

# The Simulation Experiment Description Markup Language

Frank T. Bergmann

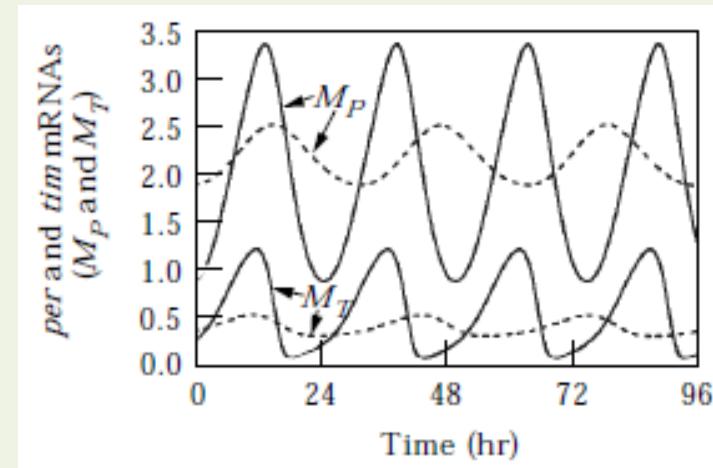
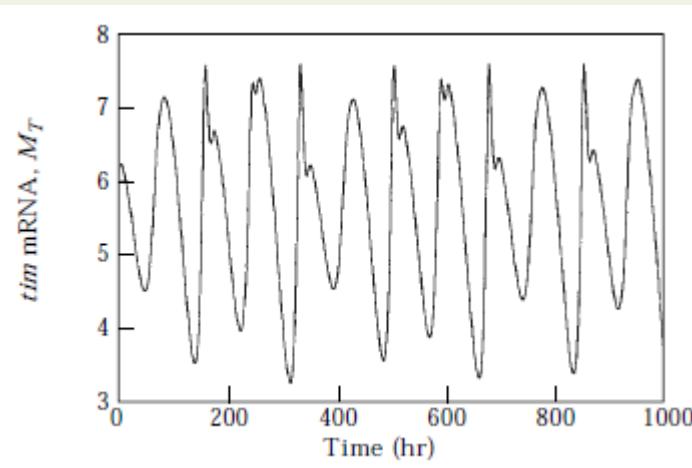
HARMONY, NY

# **MOTIVATION**

# Motivation

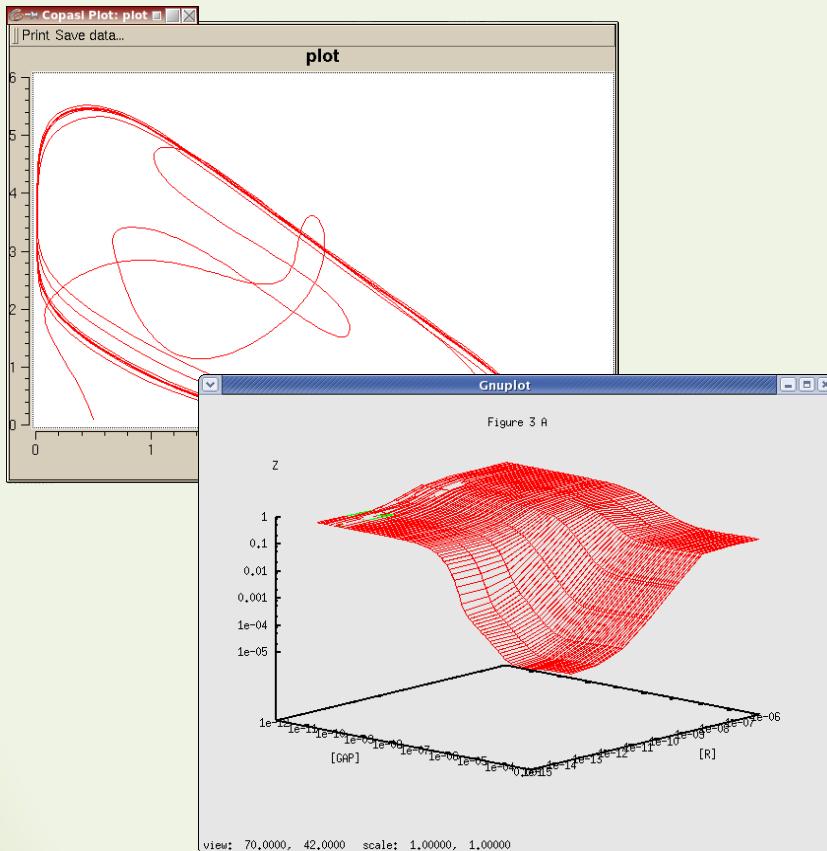
## Chaos and Birhythmicity in a Model for Circadian Oscillations of the PER and TIM Proteins in *Drosophila*

JEAN-CHRISTOPHE LELOUP AND ALBERT GOLDBETER\*



# Motivation

BM 22



BM 86

- Changes in model parameterization
- Use of a number of different models in one experiment
- Choice of correct simulation algorithm
- Post-processing of the result data, e.g. normalization, logarithmic scale ...

