The Bio-PEPA Tool Suite

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Introduction

Bio-PEPA 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.

Context

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.

The Bio-PEPA languge

Sequential component (species component)

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Depending on the interpretation, this quantity may be:

- number of molecules (SSA),
- concentration (ODE) or
- a level within a semi-quantitative model (CTMC).

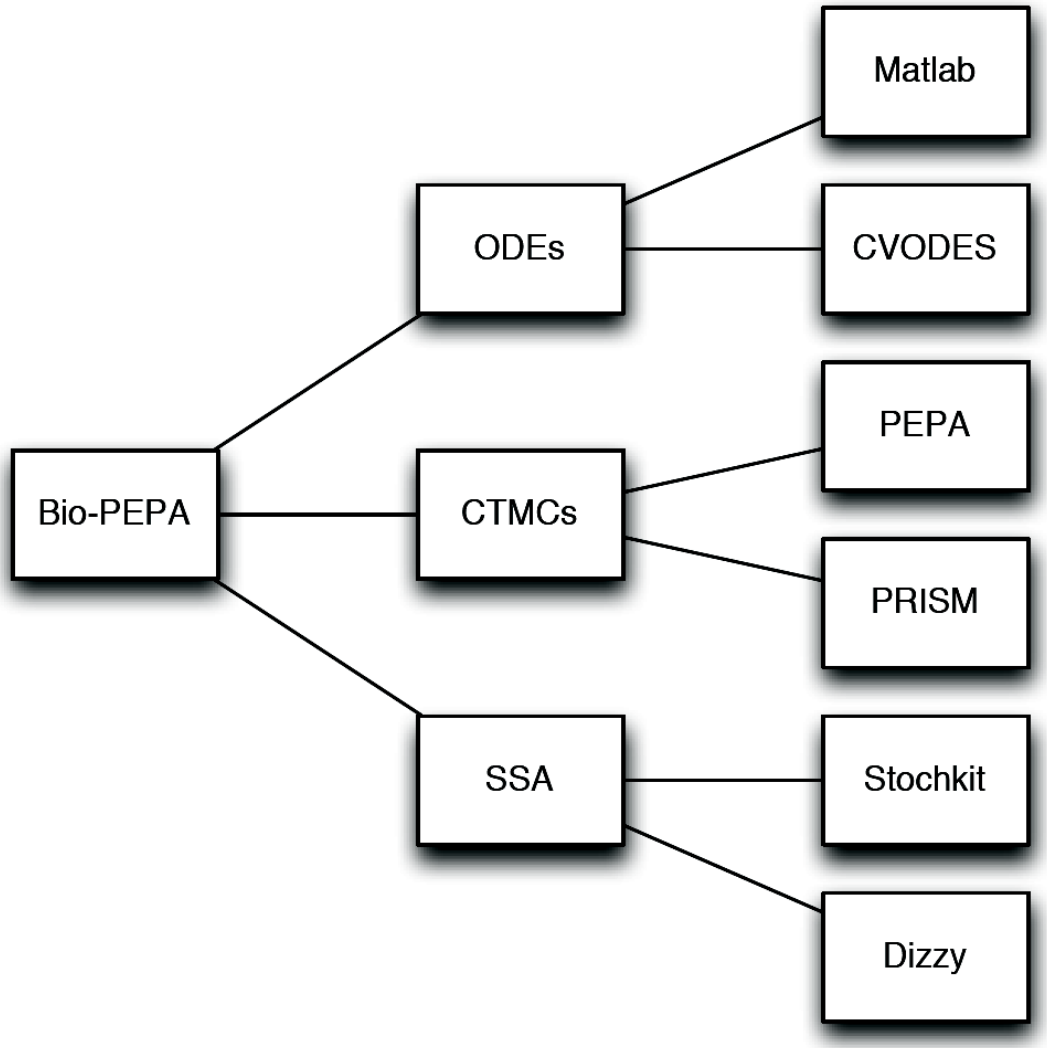
Software Tools

Two software tools are available for modelling with Bio-PEPA,

- the Bio-PEPA Workbench, and
- the Bio-PEPA Eclipse Plugin.

