Version 2

Nested Simulation Proposal

A proposal for extending SED-ML L1V1

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Contents

About this document

This document describes a second version of the proposal for nested simulation experiments [1] for SED-ML [2]. The proposal has been updated to include the feedback received in the meantime. This proposal also provides explicit examples that go beyond the ones previously detailed on the authors blog [3].

Changes in this Version

The proposal has been updated specifically in three points:

- Removal of the “steady state” primitive. This can be achieved just as well by re-using the “one step” primitive and applying a KISAO term that reflects a steady state algorithm. (this also necessitates that the ‘step’ attribute of the “one step” is now optional, as for a steady state computation the step size is insignificant.
- Previously the nested task was only able to modify one value. There have been requests to make this more flexible and so this proposal was altered to allow multiple changes to be performed.
- The previous proposal was referring to time using a predefined string. With the release of SED-ML L1V1 we now have a way to explicitly naming it using SED-ML symbols.
- Previously there was not much detail given on the individual ranges. This time examples for every construct are included.

Summary

Instead of redefining a large number of simulation types to suite various simulation tasks, which will make it very difficult for tool developers to support SED-ML, this proposal suggests a nested simulation class that breaks down complex tasks into separate steps. This is achieved by introducing two new simulation classes: “one step”, a simulation class that performs a specified simulation algorithm and “nested simulation” a class that performs a specified simulation type a multiple times (where the exact number is specified through a “range” construct while allowing specific aspects of the model to change (in the simplest case that would be by advancing the simulation time). This approach is easy to implement for tool developers and covers a large number of commonly carried out simulation experiments: parameter scans or collecting stochastic traces by running a simulation multiple times.

The Proposal

This section discusses the two new simulation classes.

New Simulation Class: oneStep

This calculates one further output step for the model from its current state. Note that this does NOT necessarily equate to one integration step. The simulator is allowed to take as many steps as needed, all that has to be fulfilled with this simulation class, is that, at the end, the desired output time is reached.

```
<listOfSimulations>
  <oneStep id="s1" step="0.1">
    <algorithm kisaoID="KISAO:0000019" />
  </oneStep>
</listOfSimulations>
```

This example defines a simulation step of a deterministic simulation which advances the associated model from its current time to current time + 0.1, as the next output step.

step

The oneStep class has one optional attribute “step”. It defines the next output step that should be reached by the algorithm. In the previous version of the proposal the step variable was mandatory. However, due to the suggestions to remove the “steady state” simulation class and combine it with “one step” the “step” attribute becomes meaningless in some scenarios.

In order to use the “oneStep” class to bring a model to steady state one would simply reference a KISAO algorithm that represents a steady state computation (as for example implemented by NLEQ or Kinsolve). In my implementation I use “KISAO:0000282” or a related one.

New Simulation Class: nestedSimulation

Nested simulations are the core of this proposal. The name comes from the fact, that this simulation class references *another* simulation task that will be carried out. A nested simulation task basically consists of the following steps:

1. Compute the current value of ranges
2. Apply the changes defined
3. Run the specified *orginalTask* on the model
4. If *resetModel* is defined, reset the model to initial conditions
5. If we have more values within the range specified in the *range* attribute go to 1, otherwise end.

The overall structure of the *nestedSimulation* class is as follows:

```
<nestedSimulation id="s3" resetModel="false" originalTask="task1" range="current">
  <algorithm kisaoID="KISAO:0000019" />
  <ranges>
    <vectorRange id="current">
        <value> 1 </value>
        <value> 4 </value>
        <value> 10 </value>
    </vectorRange>
  </ranges>
  <changes>
    <setValue target="/sbml/model/listOfParameters/parameter[@id='w']">
```

```
    <listOfVariables>
        <variable id="val" name="current range value" target="#current" />
    </listOfVariables>
    <math>
        <ci> val </ci>
    </math>
   </setValue>
  </changes>
</nestedSimulation>
```

Below the individual elements are described.

range attribute

The *range* attribute determines the range that this nested simulation experiment iterates over. This is akin to loop variables in programming languages. In the example above the nestedSimulation will iterate over three values: 1, 4 and 10.

resetModel attribute

The *resetModel* attribute indicates whether the model should be reset after completing a iteration of the nested simulation experiment. Consider the case where a piecewise simulation is performed. In this case you would not want the model to be reset to initial conditions after each piece of the simulation. However, in the case of collecting several stochastic traces you might want to reset the model each time.

originalTask attribute

The *originalTask* attribute allows specifying the simulation task to be performed during each iteration of the nested simulation.

Ranges

Ranges represent the iterative element of the nested simulation experiment that provides the collection of values to iterate over. In order to be able to refer to the current value of a range element, we add an id attribute. When the value of the id attribute is used in a listOfVariables within the nested simulation class it is to be extended with the current value.

There are three different range types:

UniformRange: this range is defined through a *start* value, an *end* value and a *number of points*. This is quite similar to what is today used in the UniformTimecourse simulation experiment. For example:

```
<uniformRange id="current" start="0.0" end="10.0" numberOfPoints="100" />
```

VectorRange: this range can be seen as simply a collection of values. For example:

```
<vectorRange id="current">
    <value> 1 </value>
    <value> 4 </value>
    <value> 10 </value>
</vectorRange>
```

FunctionalRange: defines a function to be evaluated in order to determine the next value. Previously the functional range was simply stated as a MathML element. However, this will not allow us to reference model elements, and so it needs to look like the computeChange element. That is we need a listOfVariables, along with the Math description. Additionally we need another attribute that specifies an index variable "index" so that we can evaluate the function at different points. This variable can be used in the MathML expression. The value to be used for the index is provided by another range when the functionalRange is invoked. For example:

```
<functionalRange id="current" index="index">
  <listOfVariables>
     <variable id="w" name="current parameter value"
                      target="/sbml/model/listOfParameters/parameter[@id='w']" />
  </listOfVariables>
  <function>
    <math>
       <apply>
       <times/>
       <ci> w </ci>
       <ci> index </ci>
       </apply>
    </math>
  </function>
</functionalRange>
```

