Introduction

Merging of cell models is one of the main future challenges in systems biology. Many structural and dynamic models are available in the XML-derived exchange format SBML and stored in model databases like BioModels.net. Computer-assisted merging of such models would considerably facilitate building of large-scale models. A central task in model merging is the matching of individual model elements: to allow for automatic comparisons, the biological meaning of model elements must be specified by computer-readable annotations.

Our tool semanticSBML allows the user in annotating, checking, and merging of SBML models. It also allows to create SBML models directly from lists of biochemical reactions (specified, for instance, by KEGG IDs). For comparison of model elements, the program relies on semantic annotations in a standard format (MIRIAM-compliant RDF annotations with bioqualifiers).

SemanticSBML is free software developed under the GNU public license and can be downloaded and used online at www.semanticsbml.org.

Workflow for model annotation and merging

Biochemical models in SBML format

Semantic SBML: a tool for annotating, checking, and merging of biochemical models in SBML format

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MIRIAM-compliant annotations

The MIRIAM standard (“Minimum information requested in the annotation of biochemical models”) is a set of rules to ensure the formal correctness of systems biology models.

Among other things, MIRIAM describes rules for machine-readable, unique descriptions of biological objects. These rules are realised in the SBML format in the form of RDF (Resource description framework) annotations.

An SBML/MIRIAM annotation consists of three parts: the biological object to be described, a reference to an object in an external database and a qualifier that specifies a relation between the described object and the referenced object.

Model annotation

SBMLannotate allows the user to add and modify SBO terms and SBML/MIRIAM annotations: model elements are linked to unique identifiers (IDs) from a variety of databases.

For a number of databases (currently GO, KEGG, ChEBI, PubChem, 3D-MET, and CAS), IDs are stored internally, which allows users to find annotations by a string search. The program can also suggest annotations, for instance, based on the name attribute of a species element.

Model checking

SBMLcheck verifies whether the model contains readable and consistent annotations. Elements without annotations are reported to the user. Furthermore, SBMLcheck detects mistakes in the model structure, such as circular dependencies among algebraic equations (“assignment rules”) or violations of the mass conservation constraints in chemical reactions.

Model merging

SBMLmerge allows the user to merge several models: during merging, it detects and resolves various kinds of syntactic and semantic conflicts, such as conflicting variable names, elements that appear in several input models, or mathematical problems arising from the combination of equations.

For an initial automatic matching, the program searches the input models for matching elements based on their MIRIAM annotations. Afterwards, the user can rematch the elements manually. If two models assign different values to the same element property, the conflict is highlighted and the user has to choose between the alternative statements. Conflicts are displayed in several categories according to their degree of severeness.

Eventually, the program merges the models and resolves conflicts that have occurred during the merging process. The result is a new, valid SBML model, which can then be visualised as a reaction network graph.

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