

Systems biology

SBMLToolbox: an SBML toolbox for MATLAB users

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ABSTRACT

Summary: We present SBMLToolbox, a toolbox that facilitates importing and exporting models represented in the Systems Biology Markup Language (SBML) in and out of the MATLAB environment and provides functionality that enables an experienced user of either SBML or MATLAB to combine the computing power of MATLAB with the portability and exchangeability of an SBML model. SBMLToolbox supports all levels and versions of SBML.

Availability: SBMLToolbox is freely available from <http://sbml.org/software/sbmltoolbox>

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1 INTRODUCTION

The expanding field of Systems Biology has stimulated the formalization of an increasing number of biological/biochemical models. The Systems Biology Markup Language (SBML), an XML-based format for computational models of biochemical networks, is becoming accepted as a *de facto* standard for the representation of such models (Hucka *et al.*, 2004) and thus facilitates their systematic exchange.

In addition to promoting the creation of models, Systems Biology has also motivated the development of a range of software packages that can interact with these models, perform simulations and analyses on them, produce graphical representations of models and facilitate the creation of new models. However, the commercially available software package MATLAB (<http://www.mathworks.com>) provides a wide spectrum of this type of functionality combined with the facility to easily develop user-specific functions. Thus an alternative approach to that of developing new software exists in the form of developing a toolbox that provides users with an interface between basic MATLAB data structures and a format such as SBML. This not only enables users to leverage their existing skills in using the environment to work with a new format such as SBML, but it also provides a substrate enabling other analysis tools in the environment to be applied to data represented in SBML. MATLAB is a particularly attractive environment in this regard because it is already popular worldwide in both engineering and scientific research, and as the field of Systems Biology continues to attract researchers with an engineering or physical science background, the use of MATLAB within the field is likely to proliferate. Also, there currently exist many tools, both commercial and freely

available (Prajna *et al.*, 2004, <http://www.cds.caltech.edu/sostools>), that apply the computational and analytical capabilities of MATLAB to models and data in a variety of formats.

SBMLToolbox was initially developed specifically to meet two separate needs: (1) those of existing MATLAB users wishing to import SBML models and apply functionality appropriate to their goals, whether built into the environment or purpose-written and (2) those of users experienced with SBML wishing to apply the computational power of MATLAB to their models. Thus, in addition to importing SBML, the toolbox includes functionality serving as an example of using MATLAB in the manipulation and analysis of models. However, the actual analytical functionality is limited and while it is possible to simulate a range of models with the toolbox, it should not be considered a simulation tool but rather a facilitator for the development of other functions and toolboxes. To date we are aware of at least two freely available toolboxes that use SBMLToolbox for precisely this purpose; namely SBToolbox (Schmidt and Jirstrand, 2006) and SBMLSim (Remenik, 2005, <http://www.dim.uchile.cl/~demenik/SBMLSim/>).

2 FEATURES

The core functions of SBMLToolbox are for importing and exporting SBML models. The toolbox also contains a range of functions that allow a user to manipulate the content of the resulting MATLAB data structures (that is, the model being considered). A set of validation functions allow the structure to be checked for appropriate fields and the values assigned to these fields.

2.1 Import and export

SBMLToolbox offers two import functions that take an SBML model and return a MATLAB structure that replicates the Unified Modelling Language (UML) definition of an SBML model. Although the structure returned by both import functions is identical, two versions of this function are included within the toolbox: one in which the SBML file is verified against the XML Schema (Bray *et al.*, 2000, <http://www.w3.org/TR/1998/REC-xml-19980210>) for SBML (see <http://sbml.org/xml-schemas>) and a number of consistency checks are performed prior to import, and a second version in which the verification stage is skipped.

In the toolbox, the returned structure is called a MATLAB_SBML structure. It is populated with values drawn from the model being imported. Each of the SBML 'listOf' elements is reproduced as an

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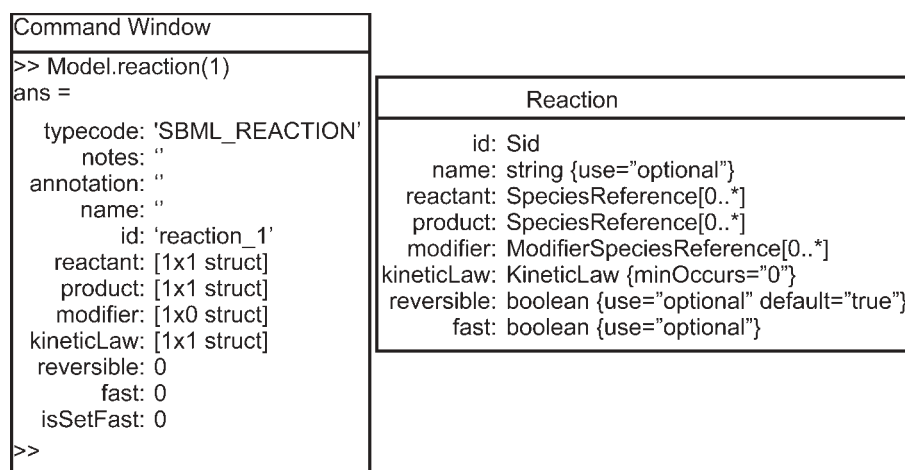


Fig. 1. MATLAB_SBML structure representing a 'reaction' and the UML definition of a 'reaction' within an SBML model.

array of structures defining the particular element, whereas each element is itself another structure. Figure 1 illustrates a portion of MATLAB_SBML corresponding to a reaction and its relationship to the definition of SBML's Reaction.