Here another example of using the values in a piecewise expression:

```
    <uniformRange id="index" start="0" end="10" numberOfPoints="100" />
    <functionalRange id="current" index="index">
      <function>
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <piecewise>
            <piece>
              <cn> 8 </cn>
              <apply>
                <lt />
                <ci> index </ci>
                <cn> 1 </cn>
              </apply>
            </piece>
            <piece>
              <cn> 0.1 </cn>
              <apply>
                <and />
                <apply>
                  <geq />
                  <ci> index </ci>
                  <cn> 4 </cn>
                </apply>
                <apply>
                  <lt />
                  <ci> index </ci>
                  <cn> 6 </cn>
                </apply>
              </apply>
            </piece>
            <otherwise>
              <cn> 8 </cn>
            </otherwise>
          </piecewise>
        </math>
      </function>
    </functionalRange>
```

Changing Values

In this version of the proposal multiple changes to the model are allowed:

```
<changes>
  <setValue target="/sbml/model/listOfParameters/parameter[@id='w']" range="current" >
   <math>
       <ci> current </ci>
   </math>
  </setValue>
</changes>
```

In order to specify the object that will receive the new value we use an xpath query in form of the target attribute. The setValue class inherits all properties from the SED-ML Variable class, and so instead of the 'target' attribute it is also possible to refer to SED-ML implicit symbols. The additional attribute 'range' describes the range object that provides the current value (see also the functionalRange examples).

If it turns out that people dislike passing in the range, we could also overload the xpath expression like so:

```
<changes>
  <setValue target="/sbml/model/listOfParameters/parameter[@id='w']" >
   <listOfVariables>
       <variable id="val" name="current range value" target="//*[@id='current']" />
   </listOfVariables>
   <math>
       <ci> val </ci>
   </math>
  </setValue>
</changes>
```

Note: how in the example above the XPath expression references the value of the range. It does so by selecting an element with the id 'current'. Since in SED-ML identifiers are unique this will work. For implementation that means if in a variable neither modelReference nor taskReference is given, the current document is to be used.

Discussion / Known Issues

The nested simulation construct explained above is easy to implement and versatile. It can be implemented to construct arbitrarily complex datasets. This section details the known issues this brings along.

Combining nested simulations

Since the "originalTask" attribute of a nested simulation object allows referencing other nested simulation tasks it is possible to combine them. This becomes useful when for example performing a 2D parameter scan:

1. A first task would apply a steady state simulation to a model
2. A second task describes a "nestedSimulation" over the first task in order to scan over parameter 1

3. A third task describes another nestedSimulation over the second task in order to scan over a different parameter 2.

Of course this can be continued into higher dimensions.

Collecting data from a nested simulation

This proposal only describes the *task* aspect, that is how to generate the data. What is not described is how to describe its visualization. When implementing the nested simulation task it would be best to have it generate a dataset of arbitrary dimensions, and present them to the user to let them slice the data as desired. The SED-ML community is discussing several alternative ways on how to deal with higher dimensional DataGenerators (one proposal involved using NuML [4, 5], and another to allow arbitrary MathML expressions [6]).

No matter which direction is chosen on how to describe the plots it the necessity of generating the results exists, and this proposal addresses them.

Semantics of a Nested Simulation Task

This proposal favors the approach of defining a general nested simulation task. Once implemented, it will allow a tool to perform a large number of different simulations. To add semantic information to the task it suffices to register a KISAO term for the specific task used, or to annotate it using MIRIAM RDF annotations on the task itself.

The author strongly believes this is preferable to the situation where we would need to define a vast number of individual simulation tasks like: 1D ParameterScan, 2D ParameterScan, 1D Logarithmic-ParameterScan or a RepeatedSimulation.

Acknowledgements

Thanks go to the SED-ML Editors as well as the SED-ML community for suggestions on the previous proposal and to Brett Olivier for implementing the previous proposal. Finally thanks to the Saurolab, University of Washington that is hosting the SED-ML Web Tools application.

