

Modelling randomness in biological systems

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Abstract: This poster presents an extension to the Open Source project *The Petri Net Kernel* (Kindler and Weber 2001). This extension facilitates the simulation of biological systems using Stochastic Petri Nets (SPNs). I explain the terminology of SPNs and an interpretation of SPNs to represent chemical reactions. In the third section I will illustrate possible applications of this software using a well-known model system, the *Volterra-Lotka* set of coupled reactions.

Introduction

The Petri Net theory was developed by Adam Petri (Petri 1962). With their stochastic extension, Petri Nets can be used to gather qualitative and quantitative information of a model.

A Stochastic Petri Net (SPN) consists of **places** and **transitions**. Each place represents a distinct molecular species. Places contain tokens which represent individual molecules. The number of token in a place is called the marking and the **global marking**, the number of token in each place, is the current state of the system.

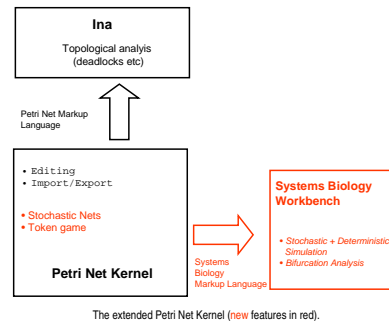
Transitions represent chemical reactions. They are connected with places through **arcs**. Input places represent reactants and output places represent products of the reaction. Each arc has a **weight** which represents the stoichiometric coefficients of the molecular species that participate in the reaction.

In a SPN, each transition has an associated **rate**. If the transition is enabled, that is in all of its input places there are at least as much tokens as specified by the weight of the corresponding arc, then the transition **fires** with an exponentially distributed delay. The SPN can be simulated by computing the delay for each enabled transition and by executing the transition with the smallest delay. This particular way to simulate the net corresponds to the Gillespie-Algorithm.

Implementation

I developed a SPN module for the *Systems Biology Workbench* (SBW) which is based on the Open Source project *The Petri Net Kernel* (Kindler and Weber 2001). This kernel offers an infrastructure for the editing and simulation of various Petri Nets and graph structures. I extended it by the following features:

- **Stochastic Simulation:** Using the implemented connection to the Systems Biology Workbench, the net can be simulated with the Gillespie, Tau-Leap or Gibson-Bruck algorithm.
- **SBML Support:** Petri Nets can be imported from and exported to SBML. Reactions are mapped on transitions and species on places as described above.
- **The Token Game for Stochastic Nets:** SPNs can be simulated by visualizing the movement of tokens through the network.



The extended Petri Net Kernel (new features in red).

Experiments

In order to show possible applications of this software, I modelled the so-called *Volterra-Lotka reactions* as a Petri Net. The Gillespie algorithm was used to simulate this set of coupled reactions:

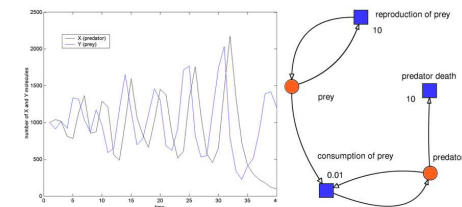


This model can also be seen as a simple description of a predator-prey ecosystem. In this case, Y represents the prey which reproduces itself in reaction (1). Reaction (2) describes how Y , the predator species, reproduces by feeding on the prey. Reaction (3) models the demise of Y through natural causes.

These reaction have been extensively modelled using different deterministic and stochastic approaches. One can show that the steady state of this system is characterized by $Y = c_3/c_2$ and $X = c_1/c_2$. But it was also shown that this system exhibits an oscillatory behaviour if modelled stochastically. I simulated the system by mapping the Petri Net to its SBML representation and simulating its dynamics with the Gillespie algorithm. With the initial conditions $X = Y = 1000$, $c_1 = c_3 = 10$ and $c_2 = 0.01$, a deterministic approach predicts that this situation

will persist indefinitely (Gillespie 1976).

The left plot gives the time evolution of the number of X and Y molecules and reveals the expected fluctuations: a rise in the prey population provides food for the predators and hence is followed shortly by a rise in the predator population.



Conclusions and future work

The strong oscillatory behaviour of the Lotka-Volterra system would not have been possible to predict using deterministic approaches. This underlines the need for stochastic approaches to biological models. The extended Petri Net Kernel has proven to be able to fulfil this need.

In the near future, I will use this software to model circadian rhythms in plants that also show an erratic behaviour. I also intend to make the simulation of the SPN more efficient by implementing more suitable algorithms.

References

- Daniel T. Gillespie (1976). A general method for numerically simulating the stochastic time evolution of coupled chemical reactions. *J. Comput. Phys.* **22** pp. 403-434
- E. Kindler and M. Weber (2001). The Petri Net Kernel - An Infrastructure for Building Petri Net Tools. *Software Tools for Technology Transfer (STTT)* 3(4), pp. 486-497
- C.A. Petri (1962). Kommunikation mit Automaten *Institut für Instrumentelle Mathematik Bonn, Schriften des IIM Nr.3*

