V11B
SBML und Modell-Erstellung

22. Januar 2015

Übersicht

Austausch und Archivierung von biochemischen Modellen
=> SBML

Diffusion plus Reaktionen
=> Virtual Cell

Komplexität der Modelle
=> BioNetGen

Systems Biology Markup Language

XML-Dialekt für Speicherung und Austausch biochemischer Modelle
=> Archivierung
=> Transfer von Modellen in andere Softwaretools

Acknowledgements

We are deeply indebted to the many funding agencies and organizations that have supported SBML over the years.

Since 2003, primary support for the continued development of SBML, as well as supporting software and activities, has come from the **National Institute of General Medical Sciences (NIH/NIGMS)** under grants R01 GM070923 and R01 GM077671. Additional support is provided by the **California Institute of Technology** (USA) and **Keio University** (Japan).

The development of SBML from its inception through 2003 was principally funded by the **Japan Science and Technology Agency** under the **ERATO Kitano Symbiotic Systems Project**.

Additional support has in the past been provided by the following organizations and agencies: the **Systems Biology Institute** (Japan), the **University of Hertfordshire** (UK), the **Molecular Sciences Institute** (USA), the **National Human Genome Research Institute** (USA), the **International Joint Research Program of NEDO** (Japan), the **ERATO-SORST** Program of the Japan Science and Technology Agency (Japan), the **Ministry of Agriculture** (Japan), the **Ministry of Education, Culture, Sports, Science and Technology** (Japan), the **BBSRC e-Science Initiative** (UK), the **DARPA IPTO Bio-Computation Program** (USA), the Army Research Office's **Institute for Collaborative Biotechnologies** (USA), and the **Air Force Office of Scientific Research** (USA).

von http://sbml.org/Acknowledgments

SBML <= XML

XML = eXtensible Markup Language

- hierarchische Baumstruktur:
  => Schachtelung von <Object> … </Object> oder <Objekt [Parameter…]/>
- genau ein Wurzelobjekt: <sbml…>

Aktuelle Dialekte: siehe http://sbml.org/Documents/Specifications

SBML Level 1, Version 2
http://www.sbml.org/specifications/sbml-level-1/version-2/sbml-level-1-v2.pdf

SBML Level 2, Version 4, Release 1
http://precedings.nature.com/documents/2715/version/1

Level:
globale Zielrichtung,
Sprachumfang

Version:
Features und
Definitionen

Release:
Bug-fixes

Was ist enthalten?

beginning of model definition
- list of function definitions (optional)
- list of unit definitions (optional)
- list of compartment types (optional)
- list of species types (optional)
- list of compartments (optional)
- list of species (optional)
- list of parameters (optional)
- list of initial assignments (optional)
- list of rules (optional)
- list of constraints (optional)
- list of reactions (optional)
- list of events (optional)

end of model definition

http://sbml.org/More_Detailed_Summary_of_SBML

Ein Beispiel

$$E + S \underset{k_{off}}{\overset{k_{on}}{<=>}} ES \overset{k_{cat}}{=>} E + P$$

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="3" xmlns="http://www.sbml.org/sbml/level2/version3">
  <model name="EnzymaticReaction">
    <listOfUnitDefinitions>
      <unitDefinition id="per_second">
        <listOfUnits>
          <unit kind="second" exponent="-1"/>
        </listOfUnits>
      </unitDefinition>
      <unitDefinition id="litre_per_mole_per_second">
        <listOfUnits>
          <unit kind="mole"   exponent="-1"/>
          <unit kind="litre"  exponent="1"/>
          <unit kind="second" exponent="-1"/>
        </listOfUnits>
      </unitDefinition>
    </listOfUnitDefinitions>
    <listOfCompartments>
      <compartment id="cytosol" size="1e-14"/>
    </listOfCompartments>
    <listOfSpecies>
      <species compartment="cytosol" id="ES" initialAmount="0"     name="ES"/>
      <species compartment="cytosol" id="P"  initialAmount="0"     name="P"/>
      <species compartment="cytosol" id="S"  initialAmount="1e-20" name="S"/>
      <species compartment="cytosol" id="E"  initialAmount="5e-21" name="E"/>
    </listOfSpecies>
    <listOfReactions>
      <reaction id="veq">
        <listOfReactants>
          <speciesReference species="E"/>
          <speciesReference species="S"/>
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="ES"/>
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times/>
              <ci>cytosol</ci>
              <apply>
                <minus/>
                <apply>
                  <times/>
                  <ci>kon</ci>
                  <ci>E</ci>
                  <ci>S</ci>
                </apply>
                <apply>
                  <times/>
                  <ci>koff</ci>
                  <ci>ES</ci>
                </apply>
              </apply>
            </apply>
          </math>
          <listOfParameters>
            <parameter id="kon"  value="1000000" units="litre_per_mole_per_second"/>
            <parameter id="koff" value="0.2"     units="per_second"/>
          </listOfParameters>
        </kineticLaw>
      </reaction>
      <reaction id="vcat" reversible="false">
        <listOfReactants>
          <speciesReference species="ES"/>
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="E"/>
          <speciesReference species="P"/>
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times/>
              <ci>cytosol</ci>
              <ci>kcat</ci>
              <ci>ES</ci>
            </apply>
          </math>
          <listOfParameters>
            <parameter id="kcat" value="0.1" units="per_second"/>
          </listOfParameters>
        </kineticLaw>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

