

Simulation Experiment Description

Markup Language (SED-ML) :

Level 1 Version 3

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<http://identifiers.org/combine.specifications/sed-ml.level-1.version-3>

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1. Introduction

The number of available computational models of biological systems is growing at an ever increasing pace. At the same time, their size and complexity are also increasing. The need to build on existing studies by reusing models therefore becomes more imperative. It is now generally accepted that one needs to be able to exchange the biochemical and mathematical structure of models. The efforts to standardise the representation of computational models in various areas of biology, such as the *Systems Biology Markup Language* (SBML, [15]), *CellML* [8] or *NeuroML* [12], resulted in such an increase of the exchange and re-use of models. However, the description of the structure of models is not sufficient to enable the reproduction of simulation results. One also needs to describe the procedures the models are subjected to, as described by the *Minimum Information About a Simulation Experiment (MIASE)* [22].

This document presents Level 1 Version 3 of the *Simulation Experiment Description Markup Language* (SED-ML), a computer-readable format for encoding simulation experiments. SED-ML files are encoded in the *Extensible Markup Language* (XML) [4]. The SED-ML format is defined by an XML Schema [11]. Level 1 Version 3 is the successor of Level 1 Version 2 and Level 1 Version 1, which is described in [23].

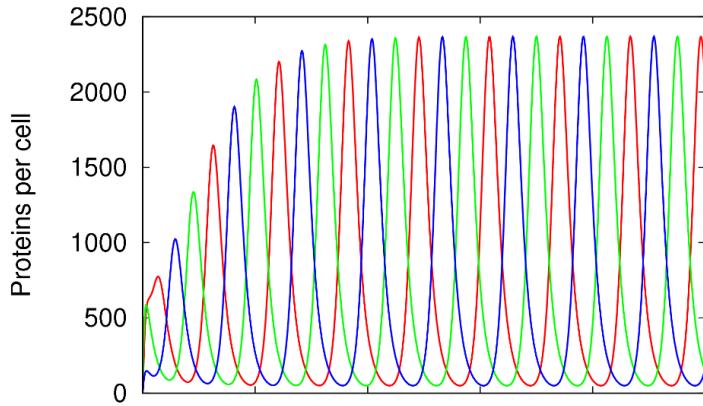


Figure 1.1: Time-course simulation of the repressor model, imported from BioModels Database and simulated in COPASI. The number of repressor proteins lacI, tetR and cI is shown. (taken from [22])

1.1 Motivation: A sample experiment

TODO MK: add sample experiment to examples in appendix

The *repressor* is a rather small, though famous, model that is capable of displaying rich and variable behaviors. We will use this model to demonstrate how a simulation experiment can be described simply and effectively.

The *repressor* is a synthetic oscillating network of transcription regulators in Escherichia coli [10]. The network is composed of the three repressor genes Lactose Operon Repressor (lacI), Tetracycline Repressor (tetR) and Repressor CI (cI), which code for proteins binding to the promoter of the other, blocking their transcription. The three inhibitions together in tandem, form a cyclic negative-feedback loop. To describe the interactions of the molecular species involved in the network, the authors built a simple mathematical model of coupled first-order differential equations. All six molecular species included in the network (three mRNAs, three repressor proteins) participated in creation (transcription/translation) and degradation processes. The model was used to determine the influence of the various parameters on the dynamic behavior of the system. In particular, parameter values were sought which induce stable oscillations in the concentrations of the system components. Oscillations in the levels of the three repressor proteins are obtained by numerical integration.

1.1.1 A time-course simulation

The first experiment we intend to run on the model is the simulation that will lead to the oscillation shown in Figure 1c of the reference publication [10]. This simulation experiment can be described as:

1. Import the model identified by the Unified Resource Identifier (URI) [3] urn:miriam:biomodels_db:BIOMD0000000012.
2. Select a deterministic method.
3. Run a uniform time course simulation for 1000 min with an output interval of 1 min.
4. Plot the amount of `lacI`, `tetR` and `cI` against time in a 2D Plot.

Following those steps and performing the simulation in the simulation tool COPASI [13] led to the result shown in Figure 1.1.

1.1.2 Applying pre-processing

The fine-tuning of the model can be shown by adjusting parameters before simulation. When changing the initial values of the parameters *protein copies per promoter* and *leakiness in protein copies per promoter* the system's behavior switches from sustained oscillation to asymptotic steady-state. The adjustments leading to that behavior may be described as:

1. Import the model as above.



Figure 1.2: Time-course simulation of the repressilator model, imported from BioModels Database and simulated in COPASI after modification of the initial values of the protein copies per promoter and the leakiness in protein copies per promoter. The number of repressor proteins lacI, tetR and cI is shown. (taken from [22])

2. Change the value of the parameter `tps_repr` from “0.0005” to “1.3e-05”.
3. Change the value of the parameter `tps_active` from “0.5” to “0.013”.
4. Select a deterministic method.
5. Run a uniform time course for the duration of 1000 min with an output interval of 1 min.
6. Plot the amount of lacI, tetR and cI against time in a 2D Plot.

Figure 1.2 shows the result of the simulation.

1.1.3 Applying post-processing

The raw numerical output of the simulation steps may be subjected to data post-processing before plotting or reporting. In order to describe the production of a normalized plot of the time-course in the first example (section 1.1.1), depicting the influence of one variable on another (in phase-planes), one could define the following further steps:

(Please note that the description steps 1 - 4 remain as given in section 1.1.1 above.)

5. Collect lacI(t) , tetR(t) and cI(t).
6. Compute the highest value for each of the repressor proteins, $\max(\text{lacI}(t))$, $\max(\text{tetR}(t))$, $\max(\text{cI}(t))$.
7. Normalize the data for each of the repressor proteins by dividing each time point by the maximum value, i. e. $\text{lacI}(t)/\max(\text{lacI}(t))$, $\text{tetR}(t)/\max(\text{tetR}(t))$, and $\text{cI}(t)/\max(\text{cI}(t))$.
8. Plot the normalized lacI protein as a function of the normalized cI, the normalized cI as a function of the normalized tetR protein, and the normalized tetR protein against the normalized lacI protein in a 2D plot.

Figure 1.3 on the following page illustrates the result of the simulation after post-processing of the output data.

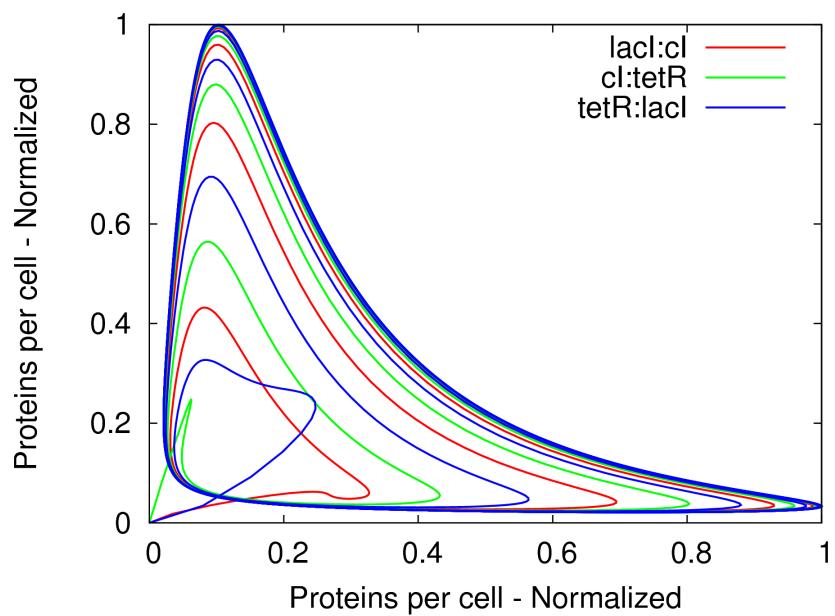


Figure 1.3: Time-course simulation of the repressilator model, imported from BioModels Database and simulated in COPASI, showing the normalized temporal evolution of repressor proteins *lacI*, *tetR* and *cI* in phase-plane. (taken from [22])

2. SED-ML technical specification

This document represents the technical specification of SED-ML. We also provide an XML Schema [21] and a UML class diagram representation of that XML Schema (Appendix A). UML class diagrams are a subset of the *Unified Markup Language* notation (UML, [19]). Sample experiment descriptions are given as XML snippets that comply with the XML Schema.

It should however be noted that some of the concepts of SED-ML cannot be captured using XML Schema alone. In these cases it is this specification that is considered the normative document.

2.1 Conventions used in this document

2.1.1 UML Classes

A SED-ML UML class (Figure 2.1) consists of a class name (**ClassName**) and a number of attributes (**attribute**) each of a specific data type (**type**). The SED-ML UML specification does not make use of UML operations.



Figure 2.1: SED-ML UML class with class names and attributes

SED-ML class names always begin with upper case letters. If they are composed of different words, the camel case style is used, as in e.g. **DataGenerator**.

2.1.2 UML Relationships

2.1.2.1 UML Relation Types

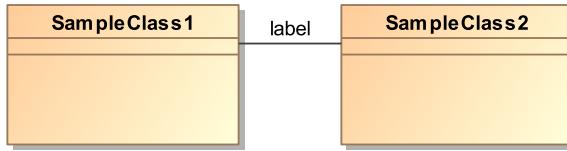


Figure 2.2: UML Class connectors

Links between classes specify the connection of objects with each other (Figure 2.2). The different relation types used in the SED-ML specification include aggregation, composite aggregation, and generalisation. The label on the line is called symbol (**label**) and describes the relation of the objects of both classes.

The **association** (Figure 2.3) indicates the existence of a connection between the objects of the participating classes. Often associations are directed to show how the label should be read (in which direction). Associations can be uni-directional (one arrowhead), or bidirectional (zero or two arrowheads).

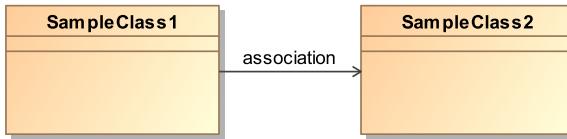


Figure 2.3: UML Association

The **aggregation** (Figure 2.4 on the following page, top) indicates that the objects of the participating classes are connected in a way that one class (**Whole**) consists of several parts (**Part**). In an aggregation, the parts may be independent of the whole. For example, a car (**Whole**) has several parts called wheel (**Part**); however, the wheels can exist independently of the car while the car requires the wheels in order to function.

The **composite aggregation** (Figure 2.4 on the next page, bottom) indicates that the objects of the participating classes are connected in a way that one class (**Whole**) consists of several parts (**Part**). In

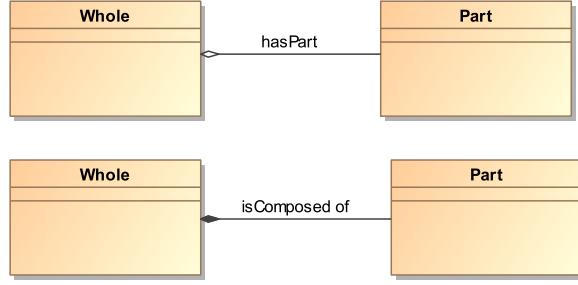


Figure 2.4: UML Aggregation (top) and Composition (bottom)

contrast to the aggregation, the subelements (**Part**) are dependent on the parent class (**Whole**). An example is that a university (**Whole**) consists of a number of departments (**Part**) which have a so-called “lifetime responsibility” with the university, e.g. if the university vanishes, the departments will vanish with it [1].

The **generalisation** (Figure 2.5) allows to extend classes (**BaseClass**) by additional properties. The derived class (**DerivedClass**) inherits all properties of the base class and defines additional ones. In the given example, an instance of **DerivedClass** has two attributes **attribute1** and **attribute2**.

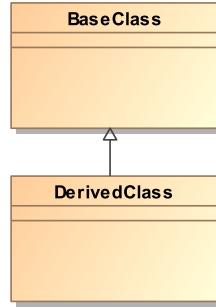


Figure 2.5: UML Generalisation

2.1.2.2 UML multiplicity

UML multiplicity defines the number of objects in one class that can be related to one object in the other class (also known as **cardinality**). Possible types of multiplicity include values (1), ranges (1..4), intervals (1,3,9), or combinations of ranges and intervals. The standard notation for “many” is the asterisk (*).

Multiplicity can be defined for both sides of a relationship between classes. The default relationship is “many to many”. The example in Figure 2.6 expresses that a class is given by a professor, and a professor might give one to many classes.

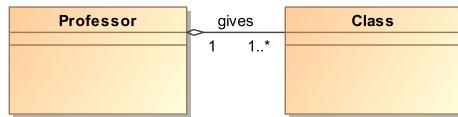


Figure 2.6: UML Multiplicity in an Aggregation

2.1.3 XML Schema language elements

The main building blocks of an XML Schema specification are:

- simple and complex types
- element specifications
- attribute specifications

XML Schema [definitions](#) create new types, [declarations](#) define new elements and attributes. The definition of new (simple and complex) types can be based on a number of already existing, predefined types (string, boolean, float). Simple types are restrictions or extensions of predefined types. Complex types describe how attributes can be assigned to elements and how elements can contain further elements. The current SED-ML XML Schema only makes use of *complex type definitions*. An example for a complex type definition is given in Listing 2.1:

```

1 <xs:element name="computeChange">
2   <xs:complexType>
3     <xs:complexContent>
4       <xs:extension base="SEDBase">
5         <xs:sequence>
6           <xs:element ref="listOfVariables" minOccurs="0" />
7           <xs:element ref="listOfParameters" minOccurs="0" />
8           <xs:element ref="math" />
9         </xs:sequence>
10        <xs:attribute name="target" use="required" type="xs:token" />
11      </xs:extension>
12    </xs:complexContent>
13  </xs:complexType>
14 </xs:element>
```

Listing 2.1: Complex Type definition of the SED-ML `computeChange` element

It shows the declaration of an element called `computeChange` that is used in SED-ML to change mathematical expressions. The element is defined using an *unnamed* complex type which is built of further elements called `listOfVariables`, `listOfParameters`, and `math`. Additionally, the element `computeChange` has an attribute `target` declared. Please note that the definition of the elements inside the complex type are only referred to and will be found elsewhere in the schema.

The nesting of elements in the schema can be expressed using the `xs:sequence` (a sequence of elements), `xs:choice` (an alternative of elements to choose from), or `xs:all` (a set of elements that can occur in any order) concepts. The current SED-ML XML Schema only uses the *sequence* of elements.

2.1.3.1 Multiplicities

The standard multiplicity for each defined `element` is 1. Explicit multiplicity is to be defined using the `minOccurs` and `maxOccurs` attributes inside the complex type definition, as shown in Listing 2.2.

```

1 <xs:element name="dataGenerator">
2   <xs:complexType>
3     <xs:complexContent>
4       <xs:extension base="SEDBase">
5         <xs:sequence>
6           <xs:element ref="listOfVariables" minOccurs="0" />
7           <xs:element ref="listOfParameters" minOccurs="0" />
8           <xs:element ref="math" />
9         </xs:sequence>
10        <xs:attributeGroup ref="idGroup" />
11      </xs:extension>
12    </xs:complexContent>
13  </xs:complexType>
14 </xs:element>
```

Listing 2.2: Multiplicity for complex types in XML Schema

In this example, the `dataGenerator` type is build of a sequence of three elements: The `listOfVariables` element is not necessary for the definition of a valid `dataGenerator` XML structure (it may occur 0 times or once). The same is true for the `listOfParameters` element (it may as well occur 0 times or once). The `math` element, however, uses the implicit standard multiplicity – it must occur exactly 1 time in the `dataGenerator` specification.

2.1.4 Type extensions

XML Schema offers mechanisms to restrict and extend previously defined complex types. Extensions add element or attribute declarations to existing types, while restrictions restrict the types by adding further characteristics and requirements (facets) to a type. An example for a type extension is given in Listing 2.3.

```

1   <xs:element name="sedML">
2       <xs:complexType>
3           <xs:complexContent>
4               <xs:extension base="SEDBase">
5                   <xs:sequence>
6                       <xs:element ref="listOfSimulations" minOccurs="0" />
7                       <xs:element ref="listOfModels" minOccurs="0" />
8                       <xs:element ref="listOfTasks" minOccurs="0" />
9                       <xs:element ref="listOfDataGenerators" minOccurs="0" />
10                      <xs:element ref="listOfOutputs" minOccurs="0" />
11                  </xs:sequence>
12                  <xs:attribute name="level" type="xs:decimal" use="required"
13                      fixed="1" />
14                  <xs:attribute name="version" type="xs:decimal" use="required"
15                      fixed="2" />
16              </xs:extension>
17          </xs:complexContent>
18      </xs:complexType>
19  </xs:element>

```

Listing 2.3: Definition of the sedML type through extension of SEDBase in SED-ML

The **sedML** element is an extension of the previously defined **SEDBase** type. It extends **SEDBase** by a sequence of five additional elements (**listOfSimulations**, **listOfModels**, **listOfTasks**, **listOfDataGenerators**, and **listOfOutputs**) and two new attributes **version** and **level**.

2.2 Concepts used in SED-ML

2.2.1 MathML subset

SED-ML files may encode pre-processing steps applied to the computational model, as well as post processing applied to the raw simulation data before output. The corresponding mathematical expressions are encoded using MathML 2.0 [5]. MathML is an international standard for encoding mathematical expressions using XML. It is also used as a representation of mathematical expressions in other formats, such as SBML and CellML, two of the languages supported by SED-ML.

2.2.1.1 MathML elements

In order to support for the SED-ML format easier to implement we restrict the MathML subset to the following elements:

- *token*: `cn`, `ci`, `csymbol`, `sep`
- *general*: `apply`, `piecewise`, `piece`, `otherwise`, `lambda`
- *relational operators*: `eq`, `neq`, `gt`, `lt`, `geq`, `leq`
- *arithmetic operators*: `plus`, `minus`, `times`, `divide`, `power`, `root`, `abs`, `exp`, `ln`, `log`, `floor`, `ceiling`, `factorial`
- *logical operators*: `and`, `or`, `xor`, `not`
- *qualifiers*: `degree`, `bvar`, `logbase`
- *trigonometric operators*: `sin`, `cos`, `tan`, `sec`, `csc`, `cot`, `sinh`, `cosh`, `tanh`, `sech`, `csch`, `coth`, `arcsin`, `arccos`, `arctan`, `arcsec`, `arccsc`, `arccot`, `arcsinh`, `arccosh`, `arctanh`, `arcsech`, `arccsch`, `arccoth`
- *constants*: `true`, `false`, `notanumber`, `pi`, `infinity`, `exponentiale`
- *MathML annotations*: `semantics`, `annotation`, `annotation-xml`

2.2.1.2 MathML Symbols

All the operations listed above only operate on *scalar* values. However, as one of SED-ML's aims is to provide post processing on the results of simulation experiments, we need to enhance this basic set of operations by some aggregate functions. Therefore a defined set of MathML symbols that represent vector values are supported by SED-ML Level 1 Version 3. To simplify the use of SED-ML L1V2 the only symbols to be used are the identifiers of variables defined in the `listOfVariables` of `DataGenerators`. These variables represent the data collected from the simulation experiment with the associated task.

2.2.1.3 MathML functions

The following aggregate functions are available for use in SED-ML Level 1 Version 3.

- *min*: Where the minimum of a variable represents the smallest value the simulation experiment yielded (Listing 2.4).

```
1 <apply>
2   <csymbol encoding="text" definitionURL="http://sed-ml.org/#min">
3     min
4   </csymbol>
5   <ci> variableId </ci>
6 </apply>
```

Listing 2.4: Example for the use of the MathML `min` function.

- *max*: Where the maximum of a variables represents the largest value the simulation experiment yielded (Listing 2.5).

```
1 <apply>
2   <csymbol encoding="text" definitionURL="http://sed-ml.org/#max">
3     max
4   </csymbol>
5   <ci> variableId </ci>
6 </apply>
```

Listing 2.5: Example for the use of the MathML `max` function.

- *sum*: All values of the variable returned by the simulation experiment are summed (Listing 2.6).

```

1 <apply>
2   <csymbol encoding="text" definitionURL="http://sed-ml.org/#sum">
3     sum
4   </csymbol>
5   <ci> variableId </ci>
6 </apply>

```

Listing 2.6: Example for the use of the MathML `sum` function.

- *product*: All values of the variable returned by the simulation experiment are multiplied (Listing 2.7).

```

1 <apply>
2   <csymbol encoding="text" definitionURL="http://sed-ml.org/#product">
3     product
4   </csymbol>
5   <ci> variableId </ci>
6 </apply>

```

Listing 2.7: Example for the use of the MathML `product` function.

These represent the only exceptions. At this point SED-ML Level 1 Version 3 does not define a complete algebra of vector values. For more information see the description of the [DataGenerator](#) class.

2.2.2 URI Scheme

URIs are needed at different points in SED-ML Level 1 Version 3. Firstly, they are the preferred mechanism to refer to model encodings. Secondly, they are used to specify the language of the referenced model. Thirdly, they enable addressing implicit model variables. Finally, annotations of SED-ML elements should be provided with a standardised annotation scheme.

The use of a standardised URI Scheme ensures long-time availability of particular information that can unambiguously be identified.

2.2.2.1 Model references

The preferred way for referencing a model from a SED-ML file is adopted from the [MIRIAM URI Scheme](#). MIRIAM enables identification of a data resource (in this case a model resource) by a predefined URN. A data entry inside that resource is identified by an ID. That way each single model in a particular model repository can be unambiguously referenced. To become part of MIRIAM resources, a model repository must ensure permanent and consistent model references, that is stable IDs.

One model repository that is part of MIRIAM resources is the [BioModels Database](#) [17]. Its data resource name in MIRIAM is `urn:miriam:biomodels.db`. To refer to a particular model, a standardised identifier scheme is defined in [MIRIAM Resources](#)¹. The ID entry maps to a particular model in the model repository. That model is never deleted. A sample BioModels Database ID is `BIOMD0000000048`. Together with the data resource name it becomes unambiguously identifiable by the URN `urn:miriam:biomodels.db:BIOMD0000000048` (in this case referring to the 1999 Kholodenko model on EGFR signaling).

SED-ML recommends to follow the above scheme for model references, if possible. SED-ML does not specify how to resolve the URNs. However, MIRIAM Resources offers web services to do so². For the above example of the `urn:miriam:biomodels.db:BIOMD0000000048` model, the resolved URL may look like:

- <http://biomodels.caltech.edu/BIOMD0000000048> or
- <http://www.ebi.ac.uk/biomodels-main/BIOMD0000000048>

depending on the physical location of the resource chosen to resolve the URN.

An alternative means to obtain a model may be to provide a single resource containing necessary models and a SED-ML file. Although a specification of such a resource is beyond the scope of this document, one proposal – COMBINE archive format – is described in Appendix 3. Further information on the `source` attribute referencing the model location is provided in Section 2.4.4.2.

¹<http://www.ebi.ac.uk/miriam/>

²<http://www.ebi.ac.uk/miriam/>

2.2.2.2 Language references

To specify the language a model is encoded in, a set of pre-defined SED-ML URNs can be used. The structure of SED-ML language URNs is `urn:sedml:language:name.version`. SED-ML allows to specify a model representation format very generally as being XML, if no standardised representation format has been used to encode the model. On the other hand, one can be as specific as defining a model being in a particular version of a language, as “SBML Level 2, Version 2, Revision 1”.

The list of URNs is available from <http://sed-ml.org/>. Further information on the `language` attribute is provided in Section 2.4.4.1.

2.2.2.3 Implicit variables

Some variables used in an experiment are not explicitly defined in the model, but may be implicitly contained in it. For example, to plot a variable’s behaviour over time, that variable is defined in an SBML model, while `time` is not explicitly defined.

To overcome this issue and allow SED-ML to refer to such variables in a common way, the notion of *implicit variables* is used. Those variables are called `symbols` in SED-ML. They are defined following the idea of MIRIAM URNs and using the SED-ML URN scheme. The structure of the URNs is `urn:sedml:symbol:implicit variable`. To refer from a SED-ML file to the definition of `time`, for example, the URN is `urn:sedml:symbol:time`.

The list of predefined symbols is available from the SED-ML site on <http://sed-ml.org/>. From that source, a mapping of SED-ML symbols on existing concepts in the languages supported by SED-ML is provided.

2.2.2.4 Annotations

When annotating SED-ML elements with semantic `annotations`, the [MIRIAM URI Scheme](#) should be used. In addition to providing the data type (e.g. PubMed) and the particular data entry inside that data type (e.g. 10415827), the relation of the annotation to the annotated element should be described using the standardised [biomodels.net qualifier](#). The list of qualifiers, as well as further information about their usage, is available from <http://www.biomodels.net/qualifiers/>.

2.2.3 XPath usage

XPath is a language for finding information in an XML document [6]. Within Level 1 Version 3, XPath version 1 expressions are used to identify nodes and attributes within an XML representation of a biological model in the following ways:

1. Within a `Variable` definition, where XPath identifies the model variable required for manipulation in SED-ML.
2. Within a `Change` definition, where XPath is used to identify the target XML to which a change should be applied.

For proper application, XPath expressions should contain prefixes that allow their resolution to the correct XML namespace within an XML document. For example, the XPath expression referring to a species `X` in an SBML model:

`/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='X'] ✓ -CORRECT`

is preferable to

`/sbml/model/listOfSpecies/species[@id='X'] ✗ -INCORRECT`

which will only be interpretable by standard XML software tools if the SBML file declares no namespaces (and hence is invalid SBML).

Following the convention of other XPath host languages such as XPointer and XSLT, the prefixes used within XPath expressions must be declared using namespace declarations within the SED-ML document, and be in-scope for the relevant expression. Thus for the correct example above, there must also be an ancestor element of the node containing the XPath expression that has an attribute like:

`xmlns:sbml='http://www.sbml.org/sbml/level3/version1/core'`

(a different namespace URI may be used; the key point is that the prefix ‘sbml’ must match that used in the XPath expression).

2.2.4 KiSAO

The Kinetic Simulation Algorithm Ontology (KiSAO, [7]) is used in SED-ML to specify simulation algorithms and uniquely identify algorithm parameters. KiSAO is a community-driven approach of classifying and structuring simulation approaches by model characteristics and numerical characteristics. The ontology is available in OWL format from BioPortal at <http://purl.bioontology.org/ontology/KiSAO>.

SED-ML refers to terms from KiSAO as referencing a simulation algorithm, or its parameters, solely through a name is error prone and ambiguous. After all, typing mistakes or language differences complicate the identification of the correct algorithm. Additionally, many algorithms exist under multiple names or abbreviation.

The identification of a simulation algorithm through KiSAO not only identifies the simulation algorithm to be used in the SED-ML simulation, it also enables software to find a related algorithm, if the specific implementation is not available. For example, software could decide to use the CVODE integration library for an analysis instead of a specific Runge Kutta 4,5 implementation.

Should a particular simulation algorithm not exist within KiSAO, please request one from the project homepage at <http://www.biomodels.net/kisao/>.

2.2.5 SED-ML resources

Information on SED-ML can be found on <http://sed-ml.org>. The SED-ML XML Schema, the UML schema and related implementations, libraries, validators and so on can be found on the SED-ML sourceforge project page <http://sed-ml.svn.sourceforge.net/>.

2.3 General attributes and classes

In this section we introduce attributes and concepts used repeatedly throughout the SED-ML specification.

2.3.1 id

Most objects in SED-ML carry an `id` attribute. The `id` attribute, if it exists for an object, is always required and identifies SED-ML constituents unambiguously. The data type for `id` is `SIId` which is a datatype derived from the basic XML type `string`, but with restrictions about the characters permitted and the sequences in which those characters may appear. The definition is shown in Figure 2.7.

```
letter ::= 'a'...'z', 'A'...'Z'  
digit ::= '0'...'9'  
idChar ::= letter | digit | '_'  
SIId ::= ( letter | '_' ) idChar*
```

Figure 2.7: The definition of the type `SIId`

For a detailed description see also the SBML specification on the “Type `SIId`” [14, p. 11].

All `ids` have a global scope, i. e. the `id` must be unambiguous throughout a whole SED-ML document. As such it identifies the constituent it is related to.

An example for a defined `id` is given in Listing 2.8.

```
1 <model id="m00001" language="urn:sedml:language:sbml" source="urn:miriam:biomodels.db:BIOMD0000000012">  
2 [MODEL DEFINITION]  
3 </model>
```

Listing 2.8: SED-ML identifier definition, e. g. for a model

The defined model carries the `id m00001`. If the model is referenced elsewhere in the SED-ML document, it is referred to by that `id`.

2.3.2 name

Besides an `id`, a SED-ML constituent may carry an optional `name`. However, names do not have identifying character; several SED-ML constituents may carry the same name. The purpose of the `name` attribute is to keep a human-readable name of the constituent, e. g. for display to the user. In the XML Schema representation, names are of the data type `String`.

Listing 2.9 extends the model definition in Listing 2.8 by a model name.

```
1 <model id="m00001" name="Circadian oscillator" language="urn:sedml:language:sbml" source="urn:miriam:biomodels.db:BIOMD0000000012">  
2 [MODEL DEFINITION]  
3 </model>
```

Listing 2.9: SED-ML name definition, e. g. for a model

2.3.3 SEDBase

`SEDBase` is the base class of SED-ML Level 1 Version 3. All other classes are derived from it. As such it provides means to attach additional information on all other classes (Figure 2.8 on the next page). That information can be specified by human readable `Notes` or custom `Annotations`.

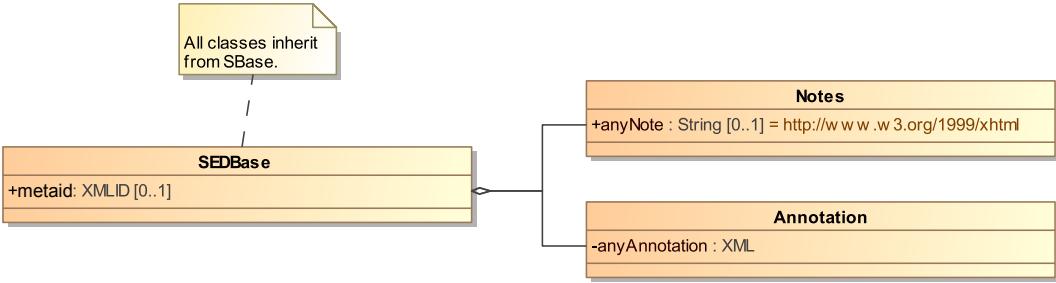


Figure 2.8: The *SEDBase* class

Table 2.1 shows all attributes and sub-elements for the *SEDBase* element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
sub-elements	description
notes ^o	page 19
annotation ^o	page 20

Table 2.1: Attributes and nested elements for *SEDBase*. xy^o denotes optional elements and attributes.

2.3.3.1 *metaid*

The main purpose of the *metaid* attribute is to attach semantic annotations in form of the *Annotation* class to SED-ML elements. The type of *metaid* is XML ID and as such the *metaid* attribute is globally unique throughout the whole SED-ML document.

An example showing how to link a semantic annotation to a SED-ML object via the *metaid* is given in the *Annotation* class description.

2.3.3.2 *Notes*

A *note* is considered a human-readable description of the element it is assigned to. It serves to display information to the user. Instances of the *Notes* class may contain any valid XHTML [20], ranging from short comments to whole HTML pages for display in a Web browser. The namespace URL for XHTML content inside the *Notes* class is <http://www.w3.org/1999/xhtml>. It may either be declared in the *sedML XML element*, or directly used in top level XHTML elements contained within the *notes* element. For further options of how to set the namespace and detailed examples, please refer to [14, p. 14].

Table 2.2 shows all attributes and sub-elements for the *Notes* element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
xmlns:string “http://www.w3.org/1999/xhtml”	page 22
sub-elements	
<i>well-formed content permitted in XHTML</i>	

Table 2.2: Attributes and nested elements for *Notes*. xy^o denotes optional elements and attributes.

