Computational analysis of biological networks

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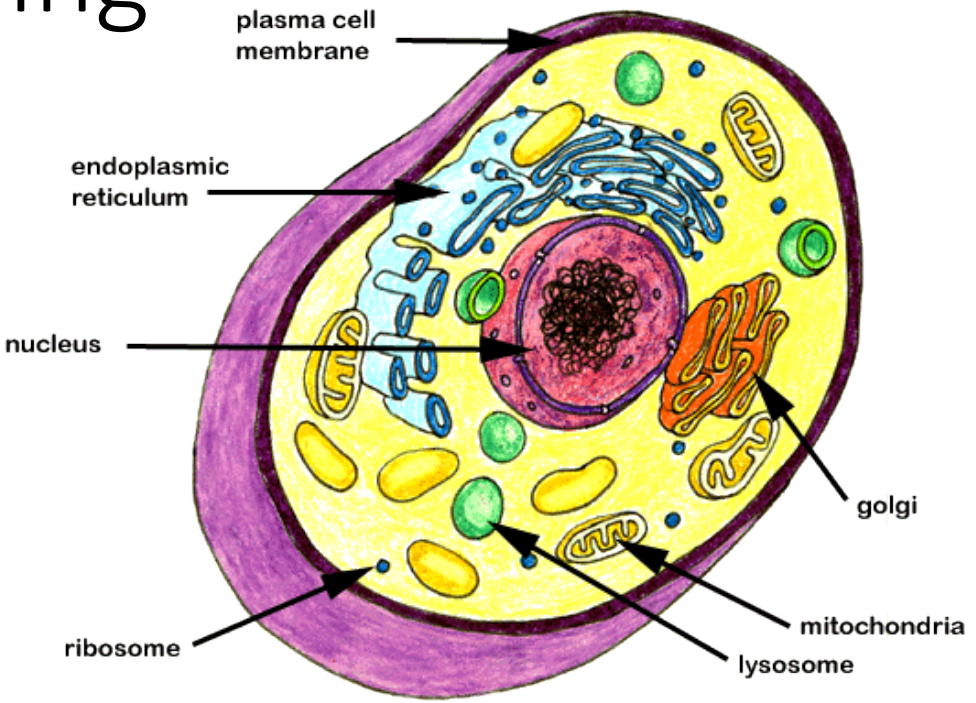
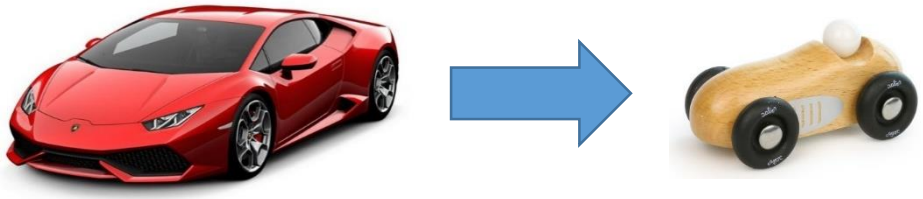
THESES 2019 - Pisa

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

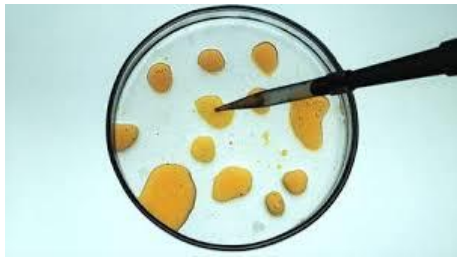
A model is a “manageable” representation of the system that focuses on the aspects that are relevant for the functionality of interest

