Stochastic Simulation GUI for Biochemical Networks

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ABSTRACT

Motivation: This paper describes the development of a useful graphical user interface for stochastic simulation of biochemical networks which allows model builders to run stochastic simulations of their models and perform statistical analysis on the results. These include the construction of correlations power-spectral densities and transfer functions between selected inputs and outputs. Availability: The software is licensed under the BSD open source license and is available at http://sourceforge.net/projects/jdesigner. In addition, a more detailed account of the algorithms employed in the tool can be found at the Wiki at http://www.sys-bio.org/sbwWiki. Contact: Ravishankar Rao Vallabhajosyula: rrao@kgi.edu

1 INTRODUCTION

The complexity of biochemical networks arises from the nature of the interaction of various biochemical species. When large numbers of participants are present, their time evolution can be described by a system of differential equations. However, in cases where the species numbers are low, this has to be replaced by a stochastic approach. A number of algorithms have been developed in the recent years for such problems, improving over the original Stochastic Simulation Algorithm (Gillespie, 1977) and have been incorporated into tools such as COPASI (Hoops et al., 2006), Dizzy (Ramsey et al., 2005) and BioNetS (Adalsteinsson et al., 2004). While most of these tools can be used only for simulation, a few like BioNetS allow construction of probability density histograms and power spectral densities. The application described in this paper enables additional analysis capabilities such as construction of correlations between species, power spectral densities as well as transfer functions.

2 CAPABILITIES

The user interface and the Gillespie simulator it interacts with were built in C# using the Systems Biology Workbench (Sauro et al., 2003). Users can perform the following tasks, as shown in Figure 1.

Data Generation: Users can load biochemical models in SBML to perform stochastic simulation. Data can be generated on an evenly spaced time-grid or by updating the species numbers by a specified value. The first option enables users to carry out statistical analysis, compute Power Spectral Densities as well as Transfer Functions.

Probability Density: Each data run is converted to a histogram representative of the spread. Averaging these over all the generated runs yields a histogram of the ensemble averaged probability.

Ensemble Averages: Population means and standard deviations for all time points are obtained by averaging the entire set of runs. These can be compared with deterministic results for the same model.

Correlations: For data generated using an evenly spaced time grid, auto and cross-correlations (Chatfield, 2004) are computed between all the species in the network for each run as well as the ensemble.

Power Spectral Densities: PSDs can provide information on noise filtering characteristics of biochemical networks (Simpson et al., 2003). These are computed using the publicly available Exocortex.DSP signal processing toolbox (Exocortex, 2003).

Transfer Functions: These are response functions that relate system outputs to inputs (Williams et al., 1972).

Creating Noise Sources: This tool allows conversion of boundary nodes into floating nodes by means of a SBMLModifier module that interfaces with libSBML (http://www.sbml.org/software/libsbml/).

Testing Application: This is a companion tool that has been built to allow users to test the correctness of the simulator implementation and is based on the discrete stochastic model testing suite (http://www.calibayes.ncl.ac.uk/Resources/dsms/overview).

3 FUTURE DIRECTIONS

While the present version allows data generated by the simulator to access the analysis capabilities, future versions could allow experimental data to be loaded into the application to carry out the same analysis for comparison with model results.

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REFERENCES


Fig. 1. Stochastic Simulation Graphical Interface: Panel 1: (a) Options for loading and running the models, (b) simulator options for data generation, (c) data sampling, (d) display settings, (e) generating correlations and power spectral densities, (f) options for noise injection at one or more boundary nodes, and (g) for plotting transfer functions. Panel 2: A linear chain network with three species (with initial numbers set to zero), and rate constants for reactions given as 0.1, 0.05, 0.06667 and 0.1 respectively. The boundary species "Node0" has a value of 100. SBML modification allows creation of a new network, shown in the right part of the top panel, with "Node0" converted from a boundary node to a floating node. Panel 3: Plots showing (a) time histories of species in the modified model, along with the probability density histogram of Node1, (b) Ensemble averages and standard deviations, (c) Auto-correlation and Power Spectral Densities and (d) Transfer functions between selected input and output nodes (in this case between Node0 and Node3), and lastly, Panel 4: (a) Graphical Interface for testing the stochastic simulator using the Discrete Stochastic Model Test Suite. Out of range normalized means in (b) and standard deviations in (c) appear in orange.