

Master thesis topics on computational analysis of biological networks

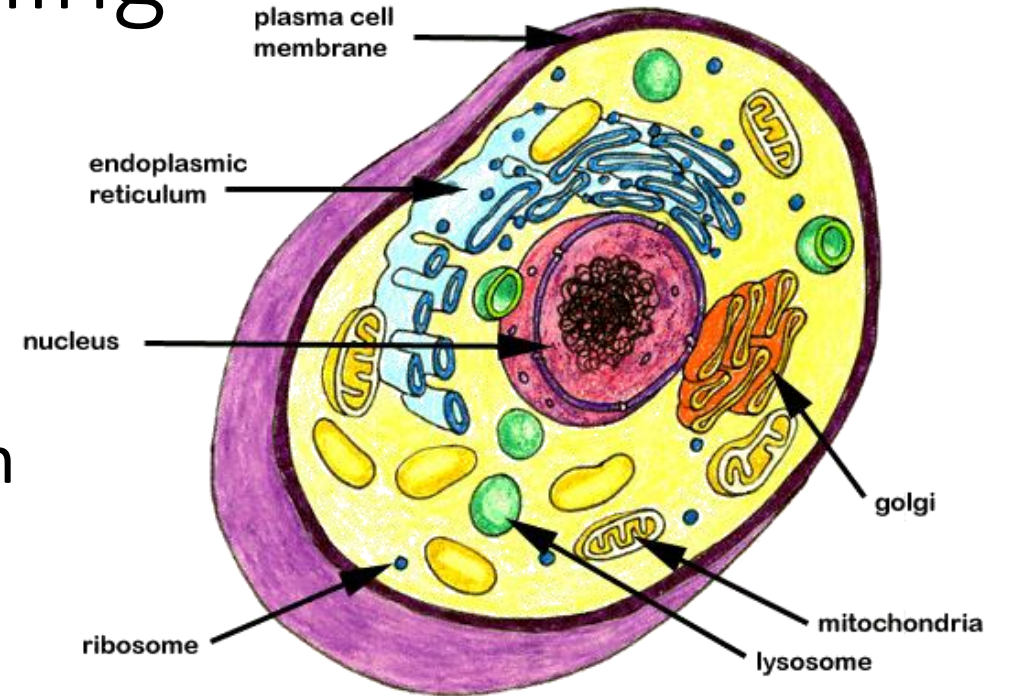
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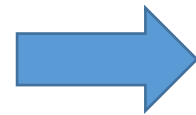
<http://pages.di.unipi.it/milazzo>

Understanding cell functioning

- Many **diseases** (e.g. **cancer**) are the result of **malfunctioning of cells**
- **Understanding** the mechanisms of cell functioning is essential in order to design **new therapies**
- **Understanding** requires **modeling**



System under study



Model

A **model** is a “manageable” representation of the system that focuses on the aspects that are relevant for the functionality of interest

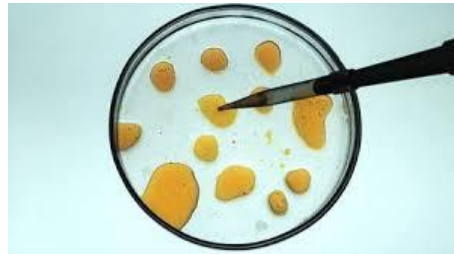
“*in silico*” models of biological systems

Modeling approaches in the context of the **life sciences** are:

