SED-ML
Simulation Experiment Description Language

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CellML & Co Workshop
Auckland, April 2009

Outline

- SED-ML
    - Some technical details
    - Main structure
- Examples, examples, examples
- Outstanding issues
- Jlibsedml (Stuart)

SED-ML is …

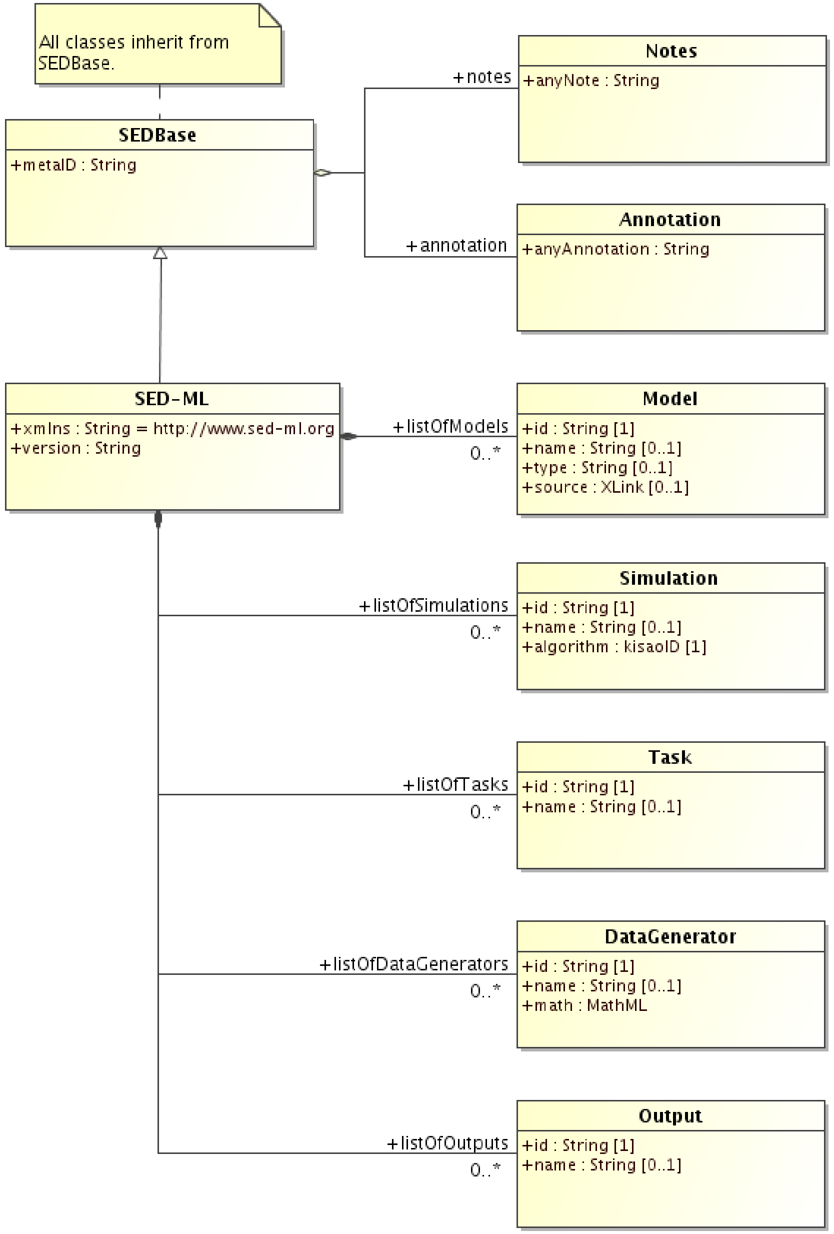
- … a community effort
- … [hopefully] “MIASE-compliant” [in the future]
- … an XML format (**XML Schema**)
- … also available as a **UML model**

http://www.ebi.ac.uk/compneur-srv/sed-ml

- … using **Xpath** to address (XML) elements in the model

Example: `/model/component[@cmeta:id='MT']`

Main Structure (1)



All classes inherit from SEDBase.

SEDBase
+metaID : String

+notes

Notes
+anyNote : String

+annotation

Annotation
+anyAnnotation : String

SED-ML
+xmlns : String = http://www.sed-ml.org
+version : String

+listOfModels 0..*

Model
+id : String [1]
+name : String [0..1]
+type : String [0..1]
+source : XLink [0..1]

+listOfSimulations 0..*

Simulation
+id : String [1]
+name : String [0..1]
+algorithm : kisaoID [1]

+listOfTasks 0..*

Task
+id : String [1]
+name : String [0..1]

