A weakly relational domain to detect potential polymerisation events in signaling pathways.

Internship proposal, Master 2 MPRI, year 2014-2015

Supervisor:	Jérôme Feret
Internship location:	Département d'informatique de l'École normale supérieure, Paris, France
Course:	M2-6: Abstract interpretation: application to verification and static analysis
Contact: Contact :	feret@ens.fr
	http://www.di.ens.fr/∼feret

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 [2, 4]).

Kappa [3] 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 a programming environment, so as to increase the level of confidence in the models that are written this way. This programming environment is made of several static analyses which compute basic properties about the model: they detect relationships between the state of different sites in proteins, they detect that some rules can never be triggered, and so on and so forth. Each abstraction are mainly local, which means that they abstract properties about proteins, or a subset of neighbouring proteins, but do not consider more global properties about bio-molecular complexes.

The goal of this internship is to design a new abstract domain to detect the rules which can create polymers (that is arbitrary long chains of proteins). More formally, a polymer is a chemical species which can be projected on a cycle of a given graph (or equivalently which contain a pattern that can be repeated infinitely many times). This is a global property.

Expected works

The intern shall design a weakly relational domain [5, 6] so as to infer the relationships between the states of the pairs proteins which can belong to a same bio-molecular complexes, and use this information to detect which rules can potentially create polymers. The proposed domain shall be proved correct. The domain will be plugged into the development plate-form [1].

References

[1] Pierre Boutillier, Jérôme Feret, Jean Krivine, and Lý Kim Quyên. http://www.kappalanguage.org.

[2] Vincent Danos, Jérôme Feret, Walter Fontana, and Jean Krivine. Abstract interpretation of cellular signalling networks. In *Proceedings of the 9th International Conference on Verification, Model Checking and Abstract Interpretation (VMCAI'08)*, volume 4905, pages 42–58, 2008.

[3] Vincent Danos and Cosimo Laneve. Core formal molecular biology. *Theoretical Computer Science*, 325:69–110, 2003.

[4] J. Feret. Reachability analysis of biological signalling pathways by abstract interpretation. In T.E. Simos, editor, *Proceedings of the International Conference of Computational Methods in Sciences and Engineering, ICCMSE '2007, Corfu, Greece*, number 963.(2) in American Institute of Physics Conference Proceedings, pages 619–622, Corfu, Greece, 25–30 September 2007. American Institute of Physics.

[5] Antoine Miné. The octagon abstract domain. In *WCRE*, page 310, 2001.

[6] Antoine Miné. A few graph-based relational numerical abstract domains. In *Static Analysis, 9th International Symposium, SAS 2002, Madrid, Spain, September 17-20, 2002, Proceedings*, pages 117–132, 2002.