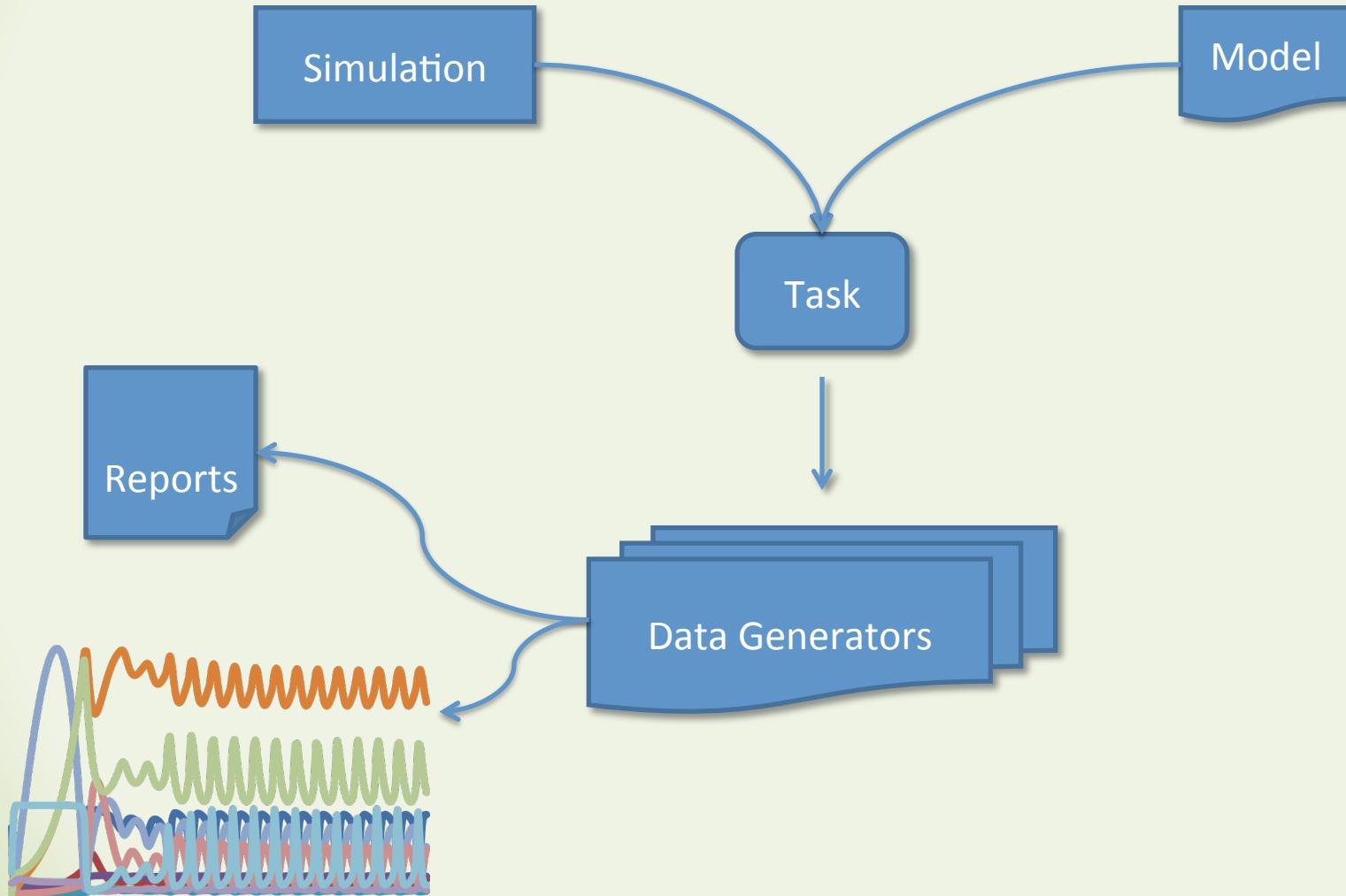
# **HOW DOES SED-ML HELP?**

# Repeatable simulation experiments

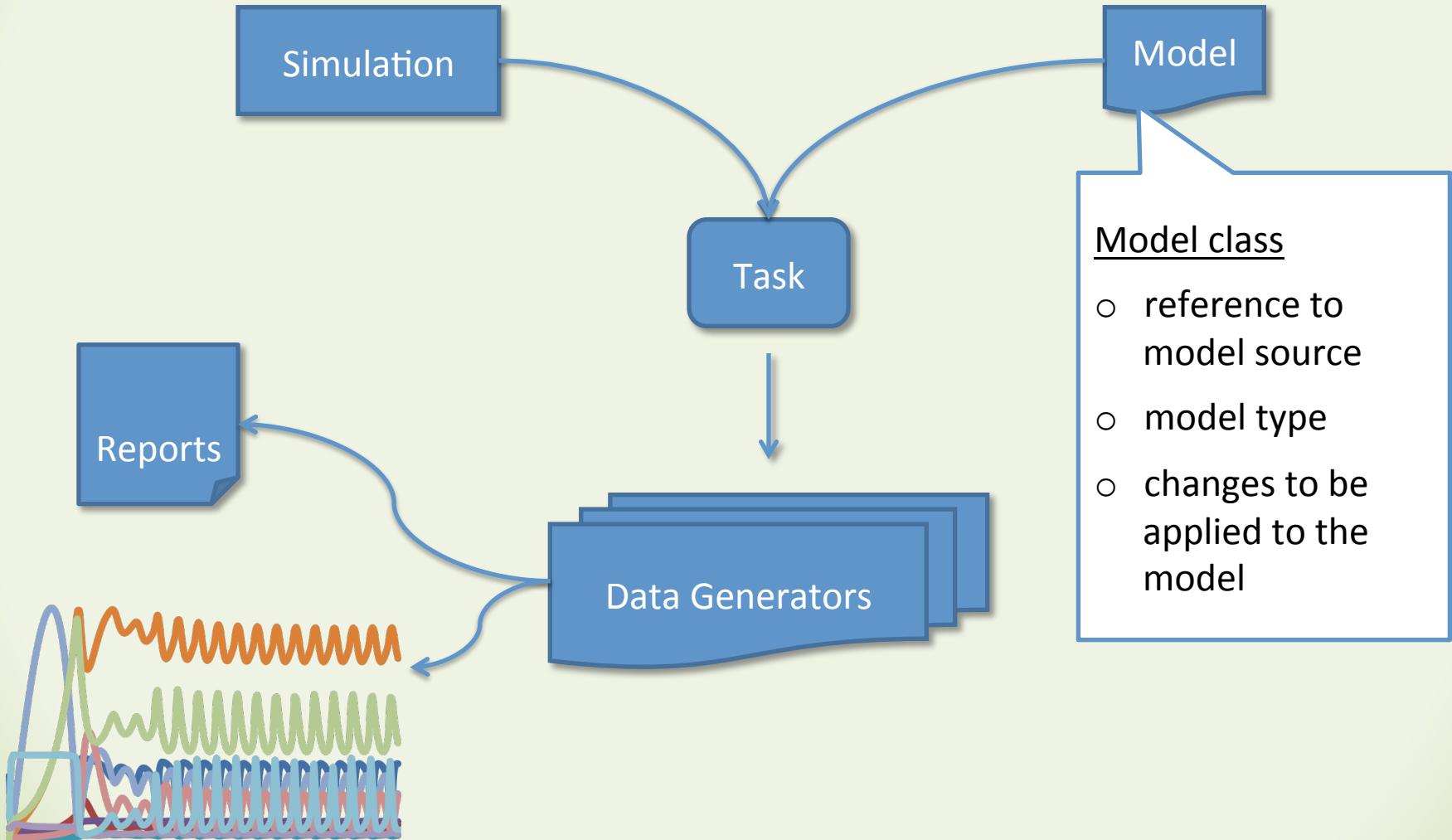
Simulation Experiment Description – Markup Language (SED-ML):

Is a language that aims to standardize the exchange of simulation experiments, independently from the model description language and the simulation tool.