Both modelling tools allow the user to analyse their model both in the discrete stochastic regime and in the deterministic continuous regime while maintaining only a single source in the Bio-PEPA language.

The Bio-PEPA Workbench



Stochastic simulation

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.

Model-checking

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.

Each species component gives rise to one PRISM module.

Custom rate expressions are generated to ensure that the generated PRISM model correctly reflects the dynamic behaviour of the input Bio-PEPA model.

Continuous simulation

For continuous simulation, the Bio-PEPA Workbench generates the reaction rate equations in the form of a system of coupled ODEs.

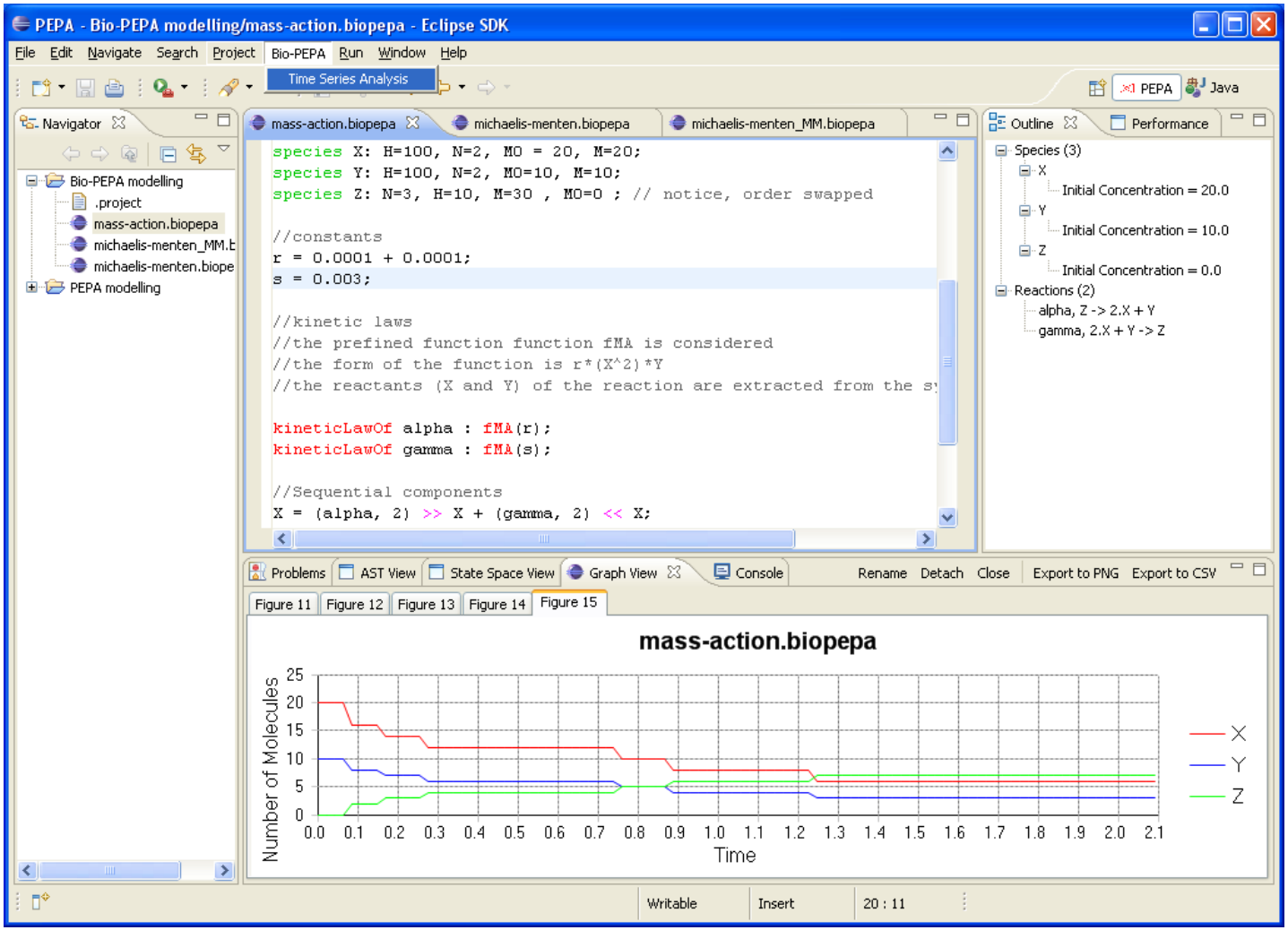
The system variables of the ODEs allow us to determine the quantity of each chemical species in the reaction at any point up to a finite time horizon, and in the long run.

