From species to pathway and tissue as process

[Extended Abstract]

Muffy Calder
School of Computing Science
University of Glasgow
Glasgow, Scotland
Muffy.Calder@glasgow.ac.uk

Oana Andrei
School of Computing Science
University of Glasgow
Glasgow, Scotland
Oana.Andrei@glasgow.ac.uk

Andrea Degasperi
School of Computing Science
University of Glasgow
Glasgow, Scotland
andrea@dcs.gla.ac.uk

Robin Donaldson
School of Computing Science
University of Glasgow
Glasgow, Scotland
radonaldson54@gmail.com

Process algebras were originally designed for modelling concurrent computations. Over the last decade, computer scientists have explored their application to modelling biomolecular processes, with considerable success. A predominant abstraction is *molecule-as-process* [RSS01, Car08], where each process represents a molecule. Analysis is by simulation and in a stochastic setting, there is a clear correspondence with stochastic simulation as proposed by Gillespie [Gil77].

An alternative abstraction is *species-as-process* [CGH06, CH09b], based on models that are continuous time Markov chains (CTMC) with levels of concentration. This population-based abstraction allows control of the granularity of representation, at one end of the spectrum corresponding to Gillespie simulation and at the other end, ordinary differential equations. A key feature of this style is it permits a range of analysis techniques in addition to simulation, namely relations (e.g. bisimulation) and model-checking properties expressed in qualitative and quantitative logics.

Within the *species-as-process* paradigm, a useful style has been *reagent-centric* models[CH09a], where all reagents in a reaction map to processes, whose variation reflect decrease through consumption and increase through product formation (consumers and producers). The reagent-centric style of modelling provides a distributed view of a system and is easily represented in a state-based formalism where state variables represent levels of concentration. An example is the language of reactive modules used in the PRISM model-checker [KNP02]. Whilst this language is not strictly a process algebra: processes are represented by modules, there is process algebraic synchronisation between modules. Moreover, modules can be generic.

This talk gives an overview of recent advances and applications of the *reagent-centric* modelling paradigm, extending basic reasoning about concentration levels and then developing higher level concepts such as *pathway-as-process* and *tissue-as-process*.

We consider how to extend basic reasoning about concentration levels by the addition of *trend formulas*, state formulas that represent ascending or descending trends of concentration [AC10]. These are similar to the sign of a first-order derivative, but in a stochastic setting. We then consider extending the *species-as-process* paradigm to *pathway-as-process*. While still adopting the reagent-centric style, we model a signalling pathway as a (synchronising) parallel composition (with renaming) of instances of generic modules, which have both internal and external reactions. The motivation is to investigate pathway interactions, known as crosstalk, and so pathways are themselves composed. We show how we can use a quantitative logic to detect cross-talk, and a qualitative logic to characterise the type of crosstalk [DC10b]. Finally, we describe a new stochastic process algebra for modelling different levels of abstraction, specifically biochemistry and tissue. The algebra is motivated by modelling pattern formation based on reaction-diffusion equations. Processes represent both biochemical species and tissues at certain locations; an explicit notion of geometrical space is embedded in the algebra. Synchronisation between the two levels is through special actions called hooks [DC10a]. The ultimate goal is to be able to compare models of similar tissue formation, but with different underlying biochemistry.

CMSB 2010 Trento, Italy

1. REFERENCES

[AC10] O. Andrei and M. Calder. A model and analysis of the AKAP scaffold. *Proceedings CS2Bio 2010, To appear in ENTCS*, 2010.

[Car08] Luca Cardelli. On process rate semantics. *Theoretical Computer Science*, 391(1):190–215, 2008.

[CGH06] M. Calder, S. Gilmore, and J. Hillston. Modelling the influence of RKIP on the ERK signalling pathway using the stochastic process algebra PEPA. *Trans. on Computat. Syst. Biol. VII*, 4230:1–23, 2006.

[CH09a] M. Calder and J. Hillston. Process algebra modelling styles for biomolecular processes.

Transactions on Computational Systems Biology, LNBI, 2009.

[CH09b] F. Ciochetta and J. Hillston. Bio-PEPA: a framework for modelling and analysis of biological systems. *Theoretical Computer Science*, 410(33), 2009.

[DC10a] A. Degasperi and M. Calder. Process algebra with hooks for models of pattern formation. *Proceedings CS2Bio 2010, To appear in ENTCS*, 2010.

[DC10b] R. Donaldson and M. Calder. Modelling and analysis of biochemical signalling pathway crosstalk. *Proceedings of FBTC (From Biology to Concurrency), EPTCS*, pages 40–44, 2010.

[Gil77] D. Gillespie. Exact stochastic simulation of coupled chemical reactions. *The Journal of Physical Chemistry*, 81(25):2340 –2361, 1977.

[KNP02] M. Kwiatkowska, G. Norman, and D. Parker. PRISM: Probabilistic Symbolic Model Checker. *Lecture Notes in Computer Science*, 2324:200–204, 2002.

[RSS01] A. Regev, W. Silverman, and E. Shapiro. Representation and simulation of biochemical processes using π-calculus process algebra. *Pacific Symposium on Biocomputing 2001 (PSB 2001)*, pages 459–470, 2001.