Extending the philosophy of the general public licenses to the development of software tools in systems biology: A power-law module for the Matlab SBToolbox

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Abstract

The SBToolbox is a recently developed Matlab toolbox for Systems Biology (Schmidt et al, 2006). The SBToolbox is an open software environment in which *systems biologists* can develop new methodologies for the analysis of biochemical systems modelled as sets of ordinary differential equations.
This article presents a fully operative software module designed to expand the current version of the SBToolbox with several functions especially for the analysis of power-law models.

1. Introduction

1.1. Systems biology and software development. Systems biology is an emerging field in science where knowledge coming from the experimental biology and the theory of systems is merged to analyse the properties of living system at the cellular level. The complexity of cell biological systems requires the development of new appropriate software tools. This new software must be computationally powerful but *easy to use* since most of its potential users are not experts in computer science. Moreover, any attempt to design a new software must be based on an environment open to changes and to the integration of new methods that might be developed in future.

1.2. SBToolbox: a general public license Matlab toolbox for systems biology. The SBToolbox is a recent Matlab toolbox for Systems Biology developed in the Fraunhofer-Chalmers Research Centre of Göteborg (Schmidt et al, 2006). This toolbox is an open and extensible software environment in which *systems biologists* can explore ideas and new methodologies for the analysis and simulation of biochemical systems modelled as sets of ordinary differential equations.
The aim was to develop a user-friendly and user-extensible software framework that facilitates work and the exchange of methods and data between researchers. For that purpose, the software was developed as a toolbox for the widely used mathematical software Matlab^{TM}, which is a standard in several fields of the scientific and technological research. The users can access all data structures generated by the SBToolbox which results in full control over the tasks to be performed and facilitates the development of new functions and algorithms. With this idea, the toolbox was developed as a General Public License software allowing modifications by the user and the integration of new methods and algorithms.
The current version of the SBToolbox includes functions related to modelling and simulation, import/export of SBML models, stability analysis, bifurcation analysis, network identification and other features.

1.3. Power-law models in systems biology. An alternative approach, not yet considered in the SBToolbox, to model biochemical systems, are models developed in the formalisms included in Biochemical System Theory (Savageau 1969a,b; for a recent revision about BST formalism, see Voit 2000, and Torres and Voit 2002). In this modelling framework, the chemical processes that integrate biochemical networks are modelled by using power-law expansions in the variables of the system and then included in ordinary differential equations:

$$\frac{dX_i}{dt} = \sum_j c_{ij} \cdot \gamma_j \cdot \prod_{k=1}^{p} X_j^{gjk} \qquad i = 1 \ldots n_d$$

where X_i are the n_d variables of the model (representing metabolite concentrations, protein concentrations or levels of gene expression), and c_{ij}, $_{.j}$and g_{jk} are different kinds of parameters defining the dynamic of the system.

These power-law models are a wider framework to model the complex chemical interactions occurring in cellular biological systems with significant computational and analytical advantages. Models using power-law expansions have been used during the last 35 years to model and analyse several kinds of biochemical systems including metabolic systems, genetic networks, and cascades of expression, and now in cellular signal transduction systems.

1.4. Objective of the work. The aim of this project was to design and implement a fully operative software module to expand the current version of the SBToolbox with several functions especially designed for the analysis of power-law models. Two different kinds of power-law models were considered, S-system and GMA models, and specific functions were developed for the analysis of both kinds of models.

Additionally, we wanted to show that the philosophy of GPL software, based on free availability of software and open collaboration between users and developers, can be a powerful tool to boost the development of software specifically intended for systems biology.

2. Discussion

2.1. Structure of the module. The software was developed as an add-on module to the original toolbox. All the functions are collected in a folder that has to be placed in the root directory of the SBToolbox. The interaction with the underlying toolbox is described in the Figure 1.

The information about the model is extracted from the basic data structure of the SBToolbox and converted into a new specific data structure that contains the essential information about the power-law model (variables, state values, matrices of kinetic orders and vectors with rate constants). The functions for the analysis of power-Law models extract the required information from this data structure and compute the results. Finally, modifications in the model can be stored in the SBToolbox formatted text file and be reused in future.

In this way, either the functions of the basic distribution or the functions of the power-law module can be used with the information contained in the SB data structure and stored in the SBToolbox formatted textfile.