Nochmal:

$$E + S \underset{k_{off}}{\overset{k_{on}}{<=>}} ES \overset{k_{cat}}{=>} E + P$$

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="3" xmlns="http://www.sbml.org/sbml/level2/version3">
   <model name="EnzymaticReaction">
      <listOfUnitDefinitions>
         :
       </listOfUnitDefinitions>
      <listOfCompartments>
         <compartment id="cytosol" size="1e-14"/>
      </listOfCompartments>
      <listOfSpecies>
         <species compartment="cytosol" id="ES" initialAmount="0"     name="ES"/>
         <species compartment="cytosol" id="P"  initialAmount="0"     name="P"/>
         <species compartment="cytosol" id="S"  initialAmount="1e-20" name="S"/>
         <species compartment="cytosol" id="E"  initialAmount="5e-21" name="E"/>
      </listOfSpecies>
      <listOfReactions>
         :
      </listOfReactions>
   </model>
</sbml>
```

Details: Einheiten

```
<listOfUnitDefinitions>
        <unitDefinition id="per_second">
                <listOfUnits>
            <unit kind="second" exponent="-1"/>
        </listOfUnits>
    </unitDefinition>
    <unitDefinition id="litre_per_mole_per_second">
        <listOfUnits>
            <unit kind="mole"    exponent="-1"/>
            <unit kind="litre"  exponent="1"/>
            <unit kind="second" exponent="-1"/>
        </listOfUnits>
    </unitDefinition>
</listOfUnitDefinitions>
```

per_seconds := s^{-1}

$$\frac{\text{litre}}{\text{mol s}}$$

SBML Software Guide/SBML Software Matrix – SBML.org

http://sbml.org/SBML_Software_Guide/SBML_Software_Matrix

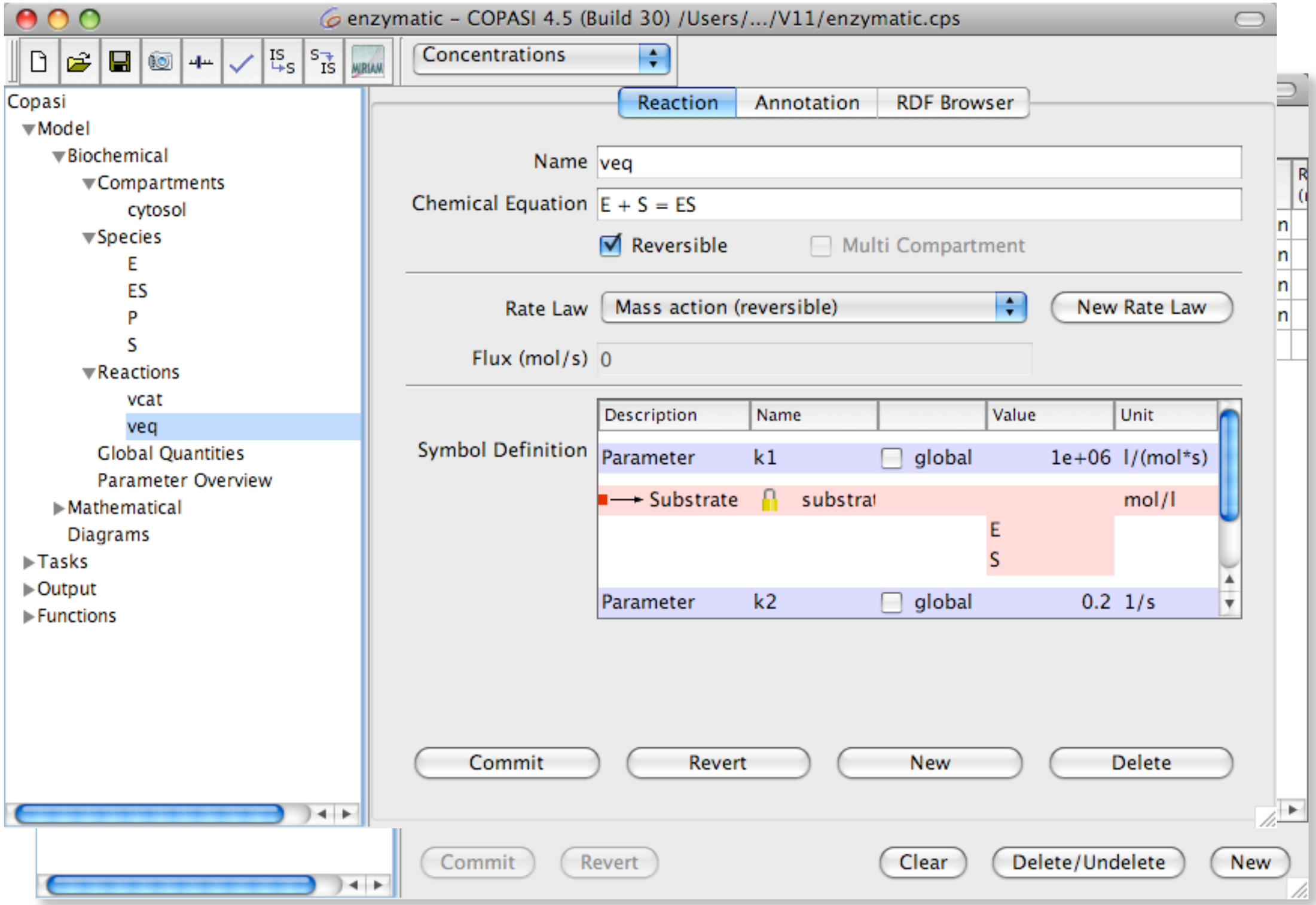
Google

SBML Software Matrix

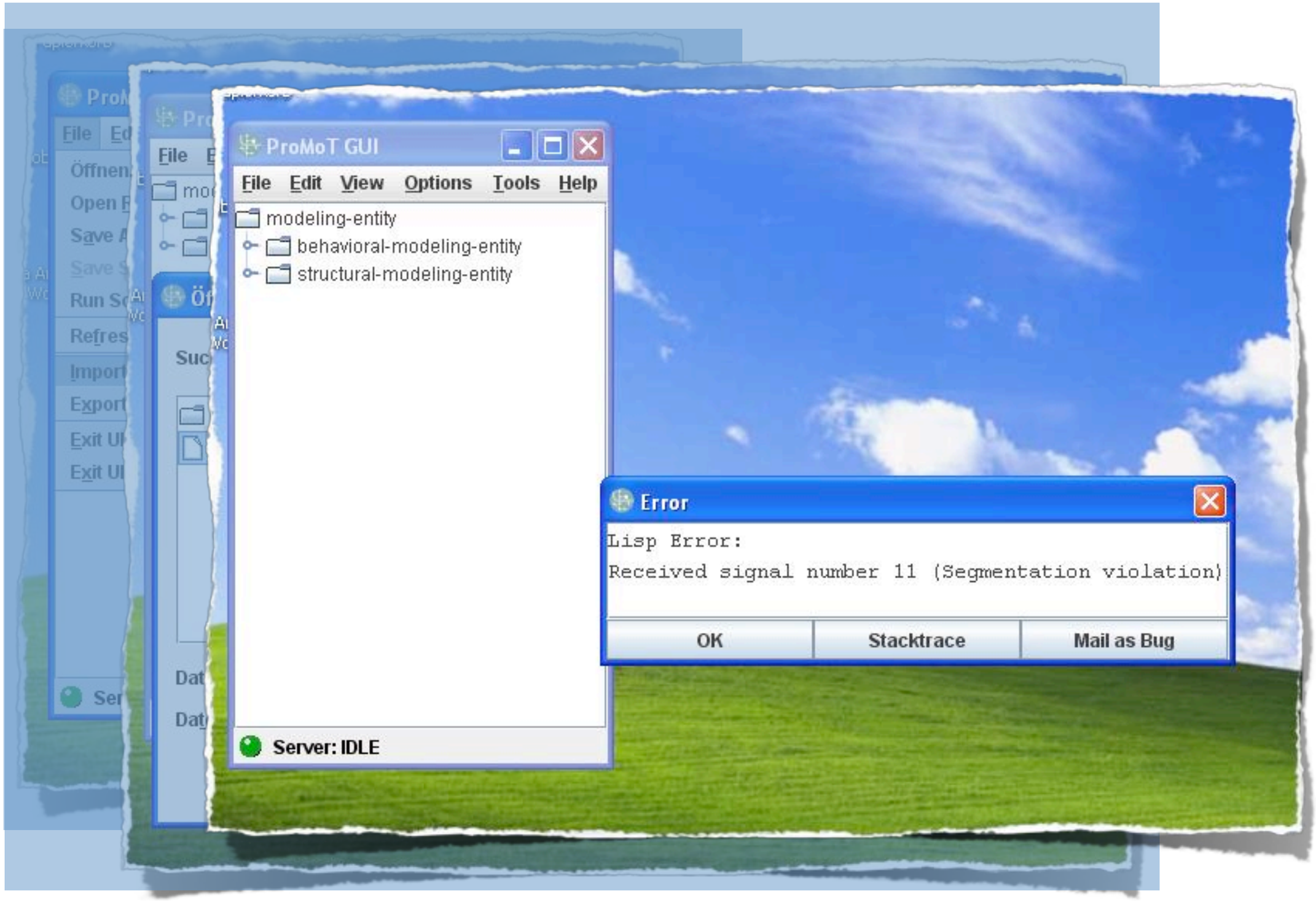
This matrix provides an at-a-glance summary of software known to us to provide some degree of support for reading, writing, or otherwise working with SBML. The columns' meanings are explained below. For a list of longer descriptions grouped into themes, please see our **SBML Software Summary** page.

	Capabilities					Frameworks							API	Dep.	Platforms	SBML		Availabil.		
	Creation	Simulation	Analysis	Database	Utility	ODE	DAE	PDE	Stochastic	Events	Logical	Other				Import	Export	Open source	Academic use	Commercial use
Cellware	•	•				•									L,W,M	•		•	F	$
CL-SBML					•							•	LISP	LISP	L	•		•	F	F
CLEML												•			L,W	•	•		F	F
COBRA			•		•	•						•		MATLAB	L,W,M	•	•	•	F	F
ConsensusPathDB					•										B	•	•	•	F	F
COPASI	•	•	•		•	•			•				C++, Java, Python		L,W,M	•	•	•	F	$
Cyto-Sim		•			•				•						L,W,M				F	F
Cytoscape	•				•								Java		L,W,M	•		•	F	F
DBSolve		•	•		•	•										•	•		F	F
Dizzy		•				•			•						L,W,M	•	•	•	F	F
E-CELL	•	•				•			•						L,W		•	•	F	F
ecellJ					•												•		F	F
EPE	•			•		•							Java		L,W, M		•		F	F
ESS		•							•					BSP				•	F	F

Import nach Copasi



Interoperabilität?



Details: eine Reaktion