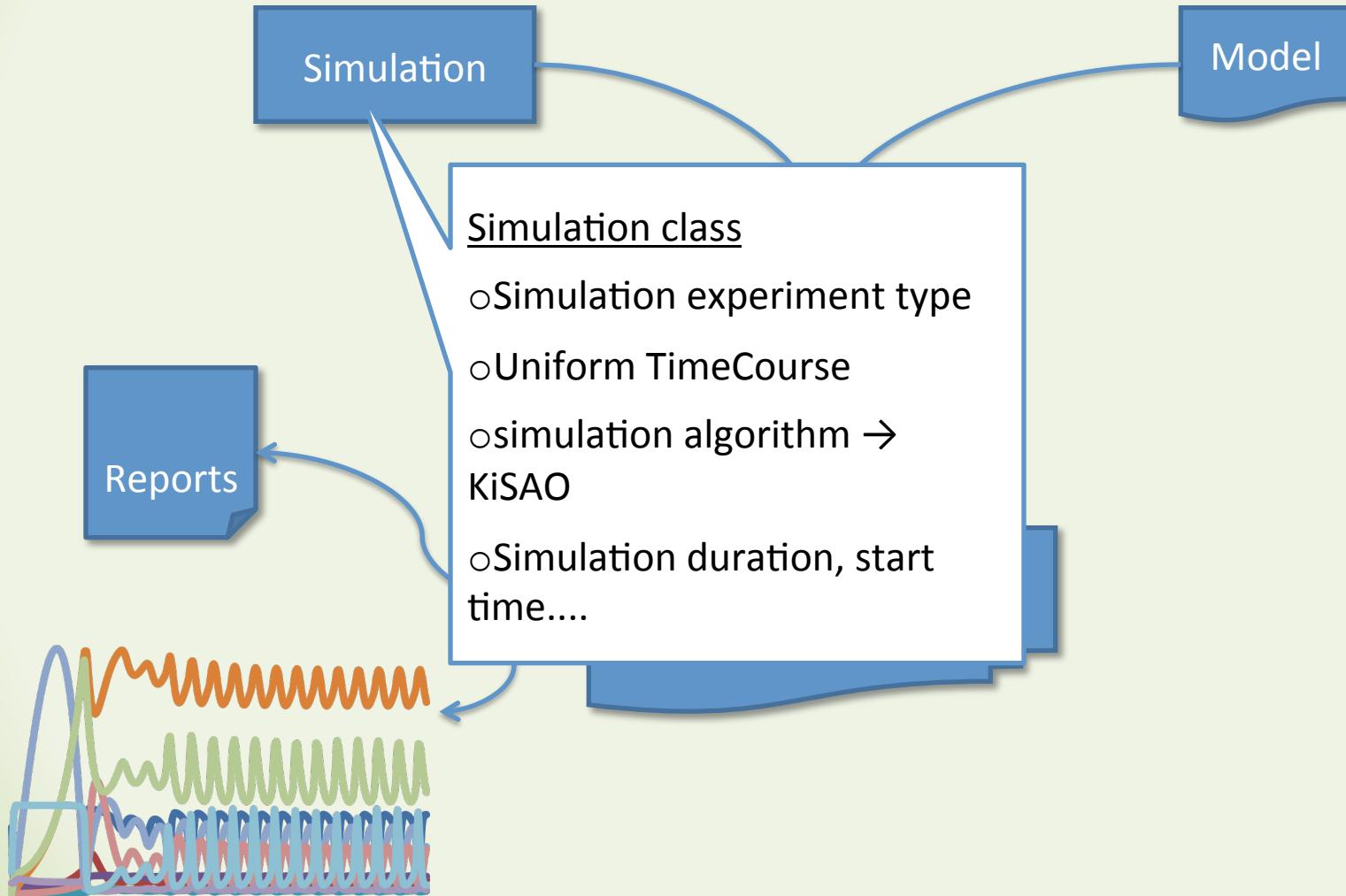
# Repeatable simulation experiments



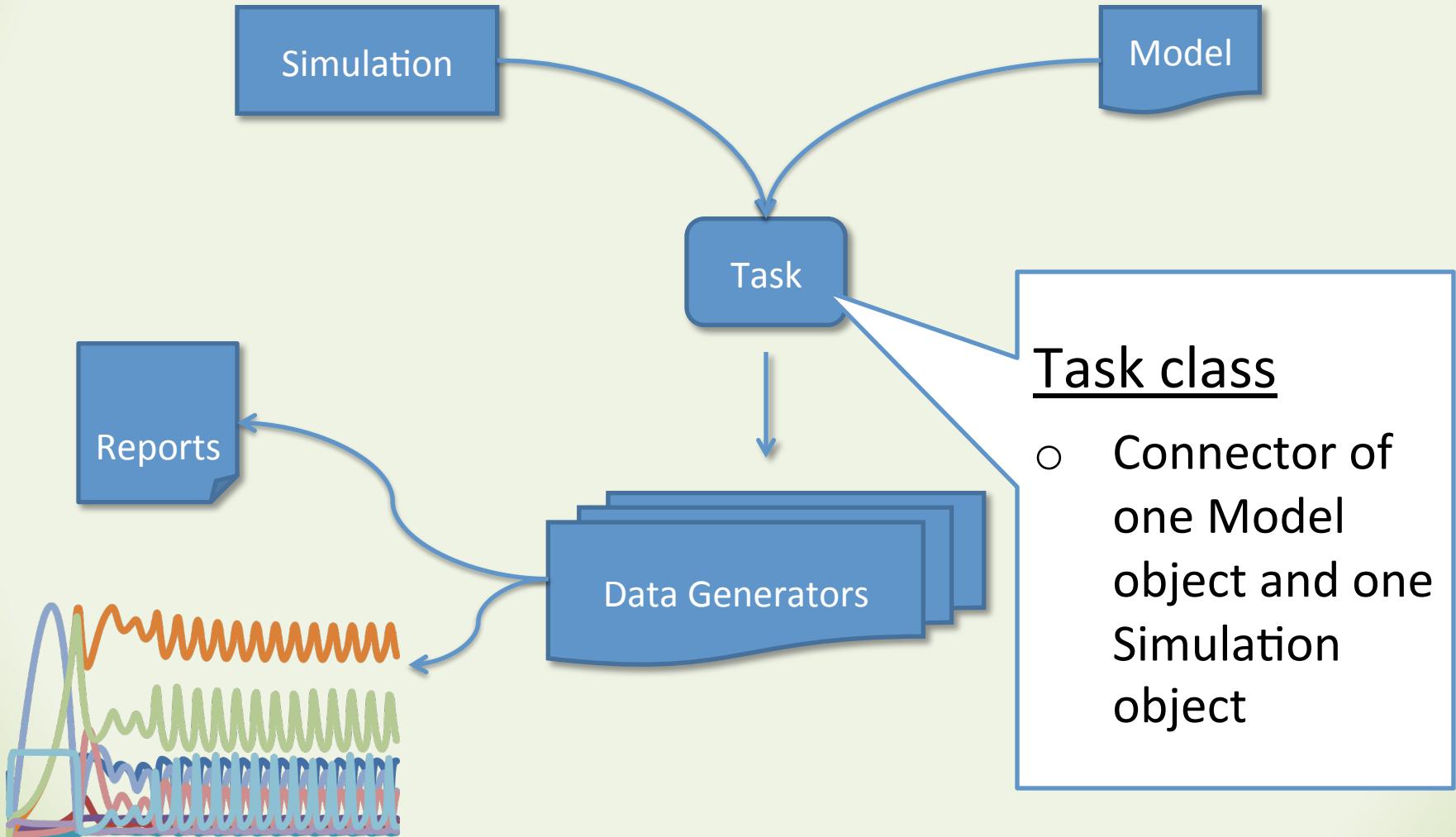
# Repeatable simulation experiments



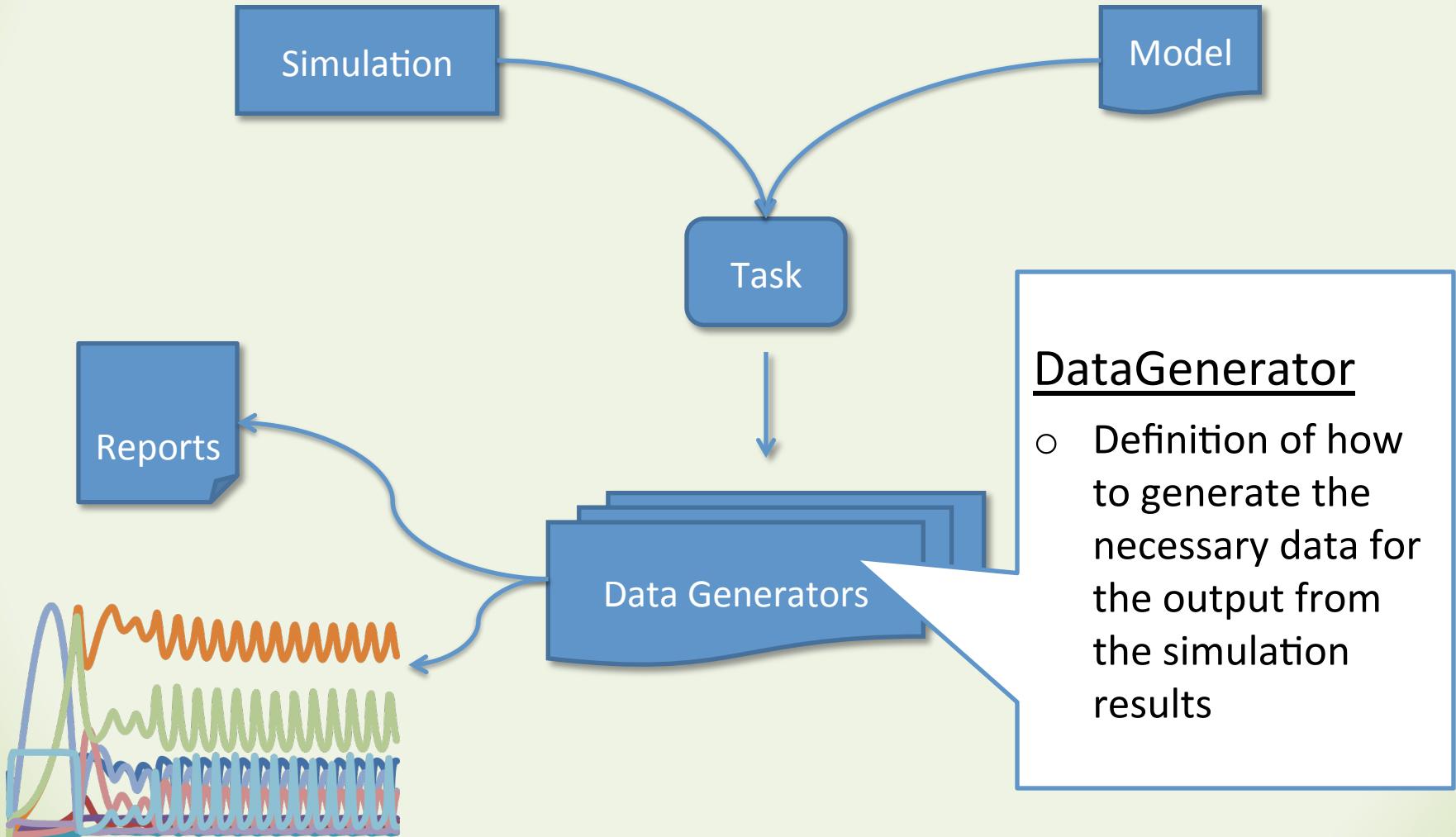
# Repeatable simulation experiments



# Repeatable simulation experiments



# Repeatable simulation experiments



# SED-ML Main Concepts



- No storage of simulation results
- SBRML
- No description of the layout of the output curves