Notes does not have any further sub-elements defined in SED-ML, nor attributes associated with it.

Listing 2.10 shows the use of the *notes* element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <sedML [...]>
2   <notes>
3     <p xmlns="http://www.w3.org/1999/xhtml">The enclosed simulation description shows the oscillating
      behaviour of
4       the Repressilator model using deterministic and stochastic simulators.</p>
5   </notes>
6 </sedML>

```

Listing 2.10: *The notes element*

In this example, the namespace declaration is inside the `notes` element and the note is related to the `sedML` root element of the SED-ML file. A note may, however, occur inside *any* SED-ML XML element, except `note` itself and `annotation`.

2.3.3.3 Annotation

An `annotation` is considered a computer-processable piece of information. Annotations may contain any valid XML content. For further guidelines on how to use annotations, we would like to encourage the reading of the corresponding section in the SBML specification [14, pp. 14-16]. The style of annotations in SED-ML is briefly described in Section 2.2.4 on page 16.

Table 2.3 shows all attributes and sub-elements for the `Annotation` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
<i>none</i>	
sub-elements	description
<i>none</i> in the SED-ML namespace	

Table 2.3: *Attributes and nested elements for Annotation.* xy^o denotes optional elements and attributes.

Listing 2.11 shows the use of the `annotation` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <sedML>
2   [...]
3   <model id="model1" metaid="_001" language="urn:sedml:language:cellml"
4     source="http://models.cellml.org/workspace/leloup_gonze_goldbeter_1999/@rawfile/
      d6613d7e1051b3eff2bb1d3d419a445bb8c754ad/leloup_gonze_goldbeter_1999_a.cellml" >
5     <annotation>
6       <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#"
7         xmlns:bqmodel="http://biomodels.net/model-qualifiers/">
8         <rdf:Description rdf:about="#_001">
9           <bqmodel:isDescribedBy>
10            <rdf:Bag>
11              <rdf:li rdf:resource="urn:miriam:pubmed:10415827"/>
12            </rdf:Bag>
13          </bqmodel:isDescribedBy>
14        </rdf:Description>
15      </rdf:RDF>
16    </annotation>
17  </model>
18  [...]
19 </sedML>

```

Listing 2.11: *The annotation element*

In that example, a SED-ML `model` element is annotated with a reference to the original publication. The `model` contains an `annotation` that uses the `biomodels.net model-qualifier` `isDescribedBy` to link to the external resource `urn:miriam:pubmed:10415827`. In natural language the annotation content could be interpreted as “The model *is described by* the published article available from *pubmed* under ID *10643740*”. The example annotation follows the proposed `URI Scheme` suggested by the MIRIAM reference standard. The MIRIAM URN can be resolved to the PubMED (<http://pubmed.gov>) publication with ID 10415827, namely the article “Alternating oscillations and chaos in a model of two coupled biochemical oscillators driving successive phases of the cell cycle.” published by Romond et al. in 1999.

2.3.4 SED-ML top level element

Each SED-ML Level 1 Version 3 document has a main class called SED-ML which defines the document's structure and content (Figure 2.9). It consists of several parts; the parts are all connected to the SED-ML class through aggregation: the DataDescription class (for resolving external data, see Section 2.4.1), the Model class (for model specification, see Section 2.4.4), the Simulation class (for simulation setup specification, see Section 2.4.6), the AbstractTask class (for the linkage of models and simulation setups, see Section 2.4.7), the DataGenerator class (for the definition of post-processing, see Section 2.4.10), and the Output class (for the output specification, see Section 2.4.11). All of them are shown in Figure 2.9 and will be explained in more detail in the relevant sections of this document.

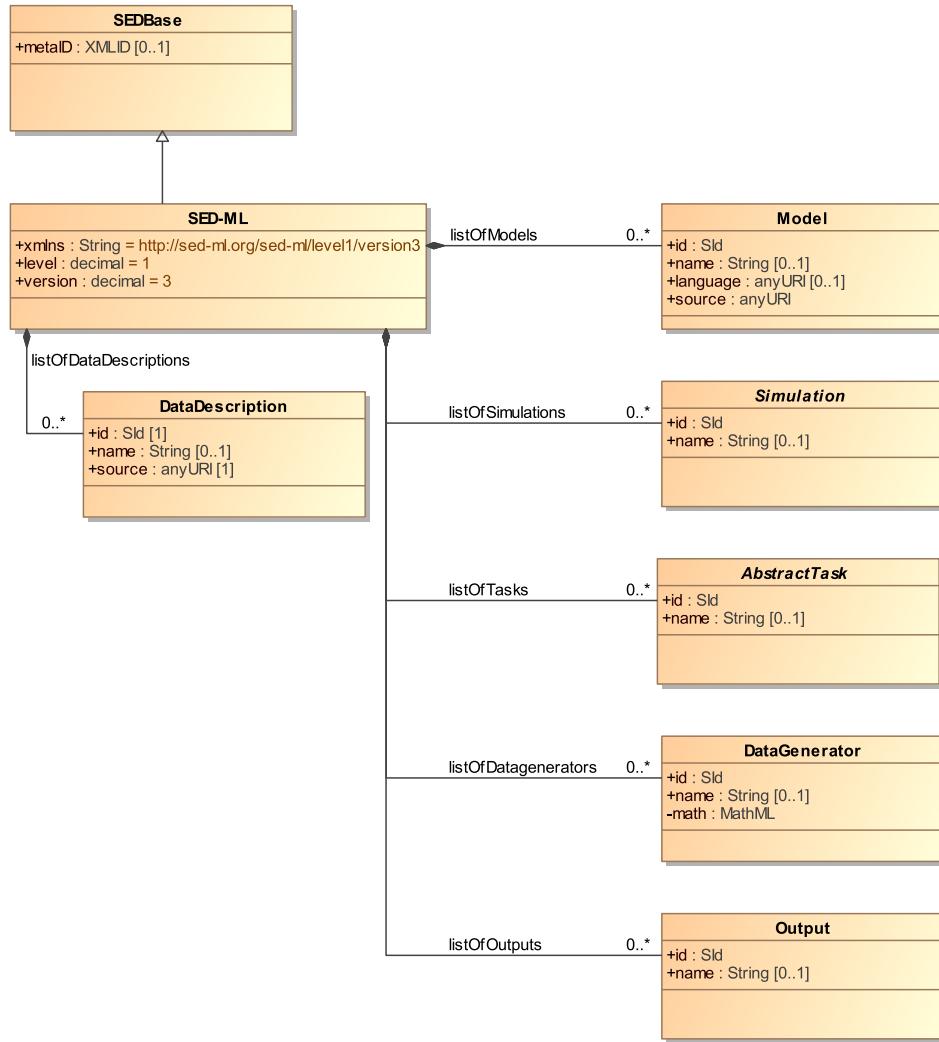


Figure 2.9: The sub-classes of SED-ML

Table 2.4 on the next page shows all attributes and sub-elements for the SED-ML element as defined by the SED-ML Level 1 Version 3 XML Schema.

A SED-ML document needs to have the SED-ML namespace defined through the mandatory `xmlns` attribute. In addition, the SED-ML `level` and `version` attributes are mandatory.

The basic XML structure of a SED-ML file is shown in listing 2.12.

```

1  <?xml version="1.0" encoding="utf-8"?>
2  <sedML xmlns:math="http://www.w3.org/1998/Math/MathML"
3      xmlns="http://sed-ml.org/sed-ml/level1/version3" level="1" version="3">
4      <listOfDataDescriptions />
5      [DATA REFERENCES AND TRANSFORMATIONS]
  
```

attribute	description
metaid ^o	page 19
xmlns	page 22
level	page 22
version	page 22
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
listOfDataDescriptions ^o	page ??
listOfModels ^o	page 29
listOfSimulations ^o	page 30
listOfTasks ^o	page 31
listOfDataGenerators ^o	page 31
listOfOutputs ^o	page 32

Table 2.4: Attributes and nested elements for [SED-ML](#). xy^o denotes optional elements and attributes.

```

6  <listOfModels />
7  [MODEL REFERENCES AND APPLIED CHANGES]
8  <listOfSimulations />
9  [SIMULATION SETUPs]
10 <listOfTasks />
11 [MODELS LINKED TO SIMULATIONS]
12 <listOfDataGenerators />
13 [DEFINITION OF POST-PROCESSING]
14 <listOfOutputs />
15 [DEFINITION OF OUTPUT]
16 </sedML>

```

Listing 2.12: The SED-ML root element

The root element of each SED-ML XML file is the `sedML` element, encoding `version` and `level` of the file, and setting the necessary namespaces. Nested inside the `sedML` element are the six lists serving as containers for the encoded data (`listOfDataDescriptions` for all external data sources, `listOfModels` for all models, `listOfSimulations` for all simulations, `listOfTasks` for all tasks, `listOfDataGenerators` for all post-processing definitions, and `listOfOutputs` for all output definitions).

2.3.4.1 `xmlns`

The `xmlns` attribute declares the namespace for the SED-ML document. The pre-defined namespace for SED-ML documents is <http://sed-ml.org/sed-ml/level1/version3>.

In addition, SED-ML makes use of the `MathML` namespace <http://www.w3.org/1998/Math/MathML> to enable the encoding of mathematical expressions in MathML 2.0. SED-ML uses a subset of MathML as described in Section 2.2.1 on page 14.

SED-ML `notes` use the XHTML namespace <http://www.w3.org/1999/xhtml>. The `Notes` class is described in Section 2.3.3.2 on page 19.

Additional external namespaces might be used in `annotations`.

2.3.4.2 `level`

The current SED-ML `level` is “level 1”. Major revisions containing substantial changes will lead to the definition of forthcoming levels.

The `level` attribute is **required** and its value is a **fixed** decimal. For SED-ML Level 1 Version 3 the value is set to 1, as shown in the example in Listing 2.12.

2.3.4.3 `version`

The current SED-ML `version` is “version 2”. Minor revisions containing corrections and refinements of SED-ML elements, or new constructs which do not affect backwards compatibility, will lead to the definition of forthcoming versions.

The `version` attribute is **required** and its value is a **fixed** decimal. For SED-ML Level 1 Version 3 the value is set to 2, as shown in the example in Listing 2.12.

2.3.5 Reference relations

The **reference** concept is used to refer to a particular element inside the SED-ML document. It may occur in six different ways in the SED-ML document:

1. as an association between two **Models** (**modelReference**),
2. as an association between a **Variable** and a **Model** (**modelReference**),
3. as an association between a **Variable** and an **AbstractTask** (**taskReference**),
4. as an association between a **Task** and the simulated **Model** (**modelReference**),
5. as an association between a **Task** and the **Simulation** run (**simulationReference**), or
6. as an association between an **Output** and a **DataGenerator** (**dataReference**).

The definition of a **Task** object requires a reference to a particular Model object (**modelReference**, see Section 2.3.5.1 on page 23); furthermore, the Task object must be associated with a particular Simulation object (**simulationReference**, see Section 2.3.5.3 on page 24).

Depending on the use of the **reference** relation in connection with a **Variable** object, it may take different roles:

- a. The **reference** association might occur between a Variable object and a Model object, e.g. if the variable is to define a **Change**. In that case the **variable** element contains a **modelReference** to refer to the particular model that contains the variable used to define the change (see Section 2.3.5.1 on page 23).
- b. If the **reference** is used as an association between a Variable object and an AbstractTask object inside the **dataGenerator** class, then the **variable** element contains a **taskReference** to unambiguously refer to an observable in a given task (see Section 2.3.5.2 on page 24).

Four different types of **data references** exist in SED-ML Level 1 Version 3. They are used depending on the *type* of output for the simulation. A 2d plot has an **xDataReference** and a **yDataReference** assigned. A 3D plot has in addition a **zDataReference** assigned. To define a report, each data column has a **dataReference** assigned.

2.3.5.1 **modelReference**

The **modelReference** either represents a relation between two **Model** objects, a **Variable** object and a **Model** object, or a relation between a **Task** object and a **Model** object.

The **source** attribute of a **Model** is allowed to reference either a URI or an **SIId** to a second **Model**. Constructs where a model **A** refers to a model **B** and **B** to **A** (directly or indirectly) are invalid.

If pre-processing needs to be applied to a model before simulation, then the model update can be specified by creating a **Change** object. In the particular case that a change must be calculated with a mathematical function, variables need to be defined. To refer to an existing entity in a defined **Model**, the **modelReference** is used.

The **modelReference** attribute of the **variable** element contains the **id** of a model that is defined in the document. Listing 2.13 shows the use of the **modelReference** element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```
1 <model id="m0001" [...]>
2   <listOfChanges>
3     <computeChange>
4       <listOfVariables>
5         <variable id="v1" modelReference="cellML" target="/cellml:model/cellml:component[@cmeta:id='MP']/
6           cellml:variable[@name='vSP']/@initial_value" />
7         [...]
8       </listOfVariables>
9       <listOfParameters [...] />
10      <math>
11        [CALCULATION OF CHANGE]
12      </math>
13    </computeChange>
14  </listOfChanges>
15  [...]
```

```
15 </model>
```

Listing 2.13: SED-ML `modelReference` attribute inside a variable definition of a `computeChange` element

In the example, a change is applied on model `m0001`. In the `computeChange` element a list of variables is defined. One of those variable is `v1` which is defined in another model (`cellML`). The XPath expression given in the `target` attribute identifies the variable in the model which carries the ID `cellML`.

The `modelReference` is also used to indicate that a `Model` object is used in a particular `Task`. Listing 2.14 shows how this can be done for a sample SED-ML document.

```
1 <listOfTasks>
2   <task id="t1" name="Baseline" modelReference="model1" simulationReference="simulation1" />
3   <task id="t2" name="Modified" modelReference="model2" simulationReference="simulation1" />
4 </listOfTasks>
```

Listing 2.14: SED-ML `modelReference` definition inside a `task` element

The example defines two different tasks; the first one applies the simulation settings of `simulation1` on `model1`, the second one applies the same simulation settings on `model2`.

2.3.5.2 `taskReference`

`DataGenerator` objects are created to apply post-processing to the simulation results before final output.

For certain types of post-processing `Variable` objects need to be created. These link to a `task` defined within the `listOfTasks` from which the model that contains the variable of interest can be inferred. A `taskReference` association is used to realise that link from a `Variable` object inside a `DataGenerator` to an `AbstractTask` object. Listing 2.15 gives an example.

```
1 <listOfDataGenerators>
2   <dataGenerator id="tg3" name="tim mRNA (difference v1-v2+20)">
3     <listOfVariables>
4       <variable id="v1" taskReference="t1" [...] />
5     </listOfVariables>
6     <math [...] />
7   </dataGenerator>
8 </listOfDataGenerators>
```

Listing 2.15: SED-ML `taskReference` definition inside a `dataGenerator` element

The example shows the definition of a variable `v1` in a `dataGenerator` element. The variable appears in the model that is used in task `t1`. The task definition of `t1` might look as shown in Listing 2.16.

```
1 <listOfTasks>
2   <task id="t1" name="task definition" modelReference="model1" simulationReference="simulation1" />
3 </listOfTasks>
```

Listing 2.16: Use of the reference relations in a task definition

Task `t1` references the model `model1`. Therefore we can conclude that the variable `v1` defined in Listing 2.15 targets an element of the model with ID `model1`. The targeting process itself will be explained in section 2.3.6.1 on page 26.

2.3.5.3 `simulationReference`

The `simulationReference` is used to refer to a particular `Simulation` in a `Task`. Listing 2.14 shows the reference to a defined simulation for a sample SED-ML document. In the example, both tasks `t1` and `t2` use the simulation settings defined in `simulation1` to run the experiment.

2.3.5.4 `dataReference`

The `dataReference` is used to refer to a particular `DataGenerator` instance from an `Output` instance. Listing 2.17 shows the reference to a defined data set for a sample SED-ML document.

```
1 <listOfOutputs>
2   <plot2D id="p1" [...] >
3     <curve id="c1" xDataReference="dg1" yDataReference="dg2" />
4     [...]
5   </plot>
6 </listOfOutputs>
```

Listing 2.17: Example for the use of data references in a curve definition

In the example, the output type is a 2D plot, which defines one curve with id **c1**. A curve must refer to two different data generators which describe how to procure the data that is to be plotted on the x-axis and y-axis respectively.

2.3.6 Variable

Variables are references to already existing entities, either existing in one of the defined **models** or implicitly defined **symbols** (Figure 2.10).

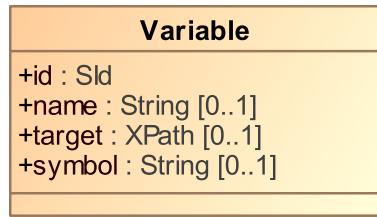


Figure 2.10: The *Variable* class

If the variable is defined through a reference to a model constituent, such as an SBML species, or to an entity within the SED-ML file itself, then the reference is specified using the **target** attribute. If the variable is defined through a reference to an **implicit variable**, rather than one explicitly appearing in the model, then the **symbol** attribute is used, which holds a SED-ML **URI**. A **variable** is always placed inside a **listOfVariables**. The **symbol** and **target** attributes must not be used together in a single instance of **Variable**, although at least one must be present.

Table 2.5 shows all attributes and sub-elements for the **Variable** element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
target	page 26
symbol	page 27
taskReference	page 24
modelReference	page 23
sub-elements	description
notes ^o	page 19
annotation ^o	page 20

Table 2.5: Attributes and nested elements for **Variable**. xy^o denotes optional elements and attributes.

A **variable** element must contain a **taskReference** if it occurs inside a **listOfVariables** inside a **dataGenerator** element. A **variable** element must contain a **modelReference** if it occurs inside a **listOfVariables** inside a **computeChange** element. A **variable** element appearing within a **functionalRange** or **setValue** element must contain a **modelReference** if and only if it references a model variable.

Listing 2.18 shows the use of the **variable** element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <sedML>
2   <listOfModels>
3     <model [...]>
4       <listOfChanges>
5         <computeChange target="TARGET ELEMENT OR ATTRIBUTE">
6           <listOfVariables>
7             <variable id="v1" name="maximum velocity"
8               target="XPath TO A MODEL ELEMENT OR ATTRIBUTE IN ANY SPECIFIED MODEL" />
  
```

```

9      [FURTHER VARIABLE DEFINITIONS]
10     </listOfVariables>
11     [...]
12     </computeChange>
13     </listOfChanges>
14     [...]
15     </model>
16     [...]
17   </listOfModels>
18   <listOfDataGenerators>
19     <dataGenerator [...]>
20       <listOfVariables>
21         <variable id="v2" name="time" taskReference="task1" symbol="urn:sedml:symbol:time" />
22         [FURTHER VARIABLE DEFINITIONS]
23       </listOfVariables>
24     </dataGenerator>
25   </listOfDataGenerators>
26   [...]
27 </sedML>

```

Listing 2.18: SED-ML variable definitions inside the `computeChange` element and inside the `dataGenerator` element

Listing 2.18 defines a variable `v1` (line 7) to compute a change on a model constituent (referenced by the `target` attribute on `computeChange` in line 5). The value of `v1` corresponds with the value of the targeted model constituent referenced by the `target` attribute in line 8. The second variable, `v2` (line 21), is used inside a `dataGenerator`. As the variable is `time` as used in `task1`, the `symbol` attribute is used to refer to the SED-ML URI for time (line 21).

2.3.6.1 target

An instance of `Variable` can refer to a model constituent inside a particular `model` through an `XPath` expression stored in the `target` attribute.

`XPath` can be used to unambiguously identify an element or attribute in an XML file.

The `target` attribute may also be used to reference an entity within the SED-ML file itself, by containing a fragment identifier consisting of a hash character (#) followed by the `id` of the desired element. As of SED-ML Level 1 Version 3 this is only used to refer to `ranges` within a `repeatedTask` (see Listing 2.50 for an example).

Listing 2.19 shows the use of the `target` attribute in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1  <listOfVariables>
2    <variable id="v1" name="TetR protein" taskReference="task1"
3      target="/sbml:sbml/sbml:listOfSpecies/sbml:species[@id='PY']" />
4  </listOfVariables>

```

Listing 2.19: SED-ML target definition

It should be noted that the identifier and names inside the SED-ML document do not *have* to match the identifiers and names that the model and its constituents carry in the model definition. In listing 2.19, the variable with ID `v1` is defined. It is described as the `TetR protein`. The reference points to a species in the referenced SBML model. The particular species can be identified through its ID in the SBML model, namely `PY`. However, SED-ML also permits using identical identifiers and names as in the referenced models. The following Listing 2.20 is another valid example for the specification of a variable, but uses the same naming in the variable definition as in the original model (as opposed to Listing 2.19):

```

1  <listOfVariables>
2    <variable id="PY" name="TetR protein" taskReference="task1"
3      target="/sbml:sbml/sbml:listOfSpecies/sbml:species[@id='PY']" />
4  </listOfVariables>

```

Listing 2.20: SED-ML variable definition using the original model identifier and name in SED-ML

```

1 <sbml [...]>
2   <listOfSpecies>
3     <species metaid="PY" id="PY" name="TetR protein" [...]>
4       [...]
5     </species>
6   </listOfSpecies>
7   [...]
8 </sbml>

```

Listing 2.21: Species definition in the referenced model (extracted from urn:miriam:biomodels.db:BIOMD0000000012)

The XPath expression used in the `target` attribute unambiguously leads to the particular place in the XML SBML model – the species is to be found in the `sbml` element, and there inside the `listOfSpecies` (Listing 2.21 on the preceding page). Note that while it is possible to write XPath expressions that select multiple nodes within a referenced model, when used within a `target` attribute a single element or attribute *must* be selected by the expression.

2.3.6.2 symbol

Symbols are predefined, implicit variables that can be called in a SED-ML file by referring to the defined URNs representing that variable's concept. The notion of implicit variables is explained in Section 2.2.2.3 on page 16.

Listing 2.22 shows the use of the `symbol` attribute in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema. The example encodes a computed change of model `m001`. To specify that change, a symbol is defined (i.e. the SED-ML symbol for `time` is assigned to the variable `t1`). How to compute the change itself is explained in Section 2.4.5.6.

```

1  <listOfVariables>
2    <variable id="t1" name="time" taskReference="task1"
3      symbol="urn:sedml:symbol:time" />
4  </listOfVariables>
```

Listing 2.22: SED-ML symbol definition

2.3.7 Parameter

The SED-ML `Parameter` class creates instances with a constant value (Figure 2.11).

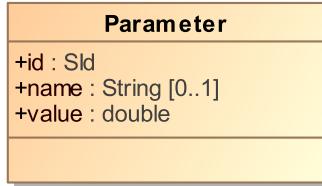


Figure 2.11: The Parameter class

SED-ML allows the use of named parameters wherever a mathematical expression is defined to compute some value (e.g. in `ComputeChange`, `FunctionalRange` or `DataGenerator`). In all cases the parameter definitions are local to the particular class defining them. A benefit of naming parameters rather than including numbers directly within the mathematical expression is that `notes` and `annotations` may be associated with them.

Table 2.6 shows all attributes and sub-elements for the `parameter` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
value	page 28
sub-elements	description
notes ^o	page 19
annotation ^o	page 20

Table 2.6: Attributes and nested elements for `parameter`. xy^o denotes optional elements and attributes.

A parameter can unambiguously be identified through its given `id`. It may additionally carry an optional

`name`. Each parameter has one associated `value`.

Listing 2.23 shows the use of the `parameter` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema. The listing shows the definition of a parameter `p1` with the `value="40"` assigned.

```
1 <listOfParameters>
2   <parameter id="p1" name="KM" value="40" />
3 </listOfParameters>
```

Listing 2.23: The definition of a parameter in SED-ML

2.3.7.1 `value`

Each `parameter` has exactly one fixed `value`. The `value` attribute of XML data type `Double` is required for each `parameter` element.

2.3.8 `ListOf*` containers

SED-ML `listOf*` elements serve as containers for a collection of objects of the same type. For example, the `listOfModels` contains all `Model` objects of a SED-ML document. Lists do not carry any further semantics nor do they add additional attributes to the language. They might, however, be annotated with `Notes` and `Annotations` as they are derived from `SEDBase`. All `listOf*` elements are optional in a SED-ML document.

2.3.8.1 `listOfDataDescriptions`: The `dataDescription` definition container

TODO: WRITE, see issue <https://github.com/SED-ML/sed-ml/issues/9>

2.3.8.2 `listOfVariables`: The `variable` definition container

SED-ML uses the `variable` concept to refer to existing entities inside a model. The container for all variables is `listOfVariables` (Figure 2.12). It includes all variables that need to be defined to either describe a change in the model by means of mathematical equations (`ComputeChange`) or to set up a `dataGenerator`.

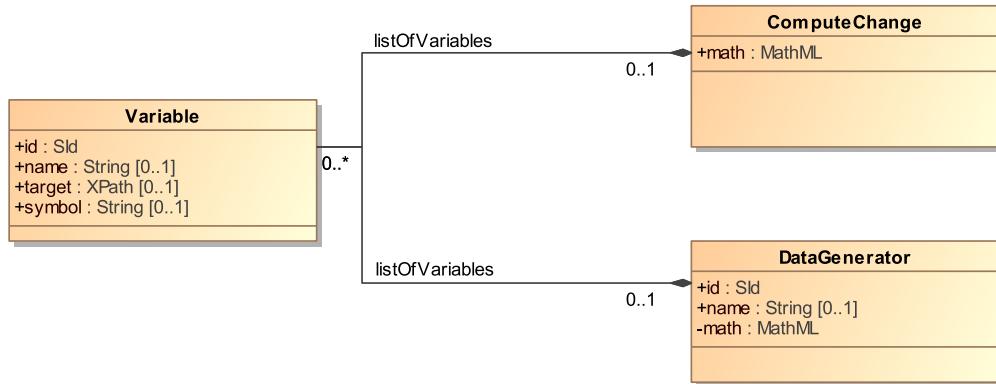


Figure 2.12: The SED-ML `listOfVariables` container

Listing 2.24 shows the use of the `listOfVariables` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema. The `listOfVariables` is optional and may contain zero to many variables.

```
1 <listOfVariables>
2   <variable id="v1" name="maximum velocity" taskReference="task1"
3     target="/cellml:model/cellml:component[@cmeta:id='MP']/cellml:variable[@name='vsP']/@initial_value"
4   />
5   <variable id="v2" taskReference="task2" symbol="urn:sedml:symbol:time" />
6 </listOfVariables>
```

Listing 2.24: SED-ML `listOfVariables` element

2.3.8.3 `listOfParameters`: The parameter definition container

All `parameters` needed throughout the simulation experiment, whether to compute a change on a model prior to or during simulation (`ComputeChange` and `SetValue`), to compute values in a `FunctionalRange`, or to set up a `DataGenerator`, are defined inside a `listOfParameters` (Figure 2.13).

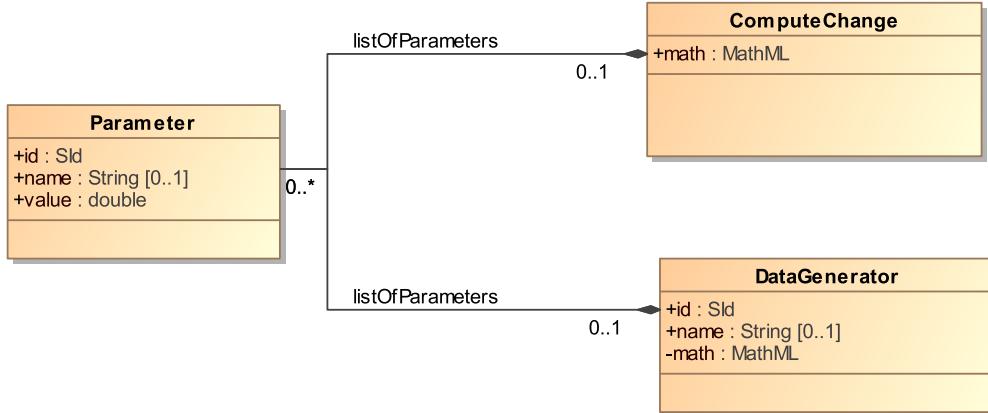


Figure 2.13: The SED-ML `listOfParameters` container

Listing 2.25 shows the use of the `listOfParameters` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema. The element is optional and may contain zero to many parameters.

```

1 <listOfParameters>
2   <parameter id="p1" value="1" />
3   <parameter id="p2" name="Kadp_2" value="0.23" />
4 </listOfParameters>
  
```

Listing 2.25: SED-ML `listOfParameters` element

2.3.8.4 `listOfModels`: The model description container

In order to specify a simulation experiment, the participating models have to be defined. SED-ML uses the `listOfModels` container for all necessary models (Figure 2.14).

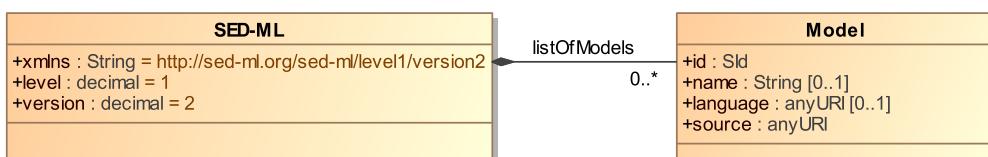


Figure 2.14: The SED-ML `listOfModels` container

Listing 2.26 shows the use of the `listOfModels` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema. The `listOfModels` is optional and may contain zero to many models. However, if the Level 1 Version 3 document contains one or more `Task` elements, at least one `Model` element must be defined to which the `Task` element refers (c.f. Section 2.3.5.1 on page 23).

```

1 <listOfModels>
2   <model id="m0001" language="urn:sedml:language:sbml"
3     source="urn:miriam:biomodels.db:BIOMD0000000012" />
4   <model id="m0002" language="urn:sedml:language:cellml"
5     source="http://models.cellml.org/workspace/leloup_gonze_goldbeter_1999/@@rawfile/
6       d6613d7e1051b3eff2bb1d3d419a445bb8c754ad/leloup_gonze_goldbeter_1999_a.cellml" />
6 </listOfModels>
  
```

Listing 2.26: SED-ML `listOfModels` element

2.3.8.5 `listOfChanges`: The change definition container

The `listOfChanges` contains the defined changes to be applied to a particular `model` (Figure 2.15).



Figure 2.15: The SED-ML `listOfChanges` container

It always occurs as an optional subelement of the `model` element.

Listing 2.27 shows the use of the `listOfChanges` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema. The `listOfChanges` is nested inside the `model` element.

```

1 <model id="m0001" [...]>
2   <listOfChanges>
3     [CHANGE DEFINITION]
4   </listOfChanges>
5 </model>
  
```

Listing 2.27: The SED-ML `listOfChanges` element, defining a change on a model

2.3.8.6 `listOfSimulations`: The simulation description container

The `listOfSimulations` element is the container for `simulation` descriptions (Figure 2.16).

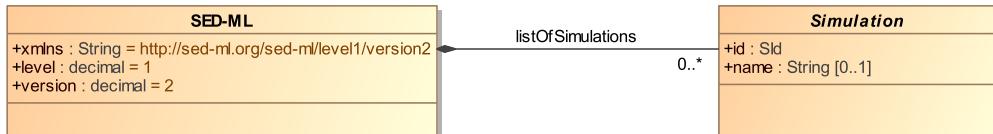


Figure 2.16: The `listOfSimulations` container

Listing 2.28 shows the use of the `listOfSimulations` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfSimulations>
2   <simulation id="s1" [...]>
3     [UNIFORM TIMECOURSE DEFINITION]
4   </simulation>
5   <simulation id="s2" [...]>
6     [UNIFORM TIMECOURSE DEFINITION]
7   </simulation>
8 </listOfSimulations>
  
```

Listing 2.28: The SED-ML `listOfSimulations` element, containing two simulation setups

The `listOfSimulations` is optional and may contain zero to many simulations. However, if the Level 1 Version 3 document contains one or more `Task` elements, at least one `Simulation` element must be defined to which the `Task` element refers — see section 2.3.5.3 on page 24.