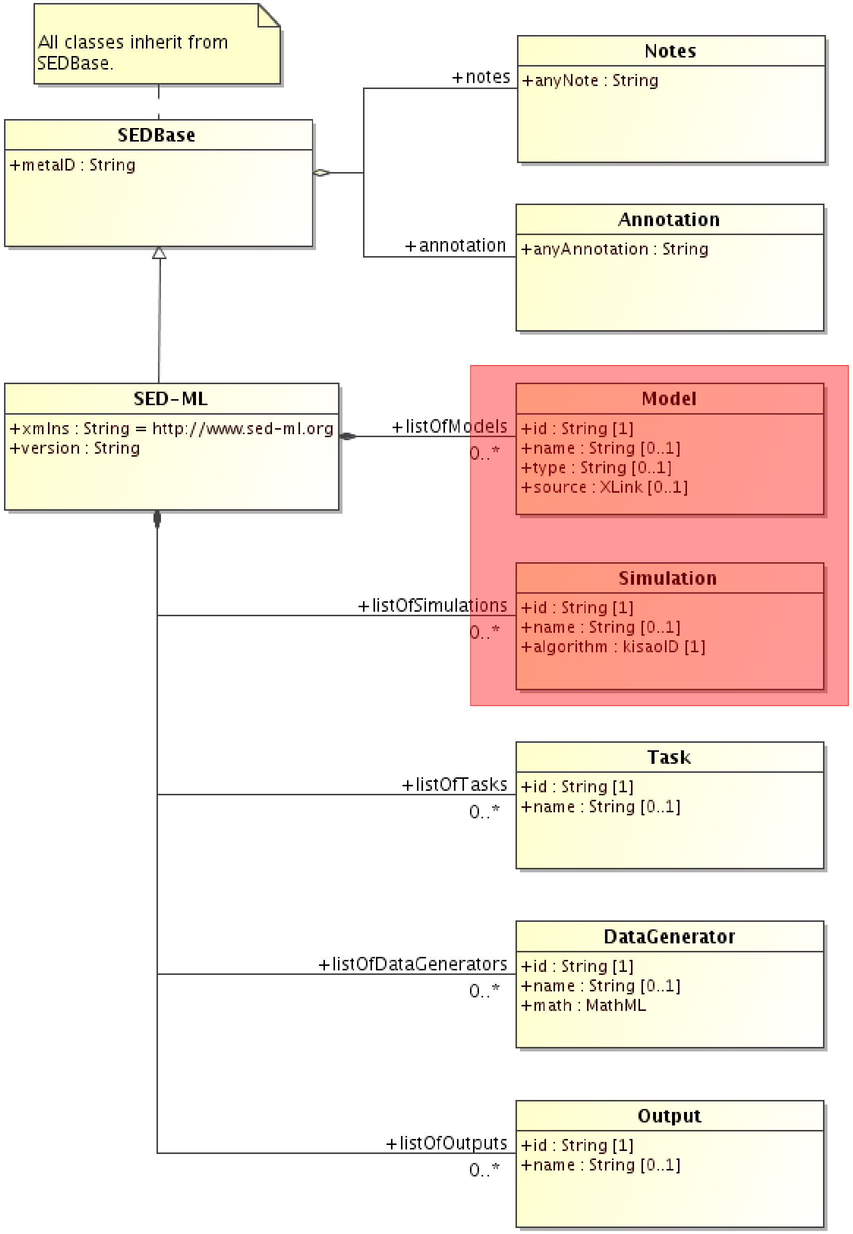
+listOfDataGenerators 0..*

DataGenerator
+id : String [1]
+name : String [0..1]
+math : MathML

+listOfOutputs 0..*

Output
+id : String [1]
+name : String [0..1]

Main Structure (1)