Examples

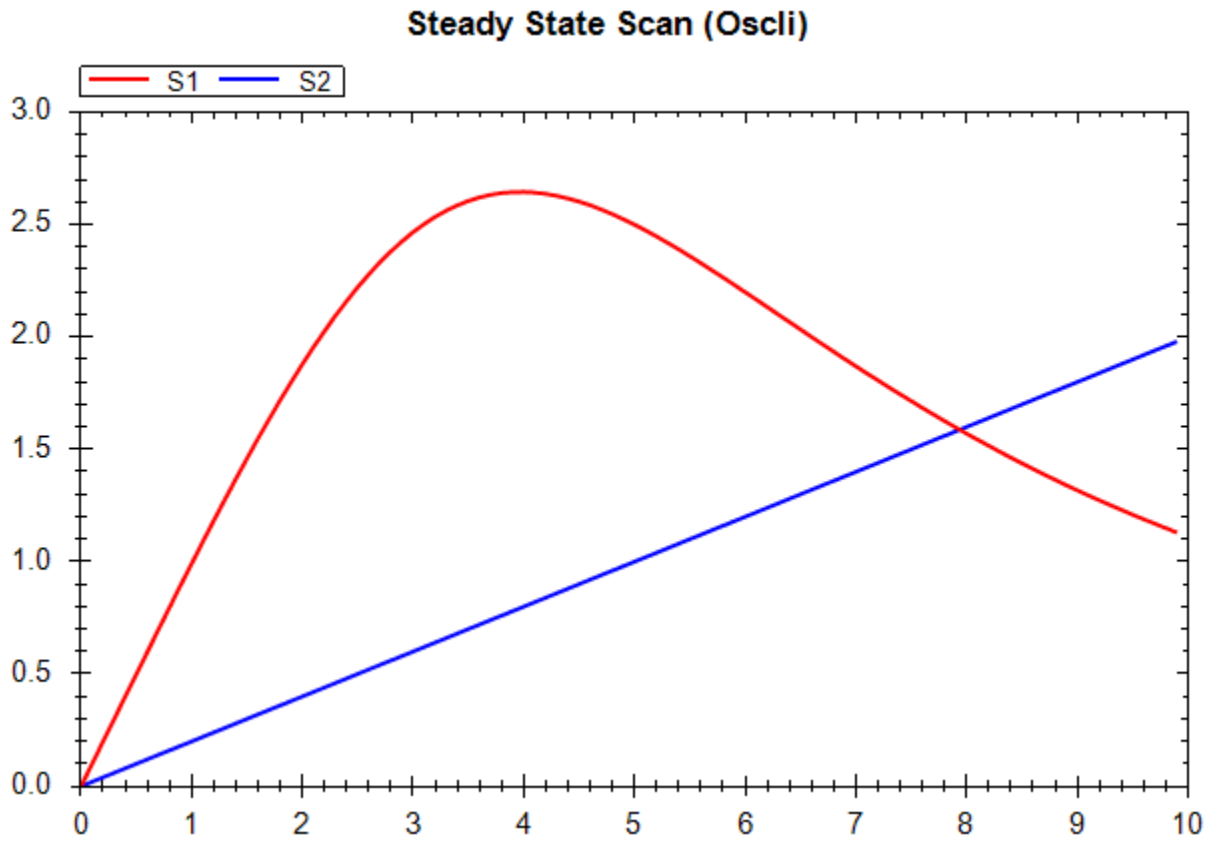
The following examples have been produced by libSedML [7]. The current version has prototypical support for the nested simulation task outlined above. The web application SED-ML Web Tools [8] have also been upgraded to be able to simulate them.

1D Steady State Parameter Scan

In this simple task one nested simulation task calls out to a oneStep task (performing a steady state computation) and varies a parameter to get different responses.

In the description below the range to be used in the setValue construct uses the Xpath variant as described above. To see the use of the 'range' attribute see the next example.

The Results



The Description

```
<?xml version="1.0" encoding="utf-8"?>
<!-- Written by libSedML v1.1.4396.33801 see http://libsedml.sf.net -->
<sedML level="1" version="1" xmlns="http://sed-ml.org/">
  <listOfSimulations>
    <oneStep id="steady1">
      <algorithm kisaoID="KISAO:0000282" />
    </oneStep>
    <nestedSimulation id="nested1" resetModel="true" originalTask="task2" range="current">
      <ranges>
        <uniformRange id="current" start="0" end="10" numberOfPoints="100" />
      </ranges>
```