2.3.8.7 `listOfAlgorithmParameters`: The container for algorithm parameters

The `listOfAlgorithmParameters` contains the the settings for the simulation algorithm used in a simulation experiment. It may list several instances of the `AlgorithmParameter` class.

Listing 2.29 on the next page shows the use of the `listOfAlgorithmParameters` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema. The `listOfAlgorithmParameters` is optional and may contain zero to many parameters.

```

1 <listOfAlgorithmParameters>
2   <algorithmParameter kisaoID="KISAO:0000211" value="23"/>
3 </listOfAlgorithmParameters>

```

Listing 2.29: SED-ML `listOfAlgorithmParameters` element

2.3.8.8 `listOfTasks`: The task specification container

The `listOfTasks` element contains the defined tasks for the simulation experiment (Figure 2.17).



Figure 2.17: The SED-ML `listOfTasks` container

Listing 2.30 shows the use of the `listOfTasks` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfTasks>
2   <task id="t1" name="simulating v1" modelReference="m1" simulationReference="s1">
3     [FURTHER TASK DEFINITIONS]
4   </listOfTasks>

```

Listing 2.30: The SED-ML `listOfTasks` element, defining one task

The `listOfTasks` is optional and may contain zero to many tasks, each of which is an instance of a subclass of `AbstractTask`. However, if the Level 1 Version 3 document contains a `DataGenerator` element with at least one `Variable` element, at least one `task` must be defined to which variable(s) in the `DataGenerator` element refer — see Section 2.3.5.2 on page 24.

2.3.8.9 `listOfDataGenerators`: The post-processing container

In SED-ML, all variable- and parameter values that shall be used in the `Output` class need to be defined as a `dataGenerator` beforehand. The container for those data generators is the `listOfDataGenerators` (Figure 2.18).

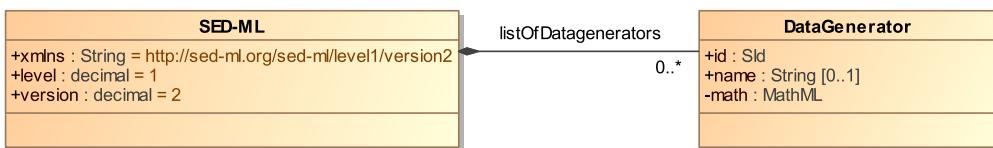


Figure 2.18: The SED-ML `listOfDataGenerators` container

Listing 2.31 shows the use of the `listOfDataGenerators` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfDataGenerators>
2   <dataGenerator id="d1" name="time">
3     [DATA GENERATOR DEFINITION FOLLOWING]
4   </dataGenerator>
5   <dataGenerator id="LaCI" name="LaCI repressor">
6     [DATA GENERATOR DEFINITION FOLLOWING]
7   </dataGenerator>
8 </listOfDataGenerators>

```

Listing 2.31: The `listOfDataGenerators` element, defining two data generators time and LaCI repressor

The `listOfDataGenerators` is optional and in general may contain zero to many `DataGenerators`. However, if the Level 1 Version 3 document contains an `Output` element, at least one `DataGenerator` must

be defined to which the **Output** element refers - see section 2.3.5.4 on page 24.

2.3.8.10 *listOfOutputs: The output specification container*

The **listOfOutputs** container holds the output specifications for a simulation experiment.

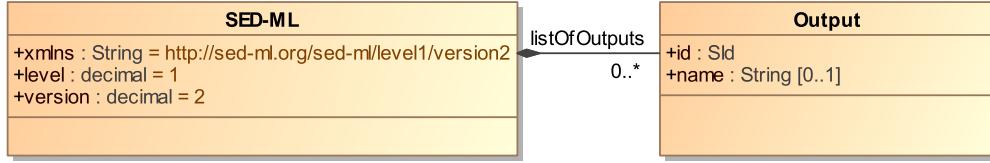


Figure 2.19: The SED-ML *listOfOutputs* container

The output can be defined as either a **report**, a **plot2D** or as a **plot3D**.

Listing 2.32 shows the use of the **listOfOutputs** element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema. The **listOfOutputs** is optional and may contain zero to many outputs.

```
1 <listOfOutputs>
2   <report id="report1">
3     [REPORT DEFINITION FOLLOWING]
4   </report>
5   <plot2D id="plot1">
6     [2D PLOT DEFINITION FOLLOWING]
7   </plot2D>
8 </listOfOutputs>
```

Listing 2.32: The *listOfOutput* element

2.4 SED-ML Components

In this section we describe the major components of SED-ML. We use the UML notation presented in section 2.1.1, and we show the use of SED-ML with XML examples. In addition, we provide an XML Schema in Appendix B.

2.4.1 DataDescription

The [DataDescription](#) class (Figure 2.20) references a file containing data points, along with a description on how to access that file, and what information to extract from it.

The [DataDescription](#) class introduces three attributes: the required attributes `id` and `source` and the optional attribute `name`. Additionally two elements are defined: `dimensionDescription` and `listOfDataSources`.

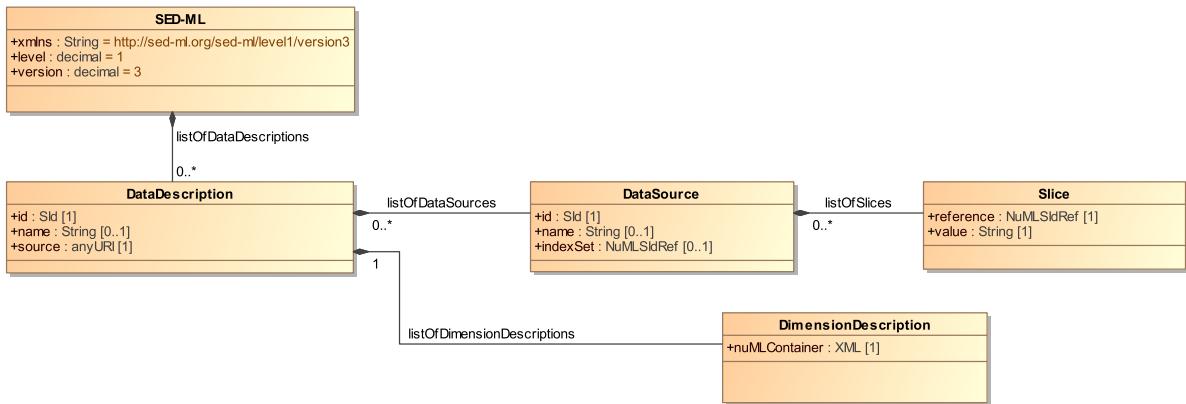


Figure 2.20: The SED-ML `DataDescription` class

Table 2.7 shows all attributes and sub-elements for the `dataDescription` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
source	page 33
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
dimensionDescription ^o	page 34
listOfDataSources ^o	page 34

Table 2.7: Attributes and nested elements for `dataDescription`. xy^o denotes optional elements and attributes.

2.4.1.1 The `id` and `name` attributes

The attribute `id` of type `SIId` is meant to uniquely identify the `dataDescription` element, while the optional `name` attribute of type `string`, is there to provide a human readable representation if desired.

2.4.1.2 The `source` attribute

Analog to how the `source` attribute on the `Model` is handled, this attribute provides a location of a data file. In order to resolve the `source` attribute, the same mechanisms are allowed as for `Model` element:

be it a local file system, a relative link or an online resource.

TODO: document the CSV option, the following is not correct

PLEASE NOTE: THE COMMUNITY DECIDED, THAT THE FILE WILL ALWAYS BE ENCODED IN THE NUML FORMAT.

Listing 2.34 shows the use of the `dataDescription` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1   <dataDescription id="Data1" name="Oscli Time Course Data"
2     source="http://svn.code.sf.net/p/libsedml/code/trunk/Samples/data/oscli.numl" >
3   ...
4 </dataDescription>
```

Listing 2.33: SED-ML `dataDescription` element

2.4.1.3 `dimensionDescription`

The `dimensionDescription` element is the data description from an NuML file. Consider for example:

```

1   <dimensionDescription>
2     <compositeDescription indexType="double" id="time" name="time"
3       xmlns="http://www.nucl.org/numl/level1/version1">
4       <compositeDescription indexType="string" id="SpeciesIds" name="SpeciesIds">
5         <atomicDescription valueType="double" name="Concentration" />
6       </compositeDescription>
7     </compositeDescription>
8   </dimensionDescription>
```

Listing 2.34: SED-ML `dimensionDescription` element

Here a nested NuML `componentDescription` with `time` spanning one dimension and `SpeciesIds` another. This two dimensional space is then filled with `double` values representing concentrations.

2.4.1.4 `listOfDataSources`

The `listOfDataSources` contains one or more `DataSource` elements that are then used in the remainder of the SED-ML document.

2.4.2 `DataSource`

The `DataSource` class (Figure ??) extracts chunks out of the data file provided by the outer `DataDescription` element.

The `DataSource` class introduces three attributes: the required attribute `id` and the optional attribute `indexSet` and `name`. Additionally the `listOfSlices` element is defined.

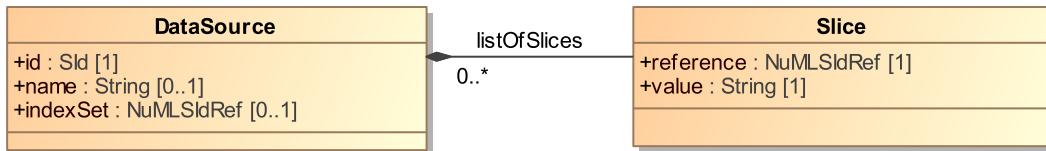


Figure 2.21: The SED-ML `DataSource` class

Table ?? shows all attributes and sub-elements for the `dataSource` element as defined by the SED-ML Level 1 Version 3 XML Schema.

2.4.2.1 `The id and name attributes`

The attribute `id` of type `SId` is meant to uniquely identify the `dataSource` element, while the optional `name` attribute of type `string`, is there to provide a human readable representation if desired.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
indexSet	page ??
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
listOfSlices ^o	page ??

Table 2.8: Attributes and nested elements for `dataSource`. xy^o denotes optional elements and attributes.

2.4.2.2 The indexSet attribute

Since data elements in NuML are either values, or indices, the `DataSource` element needs two ways of addressing those elements. The `indexSet` attribute allows to address all indices provided by NuML elements with `indexType`. For example in for the `time componentDescription` above, a `dataSource`:

```
1 <dataSource id="dataTime" indexSet="time" />
```

would extract the set of all timepoints stored in the index. Similarly:

```
1 <dataSource id="allIds" indexSet="SpeciesIds" />
```

would extract all the species id strings stored in that index set. Valid values for `indexSet` are all NuML Id elements declared in the `dimensionDescription`. If the `indexSet` attribute is specified the corresponding `dataSource` may not define any `slice` elements.

2.4.2.3 listOfSlices

The `listOfSlices` contains one or more `Slice` elements that are then used in the remainder of the SED-ML document.

2.4.2.4 Using the dataSource elements

Once the `DataSource` elements are defined, they can be reused anywhere in the SED-ML Description. Specifically their `id` attribute can be referenced within the `listOfVariables` of `DataGenerators`, `computeChange` or `setValue` objects. Here an example that re-uses the data source `dataS1`:

```
1 <dataGenerator id="dgDataS1" name="S1 (data)">
2   <listOfVariables>
3     <variable id="varS1" modelReference="model1" target="#dataS1" />
4   </listOfVariables>
5   <math xmlns="http://www.w3.org/1998/Math/MathML">
6     <ci> varS1 </ci>
7   </math>
8 </dataGenerator>
```

This represents a change from Level 1 Version 1 and Level 1 Version 2, in which a `taskReference` was always present for a `variable` in a data generator.

To indicate that the target is an entity defined within the current SED-ML description the hashtag (#) with the reference to an `id` was used. Additionally, this example uses the `modelReference`, in order to facilitate a mapping of the data encoded in the NuML document with a given model.

2.4.3 Slice

If a `DataSource` does not define the `indexSet` attribute, it will contain `Slice` elements. Each slice removes one dimension from the data hypercube.

The `Slice` class introduces two required attributes: `reference` and `value`.



Figure 2.22: The SED-ML Slice class

Table ?? shows all attributes and sub-elements for the `slice` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
reference	page ??
value	page ??
sub-elements	description
notes ^o	page 19
annotation ^o	page 20

Table 2.9: Attributes and nested elements for `slice`. xy^o denotes optional elements and attributes.

2.4.3.1 The reference attribute

The `reference` attribute references one of the indices described in the `dimensionDescription`. In the example above, valid values would be: `time` and `SpeciesIds`.

2.4.3.2 The value attribute

The `value` attribute takes the value of a specific index in the referenced set of indices. For example:

```

1      <dataSource id="dataS1">
2          <listOfSlices>
3              <slice reference="SpeciesIds" value="S1" />
4          </listOfSlices>
5      </dataSource>

```

would isolate the index set of all species ids specified, to only the single entry for `S1`, however over the full range of the `time` index set. As stated before, there could be multiple slice elements present, so it would be feasible to slice the data again, to obtain a single time point, for example the initial one:

```

1      <dataSource id="dataS1">
2          <listOfSlices>
3              <slice reference="time" value="0" />
4              <slice reference="SpeciesIds" value="S1" />
5          </listOfSlices>
6      </dataSource>

```

2.4.4 Model

The `Model` class defines the models to be used in the simulation experiment (Figure 2.23).



Figure 2.23: The SED-ML Model class

Each instance of the **Model** class has an unambiguous and mandatory `id`. An additional, optional `name` may be given to the model.

The `language` may be specified, defining the format the model is encoded in, if such a format exists. Example formats are SBML or CellML.

The **Model** class refers to the particular model of interest through the `source` attribute. The restrictions on the model reference are

- The model must be encoded in an XML format.
- To refer to the model encoding language, a reference to a valid definition of that XML format must be given (`language` attribute).
- To refer to a particular model in an external resource, an unambiguous reference must be given (`source` attribute).

A model might need to undergo preprocessing before simulation. Those pre-processing steps are specified in the SED-ML **Change** class.

Table 2.10 shows all attributes and sub-elements for the `model` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
<code>metaid^o</code>	page 19
<code>id</code>	page 18
<code>name^o</code>	page 18
<code>language^o</code>	page 39
<code>source</code>	page 39
sub-elements	description
<code>notes^o</code>	page 19
<code>annotation^o</code>	page 20
<code>change^o</code>	page 40

Table 2.10: Attributes and nested elements for `model`. xy^o denotes optional elements and attributes.

Listing 2.35 shows the use of the `model` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfModels>
2   <model id="m0001" language="urn:sedml:language:sbml"
3     source="urn:miriam:biomodels.db:BIOMD0000000012">
4     <listOfChanges>
5       <change>
6         [MODEL PRE-PROCESSING]
7       </change>
8     </listOfChanges>
9   </model>
10  <model id="m0002" language="urn:sedml:language:sbml" source="m0001">
11    <listOfChanges>
12      [MODEL PRE-PROCESSING]
13    </listOfChanges>
14  </model>
15  <model id="m0003" language="urn:sedml:language:cellml" source="http://models.cellml.org/workspace/
    leloup_gonze_goldbeter_1999/@rawfile/d6613d7e1051b3eff2bb1d3d419a445bb8c754ad/
    leloup_gonze_goldbeter_1999_a.cellml">

```

```

16   [MODEL PRE-PROCESSING]
17 </model>
18 </listOfModels>
```

Listing 2.35: SED-ML model element

The above `listOfModels` contains three models: The first model `m0001` is the Repressilator model taken from BioModels Database. The original model is available from <urn:miriam:biomodels.db:BIOMD0000000012>. For the SED-ML simulation, the model might undergo preprocessing, described in the `change` element (lines 5-7). Based on the description of the first model `m0001`, the second model is built. It refers to the model `m001` in the `source` attribute, that is the modified version of the Repressilator model. `m002` might then have even further changes applied to it on top of the changes defined in the pre-processing of `m0001`. The third model in the code example above (lines 13-15) is a different model in CellML representation. `m003` is the model available from the given URL in the `source` attribute. Again, it might have additional pre-processing applied to it before used in the simulation.

2.4.4.1 language

The evaluation of a SED-ML document is required in order for software to decide whether or not it can be used in a particular simulation environment. One crucial criterion is the particular model representation language used to encode the model. A simulation software usually only supports a small subset of the representation formats available to model biological systems computationally.

To help software decide whether or not it supports a SED-ML description file, the information on the model encoding for each referenced model can be provided through the `language` attribute, as the description of a language name and version through an unrestricted `String` is error-prone. A prerequisite for a language to be fully supported by SED-ML is that a formalised language definition, e.g. an XML Schema, is provided online. SED-ML also defines a set of standard URIs to refer to particular language definitions. The list of URNs for languages so far associated with SED-ML is available from the SED-ML web site on <http://sed-ml.org/> (Section 2.2.2.2 on page 16). To specify language and version, following the idea of MIRIAM URNs, the SED-ML URN scheme `urn:sedml:language:language name` is used. A model's language being "SBML Level 2 Version 2" can be referred to, for example, through the URN `urn:sedml:language:sbml.level-2.version-2`.

The `language` attribute is optional in the XML representation of a SED-ML file. If it is not explicitly defined in the SED-ML file, the default value for the `language` attribute is `urn:sedml:language:xml`, referring to any XML based model representation.

However, the use of the `language` attribute is strongly encouraged for two reasons. Firstly, it helps a user decide whether or not he is able to run the simulation, that is to parse the model referenced in the SED-ML file. Secondly, the language attribute is also needed to decide how to handle the implicit variables in the `Variable` class, as the interpretation of implicit variables depends on the language of the representation format. The concept of implicit variables has been introduced in Section 2.2.2.3 on page 16.

2.4.4.2 source

To make a model available for the execution of a SED-ML file, the model `source` must be specified through either a URI or a reference to an `SId` of an existing Model.

The URI should preferably point to a public, consistent location that provides the model description file and follows the proposed [URI Scheme](#). References to curated, open model bases are recommended, such as the BioModels Database. However, any resource registered with MIRIAM resources³ can easily be referenced. Even without a MIRIAM URN, SED-ML can be used (Section 2.2.2.1 on page 15).

An example for the definition of a model, and using the [URI scheme](#) is given in Listing 2.36.

```

1 <model id="m1" name="repressilator" language="urn:sedml:language:sbml"
2   source="urn:miriam:biomodels.db:BIOMD0000000012">
3   <listOfChanges>
4     [MODEL PRE-PROCESSING]
5   </listOfChanges>
6 </model>
```

Listing 2.36: The SED-ML source element, using the URI scheme

³<http://www.ebi.ac.uk/miriam/main/>

The example defines one model `m1`. `urn:miriam:biomodels.db:BIOMD0000000012` defines the source of the model code. The MIRIAM URN can be resolved into the SBML model stored in BioModels Database under ID `BIOMD0000000012` using the MIRIAM web service. The resulting URL is <http://www.ebi.ac.uk/biomodels-main/BIOMD0000000012>.

An example for the definition of a model and using a URL is given in Listing 2.37.

```
1 <model id="m1" name="repressilator" language="urn:sedml:language:cellml"
2   source="http://models.cellml.org/exposure/bba4e39f2c7ba8af51fd045463e7bdd3/aguda_b_1999.cellml">
3   <listOfChanges />
4 </model>
```

Listing 2.37: The SED-ML `source` element, using a URL

In the example one model is defined. The `language` of the model is `CellML`. As the CellML model repository currently does not provide a MIRIAM URI for model reference, the `URL` pointing to the model code is used to refer to the model. The URL is given in the `source` attribute.

2.4.5 Change

SED-ML not only allows to use the sole model for simulation, but also enables the description of [changes](#) to be made on the model before simulation (Figure 2.24 on the following page). Changes can be of three distinct types:

1. Changes on attributes of the model's XML representation ([ChangeAttribute](#))
2. Changes on any XML snippet of the model's XML representation ([AddXML](#), [ChangeXML](#), [RemoveXML](#))
3. Changes based on mathematical calculations ([ComputeChange](#))

The [Change](#) class is abstract and serves as the base class for different types of changes. Therefore, a SED-ML document will only contain the derived classes, i.e. [ChangeAttribute](#), [AddXML](#), [ChangeXML](#), [RemoveXML](#), or [ComputeChange](#).

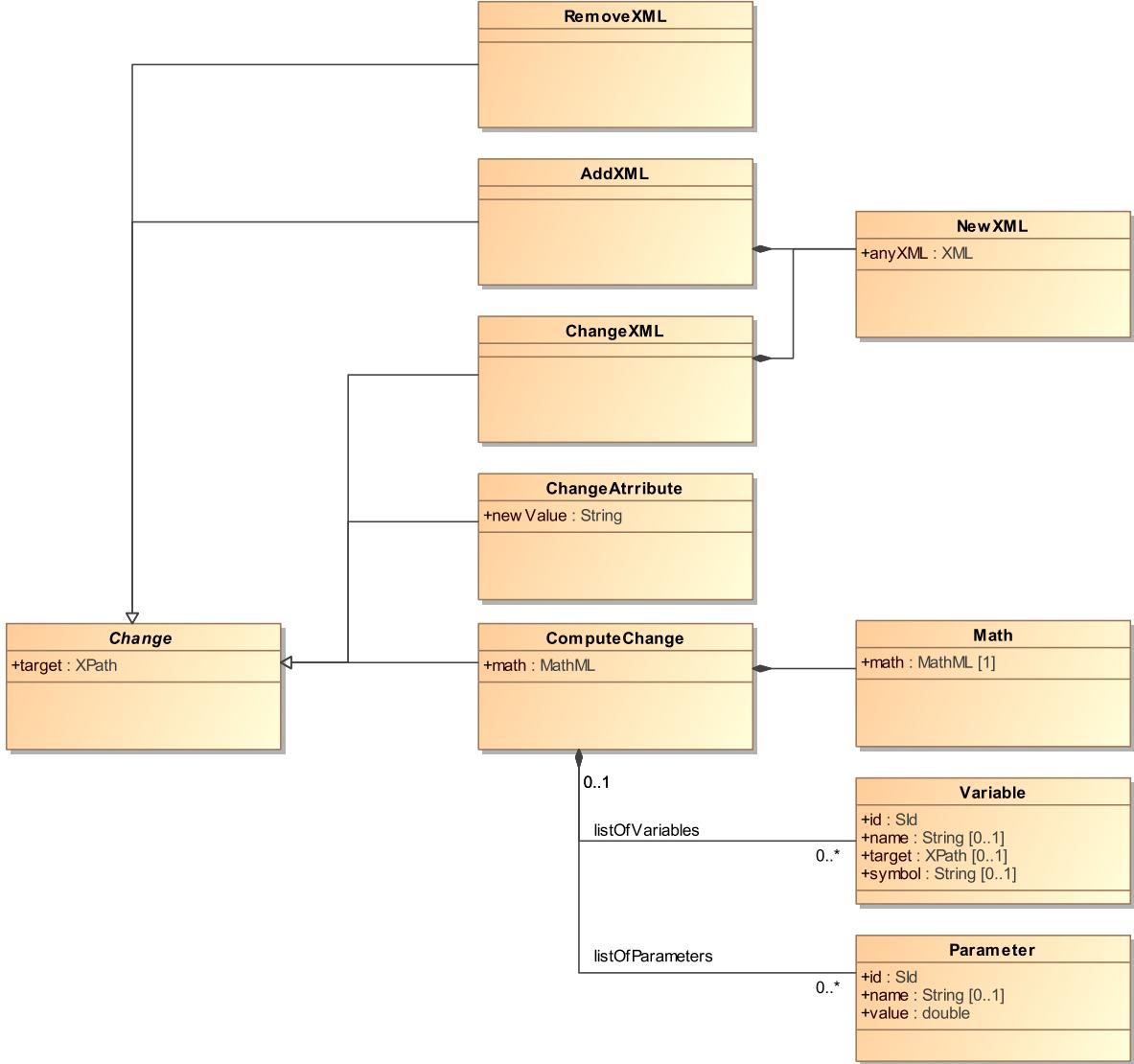


Figure 2.24: The SED-ML Change class

Table 2.11 shows all attributes and sub-elements for the `change` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
<code>metaid^o</code>	page 19
<code>id</code>	page 18
<code>name^o</code>	page 18
<code>target</code>	page 26
sub-elements	description
<code>notes^o</code>	page 19
<code>annotation^o</code>	page 20

Table 2.11: Attributes and nested elements for `change`. xy^o denotes optional elements and attributes.

Each Change has a `target` attribute that holds a valid XPath expression pointing to the XML element or XML attribute that is to undergo the defined changes. Except for the cases of `ChangeXML` and `RemoveXML`, this XPath expression must always select a *single* element or attribute within the relevant

model.

2.4.5.1 NewXML

The `newXML` element provides a piece of XML code (Figure 2.24 on the preceding page). `NewXML` must hold a valid piece of XML which after insertion into the original model must lead to a valid model file, according to the model language specification (as given by the `language` attribute).

Table 2.12 shows all attributes and sub-elements for the `newXML` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
<code>none</code>	
sub-elements	description
<code>anyXML</code>	

Table 2.12: Attributes and nested elements for `newXML`. xy^o denotes optional elements and attributes.

The `newXML` element is used at two different places inside SED-ML Level 1 Version 3:

1. If it is used as a sub-element of the `addXML` element, then the XML it contains is to be *inserted as a child* of the XML element addressed by the XPath.
2. If it is used as a sub-element of the `changeXML` element, then the XML it contains is to *replace* the XML element addressed by the XPath.

Examples are given in the relevant change class definitions.

2.4.5.2 AddXML

The `AddXML` class specifies a snippet of XML that is to be added as a child of the element selected by the XPath expression in the `target` attribute (Figure 2.25). The new piece of XML code is provided by the `NewXML` class.



Figure 2.25: The SED-ML `AddXML` class

Table 2.13 shows all attributes and sub-elements for the `addXML` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
<code>metaid^o</code>	page 19
<code>id</code>	page 18
<code>name^o</code>	page 18
<code>target</code>	page 26
sub-elements	description
<code>notes^o</code>	page 19
<code>annotation^o</code>	page 20
<code>newXML</code>	page 42

Table 2.13: Attributes and nested elements for `addXML`. xy^o denotes optional elements and attributes.

An example for a change that adds an additional parameter to a model is given in Listing 2.38.

```

1 <model language="urn:sedml:language:sbml" [...]>
2   <listOfChanges>
3     <addXML target="/sbml:sbml/sbml:model/sbml:listOfParameters" >
4       <newXML>
5         <parameter metaid="metaid_0000010" id="V_mT" value="0.7" />
6       </newXML>
7     </addXML>
8   </listOfChanges>
9 </model>
```

Listing 2.38: The `addXML` element with its `newXML` sub-element

The code of the model is changed so that a parameter with ID `V_mT` is added to its list of parameters. The `newXML` element adds an additional XML element to the original model. The element's name is `parameter` and it is added to the existing parent element `listOfParameters` that is addressed by the XPath expression in the `target` attribute.

2.4.5.3 ChangeXML

The `ChangeXML` class allows you to replace any XML element(s) in the model that can be addressed by a valid XPath expression (Figure 2.26).

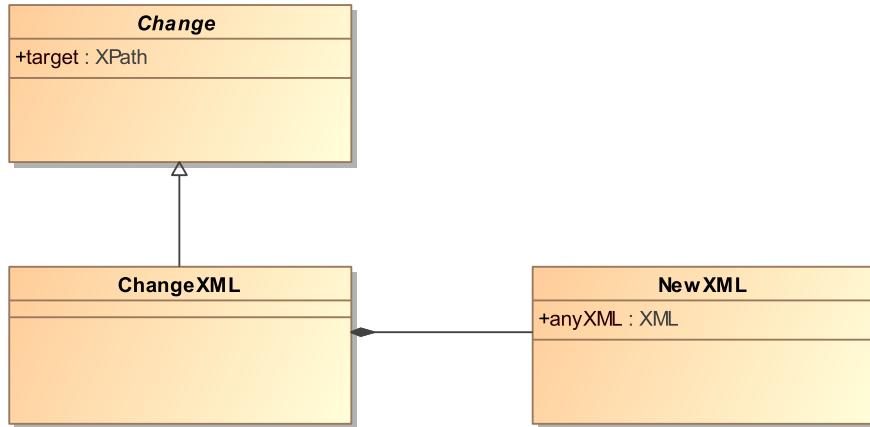


Figure 2.26: The `ChangeXML` class

The XPath expression is specified in the required `target` attribute (Section 2.3.6.1 on page 26). The replacement XML content is specified in the `NewXML` class.

Table 2.14 shows all attributes and sub-elements for the `changeXML` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
target	page 26
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
newXML	page 42

Table 2.14: Attributes and nested elements for `changeXML`. xy^o denotes optional elements and attributes.

An example for a change that adds an additional parameter to a model is given in Listing 2.39.

```

1 <model [...]>
2   <listOfChanges>
3     <changeXML target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='V_mT']" >
4       <newXML>
5         <parameter metaid="metaid_0000010" id="V_mT_1" value="0.7" />
6         <parameter metaid="metaid_0000050" id="V_mT_2" value="4.6"> />
7       </newXML>
8     </changeXML>
9   </listOfChanges>
10 </model>

```

Listing 2.39: The `changeXML` element

The code of the model is changed in the way that its parameter with ID `V_mT` is substituted by two other parameters `V_mT_1` and `V_mT_2`. The `target` attribute defines that the parameter with ID `V_mT` is to be changed. The `newXML` element then specifies the XML that is to be exchanged for that parameter.

2.4.5.4 RemoveXML

The `RemoveXML` class can be used to delete XML elements or attributes in the model that are addressed by the XPath expression (Figure 2.27).

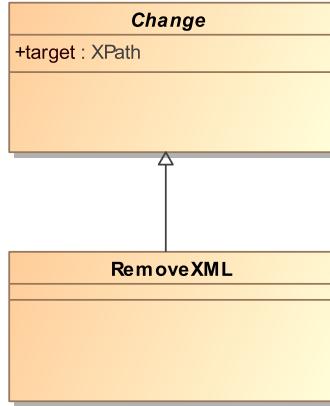


Figure 2.27: The `RemoveXML` class

The XPath is specified in the required `target` attribute.

Table 2.15 shows all attributes and sub-elements for the `removeXML` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
target	page 26
sub-elements	description
notes ^o	page 19
annotation ^o	page 20

Table 2.15: Attributes and nested elements for `removeXML`. xy^o denotes optional elements and attributes.

An example for the removal of an XML element from a model is given in Listing 2.40.

```

1 <model [...]>
2   <listOfChanges>
3     <removeXML target="/sbml:sbml/sbml:model/sbml:listOfReactions/sbml:reaction[@id='J1']" />
4   </listOfChanges>

```

```
5  </model>
```

Listing 2.40: The `removeXML` element

The code of the model is changed by deleting the reaction with ID `V_mT` from the model's list of reactions.

2.4.5.5 ChangeAttribute

The `ChangeAttribute` class allows to define updates on the XML attribute values of the corresponding model (Figure 2.28).



Figure 2.28: The `ChangeAttribute` class

The `ChangeXML` class covers the possibilities provided by the `ChangeAttribute` class. That is, everything that can be expressed by a `ChangeAttribute` construct can also be expressed by a `ChangeXML`. However, for the common case of changing an attribute value `ChangeAttribute` is easier to use, and so it is recommended to use the `ChangeAttribute` for any changes of an XML attribute's value, and to use the more general `ChangeXML` for other cases.

`ChangeAttribute` requires to specify the `target` of the change, i.e. the location of the addressed XML attribute, and also the `new value` of that attribute. Note that the XPath expression in the `target` attribute must select a single attribute within the corresponding model.