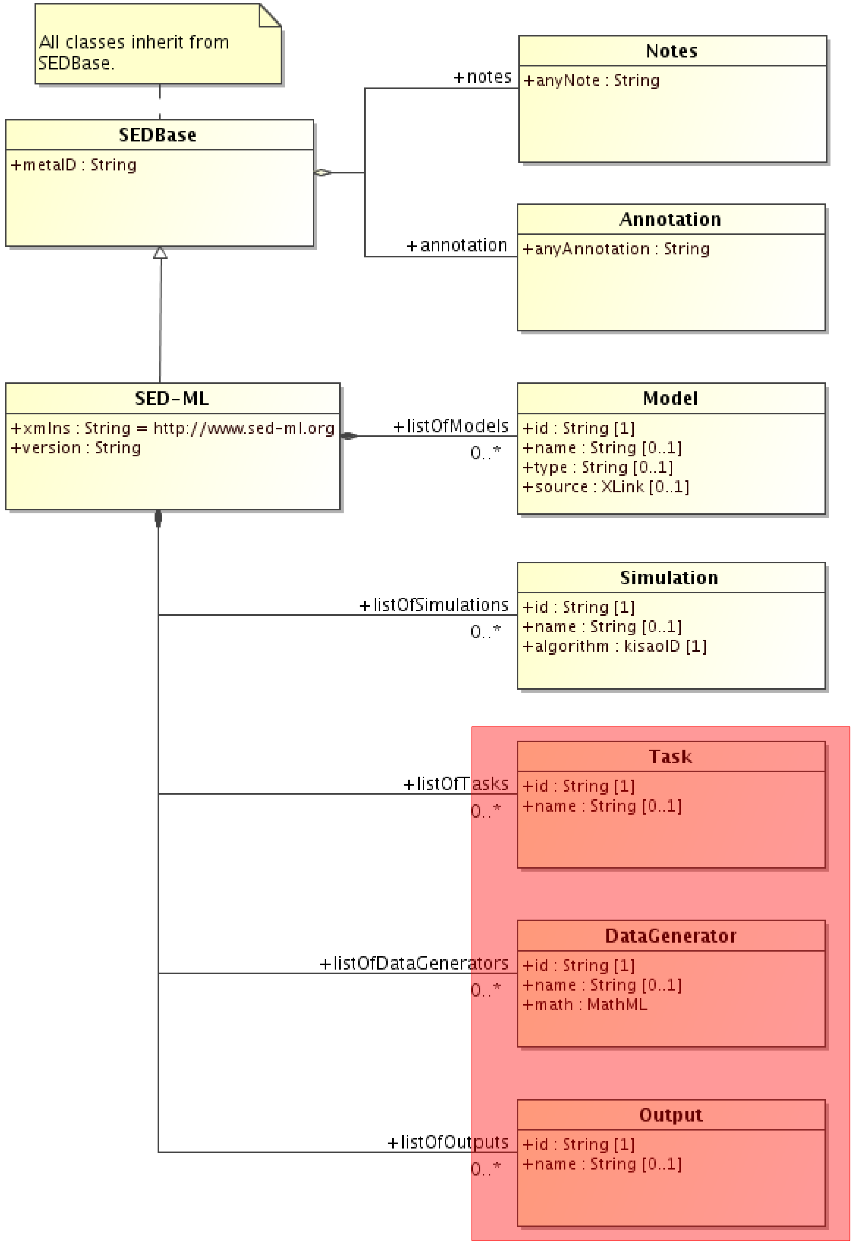
Model Class

- References to models used during simulation experiment
- Changes before simulation

Simulation Class

- Definition of simulation type, method and duration …

Main Structure (2)



Task Class

- Combination of a simulation and a model

DataGenerator Class

- Definition of variables to be used in the output

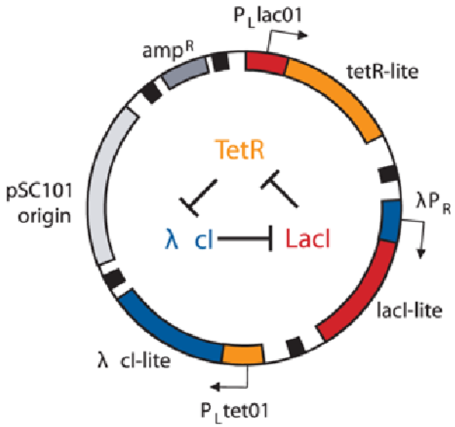
Output Class

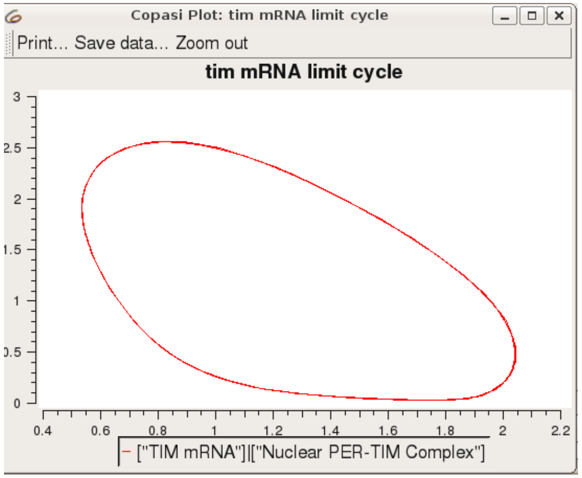
- Output type
- Link to DataGenerators

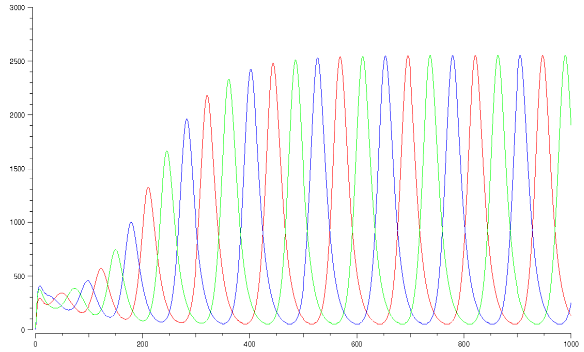
SED-ML can be used to define many experiments.

