Approximate model reduction for the differential semantics of rule-based models

Internship proposal, Master 2 MPRI, year 2014-2015

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Note: Other internships are possible on the topic of static analysis, abstract interpretation, and applications to Systems Biology. Please contact the internship supervisor for more information.

Motivation

Mechanistic models of systems of interaction between proteins are difficult to design and to analyse because of the large combinatorial complexity. Indeed, proteins can gather together or activate one another, and thus they can form many bio-molecular complexes (see [4, 6]).

Kappa [5] is formal language to describe these models by the means of graph rewrite rules. In particular, these rules are context free, they describe transformations between patterns, and there is no need to describe explicitly the whole structure of bio-molecular complexes. Kappa comes with several semantics. In particular, the differential semantics describe the evolution of the concentration of each bio-molecular complexes as the solution of a system of ordinary polynomial equations. Thus even if context free rules solve the problem describing the system, combinatorial issues raise again when one want to write (or solve) the differential semantics of these systems.

In [7, 3, 2], we have proposed a framework for the model reduction of the differential semantics of Kappa. This framework is based on a static analysis that inspect the rewrite rules and detect a change of variables. As a result, in compute a smaller differential system, the solution of which is an exact projection of the initial system (which does not need to be written explicitly). In this internship, we propose an complementary approach, given a set of patterns of interest, we would like to derive a system of ordinary differential equation so as to compute timely-dependent bounds for the concentration of these patterns. This framework will allow to tune the trade-off between accuracy and complexity, while having a sound estimation of the numerical approximations. For instance, it will allow to truncate the set of variables if there are too many of them (even after exact model reduction), and to apply different relational abstractions over the concentrations of the patterns of interest.
Expected works

The intern shall design a framework for deriving sound equations for the lower and the upper bounds of the concentration of some bio-molecular patterns in a rule-based model. In particular, this derivation will use two basic operations, one partitioning primitive, so as to split the state of the system into two parts and to apply different kind of abstractions to each of them, and a reduced product so as to combine different kinds of properties and to refine what is known about a part of the state, and thus to describe more precise equations. This framework will be implanted and integrated in the development plate-form of Kappa [1].

References