# SED-ML L1 V1 Released!

- final version available from

<http://sed-ml.org>

**Simulation Experiment Description Markup  
Language (SED-ML) :  
Level 1 Version 1**

March 25, 2011

**Editors**

Dagmar Waltemath  
Frank T. Bergmann  
Richard Adams  
Nicolas Le Novère  
*University of Rostock, Germany*  
*University of Washington, Seattle, USA*  
*University of Edinburgh, UK*  
*European Bioinformatics Institute, UK*

The latest release of the Level 1 Version 1 specification is available at  
<http://sed-ml.org/>

To discuss any aspect of the current SED-ML specification as well as language details, please send your messages to the mailing list  
[sed-ml-discuss@lists.sourceforge.net](mailto:sed-ml-discuss@lists.sourceforge.net).

To get subscribed to the mailing list, please write to the same address  
[sed-ml-discuss@lists.sourceforge.net](mailto:sed-ml-discuss@lists.sourceforge.net).

To contact the authors of the SED-ML specification, please write to  
[sed-ml-editors@lists.sourceforge.net](mailto:sed-ml-editors@lists.sourceforge.net)



# SED-ML

```
<?xml version="1.0" encoding="UTF-8"?>
<!-- Written by libSedML v1.1.4092.21172 see http://libsedml.sf.net -->
- <sedML xmlns="http://www.biomodels.net/sed-ml">
  - <listOfSimulations>
    - <uniformTimeCourse numberOfPoints="1000" outputEndTime="380" outputStartTime="0" initialTime="0" id="simulation1">
      <algorithm kisaoID="KISAO:0000019"/>
    </uniformTimeCourse>
  </listOfSimulations>
  - <listOfModels>
    <model language="urn:sedml:language:sbml" id="model1" source="urn:miriam:biomodels.db:BIOMD0000000021" name="Circadian
      Oscillations"/>
    - <model language="urn:sedml:language:sbml" id="model2" source="model1" name="Circadian Chaos">
      - <listOfChanges>
        <changeAttribute newValue="0.28" target="/sbml:	sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id="V_mT"]/@value"/>
        <changeAttribute newValue="4.8" target="/sbml:	sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id="V_dT"]/@value"/>
      </listOfChanges>
    </model>
  </listOfModels>
  - <listOfTasks>
    <task id="task1" simulationReference="simulation1" modelReference="model1"/>
    <task id="task2" simulationReference="simulation1" modelReference="model2"/>
  </listOfTasks>
  - <listOfDataGenerators>
    - <dataGenerator id="time" name="time">
      - <listOfVariables>
        <variable id="t" symbol="urn:sedml:symbol:time" taskReference="task1"/>
      </listOfVariables>
      - <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> t </ci>
      </math>
    </dataGenerator>
    - <dataGenerator id="tim1" name="tim mRNA">
      - <listOfVariables>
        <variable id="v1" target="/sbml:	sbml:	sbml:	model/sbml:listOfSpecies/sbml:species[@id='Mt']" taskReference="task1"/>
      </listOfVariables>
      - <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> v1 </ci>
      </math>
    </dataGenerator>
```

# SED-ML

```
<?xml version="1.0" encoding="UTF-8"?>
<!-- Written by libSedML v1.1.4092.21172 see http://libsedml.sf.net -->
- <sedML xmlns="http://www.biomodels.net/sed-ml">
  - <listOfSimulations>
    - <uniformTimeCourse numberOfPoints="1000" outputEndTime="380" outputStartTime="0" initialTime="0" id="simulation1">
      <algorithm kisaoID="KISAO:0000019"/>
    </uniformTimeCourse>
  </listOfSimulations>
  - <listOfModels>
    <model language="urn:sedml:language:sbml" id="model1" source="urn:miriam:biomodels.db:BIOMD0000000021" name="Circadian Oscillations"/>
    - <model language="urn:sedml:language:sbml" id="model2" source="model1" name="Circadian Chaos">
      - <listOfChanges>
        <changeAttribute newValue="0.28" target="/sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id='V_mT']/@value"/>
        <changeAttribute newValue="4.8" target="/sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id='V_dT']/@value"/>
      </listOfChanges>
    </model>
  </listOfModels>
  - <listOfTasks>
    <task id="task1" name="Task 1">
      <algorithm kisaoID="KISAO:0000019"/>
    </task>
  </listOfTasks>
  - <listOfDataGenerators>
    - <dataGenerator id="time" name="time">
      - <listOfVariables>
        <variable id="t" symbol="urn:sedml:symbol:time" taskReference="task1"/>
      </listOfVariables>
      - <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> t </ci>
      </math>
    </dataGenerator>
    - <dataGenerator id="tim1" name="tim mRNA">
      - <listOfVariables>
        <variable id="v1" target="/sbml:	sbml:	model/sbml:listOfSpecies/sbml:species[@id='Mt']" taskReference="task1"/>
      </listOfVariables>
      - <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> v1 </ci>
      </math>
    </dataGenerator>
  </listOfDataGenerators>
</sedML>
```

# SED-ML

```
<?xml version="1.0" encoding="UTF-8"?>
<!-- Written by libSedML v1.1.4092.21172 see http://libsedml.sf.net -->
- <sedML xmlns="http://www.biomodels.net/sed-ml">
  - <listOfSimulations>
    - <uniformTimeCourse numberOfPoints="1000" outputEndTime="380" outputStartTime="0" initialTime="0" id="simulation1">
      <algorithm kisaoID="KISAO:0000019"/>
    </uniformTimeCourse>
  </listOfSimulations>
  - <listOfModels>
    <model language="urn:sedml:language:sdml" id="model1" source="urn:miriam:biomodels.db:BIOMD0000000021" name="Circadian
      Oscillations"/>
    - <model language="urn:sedml:language:sbml" id="model2" source="model1" name="Circadian Chaos">
      - <listOfChanges>
        <changeAttribute newValue="0.28" target="/sbml:	sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id='V_mT']/@value"/>
        <changeAttribute newValue="4.8" target="/sbml:	sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id='V_dT']/@value"/>
      </listOfChanges>
    </model>
  </listOfModels>
  - <listOfTasks>
    <task id="task1" type="DataGenerator" name="Data Generation">
      <taskInput id="task1_in" target="model2" value="0.28" type="Parameter" name="Initial Value of V_mT" description="Initial value of V_mT for the model 2 simulation."/>
      <taskOutput id="task1_out" target="output1" value="0.28" type="Parameter" name="Final Value of V_mT" description="Final value of V_mT after simulation 1."/>
    </task>
  </listOfTasks>
  - <listOfDataGenerators>
    - <dataGenerator id="dataGen1" name="Data Generator 1">
      <listOfVariables>
        <variable id="t" target="/sbml:	sbml:	sbml:	model/sbml:listOfSpecies/sbml:species[@id='Mt']" taskReference="task1"/>
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> t </ci>
      </math>
    </dataGenerator>
    - <dataGenerator id="tim1" name="tim mRNA">
      <listOfVariables>
        <variable id="v1" target="/sbml:	sbml:	sbml:	model/sbml:listOfSpecies/sbml:species[@id='Mt']" taskReference="task1"/>
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> v1 </ci>
      </math>
    </dataGenerator>
  </listOfDataGenerators>
  - <listOfOutputs>
    <output id="output1" target="output1" type="Text" name="Output 1" description="Output 1 description."/>
  </listOfOutputs>
</sedML>
```