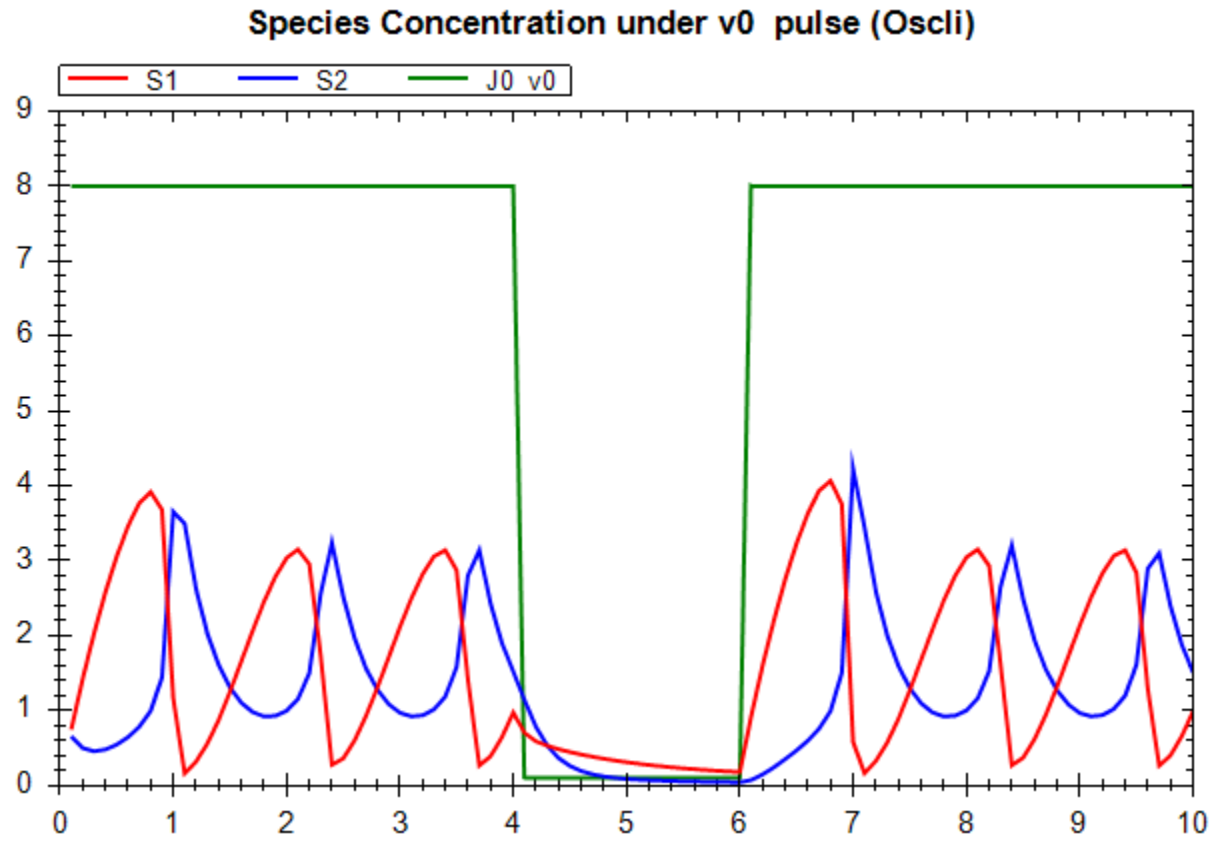
```
      <changes>
        <setValue target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J0_v0']">
          <listOfVariables>
            <variable id="val" name="current loop value" target="//*[@id='current']" />
          </listOfVariables>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <ci> val </ci>
          </math>
        </setValue>
      </changes>
    </nestedSimulation>
  </listOfSimulations>
  <listOfModels>
    <model id="model1" language="urn:sedml:language:sbml"
source="http://libsedml.svn.sourceforge.net/viewvc/libsedml/trunk/Samples/models/oscli.xml" />
  </listOfModels>
  <listOfTasks>
    <task id="task1" modelReference="model1" simulationReference="nested1" />
    <task id="task2" modelReference="model1" simulationReference="steady1" />
  </listOfTasks>
  <listOfDataGenerators>
    <dataGenerator id="J0_v0_1" name="J0_v0">
      <listOfVariables>
        <variable id="J0_v0" name="J0_v0" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J0_v0']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> J0_v0 </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="S1_1" name="S1">
      <listOfVariables>
        <variable id="S1" name="S1" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='S1']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> S1 </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="S2_1" name="S2">
      <listOfVariables>
        <variable id="S2" name="S2" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='S2']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> S2 </ci>
      </math>
    </dataGenerator>
  </listOfDataGenerators>
  <listOfOutputs>
    <plot2D id="plot1" name="Steady State Scan (Oscli)">
      <listOfCurves>
        <curve id="curve1" logX="false" logY="false" xDataReference="J0_v0_1" yDataReference="S1_1" />
        <curve id="curve2" logX="false" logY="false" xDataReference="J0_v0_1" yDataReference="S2_1" />
      </listOfCurves>
    </plot2D>
    <report id="report1" name="Steady State Values">
      <listOfDataSets>
        <dataSet id="col1" dataReference="J0_v0_1" label="" />
        <dataSet id="col2" dataReference="S1_1" label="" />
        <dataSet id="col3" dataReference="S2_1" label="" />
      </listOfDataSets>
    </report>
  </listOfOutputs>
</sedML>
```

Perturbing a Simulation

Often it is interesting to see how the dynamic behavior of a model changes when some perturbations are applied to the model. In this example we include one nested simulation task that makes repeated use of a oneStep task (that advances an ODE integration to the next output step). During the steps one parameter is modified effectively killing the oscillations in a model. Once the value is reset the oscillations recover.

Note: In the example below we use a functionalRange, although the same result could also be achieved using the setValue element directly.

The Results



The Description

```
<?xml version="1.0" encoding="utf-8"?>
<!-- Written by libSedML v1.1.4396.37631 see http://libsedml.sf.net -->
<sedML level="1" version="1" xmlns="http://sed-ml.org/">
  <listOfSimulations>
    <oneStep id="stepper" step="0.1">
      <algorithm kisaoID="KISAO:0000019" />
    </oneStep>
    <nestedSimulation id="nested1" resetModel="false" originalTask="task2" range="index">
      <ranges>
        <uniformRange id="index" start="0" end="10" numberOfPoints="100" />
        <functionalRange id="current" index="index">
          <listOfVariables>
            <variable id="val" name="current loop value" target="//*[@id='current']" />
          </listOfVariables>
```

```
          <function>
            <math xmlns="http://www.w3.org/1998/Math/MathML">
              <piecewise>
                <piece>
                  <cn> 8 </cn>
                  <apply>
                    <lt />
                    <ci> index </ci>
                    <cn> 1 </cn>
                  </apply>
                </piece>
                <piece>
                  <cn> 0.1 </cn>
                  <apply>
                    <and />
                    <apply>
                      <geq />
                      <ci> index </ci>
                      <cn> 4 </cn>
                    </apply>
                    <apply>
                      <lt />
                      <ci> index </ci>
                      <cn> 6 </cn>
                    </apply>
                  </apply>
                </piece>
                <otherwise>
                  <cn> 8 </cn>
                </otherwise>
              </piecewise>
            </math>
          </function>
        </functionalRange>
      </ranges>
      <changes>
        <setValue target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J0_v0']">
          <listOfVariables>
            <variable id="val" name="current value" target="//*[@id='current']" />
          </listOfVariables>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <ci> val </ci>
          </math>
        </setValue>
      </changes>
    </nestedSimulation>
  </listOfSimulations>
  <listOfModels>
    <model id="model1" language="urn:sedml:language:sbml"
source="http://libsedml.svn.sourceforge.net/viewvc/libsedml/trunk/Samples/models/oscli.xml" />
  </listOfModels>
  <listOfTasks>
    <task id="task1" modelReference="model1" simulationReference="nested1" />
    <task id="task2" modelReference="model1" simulationReference="stepper" />
  </listOfTasks>
  <listOfDataGenerators>
    <dataGenerator id="time_1" name="time">
      <listOfVariables>
        <variable id="time" name="time" taskReference="task1" target="time" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> time </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="J0_v0_1" name="J0_v0">
      <listOfVariables>
        <variable id="J0_v0" name="J0_v0" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J0_v0']" />
      </listOfVariables>
```