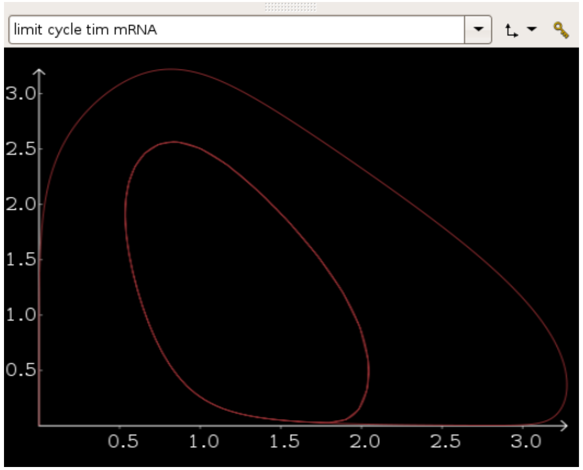
- Simulation experiment encoding
  model perturbations, simulation settings, output
- Experiments using more than one model *listOfModels*
- Experiments using models from different formalisms,
  e.g. simulations using an SBML model and a CellML model
- Experiments on one model, but using different simulation methods *listOfSimulations*
- Sequential Experiments
  Steady state analysis for an SBML model, using the parameter values for simulation of a CellML model
- *What more could you think of?*

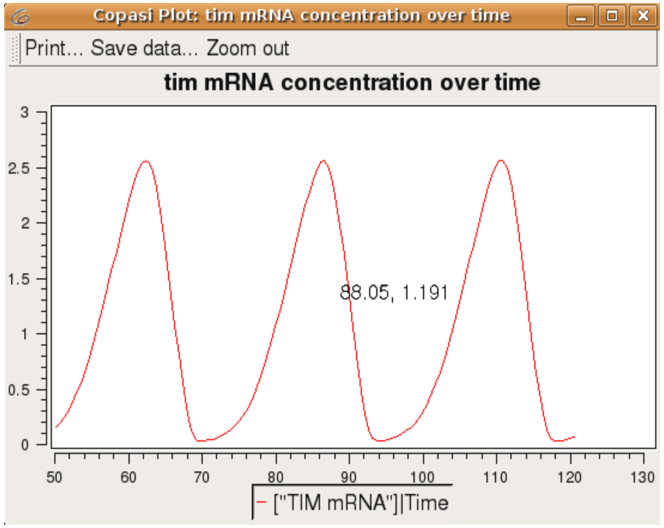
SED-ML : Examples

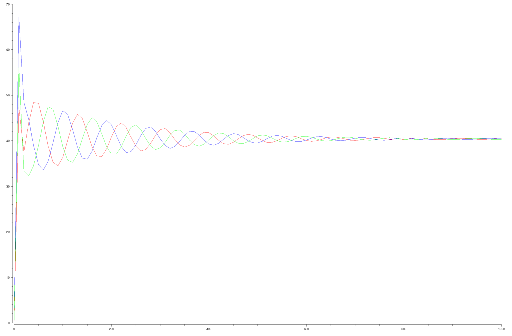












Using SED-ML to describe a simple simulation (1)

1. Take the Repressilator model

```
<model id="model1" name="Repressilator" type="SBML"
source="urn:miriam:biomodels.db:BIOMD0000000012" />
```

2. Run a time course with a deterministic simulator (LSODA)

```
<uniformTimeCourse id="simulation1"
algorithm="KiSAO:0000088" initialTime="0"
outputStartTime="0" outputEndTime="1000"
numberOfPoints="1000" />
```

3. Simulate the model with the defined simulation settings

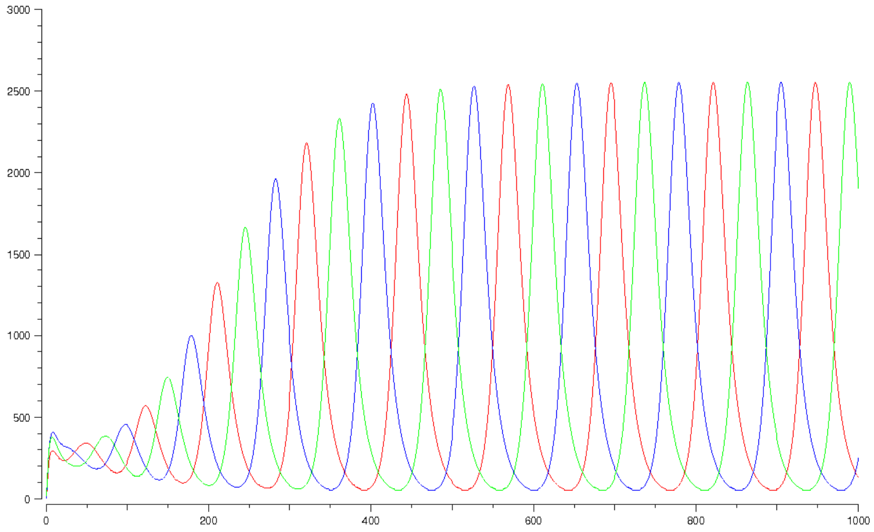
```
<task id="task1" modelReference="model1"
simulationReference="simulation1"/>
```

Using SED-ML to describe a simple simulation (2)

4. Plot the protein numbers of over time

```
<dataGenerator id="LaCI" name="LaCI repressor">
<variable id="v4" taskReference="task2" target="/
sbml/model/listOfSpecies/species[@id='PX']" />
```

```
<plot2D id="plot1"
name="protein numbers">
<listOfCurves>
<curve xDataReference="time"
yDataReference="LaCI" />
[..]
</listOfCurves>
</plot2D>
```



