2017-00190 - Model reduction by tropical algebra constraint solving (research internship)

Level of qualifications required: Bachelor's degree or equivalent
Fonction: Internship Research

About Inria
Inria, the French National Institute for computer science and applied mathematics, promotes “scientific excellence for technology transfer and society”. Graduates from the world's top universities, Inria's 2,700 employees rise to the challenges of digital sciences. With its open, agile model, Inria is able to explore original approaches with its partners in industry and academia and provide an efficient response to the multidisciplinary and application challenges of the digital transformation. Inria is the source of many innovations that add value and create jobs.

About the research centre or Inria department
Located at the heart of the main national research and higher education cluster, member of the Université Paris Saclay, a major actor in the French Investments for the Future Programme (Idex, LabEx, IRT, Equipex) and partner of the main establishments present on the plateau, the centre is particularly active in three major areas: data and knowledge; safety, security and reliability; modelling, simulation and optimisation (with priority given to energy).

The 450 researchers and engineers from Inria and its partners who work in the research centre's 31 teams, the 100 research support staff members, the high-level equipment at their disposal (image walls, high-performance computing clusters, sensor networks), and the privileged relationships with prestigious industrial partners, all make Inria Saclay Île-de-France a key research centre in the local landscape and one that is oriented towards Europe and the world.

Context
This research internship is offered at Inria Saclay IdF (https://www.inria.fr/en/centre/saclay) in the LIFEWARE project-team (http://lifeware.inria.fr). This team works in computational systems biology and develops the Biochemical Abstract Machine (BIOCHAM http://lifeware.inria.fr/biocham4) software for modeling, analyzing and now synthesizing biochemical reaction networks (CRNs) using methods from fundamental computer science and mathematics. The software developments are expected to be integrated in BIOCHAM.

The internship will be supervised by François Fages who has supervised 29 Ph.D. theses in his career, the last defended in May 2016, and who currently is 100% available with no Ph.D. student.

Assignment
Model reduction is a central topic in differential dynamical systems theory, for reducing the complexity of differential equations, finding important parameters, and developing multi-scale models for instance. While perturbation theory is a standard mathematical tool to analyze the different time scales of a dynamical system, and decompose the system according to fast-slow dynamics, in the domain of computational systems biology, the biochemical reaction networks under consideration involve several tenths of variables which appeal for automated reasoning methods.

Tropicalization is a mathematical method for analysing polynomial equations in the (min,+) or (max,plus) semiring. The intuitive idea is to reason on the orders of magnitude of concentrations and kinetic parameters which are expressed by the logarithm of their values, hence the (min,+) algebra for polynomials. We have shown that Constraint Logic Programming can be used to efficiently solve tropical equation problems for identifying the dominating monomials and reactions in a network, and...
then simplifying the dynamics in the different regions of the phase space corresponding to different regimes (i.e. Quasi Steady State or Quasi Equilibrium assumptions).

The goal of this research internship is to generalize our tropical equation solver based on constraint programming and to develop the model reduction method by stating precise approximation results (e.g. using Tikhonov theorem) at least in simple examples like the Michaelis-Menten enzymatic reaction. The method will be implemented in our modeling environment Biocham.

**Main activities**

Our first results on this subject have been published in


The work will consist in

- generalizing the CLP solver to handle inequalities instead of equalities, with accurate translation from polynomials to (min,+) intervals,
- developing correctness criteria for the simplified system (e.g. stability conditions of Tikhonov theorem)
- implementing the model reduction method and evaluating it on models from the BioModels repository.

Further reading:


**Skills**

This subject requires common and basic knowledge on differential equations, linear algebra, algorithms and programming.

There is no specific prerequisite for this internship. However, some specific knowledge on either constraint programming, Prolog, control theory, or computational systems biology will be a plus.

**Benefits package**

- Subsidised catering service
- Partially-reimbursed public transport
- Social security
- Paid leave
- Flexible working hours
- Sports facilities

**Remuneration**

500 euros/month + living compensation for foreigners