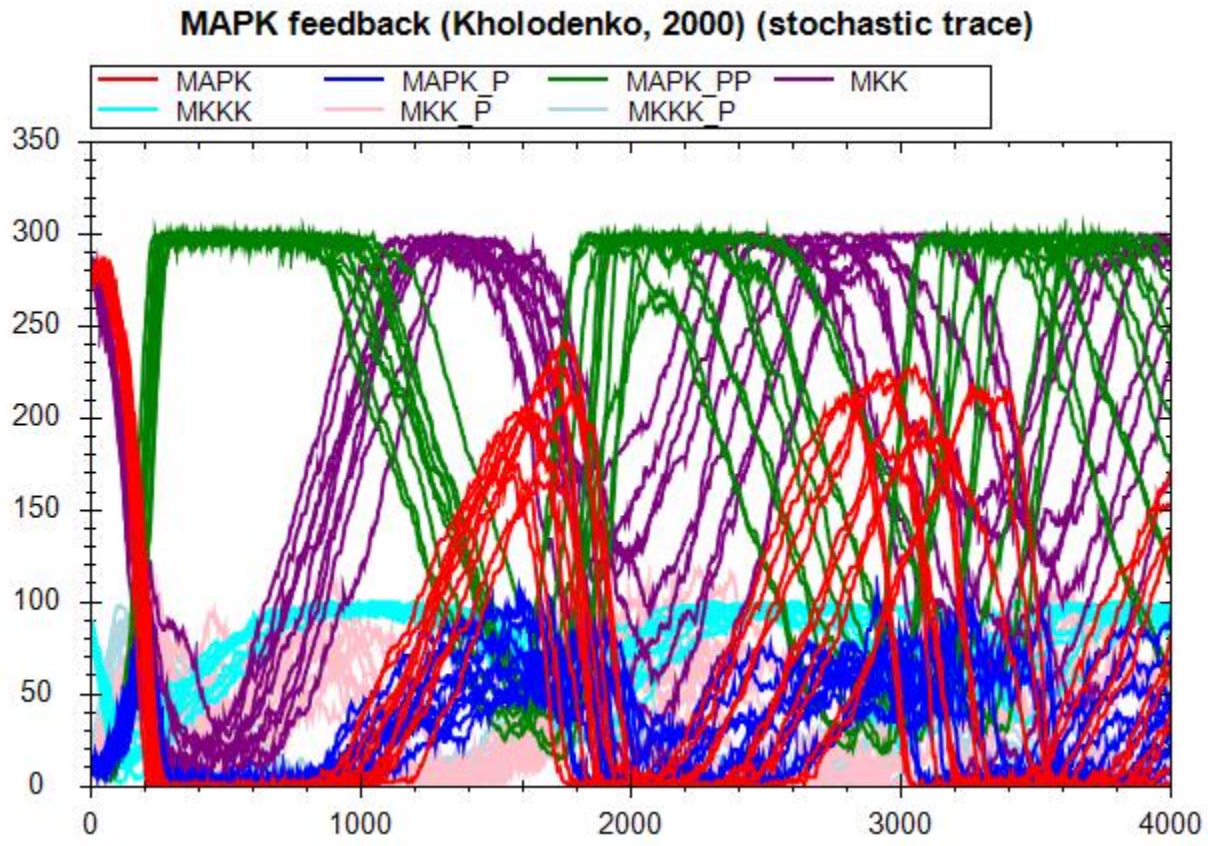
```
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> J0_v0 </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="S1_1" name="S1">
      <listOfVariables>
        <variable id="S1" name="S1" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='S1']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> S1 </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="S2_1" name="S2">
      <listOfVariables>
        <variable id="S2" name="S2" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='S2']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> S2 </ci>
      </math>
    </dataGenerator>
  </listOfDataGenerators>
  <listOfOutputs>
    <plot2D id="plot1" name="Species Concentration under v0  pulse (Oscli)">
      <listOfCurves>
        <curve id="curve1" logX="false" logY="false" xDataReference="time_1" yDataReference="S1_1" />
        <curve id="curve2" logX="false" logY="false" xDataReference="time_1" yDataReference="S2_1" />
        <curve id="curve3" logX="false" logY="false" xDataReference="time_1" yDataReference="J0_v0_1" />
      </listOfCurves>
    </plot2D>
    <report id="report1" name="Species Concentration under v0  pulse (Oscli)">
      <listOfDataSets>
        <dataSet id="col0" dataReference="time_1" label="" />
        <dataSet id="col1" dataReference="J0_v0_1" label="" />
        <dataSet id="col2" dataReference="S1_1" label="" />
        <dataSet id="col3" dataReference="S2_1" label="" />
      </listOfDataSets>
    </report>
  </listOfOutputs>
</sedML>
```

Repeated Stochastic Simulation

NOTE: Since this example produces three dimensional results (time, species concentration, multiple repeats). Currently we do not have a way for post-processing these values. In my implementation of plots I allow higher dimensional values and flatten them by overlaying them onto the desired plot.

Running just one stochastic trace does not give you a complete picture of the behavior of a system. A large number of traces are needed to provide a result. In this example we perform just ten traces of a simulation to give the general idea. Here we have one nested simulation task running over a repeated uniform time course simulation (performing a stochastic simulation run).