The Bio-PEPA 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.

Users can compare stochastic ensembles of independent simulation runs with the mean trajectory obtained by generating the differential equation model and numerically integrating this.

The Bio-PEPA Eclipse Plugin



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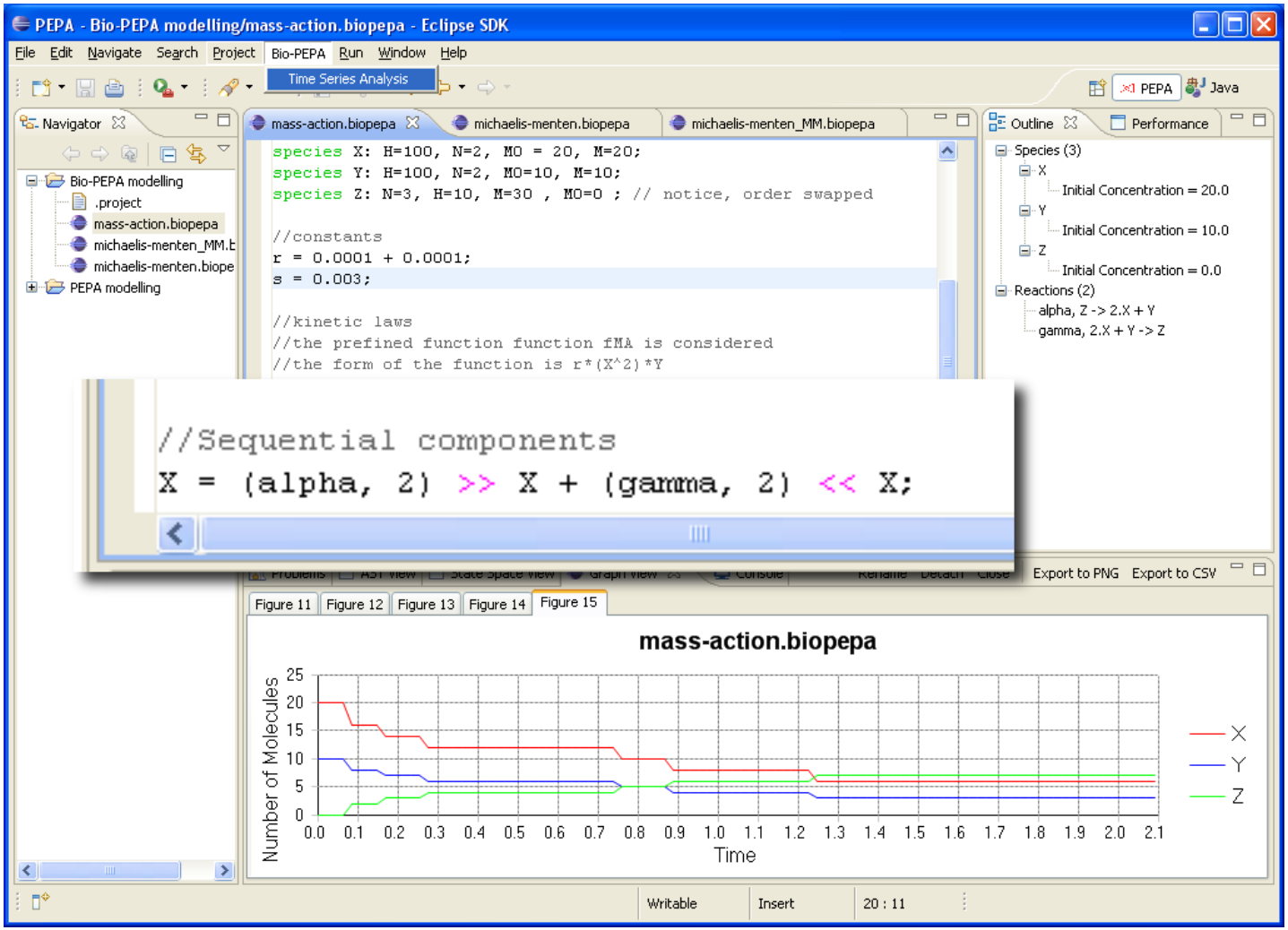

