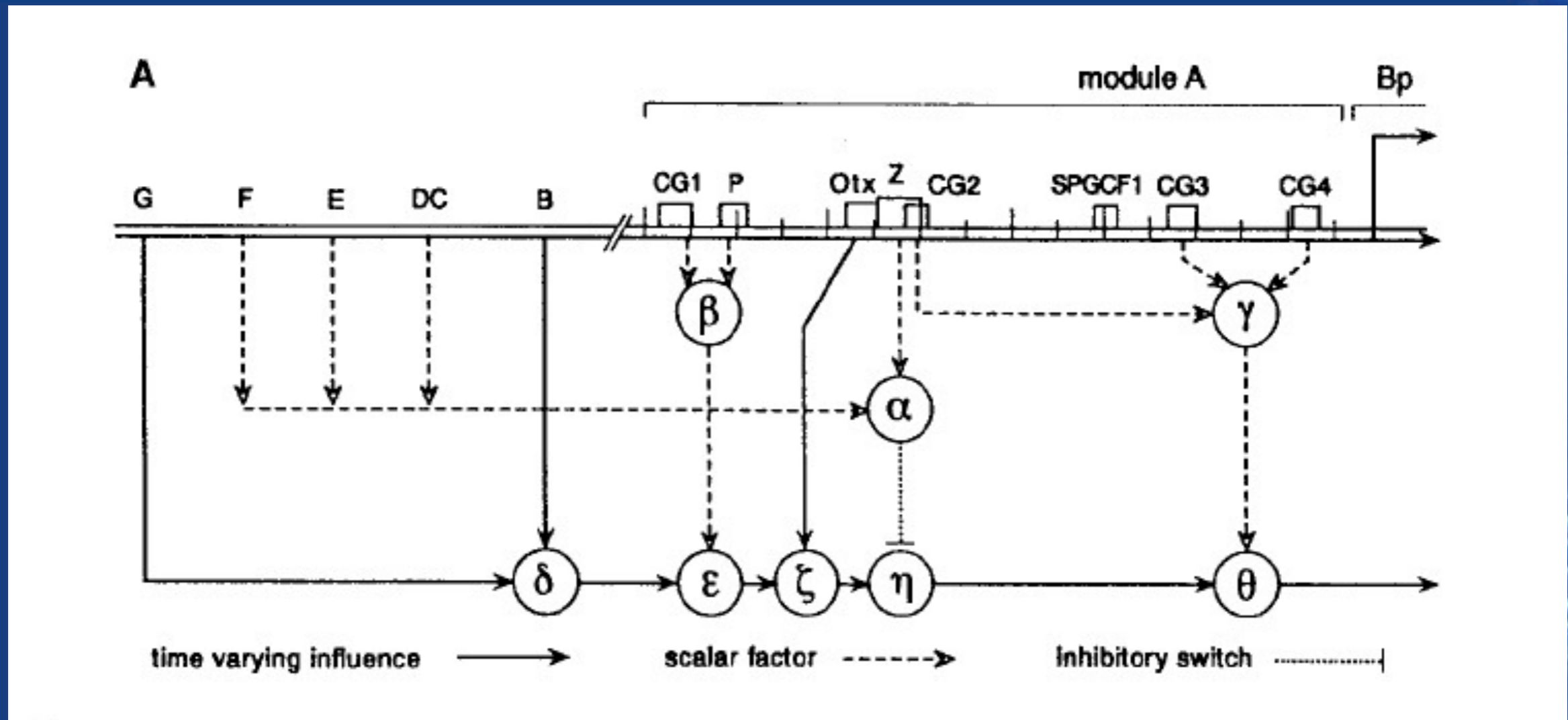
# What is complex about biological systems?



I. Biological parts interact in large networks.



# What is complex about biological systems?



Yuh, Bolouri, Davidson, Science, 1998

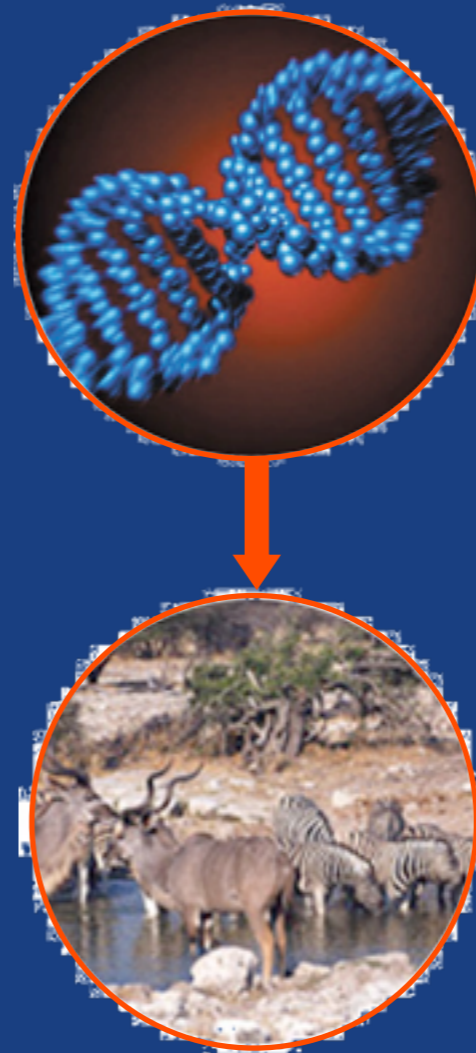
# What is complex about biological systems?