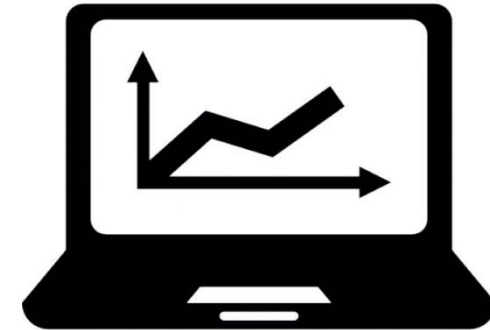
in vivo



in vitro



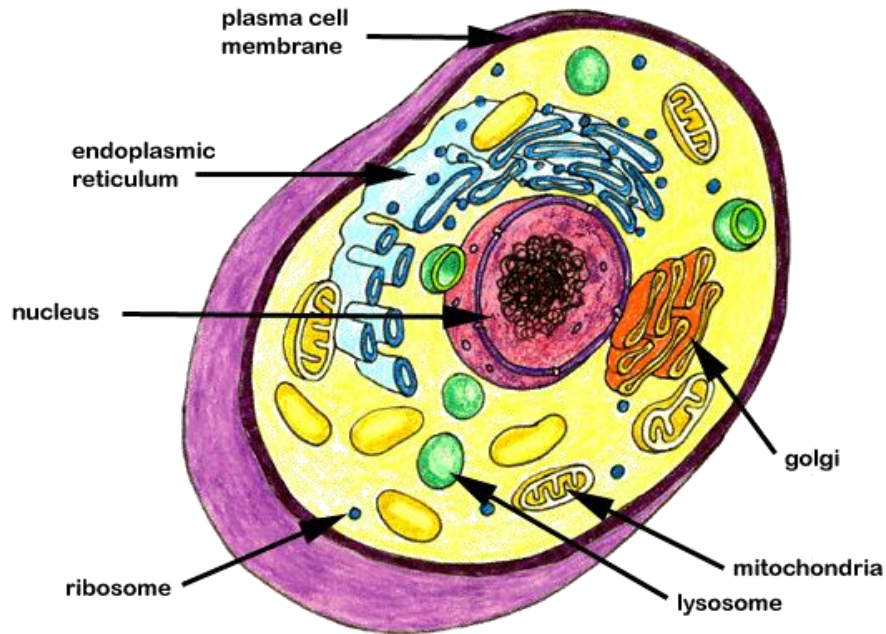
in silico



“*in silico*” models:

- aim at replicating biological processes in a **virtual environment**
- enable analysis by means of **simulation**, **machine learning** and **formal methods**
- can be used to make **predictions**

Cell functioning in few (very rough) words

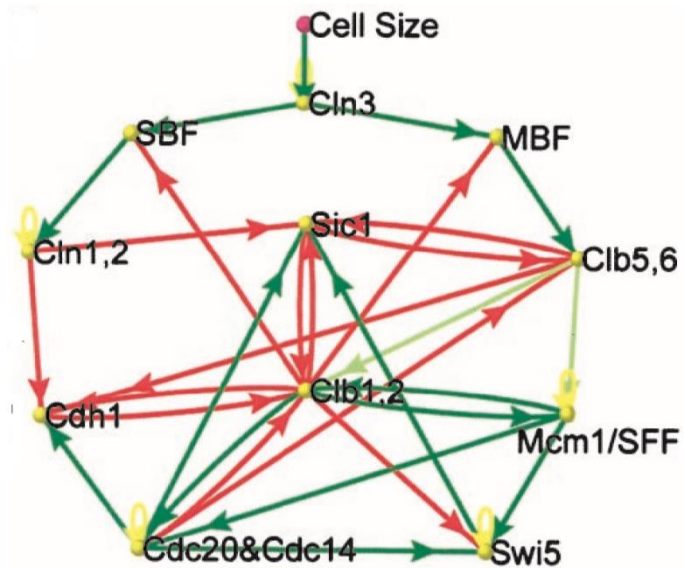


- **DNA** is the **source code** of the cell
 - Many genes are translated into proteins, that are the real «workers» inside the cell
 - Genes can **activate/inhibit** each other in order to turn on/off cell functionalities
- **Proteins** do the job!
 - Many types: enzymes, membrane channels, transporters, structural ones, ...
 - They cooperate by participating together in **chemical reactions**
 - A network of chemical reactions related to a specific functionality is called «**pathway**»