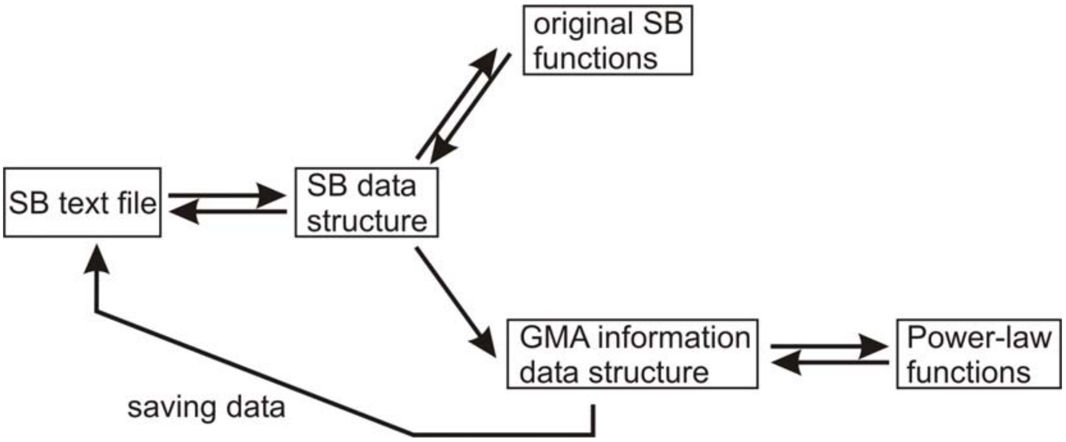


Figure 1. Structure of the Power-law module and interaction with the functions of the original SBToolbox.

2.2. Basic functions. The functions offered by the module allow the analysis of two different kinds of power-law models: S-system and GMA models (see Voit 2000 for further explanations about the features of these models). Models with mass conservation laws cannot be analysed with the current distribution, but this option will be available in the next version.
The module contains functions for the calculation of steady states, stability analysis, and assessment of the robustness and responsibility of the system using logarithmic gains and sensitivities. A function developed to facilitate the plotting of log gains and sensitivities is also available (Figure 2).

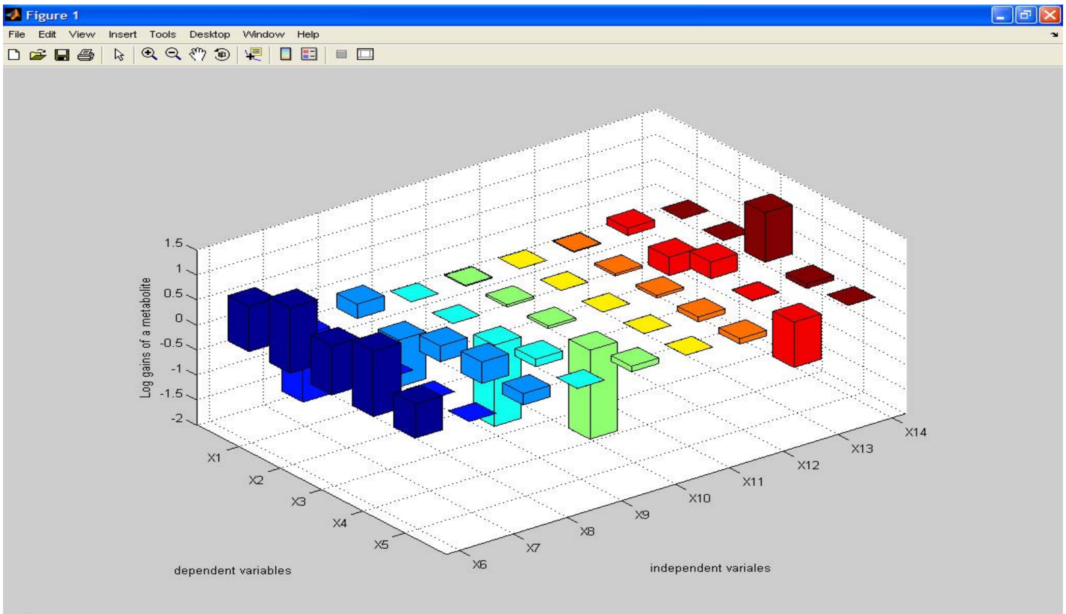


Figure 2. Plot of the logarithmic gains of an S-System model using the function *S_plots*.

Figure 3 shows how the different functions in the module interact. Once one has generated the data structure with the essential information, the steady state of the system is calculated. With the values of this computed steady state, the other functions, which analyse the properties of such state, can be calculated. Finally, either the log gains or the sensitivities of the model can be visualized by using the appropriate function for plotting (*GMA_plots*, see Figure 3).