**language = "urn:sedml:language:sbml"**  
**name = "Circadian Oscillations"/>**

**language = "urn:sedml:language:sbml"**

# SED-ML

```
<?xml version="1.0" encoding="UTF-8"?>
<!-- Written by libSedML v1.1.4092.21172 see http://libsedml.sf.net -->
- <sedML xmlns="http://www.biomodels.net/sed-ml">
  - <listOfSimulations>
    - <uniformTimeCourse numberOfPoints="1000" outputEndTime="380" outputStartTime="0" initialTime="0" id="simulation1">
      <algorithm kisaoID="KISAO:0000019"/>
    </uniformTimeCourse>
  </listOfSimulations>
  - <listOfModels>
    <model language="urn:sedml:language:sbml" id="model1" source="urn:miriam:biomodels.db:BIOMD0000000021" name="Circadian
      Oscillations"/>
    - <model language="urn:sedml:language:sbml" id="model2" source="model1" name="Circadian Chaos">
      - <listOfChanges>
        <change>
        <change>
      </listOfChanges>
    </model>
  </listOfModels>
  - <listOfTasks>
    <task id="task1" simulationReference="simulation1" modelReference="model1"/>
    <task id="task2" simulationReference="simulation1" modelReference="model2"/>
  </listOfTasks>
  - <listOfDataGenerators>
    - <dataGenerator id="time" name="time">
      - <listOfVariables>
        <variable id="t" symbol="urn:sedml:symbol:time" taskReference="task1"/>
      </listOfVariables>
      - <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> t </ci>
      </math>
    </dataGenerator>
    - <dataGenerator id="tim1" name="tim mRNA">
      - <listOfVariables>
        <variable id="v1" target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='Mt']" taskReference="task1"/>
      </listOfVariables>
      - <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> v1 </ci>
      </math>
    </dataGenerator>
```

symbol="urn:sedml:symbol:time"

The diagram illustrates the use of the 'symbol' attribute in the SED-ML XML code. A red box highlights the 'symbol' attribute in the variable element of the first data generator. Two blue arrows point from this red box to a white callout box containing the text 'symbol="urn:sedml:symbol:time"'. The callout box also contains two additional lines of code: '<math>["V\_mT"]/@value</math>' and '<math>["V\_dT"]/@value</math>'. The entire XML code is displayed in a monospaced font.

# **IMPLEMENTATION**

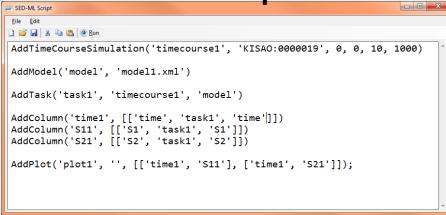
<http://libsedml.sf.net>

The screenshot shows a web browser window with the title "libSedML – Libraries and Tools supporting SED-ML". The address bar contains the URL "http://libsedml.sourceforge.net/". The page content includes a navigation menu with links to "Welcome", "Screenshots", "Libraries", "SedMLScript", and "Simulation Tool". Below the menu, a large section features the text "libSedML - Libraries and Tools supporting SED-ML" in a large, bold, white font. A code snippet in XML syntax is displayed, illustrating SED-ML elements like <notes>, <listOfSimulations>, and <model>.

```
<?xml version="1.0" encoding="utf-8"?>
<sedML version="0.1" xmlns="http://www.biomodels.net/sed-ml" >
  <notes>Changing a system from oscillation to chaos</notes>
  <listOfSimulations>
    <uniformTimeCourse id="simulation1"
      algorithm="KiSAO:0000071" initialTime="0" outputStartTime=
    </listOfSimulations>
    <listOfModels>
      <model id="model1" name="Circadian Oscillations" type="SBM"
        <model id="model2" name="Circadian Chaos" type="SBML" sou
```

# Implementation

SED-ML Script Editor



```
SED-ML Script
File Edit Help
AddTimeCourseSimulation('timecourse1', 'KISAO:0000019', 0, 0, 10, 1000)
AddModel('model', 'model1.xml')
AddTask('task1', 'timecourse1', 'model1')
AddColumn('time1', [[['time', 'task1', 'time']]])
AddColumn('S11', [[['S1', 'task1', 'S1']]])
AddColumn('S21', [[['S2', 'task1', 'S2']]])
AddPlot('plot1', '', [['time1', 'S11'], ['time1', 'S21']]);

```



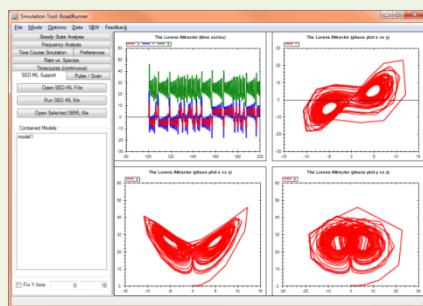
libSedMLScript



libSedML



libSedMLRunner



Simulation Tool



*RoadRunner*  
*JSim*

*iBioSim*

# Implementation

```
<?xml version="1.0" encoding="UTF-8"?
<!-- Written by libSedML v1.1.4 -->
<sedML xmlns="http://www.sedml.org/sedml/1.1">
    <listOfSimulations>
        <uniformTimeCourseSimulation id="simulation1">
            <algorithm kisaoID="KISAO_0000071"/>
        </uniformTimeCourseSimulation>
    </listOfSimulations>
    <listOfModels>
        <model language="urn:nbn:de:hbz:5:1-100000000021">
            <name>oscillations</name>
            <uri>http://miriam.biomodels.net/BIOMD00000000021</uri>
            <version>1.0</version>
            <description>A model of gene oscillations</description>
            <parameters>
                <parameter id="V_mT" value="0.28" type="double" unit="molar" constant="true" binding="task1"></parameter>
                <parameter id="V_dT" value="4.8" type="double" unit="molar" constant="true" binding="task2"></parameter>
            </parameters>
            <species>
                <species id="v1" name="mRNA" initialConcentration="100" compartment="cell" type="compartment" binding="task1"></species>
                <species id="v2" name="protein" initialConcentration="0" compartment="cell" type="compartment" binding="task2"></species>
            </species>
            <reactions>
                <reaction id="r1" type="massAction" binding="task1">
                    <math>\text{v1} \rightarrow \text{v2}; \text{v1} - \text{v2} + 20</math>
                </reaction>
                <reaction id="r2" type="massAction" binding="task2">
                    <math>\text{v2} \rightarrow \text{v1}; \text{v2} - \text{v1} + 20</math>
                </reaction>
            </reactions>
        </model>
    </listOfModels>
    <listOfTasks>
        <task id="task1" simulation="simulation1">
            <speciesAssignment species="v1" compartment="cell" value="100" binding="task1"/>
        </task>
        <task id="task2" simulation="simulation1">
            <speciesAssignment species="v2" compartment="cell" value="0" binding="task2"/>
        </task>
    </listOfTasks>
    <listOfDataGenerators>
        <dataGenerator id="tin">
            <listOfVariables>
                <variable id="t" type="double" unit="second" binding="task1"></variable>
            </listOfVariables>
            <math xmlns="http://www.w3.org/1998/Math/MathML">
                <ci> t </ci>
            </math>
        </dataGenerator>
        <dataGenerator id="tout">
            <listOfVariables>
                <variable id="v1" type="double" unit="molar" binding="task1"></variable>
                <variable id="v2" type="double" unit="molar" binding="task2"></variable>
            </listOfVariables>
            <math xmlns="http://www.w3.org/1998/Math/MathML">
                <ci> v1 </ci>
            </math>
        </dataGenerator>
    </listOfDataGenerators>

```

AddTimeCourseSimulation('simulation1', 'KiSA0:0000071', 0, 50, 1000, 1000)

AddModel('model1', 'urn:miriam:biomodels.db:BIOMD00000000021')

AddModel('model2', 'model1')

AddParameterChange('model2', 'V\_mT', '0.28')

AddParameterChange('model2', 'V\_dT', '4.8')