The Results



The Description

```
<?xml version="1.0" encoding="utf-8"?>
<!-- Written by libSedML v1.1.4397.33034 see http://libsedml.sf.net -->
<sedML level="1" version="1" xmlns="http://sed-ml.org/">
  <listOfSimulations>
    <uniformTimeCourse id="timecourse1" initialTime="0" outputStartTime="0" outputEndTime="4000"
numberOfPoints="1000">
      <algorithm kisaoID="KISAO:0000241" />
    </uniformTimeCourse>
    <nestedSimulation id="nested1" resetModel="true" originalTask="task2" range="current">
      <ranges>
        <uniformRange id="current" start="0" end="10" numberOfPoints="10" />
      </ranges>
    </nestedSimulation>
  </listOfSimulations>
  <listOfModels>
    <model id="model1" language="urn:sedml:language:sbml" source="c:\users\fbergmann\documents\sbml
models\BorisEjb.xml" />
  </listOfModels>
  <listOfTasks>
    <task id="task2" modelReference="model1" simulationReference="timecourse1" />
    <task id="task1" modelReference="model1" simulationReference="nested1" />
  </listOfTasks>
  <listOfDataGenerators>
    <dataGenerator id="time1" name="time">
      <listOfVariables>
        <variable id="time" taskReference="task1" symbol="urn:sedml:symbol:time" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> time </ci>
```

```
      </math>
    </dataGenerator>
    <dataGenerator id="MAPK1" name="MAPK">
      <listOfVariables>
        <variable id="MAPK" name="MAPK" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='MAPK']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> MAPK </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="MAPK_P1" name="MAPK_P">
      <listOfVariables>
        <variable id="MAPK_P" name="MAPK_P" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='MAPK_P']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> MAPK_P </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="MAPK_PP1" name="MAPK_PP">
      <listOfVariables>
        <variable id="MAPK_PP" name="MAPK_PP" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='MAPK_PP']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> MAPK_PP </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="MKK1" name="MKK">
      <listOfVariables>
        <variable id="MKK" name="MKK" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='MKK']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> MKK </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="MKK_P1" name="MKK_P">
      <listOfVariables>
        <variable id="MKK_P" name="MKK_P" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='MKK_P']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> MKK_P </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="MKKK1" name="MKKK">
      <listOfVariables>
        <variable id="MKKK" name="MKKK" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='MKKK']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> MKKK </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="MKKK_P1" name="MKKK_P">
      <listOfVariables>
        <variable id="MKKK_P" name="MKKK_P" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='MKKK_P']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> MKKK_P </ci>
      </math>
    </dataGenerator>
  </listOfDataGenerators>
  <listOfOutputs>
    <plot2D id="plot1" name="MAPK feedback (Kholodenko, 2000) (stochastic trace)">
      <listOfCurves>
```

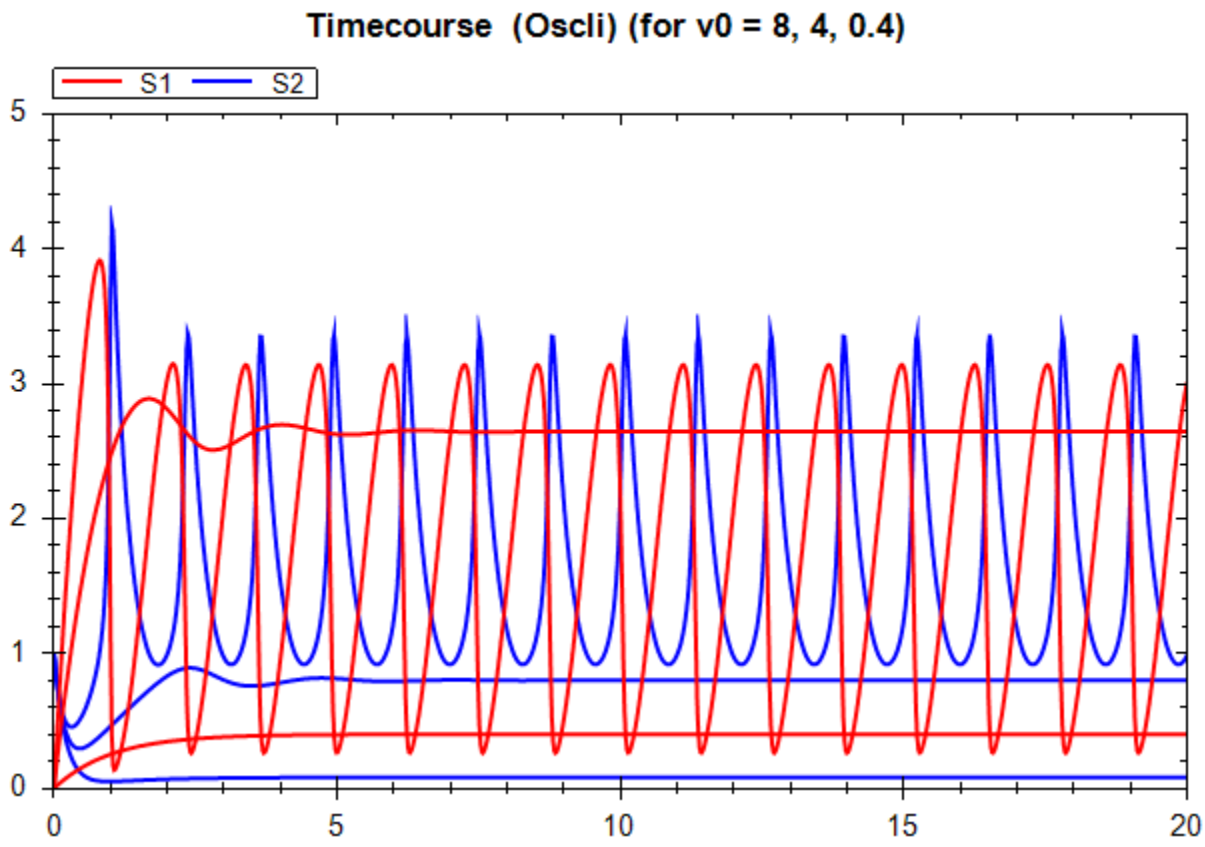
```
        <curve id="curve1" logX="false" logY="false" xDataReference="time1" yDataReference="MAPK1" />
        <curve id="curve2" logX="false" logY="false" xDataReference="time1" yDataReference="MAPK_P1" />
        <curve id="curve3" logX="false" logY="false" xDataReference="time1" yDataReference="MAPK_PP1" />
        <curve id="curve4" logX="false" logY="false" xDataReference="time1" yDataReference="MKK1" />
        <curve id="curve5" logX="false" logY="false" xDataReference="time1" yDataReference="MKKK1" />
        <curve id="curve6" logX="false" logY="false" xDataReference="time1" yDataReference="MKK_P1" />
        <curve id="curve7" logX="false" logY="false" xDataReference="time1" yDataReference="MKKK_P1" />
      </listOfCurves>
    </plot2D>
  </listOfOutputs>
</sedML>
```