Table 2.16 shows all attributes and sub-elements for the `changeAttribute` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
target	page 26
newValue	page 45
sub-elements	description
notes ^o	page 19
annotation ^o	page 20

Table 2.16: Attributes and nested elements for `ChangeAttribute`. xy^o denotes optional elements and attributes.

2.4.5.1 newValue

The mandatory `newValue` attribute assigns a new value to the targeted XML attribute.

The example in Listing 2.41 shows the update of the initial concentration of two parameters inside an SBML model.

```
1 <model id="model1" name="Circadian Chaos" language="urn:sedml:language:sbml"
2   source="urn:miriam:biomodels.db:BIOMD0000000021">
3   <listOfChanges>
4     <changeAttribute target="/sbml:	sbml/sbml:	model/sbml:listOfParameters/sbml:parameter[@id='V_mT']/@value"
5       newValue="0.28"/>
6     <changeAttribute target="/sbml:	sbml/sbml:	model/sbml:listOfParameters/sbml:parameter[@id='V_dT']/@value"
6       newValue="4.8"/>
7   </listOfChanges>
```

```
7  </model>
```

Listing 2.41: The `changeAttribute` element and its `newValue` attribute

2.4.5.6 ComputeChange

The `ComputeChange` class permits to change, prior to the experiment, the numerical value of any element or attribute of a model addressable by an XPath expression, based on a calculation (Figure 2.29).

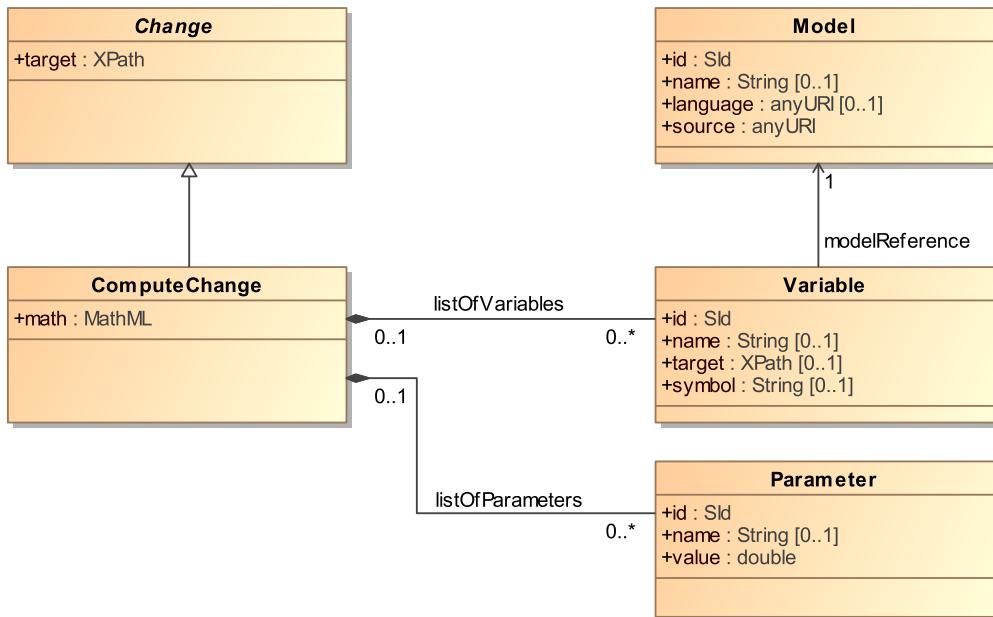


Figure 2.29: The `ComputeChange` class

The computed new value is described by a mathematical expression using a subset of `MathML` (see section 2.2.1 on page 14). The computation can use the value of variables from any model defined in the simulation experiment. Those `variables` need to be defined, and can then be addressed by their ID. A variable used in a `ComputeChange` must carry a `modelReference` attribute (page 23) but no `taskReference` attribute (page 24). To carry out the calculation it may be necessary to introduce additional parameters, that are not defined in any of the models used by the experiment. This is done through the `parameter` class, and such parameters are thereafter referred to by their ID. Finally, the change itself is specified using an instance of the `Math` class.

Note that where a `ComputeChange` refers to another model, that model is not allowed to be modified by `ComputeChanges` which directly or indirectly refer to this model. In other words, cycles in the definitions of computed changes are prohibited, since then the new values would not be well defined.

Table 2.17 on the next page shows all attributes and sub-elements for the `computeChange` element as defined by the SED-ML Level 1 Version 3 XML Schema.

2.4.5.6.1 Math

The `Math` element encodes mathematical functions. If used as an element of the `ComputeChange` class, it computes the change of the element or attribute addressed by the `target` attribute. Level 1 Version 3 supports the subset of MathML 2.0 shown in section 2.2.1.

Listing 2.42 shows the use of the `computeChange` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```
1  <model [...]>
2      <computeChange target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='sensor']">
3          <listOfVariables>
4              <variable modelReference="model1" id="R" name="regulator"
5                  target="/sbml:sbml/sbml:model/sbml:listOfSpecies/sbml:species[@id='regulator']" />
```

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
target	page 26
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
listOfVariables ^o	page 28
listOfParameters ^o	page 29
math	page 46

Table 2.17: Attributes and nested elements for `computeChange`. xy^o denotes optional elements and attributes.

```

6      <variable modelReference="model2" id="S" name="sensor"
7          target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='sensor']" />
8      <listOfVariables/>
9      <listOfParameters>
10     <parameter id="n" name="cooperativity" value="2">
11     <parameter id="K" name="sensitivity" value="1e-6">
12     <listOfParameters/>
13     <math xmlns="http://www.w3.org/1998/Math/MathML">
14         <apply>
15             <times />
16             <ci>S</ci>
17             <apply>
18                 <divide />
19                 <apply>
20                     <power />
21                     <ci>R</ci>
22                     <ci>n</ci>
23                 </apply>
24                 <apply>
25                     <plus />
26                     <apply>
27                         <power />
28                         <ci>K</ci>
29                         <ci>n</ci>
30                     </apply>
31                     <apply>
32                         <power />
33                         <ci>R</ci>
34                         <ci>n</ci>
35                     </apply>
36                 </apply>
37             </apply>
38         </math>
39     </computeChange>
40   </listOfChanges>
41 </model>
```

Listing 2.42: The `computeChange` element

The example in Listing 2.42 computes a change of the variable `sensor` of the model `model2`. To do so, it uses the value of the variable `regulator` coming from model `model1`. In addition, the calculation used two additional parameters, the cooperativity `n`, and the sensitivity `K`. The mathematical expression in the mathML then computes the new initial value of `sensor` using the equation:

$$S = S \times \frac{R^n}{K^n + R^n} .$$

2.4.6 Simulation

A simulation is the execution of some defined algorithm(s). Simulations are described differently depending on the type of simulation experiment to be performed (Figure 2.30 on the next page).

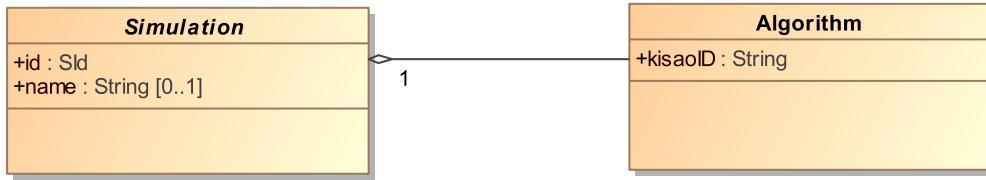


Figure 2.30: The SED-ML `Simulation` class

Simulation is an abstract class and serves as the container for the different types of simulation experiments. SED-ML Level 1 Version 3 offers the predefined simulation classes `UniformTimeCourse`, `OneStep` and `SteadyState`. Further simulation classes are planned for future versions of SED-ML, including simulation classes for bifurcation analysis. Simulation algorithms used for the execution of a simulation setup are defined in the **Algorithm** class.

Table 2.18 shows all attributes and sub-elements for the `simulation` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
<code>metaid^o</code>	page 19
<code>id</code>	page 18
<code>name^o</code>	page 18
sub-elements	description
<code>notes^o</code>	page 19
<code>annotation^o</code>	page 20
<code>algorithm</code>	page 48

Table 2.18: Attributes and nested elements for `simulation`. xy^o denotes optional elements and attributes.

Listing 2.43 shows the use of the `simulation` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfSimulations>
2   <uniformTimeCourse [...]>
3     [SIMULATION SPECIFICATION]
4   </uniformTimeCourse>
5   <uniformTimeCourse [...]>
6     [SIMULATION SPECIFICATION]
7   </uniformTimeCourse>
8 </listOfSimulations>

```

Listing 2.43: The SED-ML `listOfSimulations` element, defining two different simulations

Two timecourses with uniform range are defined.

2.4.6.1 Algorithm

SED-ML makes use of the **KiSAO ontology** (Section 2.2.4 on page 17) to refer to a term in the controlled vocabulary identifying the particular simulation algorithm to be used in the simulation.

Each instance of the `Simulation` class must contain one reference to a simulation algorithm (Figure 2.31 on the following page).

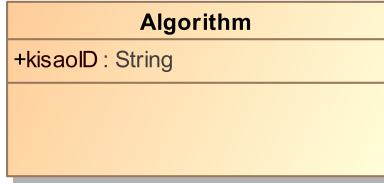


Figure 2.31: The `Algorithm` class

Each instance of the `Algorithm` class must contain a `KiSAO` reference to a simulation algorithm. The reference should define the simulation algorithm to be used in the simulation as precisely as possible, and should be defined in the correct syntax, as defined by the regular expression `KISA0:[0-9]{7}`.

The `Algorithm` class contains an optional list of parameters (`algorithmParameter`) that are used to parameterize the particular algorithm used in the simulation.

Table 2.19 shows all attributes and sub-elements for the `Algorithm` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
kisaoID	page 17
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
algorithmParameter ^o	page 49

Table 2.19: Attributes and nested elements for `algorithm`. `xyo` denotes optional elements and attributes.

The example given in code snippet in Listing 2.43, completed by algorithm definitions results in the code given in Listing 2.44.

```

1 <listOfSimulations>
2   <uniformTimeCourse id="s1" name="time course simulation over 100 minutes" [...]>
3     <algorithm kisaoID="KISA0:0000030" />
4   </uniformTimeCourse>
5   <uniformTimeCourse id="s2" name="time course definition for concentration of p" [...]>
6     <algorithm kisaoID="KISA0:0000021" />
7   </uniformTimeCourse>
8 </listOfSimulations>

```

Listing 2.44: The SED-ML `algorithm` element for two different time course simulations, defining two different algorithms. `KISA0:0000030` refers to the Euler forward method ; `KISA0:0000021` refers to the StochSim nearest neighbor algorithm.

For both simulations, one algorithm is defined. In the first simulation `s1` a deterministic approach has been chosen (Euler forward method), in the second simulation `s2` a stochastic approach is used (Stochsim nearest neighbor).

2.4.6.2 AlgorithmParameter

The `AlgorithmParameter` class allows to parameterize a particular simulation algorithm. The set of possible parameters for a particular instance is determined by the algorithm that is referenced by the `kisaoID` of the enclosing `algorithm` element. Parameters of simulation algorithms are unambiguously referenced by the mandatory `kisaoID` attribute. Their value is set in the mandatory `value` attribute.

```

1 <algorithm kisaoID="KISA0:0000032">
2   <listOfAlgorithmParameters>
3     <algorithmParameter kisaoID="KISA0:0000211" value="23"/>
4   </listOfAlgorithmParameters>
5 </algorithm>

```

Listing 2.45: The SED-ML `algorithmParameter` element setting the parameter value for the simulation algorithm. `KISA0:0000032` refers to the explicit fourth-order Runge-Kutta method;

KISAO:00000211 refers to the absolute tolerance.

2.4.6.3 UniformTimeCourse



Figure 2.32: The `UniformTimeCourse` class

Table 2.20 shows all attributes and sub-elements for the `uniformTimeCourse` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
initialTime	page 50
outputStartTime	page 50
outputEndTime	page 51
numberOfPoints	page 51
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
algorithm	page 48

Table 2.20: Attributes and nested elements for `uniformTimeCourse`. xy^o denotes optional elements and attributes.

Listing 2.46 shows the use of the `uniformTimeCourse` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfSimulations>
2   <uniformTimeCourse id="s1" name="time course simulation of variable v1 over 100 minutes"
3     initialValue="0" outputStartTime="0" outputEndTime="2500" numberOfPoints="1000">
4     <algorithm [...] />
5   </uniformTimeCourse>
6 </listOfSimulations>
  
```

Listing 2.46: The SED-ML `uniformTimeCourse` element, defining a uniform time course simulation over 2500 time units with 1000 simulation points.

2.4.6.3.1 initialTime

The attribute `initialTime` of type `double` represents the time from which to start the simulation. Usually this will be `0`. Listing 2.46 shows an example.

2.4.6.3.2 outputStartTime

Sometimes a researcher is not interested in simulation results at the start of the simulation (i.e. the initial time). To accommodate this in SED-ML the `uniformTimeCourse` class uses the attribute `outputStartTime` of type `double`. To be valid the `outputStartTime` cannot be before `initialTime`. For an example, see Listing 2.46.

2.4.6.3.3 `outputEndTime`

The attribute `outputEndTime` of type `double` marks the end time of the simulation. See Listing 2.46 for an example.

2.4.6.3.4 `numberOfPoints`

When executed, the `uniformTimeCourse` simulation produces output on a regular grid starting with `outputStartTime` and ending with `outputEndTime`. The attribute `numberOfPoints` of type `integer` describes the number of points expected in the result. Software interpreting the `uniformTimeCourse` is expected to produce a first outputPoint at time `outputStartTime` and then `numberOfPoints` output points with the results of the simulation. Thus a total of `numberOfPoints + 1` output points will be produced.

Just because the output points lie on the regular grid described above, this does not mean that the simulation algorithm has to work with the same step size. Usually the step size the simulator chooses will be adaptive and much smaller than the required output step size. On the other hand a stochastic simulator might not have any new events occurring between two grid points. Nevertheless the simulator has to produce data on this regular grid. For an example, see Listing 2.46.

2.4.6.4 `OneStep`

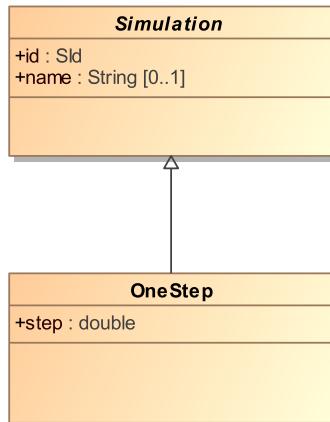


Figure 2.33: The `OneStep` class

The SED-ML `oneStep` 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. However, after running `oneStep`, the desired output time is reached.

Table 2.21 shows all attributes and sub-elements for the `oneStep` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
<code>metaid^o</code>	page 19
<code>id</code>	page 18
<code>name^o</code>	page 18
<code>step</code>	page 52
sub-elements	description
<code>notes^o</code>	page 19
<code>annotation^o</code>	page 20
<code>algorithm</code>	page 48

Table 2.21: Attributes and nested elements for `oneStep`. xy^o denotes optional elements and attributes.

Listing 2.47 shows the use of the `oneStep` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfSimulations>
2   <oneStep id="s1" step="0.1">
3     <algorithm kisaoID="KISAO:0000019" />
4   </oneStep>
5 </listOfSimulations>
```

Listing 2.47: The SED-ML `oneStep` element, specifying to apply the simulation algorithm for another output step of size 0.1.

2.4.6.4.1 step

The `oneStep` class has one required attribute `step` of type `double`. It defines the next output point that should be reached by the algorithm, by specifying the increment from the current output point. Listing 2.47 shows an example.

2.4.6.5 SteadyState

The `SteadyState` class represents a steady state computation (as for example implemented by NLEQ or Kinsolve).

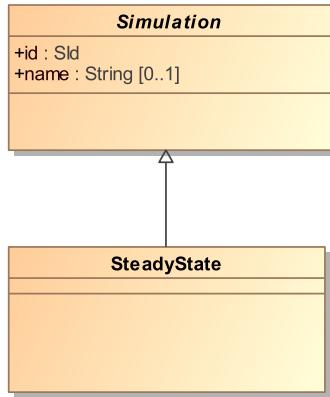


Figure 2.34: The `SteadyState` class

Table 2.22 shows all attributes and sub-elements for the `steadyState` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
algorithm	page 48

Table 2.22: Attributes and nested elements for `steadyState`. xy^o denotes optional elements and attributes.

Listing 2.48 shows the use of the `steadyState` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfSimulations>
2   <steadyState id="steady">
3     <algorithm kisaoID="KISAO:0000282" />
4   </steadyState >
```

```
s </listOfSimulations>
```

Listing 2.48: The SED-ML `steadyState` element, defining a steady state simulation with id `steady`.

2.4.7 Abstract Task

An abstract task in SED-ML represents the base class for all SED-ML tasks. It is not meant to be instantiated directly.

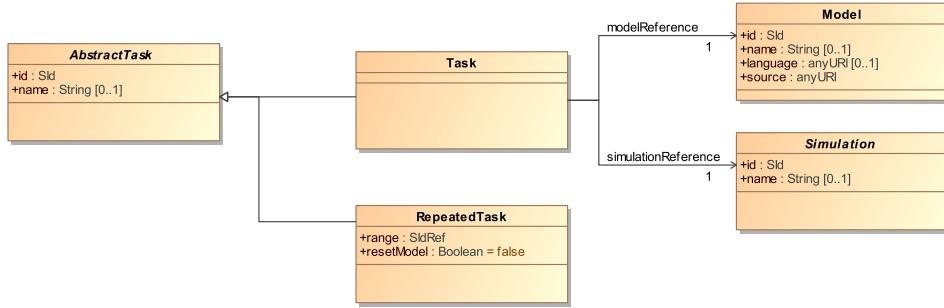


Figure 2.35: The SED-ML Abstract Task class

Table 2.23 shows all attributes and sub-elements for the `abstractTask` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
<code>metaid^o</code>	page 19
<code>id</code>	page 18
<code>name^o</code>	page 18
sub-elements	description
<code>notes^o</code>	page 19
<code>annotation^o</code>	page 20

Table 2.23: Attributes and nested elements for `abstractTask`. xy^o denotes optional elements and attributes.

2.4.8 Task

A task in SED-ML links a `model` to a certain `simulation` description via their respective identifiers (Figure 2.36 on the next page), using the `modelReference` and the `simulationReference`. The task class receives the `id` and `name` attributes from the `AbstractTask`.

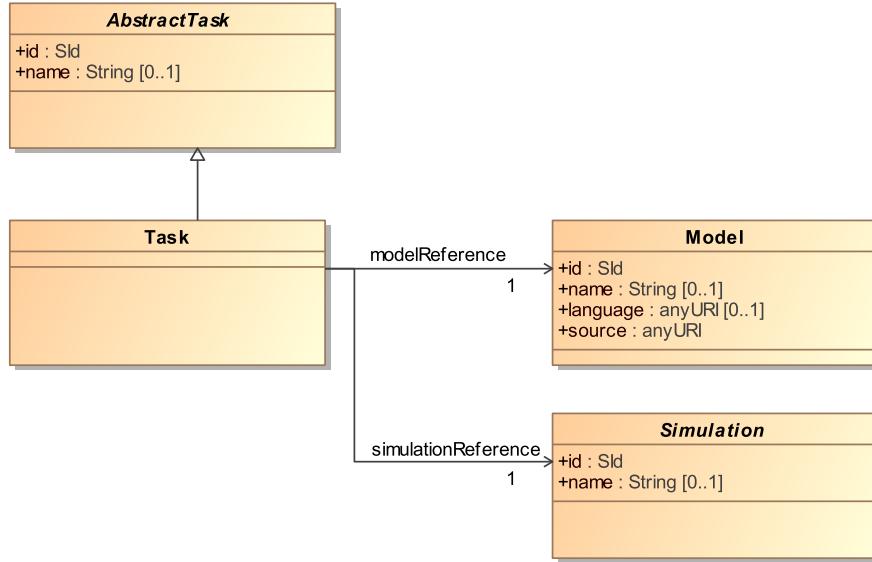


Figure 2.36: The SED-ML Task class

In SED-ML Level 1 Version 3 it is only possible to link one simulation description to one model at a time. However, one can define as many tasks as needed within one experiment description. Please note that the tasks may be executed in any order, as determined by the implementation.

Table 2.24 shows all attributes and sub-elements for the `task` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
modelReference	page 23
simulationReference	page 24
sub-elements	description
notes ^o	page 19
annotation ^o	page 20

Table 2.24: Attributes and nested elements for `task`. xy^o denotes optional elements and attributes.

Listing 2.49 shows the use of the `task` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfTasks>
2   <task id="t1" name="task definition" modelReference="model1"
3     simulationReference="simulation 1" />
4   <task id="t2" name="another task definition" modelReference="model2"
5     simulationReference="simulation 1" />
6 </listOfTasks>

```

Listing 2.49: The `task` element

In the example, a simulation setting `simulation1` is applied first to `model1` and then is applied to `model2`.

2.4.9 Repeated Task

The `repeatedTask` class provides a generic looping construct, allowing complex tasks to be represented by composing separate steps. It performs a specified task (or sequence of tasks) multiple times (where the exact number is specified through a `range` construct), while allowing specific quantities in the model to be altered at each iteration (as defined in the `listOfChanges`).

The `RepeatedTask` inherits from `AbstractTask`. Additionally it has two required attributes `range` and `resetModel` as well as child elements `listOfRanges`, `listOfChanges` and `listOfSubTasks`. Of these only `listOfChanges` is optional.

Note that the order of activities within each iteration of a `repeatedTask` is as follows. Firstly the model is reset, if specified by the `resetModel` attribute. Secondly any changes to the model specified by `setValue` elements are made. Finally, the `subTasks` are executed once each in order.

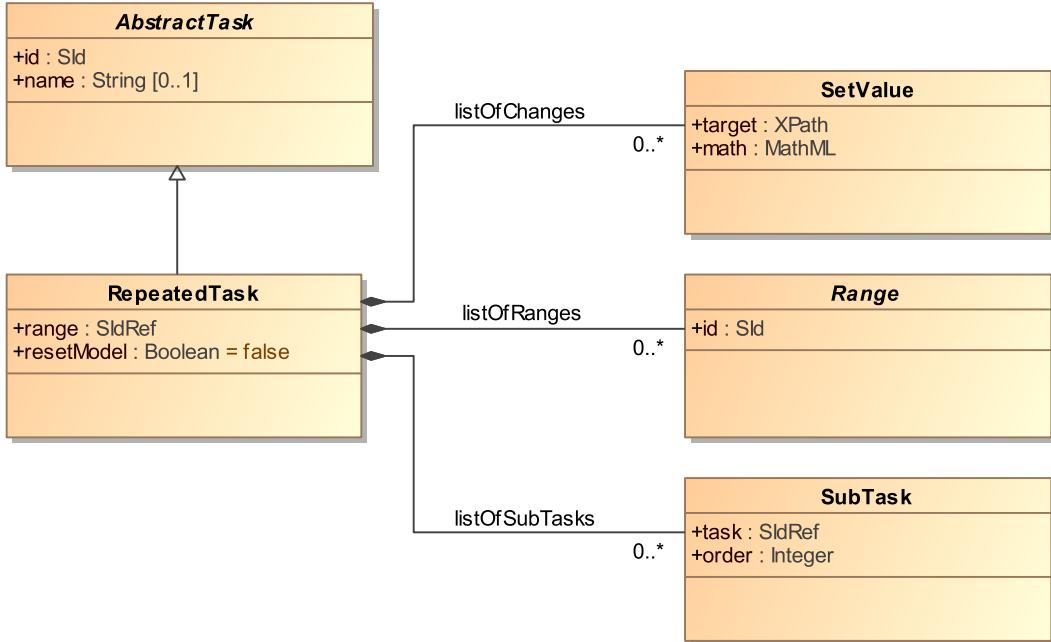


Figure 2.37: The SED-ML `RepeatedTask` class

Table 2.25 shows all attributes and sub-elements for the `repeatedTask` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
range	page 56
resetModel	page 56

sub-elements	description
notes ^o	page 19
annotation ^o	page 20
range	page 56
change ^o	page 59
subTask ^o	page 59

Table 2.25: Attributes and nested elements for `repeatedTask`. xy^o denotes optional elements and attributes.

Listing 2.50 shows the use of the `repeatedTask` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <task id="task1" modelReference="model1" simulationReference="simulation1" />
2
3 <repeatedTask id="task3" resetModel="false" range="current"
4   xmlns:s='http://www.sbml.org/sbml/level3/version1/core'>

```

```

5   <listOfRanges>
6     <vectorRange id="current">
7       <value> 1 </value>
8       <value> 4 </value>
9       <value> 10 </value>
10    </vectorRange>
11  </listOfRanges>
12  <listOfChanges>
13    <setValue target="/s:sbml/s:model/s:listOfParameters/s:parameter[@id='w']" modelReference="model1">
14      <listOfVariables>
15        <variable id="val" name="current range value" target="#current" />
16      </listOfVariables>
17      <math xmlns="http://www.w3.org/1998/Math/MathML">
18        <ci> val </ci>
19      </math>
20    </setValue>
21  </listOfChanges>
22  <listOfSubTasks>
23    <subTask task="task1" />
24  </listOfSubTasks>
25 </repeatedTask>

```

Listing 2.50: The `repeatedTask` element

In the example, `task1` is repeated three times, each time with a different value for a model parameter `w`.

2.4.9.1 The `range` attribute

The `repeatedTask` class has a required attribute `range` of type `SIId`. It specifies which `range` defined in the `listOfRanges` this repeated task iterates over. Listing 2.50 shows an example of a `repeatedTask` iterating over a single range comprising the values: 1, 4 and 10. If there are multiple ranges in the `listOfRanges`, then only the `master range` identified by this attribute determines how many iterations there will be in the `repeatedTask`. All other ranges must allow for at least as many iterations as the master range, and will be moved through in lock-step; their values can be used in `setValue` constructs.

2.4.9.2 The `resetModel` attribute

The `repeatedTask` class has a required attribute `resetModel` of type `boolean`. It specifies whether the model should be reset to the initial state before processing an iteration of the defined `subTasks`. Here initial state refers to the state of the model as given in the `listOfModels`. In the example in Listing 2.50 the repeated task is not to be reset, so a change is made, `task1` is carried out, another change is made, then `task1` continues from there, another change is applied, and `task1` is carried out a last time.

2.4.9.3 The `listOfRanges`

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, an `id` attribute is added. When the value of the `id` attribute is used in a `listOfVariables` within the repeated task class its value is to be replaced with the current value of the range.

There are three different range types permitted in the `listOfRanges`: `UniformRange`, `VectorRange` and `FunctionalRange`. They each inherit from an abstract `Range` class.

2.4.9.3.1 Range

The `Range` class is abstract and exists solely as the base class for the different types of range. Therefore, a SED-ML document will only contain the derived classes listed below.

2.4.9.3.2 UniformRange

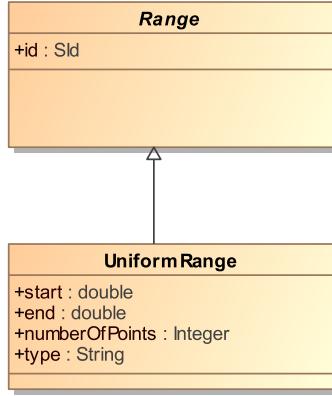


Figure 2.38: The SED-ML `UniformRange` class

The **UniformRange** is quite similar to what is used in the [UniformTimeCourse](#) simulation class. This range is defined through four mandatory attributes: `start`, the start value; `end`, the end value and `numberOfPoints` that contains the number of points the range contains. A fourth attribute `type` that can take the values `linear` or `log` determines whether to draw the values logarithmically (with a base of 10) or linearly.

For example:

```

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

Listing 2.51: The `UniformRange` element

As for [UniformTimeCourse](#), this range will actually produce 101 values uniformly spaced on the interval [0, 10], in ascending order.

The following logarithmic example generates the three values 1, 10 and 100.

```

1      <uniformRange id="current" start="1.0" end="100.0" numberOfPoints="2" type="log" />
  
```

Listing 2.52: The `UniformRange` element with a logarithmic range.

2.4.9.3.3 VectorRange

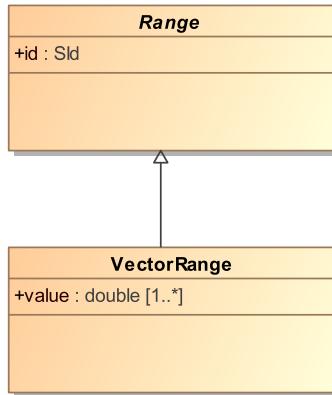


Figure 2.39: The SED-ML `VectorRangeClass` class

A **VectorRange** describes an ordered collection of real values, listing them explicitly within child `value` elements. For example, the range below iterates over the values 1, 4 and 10 in that order.

```

1   <vectorRange id="current">
2       <value> 1 </value>
3       <value> 4 </value>
4       <value> 10 </value>
5   </vectorRange>

```

Listing 2.53: The `VectorRange` element

2.4.9.3.4 FunctionalRange

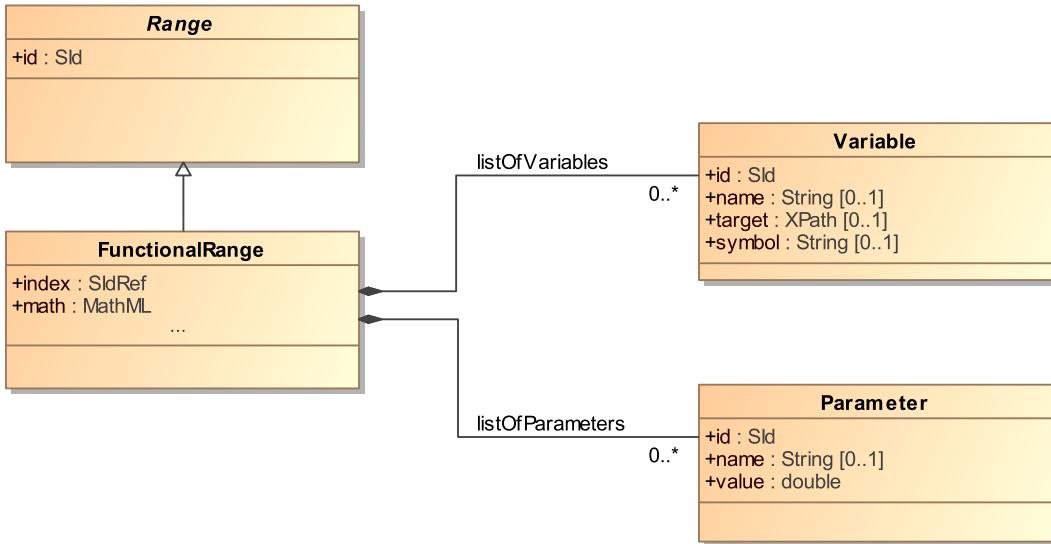


Figure 2.40: The SED-ML `FunctionalRange` class

A `FunctionalRange` constructs a range through calculations that determine the next value based on the value(s) of other range(s) or model variables. In this it is quite similar to the `ComputeChange` element, and shares some of the same child elements. It consists of an optional attribute `range`, two optional elements `listOfVariables` and `listOfParameters`, and a required element `math`.

The optional attribute `range` may be used as a shorthand to specify the `id` of another `Range`. The current value of the referenced range may then be used within the function defining this `FunctionalRange`, just as if that range had been referenced using a `variable` element, except that the `id` of the range is used directly. In other words, whenever the expression contains a `ci` element that contains the value specified in the `range` attribute, the value of the referenced range is to be inserted.