AddTask('task1', 'simulation1', 'model1')

AddTask('task2', 'simulation1', 'model2')

AddColumn('time', [['time', 'task1', 'time']])

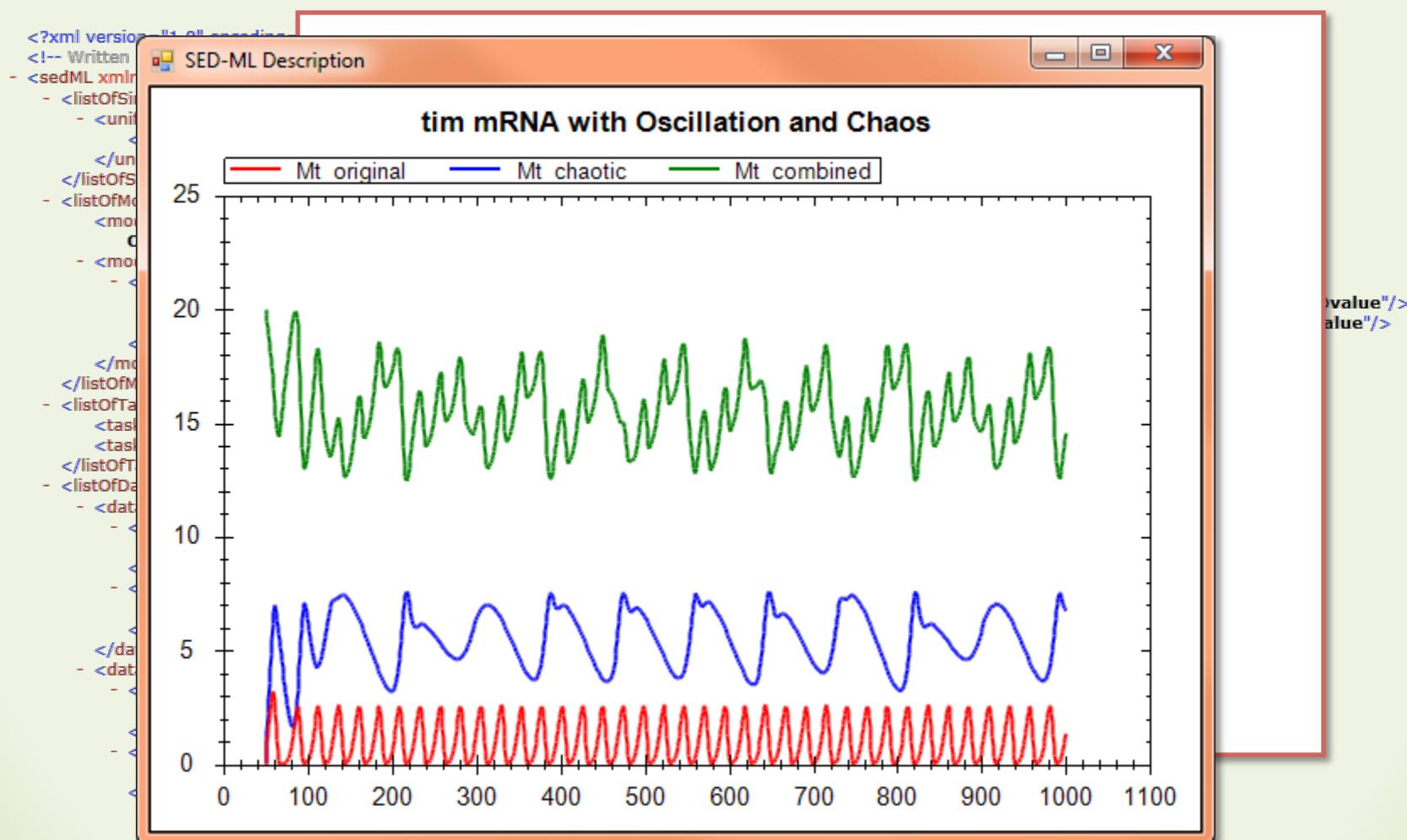
AddColumn('Mt\_original', [['v1', 'task1', 'Mt']])

AddColumn('Mt\_chaotic', [['v2', 'task2', 'Mt']])

AddColumn('Mt\_combined', [['v1', 'task1', 'Mt'], ['v2', 'task2', 'Mt']], 'v1 - v2 + 20')

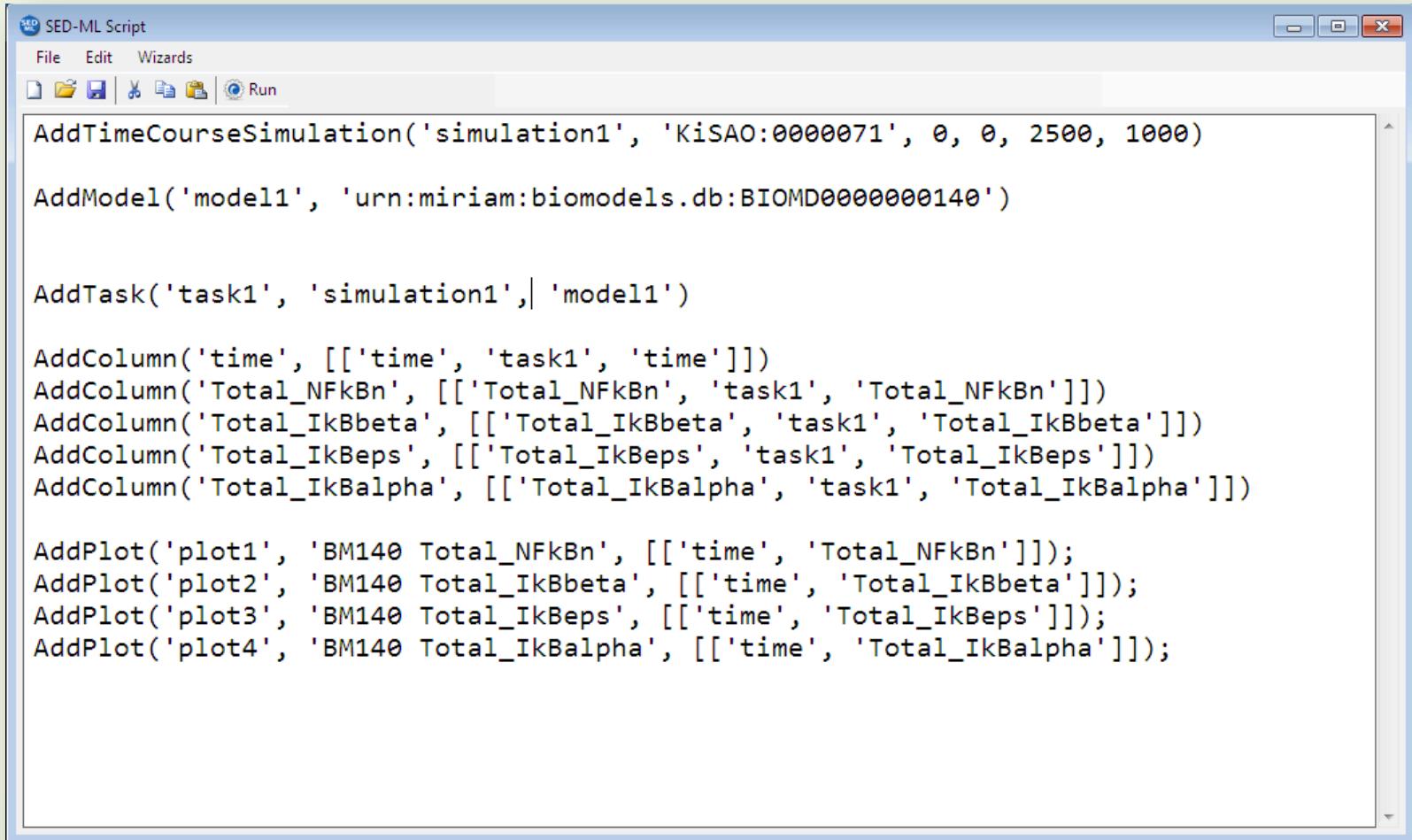
AddPlot('plot1', 'tim mRNA with Oscillation and Chaos', [['time', 'Mt\_original'], ['time', 'Mt\_chaotic'], ['time', 'Mt\_combined']]);