EMBL-EBI

Using SED-ML to show different model behaviours (oscillation vs stable steady state) (1)

1. Take the Repressilator model

```
<model id="model2" name="Repressilator" type="SBML"
source="model1" />
```

2. Change the relevant parameter (alpha)

```
<listOfChanges>
<changeAttribute
target="/sbml/model/listOfParameters/
parameter[@id='alpha']" newValue="9" />
</listOfChanges>
```

Using SED-ML to show different model behaviours (oscillation vs stable steady state) (2)

3. Run a time course with a deterministic simulator (LSODA)

```
<uniformTimeCourse id="simulation1"
algorithm="KiSAO:0000088" initialTime="0"
outputStartTime="0" outputEndTime="1000"
numberOfPoints="1000" />
```

4. Simulate the model with the defined simulation settings

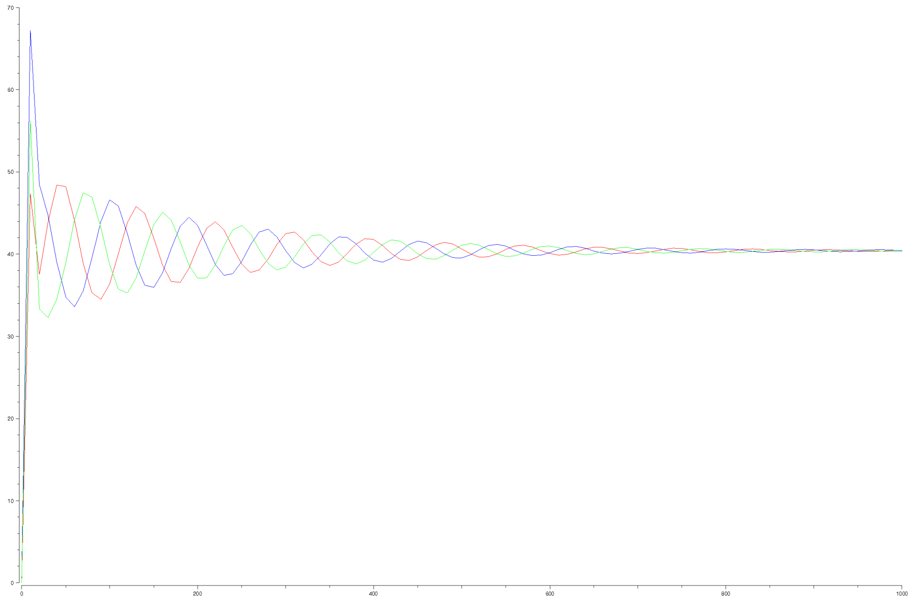
```
<task id="task1" modelReference="model2"
simulationReference="simulation1"/>
```

Using SED-ML to show different model behaviours (oscillation vs stable steady state) (3)

5. Plot the protein numbers over time

```
<dataGenerator id="LaCI" name="LaCI repressor">
<variable id="v4" taskReference="task2" target="/
sbml/model/listOfSpecies/species[@id='PX']" />

<plot2D id="plot1"
name="protein numbers">
<listOfCurves>
<curve xDataReference="time"
yDataReference="LaCI" />
[..]
</listOfCurves>
</plot2D>
```



Using SED-ML to simulate models of different formats (Circadian Oscillations in SBML) (1)

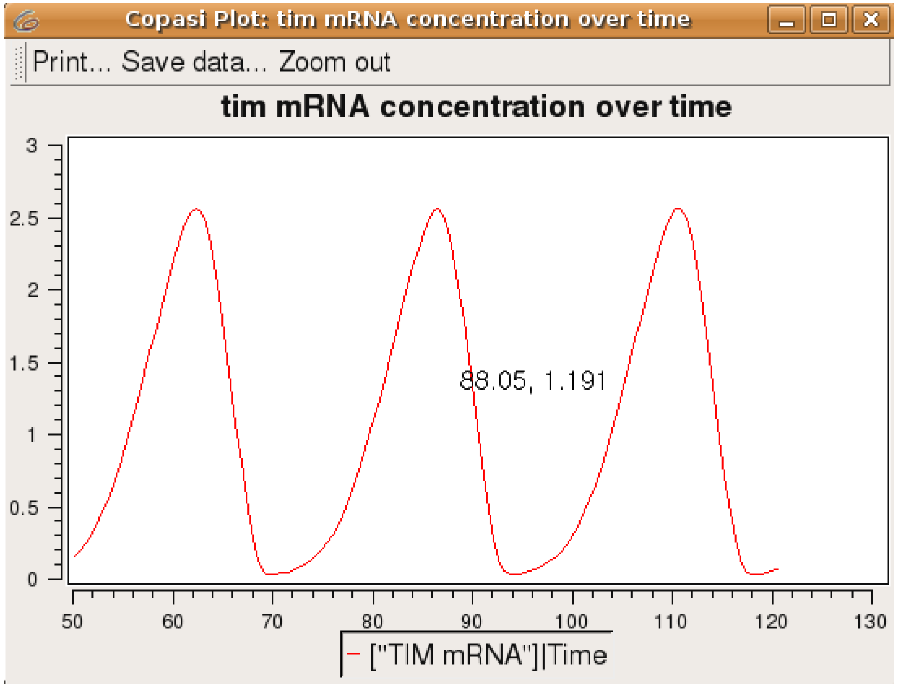
1. Take the (Leloup,99) model
   ```
   <model id="model1" name="Circadian Oscillations"
   type="SBML" source="urn:miriam:biomodels.db:
   BIOMD0000000021" />
   ```
2. Run a time course with a deterministic simulator (LSODE)
   ```
   <uniformTimeCourse id="simulation1"
   algorithm="KiSAO:0000071" numberOfPoints="1000" />
   ```
3. Simulate the model with the defined simulation settings
   ```
   <task id="task1" modelReference="model1"
   simulationReference="simulation1"/>
   ```