```
<listOfReactions>     :
        <reaction id="vcat" reversible="false">
            <listOfReactants>
                <speciesReference species="ES"/>
            </listOfReactants>
            <listOfProducts>
                <speciesReference species="E"/>
                <speciesReference species="P"/>
            </listOfProducts>
            <kineticLaw>
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                    <apply>
                        <times/>
                        <ci>cytosol</ci>
                        <ci>kcat</ci>
                        <ci>ES</ci>
                    </apply>
                </math>
                <listOfParameters>
                    <parameter id="kcat" value="0.1" units="per_second"/>
                </listOfParameters>
            </kineticLaw>
        </reaction>
</listOfReactions>
```

$$E + S \underset{k_{off}}{\overset{k_{on}}{<=>}} ES \overset{k_{cat}}{=>} E + P$$

$$\Rightarrow \frac{dN}{dt} = V_{cytosol}\, k_{cat}\, [ES]$$

lokaler Parameter!

SBML lesbar machen

http://webservices.cs.uni-tuebingen.de/

Dräger A, Planatscher H, Wouamba DM, Schröder A, Hucka M, Endler L, Golebiewski M, Müller W, and Zell A: “SBML2LaTeX: Conversion of SBML files into human-readable reports”, Bioinformatics 2009

Drei Minuten später:

convert

Please download your result here: 07ff0064-6af4-4eb5-bea1-906da1fbcd86-request.pdf

Submit another file

SBML Model Report

Model name: “EnzymaticReaction”

SBML2LaTeX

June 30, 2009

1 General Overview

This is a document in SBML Level 2 Version 3 format. Table 1 gives an overview of the quantities of all components of this model.

Table 1: The SBML components in this model.
All components are described in more detail in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	4
events	0	constraints	0
reactions	2	function definitions	0
global parameters	0	unit definitions	2
rules	0	initial assignments	0

2 Unit Definitions

This is an overview of seven unit definitions. The units `substance`, `volume`, `area`, `length`, and `time` are predefined by SBML and not mentioned in the model.

2.1 Unit `per_second`

Definition s^{-1}

2.2 Unit `litre_per_mole_per_second`

Definition $mol^{-1} \cdot l \cdot s^{-1}$

2.3 Unit `substance`

Notes Mole is the predefined SBML unit for `substance`.

Definition mol

2.4 Unit `volume`

Notes Litre is the predefined SBML unit for `volume`.

Definition l

2.5 Unit `area`

Notes Square metre is the predefined SBML unit for `area` since SBML Level 2 Version 1.

Definition m^2

2.6 Unit `length`

Notes Metre is the predefined SBML unit for `length` since SBML Level 2 Version 1.

Definition m

2.7 Unit `time`

Notes Second is the predefined SBML unit for `time`.

Definition s

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
cytosol			3	10^{-14}	l	☑	

3.1 Compartment cytosol

This is a three-dimensional compartment with a constant size of 10^{-14} litre.

4 Species

This model contains four species. Section 6 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
ES	ES	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
P	P	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
S	S	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
E	E	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Reactions

This model contains two reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by one or more modifiers, the identifiers of the modifier species are written above the reaction arrow.

Table 4: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	veq		$\mathrm{E} + \mathrm{S} \rightleftharpoons \mathrm{ES}$	
2	vcat		$\mathrm{ES} \longrightarrow \mathrm{E} + \mathrm{P}$	

5.1 Reaction veq

This is a reversible reaction of two reactants forming one product.

Reaction equation

$$\mathrm{E} + \mathrm{S} \rightleftharpoons \mathrm{ES} \tag{1}$$

Reactants

Table 5: Properties of each reactant.

Id	Name	SBO
E	E	
S	S	

Product

Table 6: Properties of each product.

Id	Name	SBO
ES	ES	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$\nu_1 = \mathrm{vol}(\mathtt{cytosol}) \cdot (\mathtt{kon} \cdot [\mathrm{E}] \cdot [\mathrm{S}] - \mathtt{koff} \cdot [\mathrm{ES}]) \tag{2}$$

Table 7: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kon			1000000.0	$\mathrm{mol}^{-1} \cdot 1 \cdot \mathrm{s}^{-1}$	☑
koff			0.2	s^{-1}	☑

6 Derived Rate Equations

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rates of change of each species.

6.1 Species ES

Name ES

Initial amount 0 mol

This species takes part in two reactions (as a reactant in vcat and as a product in veq).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ES} = v_1 - v_2 \tag{5}$$

6.2 Species P

Name P

Initial amount 0 mol

This species takes part in one reaction (as a product in vcat).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P} = v_2 \tag{6}$$

6.3 Species S

Name S

Initial amount 10^{-20} mol

This species takes part in one reaction (as a reactant in veq).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S} = -v_1 \tag{7}$$

6.4 Species E

Name E

Initial amount $5 \cdot 10^{-21}$ mol

This species takes part in two reactions (as a reactant in veq and as a product in vcat).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E} = v_2 - v_1 \tag{8}$$

es gibt bereits sehr viele Modelle