<b>B</b>	
<b>if (F = 1 or E = 1 or CD = 1) and (Z = 1)</b>	Repression functions of modules F, E, and DC mediated by Z site
$\alpha = 1$	
<b>else</b> $\alpha = 0$	
<b>if (P = 1 and CG<sub>1</sub> = 1)</b>	Both P and CG <sub>1</sub> needed for synergistic link with module B
$\beta = 2$	
<b>else</b> $\beta = 0$	
<b>if (CG<sub>2</sub> = 1 and CG<sub>3</sub> = 1 and CG<sub>4</sub> = 1)</b>	Final step up of system output
$\gamma = 2$	
<b>else</b> $\gamma = 1$	
$\delta(t) = B(t) + G(t)$	Positive input from modules B and G
$\varepsilon(t) = \beta * \delta(t)$	Synergistic amplification of module B output by CG <sub>1</sub> -P subsystem
<b>if (<math>\varepsilon(t) = 0</math>)</b>	Switch determining whether Otx site in module A, or upstream modules (i.e., mainly module B), will control level of activity
$\xi(t) = Otx(t)$	
<b>else</b> $\xi(t) = \varepsilon(t)$	
<b>if (<math>\alpha = 1</math>)</b>	Repression function inoperative in endoderm but blocks activity elsewhere
$\eta(t) = 0$	
<b>else</b> $\eta(t) = \xi(t)$	
$\Theta(t) = \gamma * \eta(t)$	Final output communicated to BTA



# What is complex about biological systems?

DNA  
mRNA  
Proteins  
Pathways/Modules  
Cells  
Tissues  
Organs  
Individuals  
Populations  
Ecosystems



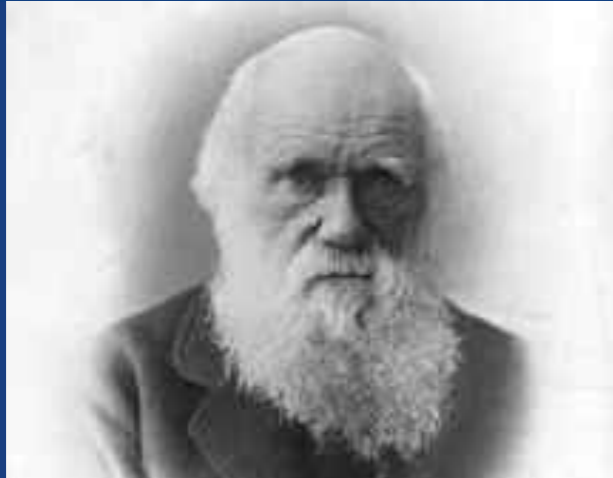
## 2. Different levels interact.



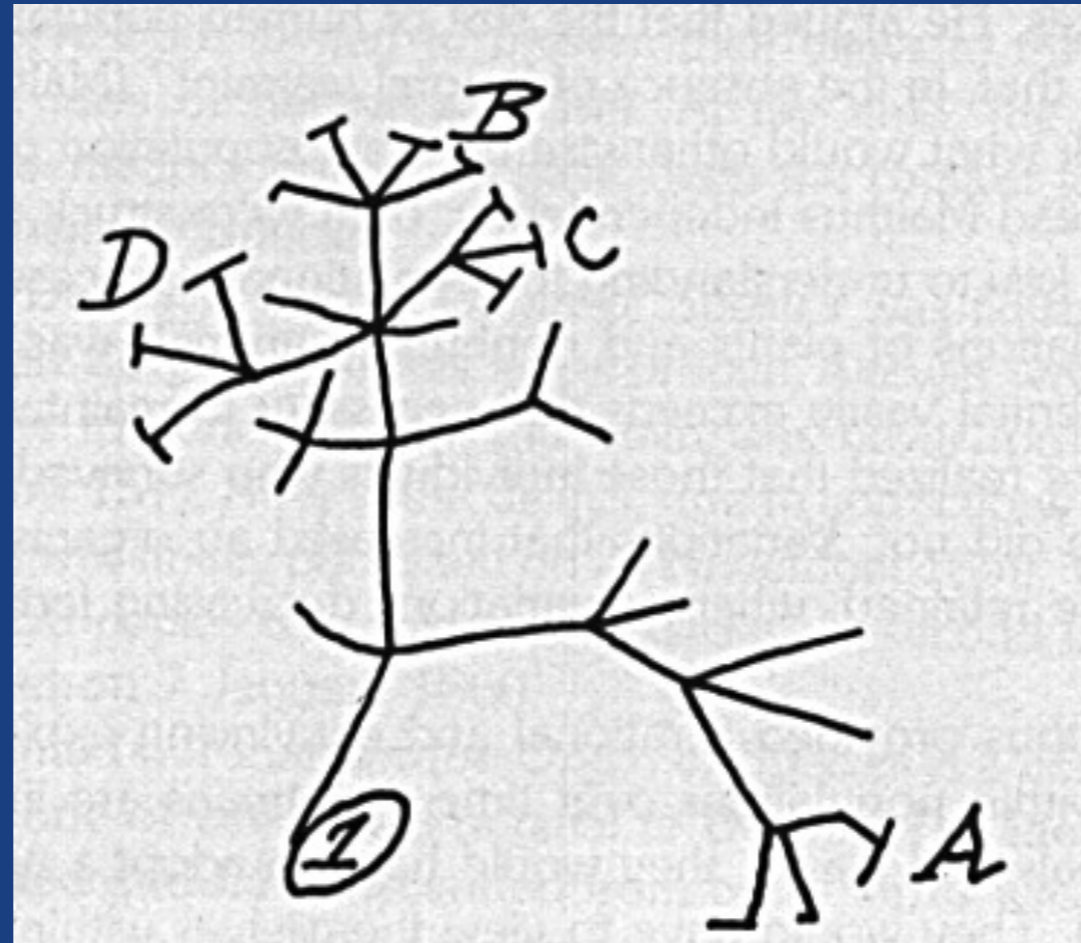
# What is complex about biological systems?