Using SED-ML to simulate models of different formats (Circadian Oscillations in SBML) (2)

4. Plot the tim mRNA concentration over time

```
<variable id="v1" taskReference="task1"
target="/sbml/model/listOfSpecies/
species[@id='Mt']" />

<plot2D>
<listOfCurves>
<curve xDataReference="time"
 yDataReference="tim1" />
</listOfCurves>
<plot2D>
```



Using SED-ML to simulate models of different formats (Circadian Oscillations in CellML) (1)

1. Take the (Leloup,99) model

```
<model id="model1" name="Circadian Oscillations"
type="CellML" source="http://www.cellml.org/
models/leloup_gonze_goldbeter_1999_version02" />
```

2. Change the parameters in the model according to the paper

```
<changeAttribute target="/model/
component[@cmeta:id='MP']/variable[@name='vsP']/@in
itial_value" newValue="1"/>
```

3. Run a time course with a deterministic simulator (LSODE)

```
<uniformTimeCourse id="simulation1"
algorithm="KiSAO:0000071" numberOfPoints="1000" />
```

Using SED-ML to simulate models of different formats (Circadian Oscillations in CellML) (2)

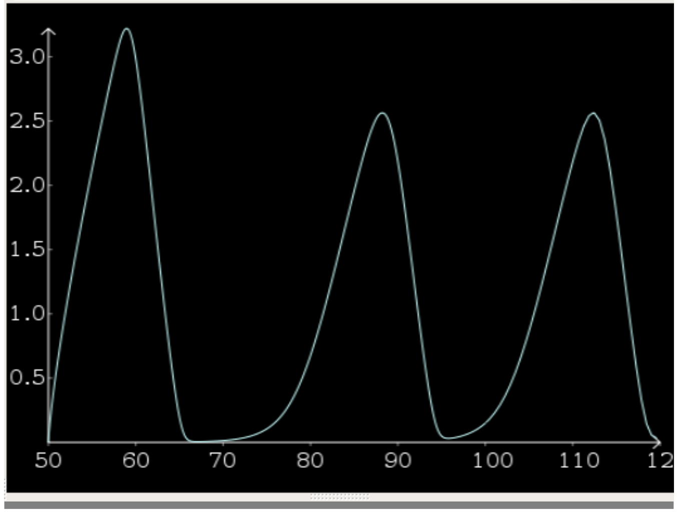
4. Simulate the model with the simulation settings

```
<task id="task1" modelReference="model1"
simulationReference="simulation1"/>
```

5. Plot the tim mRNA concentration over time

```
<variable id="v1" taskReference="task1"
target="/model/component[@cmeta:id='MT']″ />

<plot2D>
<listOfCurves>
<curve xDataReference="time"
yDataReference="tim1" />
```