In the `listOfVariables`, `variable` elements define identifiers referring to model variables or range values, which may then be used within the `math` expression. These references always retrieve the `current` value of the model variable or range at the current iteration of the enclosing `repeatedTask`. For a model not being simulated by any `subTask`, the initial state of the model is used.

The `function` encompasses the mathematical expression that is used to compute the value for the functional range at each iteration of the enclosing `repeatedTask`.

For example:

```

1   <functionalRange id="current" range="index"
2       xmlns:s="http://www.sbml.org/sbml/level3/version1/core">
3       <listOfVariables>
4           <variable id="w" name="current parameter value" modelReference="model2"
5               target="/s:sbml/s:model/s:listOfParameters/s:parameter[@id='w']" />
6       </listOfVariables>
7       <math xmlns="http://www.w3.org/1998/Math/MathML">
8           <apply>
9               <times/>
10              <ci> w </ci>
11              <ci> index </ci>
12          </apply>
13      </math>

```

```
14    </functionalRange>
```

Listing 2.54: An example of a `functionalRange` where a parameter `w` of model `model2` is multiplied by `index` each time it is called.

Here is another example, this time using the values in a piecewise expression:

```
1      <uniformRange id="index" start="0" end="10" numberofPoints="100" />
2      <functionalRange id="current" range="index">
3          <math xmlns="http://www.w3.org/1998/Math/MathML">
4              <piecewise>
5                  <piece>
6                      <cn> 8 </cn>
7                      <apply>
8                          <lt />
9                          <ci> index </ci>
10                         <cn> 1 </cn>
11                     </apply>
12                 </piece>
13                 <piece>
14                     <cn> 0.1 </cn>
15                     <apply>
16                         <and />
17                         <apply>
18                             <geq />
19                             <ci> index </ci>
20                             <cn> 4 </cn>
21                         </apply>
22                         <apply>
23                             <lt />
24                             <ci> index </ci>
25                             <cn> 6 </cn>
26                         </apply>
27                     </apply>
28                 </piece>
29                 <otherwise>
30                     <cn> 8 </cn>
31                 </otherwise>
32             </piecewise>
33         </math>
34     </functionalRange>
```

Listing 2.55: A `functionalRange` element that returns 8 if `index` is smaller than 1, 0.1 if `index` is between 4 and 6, and 8 otherwise.

2.4.9.4 The `listOfChanges`

The `listOfChanges` element, when present, contains one or more `setValue` elements. These elements allow the modification of values in the model prior to the next execution of the `subTasks`.

A `setValue` element inherits from the `computeChange` class, which allows it to compute arbitrary expressions involving a number of variables and parameters. The element `setValue` adds a mandatory `modelReference` attribute, and two optional attributes `range` and `symbol`.

The value to be changed is identified via the combination of the attributes `modelReference` and either `symbol` or `target`, in order to select an implicit or explicit variable within the referenced model.

As in `functionalRange`, the attribute `range` may be used as a shorthand for referring to the range whose values will be used to compute a value for the specified model element.

The child `math` contains the expression computing the value by referring to optional parameters, variables or ranges. Again as for `functionalRange`, variable references always retrieve the `current` value of the model variable or range at the current iteration of the enclosing `repeatedTask`. For a model not being simulated by any `subTask`, the initial state of the model is used.

```
1      <listOfChanges>
2          <setValue target="/s:sbml/s:model/s:listOfParameters/s:parameter[@id='w']"
3              range="current" modelReference="model1">
4              <math xmlns="http://www.w3.org/1998/Math/MathML">
5                  <ci> current </ci>
6              </math>
7          </setValue>
8      </listOfChanges>
```

Listing 2.56: A `setValue` element setting `w` to the values of the range with id `current`.

2.4.9.5 The `listOfSubTasks`

The `listOfSubTasks` contains one or more `subTask` elements that specify what simulations are to be performed by the `RepeatedTask`. All `subTasks` have to be carried out sequentially, each continuing from

the current model state (i.e. as at the end of the previous `subTask`, assuming it simulates the same model), and with their results concatenated (thus appearing identical to a single complex simulation). The `subTask` itself has one required attribute `task` that references the `id` of another task defined in the `listOfTasks`. The order in which to run multiple `subTasks` should be specified using `order` attributes on the `subTask` elements; if these are omitted the ordering is given by the order of the `subTask` elements. In order to establish that one `subTask` should be carried out before another its `order` attribute has to have a lower number (c.f. Listing 2.57).

```

1  <listOfSubTasks>
2    <subTask task="task1" order="2"/>
3    <subTask task="task2" order="1"/>
4  </listOfSubTasks>
```

Listing 2.57: The `subTask` element. In this example the task `task2` has to be carried out before `task1`.

2.4.10 DataGenerator

The `DataGenerator` class prepares the raw simulation results for later output (Figure 2.41). It encodes the post-processing to be applied to the simulation data. The post-processing steps could be anything, from simple normalisations of data to mathematical calculations.

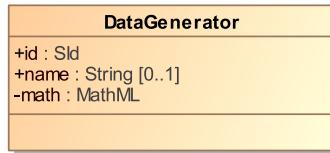


Figure 2.41: The SED-ML `DataGenerator` class

Each instance of the `DataGenerator` class is identifiable within the experiment by its unambiguous `id`. It can be further characterised by an optional `name`. The related `Math` class contains a mathML expression for the calculation of the data generator. Mathematical functions available for the specification of data generators are given in Section 2.2.1 on page 14. `Variable` and `Parameter` instances can be used to encode the mathematical expression.

Table 2.26 shows all attributes and sub-elements for the `dataGenerator` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18

sub-elements	description
math	page 46
notes ^o	page 19
annotation ^o	page 20
variable ^o	page 25
parameter ^o	page 27

Table 2.26: Attributes and nested elements for `dataGenerator`. xy^o denotes optional elements and attributes.

Listing 2.58 shows the use of the `dataGenerator` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1  <listOfDataGenerators>
2    <dataGenerator id="d1" name="time">
3      <listOfVariables>
4        <variable id="time" taskReference="task1" symbol="urn:sedml:symbol:time" />
5      </listOfVariables >
```

```

6   <listOfParameters />
7   <math xmlns="http://www.w3.org/1998/Math/MathML">
8     <ci> time </ci>
9   </math>
10  </dataGenerator>
11  <dataGenerator id="d2" name="LaCI repressor">
12    <listOfVariables>
13      <variable id="v1" taskReference="task1"
14        target="/sbml:sbml:sbml:model:sbml:listOfSpecies/
15          sbml:species[@id='PX']" />
16    </listOfVariables>
17    <math:math>
18      <math:ci>v1</math:ci>
19    </math:math>
20  </dataGenerator>
21 </listOfDataGenerators>

```

Listing 2.58: Definition of two `dataGenerator` elements, time and LaCI repressor

The `listOfDataGenerator` contains two `dataGenerator` elements. The first one, `d1`, refers to the task definition `t1` (which itself refers to a particular model), and from the corresponding model it reuses the symbol `time`. The second one, `d2`, references a particular species defined in the same model (and referred to via the `taskReference="t1"`). The model species with ID `PX` is reused for the data generator `d2` without further post-processing.

2.4.11 Output

The `Output` class describes how the results of a simulation should be presented to the user (Figure 2.42).

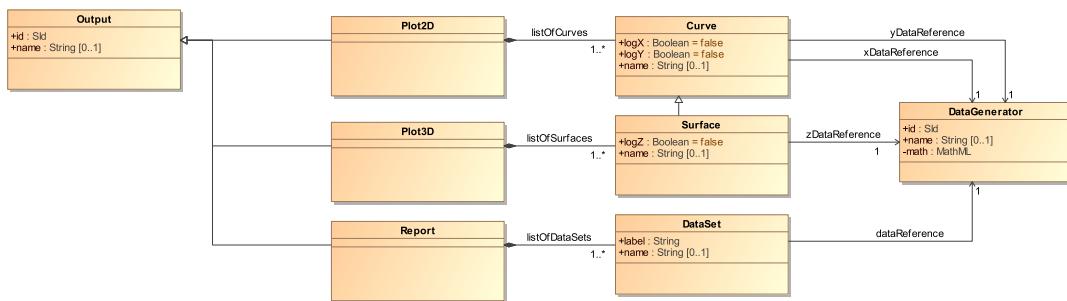


Figure 2.42: The SED-ML Output class

It does not contain the data itself, but the type of output and the `data generators` used to produce a particular output.

The types of output pre-defined in SED-ML Level 1 Version 3 are plots and `reports`. The output can be defined as a `2D plot` or alternatively as a `3D plot`.

Note that even though the terms “`2D plot`” and “`3D plot`” are used, the exact type of plot is not specified. In other words, whether the `3D plot` represents a surface plot, or three dimensional lines in space, cannot be distinguished by SED-ML alone. It is expected that applications use `annotations` for this purpose.

Table 2.27 on the following page shows all attributes and sub-elements for the `output` element as defined by the SED-ML Level 1 Version 3 XML Schema.

2.4.11.1 Plot2D

A `2 dimensional plot` (Figure 2.43 on the next page) contains a number of `curve` definitions.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
plot2D ^o	page 61
plot3D ^o	page 63
report ^o	page 63

Table 2.27: Attributes and nested elements for `output`. xy^o denotes optional elements and attributes.

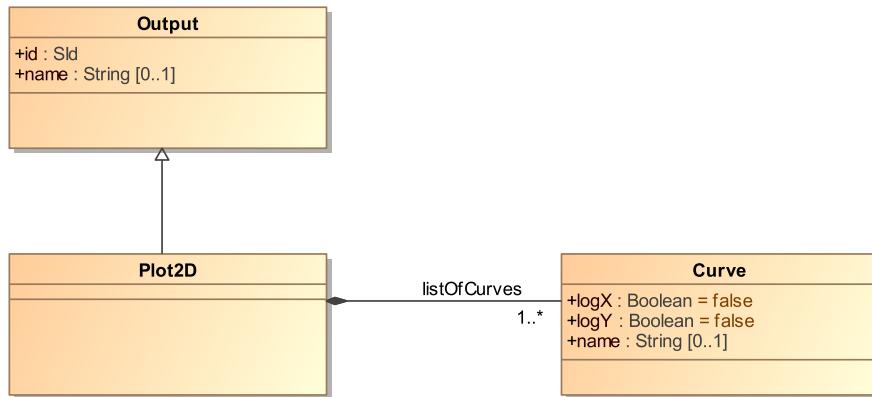


Figure 2.43: The SED-ML Plot2D class

Table 2.28 shows all attributes and sub-elements for the `plot2D` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
curve	page 64

Table 2.28: Attributes and nested elements for `plot2D`. xy^o denotes optional elements and attributes.

Listing 2.59 shows the use of the `listOfCurves` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <plot2D>
2   <listOfCurves>
3     <curve>
4       [CURVE DEFINITION]
5     </curve>
6     [FURTHER CURVE DEFINITIONS]
7   </listOfCurves>
8 </plot2D>
  
```

Listing 2.59: The `plot2D` element with the nested `listOfCurves` element

The listing shows the definition of a 2 dimensional plot containing one `curve` element inside the `listOfCurves`. The curve definition follows in Section 2.4.12.1 on [page 64](#).

2.4.11.2 Plot3D

A 3 dimensional plot (Figure 2.44) contains a number of `surface` definitions.

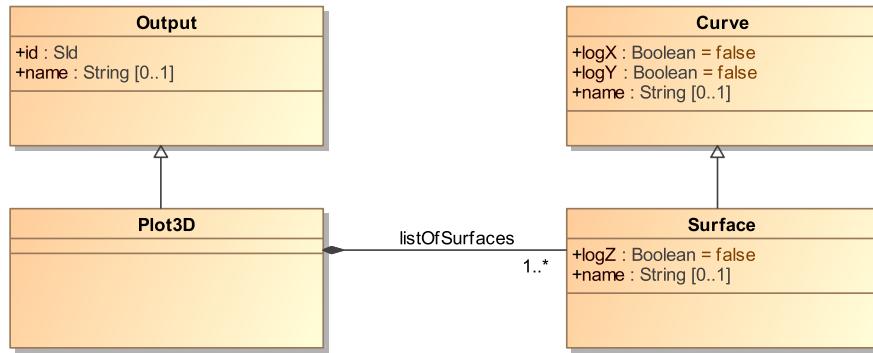


Figure 2.44: The SED-ML `Plot3D` class

Table 2.29 shows all attributes and sub-elements for the `plot3D` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
surface	page 66

Table 2.29: Attributes and nested elements for `plot3D`. xy^o denotes optional elements and attributes.

Listing 2.60 shows the use of the `plot3D` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <plot3D>
2   <listOfSurfaces>
3     <surface>
4       [SURFACE DEFINITION]
5     </surface>
6     [FURTHER SURFACE DEFINITIONS]
7   </listOfSurfaces>
8 </plot3D>
  
```

Listing 2.60: The `plot3D` element with the nested `listOfSurfaces` element

The example defines a `surface` for the 3 dimensional plot. The surface definition follows in Section 2.4.12.2 on page 66.

2.4.11.3 The Report class

The `Report` class defines a data table consisting of several single instances of the `DataSet` class (Figure 2.45 on the next page). Its output returns the simulation result in actual *numbers*. The particular columns of the report table are defined by creating an instance of the `DataSet` class for each column.

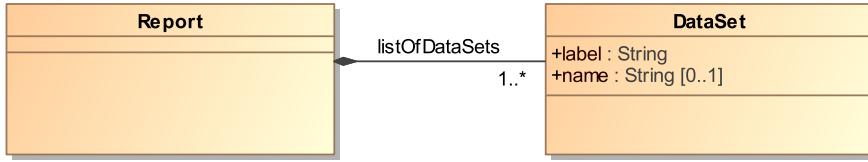


Figure 2.45: The SED-ML Report class

Table 2.30 shows all attributes and sub-elements for the `report` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
sub-elements	description
notes ^o	page 19
annotation ^o	page 20
dataSet	page 67

Table 2.30: Attributes and nested elements for `report`. xy^o denotes optional elements and attributes.

Listing 2.61 shows the use of the `listOfDataSets` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <report>
2   <listOfDataSets>
3     <dataSet>
4       [DATA REFERENCE]
5     </dataSet>
6   </listOfDataSets>
7 </report>
  
```

Listing 2.61: The `report` element with the nested `listOfDataSets` element

The simulation result itself, i.e. concrete result numbers, are not stored in SED-ML, but the directive how to *calculate* them from the output of the simulator is provided through the `dataGenerator`.

The encoding of simulation results is outside the scope of SED-ML, but other efforts exist, for example the *Systems Biology Result Markup Language* (SBRML, [9]).

2.4.12 Output components

2.4.12.1 Curve

One or more instances of the `Curve` class define a 2D plot. A `curve` needs a data generator reference to refer to the data that will be plotted on the x-axis, using the `xDataReference`. A second data generator reference is needed to refer to the data that will be plotted on the y-axis, using the `yDataReference`.

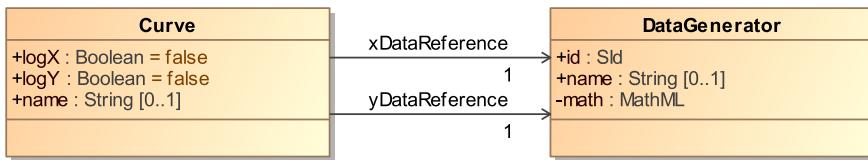


Figure 2.46: The SED-ML Curve class

Table 2.31 on the following page shows all attributes and sub-elements for the `curve` element as defined

by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
logX	page 65
xDataReference	page 65
logY	page 65
yDataReference	page 65
sub-elements	description
notes ^o	page 19
annotation ^o	page 20

Table 2.31: Attributes and nested elements for `curve`. xy^o denotes optional elements and attributes.

Listing 2.62 shows the use of the `curve` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfCurves>
2   <curve id="c1" name="v1 / time" xDataReference="dg1" yDataReference="dg2" logX="true" logY="false" />
3 </listOfCurves>
```

Listing 2.62: The SED-ML `curve` element, defining the output curve showing the result of simulation for the referenced dataGenerators

Here, only one curve is created, results shown on the x-axis are generated by the data generator `dg1`, results shown on the y-axis are generated by the data generator `dg2`. Both `dg1` and `dg2` need to be already defined in the `listOfDataGenerators`. The x-axis is plotted logarithmically.

2.4.12.1.1 `logX`

`logX` is a required attribute of the `Curve` class and defines whether or not the data output on the x-axis is logarithmic. The data type of `logX` is `boolean`. To make the output on the x-axis of a plot logarithmic, `logX` must be set to “true”, as shown in the sample Listing 2.62.

`logX` is also used in the definition of a `Surface` output.

2.4.12.1.2 `logY`

`logY` is a required attribute of the `Curve` class and defines whether or not the data output on the y-axis is logarithmic. The data type of `logY` is `boolean`. To make the output on the y-axis of a plot logarithmic, `logY` must be set to “true”, as shown in the sample Listing 2.62.

`logY` is also used in the definition of a `Surface` output.

2.4.12.1.3 `xDataReference`

The `xDataReference` is a mandatory attribute of the `Curve` object. Its content refers to a `DataGenerator` ID which denotes the `DataGenerator` object that is used to generate the output on the x-axis of a `Curve` in a `2D Plot`. The `xDataReference` data type is `string`. However, the valid values for the `xDataReference` are restricted to the IDs of already defined `DataGenerator objects`.

An example for the definition of a curve is given in Listing 2.62. `xDataReference` is also used in the definition of the x-axis of a `Surface` in a `3D Plot`.

2.4.12.1.4 `yDataReference`

The `yDataReference` is a mandatory attribute of the `Curve` object. Its content refers to a `DataGenerator` ID which denotes the `DataGenerator` object that is used to generate the output on the y-axis of a `Curve` in a `2D Plot`. The `yDataReference` data type is `string`. However, the number of valid values for the `yDataReference` is restricted to the IDs of already defined `DataGenerator objects`.

An example for the definition of a curve is given in Listing 2.62. `yDataReference` is also used in the

definition of the y-axis of a [Surface](#) in a [3D Plot](#).

2.4.12.2 Surface

A [surface](#) is a three-dimensional figure representing a simulation result (Figure 2.47).

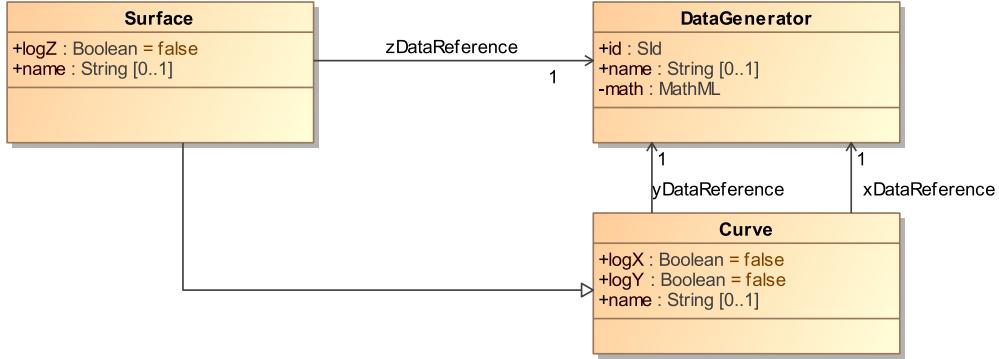


Figure 2.47: The SED-ML Surface class

Creating an instance of the [Surface](#) class requires the definition of three different axes, that is which data to plot on which axis and in which way. The aforementioned [xDataReference](#) and [yDataReference](#) attributes define the according [data generators](#) for both the x- and y-axis of a surface. In addition, the [zDataReference](#) attribute defines the output for the z-axis. All axes might be logarithmic or not. This can be specified through the [logX](#), [logY](#), and the [logZ](#) attributes in the according [dataReference](#) elements.

Table 2.32 shows all attributes and sub-elements for the [surface](#) element as defined by the SED-ML Level 1 Version 3 XML Schema. Listing 2.63 shows the use of the [surface](#) element in a SED-ML file

attribute	description
metaid ^o	page 19
id	page 18
name ^o	page 18
logX	page 65
xDataReference	page 65
logY	page 65
yDataReference	page 65
logZ	page 67
zDataReference	page 67
sub-elements	description
notes ^o	page 19
annotation ^o	page 20

Table 2.32: Attributes and nested elements for [surface](#). xy^o denotes optional elements and attributes.

as defined by the SED-ML Level 1 Version 3 XML Schema.

```

1 <listOfSurfaces>
2   <surface id="s1" name="surface" xDataReference="dg1" yDataReference="dg2" zDataReference="dg3"
3     logX="true" logY="false" logZ="false" />
4   [FURTHER SURFACE DEFINITIONS]
5 </listOfSurfaces>
  
```

Listing 2.63: The SED-ML [surface](#) element, defining the output showing the result of the referenced task

Here, only one surface is created, results shown on the x-axis are generated by the data generator dg1, results shown on the y-axis are generated by the data generator dg2, and results shown on the z-axis are generated by the data generator dg3. All dg1, dg2 and dg3 need to be already defined in the

`listOfDataGenerators`.

2.4.12.2.1 `logZ`

`logZ` is a required attribute of the `Surface` class and defines whether or not the data output on the z-axis is logarithmic. The data type of `logZ` is `boolean`. To make the output on the z-axis of a surface plot logarithmic, `logZ` must be set to “true”, as shown in the sample Listing 2.63.

2.4.12.2.2 `zDataReference`

The `zDataReference` is a mandatory attribute of the `Surface` object. Its content refers to a `dataGenerator` ID which denotes the `DataGenerator` object that is used to generate the output on the z-axis of a `3D Plot`. The `zDataReference` data type is `string`. However, the valid values for the `zDataReference` are restricted to the IDs of already defined `DataGenerator objects`.

An example using the `zDataReference` is given in Listing 2.63 on page 66.

2.4.12.3 `DataSet`

The `DataSet` class holds definitions of data to be used in the `Report` class (Figure 2.48).



Figure 2.48: The SED-ML `DataSet` class

Data sets are labeled references to instances of the `DataGenerator` class.

Table 2.33 shows all attributes and sub-elements for the `dataSet` element as defined by the SED-ML Level 1 Version 3 XML Schema.

attribute	description
<code>metaid^o</code>	page 19
<code>id</code>	page 18
<code>name^o</code>	page 18
<code>dataReference</code>	page 67
<code>label</code>	page 67
sub-elements	description
<code>notes^o</code>	page 19
<code>annotation^o</code>	page 20

Table 2.33: Attributes and nested elements for `dataSet`. xy^o denotes optional elements and attributes.

2.4.12.3.1 `label`

Each data set in a `Report` does have to carry an unambiguous `label`. A label is a human readable descriptor of a data set for use in a `report`. For example, for a tabular data set of time series results, the label could be the column heading.

2.4.12.3.2 `dataReference`

The `dataReference` attribute contains the ID of a `dataGenerator` element and as such represents a link to it. The data produced by that particular data generator fills the according data set in the `report`. Listing 2.64 on the next page shows the use of the `dataSet` element in a SED-ML file as defined by the SED-ML Level 1 Version 3 XML Schema.

```
1 <listOfDataSets>
2   <dataSet id="d1" name="v1 over time" dataReference="dg1" label="_1">
3 </listOfDataSets>
```

Listing 2.64: The SED-ML `dataSet` element, defining a data set containing the result of the referenced task

3. COMBINE archive

A COMBINE archive [2] is a single file that supports the exchange of all the information necessary for a modeling and simulation experiment in biology. A COMBINE archive file is a ZIP container that includes a manifest file, listing the content of the archive, an optional metadata file adding information about the archive and its content, and the files describing the model. The content of a COMBINE Archive consists of files encoded in COMBINE standards whenever possible, but may include additional files defined by an Internet Media Type. Several tools that support the COMBINE Archive are available, either as independent libraries or embedded in modeling software.

The COMBINE archive is described at <http://combine.org/documents/archive> and in [2].

COMBINE archives are the recommended means for distributing simulation experiment descriptions in SED-ML, the respective data and model files, and the simulation results (figures and reports).

4. Acknowledgements

The SED-ML specification is developed with the input of many people. The following individuals served as past SED-ML Editors and contributed to SED-ML specifications. Their efforts helped shape what SED-ML is today.

- Richard Adams (editor, 2011-2012)
- Frank Bergmann (editor, 2011-2014)
- Jonathan Cooper (editor, 2012-2015)
- Nicolas Le Novère (editorial advisor, 2011-2012, 2013)
- Andrew Miller (editor, 2011-2012)
- Ion Moraru (editor, 2014-2016)
- Sven Sahle (editor, 2014-2016)
- Herbert Sauro

Moreover, we would like to thank all the participants of the meetings where SED-ML has been discussed as well as the members of the SED-ML community.

A. SED-ML UML Overview

Figure A.1 shows the complete UML diagram of the SED-ML. It gives the full picture of all implemented classes (see the XML Schema definition on page 72).

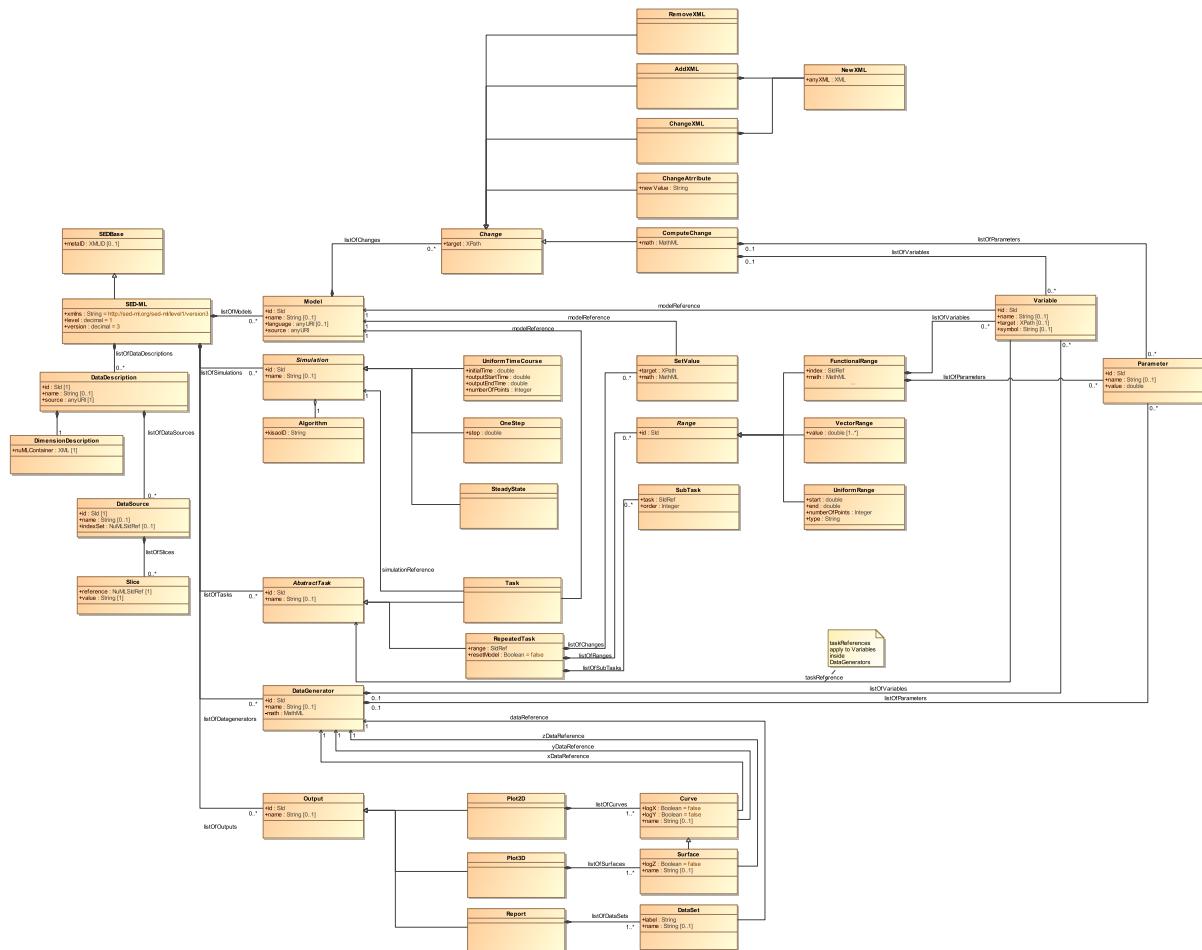


Figure A.1: The SED-ML UML class diagram

B. XML Schema

Listing B.1 shows the full SED-ML XML Schema. The code is commented inline.