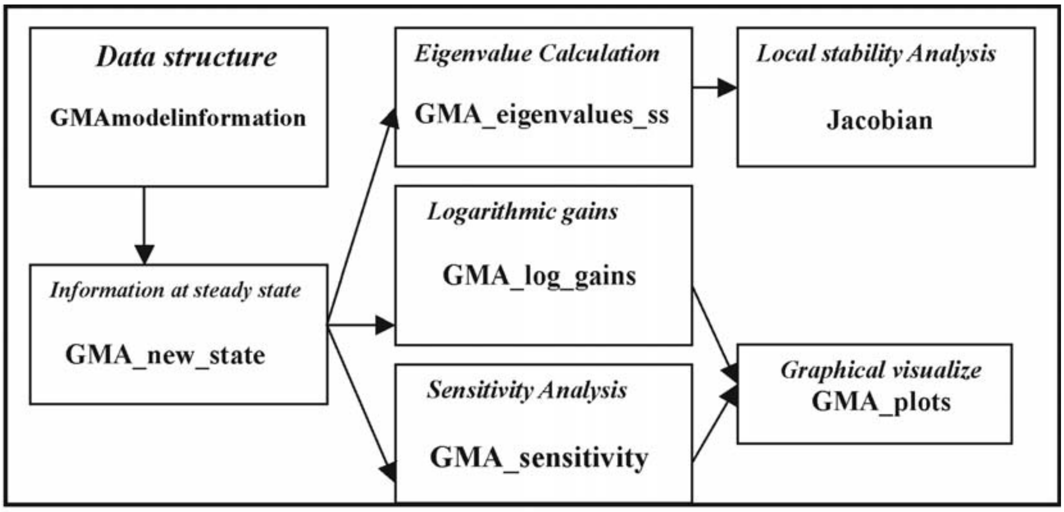
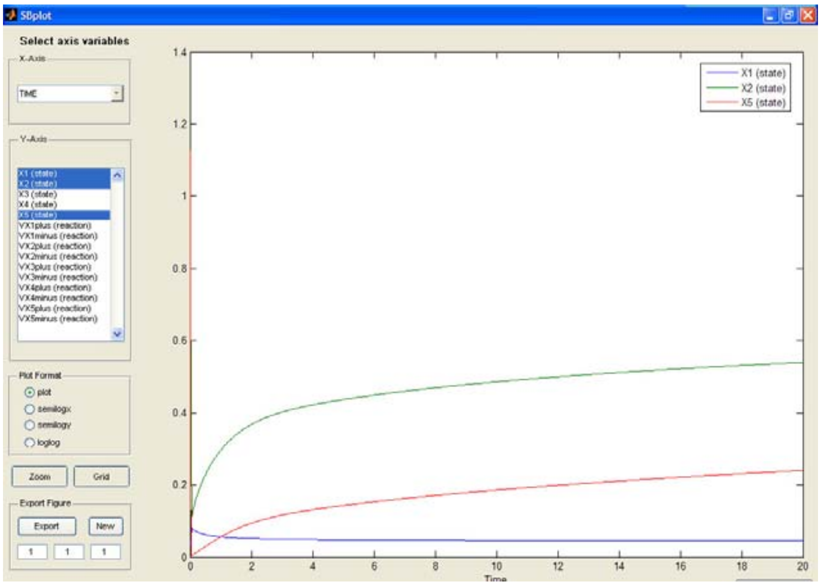


Figure 3. Interaction between the functions integrated (embedded) in the Power-law module.

The resulting model with its modifications can be translated into the SBML (Hucka et al. 2003) format using the specific function included in the underlying SBToolbox.


Select axis variables

X-Axis
TIME

Y-Axis
X1 (state)
X2 (state)
X5 (state)

Plot Format: ● plot ○ semilogx ○ semilogy ○ loglog

Export Figure: 1 1 1

Figure 4. Simulation of a Power-law model using the user interface of the SBToolbox.

3. Availability

The current version of the module, a user's manual and additional useful information will be available on the website of the Systems Biology and Bioinformatics Group at the University of Rostock:

www.sbi.uni-rostock.de

The current version of the basic SBToolbox is available on the following website:

www.sbtoolbox.org

4. Outlook

The futures intention is to improve the features of the module concerning the following elements of the analysis of power-law models:

- Development of new algorithms especially adapted to analyze systems with mass conservation.
- Development of new functions concerning the analysis of dynamical properties of biological systems modelled with power-law models.
- Implementation of functions for the optimization of biochemical systems with biotechnological and biomedical purposes.
- Integration of parameter estimation algorithms specifically designed for power law models.

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