"in silico" models of biological systems

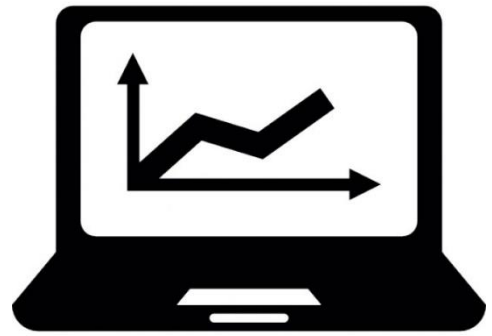
Modeling approaches in the context of the life sciences are:

in vivo

in vitro



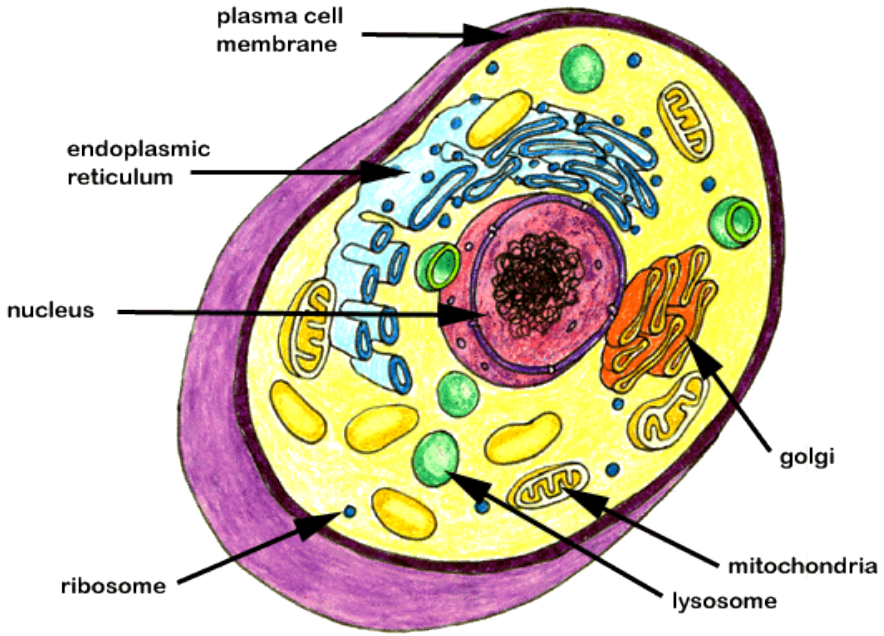
in silico



"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

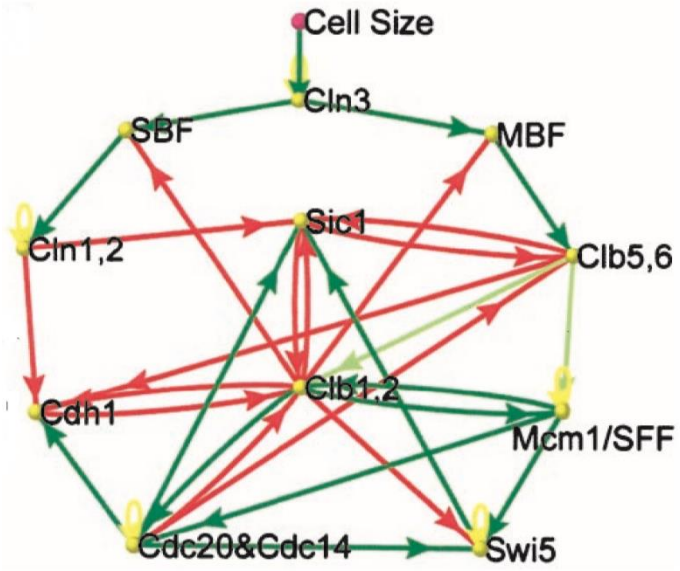


- DNA is the source code of the cell
  - Many genes are translated into proteins, that are the are the real «workers» inside the cell
  - Genes can activate/inhibit each other in order to turn on/off cell functionalities
- Proteins do the job!
  - Many types: enzymes, membrane channels, transporters, 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