# What is complex about biological systems?



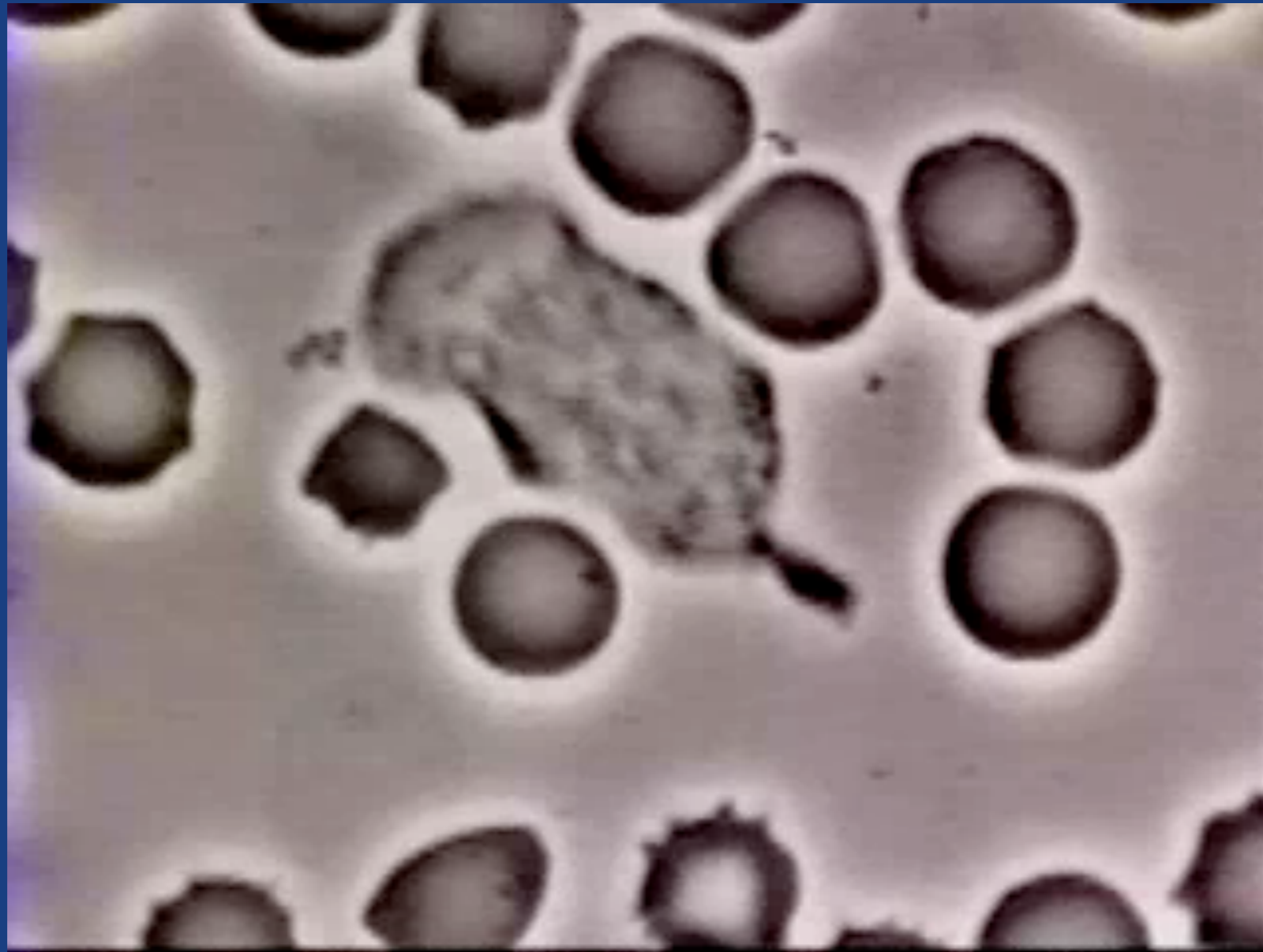
Charles Darwin



1837

3. Different parts are related by evolution.

# What is complex about biological systems?

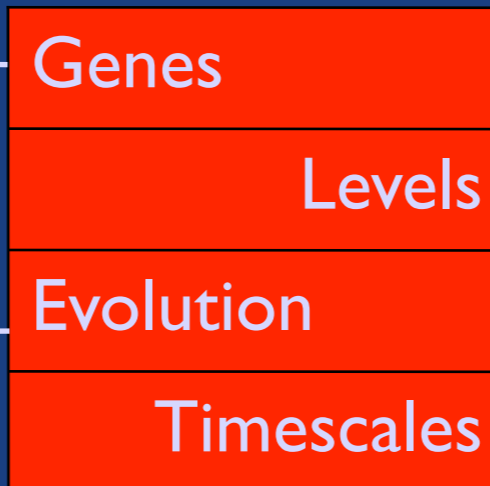
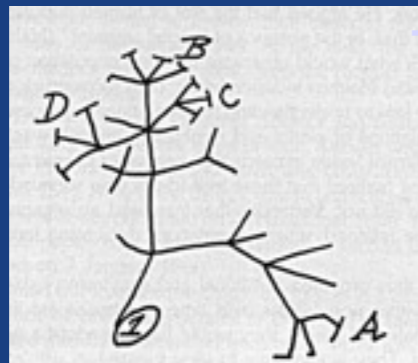
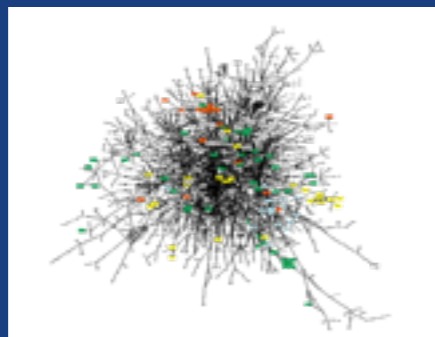