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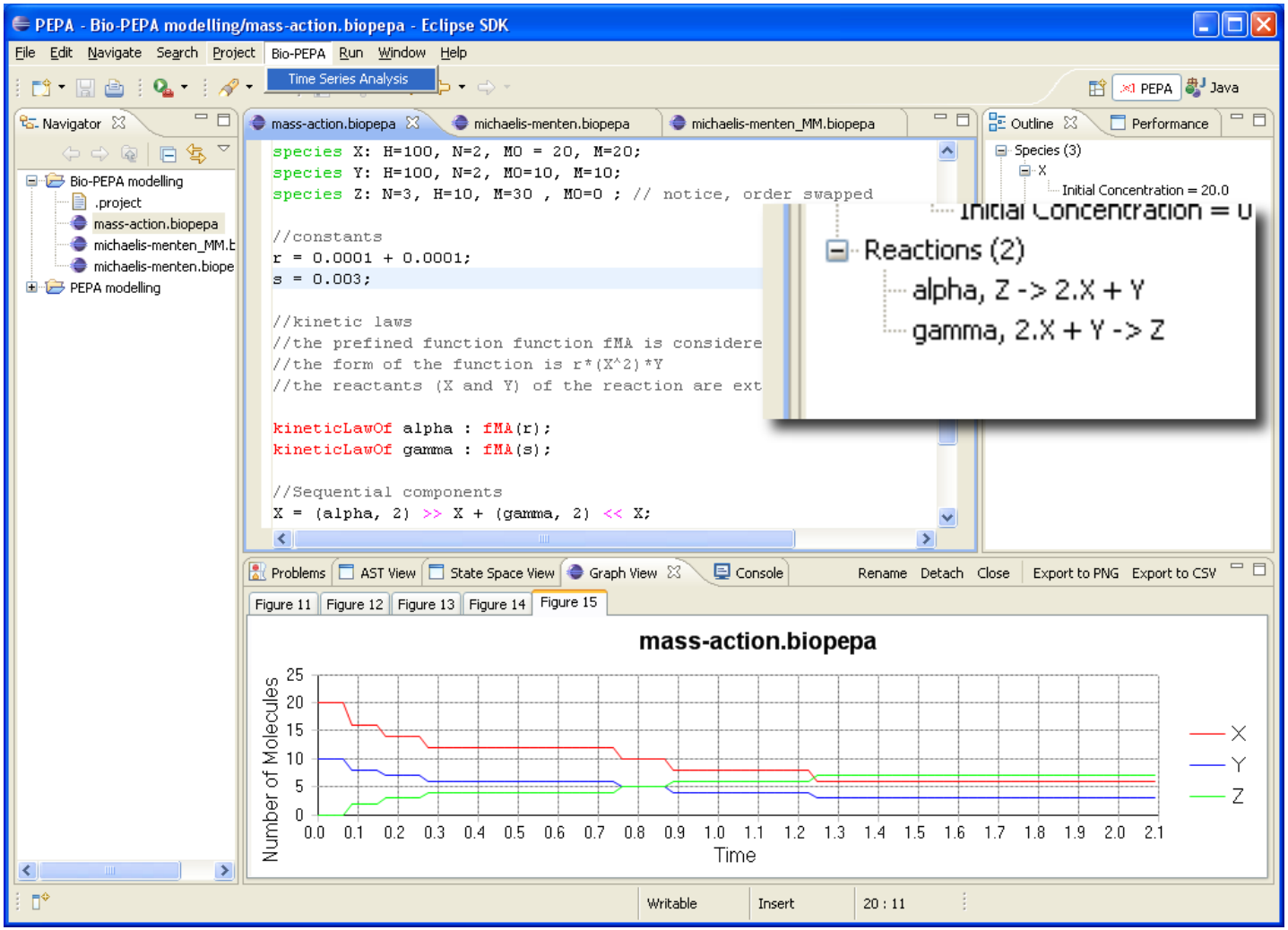