Biological networks

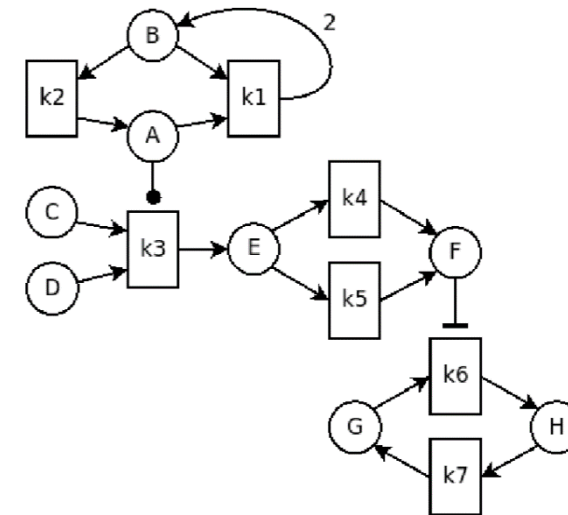
- Cellular processes can be described in terms of **networks**, such as:

Gene regulatory networks



Describe influence relationships
(**activation**/**inhibition**) between genes

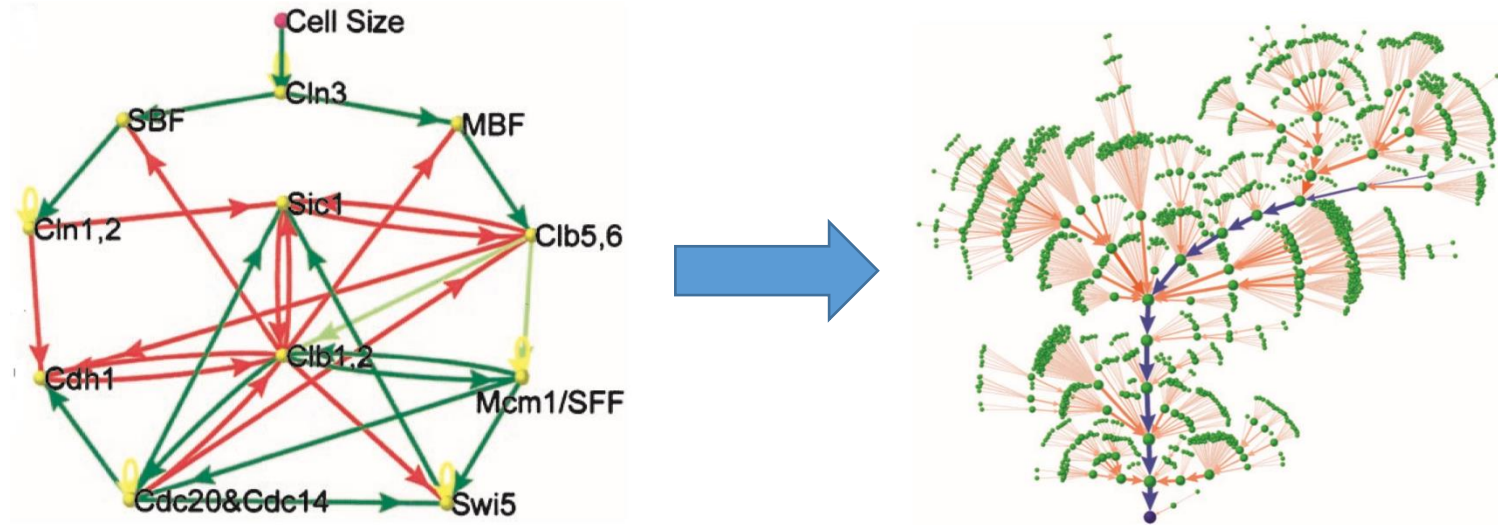
Biochemical pathways



Describe **chemical reactions** in cells
involving proteins, and other molecules

Thesis topic 1: (In collaboration with R. Barbuti, R. Gori and F. Levi)