```
1 <xs:schema targetNamespace="http://sed-ml.org/sed-ml/level1/version3" xmlns="http://sed-ml.org/sed-ml/
  level1/version3"
2   xmlns:xs="http://www.w3.org/2001/XMLSchema" xmlns:math="http://www.w3.org/1998/Math/MathML"
3   elementFormDefault="qualified">
4   <xs:import namespace="http://www.w3.org/1998/Math/MathML" schemaLocation="sedml-mathml.xsd" />
5
6
7   <xs:simpleType name="SId">
8     <xs:annotation>
9       <xs:documentation>
10         The type SId is used throughout SED-ML as the
11         type of the 'id' attributes on SED-ML elements.
12       </xs:documentation>
13     </xs:annotation>
14     <xs:restriction base="xs:string">
15       <xs:pattern value="(_|[a-z]|[A-Z])(_|[a-z]|[A-Z]|[_0-9])*" />
16     </xs:restriction>
17   </xs:simpleType>
18
19   <!-- Attribute group for elements with ID & name attributes -->
20   <xs:attributeGroup name="idGroup">
21     <xs:attribute name="id" use="required" type="SId"></xs:attribute>
22     <xs:attribute name="name" use="optional" type="xs:string"></xs:attribute>
23   </xs:attributeGroup>
24
25   <!-- SED Base class -->
26   <xs:complexType name="SEDBase">
27     <xs:annotation>
28       <xs:documentation xml:lang="en">
29         The SEDBase type is the
30         base type of all main types in SED-ML. It
31         serves as a container for
32         the annotation of any part of the
33         experiment description.
34       </xs:documentation>
35     </xs:annotation>
36     <xs:sequence>
37       <xs:element ref="notes" minOccurs="0" />
38       <xs:element ref="annotation" minOccurs="0" />
39     </xs:sequence>
40   <!--
41     This must be a variable-type identifier, i.e., (Letter | '_')
42     (NCNameChar)* that is unique in the document.
43   -->
44   <xs:attribute name="metaid" type="xs:ID" use="optional"></xs:attribute>
45 </xs:complexType>
46
47   <!-- SED ML Top level element -->
48   <xs:element name="sedML">
49     <xs:complexType>
50       <xs:complexContent>
51         <xs:extension base="SEDBase">
52           <xs:sequence>
53             <xs:element ref="listOfDataDescriptions" minOccurs="0" />
54             <xs:element ref="listOfSimulations" minOccurs="0" />
55             <xs:element ref="listOfModels" minOccurs="0" />
56             <xs:element ref="listOfTasks" minOccurs="0" />
57             <xs:element ref="listOfDataGenerators" minOccurs="0" />
58             <xs:element ref="listOfOutputs" minOccurs="0" />
59           </xs:sequence>
60           <xs:attribute name="level" type="xs:decimal" use="required" fixed="1" />
61           <xs:attribute name="version" type="xs:decimal" use="required" fixed="3" />
62         </xs:extension>
63       </xs:complexContent>
64     </xs:complexType>
65   </xs:element>
66
67   <!-- notes and annotations -->
68   <xs:element name="notes">
```

```

69      <xs:complexType>
70          <xs:sequence>
71              <xs:any namespace="http://www.w3.org/1999/xhtml"
72                  processContents="skip" minOccurs="0" maxOccurs="unbounded" />
73          </xs:sequence>
74      </xs:complexType>
75  </xs:element>
76  <xs:element name="annotation">
77      <xs:complexType>
78          <xs:sequence>
79              <xs:any processContents="skip" minOccurs="0" maxOccurs="unbounded" />
80          </xs:sequence>
81      </xs:complexType>
82  </xs:element>
83
84  <!-- KiSAO ID type -->
85  <xs:simpleType name="KisaoType">
86      <xs:restriction base="xs:string">
87          <xs:pattern value="KISAO:[0-9]{7}" />
88      </xs:restriction>
89  </xs:simpleType>
90
91  <!-- global element declarations -->
92  <xs:element name="variable">
93      <xs:complexType>
94          <xs:complexContent>
95              <xs:extension base="SEDBase">
96                  <!-- at least one of taskReference or modelReference must be set -->
97                  <xs:attribute name="taskReference" type="SID" use="optional" />
98                  <xs:attribute name="modelReference" type="SID" use="optional" />
99
100                 <!-- either target or symbol have to be used in the variable definition -->
101                 <xs:attribute name="target" type="xs:token" use="optional" />
102                 <xs:attribute name="symbol" type="xs:string" use="optional" />
103                 <xs:attributeGroup ref="idGroup" />
104             </xs:extension>
105         </xs:complexContent>
106     </xs:complexType>
107  </xs:element>
108
109  <xs:element name="parameter">
110      <xs:complexType>
111          <xs:complexContent>
112              <xs:extension base="SEDBase">
113                  <xs:attributeGroup ref="idGroup" />
114                  <xs:attribute name="value" type="xs:double" use="required" />
115              </xs:extension>
116          </xs:complexContent>
117      </xs:complexType>
118  </xs:element>
119
120  <!-- The model(s) to simulate/analyse -->
121  <xs:element name="model">
122      <xs:complexType>
123          <xs:complexContent>
124              <xs:extension base="SEDBase">
125                  <xs:sequence>
126                      <xs:element ref="listOfChanges" minOccurs="0" />
127                  </xs:sequence>
128                      <xs:attribute name="language" type="xs:anyURI" use="optional"
129                          default="urn:sedml:language:xml" />
130                      <xs:attribute name="source" type="xs:anyURI" use="required" />
131                      <xs:attributeGroup ref="idGroup" />
132                  </xs:extension>
133          </xs:complexContent>
134      </xs:complexType>
135  </xs:element>
136
137  <!-- Model pre-processing changes -->
138  <xs:element name="newXML">
139      <xs:complexType>
140          <xs:sequence>
141              <xs:any processContents="skip" minOccurs="1" maxOccurs="unbounded" />
142          </xs:sequence>
143      </xs:complexType>
144  </xs:element>
145
146  <xs:element name="changeAttribute">
147      <xs:complexType>
148          <xs:complexContent>
149              <xs:extension base="SEDBase">
150                  <xs:attribute name="target" use="required" type="xs:token" />
151                  <xs:attribute name="newValue" type="xs:string" use="required" />
152              </xs:extension>
153          </xs:complexContent>
154      </xs:complexType>
155  </xs:element>
156
157  <xs:element name="changeXML">
```

```

158      <xs:complexType>
159          <xs:complexContent>
160              <xs:extension base="SEDBase">
161                  <xs:sequence>
162                      <xs:element ref="newXML" />
163                  </xs:sequence>
164                  <xs:attribute name="target" use="required" type="xs:token" />
165              </xs:extension>
166          </xs:complexContent>
167      </xs:complexType>
168  </xs:element>
169
170  <xs:element name="addXML">
171      <xs:complexType>
172          <xs:complexContent>
173              <xs:extension base="SEDBase">
174                  <xs:sequence>
175                      <xs:element ref="newXML" />
176                  </xs:sequence>
177                  <xs:attribute name="target" use="required" type="xs:token" />
178              </xs:extension>
179          </xs:complexContent>
180      </xs:complexType>
181  </xs:element>
182
183  <xs:element name="removeXML">
184      <xs:complexType>
185          <xs:complexContent>
186              <xs:extension base="SEDBase">
187                  <xs:attribute name="target" use="required" type="xs:token" />
188              </xs:extension>
189          </xs:complexContent>
190      </xs:complexType>
191  </xs:element>
192
193  <xs:complexType name="ComputeChange">
194      <xs:complexContent>
195          <xs:extension base="SEDBase">
196              <xs:sequence>
197                  <xs:element ref="listOfVariables" minOccurs="0" />
198                  <xs:element ref="listOfParameters" minOccurs="0" />
199                  <xs:element ref="math:math" />
200              </xs:sequence>
201              <xs:attribute name="target" use="required" type="xs:token" />
202          </xs:extension>
203      </xs:complexContent>
204  </xs:complexType>
205
206  <xs:element name="computeChange" type="ComputeChange"/>
207
208
209  <!-- The simulation/analysis algorithms to use -->
210  <xs:element name="algorithm">
211      <xs:complexType>
212          <xs:complexContent>
213              <xs:extension base="SEDBase">
214                  <xs:sequence>
215                      <xs:element ref="listOfAlgorithmParameters" minOccurs="0"/>
216                  </xs:sequence>
217                  <xs:attribute name="kisaoID" type="KisaoType" use="required" />
218              </xs:extension>
219          </xs:complexContent>
220      </xs:complexType>
221  </xs:element>
222
223  <xs:element name="algorithmParameter">
224      <xs:complexType>
225          <xs:complexContent>
226              <xs:extension base="SEDBase">
227                  <xs:attribute name="kisaoID" type="KisaoType" use="required"/>
228                  <xs:attribute name="value" type="xs:string" use="required"/>
229              </xs:extension>
230          </xs:complexContent>
231      </xs:complexType>
232  </xs:element>
233
234  <xs:complexType name="Simulation">
235      <xs:complexContent>
236          <xs:extension base="SEDBase">
237              <xs:sequence>
238                  <xs:element ref="algorithm" />
239              </xs:sequence>
240              <xs:attributeGroup ref="idGroup" />
241          </xs:extension>
242      </xs:complexContent>
243  </xs:complexType>
244
245  <xs:element name="uniformTimeCourse">
246      <xs:complexType>

```

```

247     <xs:complexContent>
248         <xs:extension base="Simulation">
249             <xs:attribute name="outputStartTime" type="xs:double" use="required" />
250             <xs:attribute name="outputEndTime" type="xs:double" use="required" />
251             <xs:attribute name="numberOfPoints" type="xs:integer" use="required" />
252             <xs:attribute name="initialTime" type="xs:double" use="required" />
253         </xs:extension>
254     </xs:complexContent>
255   </xs:complexType>
256 </xs:element>
257
258 <xs:element name="oneStep">
259     <xs:complexType>
260         <xs:complexContent>
261             <xs:extension base="Simulation">
262                 <xs:attribute name="step" type="xs:double" use="required"/>
263             </xs:extension>
264         </xs:complexContent>
265     </xs:complexType>
266 </xs:element>
267
268 <xs:element name="steadyState">
269     <xs:complexType>
270         <xs:complexContent>
271             <xs:extension base="Simulation">
272                 <!-- There is actually no difference from the base type here -->
273             </xs:extension>
274         </xs:complexContent>
275     </xs:complexType>
276 </xs:element>
277
278 <!-- The various task elements inherit from AbstractTask -->
279 <xs:complexType name="AbstractTask">
280     <xs:complexContent>
281         <xs:extension base="SEDBase">
282             <xs:attributeGroup ref="idGroup" />
283         </xs:extension>
284     </xs:complexContent>
285 </xs:complexType>
286
287 <xs:element name="task">
288     <xs:complexType>
289         <xs:complexContent>
290             <xs:extension base="AbstractTask">
291                 <xs:attribute name="simulationReference" type="SId" use="required" />
292                 <xs:attribute name="modelReference" type="SId" use="required" />
293             </xs:extension>
294         </xs:complexContent>
295     </xs:complexType>
296 </xs:element>
297
298 <xs:element name="repeatedTask">
299     <xs:complexType>
300         <xs:complexContent>
301             <xs:extension base="AbstractTask">
302                 <xs:sequence>
303                     <xs:element ref="listOfRanges"/>
304                     <xs:element name="listOfChanges" type="repeatedTaskListOfChanges"
305                         minOccurs="0" />
306                     <xs:element ref="listOfSubTasks"/>
307                 </xs:sequence>
308                 <xs:attribute name="range" type="SId" use="required"/>
309                 <xs:attribute name="resetModel" type="SId" use="required"/>
310             </xs:extension>
311         </xs:complexContent>
312     </xs:complexType>
313 </xs:element>
314
315 <!-- Child elements of repeatedTask -->
316 <xs:complexType name="Range">
317     <xs:complexContent>
318         <xs:extension base="SEDBase">
319             <xs:attributeGroup ref="idGroup"/>
320         </xs:extension>
321     </xs:complexContent>
322 </xs:complexType>
323
324 <xs:simpleType name="LogOrLinear">
325     <xs:restriction base="xs:string">
326         <xs:enumeration value="log"/>
327         <xs:enumeration value="linear"/>
328     </xs:restriction>
329 </xs:simpleType>
330
331 <xs:element name="uniformRange">
332     <xs:complexType>
333         <xs:complexContent>
334             <xs:extension base="Range">
335                 <xs:attribute name="start" type="xs:double"/>

```

```

336             <xs:attribute name="end" type="xs:double"/>
337             <xs:attribute name="numberOfPoints" type="xs:integer"/>
338             <xs:attribute name="type" type="LogOrLinear"/>
339         </xs:extension>
340     </xs:complexContent>
341   </xs:complexType>
342 </xs:element>
343
344 <xs:element name="vectorRange">
345   <xs:complexType>
346     <xs:complexContent>
347       <xs:extension base="Range">
348         <xs:sequence>
349           <xs:element name="value" type="xs:double" maxOccurs="unbounded"/>
350         </xs:sequence>
351       </xs:extension>
352     </xs:complexContent>
353   </xs:complexType>
354 </xs:element>
355
356 <xs:element name="functionalRange">
357   <xs:complexType>
358     <xs:complexContent>
359       <xs:extension base="Range">
360         <xs:sequence>
361           <xs:element ref="listOfVariables" minOccurs="0" />
362           <xs:element ref="listOfParameters" minOccurs="0" />
363           <xs:element ref="math:math" />
364         </xs:sequence>
365         <xs:attribute name="range" type="SId" use="optional"/>
366       </xs:extension>
367     </xs:complexContent>
368   </xs:complexType>
369 </xs:element>
370
371 <xs:element name="setValue">
372   <xs:complexType>
373     <xs:complexContent>
374       <xs:extension base="ComputeChange">
375         <xs:attribute name="modelReference" type="SId" use="required"/>
376         <xs:attribute name="range" type="SId" use="optional"/>
377         <xs:attribute name="symbol" type="xs:string" use="optional"/>
378       </xs:extension>
379     </xs:complexContent>
380   </xs:complexType>
381 </xs:element>
382
383 <xs:element name="subTask">
384   <xs:complexType>
385     <xs:complexContent>
386       <xs:extension base="SEDBase">
387         <xs:attribute name="task" type="SId" use="required"/>
388         <xs:attribute name="order" type="xs:integer" use="optional"/>
389       </xs:extension>
390     </xs:complexContent>
391   </xs:complexType>
392 </xs:element>
393
394 <!-- Post-processing using a data generator -->
395 <xs:element name="dataGenerator">
396   <xs:complexType>
397     <xs:complexContent>
398       <xs:extension base="SEDBase">
399         <xs:sequence>
400           <xs:element ref="listOfVariables" minOccurs="0" />
401           <xs:element ref="listOfParameters" minOccurs="0" />
402           <xs:element ref="math:math" />
403         </xs:sequence>
404         <xs:attributeGroup ref="idGroup" />
405       </xs:extension>
406     </xs:complexContent>
407   </xs:complexType>
408 </xs:element>
409
410 <!-- Simulation experiment outputs -->
411 <xs:element name="plot2D">
412   <xs:complexType>
413     <xs:complexContent>
414       <xs:extension base="SEDBase">
415         <xs:sequence>
416           <xs:element ref="listOfCurves" minOccurs="0" />
417         </xs:sequence>
418         <xs:attributeGroup ref="idGroup" />
419       </xs:extension>
420     </xs:complexContent>
421   </xs:complexType>
422 </xs:element>
423
424 <xs:element name="plot3D">
```

```

425      <xs:complexType>
426          <xs:complexContent>
427              <xs:extension base="SEDBase">
428                  <xs:sequence>
429                      <xs:element ref="listOfSurfaces" minOccurs="0" />
430                  </xs:sequence>
431                  <xs:attributeGroup ref="idGroup" />
432              </xs:extension>
433          </xs:complexContent>
434      </xs:complexType>
435  </xs:element>
436
437  <xs:element name="report">
438      <xs:complexType>
439          <xs:complexContent>
440              <xs:extension base="SEDBase">
441                  <xs:sequence>
442                      <xs:element ref="listOfDataSets" minOccurs="0" />
443                  </xs:sequence>
444                  <xs:attributeGroup ref="idGroup" />
445              </xs:extension>
446          </xs:complexContent>
447      </xs:complexType>
448  </xs:element>
449
450  <xs:element name="curve">
451      <xs:complexType>
452          <xs:complexContent>
453              <xs:extension base="SEDBase">
454                  <xs:attributeGroup ref="idGroup" />
455                  <xs:attribute name="yDataReference" type="SId" use="required" />
456                  <xs:attribute name="xDataReference" type="SId" use="required" />
457
458                  <xs:attribute name="logY" use="required" type="xs:boolean" />
459                  <xs:attribute name="logX" use="required" type="xs:boolean" />
460              </xs:extension>
461          </xs:complexContent>
462      </xs:complexType>
463  </xs:element>
464
465  <xs:element name="surface">
466      <xs:complexType>
467          <xs:complexContent>
468              <xs:extension base="SEDBase">
469                  <xs:attributeGroup ref="idGroup" />
470                  <xs:attribute name="yDataReference" type="SId" use="required" />
471                  <xs:attribute name="xDataReference" type="SId" use="required" />
472                  <xs:attribute name="zDataReference" type="SId" use="required" />
473                  <xs:attribute name="logY" use="required" type="xs:boolean" />
474                  <xs:attribute name="logX" use="required" type="xs:boolean" />
475                  <xs:attribute name="logZ" use="required" type="xs:boolean" />
476              </xs:extension>
477          </xs:complexContent>
478      </xs:complexType>
479  </xs:element>
480
481  <xs:element name="dataSet">
482      <xs:complexType>
483          <xs:complexContent>
484              <xs:extension base="SEDBase">
485                  <xs:attribute name="dataReference" type="SId" use="required" />
486                  <xs:attribute name="label" use="required" type="xs:string" />
487                  <xs:attributeGroup ref="idGroup" />
488              </xs:extension>
489          </xs:complexContent>
490      </xs:complexType>
491  </xs:element>
492
493  <!-- listOf elements -->
494  <xs:element name="listOfVariables">
495      <xs:complexType>
496          <xs:complexContent>
497              <xs:extension base="SEDBase">
498                  <xs:sequence>
499                      <xs:element ref="variable" minOccurs="0" maxOccurs="unbounded" />
500                  </xs:sequence>
501              </xs:extension>
502          </xs:complexContent>
503      </xs:complexType>
504  </xs:element>
505
506  <xs:element name="listOfParameters">
507      <xs:complexType>
508          <xs:complexContent>
509              <xs:extension base="SEDBase">
510                  <xs:sequence>
511                      <xs:element ref="parameter" minOccurs="0" maxOccurs="unbounded" />
512                  </xs:sequence>
513              </xs:extension>

```

```

514         </xs:complexContent>
515     </xs:complexType>
516   </xs:element>
517
518   <xs:element name="listOfAlgorithmParameters">
519     <xs:complexType>
520       <xs:complexContent>
521         <xs:extension base="SEDBase">
522           <xs:sequence>
523             <xs:element ref="algorithmParameter" minOccurs="0" maxOccurs="unbounded" />
524           </xs:sequence>
525         </xs:extension>
526       </xs:complexContent>
527     </xs:complexType>
528   </xs:element>
529
530   <xs:element name="listOfTasks">
531     <xs:complexType>
532       <xs:complexContent>
533         <xs:extension base="SEDBase">
534           <xs:choice minOccurs="0" maxOccurs="unbounded">
535             <xs:element ref="task" />
536             <xs:element ref="repeatedTask" />
537           </xs:choice>
538         </xs:extension>
539       </xs:complexContent>
540     </xs:complexType>
541   </xs:element>
542
543   <xs:element name="listOfDataDescriptions">
544     <xs:complexType>
545       <xs:complexContent>
546         <xs:extension base="SEDBase">
547           <xs:choice minOccurs="0" maxOccurs="unbounded">
548             <xs:element ref="dataDescription"/>
549           </xs:choice>
550         </xs:extension>
551       </xs:complexContent>
552     </xs:complexType>
553   </xs:element>
554
555   <xs:element name="dataDescription">
556     <xs:complexType>
557       <xs:complexContent>
558         <xs:extension base="SEDBase">
559           <xs:sequence>
560             <xs:element ref="dimensionDescription" />
561             <xs:element ref="listOfDataSources" />
562           </xs:sequence>
563             <xs:attribute name="source" type="xs:anyURI" use="required" />
564             <xs:attributeGroup ref="idGroup" />
565           </xs:extension>
566         </xs:complexContent>
567       </xs:complexType>
568   </xs:element>
569
570   <xs:element name="dimensionDescription">
571     <xs:complexType>
572       <xs:sequence>
573         <xs:any namespace="http://www.numl.org/numl/level1/version1"
574           processContents="skip" minOccurs="0" maxOccurs="unbounded" />
575       </xs:sequence>
576     </xs:complexType>
577   </xs:element>
578
579   <xs:element name="listOfDataSources">
580     <xs:complexType>
581       <xs:complexContent>
582         <xs:extension base="SEDBase">
583           <xs:choice minOccurs="0" maxOccurs="unbounded">
584             <xs:element ref="dataSource" />
585           </xs:choice>
586         </xs:extension>
587       </xs:complexContent>
588     </xs:complexType>
589   </xs:element>
590
591   <xs:element name="dataSource">
592     <xs:complexType>
593       <xs:complexContent>
594         <xs:extension base="SEDBase">
595           <xs:sequence>
596             <xs:element ref="listOfSlices" minOccurs="0" maxOccurs="unbounded" />
597           </xs:sequence>
598             <xs:attribute name="indexSet" type="SIid" use="optional" />
599             <xs:attributeGroup ref="idGroup" />
600           </xs:extension>
601         </xs:complexContent>
602   </xs:complexType>

```

```

603      </xs:element>
604
605      <xs:element name="listOfSlices">
606          <xs:complexType>
607              <xs:complexContent>
608                  <xs:extension base="SEDBase">
609                      <xs:choice minOccurs="0" maxOccurs="unbounded">
610                          <xs:element ref="slice"/>
611                      </xs:choice>
612                  </xs:extension>
613              </xs:complexContent>
614          </xs:complexType>
615      </xs:element>
616
617      <xs:element name="slice">
618          <xs:complexType>
619              <xs:complexContent>
620                  <xs:extension base="SEDBase">
621                      <xs:attribute name="reference" type="SID" use="required" />
622                      <xs:attribute name="value" type="xs:string" use="required" />
623                  </xs:extension>
624              </xs:complexContent>
625          </xs:complexType>
626      </xs:element>
627
628      <xs:element name="listOfSimulations">
629          <xs:complexType>
630              <xs:complexContent>
631                  <xs:extension base="SEDBase">
632                      <xs:choice minOccurs="0" maxOccurs="unbounded">
633                          <xs:element ref="uniformTimeCourse"/>
634                          <xs:element ref="oneStep"/>
635                          <xs:element ref="steadyState"/>
636                      </xs:choice>
637                  </xs:extension>
638              </xs:complexContent>
639          </xs:complexType>
640      </xs:element>
641
642      <xs:element name="listOfOutputs">
643          <xs:complexType>
644              <xs:complexContent>
645                  <xs:extension base="SEDBase">
646                      <xs:choice minOccurs="0" maxOccurs="unbounded">
647                          <xs:element ref="plot2D" />
648                          <xs:element ref="plot3D" />
649                          <xs:element ref="report" />
650                      </xs:choice>
651                  </xs:extension>
652              </xs:complexContent>
653          </xs:complexType>
654      </xs:element>
655
656      <xs:element name="listOfModels">
657          <xs:complexType>
658              <xs:complexContent>
659                  <xs:extension base="SEDBase">
660                      <xs:sequence>
661                          <xs:element ref="model" minOccurs="0" maxOccurs="unbounded" />
662                      </xs:sequence>
663                  </xs:extension>
664              </xs:complexContent>
665          </xs:complexType>
666      </xs:element>
667
668      <xs:element name="listOfDataGenerators">
669          <xs:complexType>
670              <xs:complexContent>
671                  <xs:extension base="SEDBase">
672                      <xs:sequence>
673                          <xs:element ref="dataGenerator" minOccurs="0" maxOccurs="unbounded" />
674                      </xs:sequence>
675                  </xs:extension>
676              </xs:complexContent>
677          </xs:complexType>
678      </xs:element>
679
680      <xs:element name="listOfCurves">
681          <xs:complexType>
682              <xs:complexContent>
683                  <xs:extension base="SEDBase">
684                      <xs:sequence>
685                          <xs:element ref="curve" maxOccurs="unbounded" />
686                      </xs:sequence>
687                  </xs:extension>
688              </xs:complexContent>
689          </xs:complexType>
690      </xs:element>
691

```

```

692     <xs:element name="listOfSurfaces">
693         <xs:complexType>
694             <xs:complexContent>
695                 <xs:extension base="SEDBase">
696                     <xs:sequence>
697                         <xs:element ref="surface" maxOccurs="unbounded" />
698                     </xs:sequence>
699                 </xs:extension>
700             </xs:complexContent>
701         </xs:complexType>
702     </xs:element>
703
704     <xs:element name="listOfDataSets">
705         <xs:complexType>
706             <xs:complexContent>
707                 <xs:extension base="SEDBase">
708                     <xs:sequence>
709                         <xs:element ref="dataSet" maxOccurs="unbounded" />
710                     </xs:sequence>
711                 </xs:extension>
712             </xs:complexContent>
713         </xs:complexType>
714     </xs:element>
715
716     <xs:element name="listOfChanges">
717         <xs:complexType>
718             <xs:complexContent>
719                 <xs:extension base="SEDBase">
720                     <xs:choice minOccurs="0" maxOccurs="unbounded">
721                         <xs:element ref="changeAttribute" />
722                         <xs:element ref="changeXML" />
723                         <xs:element ref="addXML" />
724                         <xs:element ref="removeXML" />
725                         <xs:element ref="computeChange" />
726                     </xs:choice>
727                 </xs:extension>
728             </xs:complexContent>
729         </xs:complexType>
730     </xs:element>
731
732     <xs:element name="listOfRanges">
733         <xs:complexType>
734             <xs:complexContent>
735                 <xs:extension base="SEDBase">
736                     <xs:choice maxOccurs="unbounded">
737                         <xs:element ref="uniformRange" />
738                         <xs:element ref="vectorRange" />
739                         <xs:element ref="functionalRange" />
740                     </xs:choice>
741                 </xs:extension>
742             </xs:complexContent>
743         </xs:complexType>
744     </xs:element>
745
746     <xs:complexType name="repeatedTaskListOfChanges">
747         <xs:complexContent>
748             <xs:extension base="SEDBase">
749                 <xs:sequence>
750                     <xs:element ref="setValue" minOccurs="0" maxOccurs="unbounded" />
751                 </xs:sequence>
752             </xs:extension>
753         </xs:complexContent>
754     </xs:complexType>
755
756     <xs:element name="listOfSubTasks">
757         <xs:complexType>
758             <xs:complexContent>
759                 <xs:extension base="SEDBase">
760                     <xs:sequence>
761                         <xs:element ref="subTask" maxOccurs="unbounded" />
762                     </xs:sequence>
763                 </xs:extension>
764             </xs:complexContent>
765         </xs:complexType>
766     </xs:element>
767 </xs:schema>

```

Listing B.1: The SED-ML XML Schema definition

C. Examples

This appendix presents selected SED-ML examples. These examples are only illustrative and do not intend to demonstrate the full capabilities of SED-ML. For a more comprehensive view of the SED-ML features refer to the specification (Chapter 2) and to additional SED-ML examples are available from <http://sed-ml.org/>.

The presented examples use models encoded in SBML and CellML. SED-ML is not restricted to those formats, but can be used with models encoded in formats serialized in XML. A list of formats known to have been used with SED-ML is available on <http://sed-ml.org/>.

C.1 Le Loup Model (SBML)

The following example provides a SED-ML description for the simulation of the model based on the publication by Leoup, Gonze and Goldbeter “Limit Cycle Models for Circadian Rhythms Based on Transcriptional Regulation in Drosophila and Neurospora” (PubMed ID: 10643740).

This model is referenced by its SED-ML ID `model1` and refers to the model with the MIRIAM URN [urn:miriam:biomodels.db:BIOMD0000000021](#). Software applications interpreting this example know how to dereference this URN and access the model in BioModels Database [16].

A second model is defined in l. 11 of the example, using `model1` as a source and applying even further changes to it, in this case updating two model parameters.

One simulation setup is defined in the `listOfSimulations`. It is a `uniformTimeCourse` over 380 time units, providing 1000 output points. The algorithm used is the CVODE solver, as denoted by the KiSAO ID `KiSAO:0000019`.

A number of `dataGenerators` are defined in ll. 23-62. Those are the prerequisite for defining the outputs of the simulation. The first dataGenerator named `time` collects the simulation time. `tim1` in l. 31 maps on the `Mt` entity in the model that is used in `task1` which here is the model with ID `model1`. The dataGenerator named `per-tim1` in l. 39 maps on the `Cn` entity in `model1`. Finally the fourth and fifth dataGenerators map on the `Mt` and `per-tim` entity respectively in the updated model with ID `model2`.

The `output` defined in the experiment consists of three 2D plots. The first plot has two different curves (ll. 65-70) and provides the time course of the simulation using the `tim` mRNA concentrations from both simulation experiments. The second plot shows the `per-tim` concentration against the `tim` concentration for the oscillating model. And the third plot shows the same plot for the chaotic model. The resulting three plots are shown in Figure C.1.

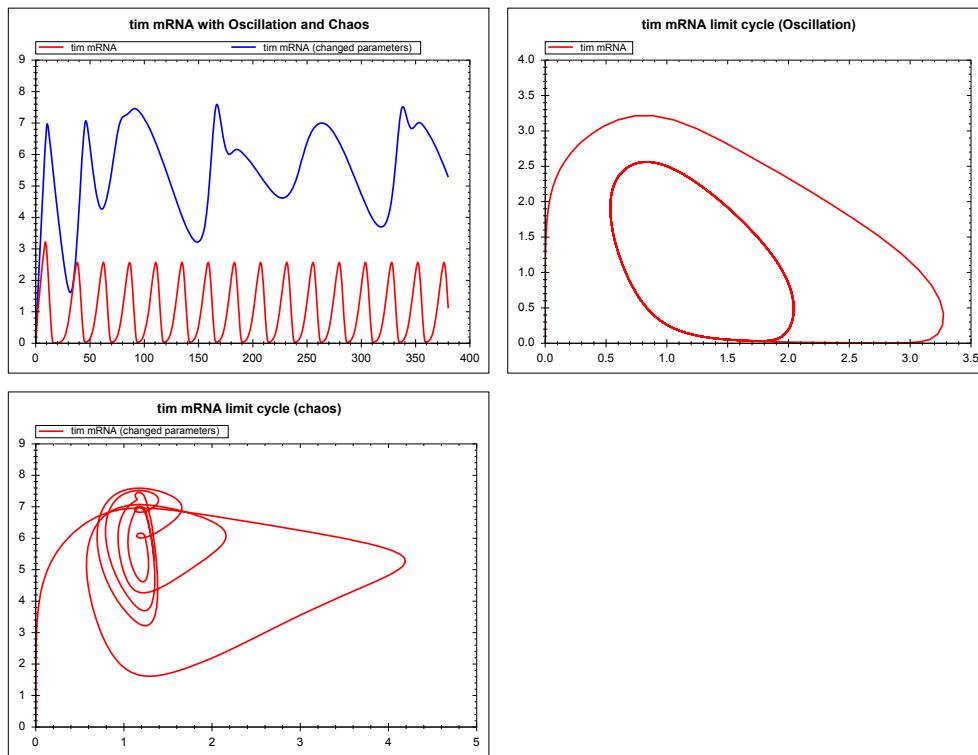


Figure C.1: The simulation result gained from the simulation description given in Listing C.1

```

1 <?xml version="1.0" encoding="utf-8"?>
2 <!-- Written by libSedML v1.1.4092.21172 see http://libsedml.sf.net -->
3 <sedML xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
4   xsi:schemaLocation="http://sed-ml.org/ sed-ml-L1-V1.xsd" xmlns="http://sed-ml.org/sed-ml/level1/version3
    " level="1"
5   version="3">
```