## 4. Interacting timescales.



# What is complex about biological systems?

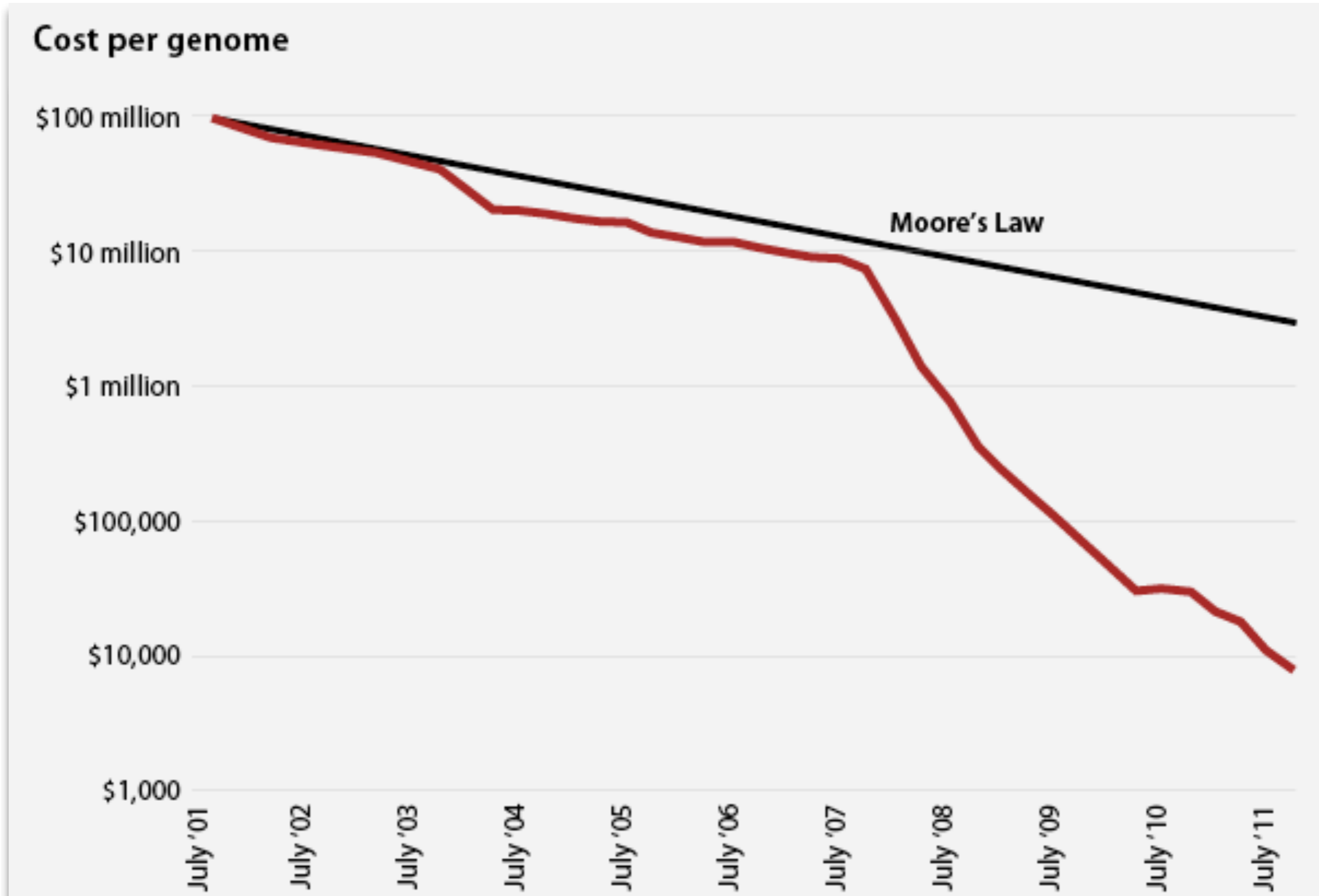
*Four nonlinear contexts.*



[wehi.edu.au](http://wehi.edu.au)