Formal analysis of gene regulatory network dynamics

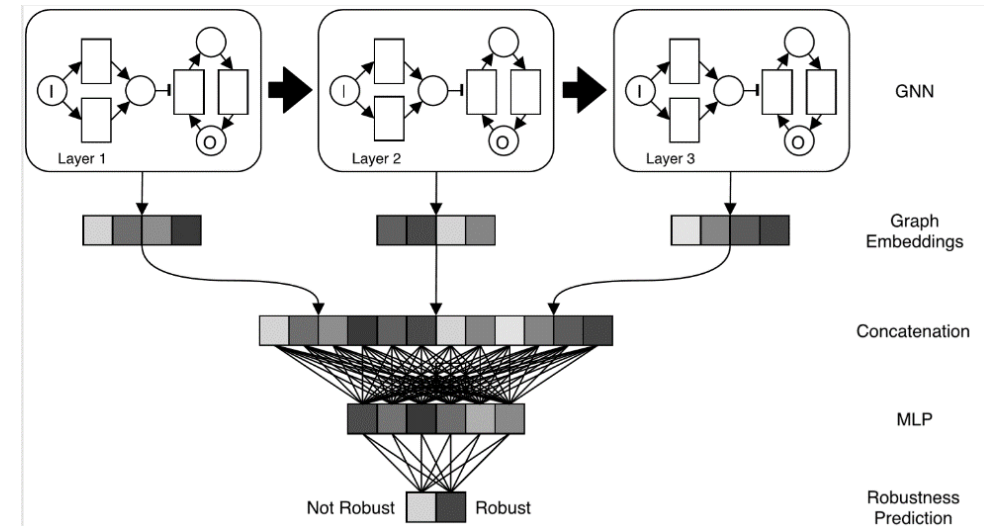
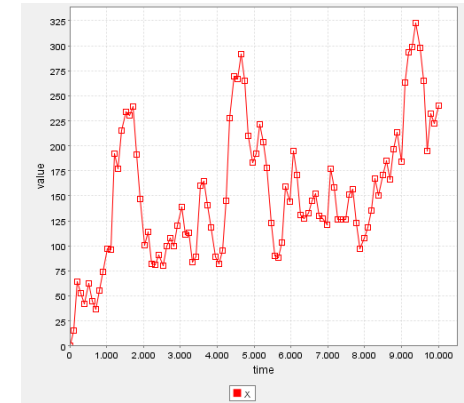
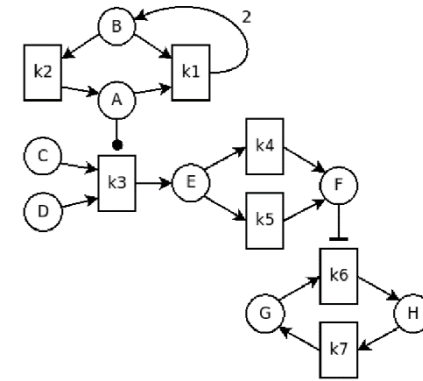


- The **dynamics** of a gene regulatory network can be described as a **transition system** in which states are gene activation configurations
- **Formal methods** can be developed and applied to study dynamical properties on the transition system
 - e.g. to study causes leading to configurations associated with diseases

Thesis topic 2: (In collaboration with A. Micheli and M. Podda -- CIML group)

Prediction of dynamical properties of biochemical pathways through machine learning on graphs

