The Bio-PEPA Tool Suite

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1 Introduction

Bio-PEPA [1, 2] is a timed process algebra designed specifically for the description of biological phenomena and their analysis through quantitative methods such as stochastic simulation and probabilistic model-checking.
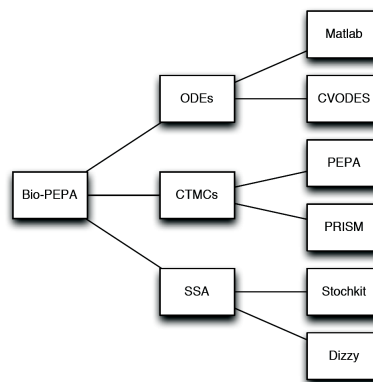
The context of application we consider is that of biochemical networks. A biochemical network is composed of n species which interact through m reactions; the dynamics of reaction j is described by a kinetic law. The quantitative behaviour of a biochemical network depends on the initial values of the involved species and on the kinetic parameters.

Two software tools are available for modelling with Bio-PEPA, the Bio-PEPA Workbench and the Bio-PEPA Eclipse Plugin. The Bio-PEPA Workbench is the research prototype tool which allows us to try out new language features and new types of analysis through rapid prototyping. The Bio-PEPA Eclipse Plugin is a polished modelling environment which targets end-users who wish to do Bio-PEPA modelling supported by a comprehensive integrated development environment. Both modelling tools allow the user to analyse their model both in the discrete stochastic regime and in the sure continuous regime while maintaining only a single source in the Bio-PEPA language.

2 The Bio-PEPA Workbench

The Bio-PEPA Workbench is a lightweight modelling tool whose primary function is to compile Bio-PEPA models into other formats for analysis by a suite of other tools. Among these are well-known tools such as Matlab and the PRISM probabilistic model-checker but the Bio-PEPA Workbench also allows users to work with the StochKit [3] simulation framework and the Sundials ODE solver suite. These are efficient C++ libraries for stochastic simulation and numerical integration of systems of differential equations.

The Bio-PEPA Workbench uses a range of other analysis tools. An outline of the tool organisation is shown below.

With respect to stochastic simulation, the Bio-PEPA Workbench generates the kinetic laws and propensity function descriptions which are needed to perform an analysis of the model via stochastic simulation using Gillespie's Stochastic Simulation Algorithm (SSA) and other stochastic simulation algorithms such as Gibson-Bruck.

As an alternative to simulation, the Bio-PEPA Workbench can also generate a CTMC model in the format accepted by the PRISM model-checker together with a reward structure and typical formulae of CSL logic which can be checked against the PRISM model [4].

With respect to continuous simulation, the Bio-PEPA Workbench generates the reaction rate equations in the form of a system of coupled ordinary differential equations where the system variables of the differential equations allow us to determine the quantity of each chemical species in the reaction at any point up to a finite time horizon, and in the long run. The Bio-PEPA Workbench uses symbolic differentiation to generate the Jacobian of the model's kinetic functions. This can be used by a numerical integrator to provide faster and more stable numerical computation of expected concentrations of chemical species. The Bio-PEPA Workbench connects to other numerical analysis packages to allow bifurcation and continuation analysis of models also.
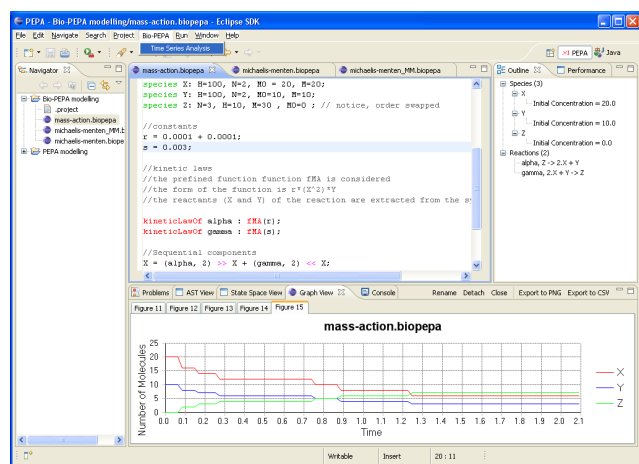
3 The Bio-PEPA Eclipse Plug-in

The Bio-PEPA Eclipse Plug-in is a rich modelling environment for Bio-PEPA which aims to provide strong support for investigating the average case dynamic behaviour

of systems. The Bio-PEPA Eclipse Plug-in supports the experimental process by allowing users to execute stochastic ensembles of independent simulation runs and to compute averages over these, which is one kind of analysis. A second kind of analysis investigates the mean trajectory directly by generating the differential equation model and numerically integrating this. Being able to compare simulation results and ODE solutions has allowed us to discover errors in published modelling studies in computational biology [5]. This illustrates the strength of a high-level modelling language such as a process calculus.

In contrast to the Bio-PEPA Workbench which uses external tools, the Eclipse Plug-in project has stochastic simulators and numerical integrators built-in making this tool much easier for non-expert users to install and use. The Bio-PEPA Eclipse Plug-in project currently supports two numerical integrators for ODEs, a Runge-Kutta implicit-explicit implementation and the Dormand-Prince adaptive step-size solver, both through the odeToJava library. All of the numerical calculation and management of the results through to visualisation in the form of graphs and charts is handled by the tool itself.

The stochastic simulators which are currently supported are Gillespie's Stochastic Simulation Algorithm (SSA) and the Gibson-Bruck algorithm. These have formally been shown to be in agreement with the Chemical Master Equation, which itself is a Markov chain. It is this structure – and the optimisations possible because of it – which allow these algorithms to analyse in a realistic time systems which would be intractable when using a state-based representation.

The Bio-PEPA Eclipse Plug-in Project is built on the PEPA Eclipse Plug-in Project [6], a state-of-the-art modelling tool for PEPA. Both tools are 100% Java, for maximum portability.

4 Future work

Future work with the Bio-PEPA tools is developing a mapping from a user-centred narrative language into Bio-PEPA, and an interface between the Systems Biology Graphical Notation (SBGN) and Bio-PEPA is currently under development by Laurence Loewe at the Centre for Systems Biology at Edinburgh. We hope that these developments will encourage users in the Life Sciences to adopt the Bio-PEPA tools because they will be able to obtain the benefits of using a high-level modelling language without needing to work directly at the process calculus level.

Availability: The Bio-PEPA software is available for free download from `http://www.biopepa.org`.

References

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