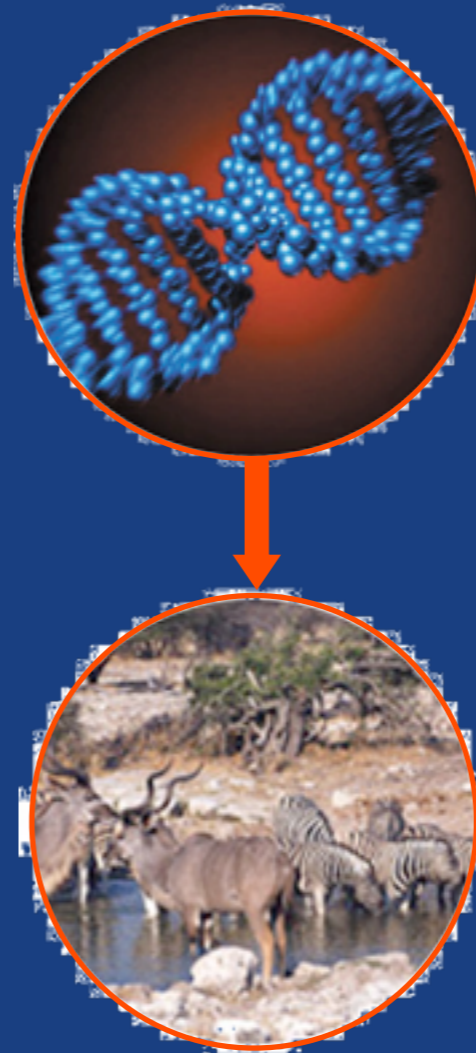
# DNA/RNA sequencing technology



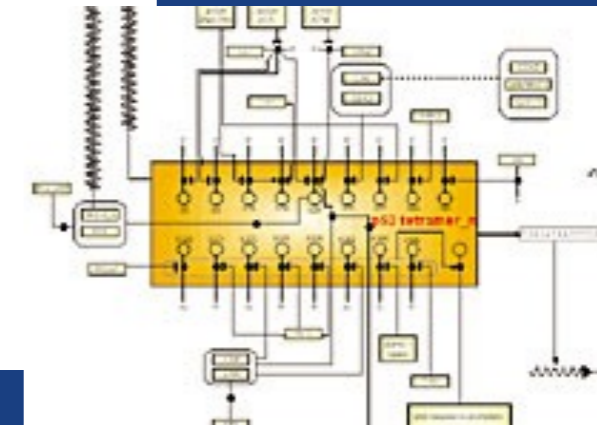
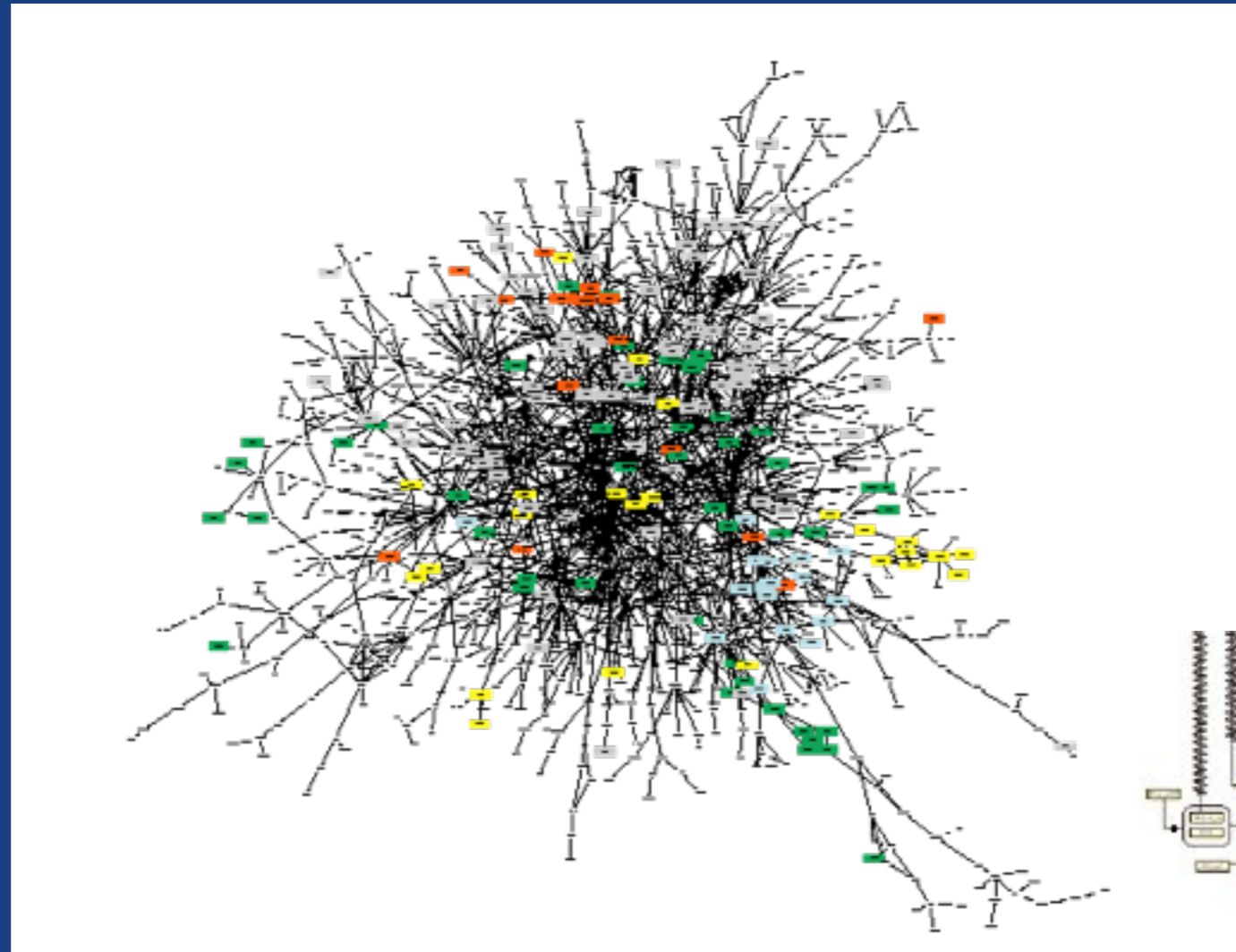


# Why do we need a digital pathway microscope?

DNA  
mRNA  
Proteins  
Pathways/Modules  
Cells  
Tissues  
Tissues  
Organs  
Individuals  
Populations  
Ecosystems