1D Time course Parameter Scan

NOTE: Since this example produces three dimensional results (time, species concentration, multiple parameter values). Currently we do not have a way for post-processing these values. In my implementation of plots I allow higher dimensional values and flatten them by overlaying them onto the desired plot.

Here we have one nested simulation task running over a repeated uniform time course simulation (performing a deterministic simulation run) after each run the parameter value is changed.

The Results



The Description

```
<?xml version="1.0" encoding="utf-8"?>
<!-- Written by libSedML v1.1.4397.33034 see http://libsedml.sf.net -->
<sedML level="1" version="1" xmlns="http://sed-ml.org/">
  <listOfSimulations>
```

```
    <uniformTimeCourse id="timecourse1" initialTime="0" outputStartTime="0" outputEndTime="20"
numberOfPoints="1000">
      <algorithm kisaoID="KISAO:0000019" />
    </uniformTimeCourse>
    <nestedSimulation id="nested1" resetModel="true" originalTask="task2" range="current">
      <ranges>
        <vectorRange id="current">
          <value>8</value>
          <value>4</value>
          <value>0.4</value>
        </vectorRange>
      </ranges>
      <changes>
        <setValue target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J0_v0']"
range="current">
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <ci> current </ci>
          </math>
        </setValue>
      </changes>
    </nestedSimulation>
  </listOfSimulations>
  <listOfModels>
    <model id="model1" language="urn:sedml:language:sbml"
source="http://libsedml.svn.sourceforge.net/viewvc/libsedml/trunk/Samples/models/oscli.xml" />
  </listOfModels>
  <listOfTasks>
    <task id="task1" modelReference="model1" simulationReference="nested1" />
    <task id="task2" modelReference="model1" simulationReference="timecourse1" />
  </listOfTasks>
  <listOfDataGenerators>
    <dataGenerator id="time1" name="time">
      <listOfVariables>
        <variable id="time" name="time" taskReference="task1" target="time" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> time </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="J0_v0_1" name="J0_v0">
      <listOfVariables>
        <variable id="J0_v0" name="J0_v0" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J0_v0']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> J0_v0 </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="S1_1" name="S1">
      <listOfVariables>
        <variable id="S1" name="S1" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='S1']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> S1 </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="S2_1" name="S2">
      <listOfVariables>
        <variable id="S2" name="S2" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='S2']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> S2 </ci>
      </math>
    </dataGenerator>
  </listOfDataGenerators>
  <listOfOutputs>
    <plot2D id="plot1" name="Timecourse  (Oscli) (for v0 = 8, 4, 0.4)">
```

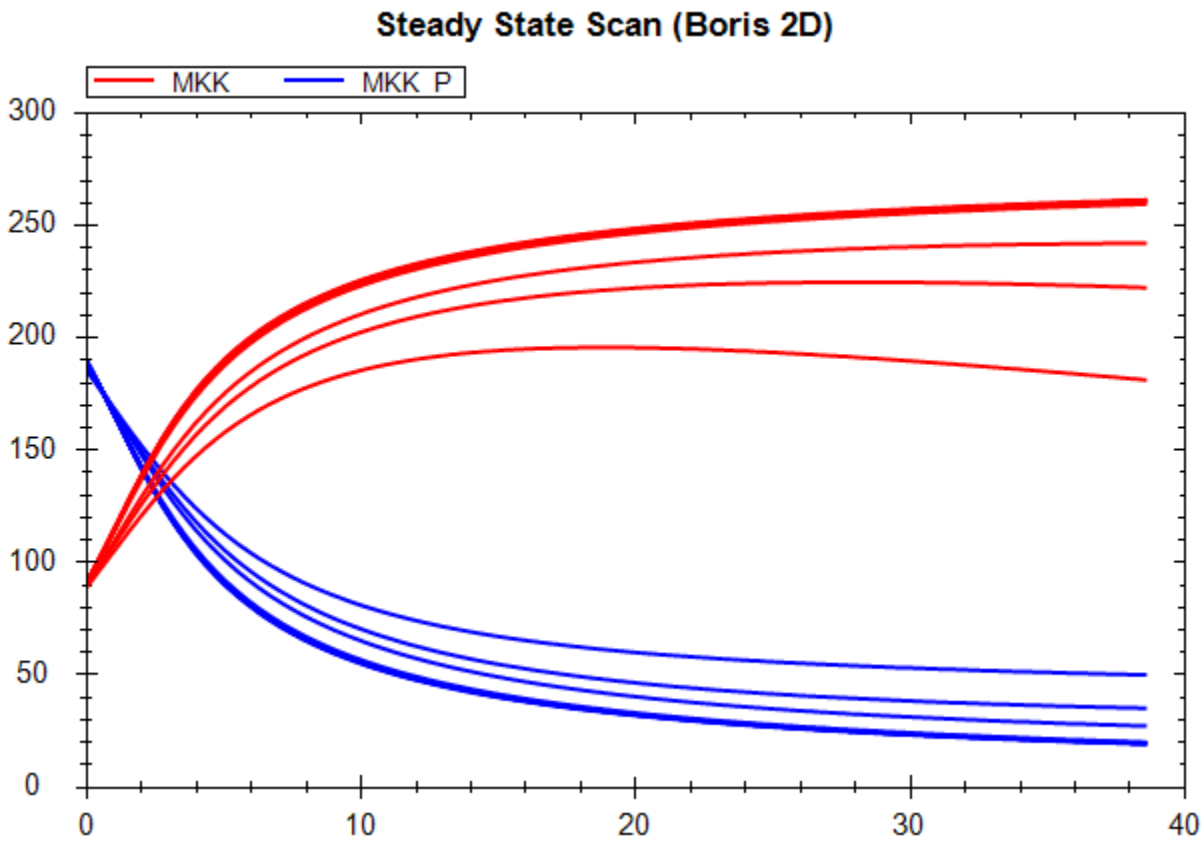
```
      <listOfCurves>
        <curve id="curve1" logX="false" logY="false" xDataReference="time1" yDataReference="S1_1" />
        <curve id="curve2" logX="false" logY="false" xDataReference="time1" yDataReference="S2_1" />
      </listOfCurves>
    </plot2D>
  </listOfOutputs>
</sedML>
```