```

6   <listOfSimulations>
7     <uniformTimeCourse id="simulation1" initialTime="0" outputStartTime="0" outputEndTime="380"
8       numberOfPoints="1000">
9         <algorithm kisaoID="KISAO:0000019" />
10    </uniformTimeCourse>
11  </listOfSimulations>
12  <listOfModels>
13    <model id="model1" name="Circadian Oscillations" language="urn:sedml:language:sbml" source=
14      "urn:miriam:biomodels.db:BIOMD0000000021" />
15    <model id="model2" name="Circadian Chaos" language="urn:sedml:language:sbml" source="model1">
16      <listOfChanges>
17        <changeAttribute target="/sbml:sbml:sbml:model/sbml:listOfParameters/sbml:parameter[@id="
18          V_mT"]@value" newValue="0.28" />
19        <changeAttribute target="/sbml:sbml:sbml:model/sbml:listOfParameters/sbml:parameter[@id="
20          V_dT"]@value" newValue="4.8" />
21      </listOfChanges>
22    </model>
23  </listOfModels>
24  <listOfTasks>
25    <task id="task1" modelReference="model1" simulationReference="simulation1" />
26    <task id="task2" modelReference="model2" simulationReference="simulation1" />
27  </listOfTasks>
28  <listOfDataGenerators>
29    <dataGenerator id="time" name="time">
30      <listOfVariables>
31        <variable id="t" taskReference="task1" symbol="urn:sedml:symbol:time" />
32      </listOfVariables>
33      <math xmlns="http://www.w3.org/1998/Math/MathML">
34        <ci> t </ci>
35      </math>
36    </dataGenerator>
37    <dataGenerator id="tim1" name="tim mRNA">
38      <listOfVariables>
39        <variable id="v1" taskReference="task1" target="/sbml:sbml:sbml:model/sbml:listOfSpecies/
40          sbml:species[@id='Mt']" />
41      </listOfVariables>
42      <math xmlns="http://www.w3.org/1998/Math/MathML">
43        <ci> v1 </ci>
44      </math>
45    </dataGenerator>
46    <dataGenerator id="per_tim1" name="nuclear PER-TIM complex">
47      <listOfVariables>
48        <variable id="v1a" taskReference="task1" target="/sbml:sbml:sbml:model/sbml:listOfSpecies/
49          sbml:species[@id='Cn']" />
50      </listOfVariables>
51      <math xmlns="http://www.w3.org/1998/Math/MathML">
52        <ci> v1a </ci>
53      </math>
54    </dataGenerator>
55    <dataGenerator id="tim2" name="tim mRNA (changed parameters)">
56      <listOfVariables>
57        <variable id="v2" taskReference="task2" target="/sbml:sbml:sbml:model/sbml:listOfSpecies/
58          sbml:species[@id='Mt']" />
59      </listOfVariables>
60      <math xmlns="http://www.w3.org/1998/Math/MathML">
61        <ci> v2 </ci>
62      </math>
63    </dataGenerator>
64    <dataGenerator id="per_tim2" name="nuclear PER-TIM complex">
65      <listOfVariables>
66        <variable id="v2a" taskReference="task2" target="/sbml:sbml:sbml:model/sbml:listOfSpecies/
67          sbml:species[@id='Cn']" />
68      </listOfVariables>
69      <math xmlns="http://www.w3.org/1998/Math/MathML">
70        <ci> v2a </ci>
71      </math>
72    </dataGenerator>
73  </listOfDataGenerators>
74  <listOfOutputs>
75    <plot2D id="plot1" name="tim mRNA with Oscillation and Chaos">
76      <listOfCurves>
77        <curve id="c1" logX="false" logY="false" xDataReference="time" yDataReference="tim1" />
78        <curve id="c2" logX="false" logY="false" xDataReference="time" yDataReference="tim2" />
79      </listOfCurves>
80    </plot2D>
81    <plot2D id="plot2" name="tim mRNA limit cycle (Oscillation)">
82      <listOfCurves>
83        <curve id="c3" logX="false" logY="false" xDataReference="per_tim1" yDataReference="tim1" />
84      </listOfCurves>
85    </plot2D>
86    <plot2D id="plot3" name="tim mRNA limit cycle (chaos)">
87      <listOfCurves>
88        <curve id="c4" logX="false" logY="false" xDataReference="per_tim2" yDataReference="tim2" />
89      </listOfCurves>
90    </plot2D>
91  </listOfOutputs>
92 </sedML>
```

Listing C.1: LeLoup Model Simulation Description in SED-ML

C.2 Le Loup Model (CellML)

The following example provides a SED-ML description for the simulation of the model based on the publication by Leloup, Gonze and Goldbeter “Limit Cycle Models for Circadian Rhythms Based on Transcriptional Regulation in Drosophila and Neurospora” (PubMed ID: 10643740). Whereas the previous example used SBML to encode the simulation experiment, here the model is taken from the CellML Model Repository [18].

The original model used in the simulation experiment is referred to using a URL (http://models.cellml.org/workspace/leloup_gonze_goldbeter_1999/@@rawfile/7606a47e222bc3b3d9117baa08d2e7246d67eedd/leloup_gonze_goldbeter_1999_a.cellml, ll. 14).

A second model is defined in l. 15 of the example, using `model1` as a source and applying even further changes to it, in this case updating two model parameters.

One simulation setup is defined in the `listOfSimulations`. It is a `uniformTimeCourse` over 380 time units, using 1000 simulation points. The algorithm used is the CVODE solver, as denoted by the KiSAO ID `KiSAO:0000019`.

A number of `dataGenerators` are defined in ll. 27-73. Those are the prerequisite for defining the output of the simulation. The dataGenerator named `tim1` in l. 37 maps on the `Mt` entity in the model that is used in `task1`, which here is the model with ID `model1`. The dataGenerator named `per-tim` in l. 46 maps on the `CN` entity in `model1`. Finally the fourth and fifth dataGenerators map on the `Mt` and `per-tim` entity respectively in the updated model with ID `model2`.

The `output` defined in the experiment consists of three 2D plots (ll. 74-91). They reproduce the same output as the previous example.

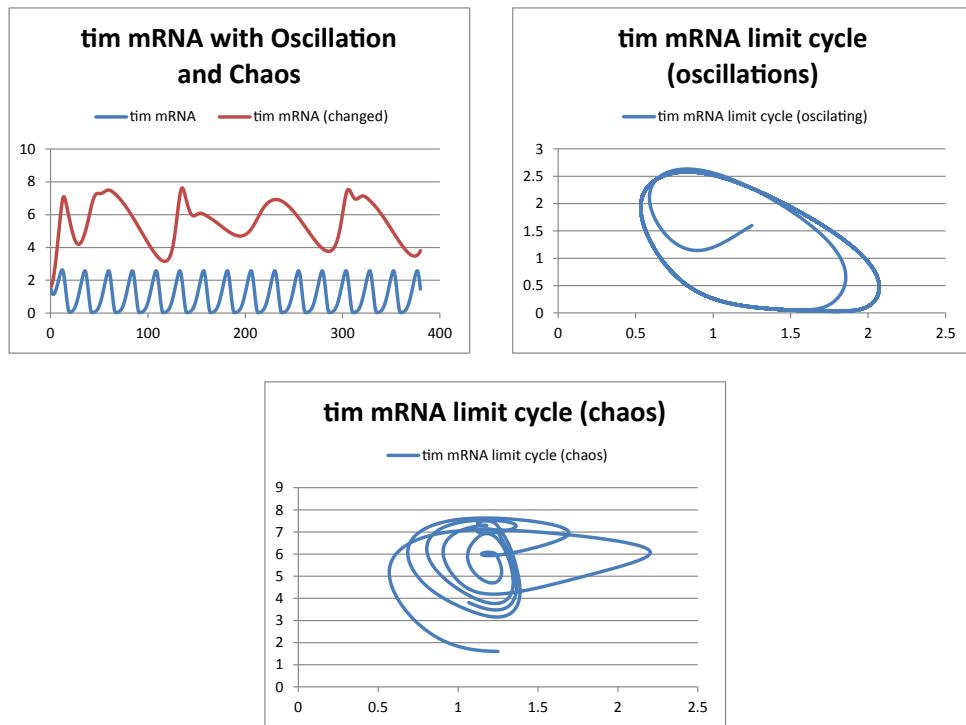


Figure C.2: The simulation result gained from the simulation description given in Listing C.2

```

1 <?xml version="1.0" encoding="utf-8"?>
2 <sedML xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
3   xsi:schemaLocation="http://sed-ml.org/ sed-ml-L1-V1.xsd"
4   xmlns:math="http://www.w3.org/1998/Math/MathML" xmlns="http://sed-ml.org/sed-ml/level1/version3" level=
5     "1" version="3">
6   <notes><p xmlns="http://www.w3.org/1999/xhtml">Comparing Limit Cycles and strange attractors for
7     oscillation in Drosophila</p></notes>
8   <listOfSimulations>
9     <uniformTimeCourse id="simulation1">

```

```

9      initialTime="0" outputStartTime="0" outputEndTime="380"
10     numberofPoints="1000" >
11       <algorithm kisaoID="KISAO:0000019"/>
12     </uniformTimeCourse>
13   </listOfSimulations>
14 </listOfModels>
15 <model id="model1" name="Circadian Oscillations" language="urn:sedml:language:cellml" source="http://
16   models.cellml.org/workspace/leloup_gonze_goldbeter_1999@@rawfile/7606
17   a47e222bc3b3d9117baa08d2e7246d67eedd/leloup_gonze_goldbeter_1999_a.cellml"/>
18 <model id="model2" name="Circadian Chaos" language="urn:sedml:language:cellml" source="model1">
19   <listOfChanges>
20     <changeAttribute target="/cellml:model/cellml:component[@name='MT']/cellml:variable[@name='vmT']/
21       @initial_value" newValue="0.28"/>
22     <changeAttribute target="/cellml:model/cellml:component[@name='T2']/cellml:variable[@name='vdT']/
23       @initial_value" newValue="4.8"/>
24   </listOfChanges>
25 </model>
26 </listOfModels>
27
28 <listOfTasks>
29   <task id="task1" name="Limit Cycle" modelReference="model1" simulationReference="simulation1"/>
30   <task id="task2" name="Strange attractors" modelReference="model2" simulationReference="simulation1"/
31   >
32 </listOfTasks>
33 <listOfDataGenerators>
34   <dataGenerator id="time" name="time">
35     <listOfVariables>
36       <variable id="t" taskReference="task1" target="/cellml:model/cellml:component[@name='environment']/
37         /cellml:variable[@name='time']" />
38     </listOfVariables>
39     <math:math>
40       <math:ci>t</math:ci>
41     </math:math>
42   </dataGenerator>
43
44   <dataGenerator id="tim1" name="tim mRNA">
45     <listOfVariables>
46       <variable id="v0" taskReference="task1" target="/cellml:model/cellml:component[@name='MT']/
47         /cellml:variable[@name='MT']" />
48     </listOfVariables>
49     <math:math>
50       <math:ci>v0</math:ci>
51     </math:math>
52   </dataGenerator>
53
54   <dataGenerator id="per_tim" name="nuclear PER-TIM complex">
55     <listOfVariables>
56       <variable id="v1" taskReference="task1" target="/cellml:model/cellml:component[@name='CN']/
57         /cellml:variable[@name='CN']" />
58     </listOfVariables>
59     <math:math>
60       <math:ci>v1</math:ci>
61     </math:math>
62   </dataGenerator>
63
64   <dataGenerator id="tim2" name="tim mRNA (changed parameters)">
65     <listOfVariables>
66       <variable id="v2" taskReference="task2" target="/cellml:model/cellml:component[@name='MT']/
67         /cellml:variable[@name='MT']" />
68     </listOfVariables>
69     <math:math>
70       <math:ci>v2</math:ci>
71     </math:math>
72   </dataGenerator>
73 </listOfDataGenerators>
74
75 <listOfOutputs>
76   <plot2D id="plot1" name="tim mRNA with Oscillation and Chaos">
77     <listOfCurves>
78       <curve id="c1" logX="false" logY="false" xDataReference="time" yDataReference="tim1" />
79       <curve id="c2" logX="false" logY="false" xDataReference="time" yDataReference="tim2" />
80     </listOfCurves>
81   </plot2D>
82   <plot2D id="plot2" name="tim mRNA limit cycle (Oscillation)">
83     <listOfCurves>
84       <curve id="c3" logX="false" logY="false" xDataReference="per_tim" yDataReference="tim1" />
85     </listOfCurves>
86   </plot2D>
87   <plot2D id="plot3" name="tim mRNA limit cycle (chaos)">

```

```
88      <listOfCurves>
89          <curve id="c4" logX="false" logY="false" xDataReference="per_time2" yDataReference="time2" />
90      </listOfCurves>
91  </plot2D>
92 </listOfOutputs>
93 </sedML>
```

Listing C.2: *LeLoup Model Simulation Description in SED-ML*

C.3 IkappaB-NF-kappaB Signaling (SBML)

The following example provides a SED-ML description for the simulation of the IkappaB-NF-kappaB signaling module based on the publication by Hoffmann, Levchenko, Scott and Baltimore “The IkappaB-NF-kappaB signaling module: temporal control and selective gene activation.” (PubMed ID: 12424381)

This model is referenced by its SED-ML ID `model1` and refers to the model with the MIRIAM URN [urn:miriam:biomodels.db:BIOMD0000000140](#). Software applications interpreting this example know how to dereference this URN and access the model in BioModels Database [16].

The simulation description specifies one simulation `simulation1`, which is a uniform timecourse simulation that simulates the model for 41 hours. `task1` then applies this simulation to the model.

As output this simulation description collects four parameters: `Total_NFkBn`, `Total_IkBbeta`, `Total_IkBeps` and `Total_IkBalpa`. These variables are to be plotted against the simulation time and displayed in four separate plots, as shown in Figure C.3.

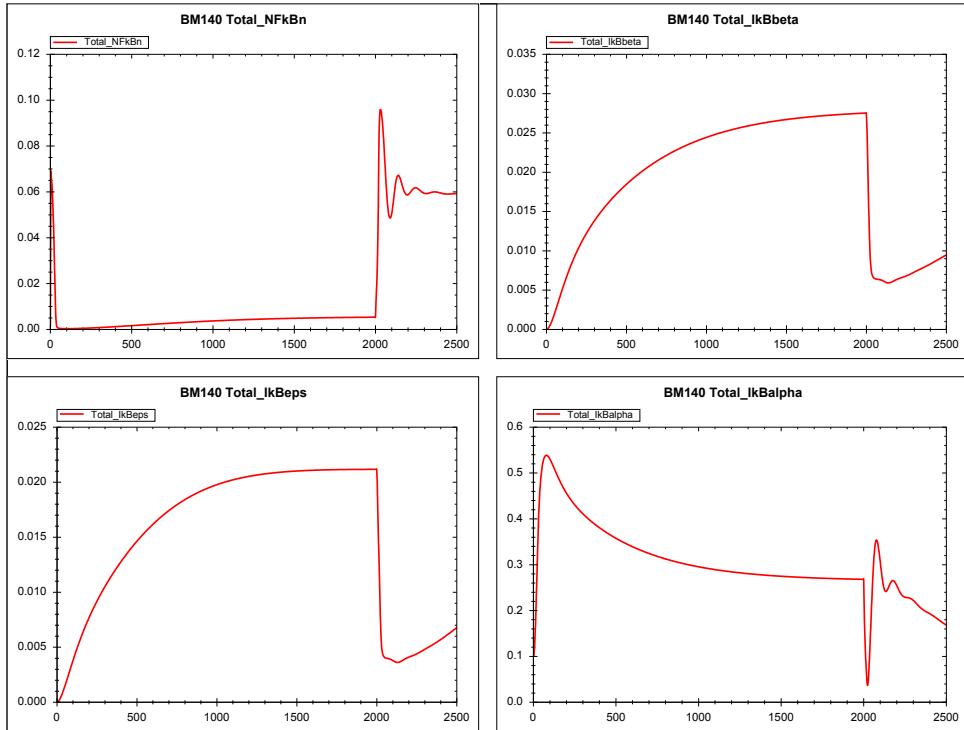


Figure C.3: The simulation result gained from the simulation description given in Listing C.3

The SED-ML description of the simulation experiment is given in Listing C.3.

```

1 <?xml version="1.0" encoding="utf-8"?>
2 <sedML xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
3   xsi:schemaLocation="http://sed-ml.org/ sed-ml-L1-V1.xsd" xmlns="http://sed-ml.org/sed-ml/level1/version3"
4     " level="1"
5   version="3">
6   <listOfSimulations>
7     <uniformTimeCourse id="simulation1"
8       initialTime="0" outputStartTime="0" outputEndTime="2500"
9       numberOfPoints="1000" >
10      <algorithm kisaoID="KISAO:0000019"/>
11    </uniformTimeCourse>
12  </listOfSimulations>
13  <listOfModels>
14    <model id="model1" language="urn:sedml:language:sbml" source="urn:miriam:biomodels.db:BIOMD0000000140"
15      "/>
16  </listOfModels>
17  <listOfTasks>
18    <task id="task1" modelReference="model1"
19      simulationReference="simulation1"/>
20  </listOfTasks>
21  <listOfDataGenerators>
22    <dataGenerator id="time" name="time">
```

```

21      <listOfVariables>
22          <variable id="time1" taskReference="task1" symbol="urn:sedml:symbol:time"/>
23      </listOfVariables>
24      <math xmlns="http://www.w3.org/1998/Math/MathML">
25          <ci>time1</ci>
26      </math>
27  </dataGenerator>
28  <dataGenerator id="Total_NFkBn" name="Total_NFkBn">
29      <listOfVariables>
30          <variable id="Total_NFkBn1" taskReference="task1"
31              target="/sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id='Total_NFkBn']"/>
32      </listOfVariables>
33      <math xmlns="http://www.w3.org/1998/Math/MathML">
34          <ci>Total_NFkBn1</ci>
35      </math>
36  </dataGenerator>
37  <dataGenerator id="Total_IkBbeta" name="Total_IkBbeta">
38      <listOfVariables>
39          <variable id="Total_IkBbeta1" taskReference="task1"
40              target="/sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id='Total_IkBbeta']" />
41      </listOfVariables>
42      <math xmlns="http://www.w3.org/1998/Math/MathML">
43          <ci>Total_IkBbeta1</ci>
44      </math>
45  </dataGenerator>
46  <dataGenerator id="Total_IkBeps" name="Total_IkBeps">
47      <listOfVariables>
48          <variable id="Total_IkBeps1" taskReference="task1"
49              target="/sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id='Total_IkBeps']" />
50      </listOfVariables>
51      <math xmlns="http://www.w3.org/1998/Math/MathML">
52          <ci>Total_IkBeps1</ci>
53      </math>
54  </dataGenerator>
55  <dataGenerator id="Total_IkBalpha" name="Total_IkBalpha">
56      <listOfVariables>
57          <variable id="Total_IkBalpha1" taskReference="task1"
58              target="/sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id='Total_IkBalpha']" />
59      </listOfVariables>
60      <math xmlns="http://www.w3.org/1998/Math/MathML">
61          <ci>Total_IkBalpha1</ci>
62      </math>
63  </dataGenerator>
64 </listOfDataGenerators>
65 <listOfOutputs>
66     <plot2D id="plot1" name="BM140 Total_NFkBn">
67         <listOfCurves>
68             <curve id="c1" logX="false" logY="false" xDataReference="time"
69                 yDataReference="Total_NFkBn" />
70         </listOfCurves>
71     </plot2D>
72     <plot2D id="plot2" name="BM140 Total_IkBbeta">
73         <listOfCurves>
74             <curve id="c2" logX="false" logY="false" xDataReference="time"
75                 yDataReference="Total_IkBbeta" />
76         </listOfCurves>
77     </plot2D>
78     <plot2D id="plot3" name="BM140 Total_IkBeps">
79         <listOfCurves>
80             <curve id="c3" logX="false" logY="false" xDataReference="time"
81                 yDataReference="Total_IkBeps" />
82         </listOfCurves>
83     </plot2D>
84     <plot2D id="plot4" name="BM140 Total_IkBalpha">
85         <listOfCurves>
86             <curve id="c4" logX="false" logY="false" xDataReference="time"
87                 yDataReference="Total_IkBalpha" />
88         </listOfCurves>
89     </plot2D>
90 </listOfOutputs>
91 </sedML>
```

Listing C.3: *IkappaB-NF-kappaB signaling Model Simulation Description in SED-ML*

C.4 Simulation Experiments with `repeatedTask`

The `repeatedTask` introduced in Level 1 Version 2 makes it possible to encode a large number of different simulation experiments. In this section several simulation experiment are presented that use the repeated tasks construct.

C.4.1 One Dimensional Steady State Parameter Scan

Here the repeated task calls out to a `oneStep` task (performing a steady state computation). Each time a parameter is carried in order to collect different responses.

In the description below the range to be used in the `setValue` construct use of the `range` attribute.

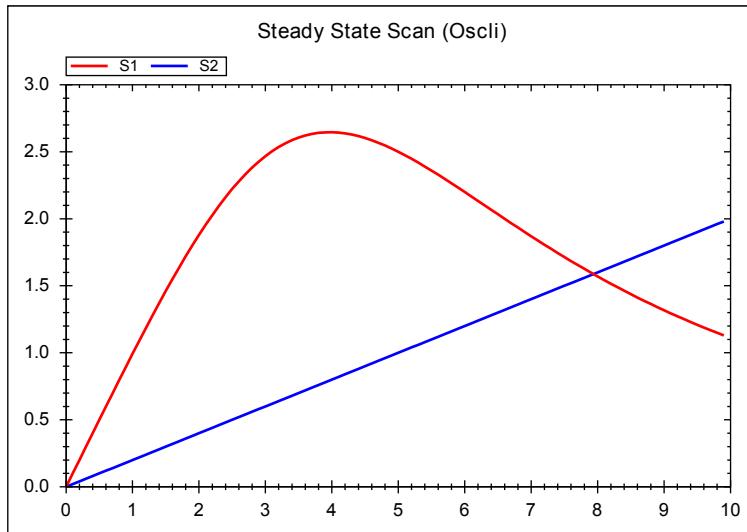


Figure C.4: The simulation result gained from the simulation description given in Listing C.4

```

1 <?xml version="1.0" encoding="utf-8"?>
2 <!-- Written by libSedML v1.1.4992.38982 see http://libsedml.sf.net -->
3 <sedML xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
4   xsi:schemaLocation="http://sed-ml.org/ sed-ml-L1-V2.xsd" xmlns="http://sed-ml.org/sed-ml/level1/version3
      " level="1"
5   version="3">
6     <listOfSimulations>
7       <steadyState id="steady1">
8         <algorithm kisaoID="KISAO:0000282" />
9       </steadyState>
10    </listOfSimulations>
11    <listOfModels>
12      <model id="model1" language="urn:sedml:language:sbml" source="http://sourceforge.net/p/libsedml/code
          /119/tree/trunk/Samples/models/oscli.xml?format=raw" />
13    </listOfModels>
14    <listOfTasks>
15      <task id="task0" modelReference="model1" simulationReference="steady1" />
16      <repeatedTask id="task1" resetModel="true" range="current">
17        <listOfRanges>
18          <uniformRange id="current" start="0" end="10" numberofPoints="100" type="linear" />
19        </listOfRanges>
20        <listOfChanges>
21          <setValue target="/sbml:sbml:sbml:model:sbml:listOfParameters:sbml:parameter[@id='J0_v0']"
22            range="current" modelReference="model1">
23            <math xmlns="http://www.w3.org/1998/Math/MathML">
24              <ci> current </ci>
25            </math>
26          </setValue>
27        </listOfChanges>
28        <listOfSubTasks>
29          <subTask order="1" task="task0" />
30        </listOfSubTasks>
31      </repeatedTask>
32    </listOfTasks>
33    <listOfDataGenerators>
34      <dataGenerator id="J0_v0_1" name="J0_v0">
35        <listOfVariables>
36          <variable id="J0_v0" name="J0_v0" taskReference="task1" target="/sbml:sbml:model/

```

```

    sbml:listOfParameters/sbml:parameter[@id='J0_v0']" />
37   </listOfVariables>
38   <math xmlns="http://www.w3.org/1998/Math/MathML">
39     <ci> J0_v0 </ci>
40   </math>
41 </dataGenerator>
42 <dataGenerator id="S1_1" name="S1">
43   <listOfVariables>
44     <variable id="S1" name="S1" taskReference="task1" target="/sbml:sbml/sbml:model/
        sbml:listOfSpecies/sbml:species[@id='S1']" />
45   </listOfVariables>
46   <math xmlns="http://www.w3.org/1998/Math/MathML">
47     <ci> S1 </ci>
48   </math>
49 </dataGenerator>
50 <dataGenerator id="S2_1" name="S2">
51   <listOfVariables>
52     <variable id="S2" name="S2" taskReference="task1" target="/sbml:sbml/sbml:model/
        sbml:listOfSpecies/sbml:species[@id='S2']" />
53   </listOfVariables>
54   <math xmlns="http://www.w3.org/1998/Math/MathML">
55     <ci> S2 </ci>
56   </math>
57 </dataGenerator>
58 </listOfDataGenerators>
59 <listOfOutputs>
60   <plot2D id="plot1" name="Steady State Scan (Oscli)">
61     <listOfCurves>
62       <curve id="curve1" logX="false" logY="false" xDataReference="J0_v0_1" yDataReference="S1_1" />
63       <curve id="curve2" logX="false" logY="false" xDataReference="J0_v0_1" yDataReference="S2_1" />
64     </listOfCurves>
65   </plot2D>
66   <report id="report1" name="Steady State Values">
67     <listOfDataSets>
68       <dataSet id="col1" dataReference="J0_v0_1" label="J0_v0" />
69       <dataSet id="col2" dataReference="S1_1" label="S1" />
70       <dataSet id="col3" dataReference="S2_1" label="S2" />
71     </listOfDataSets>
72   </report>
73 </listOfOutputs>
74 </sedML>
```

Listing C.4: SED-ML document implementing the one dimensional steady state parameter scan

C.4.2 Simulation Perturbation

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 repeated 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 causing the oscillations of a model to stop. 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.

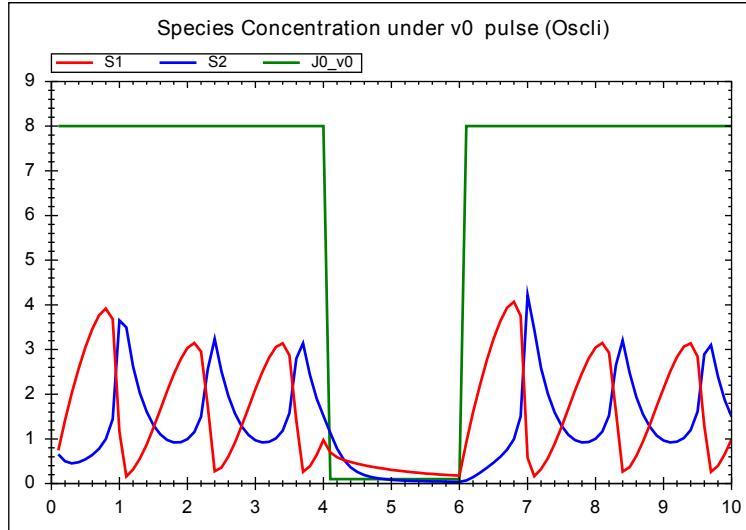


Figure C.5: The simulation result gained from the simulation description given in Listing C.5

```

1 <?xml version="1.0" encoding="utf-8"?>
2 <!-- Written by libSedML v1.1.4992.38982 see http://libsedml.sf.net -->
3 <sedML xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
4   xsi:schemaLocation="http://sed-ml.org/ sed-ml-L1-V2.xsd" xmlns="http://sed-ml.org/sed-ml/level1/version3
      " level="1"
5   version="3">
6     <listOfSimulations>
7       <oneStep id="stepper" step="0.1">
8         <algorithm kisaoID="KISAO:0000019" />
9       </oneStep>
10    </listOfSimulations>
11    <listOfModels>
12      <model id="model1" language="urn:sedml:language:sbml" source="http://sourceforge.net/p/libsedml/code
          /119/tree/trunk/Samples/models/oscli.xml?format=raw" />
13    </listOfModels>
14    <listOfTasks>
15      <task id="task0" modelReference="model1" simulationReference="stepper" />
16      <repeatedTask id="task1" resetModel="false" range="index">
17        <listOfRanges>
18          <uniformRange id="index" start="0" end="10" numberofPoints="100" type="linear" />
19          <functionalRange id="current" range="index">
20            <math xmlns="http://www.w3.org/1998/Math/MathML">
21              <piecewise>
22                <piece>
23                  <cn> 8 </cn>
24                  <apply>
25                    <lt />
26                    <ci> index </ci>
27                    <cn> 1 </cn>
28                  </apply>
29                </piece>
30                <piece>
31                  <cn> 0.1 </cn>
32                  <apply>
33                    <and />
34                    <apply>
35                      <geq />
36                      <ci> index </ci>
37                      <cn> 4 </cn>
38                    </apply>
39                    <apply>
40                      <lt />
41                      <ci> index </ci>
42                      <cn> 6 </cn>
43                    </apply>
44                  </apply>
45                </piece>
46                <otherwise>
47                  <cn> 8 </cn>
48                </otherwise>
49              </piecewise>
50            </math>
51          </functionalRange>
52        </listOfRanges>
53      <listOfChanges>
54        <setValue target="/sbml:	sbml:	sbml:	model/sbml:listOfParameters/sbml:parameter[@id='J0_v0']"
          range="current" modelReference="model1">
55          <math xmlns="http://www.w3.org/1998/Math/MathML">

```

```

57         <ci> current </ci>
58     </math>
59   </setValue>
60 </listOfChanges>
61 <listOfSubTasks>
62   <subTask order="1" task="task0" />
63 </listOfSubTasks>
64 </repeatedTask>
65 </listOfTasks>
66 <listOfDataGenerators>
67   <dataGenerator id="time_1" name="time">
68     <listOfVariables>
69       <variable id="time" name="time" taskReference="task1" target="time" />
70     </listOfVariables>
71     <math xmlns="http://www.w3.org/1998/Math/MathML">
72       <ci> time </ci>
73     </math>
74   </dataGenerator>
75   <dataGenerator id="J0_v0_1" name="J0_v0">
76     <listOfVariables>
77       <variable id="J0_v0" name="J0_v0" taskReference="task1" target="/sbml:sbml:sbml:model/
78         sbml:listOfParameters/sbml:parameter[@id='J0_v0']" />
79     </listOfVariables>
80     <math xmlns="http://www.w3.org/1998/Math/MathML">
81       <ci> J0_v0 </ci>
82     </math>
83   </dataGenerator>
84   <dataGenerator id="S1_1" name="S1">
85     <listOfVariables>
86       <variable id="S1" name="S1" taskReference="task1" target="/sbml:sbml:sbml:model/
87         sbml:listOfSpecies/sbml:species[@id='S1']" />
88     </listOfVariables>
89     <math xmlns="http://www.w3.org/1998/Math/MathML">
90       <ci> S1 </ci>
91     </math>
92   </dataGenerator>
93   <dataGenerator id="S2_1" name="S2">
94     <listOfVariables>
95       <variable id="S2" name="S2" taskReference="task1" target="/sbml:sbml:sbml:model/
96         sbml:listOfSpecies/sbml:species[@id='S2']" />
97     </listOfVariables>
98     <math xmlns="http://www.w3.org/1998/Math/MathML">
99       <ci> S2 </ci>
100      </math>
101    </dataGenerator>
102  </listOfDataGenerators>
103 <listOfOutputs>
104   <plot2D id="plot1" name="Species Concentration under v0 pulse (Oscli)">
105     <listOfCurves>
106       <curve id="curve1" logX="false" logY="false" xDataReference="time_1" yDataReference="S1_1" />
107       <curve id="curve2" logX="false" logY="false" xDataReference="time_1" yDataReference="S2_1" />
108       <curve id="curve3" logX="false" logY="false" xDataReference="time_1" yDataReference="J0_v0_1" />
109     </listOfCurves>
110   </plot2D>
111   <report id="report1" name="Species Concentration under v0 pulse (Oscli)">
112     <listOfDataSets>
113       <dataSet id="col0" dataReference="time_1" label="time" />
114       <dataSet id="col1" dataReference="J0_v0_1" label="J0_v0" />
115       <dataSet id="col2" dataReference="S1_1" label="S1" />
116       <dataSet id="col3" dataReference="S2_1" label="S2" />
117     </listOfDataSets>
118   </report>
119 </listOfOutputs>
120 </sedML>

```

Listing C.5: SED-ML document implementing the perturbation experiment

C.4.3 Repeated Stochastic Simulation

NOTE: This example produces three dimensional results (time, species concentration, multiple repeats). While Level 1 Version 2 does not include a way to post-processing these values. So it is left to the implementation on how to display them. One example would be to flatten the values by overlaying them onto the desired plot.

Running just one stochastic trace does not provide a complete picture of the behavior of a system. A large number of traces are needed to provide a result. This example demonstrates the basic use case of running ten traces of a simulation to. This is achieved by running on repeatedTask running ten uniform time course simulations (each of which performing a stochastic simulation run).

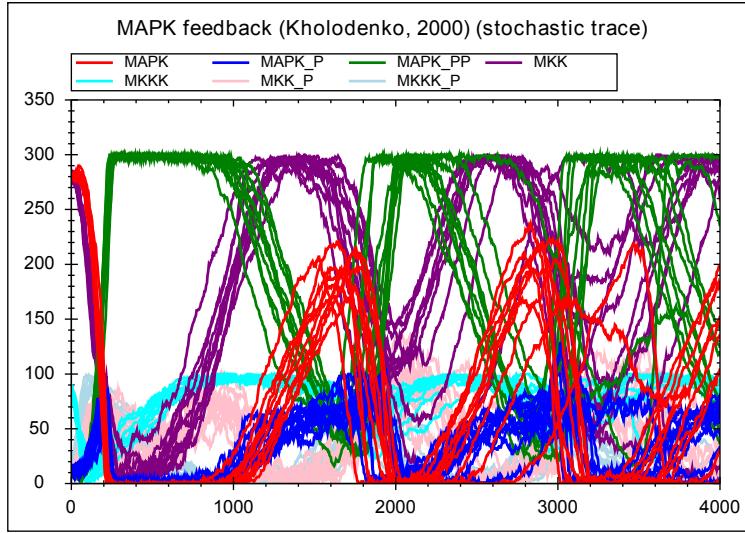


Figure C.6: The simulation result gained from the simulation description given in Listing C.6