For export, SBMLToolbox provides a function for translating a MATLAB_SBML structure back to an XML file in SBML format. As a convenience to users, the toolbox also provides additional functions allowing a MATLAB_SBML model structure to be written as a MATLAB data file known as a MAT file. This allows faster access to stored models. The use of a MATLAB MAT file also facilitates using MATLAB external library functions for the manipulation of these data files. SBMLToolbox includes functions for browsing models stored in MAT files.

2.2 Manipulation functions

One set of functions act directly on the structures and mimic the functions provided by libSBML, the library developed and maintained by the SBML Team as part of the software infrastructure supporting SBML development (Bornstein *et al.*, 2003, <http://sbml.org/software/libsbml>). Many developers of SBML compliant software are familiar with libSBML and thus this set of functions gives them an easy transition into the MATLAB environment. The functions include those for creating objects, e.g. Model_create; functions for setting field values, e.g. Compartment_setId; functions for returning field values, e.g. Reaction_getId; functions for querying whether a field value has been set, e.g. Species_isSetId and functions for adding structures to arrays within the given structure, e.g. Model_addRule.

A second set of manipulation functions in SBMLToolbox drive a set of graphical user interfaces (GUI) that display the field names and corresponding values for each element. For example, the ViewSpecies function produces a GUI that shows the name/id of the species, the compartment containing it, the initial concentration and units and so on. The GUI does not provide editing functionality; it is intended principally as a simple tool for displaying model structures, and as a starting point for users' development of more elaborate capabilities.

In order to interact with the MATLAB_SBML model structure it is necessary to extract the required information. The use of the standard MATLAB structure allows easy access to field names and indexing into arrays of structures within structures, e.g. the name of the second species in 'model' can be accessed as model.species(2).name. However the interaction with a model may be more complex and SBMLToolbox provides a third set of designed functions to return more detailed information from the model; e.g. GetRateLawsFromReactions returns two arrays, one of the names of each species in the model and the other containing the character representation of the rate law used to determine each species in the same order as the species, thus allowing the two to be paired. These functions are also replicated to return symbolic representations of the model information which facilitates the use of MATLAB's Symbolic Toolbox—an additional commercial toolbox from The Mathworks that incorporates symbolic computation into the MATLAB environment.

Finally, the MATLAB_SBML structure stores any formula/MathML in the original model as a string representation of the formula. In order to support interaction with the model, SBMLToolbox contains a set of 'convenience' functions that facilitate the manipulation of the string representations of formula; e.g. PairBrackets that determines the order in which brackets within a formula should be considered and SubstituteFunction which allows arguments to be passed to a formula defined by a function definition.

2.3 Simulation

SBMLToolbox is not intended to be a simulation tool; however, it does contain a set of example functions that allow the user to simulate an SBML model using MATLAB's built-in ODE solvers. The functionality provided includes writing out a script for use with the ODE solvers, running the solvers, and displaying the data, as well as a number of supporting functions. These functions deal with all aspects of an SBML model. The simulation output passes all the tests in the test-suite produced by the SBML Team (Finney *et al.*, 2003, http://sbml.org/wiki/Semantic_Test_Suite). The one exception is that the package does not currently handle the 'delay' feature in SBML.

3 IMPLEMENTATION

SBMLToolbox works with all versions of MATLAB from version 6.5 onwards and depends on the Xerces-C version of libSBML. The import/export functions do require compilation; however, scripts are included within the toolbox to facilitate this. There are two downloads available: a Windows installer that pre-packages the necessary libraries and precompiled functions, and a 'source' download that can be used to install the toolbox on Linux, Unix or Mac OS platforms. The functions providing interaction between a model and the symbolic toolbox obviously require the presence of the MATLAB Symbolic Toolbox; however, these functions are self-contained and the full functionality of the toolbox can be achieved without using symbols. In addition, the source download contains a number of test files, thus facilitating further development of the toolbox functions. Full documentation is included with SBMLToolbox and each function has extensive MATLAB help.

SBMLToolbox is distributed under the GNU Lesser General Public License (<http://www.gnu.org/licenses/licenses.html#LGPL>).

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REFERENCES

- Bornstein,B *et al.* (2003) LibSBML, a library designed to help you read, write, manipulate, translate and validate SBML.
- Bray,T *et al.* (2000) Extensible markup language (XML) 1.0 (second edition), W3C Recommendation 6-October-2000.
- Finney,A. *et al.* (2003) Semantic test suite.
- Hucka,M *et al.* (2004) Evolving a lingua franca and associated software infrastructure for computational systems biology: the Systems Biology Markup Language (SBML) project. *IEE Syst. Biol.*, **1**, 41–53.
- Prajna,S *et al.* (2004) SOSTOOLS: sum of squares optimization toolbox for MATLAB.
- Remenik,D (2005) SBMLSim.
- Schmidt,H and Jirstrand,M (2006) Systems Biology Toolbox for MATLAB: a computational platform for research in Systems Biology. *Bioinformatics*, **22**, 514–515.