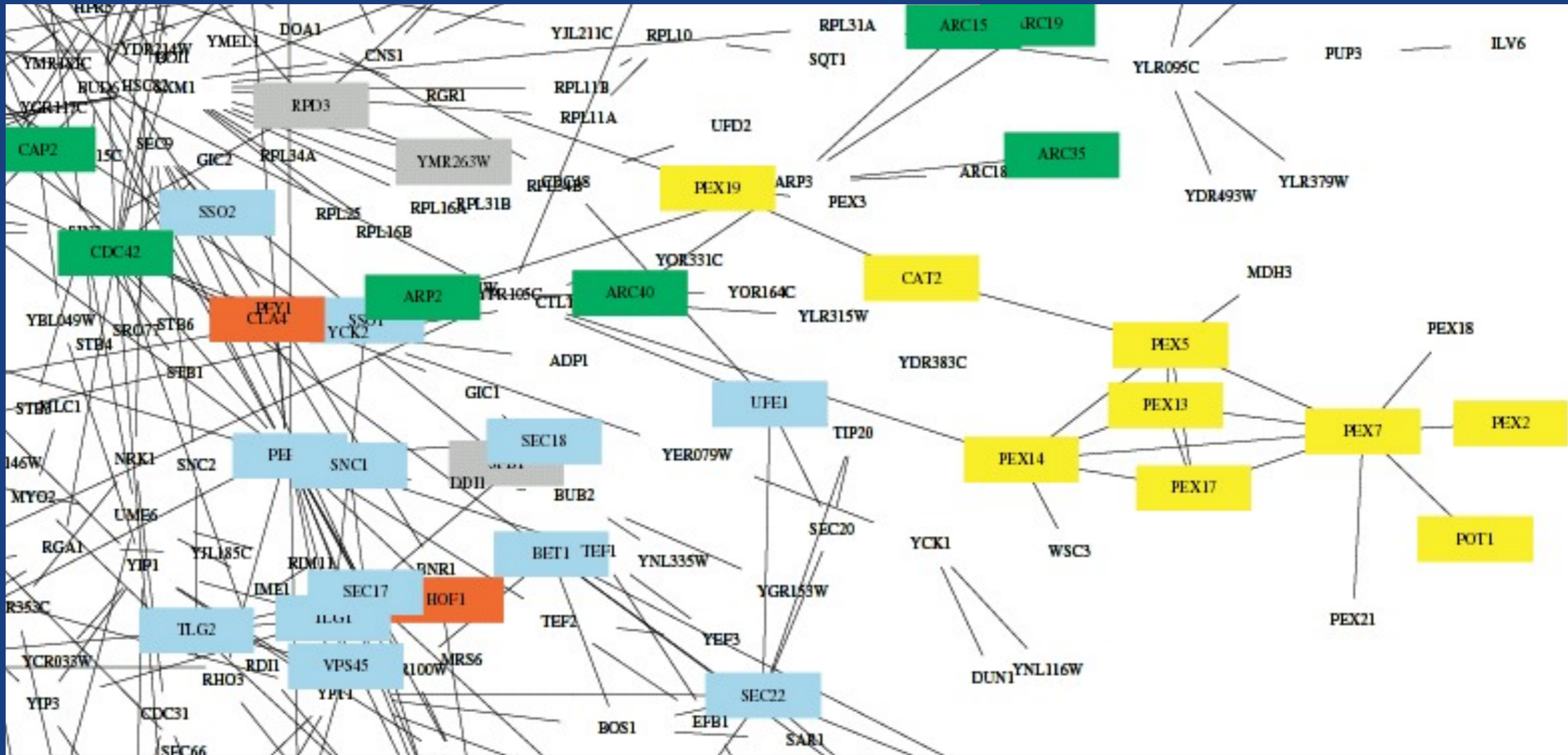
# What is complex about biological systems?



I. Biological molecules interact in large networks.



# Can we figure these out?





# Cytoscape

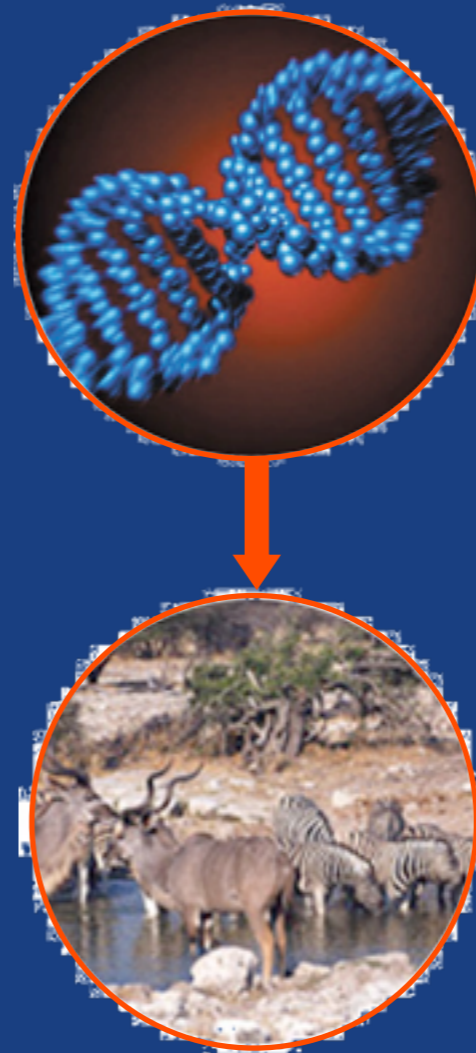
Our digital microscope

# Cytoscape, a digital microscope for cell biology

- Different qualitative and quantitative information accessible in one place
- Organized into interaction networks that represent systems
- Visual exploration goes hand in hand with statistical data exploration and analysis
- Open source and open standards
- Active community exchanging networks, know-how, and new functionality

# Why do we need a digital pathway microscope?

DNA  
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# Research questions

Why do some drugs work in person A, but not in person B?

Can you *predict* whether a drug will work for A? For B?

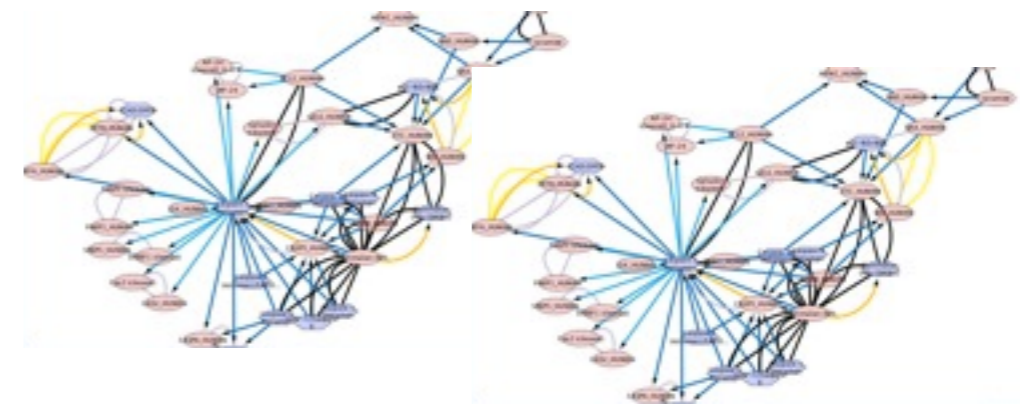
What drug combinations can/cannot do?

Why do more and more people become allergic to their environment?

How to diagnose breast cancer *before* it starts?

Can we find the better drug targets against malaria/HIV/tuberculosis/Alzheimer's/colon cancer/...