```

1 <?xml version="1.0" encoding="utf-8"?>
2 <!-- Written by libSedML v1.1.4992.38982 see http://libsedml.sf.net -->
3 <sedML xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
4   xsi:schemaLocation="http://sed-ml.org/ sed-ml-L1-V2.xsd" xmlns="http://sed-ml.org/sed-ml/level1/version3
      " level="1"
5   version="3">
6     <listOfSimulations>
7       <uniformTimeCourse id="timecourse1" initialTime="0" outputStartTime="0" outputEndTime="4000"
        numberofPoints="1000">
8         <algorithm kisaoID="KISAO:0000241" />
9       </uniformTimeCourse>
10    </listOfSimulations>
11    <listOfModels>
12      <model id="model1" language="urn:sedml:language:sbml" source="E:\Users\fbergmann\Documents\sbml
          models\borisejb.xml" />
13    </listOfModels>
14    <listOfTasks>
15      <task id="task0" modelReference="model1" simulationReference="timecourse1" />
16      <repeatedTask id="task1" resetModel="true" range="current">
17        <listOfRanges>
18          <uniformRange id="current" start="0" end="10" numberofPoints="10" type="linear" />
19        </listOfRanges>
20        <listOfSubTasks>
21          <subTask order="1" task="task0" />
22        </listOfSubTasks>
23      </repeatedTask>
24    </listOfTasks>
25    <listOfDataGenerators>
26      <dataGenerator id="time1" name="time">
27        <listOfVariables>
28          <variable id="time" taskReference="task1" symbol="urn:sedml:symbol:time" />
29        </listOfVariables>
30        <math xmlns="http://www.w3.org/1998/Math/MathML">
31          <ci> time </ci>
32        </math>
33      </dataGenerator>
34      <dataGenerator id="MAPK1" name="MAPK">
35        <listOfVariables>
36          <variable id="MAPK" name="MAPK" taskReference="task1" target="/sbml:sbml:sbml:model/
              sbml:listOfSpecies/sbml:species[@id='MAPK']" />
37        </listOfVariables>
38        <math xmlns="http://www.w3.org/1998/Math/MathML">
39          <ci> MAPK </ci>
40        </math>
41      </dataGenerator>
42      <dataGenerator id="MAPK_P1" name="MAPK_P">
43        <listOfVariables>
44          <variable id="MAPK_P" name="MAPK_P" taskReference="task1" target="/sbml:sbml:sbml:model/
              sbml:listOfSpecies/sbml:species[@id='MAPK_P']" />
45        </listOfVariables>
46        <math xmlns="http://www.w3.org/1998/Math/MathML">
47          <ci> MAPK_P </ci>
48        </math>
49      </dataGenerator>
50      <dataGenerator id="MAPK_PP1" name="MAPK_PP">
51        <listOfVariables>
52          <variable id="MAPK_PP" name="MAPK_PP" taskReference="task1" target="/sbml:sbml:sbml:model/
              sbml:listOfSpecies/sbml:species[@id='MAPK_PP']" />

```

```

53      </listOfVariables>
54      <math xmlns="http://www.w3.org/1998/Math/MathML">
55          <ci> MAPK_PP </ci>
56      </math>
57  </dataGenerator>
58  <dataGenerator id="MKK1" name="MKK">
59      <listOfVariables>
60          <variable id="MKK" name="MKK" taskReference="task1" target="/sbml:sbml/sbml:model/
61              sbml:listOfSpecies/sbml:species[@id='MKK']" />
62      </listOfVariables>
63      <math xmlns="http://www.w3.org/1998/Math/MathML">
64          <ci> MKK </ci>
65      </math>
66  </dataGenerator>
67  <dataGenerator id="MKK_P1" name="MKK_P">
68      <listOfVariables>
69          <variable id="MKK_P" name="MKK_P" taskReference="task1" target="/sbml:sbml/sbml:model/
70              sbml:listOfSpecies/sbml:species[@id='MKK_P']" />
71      </listOfVariables>
72      <math xmlns="http://www.w3.org/1998/Math/MathML">
73          <ci> MKK_P </ci>
74      </math>
75  </dataGenerator>
76  <dataGenerator id="MKKK1" name="MKKK">
77      <listOfVariables>
78          <variable id="MKKK" name="MKKK" taskReference="task1" target="/sbml:sbml/sbml:model/
79              sbml:listOfSpecies/sbml:species[@id='MKKK']" />
80      </listOfVariables>
81      <math xmlns="http://www.w3.org/1998/Math/MathML">
82          <ci> MKKK </ci>
83      </math>
84  </dataGenerator>
85  <dataGenerator id="MKKK_P1" name="MKKK_P">
86      <listOfVariables>
87          <variable id="MKKK_P" name="MKKK_P" taskReference="task1" target="/sbml:sbml/sbml:model/
88              sbml:listOfSpecies/sbml:species[@id='MKKK_P']" />
89      </listOfVariables>
90      <math xmlns="http://www.w3.org/1998/Math/MathML">
91          <ci> MKKK_P </ci>
92      </math>
93  </dataGenerator>
94  </listOfDataGenerators>
95  <listOfOutputs>
96      <plot2D id="plot1" name="MAPK feedback (Kholodenko, 2000) (stochastic trace)">
97          <listOfCurves>
98              <curve id="curve1" logX="false" logY="false" xDataReference="time1" yDataReference="MAPK1" />
99              <curve id="curve2" logX="false" logY="false" xDataReference="time1" yDataReference="MAPK_P1" />
100             <curve id="curve3" logX="false" logY="false" xDataReference="time1" yDataReference="MAPK_PP1" />
101             <curve id="curve4" logX="false" logY="false" xDataReference="time1" yDataReference="MKK1" />
102             <curve id="curve5" logX="false" logY="false" xDataReference="time1" yDataReference="MKKK1" />
103             <curve id="curve6" logX="false" logY="false" xDataReference="time1" yDataReference="MKK_P1" />
104             <curve id="curve7" logX="false" logY="false" xDataReference="time1" yDataReference="MKKK_P1" />
105         </listOfCurves>
106     </plot2D>
107  </listOfOutputs>
108 </sedML>

```

Listing C.6: SED-ML document implementing repeated stochastic runs

C.4.4 One Dimensional Time Course Parameter Scan

NOTE: This example produces three dimensional results (time, species concentration, multiple repeats). While Level 1 Version 2 does not include a way to post-processing these values. So it is left to the implementation on how to display them. One example would be to flatten the values by overlaying them onto the desired plot.

Here one repeatedTask runs repeated uniform time course simulations (performing a deterministic simulation run) after each run the parameter value is changed.

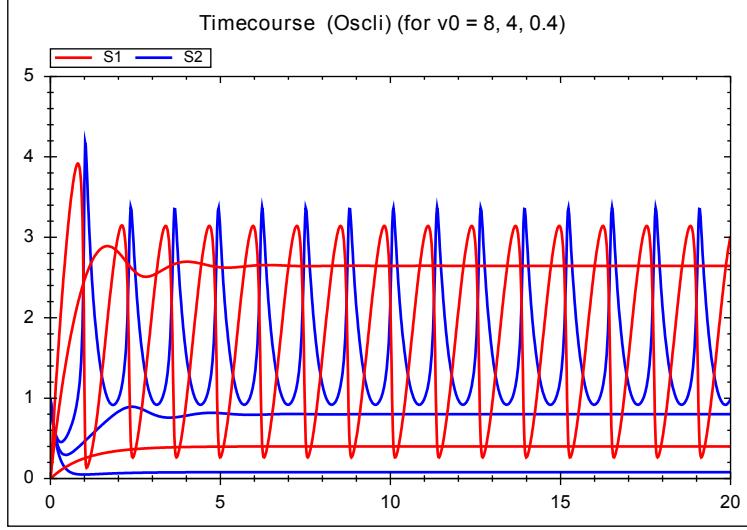


Figure C.7: The simulation result gained from the simulation description given in Listing C.7

```

1 <?xml version="1.0" encoding="utf-8"?>
2 <!-- Written by libSedML v1.1.4992.38982 see http://libsedml.sf.net -->
3 <sedML xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
4   xsi:schemaLocation="http://sed-ml.org/ sed-ml-L1-V2.xsd" xmlns="http://sed-ml.org/sed-ml/level1/version3
      " level="1"
5   version="3">
6     <listOfSimulations>
7       <uniformTimeCourse id="timecourse1" initialTime="0" outputStartTime="0" outputEndTime="20"
        numberofPoints="1000">
8         <algorithm kisaoID="KISAO:0000019" />
9       </uniformTimeCourse>
10    </listOfSimulations>
11    <listOfModels>
12      <model id="model1" language="urn:sedml:language:sbml" source="http://sourceforge.net/p/libsedml/code
          /119/tree/trunk/Samples/models/oscli.xml?format=raw" />
13    </listOfModels>
14    <listOfTasks>
15      <task id="task0" modelReference="model1" simulationReference="timecourse1" />
16      <repeatedTask id="task1" resetModel="true" range="current">
17        <listOfRanges>
18          <vectorRange id="current">
19            <value>8</value>
20            <value>4</value>
21            <value>0.4</value>
22          </vectorRange>
23        </listOfRanges>
24        <listOfChanges>
25          <setValue target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J0_v0']"
26            range="current" modelReference="model1">
27            <math xmlns="http://www.w3.org/1998/Math/MathML">
28              <ci> current </ci>
29            </math>
30          </setValue>
31        </listOfChanges>
32        <listOfSubTasks>
33          <subTask order="1" task="task0" />
34        </listOfSubTasks>
35      </repeatedTask>
36    </listOfTasks>
37    <listOfDataGenerators>
38      <dataGenerator id="time1" name="time">
39        <listOfVariables>
40          <variable id="time" name="time" taskReference="task1" target="time" />
41        </listOfVariables>
42        <math xmlns="http://www.w3.org/1998/Math/MathML">
43          <ci> time </ci>
44        </math>
45      </dataGenerator>
46      <dataGenerator id="J0_v0_1" name="J0_v0">
47        <listOfVariables>
48          <variable id="J0_v0" name="J0_v0" taskReference="task1" target="/sbml:sbml/sbml:model/
              sbml:listOfParameters/sbml:parameter[@id='J0_v0']" />
49        </listOfVariables>
50        <math xmlns="http://www.w3.org/1998/Math/MathML">
51          <ci> J0_v0 </ci>
52        </math>
53      </dataGenerator>
54      <dataGenerator id="S1_1" name="S1">
```

```

55      <listOfVariables>
56          <variable id="S1" name="S1" taskReference="task1" target="/sbml:sbml/sbml:model/
57              sbml:listOfSpecies/sbml:species[@id='S1']" />
58      </listOfVariables>
59      <math xmlns="http://www.w3.org/1998/Math/MathML">
60          <ci> S1 </ci>
61      </math>
62  </dataGenerator>
63  <dataGenerator id="S2_1" name="S2">
64      <listOfVariables>
65          <variable id="S2" name="S2" taskReference="task1" target="/sbml:sbml/sbml:model/
66              sbml:listOfSpecies/sbml:species[@id='S2']" />
67      </listOfVariables>
68      <math xmlns="http://www.w3.org/1998/Math/MathML">
69          <ci> S2 </ci>
70      </math>
71  </dataGenerator>
72  </listOfDataGenerators>
73  <listOfOutputs>
74      <plot2D id="plot1" name="Timecourse (Oscli) (for v0 = 8, 4, 0.4)">
75          <listOfCurves>
76              <curve id="curve1" logX="false" logY="false" xDataReference="time1" yDataReference="S1_1" />
77              <curve id="curve2" logX="false" logY="false" xDataReference="time1" yDataReference="S2_1" />
78          </listOfCurves>
79      </plot2D>
80  </listOfOutputs>
81 </sedML>

```

Listing C.7: SED-ML document implementing the one dimensional time course parameter scan

C.4.5 Two Dimensional Steady State Parameter Scan

NOTE: This example produces three dimensional results (time, species concentration, multiple repeats). While Level 1 Version 2 does not include a way to post-processing these values. So it is left to the implementation on how to display them. One example would be to flatten the values by overlaying them onto the desired plot.

Here a repeatedTask runs over another repeatedTask which runs over a oneStep task (performing a steady state computation). Each repeated simulation task modifies a different parameter.

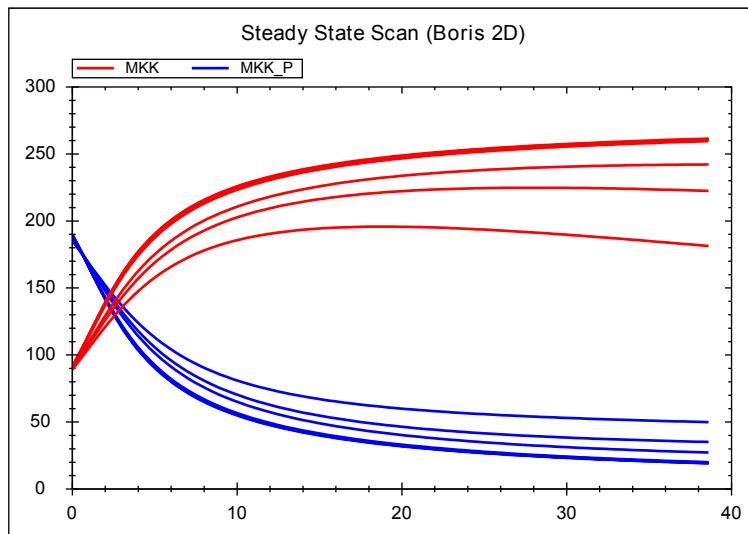


Figure C.8: The simulation result gained from the simulation description given in Listing C.8

```

1 <?xml version="1.0" encoding="utf-8"?>
2 <!-- Written by libSedML v1.1.4992.38982 see http://libsedml.sf.net -->
3 <sedML xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
4   xsi:schemaLocation="http://sed-ml.org/ sed-ml-L1-V2.xsd" xmlns="http://sed-ml.org/sed-ml/level1/version3
    " level="1"
5   version="3">
6   <listOfSimulations>
7     <steadyState id="steady1">
8       <algorithm kisaoID="KISAO:0000282" />
9     </steadyState>
10    </listOfSimulations>

```

```

11   <listOfModels>
12     <model id="model1" language="urn:sedml:language:sbml" source="E:\Users\fbergmann\Documents\sbml
13       models\borisjeb.xml" />
14   </listOfModels>
15   <listOfTasks>
16     <task id="task0" modelReference="model1" simulationReference="steady1" />
17     <repeatedTask id="task1" resetModel="false" range="current">
18       <listOfRanges>
19         <vectorRange id="current">
20           <value>1</value>
21           <value>5</value>
22           <value>10</value>
23           <value>50</value>
24           <value>60</value>
25           <value>70</value>
26           <value>80</value>
27           <value>90</value>
28           <value>100</value>
29     </vectorRange>
30   </listOfRanges>
31   <listOfChanges>
32     <setValue target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J1_KK2']"
33       range="current" modelReference="model1">
34       <math xmlns="http://www.w3.org/1998/Math/MathML">
35         <ci> current </ci>
36       </math>
37     </setValue>
38   </listOfChanges>
39   <listOfSubTasks>
40     <subTask order="1" task="task2" />
41   </listOfSubTasks>
42 </repeatedTask>
43 <repeatedTask id="task2" resetModel="false" range="current1">
44   <listOfRanges>
45     <uniformRange id="current1" start="1" end="40" numberOfPoints="100" type="linear" />
46   </listOfRanges>
47   <listOfChanges>
48     <setValue target="/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter[@id='J4_KK5']"
49       range="current1" modelReference="model1">
50       <math xmlns="http://www.w3.org/1998/Math/MathML">
51         <ci> current1 </ci>
52       </math>
53     </setValue>
54   </listOfChanges>
55   <listOfSubTasks>
56     <subTask order="1" task="task0" />
57   </listOfSubTasks>
58 </repeatedTask>
59 </listOfTasks>
60 <listOfDataGenerators>
61   <dataGenerator id="J4_KK5_1" name="J4_KK5">
62     <listOfVariables>
63       <variable id="J4_KK5" name="J4_KK5" taskReference="task1" target="/sbml:sbml:sbml:model/
64         sbml:listOfParameters/sbml:parameter[@id='J4_KK5']" />
65     </listOfVariables>
66     <math xmlns="http://www.w3.org/1998/Math/MathML">
67       <ci> J4_KK5 </ci>
68     </math>
69   </dataGenerator>
70   <dataGenerator id="J1_KK2_1" name="J1_KK2">
71     <listOfVariables>
72       <variable id="J1_KK2" name="J1_KK2" taskReference="task1" target="/sbml:sbml:sbml:model/
73         sbml:listOfParameters/sbml:parameter[@id='J1_KK2']" />
74     </listOfVariables>
75     <math xmlns="http://www.w3.org/1998/Math/MathML">
76       <ci> J1_KK2 </ci>
77     </math>
78   </dataGenerator>
79   <dataGenerator id="MKK_1" name="MKK">
80     <listOfVariables>
81       <variable id="MKK" name="MKK" taskReference="task1" target="/sbml:sbml:sbml:model/
82         sbml:listOfSpecies/sbml:species[@id='MKK']" />
83     </listOfVariables>
84     <math xmlns="http://www.w3.org/1998/Math/MathML">
85       <ci> MKK </ci>
86     </math>
87   </dataGenerator>
88   <dataGenerator id="MKK_P_1" name="MKK_P">
89     <listOfVariables>
90       <variable id="MKK_P" name="MKK_P" taskReference="task1" target="/sbml:sbml:sbml:model/
91         sbml:listOfSpecies/sbml:species[@id='MKK_P']" />
92     </listOfVariables>
93     <math xmlns="http://www.w3.org/1998/Math/MathML">
94       <ci> MKK_P </ci>

```

```

95      <listOfCurves>
96          <curve id="curve1" logX="false" logY="false" xDataReference="J4_KK5_1" yDataReference="MKK_1" />
97          <curve id="curve2" logX="false" logY="false" xDataReference="J4_KK5_1" yDataReference="MKK_P_1" /
98      >
99  </listOfCurves>
100 </plot2D>
101 <report id="report1" name="Steady State Values (Boris2D)">
102     <listOfDataSets>
103         <dataSet id="col0" dataReference="J4_KK5_1" label="J4_KK5" />
104         <dataSet id="col1" dataReference="J1_KK2_1" label="J1_KK2" />
105         <dataSet id="col2" dataReference="MKK_1" label="MKK" />
106         <dataSet id="col3" dataReference="MKK_P_1" label="MKK_P" />
107     </listOfDataSets>
108 </report>
109 </listOfOutputs>
110 </sedML>

```

Listing C.8: SED-ML document implementing the one dimensional steady state parameter scan

C.5 Referencing external data

This example demonstrates the use of the data sources in a basic SED-ML description. In this example a model is simulated (using a uniform time course simulation), that simulation result is plotted in one plot, a second plot obtains a stored result (using the data sources), extracts the `S1` and `time` column from it and renders it.

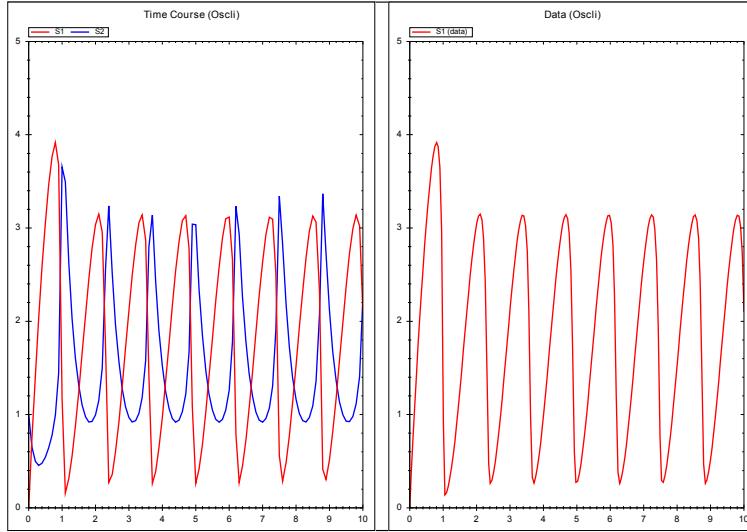


Figure C.9: The simulation result gained from the simulation description given in Listing C.9

```

1 <?xml version="1.0" encoding="utf-8"?>
2 <!-- Written by libSedML v1.1.5335.19015 see http://libsedml.sf.net -->
3 <sedML level="1" version="3" xmlns="http://sed-ml.org/sed-ml/level1/version3">
4   <listOfDataDescriptions>
5     <dataDescription id="Data1" name="Oscli Time Course Data" source="http://svn.code.sf.net/p/libsedml/
       code/trunk/Samples/data/oscli.numl">
6       <dimensionDescription>
7         <compositeDescription indexType="double" id="time" name="time" xmlns="http://www.numl.org/numl/
           level1/version1">
8           <compositeDescription indexType="string" id="SpeciesIds" name="SpeciesIds">
9             <atomicDescription valueType="double" name="Concentrations" />
10            </compositeDescription>
11        </compositeDescription>
12      </dimensionDescription>
13      <listOfDataSources>
14        <dataSource id="dataS1">
15          <listOfSlices>
16            <slice reference="SpeciesIds" value="S1" />
17          </listOfSlices>
18        </dataSource>
19        <dataSource id="dataTime" indexSet="time" />
20      </listOfDataSources>
21    </dataDescription>
22  </listOfDataDescriptions>
23  <listOfSimulations>
24    <uniformTimeCourse id="sim1" initialTime="0" outputStartTime="0" outputEndTime="10" numberOfPoints="
      100">
25      <algorithm kisaoID="KISAO:0000019">
26        <listOfAlgorithmParameters>
27          <algorithmParameter kisaoID="KISAO:0000209" value="1E-06" />
28          <algorithmParameter kisaoID="KISAO:0000211" value="1E-12" />
29          <algorithmParameter kisaoID="KISAO:0000415" value="10000" />
30        </listOfAlgorithmParameters>
31      </algorithm>
32    </uniformTimeCourse>
33  </listOfSimulations>
34  <listOfModels>
35    <model id="model1" language="urn:sedml:language:sbml" source="http://sourceforge.net/p/libsedml/code
      /119/tree/trunk/Samples/models/oscli.xml?format=raw" />
36  </listOfModels>
37  <listOfTasks>
38    <task id="task1" modelReference="model1" simulationReference="sim1" />
39  </listOfTasks>
40  <listOfDataGenerators>
41    <dataGenerator id="time_1" name="time">
42      <listOfVariables>
43        <variable id="time" name="time" taskReference="task1" symbol="urn:sedml:symbol:time" />
```

```

44      </listOfVariables>
45      <math xmlns="http://www.w3.org/1998/Math/MathML">
46          <ci> time </ci>
47      </math>
48  </dataGenerator>
49  <dataGenerator id="S1_1" name="S1">
50      <listOfVariables>
51          <variable id="S1" name="S1" taskReference="task1" target="/sbml:sbml/sbml:model/
52              sbml:listOfSpecies/sbml:species[@id='S1']" />
53      </listOfVariables>
54      <math xmlns="http://www.w3.org/1998/Math/MathML">
55          <ci> S1 </ci>
56      </math>
57  </dataGenerator>
58  <dataGenerator id="S2_1" name="S2">
59      <listOfVariables>
60          <variable id="S2" name="S2" taskReference="task1" target="/sbml:sbml/sbml:model/
61              sbml:listOfSpecies/sbml:species[@id='S2']" />
62      </listOfVariables>
63      <math xmlns="http://www.w3.org/1998/Math/MathML">
64          <ci> S2 </ci>
65      </math>
66  </dataGenerator>
67  <dataGenerator id="dgDataS1" name="S1 (data)">
68      <listOfVariables>
69          <variable id="varS1" modelReference="model1" target="#dataS1" />
70      </listOfVariables>
71      <math xmlns="http://www.w3.org/1998/Math/MathML">
72          <ci> varS1 </ci>
73      </math>
74  </dataGenerator>
75  <dataGenerator id="dgDataTime" name="Time">
76      <listOfVariables>
77          <variable id="varTime" modelReference="model1" target="#dataTime" />
78      </listOfVariables>
79      <math xmlns="http://www.w3.org/1998/Math/MathML">
80          <ci> varTime </ci>
81      </math>
82  </dataGenerator>
83 </listOfDataGenerators>
84 <listOfOutputs>
85     <plot2D id="plot1" name="Time Course (Oscli)">
86         <listOfCurves>
87             <curve id="curve1" logX="false" logY="false" xDataReference="time_1" yDataReference="S1_1" />
88             <curve id="curve2" logX="false" logY="false" xDataReference="time_1" yDataReference="S2_1" />
89         </listOfCurves>
90     </plot2D>
91     <plot2D id="plot2" name="Data (Oscli)">
92         <listOfCurves>
93             <curve id="curve3" logX="false" logY="false" xDataReference="dgDataTime" yDataReference="dgDataS1
94                 " />
95         </listOfCurves>
96     </plot2D>
97 </listOfOutputs>
98 </sedML>

```

Listing C.9: SED-ML document using *DataSource* and *DataDescription*

Bibliography

- [1] D. Bell. UML basics, Part III: The class diagram. IBM, the rational edge, 2003. http://download.boulder.ibm.com/ibmdl/pub/software/dw/rationaleedge/nov03/t_modelinguml_db.pdf.
- [2] F. T. Bergmann, R. Adams, S. Moodie, J. Cooper, M. Glont, M. Golebiewski, M. Hucka, C. Laibe, A. K. Miller, D. P. Nickerson, B. G. Olivier, N. Rodriguez, H. M. Sauro, M. Scharm, S. Soiland-Reyes, D. Waltemath, F. Yvon, and N. Le Novère. Combine archive and omex format: one file to share all information to reproduce a modeling project. *BMC bioinformatics*, 15:369, Dec. 2014.
- [3] T. Berners-Lee, R. Fielding, and L. Masinter. Uniform Resource Identifier (URI): Generic Syntax, 2005.
- [4] T. Bray, J. Paoli, C. Sperberg-McQueen, E. Maler, F. Yergeau, and J. Cowan. Extensible Markup Language (XML) 1.1 (Second Edition), 2006.
- [5] D. Carlisle, P. Ion, R. Miner, and N. Popelier. Mathematical Markup Language (MathML) version 2.0. *W3C Recommendation*, 21, 2001.
- [6] J. Clarke and S. DeRose. XML Path Language (XPath) Version 1.0, 1999.
- [7] M. Courtot, N. Juty, C. Knüpfer, D. Waltemath, A. Dräger, A. Finney, M. Golebiewski, S. Hoops, S. Keating, D. Kell, S. Kerrien, J. Lawson, A. Lister, J. Lu, R. Machne, P. Mendes, M. Pocock, N. Rodriguez, A. Villegas, S. Wimalaratne, C. Laibe, M. Hucka, and N. Le Novère. Controlled vocabularies and semantics in systems biology. *Mol Sys Biol*, 7, Oct. 2011.
- [8] A. A. Cuellar, C. M. Lloyd, P. F. Nielson, M. D. B. Halstead, D. P. Bullivant, D. P. Nickerson, and P. J. Hunter. An overview of CellML 1.1, a biological model description language. *Simulation*, 79(12):740–747, 2003.
- [9] J. Dada, I. Spasić, N. Paton, and P. Mendes. SBRML: a markup language for associating systems biology data with models. *Bioinformatics (Oxford, England)*, 26(7):932–938, April 2010.
- [10] M. Elowitz and S. Leibler. A synthetic oscillatory network of transcriptional regulators. *Nature*, 403(6767):335–338, Jan. 2000.
- [11] D. Fallside, P. Walmsley, et al. XML schema part 0: Primer. *W3C recommendation*, 2, 2001.
- [12] N. Goddard, M. Hucka, F. Howell, H. Cornelis, K. Skankar, and D. Beeman. Towards NeuroML: Model Description Methods for Collaborative Modeling in Neuroscience. *Phil. Trans. Royal Society series B*, 356:1209–1228, 2001.
- [13] S. Hoops, S. Sahle, C. Lee, J. Pahle, N. Simus, M. Singhal, L. Xu, P. Mendes, and U. Kummer. COPASI - a COmplex PAthway SImulator. *Bioinformatics (Oxford, England)*, 22(24):3067–3074, December 2006.
- [14] M. Hucka, F. Bergmann, S. Hoops, S. Keating, S. Sahle, and D. Wilkinson. The Systems Biology Markup Language (SBML): Language Specification for Level 3 Version 1 Core (Release 1 Candidate). *Nature Precedings*, January 2010.
- [15] M. Hucka, A. Finney, H. M. Sauro, H. Bolouri, J. C. Doyle, H. Kitano, A. P. Arkin, B. J. Bornstein, D. Bray, A. Cornish-Bowden, A. A. Cuellar, S. Dronov, E. D. Gilles, M. Ginkel, V. Gor, I. I. Goryanin, W. J. Hedley, T. C. Hodgman, J. H. Hofmeyr, P. J. Hunter, N. S. Juty, J. L. Kasberger, A. Kremling, U. Kummer, N. Le Novère, L. M. Loew, D. Lucio, P. Mendes, E. Minch, E. D.

- Mjolsness, Y. Nakayama, M. R. Nelson, P. F. Nielsen, T. Sakurada, J. C. Schaff, B. E. Shapiro, T. S. Shimizu, H. D. Spence, J. Stelling, K. Takahashi, M. Tomita, J. Wagner, and J. Wang. The systems biology markup language (SBML): a medium for representation and exchange of biochemical network models. *Bioinformatics*, 19(4):524–531, March 2003.
- [16] N. Le Novère, B. Bornstein, A. Broicher, M. Courtot, M. Donizelli, H. Dharuri, L. Li, H. Sauro, M. Schilstra, B. Shapiro, J. L. Snoep, and M. Hucka. BioModels Database: a free, centralized database of curated, published, quantitative kinetic models of biochemical and cellular systems. *Nucleic Acids Res*, 34(Database issue), January 2006.
- [17] C. Li, M. Donizelli, N. Rodriguez, H. Dharuri, L. Endler, V. Chelliah, L. Li, E. He, A. Henry, M. Stefan, J. Snoep, M. Hucka, N. Le Novère, and C. Laibe. BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. *BMC Systems Biology*, 4(1):92+, June 2010.
- [18] C. Lloyd, J. Lawson, P. Hunter, and P. Nielsen. The CellML model repository. *Bioinformatics*, 24(18):2122, 2008.
- [19] OMG. *UML 2.2 Superstructure and Infrastructure*, February 2009.
- [20] S. Pemberton et al. XHTML 1.0: The Extensible HyperText Markup Language—W3C Recommendation 26 January 2000. *World Wide Web Consortium (W3C)(August 2002)*, 2002.
- [21] W3C. XML Schema Part 1: Structures Second Edition. W3C Recommendation, October 2004.
- [22] D. Waltemath, R. Adams, D. Beard, F. Bergmann, U. Bhalla, R. Britten, V. Chelliah, M. Cooling, J. Cooper, E. Crampin, A. Garny, S. Hoops, M. Hucka, P. Hunter, E. Klipp, C. Laibe, A. Miller, I. Moraru, D. Nickerson, P. Nielsen, M. Nikolski, S. Sahle, H. Sauro, H. Schmidt, J. Snoep, D. Tolle, O. Wolkenhauer, and N. Le Novère. Minimum information about a simulation experiment (MIASE). *PLoS Comput Biol*, 7:e1001122, 2011.
- [23] D. Waltemath, R. Adams, F. T. Bergmann, M. Hucka, F. Kolpakov, A. K. Miller, I. I. Moraru, D. Nickerson, S. Sahle, J. L. Snoep, et al. Reproducible computational biology experiments with sed-ml—the simulation experiment description markup language. *BMC systems biology*, 5(1):198, 2011.