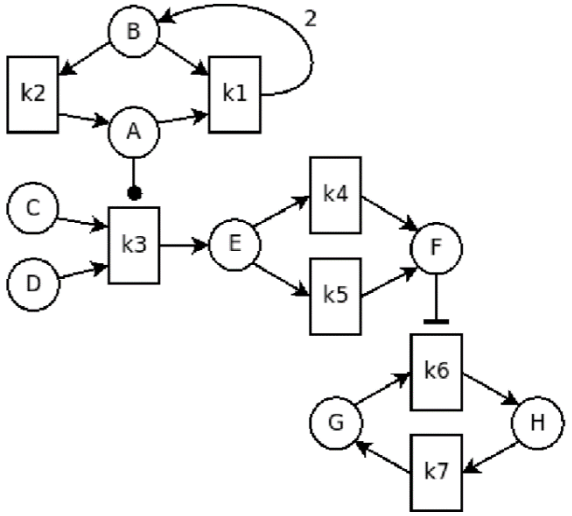
- Cellular processes can be described in terms of networks, such as:

Gene regulatory networks



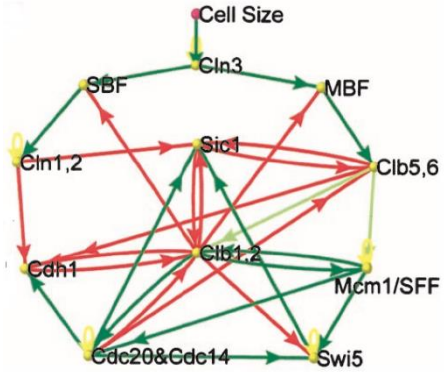
Describe influence relationships (activation/inhibition) between genes

Biochemical pathways



Describe chemical reactions in cells involving proteins, and other molecules

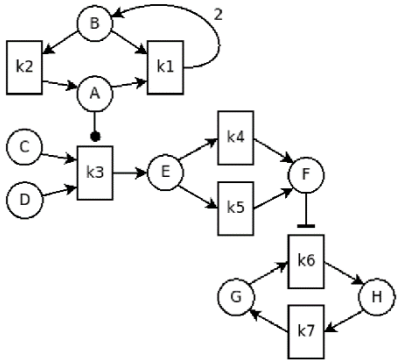
Research topics



Research topic 1:

Formal analysis of gene regulatory network dynamics

In collaboration with R. Barbuti, R. Gori and F. Levi



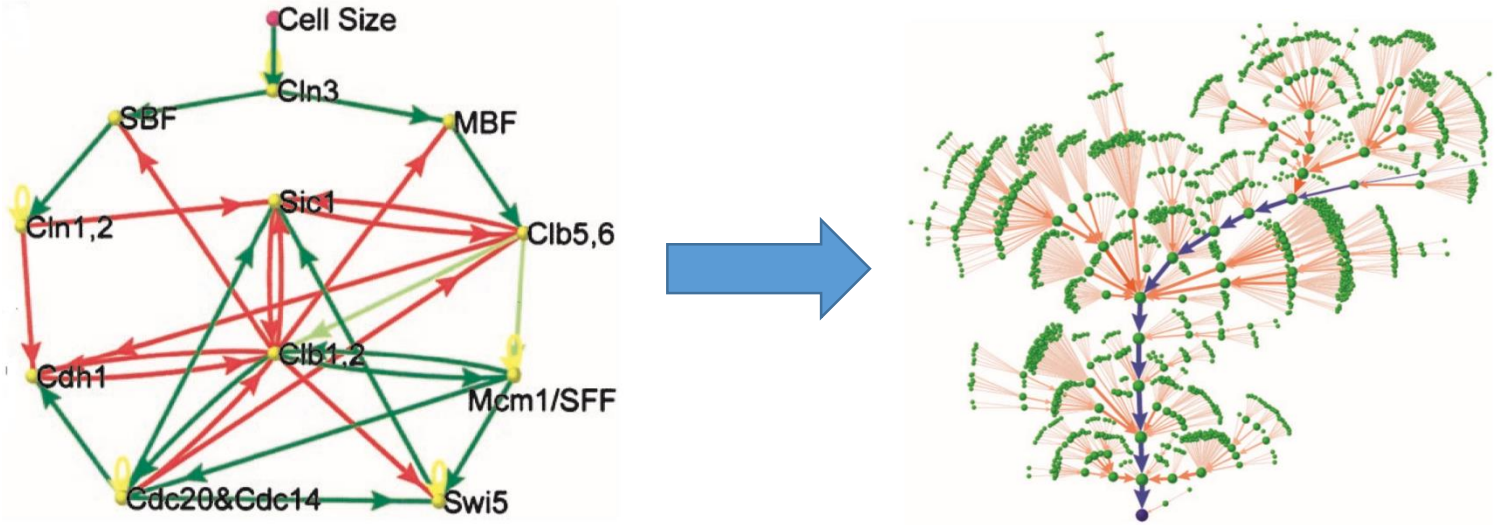
Research topic 2:

