Master internship

Petri net unfolding of biological networks

Topic: Logic and Verification, Computational Biology

Location: MExICo project team, LSV, École Normale Supérieure de Cachan, Cachan, France
(Head of LSV: Laurent Fribourg <fribourg@lsv.ens-cachan.fr>)

Advisors:

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General presentation

Biological networks, such as gene regulatory networks or signalling networks, can be modeled as automata networks or Petri nets. It results in concurrent models involved hundreds or thousands of parallel-interacting components. Aiming at capturing the dynamical landscape of those models, and ultimately proposing mutations to control the biological cells, we are interested in computing several properties, such as the attractors (live/dead locks, characterizing the long-term behaviour) and set of mutations that would trigger a re-differentiation of the cell, i.e. will change the current attractor.

Objective of the internship

In order to cope with the huge size of the networks, this internship will address the design, implementation, and evaluation of new algorithms based on Petri net unfoldings for computing dynamical properties on discrete models of biological networks. Petri net unfoldings exploit the concurrency between transitions to obtain so-called complete prefixes, that result in compact representations of all the possible behaviour of the net. Tools such as mole (http://www.lsv.ens-cachan.fr/~schwoon/tools/mole) or cunf (https://code.google.com/p/cunf) allow to compute efficiently the complete prefix of the unfolding of Petri nets.

This internship will first consist in evaluating and comparing existing algorithms for computing attractors in Petri net models of biological networks. Several variants and extensions of Petri net unfoldings will be explored in order to improve the scalability of the method. This task will involve adapting existing algorithms and implementing them to make them more efficient when applied to large biological networks. Then, new algorithms will be designed for identifying sets of components of the network for which the activation or inhibition would (1) prevent the reachability of a particular attractor from a given initial state while conserving other attractors reachability; (2) force a transition from one attractor to another given one.

This work may be continued with a PhD thesis on developing causality and concurrency theory for the formal analysis of dynamics of discrete biological networks.

Bibliographic References

M. Noual, D. Regnault and S. Sené. *About non-monotony in Boolean automata networks.* Theoretical Computer Science, 504: 12-25, 2013

R. Thomas, and M. Kaufman. *Multistationarity, the basis of cell differentiation and memory. II. Logical analysis of regulatory networks in terms of feedback circuits.* In Chaos: An Interdisciplinary Journal of Nonlinear Science, AIP, 2001, 11, 180-195 (pdf).

J. Esparza, and K. Heljanko. *Unfoldings – A Partial-Order Approach to Model Checking.* Springer, 2008 (pdf).

T. Chatain, S. Haar, L. Jezequel, L. Paulevé, and S. Schwoon. *Characterization of reachable attractors using Petri net unfoldings.* In Computational Methods in Systems Biology, LNCS, Springer, 2014 (pdf).

Expected ability of the student

- Logic, Automata, Algorithms
- Unix programming
- No particular background in biology is required.