...



*Merci !*

For more information visit

<http://cytoscape.org>  
<http://systemsbiology.fr>

**Cytoscape**  
Cytoscape: An Open Source Platform for Complex Network Analysis and Visualization

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Network Data Integration, Analysis, and Visualization in a Box

Cytoscape is an open source software platform for visualizing complex networks and integrating these with any type of attribute data. A lot of plugins are available for various kinds of problem domains, including bioinformatics, social network analysis, and semantic web.

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**NATIONAL RESOURCE FOR NETWORK BIOLOGY**

We are developing a freely available, open source suite of software technologies to enable network-based visualization, analysis, and biomedical discovery. **Cytoscape** is the flagship tool supported by NRNB. We are driving technical research and development projects, coordinating training opportunities, and actively seeking new collaborations to develop NRNB tools and apply them to biomedical research.

[Video introduction to NRNB](#)

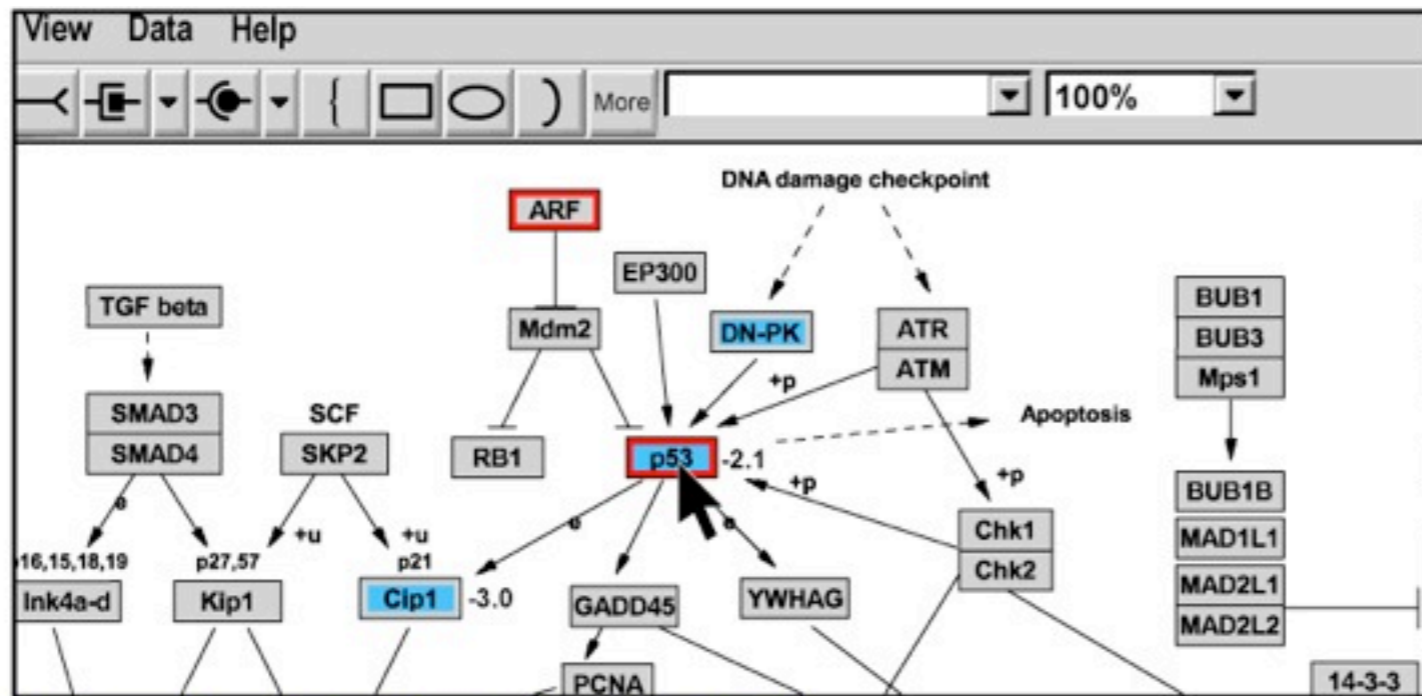
**How to Collaborate with NRNB**

**As a researcher,** we can collaborate on adapting NRNB tools

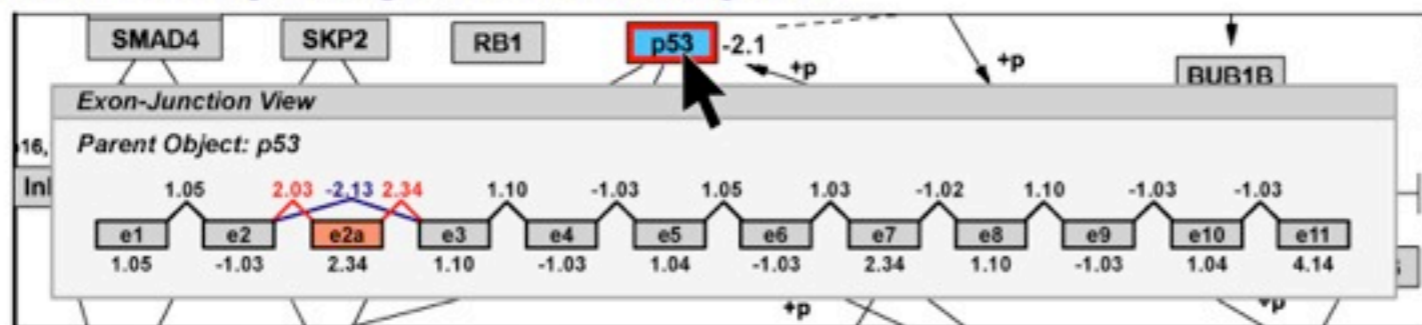
*Funded by the National Institutes of Health (USA)*