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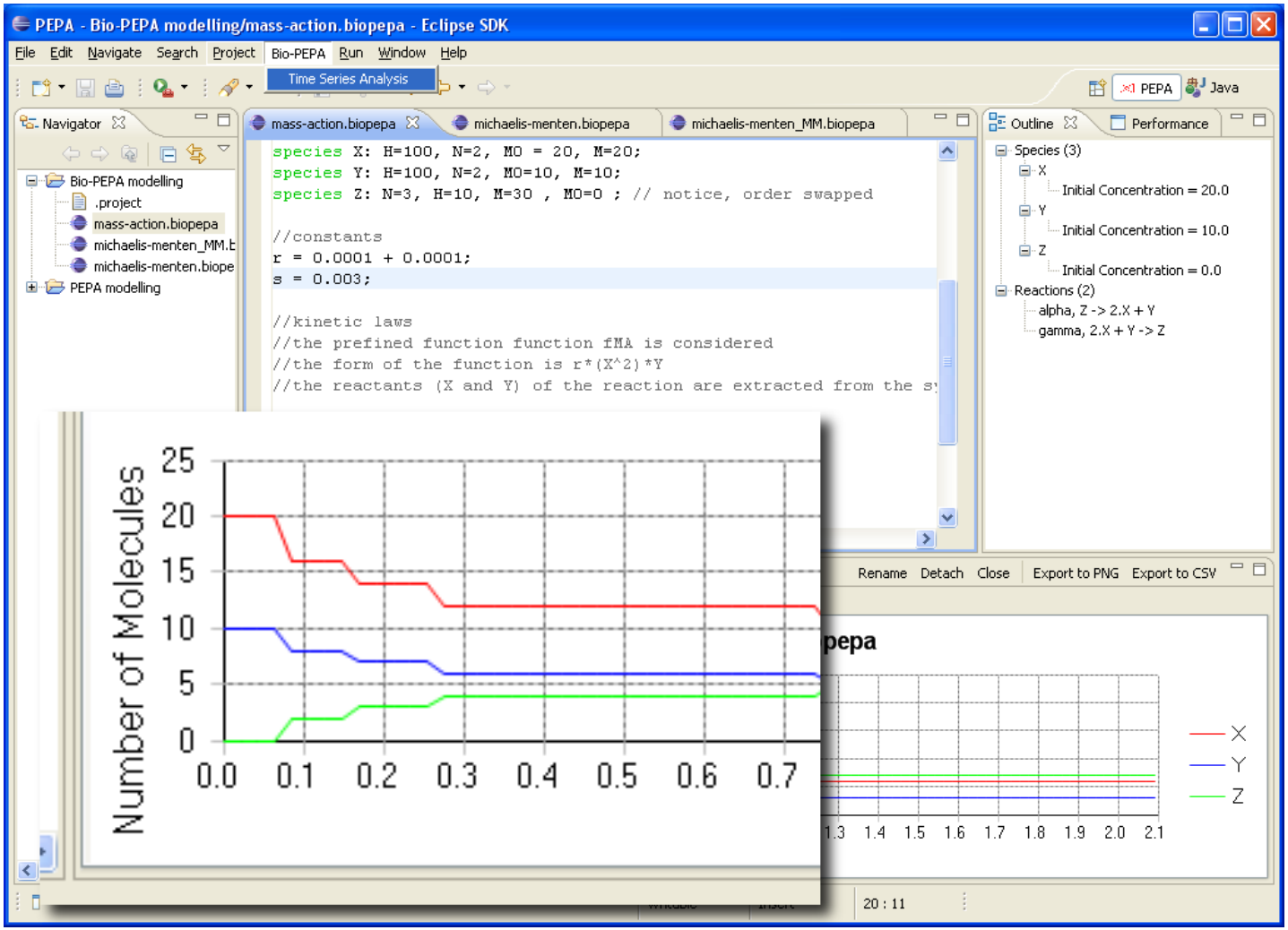
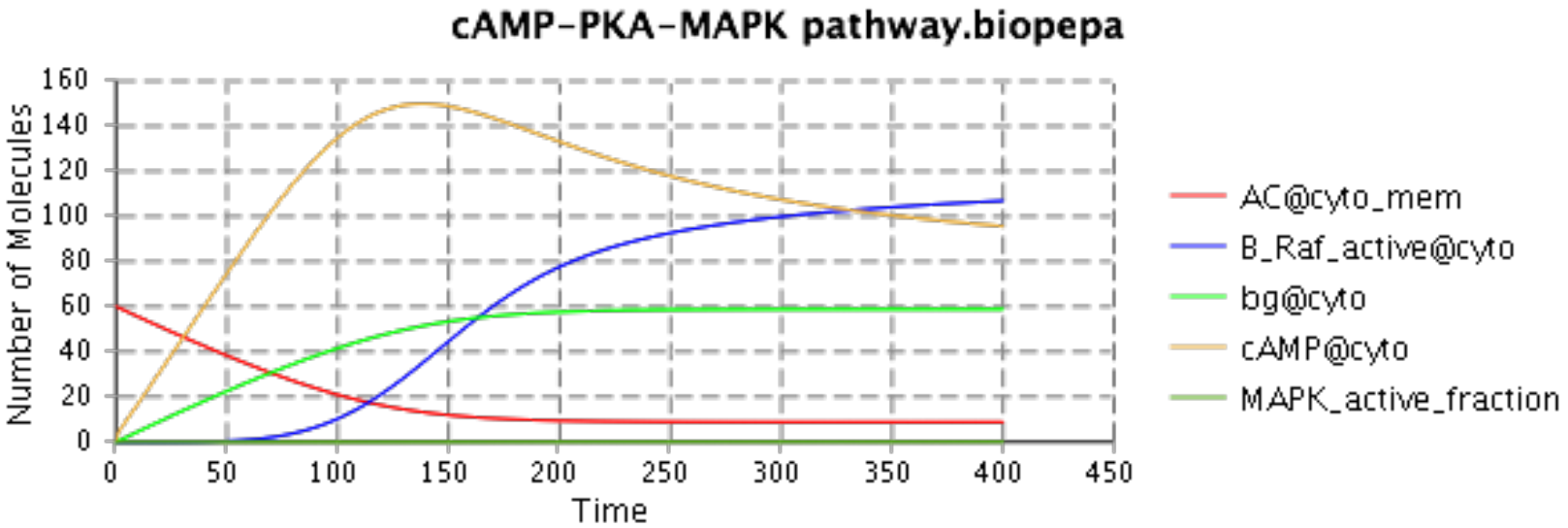


Example results



Advantages of process calculus

Being able to compare simulation results and ODE solutions has allowed us to discover errors in published modelling studies in computational biology. This illustrates the strength of a high-level modelling language such as a process calculus.

Stronger computational modelling of signalling pathways using both continuous and discrete-state methods.

M. Calder, A. Duguid, S. Gilmore, and J. Hillston.

Computational Methods in Systems Biology, Trento, Italy, 2006.

Additionally we are working on developing appropriate notions of equivalence and abstraction for biological models.

Availability

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

Acknowledgements

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- EP/E031439/1 "Stochastic Process Algebra for Biochemical Signalling Pathway Analysis".