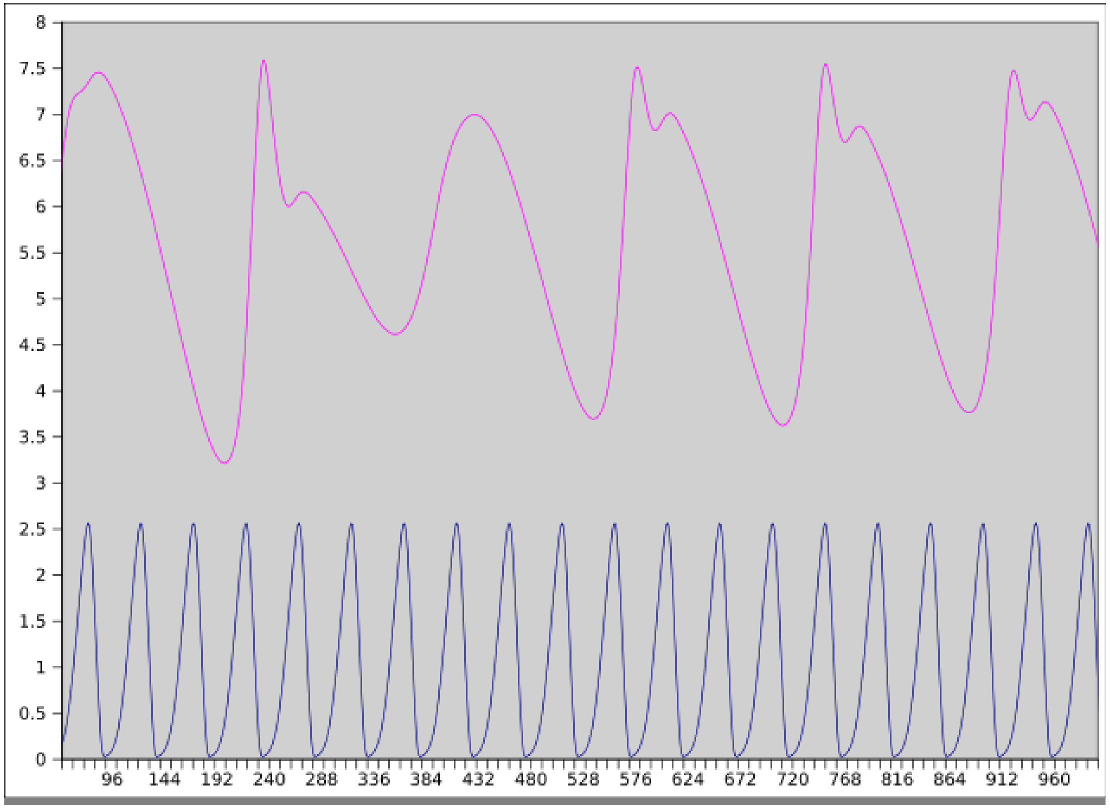
SED-ML files for both experiments are similar except element addressing (XPath)

```
<model id="model1" name="Circadian Oscillations" type="SBML"
source="urn:miriam:biomodels.db:BIOMD0000000021" />
[..]
<variable id="v1" taskReference="task1" target="/sbml/model/
listOfSpecies/species[@id='Mt']" />
<plot2D> <listOfCurves>
<curve xDataReference="time" yDataReference="tim1" />
</listOfCurves> <plot2D>
```

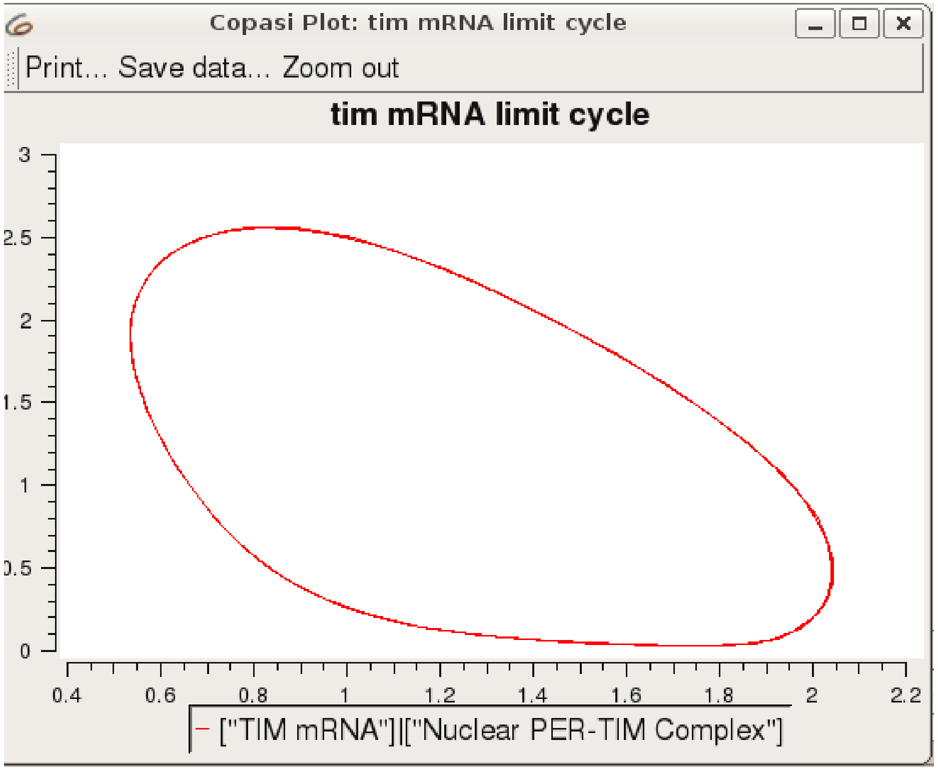
```
<model id="model1" name="Circadian Oscillations" type="CellML"
source="http://www.cellml.org/models/leloup_gonze_go
ldbeter_1999_version02" />
[..]
<variable id="v1" taskReference="task1" target="/model/
component[@cmeta:id='MT']” />
<plot2D> <listOfCurves>
<curve xDataReference="time" yDataReference="tim1" />
</listOfCurves> <plot2D>
```