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

In collaboration with A. Micheli and M. Podda (CIML group)

Research topic 1:

Formal analysis of gene regulatory network dynamics

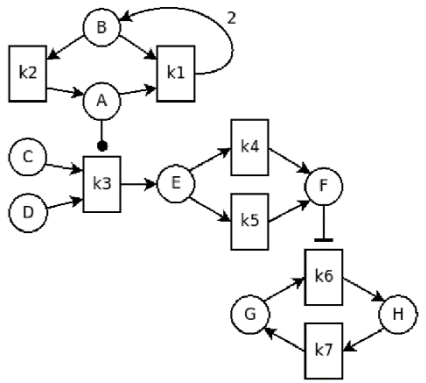


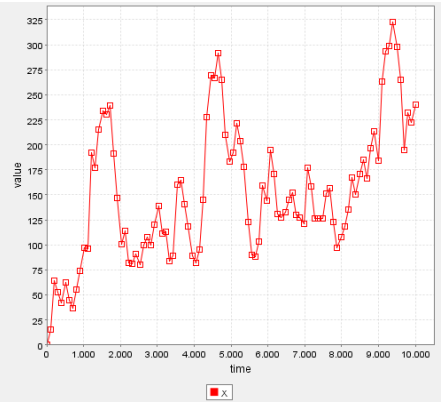
- The dynamics of a gene regulatory network can be described as a transition system in which states are gene activation configurations
- Formal methods can be developed and applied to study dynamical properties on the transition system
  - e.g. to study causes leading to configurations associated with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

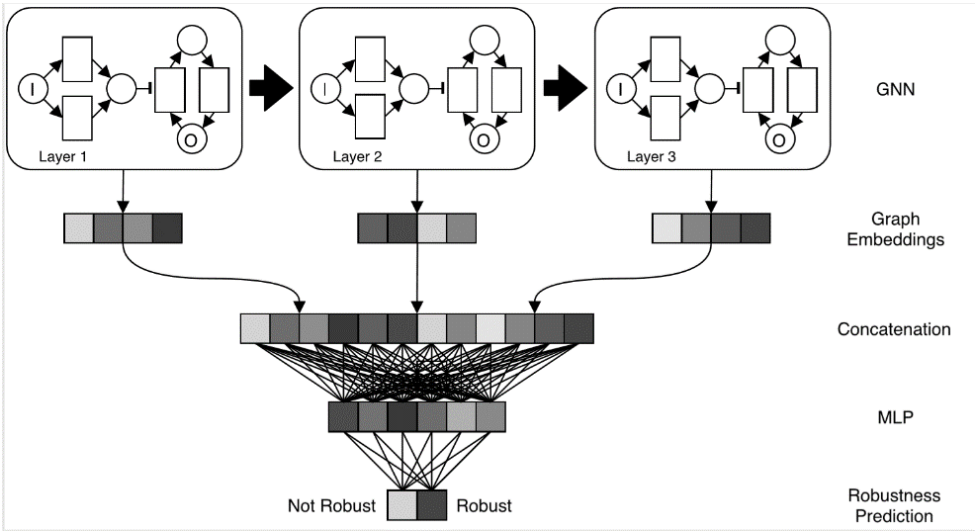
Research topic 2:

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







References

Research 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

Research 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
Submitted for publication (draft available on request)

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/