# Implementation



<http://libsedml.sf.net>

# SED-ML script editor



The screenshot shows a Windows application window titled "SED-ML Script". The menu bar includes "File", "Edit", and "Wizards". Below the menu is a toolbar with icons for file operations like Open, Save, and Run. The main area contains the following SED-ML script code:

```
AddTimeCourseSimulation('simulation1', 'KiSAO:0000071', 0, 0, 2500, 1000)

AddModel('model1', 'urn:miriam:biomodels.db:BIOMD0000000140')

AddTask('task1', 'simulation1',| 'model1')

AddColumn('time', [['time', 'task1', 'time']])

AddColumn('Total_NFkBn', [['Total_NFkBn', 'task1', 'Total_NFkBn']])

AddColumn('Total_IkBbeta', [['Total_IkBbeta', 'task1', 'Total_IkBbeta']])

AddColumn('Total_IkBeps', [['Total_IkBeps', 'task1', 'Total_IkBeps']])

AddColumn('Total_IkBalpha', [['Total_IkBalpha', 'task1', 'Total_IkBalpha']])

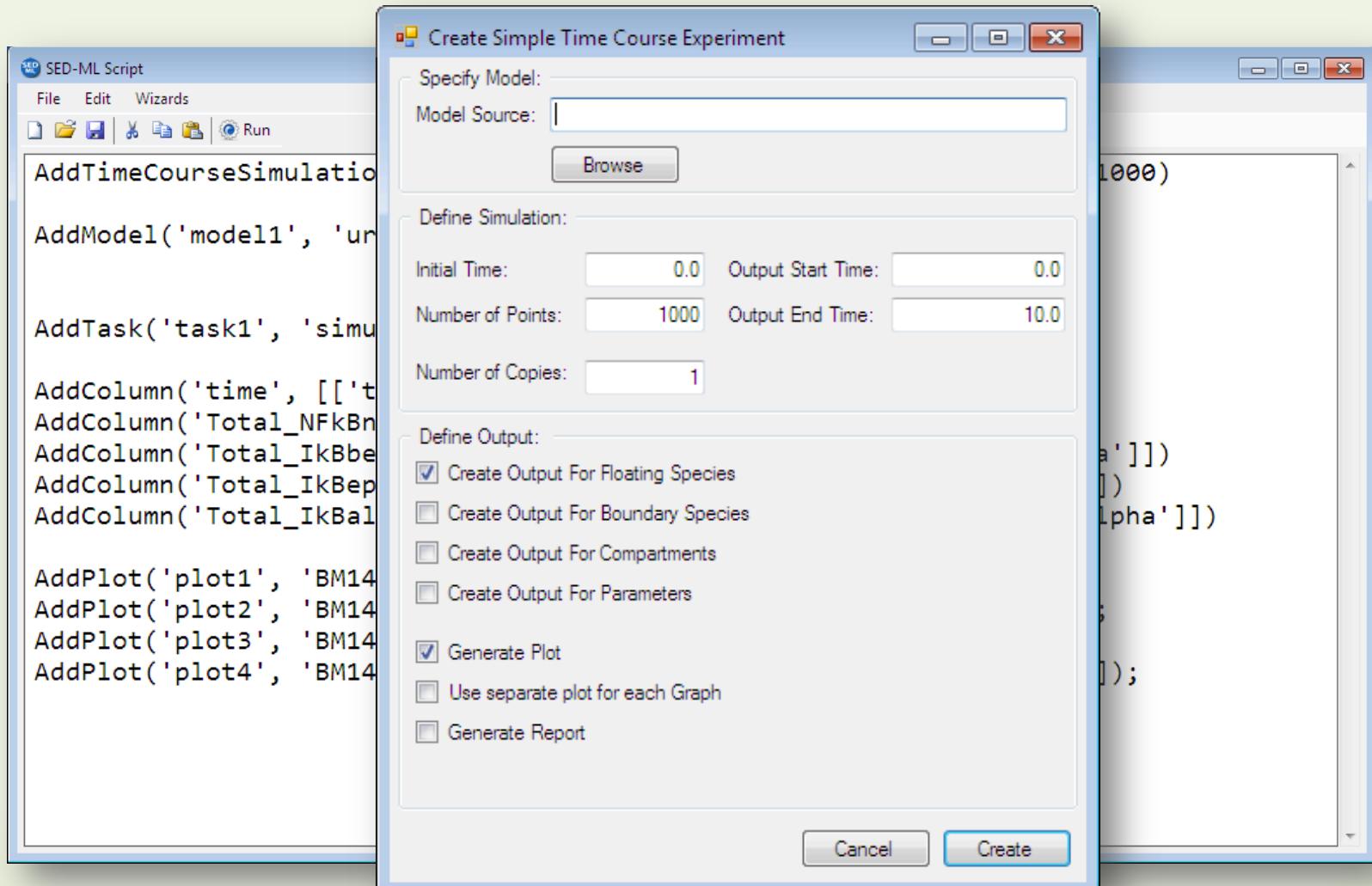
AddPlot('plot1', 'BM140 Total_NFkBn', [['time', 'Total_NFkBn']]);

AddPlot('plot2', 'BM140 Total_IkBbeta', [['time', 'Total_IkBbeta']]);

AddPlot('plot3', 'BM140 Total_IkBeps', [['time', 'Total_IkBeps']]);

AddPlot('plot4', 'BM140 Total_IkBalpha', [['time', 'Total_IkBalpha']]);
```

# SED-ML script editor



# SED-ML script editor

SED-ML Script

File Edit Wizards

Run

```
AddTimeCourseSimulation('sim1', 'K')

AddModel('model1', '/Users/fbergma

AddTask('task1', 'sim1', 'model1')

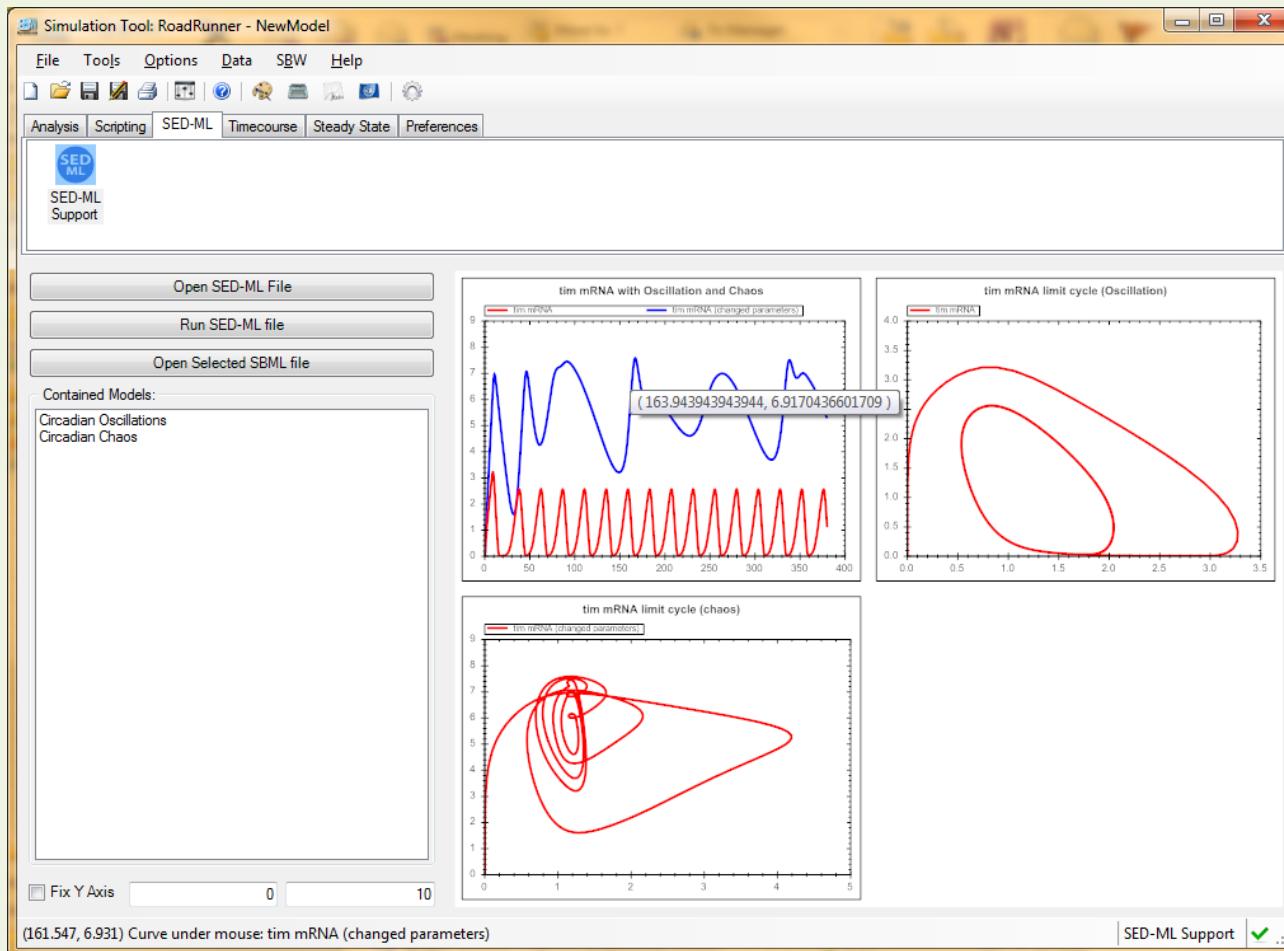
AddColumn('time', [['time', 'task1
AddColumn('X_1', [['X', 'task1', '
AddColumn('Y_1', [['Y', 'task1', '
AddColumn('Z_1', [['Z', 'task1', '

AddPlot3D('plot1', '', [['X_1', 'Y_1', 'Z_1']]));
```