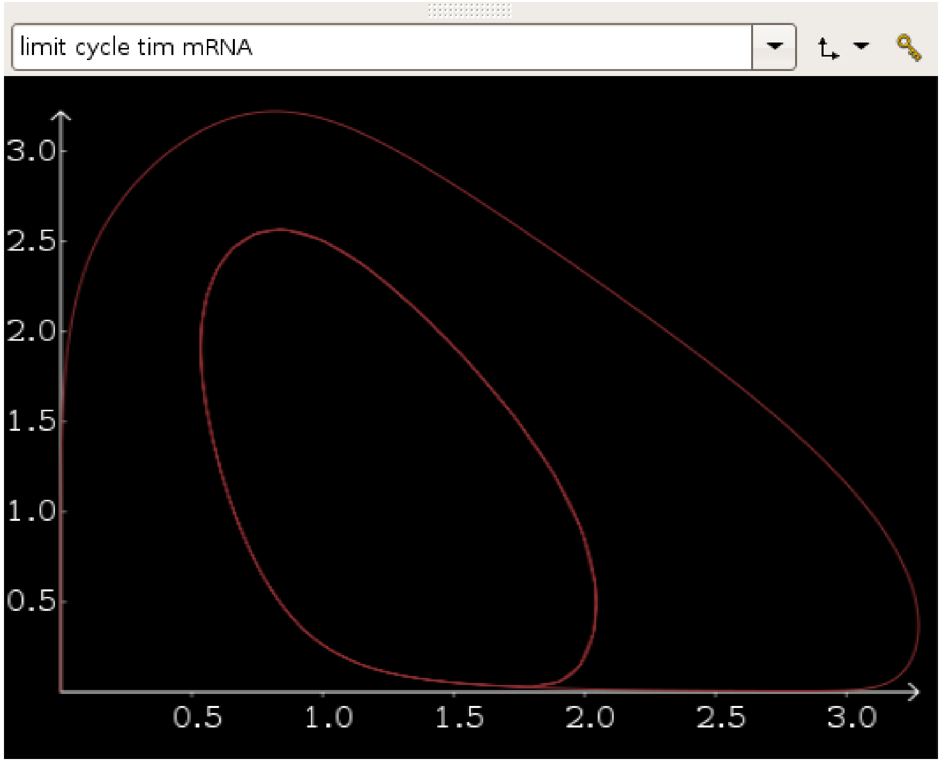
Using SED-ML to put together plots from different simulations

- Simulating the SBML (Leloup,99) in COPASI with oscillating behaviour and chaotic behaviour (changed parameters V_mT/V_dT); comparing both curves in one plot (Gnumeric Spreadsheet)



Simulation examples on Sourceforge





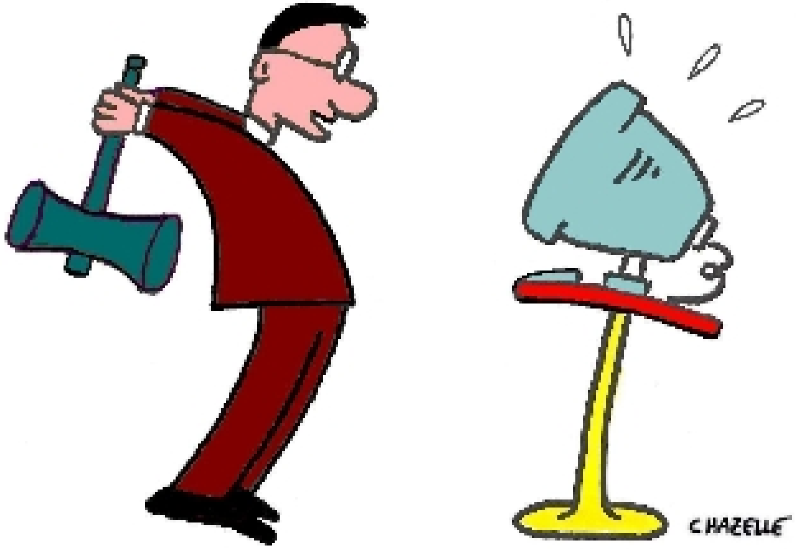
http://miase.svn.sourceforge.net/viewvc/miase/sed-ml/examples/

Outstanding Issues

- Support more simulation types
  - Supported: Uniform Time Course, AnySimulation
  - Desired: Parameter Scans, Optimisations … *Which ones would you like to encode?*
- Should we also consider to link to experiment results? And if yes, in what way?
  - Options: SBRML or link to tabular data or data files
- Technical issues
  - Xpath, Prototype implementations, Library development
  - Jlibsedml

Thanks to …

Richard Adams (JlibSED-ML)
Frank Bergman (roadrunner)
Mike Hucka
Fedor Kolpakov (BioUML)
Nicolas Le Novère
Ion Moraru (Virtual Cell)
Sven Sahle (COPASI)
Henning Schmidt (SB Toolbox)



“ What do you mean, ‘intractable’ ? ”

http://www.cs.princeton.edu/~chazelle/pics/smash.jpg

http://www.ebi.ac.uk/compneur-srv/sed-ml/

miase-discuss@lists.sourceforge.net