Network Systems Biology
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SBMLsqueezer: a CellDesigner plug-in to generate kinetic rate equations for biochemical networks

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Background

The development of complex biochemical models has been facilitated through the standardization of machine-readable representations like SBML (Systems Biology Markup Language). This effort is accompanied by the ongoing development of the human-readable diagrammatic representation SBGN (Systems Biology Graphical Notation). The graphical SBML editor CellDesigner allows direct translation of SBGN into SBML, and vice versa. For the assignment of kinetic rate laws, however, this process is not straightforward, as it often requires manual assembly and specific knowledge of kinetic equations.

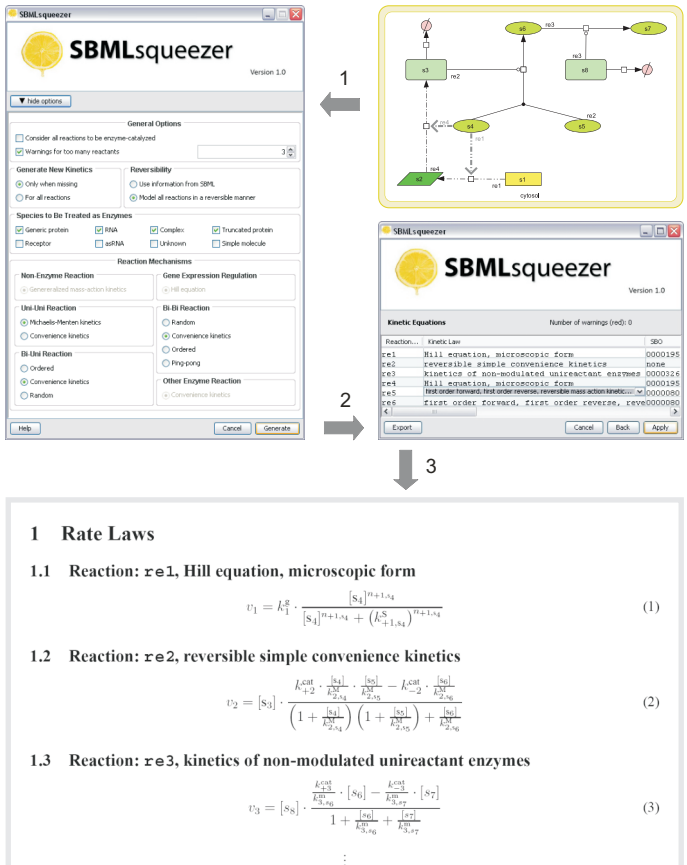

Fig. 1: The first window enables the user to specify the type of kinetics to be applied (1). By clicking on "Generate", the kinetics are compiled, presented in a table and can be altered through a list of all applicable alternative equations for each reaction (2). The results can be stored in SBML, plain text or LaTeX (3).

Results

SBMLsqueezer facilitates this modeling step via automated equation generation, overcoming the highly error-prone and cumbersome process of manually assigning kinetic equations. For each reaction the kinetic equation is derived from the stoichiometry and activatory or inhibitory relations of the process diagram. Considered rate laws are:

- Generalized mass-action rate law with numerous orders
- Uni-uni Michaelis-Menten kinetics
- Bi-uni enzyme mechanisms
  - Random-order mechanism
  - Ordered mechanism
- Bi-bi enzyme reactions
  - Random-order mechanism
  - Ordered mechanism
  - Ping-pong mechanism
- Irreversible non-modulated non-interacting Reactant Enzymes
- Convenience kinetics
  - Thermodynamically dependent form
  - Thermodynamically independent form
- Hill equation

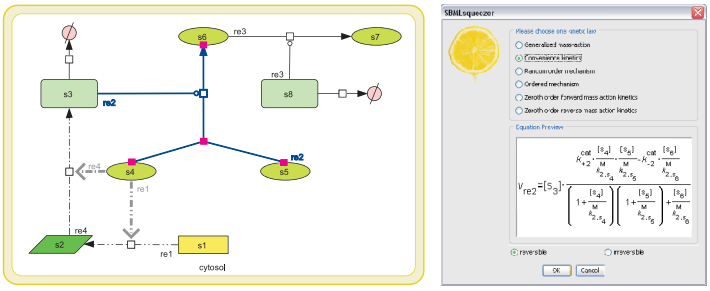

Fig. 2: Context menu to create kinetic equations for the model one by one. An analysis of the reaction ensures that only possible rate laws are selectable. An equation preview facilitates the selection of an appropriate rate equation. The reaction can be set as reversible or irreversible possibly changing the selection of available rate laws.

Conclusions

SBMLsqueezer considers the annotation of all participating reactants, products and regulators when generating rate laws for reactions. Thus, for each reaction, only applicable kinetic formulas are considered. This modeling scheme creates kinetics in accordance with the diagrammatic representation. In contrast most previously published tools have relied on the stoichiometry and generic modulators of a reaction, thus ignoring and potentially conflicting with the information expressed through the process diagram. Additional material and the source code can be found at http://www.ra.cs.uni-tuebingen.de/software/SBMLsqueezer.

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