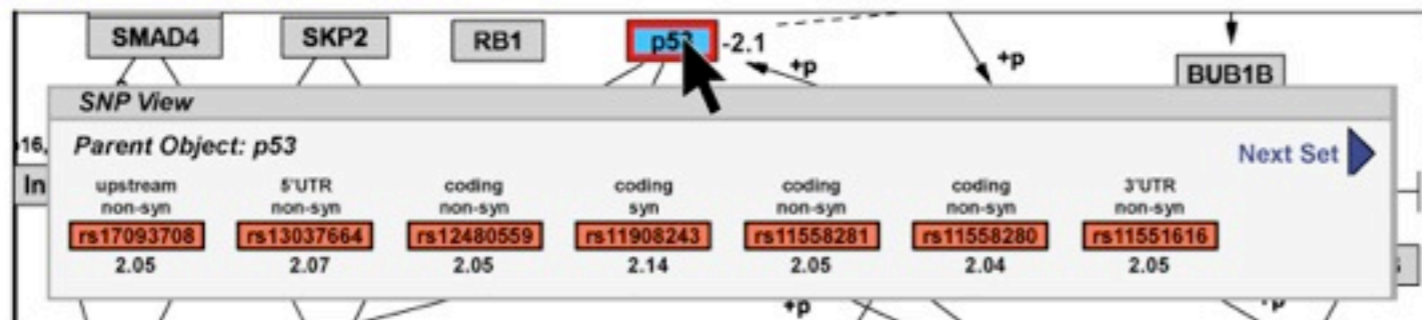
# 2A. Semantic Zooming: *from genes to exons*



## Exon and splice junction analysis



## Polymorphism analysis



**Pathway ColorSets**

**Gene/Protein Objects**

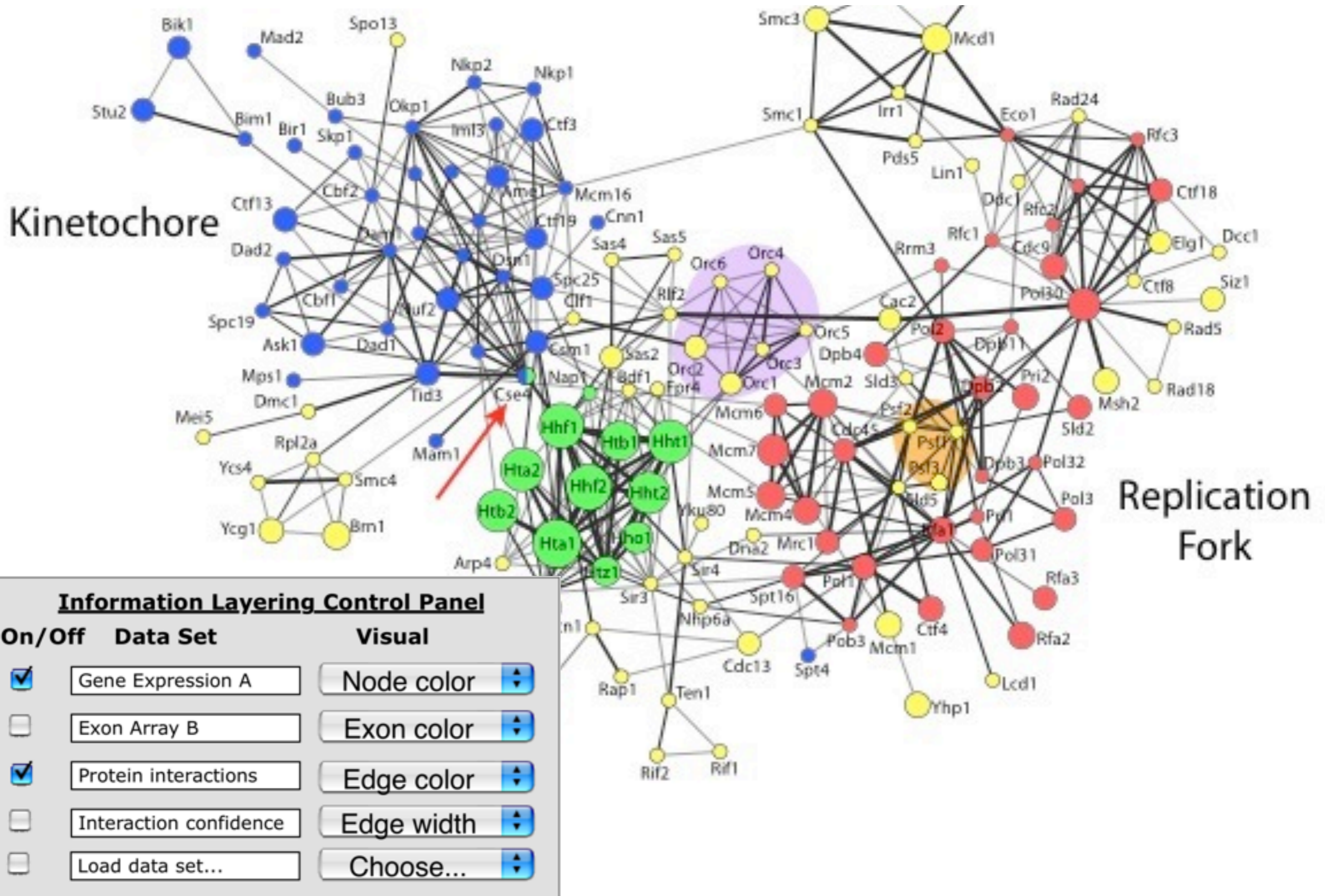
- Center Box Criterion**
  - up-regulated expression
  - down-regulated expression
  - not changed
  - not present
- Rim Criterion**
  - Differential splicing
  - No differential splicing
  - Not applicable

**Child Objects**

- Center Box Criterion**
  - up-regulated expression
  - down-regulated expression
  - not changed
  - not present
- Rim Criterion**
  - Rare variant SNPs present
  - No rare variants detected
  - Not applicable



# 2B. Information Layering



# Merci!

<http://cytoscape.org>

<http://nrnb.org>