Models and Languages for Computational Systems Biology
Session 2009–2010, Semester 2

Assignment 2

This is the second of two pieces of credit-bearing coursework for MLCSB, each marked out of 100 and each contributing 15% to the final course grade. Please submit your coursework to the collection box outside the Informatics Teaching Organisation office on level 4 of the Appleton Tower. Include a completed copy of the University "Own Work Declaration" form provided on the ITO web pages. This exercise will be marked anonymously: please use the green cover sheet provided by the ITO, writing on it the title of the course, and your name in the corner where the ITO can conceal it for anonymisation. Do not mark your name, student number, or exam number anywhere else.

Due date: 4pm Thursday 25 March 2010 (2010-03-25 16:00Z) *Ian Stark*

The aim of this exercise is to model a signalling pathway using the *BioPEPA* process algebra, and investigate the behaviour of the model. The pathway is outlined in Figure 1 with some suggested kinetic parameters.

You will need to install the BioPEPA tools, create a model of the pathway in the BioPEPA language, and execute some analyses. Finally, you should submit a written report of your investigation. Assessment will be on the basis of this report.

The exercise is somewhat open-ended: it is for you to decide what analyses to carry out, what questions about the model you might try and answer, and how to organise and present your results.

Your report should be printed, not hand-written, but there is no further constraint on format beyond being clearly readable. In particular, you may use whatever document preparation tools you find most convenient.

Resources

Start at `http://biopepa.org`. As well as the tool and documentation, this has links to technical papers describing BioPEPA, examples, and case studies. You will need to read some of these to find out more about BioPEPA modelling and the techniques required.

You might consider carrying out any of the following kinds of model analysis, or others:

- State space exploration.
- Continuous-time Markov chain (CTMC).
- Numerical analysis of CTMC transient and steady-state behaviour.
- Stochastic simulation; single or ensemble.
- Fluid approximation through ordinary differential equations (ODEs).
- Probabilistic model-checking.

You could use these analyses to address any of the following questions, or others:

- Does the pathway successfully transmit a signal?
- How long does signalling take?

- What happens when the input signal disappears?
- Is the system robust to changes in rate parameters?
- Does the qualitative behaviour of the model depend on having precise values for the parameters?
- What happens if the model is extended to include creation/degradation?
- What if the final product C catalyzes degradation of A_{PP}?

Report

Your report should include a description of your model, your analyses, and the results you obtained. Include details of code written, graphs, with web pages and screenshots if appropriate. Beyond the bare technical details, you should also discuss and comment on your investigation: the suitability of BioPEPA and its tools; limitations; possible extensions and further directions. You may wish to include an appendix with a complete record of material used; there are no size limits on the report.

You should include full references, and a bibliography listing all the papers, articles and other sources you have used in your work.

Assessment

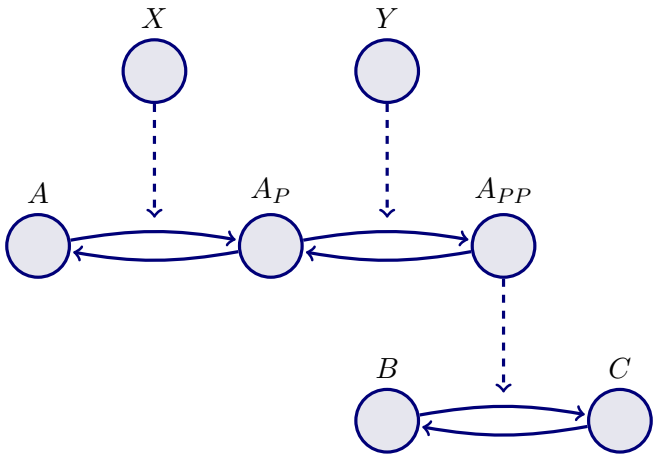
Assessment will be according to the *Extended Common Marking Scheme* of the University. The College of Science and Engineering provide a description of how this applies to coursework of this kind: see the "general description for Honours years" and "table" at the following address.

`http://www.scieng.ed.ac.uk/AA/Staff/Taught%20Student%20Admin/Assess.htm`

In particular, assessment is based on performance in the following broad areas.

- Knowledge
- Understanding and handling of key concepts
- Focus on the subject
- Critical analysis and discussion
- Literature synthesised, analysed and referenced
- Structure
- Presentation

Naturally, these are interpreted in the technical context of this specific exercise.



Volume	10^{-14}l	
Initial concentrations	$[A] = 0.05\,\mu$M	
	$[B] = 0.1\,\mu$M	
	$[X] = [Y] = 0.01\,\mu$M	with others zero.
Michaelis-Menton kinetics	$A \xrightarrow{X} A_P$	$(10\,\text{min}^{-1}, 0.06\,\mu\text{M})$
	$A_P \xrightarrow{Y} A_{PP}$	$(8\,\text{min}^{-1}, 0.1\,\mu\text{M})$
	$B \xrightarrow{A_{PP}} C$	$(3\,\text{min}^{-1}, 0.2\,\mu\text{M})$
Mass-action kinetics	$A_P \to A$	$0.1\,\text{min}^{-1}$
	$A_{PP} \to A_P$	$0.05\,\text{min}^{-1}$
	$C \to B$	$0.10\,\text{min}^{-1}$

Figure 1: A simplified signalling pathway and some sample parameters.