Modeling of biochemical networks using Monte Carlo simulations

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Introduction:
Modeling living cells are of great importance in order to understand the complicated biochemical networks in cells. Inside of living cells, molecules move in space by diffusion and when they react with each other, new compounds are formed. For systems where the molecules can be assumed to be well stirred, the space dependency can be ignored.

Living cells are usually modeled using either the deterministic Chemical Master Equation (CME) or the Stochastic Simulation Algorithm (SSA). However, CME can only be used for small scale problems and SSA have a slow convergence rate. The aim of this project was to develop a faster SSA based on Monte Carlo methods for well stirred steady state problems.

Method:
Our approach have two modifications compared to the classical SSA.

1. The time between the reaction is made longer by letting multiple reactions occur at once. This impairs the accuracy of the solution, but reduces the time it takes to reach steady state.

2. Instead of simulating a lot of trajectories at as in a normal Monte Carlo we simulate one or few trajectories until steady state is reached. Starting at that “equilibrium” we perform a full scale Monte Carlo simulation.

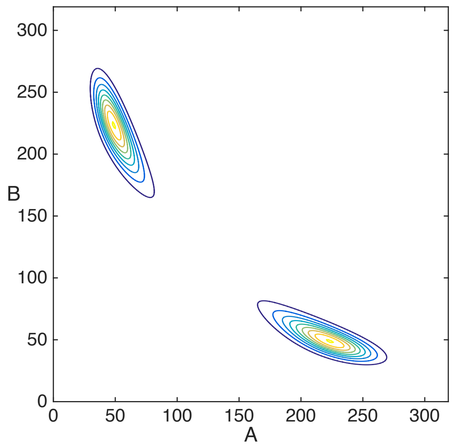

***Figure 1**. Isolines of the probability distribution at time 100’000 [s] for molecule A and B.*

Result and Conclusions:
The efficiency of the method is very much dependent of the number of used trajectories used in the simulation. As a result the Two metabolites 3D simulation is least improved, which can be seen in figure 2.

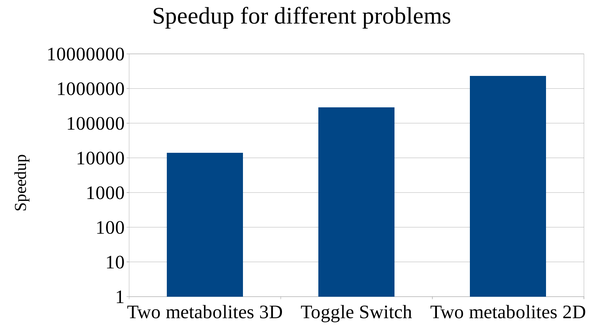

***Figure 2**. Speed up for three different reaction systems.*

The efficiency of the model is of the same reason also dependent of the number of equilibriums in the system. For a two equilibrium system, as for the *Toggle Switch,* in figure 1, enough trajectories has to be created from the start so that the equilibriums gets the correct probability distributions.