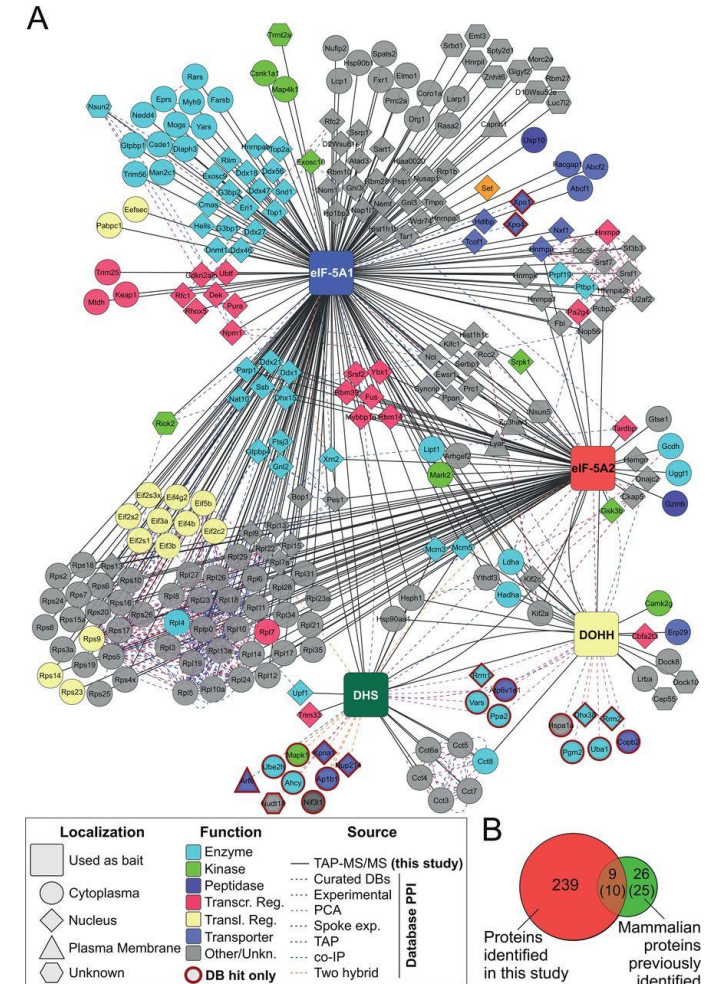
- The **dynamics** of a biochemical pathway is the **variation of the concentrations** of the involved proteins/molecules **over time**
 - It is usually studied through **simulation techniques**
- **Dynamical properties** (e.g. robustness to perturbations in initial concentrations) are often related with **structural properties** of the pathway
- **The idea:** let's construct a dataset of pathways and simulation results to be learnt by a **Graph Neural Network**
 - It could then be able to **predict dynamical properties** of new pathways without performing traditional simulations



Thesis topic 3: (In collaboration with C.Priami)

Analysis of protein interaction networks for biomedical applications

- Several analysis techniques exist for **protein-protein interaction networks** aimed at investigating relationships between proteins
- In the biomedical context it is often interesting to understand:
 - which proteins could be influenced by a disfunction of some other proteins (a **disease**)?
 - which proteins should be addressed by a new drug to be developed (**target identification**)?
 - which proteins could be influenced by a new drug (**toxicity prediction**)?
 - which existing drug could be used to treat a new disease (**drug repurposing**)?
- We would like to develop new methodologies based on protein-protein interaction networks and investigate new application cases, for instance in the context of drug repurposing



References

Thesis topic 1: Formal analysis of gene regulatory network dynamics

- R. Barbuti, R. Gori, F. Levi and P. Milazzo, **Investigating dynamic causalities in Reaction Systems**, Theoretical Computer Science 623, pages 114-145, 2016
- R. Barbuti, P. Bove, R. Gori, F. Levi and P. Milazzo, **Simulating gene regulatory networks using Reaction Systems**, Proc. of CS&P 2018, CEUR Workshop Proceedings 2240-11, 2018

Thesis topic 2: Prediction of dynamical properties of biochemical pathways through machine learning on graphs

- P. Bove, A. Micheli, P. Milazzo and M. Podda, **Prediction of dynamical properties of biochemical pathways with Graph Neural Networks**
- P. Bove, A. Micheli, P. Milazzo and M. Podda, **Preliminary Results on Predicting Robustness of Biochemical Pathways through Machine Learning on Graphs**, DataMod 2019, abstract available at <http://pages.di.unipi.it/datamod/program-and-pre-proceedings/>

Thesis topic 3: Analysis of protein interaction networks for biomedical applications

- On request...