Modeling and Analysis of Multi-Valued Biological Regulatory Networks

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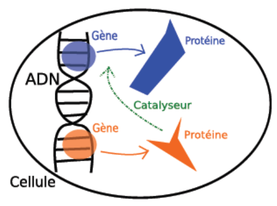
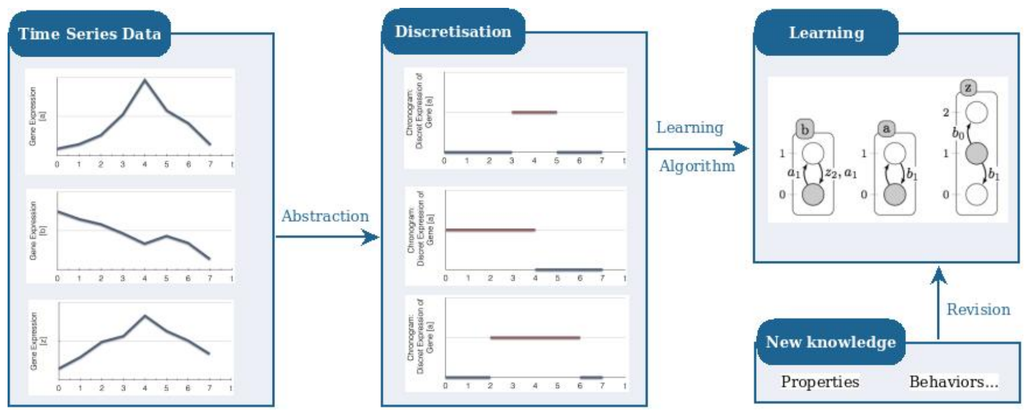
Introduction

- **Motivation**
  - → study and understand of interactions inside biological systems
  - → learn models coherent with the observations
  - → predict the system behavior after new perturbations
- Goal
  - → Automated modeling/revision of biological systems from Time Series Data
  - → Properties analysis

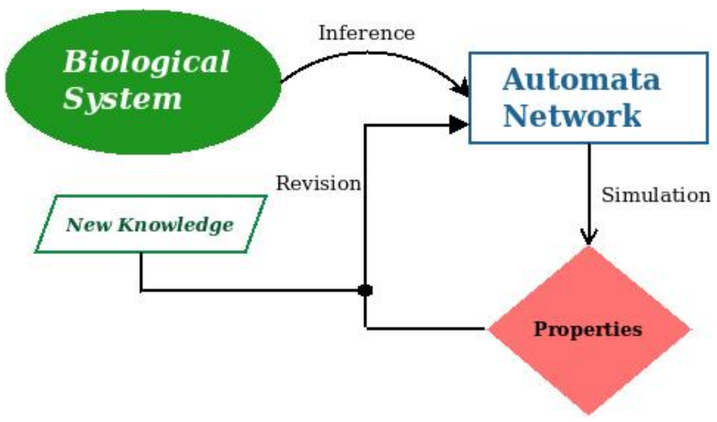


Learning models



Studying models

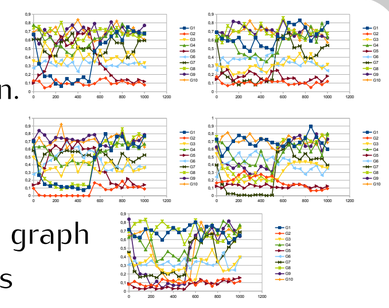
- Models are often too large to be studied exhaustively
- Usual model-checkers have to compute all states



- Properties: Steady states, basins of attraction, reachability...

Experiment: DREAM4 Challenge

- DATA [4]:
  - → 5 different time series of genes expression.
  - → Each series has different perturbations.
- GOAL:
  - → Predict the directed unsigned interaction graph
  - → Predict steady states from dual knockouts



Evaluation

- INPUT:
  - → An initial state
  - → 5 different conditions of dual genes to be knockout simultaneously
- GOAL:
  - → Predict the point attractor

Benchmark	#genes	MSE
insilico_1	100	0.052
insilico_2	100	0.042
insilico_3	100	0.033
insilico_4	100	0.033
insilico_5	100	0.052

Evaluation: precision is evaluated as the mean squared error of the difference between predicted/expected values.

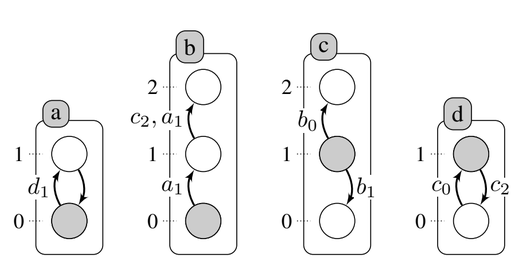
Work in progress

- Add delays for transitions: towards Timed AN
- Identify of basins of attraction
- Learn of circadian clock model (perturbations: jet lag)
- Participate to DREAM11 challenge

Automata Networks [1]

- Well adapted to large-scale models
- Qualitative levels for each component
- Atomistic representation of actions
- Very efficient to analyse dynamical properties [2,3]

Example:



Bibliography

[1] Paulevé, Magnin, Roux in TCSB, 2012
[2] Ben Abdallah, Folschette, Roux and Magnin in BIBM, IEEE, 2015
[3] Folschette, Paulevé, Inoue, Magnin, Roux in TCS, 2015
[4] Prill et al. in Science signaling, 2011