Scientific Report

First name / Family name	Cristian Versari
Nationality	Italian
Name of the *Host Organisation*	INRIA Lille - Nord Europe
First Name / family name of the *Scientific Coordinator*	Rémi Gilleron
Period of the fellowship	01/06/2011 to 31/05/2012

I – SCIENTIFIC ACTIVITY DURING YOUR FELLOWSHIP

During my ERCIM fellowship I have been collaborating with the bioComputing group in Lille, focussing on the study of techniques for the in silico analysis of biochemical systems. I carried out my research activity along two main directions.

Expressiveness of concurrent languages for biochemical modelling. The application of the pi-calculus to the modelling of biochemical processes **[1]** led to the development of several concurrent languages specifically designed for the analysis of biological systems. The React(C) language **[2]**, previously developed in collaboration with bioComputing, represents one major achievement in this area. The high computational cost usually required for the analysis of biochemical models motivated the search of fragments of React(C) whose model analysis could have been remarkably efficient. Some initial results are presented in the submitted work **[3]**, where the efficient analysis of models written in a fragment of React(C) called κf is performed through translation to standard chemical reactions.

Approximate dynamics and reduction of stochastic biochemical models. Biochemical processes are often characterized by an intrinsic stochastic nature, reason why many bio-oriented languages are equipped with a stochastic semantics. However, stochasticity is one of the main factors causing high computational costs for model analysis. Approximate analysis techniques such as *moment closure* have been recently applied with success to biochemical models, decreasing the costs of the analysis with acceptable loss of precision. In the submitted work **[4]** the regular structure typical of some biochemical networks was exploited together with moment closure to further decrease the cost of the analysis by means of model reduction based on symmetry.

[1] C. Priami, A. Regev, E. Y. Shapiro, and W. Silverman. Application of a stochastic name- passing calculus to representation and simulation of molecular processes. Inf. Process. Lett., 80(1):25–31, 2001.

[2] M. John, C. Lhoussaine, J. Niehren, and C. Versari. Biochemical reaction rules with constraints. In G. Barthe, editor, ESOP, volume 6602 of Lecture Notes in Computer Science, pages 338–357. Springer, 2011.

II – PUBLICATION(S) DURING YOUR FELLOWSHIP

[3] C. Versari and G. Zavattaro. *Complex Functional Rates in Rule-based Languages for Biochemistry.* (pending)

Abstract.

Rule-based languages (like, for example, Kappa, BioNetGen, and BioCham) have emerged as successful models for the representation, analysis, and simulation of bio-chemical systems. In particular Kappa, although based on reactions, differs from traditional chemistry as it allows for a graph-like representation of complexes. It follows the “don’t care, don’t write” approach: a rule contains the description of only those parts of the complexes that are actually involved in a reaction. Hence, given any possible combination of complexes that contain the reactants, such complexes can give rise to the reaction. In this paper we address the problem of extending the “don’t care, don’t write”

approach to cases in which the actual structure of the complexes involved in the reaction could affect it (for instance, the mass of the complexes could influence the rate). The solutions that we propose is κf, an extension of the Kappa-calculus in which rates are defined as functions of the actually involved complexes.

[4] K. Batmanov, F. Lemaire, C. Kuttler, C. Lhoussaine, C. Versari. *Symmetry-based model reduction for approximate stochastic analysis.* (pending)
Abstract.
For models of cell-to-cell communication, with many reactions and species per cell, the computational cost of stochastic simulation soon becomes intractable. Deterministic methods, while computationally more efficient, may fail to contribute reliable approximations for those models. In this paper, we suggest a reduction for models of cell-to-cell communication, based on symmetries of the underlying reaction network.
To carry out a stochastic analysis that otherwise comes at an excessive computational cost, we apply a moment closure (MC) approach. We illustrate with a community effect, that allows synchronization of a group of cells in animal development. Comparing the results of stochastic simulation with deterministic and MC approximation, we show the benefits of our approach. The reduction presented here is potentially applicable to a broad range of highly regular systems.

III – ATTENDED SEMINARS, WORKHOPS, CONFERENCES

Conferences:

- 9th International Conference on Computational Methods in Systems Biology (CMSB 2011). Institut Henri Poincaré, Paris, France. September 21-23, 2011.

Seminars:

- ERCIM ABCDE Seminar. November 10-11, 2011. Berlin, Germany.

IV – RESEARCH EXCHANGE PROGRAMME (REP)

REP Organization:	Centrum Wiskunde & Informatica (CWI), Amsterdam - The Netherlands
Dates:	May 10-16, 2012
Local scientific coordinator:	Drs. J.G. Blom

My first visit under the REP programme was focussed on the efficiency and applicability of moment closure to Biochemistry. While moment closure has been widely applied in Physics so far, it has recently turned out as an effective way to calculate the dynamics of biochemical networks under some circumstances. During my visit at CWI I had the opportunity to share the experience on the state of the art of moment closures for biochemical systems that I acquired during my collaboration with the bioComputing group in Lille: I discussed with Drs. Blom the strength and potential of such a technique, as well as its limits and frequent misuses.

REP Organization:	Department of Information Technology and Electrical Engineering - ETH Zurich
Dates:	May 17-30, 2012
Local scientific coordinator:	Prof. Heinz Koeppl

During my second visit under the REP programme I had the chance to collaborate with prof. Heinz Koeppl and his colleagues on techniques for the efficient analysis of biochemical models based on the so called *lumping* of chemical species. We discussed the conditions of applicability of such reductions and the possibility of joining them with techniques for the calculation of approximate dynamics of biochemical models.