Gnuplot (window id : 0)

view: 60.0000, 30.0000 scale: 1.00000, 1.00000

# Available in SBW!



# SBML Test Suite

- Next release of the SBML Test Suite will come with SED-ML models for all test cases:
- That's 4872 SED-ML models!

 00775-model.html
 00775-model.m
 00775-plot.jpg
 00775-results.csv
 00775-results.csv.jpg
 00775-sbml-l2v1_sedml.xml
 00775-sbml-l2v1.xml
 00775-sbml-l2v2_sedml.xml
 00775-sbml-l2v2.xml
 00775-sbml-l2v3_sedml.xml
 00775-sbml-l2v3.xml
 00775-sbml-l2v4_sedml.xml
 00775-sbml-l2v4.xml
 00775-sbml-l3v1_sedml.xml
 00775-sbml-l3v1.xml
 00775-settings.txt

# Outlook

A Simple Nested Simulation for SED-ML

Frank T. Bergmann ([fbergman@u.washington.edu](mailto:fbergman@u.washington.edu))

About this document

This document describes a simple nested Simulation Experiment for SED-ML [1] that is easy to implement and will help to broaden what SED-ML is able to encode. Currently, SED-ML effectively describes the exchange of time course simulation experiments. Through suggestions made at the Super Hackathon in New Zealand<sup>1</sup> last year, this general uniform time course simulation was extended, by applying different ranges to simulation experiments (Figure 1).

Nature Precedings : doi:10.1038/npre.2010.4257.1 : Posted 4 Mar 2010

```
classDiagram Range <|-- UniformRange
classDiagram Range <|-- VectorRange
classDiagram Range <|-- FunctionalRange
```

Figure 1: Extending Simulations Through Ranges [snippet from current proposed SED-ML object model]<sup>2</sup>

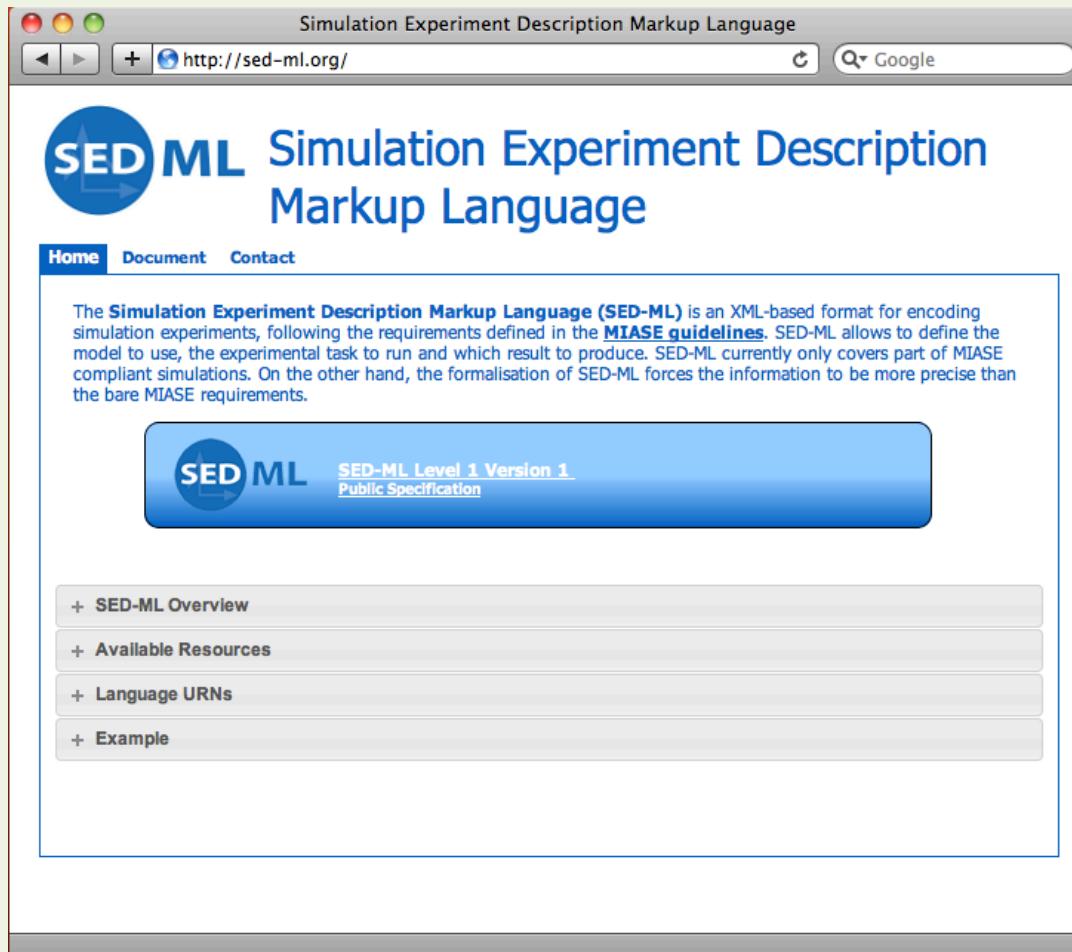
However, by directly applying these ranges to the `TimeCourse` simulation element (and other future simulation types), it will be arguably harder for the community to implement this standard. Currently available simulation tools do not have this functionality. Moreover, a custom implementation will be necessary for each simulation experiment encoded this way. Here, an alternative will be presented that will allow for the same functionality as the current proposal and, perhaps even more important, make it easy for developers to implement. It will also allow for the community to implement novel simulation experiments.

- Nested Tasks
- More Simulation Experiments
- Advanced Post processing

<sup>1</sup> <http://www.cellml.org/community/events/workshop/2009>

<sup>2</sup> <http://sed-ml.svn.sourceforge.net/viewvc/sed-ml/sed-ml/documents/sed-om/sedom-tmp.pdf>

# More Information



<http://sed-ml.org>

# Acknowledgments

Nicolas Le Nov  re, Richard Adams  
Dagmar Waltemath

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Ion Moraru  
Sven Sahle  
David Nickerson  
Henning Schmidt  
Fedor Kolpakov