2D Steady State Parameter Scan

NOTE: Since this example produces three dimensional results (species concentration, parameter1 values, parameter2 values). Currently we do not have a way for post-processing these values. In my implementation of plots I allow higher dimensional values and flatten them by overlaying them onto the desired plot.

Here we have one nested simulation task running over another nested simulation which runs over a oneStep task (performing a steady state computation). Each nested simulation task modifies a different parameter.

The Results



The Description

```
<?xml version="1.0" encoding="utf-8"?>
<!-- Written by libSedML v1.1.4397.34340 see http://libsedml.sf.net -->
<sedML level="1" version="1" xmlns="http://sed-ml.org/">
  <listOfSimulations>
    <oneStep id="steady1">
      <algorithm kisaoID="KISAO:0000282" />
```

```
    </oneStep>
    <nestedSimulation id="nested1" resetModel="false" originalTask="task3" range="current">
      <ranges>
        <vectorRange id="current">
          <value>1</value>
          <value>5</value>
          <value>10</value>
          <value>50</value>
          <value>60</value>
          <value>70</value>
          <value>80</value>
          <value>90</value>
          <value>100</value>
        </vectorRange>
      </ranges>
      <changes>
        <setValue target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J1_KK2']">
          <listOfVariables>
            <variable id="val" name="current loop value" target="//*[@id='current']" />
          </listOfVariables>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <ci> val </ci>
          </math>
        </setValue>
      </changes>
    </nestedSimulation>
    <nestedSimulation id="nested2" resetModel="false" originalTask="task2" range="current1">
      <ranges>
        <uniformRange id="current1" start="1" end="40" numberOfPoints="100" />
      </ranges>
      <changes>
        <setValue target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J4_KK5']"
range="current1">
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <ci> current1 </ci>
          </math>
        </setValue>
      </changes>
    </nestedSimulation>
  </listOfSimulations>
  <listOfModels>
    <model id="model1" language="urn:sedml:language:sbml" source="c:\users\fbergmann\documents\sbml
models\boris.xml" />
  </listOfModels>
  <listOfTasks>
    <task id="task1" modelReference="model1" simulationReference="nested1" />
    <task id="task2" modelReference="model1" simulationReference="steady1" />
    <task id="task3" modelReference="model1" simulationReference="nested2" />
  </listOfTasks>
  <listOfDataGenerators>
    <dataGenerator id="J4_KK5_1" name="J4_KK5">
      <listOfVariables>
        <variable id="J4_KK5" name="J4_KK5" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J4_KK5']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> J4_KK5 </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="J1_KK2_1" name="J1_KK2">
      <listOfVariables>
        <variable id="J1_KK2" name="J1_KK2" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J1_KK2']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> J1_KK2 </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="MKK_1" name="MKK">
```

```
      <listOfVariables>
        <variable id="MKK" name="MKK" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='MKK']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> MKK </ci>
      </math>
    </dataGenerator>
    <dataGenerator id="MKK_P_1" name="MKK_P">
      <listOfVariables>
        <variable id="MKK_P" name="MKK_P" taskReference="task1"
target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='MKK_P']" />
      </listOfVariables>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <ci> MKK_P </ci>
      </math>
    </dataGenerator>
  </listOfDataGenerators>
  <listOfOutputs>
    <plot2D id="plot1" name="Steady State Scan (Boris 2D)">
      <listOfCurves>
        <curve id="curve1" logX="false" logY="false" xDataReference="J4_KK5_1" yDataReference="MKK_1" />
        <curve id="curve2" logX="false" logY="false" xDataReference="J4_KK5_1" yDataReference="MKK_P_1" />
      </listOfCurves>
    </plot2D>
    <report id="report1" name="Steady State Values (Boris2D)">
      <listOfDataSets>
        <dataSet id="col0" dataReference="J4_KK5_1" label="" />
        <dataSet id="col1" dataReference="J1_KK2_1" label="" />
        <dataSet id="col2" dataReference="MKK_1" label="" />
        <dataSet id="col3" dataReference="MKK_P_1" label="" />
      </listOfDataSets>
    </report>
  </listOfOutputs>
</sedML>
```

References

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