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Project Description:

NFsim (http://www.nfsim.org) is a generalized stochastic reaction network simulator designed to handle systems with a large (or even infinite) state space. It has a number of features that make it ideal for handling large and complex biochemical systems, such as functionally defined rate laws and reactions that depend on local context. Therefore, it can be used to study molecular biology and genomics study for various types of cancer.

NFsim is designed to operate with the BioNetGen Language (http://bionetgen.org/). BioNetGen is a software for rule-based modeling of signal transduction based on the interactions of molecular domains

Currently, NFSIM can simulate conditional reactions only based on reactants' features. Hence, It cannot considers this fact that some undesirable features, which can be only seen in a product of some reaction, may prevent that reaction happens. Therefore, one possible Improvement to NFSIM would be adding right-hand side (RHS) functions to reaction rules.

In the project folders, following files are mainly responsible for handling these kind of functions:

- NFSIM2/NFreactions/reactions/RHSreaction.cpp
- NFSIM2/NFreactions/reactions/RHSreaction.hh

Other than these two files couple of other files are added to enable this functionality in the project.

In order to show that aforementioned modifications work properly generating some comparative results are required. Therefore, I started working on generating sample models which I believed older version cannot handle them. These models required to be tested using two version of the software. In addition, old models which were already verified by old version can be tested with the new version because the new version has to handle old models as well

Problem Statement:

- Generating results in order to verify RHS function works properly in new version of NFsim
- Modifying BionetGen 2.3 in order to make it compatible with RHS function which is new option of Nfsim

Investigation/Research:

In order to understand how the Nfsim work following paper was studied:

- Sneddon MW, Faeder JR and Emonet T. Efficient modeling, simulation and coarse-graining of biological complexity with NFsim. Nature Methods (2011) 8(2):177-83.

- Erban, Radek, Jonathan Chapman, and Philip Maini. "A practical guide to stochastic simulations of reaction-diffusion processes." arXiv preprint arXiv:0704.1908 (2007).

Analysis & Testing:

After generating different BNGL file to test RHS function it turns out that after activation of RHS macro Nfsim simulation speed magnificently reduced. In addition, in some cases a memory segmentation error terminates the simulation.

Fixing the problem of BionetGen in order to support RHS functions has two different steps. Firstly, it needs to modify Perl script to add label to righ hand side of reaction. Secondly, there are some circumstances to check labeling of the bngl files. It is required to modify corresponding functions in BioNetGen to accept RHS function.

Implementation:

After upgrading BionetGen following files are modified:

- BNG2.pl
- RateLaw.pm
- Expression.pm
- ParamList.pm
- RxnRule.pm
- BNGModel.pm

There is a Documentation of changes which is under preparation.

In order to solve the problem of simulation speed and segmentation error the code for process of duplicating Molecules is improved. Any changes regarding the code upgrades are documented in the code.