SBML Level 3 Package: Layout ('layout')

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This is a draft specification for the package 'layout' and not a normative document. Please send feedback to the Package Working Group mailing list at sbml-layout@lists.sourceforge.net

The latest release, past releases, and other materials related to this specification are available at http://sbml.org/Documents/Specifications/SBML_Level_3/Packages/Layout_(layout)

This release of the specification is available at http://sbml.org/Documents/Specifications/Layout_Level_1_Version_1



Contents

1 Introduction				
	1.1	Proposal corresponding to this package specification	3	
	1.2	Tracking number	3	
	1.3	Package dependencies	3	
	1.4	Document conventions	3	
2	Bac	kground and context	5	
3	Pac	kage syntax and semantics	7	
	3.1	Namespace URI and other declarations necessary for using this package	7	
	3.2	Coordinate System and Size	7	
	3.3	Primitive data types	8	
		3.3.1 Type SpeciesReferenceRole	8	
		3.3.2 Type xsi:type	8	
	3.4	General features	8	
		3.4.1 The Point class	8	
		3.4.2 The Dimensions class	8	
		3.4.3 The BoundingBox class	9	
		3.4.4 The Curve class	9	
			10	
			10	
	3.5	The extended Model class		
	3.6	The Layout class		
	3.7	The Graphical Object class		
	3.8	The CompartmentGlyph class		
	3.9	The SpeciesGlyph class		
	3.10	The ReactionGlyph class		
			17	
	3.11	The GeneralGlyph class		
	0.40	3.11.1 The ReferenceGlyph class		
			20	
4			22	
	4.1			
	4.2		22	
	4.3	ReactionGlyph Example		
	4.4	TextGlyph Example		
	4.5	Example using SBML Level 3 Version 1		
	4.6	Example using SBML Level 2 Version 1		
	4.7	- b 2	34	
Α			37	
			37	
			49	
Re	References 50			

1 Introduction

With the Systems Biology Markup Language (SBML) there now is a common standard for the exchange of dynamical systems data which has already been adopted by many applications in this field Hucka et al. (2011, 2003); SBML Team (2012).

In 2002 we worked on an automatic layout algorithm (Wegner and Kummer (2005)). Based on a given SBML file species and reactions should be placed automatically as a network. Since there was no way to save the final layout of the network, we started developing the layout extension. In 2003 the first draft was done and presented on the SBML workshop in St. Louis in 2004. Based on the discussions in St. Louis Ralph Gauges finalized a first specification and implementation for libSBML which was published in Gauges et al. (2006). During the next SBML meetings the layout extension was discussed heavily and also challenged by other proposals but due to the constant support from the community (e.g.: Deckard et al. (2006)), it got finally accepted as a package of SBML Level 3.

1.1 Proposal corresponding to this package specification

This specification for Layout in SBML Level 3 Version 1 is based on the proposal by the same authors, located at the following URL:

http://sbml.org/Community/Wiki/SBML_Level_3_Proposals/Layout

The tracking number in the SBML issue tracking system (SBML Team, 2010) for the Layout package activities is 3594234. The version of the proposal used as the starting point for this specification is the version of April 2005. Previous versions of the current proposal are available from:

http://otto.bioquant.uni-heidelberg.de/sbml/

Details of earlier independent proposals are provided in Section 2.

1.2 Tracking number

As initially listed in the SBML issue tracking system under: http://sourceforge.net/tracker/?func=detail&aid=3594234&group_id=71971&atid=894711.

1.3 Package dependencies

The Layout package adds additional classes to SBML Level 3 Version 1 Core and has no dependency on any other SBML Level 3 package.

1.4 Document conventions

Following the precedent set by the SBML Level 3 Version 1 Core specification document, we use UML 1.0 (Unified Modeling Language; Eriksson and Penker 1998; Oestereich 1999) class diagram notation to define the constructs provided by this package. We also use color in the diagrams to carry additional information for the benefit of those viewing the document on media that can display color. The following are the colors we use and what they represent:

■ *Black*: Items colored black in the UML diagrams are components taken unchanged from their definition in the SBML Level 3 Version 1 Core specification document.

31

33

- *Green*: Items colored green are components that exist in SBML Level 3 Version 1 Core, but are extended by this package. Class boxes are also drawn with dashed lines to further distinguish them.
- *Blue*: Items colored blue are new components introduced in this package specification. They have no equivalent in the SBML Level 3 Version 1 Core specification.

Section 1 Introduction Page 3 of 50

13

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We also use the following typographical conventions to distinguish the names of objects and data types from other entities; these conventions are identical to the conventions used in the SBML Level 3 Version 1 Core specification document:

AbstractClass: Abstract classes are classes that are never instantiated directly, but rather serve as parents of other object classes. Their names begin with a capital letter and they are printed in a slanted, bold, sans-serif type-face. In electronic document formats, the class names defined within this document are also hyperlinked to their definitions; clicking on these items will, given appropriate software, switch the view to the section in this document containing the definition of that class. (However, for classes that are unchanged from their definitions in SBML Level 3 Version 1 Core, the class names are not hyperlinked because they are not defined within this document.)

Class: Names of ordinary (concrete) classes begin with a capital letter and are printed in an upright, bold, sansserif typeface. In electronic document formats, the class names are also hyperlinked to their definitions in this specification document. (However, as in the previous case, class names are not hyperlinked if they are for classes that are unchanged from their definitions in the SBML Level 3 Version 1 Core specification.)

SomeThing, otherThing: Attributes of classes, data type names, literal XML, and generally all tokens *other* than SBML UML class names, are printed in an upright typewriter typeface. Primitive types defined by SBML begin with a capital letter; SBML also makes use of primitive types defined by XML Schema 1.0 (Biron and Malhotra, 2000; Fallside, 2000; Thompson et al., 2000), but unfortunately, XML Schema does not follow any capitalization convention and primitive types drawn from the XML Schema language may or may not start with a capital letter.

The UML diagrams in this document show the name of the class on top. Below are the attributes specific to that class. Optional attributes have some default value which may be NULL. Arrays are written in square brackets where with the valid array length within those brackets. So an array [2..] would mean that it can hold from 2 to ∞ number of objects.

For other matters involving the use of UML and XML, we follow the conventions used in the SBML Level 3 Version 1 Core specification document.

Section 1 Introduction Page 4 of 50

2 Background and context

Currently, there is no official way of encoding the layout of computational models in SBML. Software tools wishing to share this information have been using the SBML annotation scheme to store this information in proprietary form.

The layout proposal was made in early 2003, since then it has been incorporated into libSBML (Gauges et al. (2006)) and has been used by software applications (e.g.: Sahle et al. (2006), Bergmann and Sauro (2006)) for SBML Level 2 and Level 3.

The overall structure of this proposal reflects design decisions that will be detailed in this section. These decisions are mainly based on the discussion on the mailing list and during the workshop in St. Louis. It was requested that several layouts should be stored in one SBML file. And so the layout is stored in a **ListOfLayouts** as child of the the **Model** element instead of direct annotations to the model constituents.

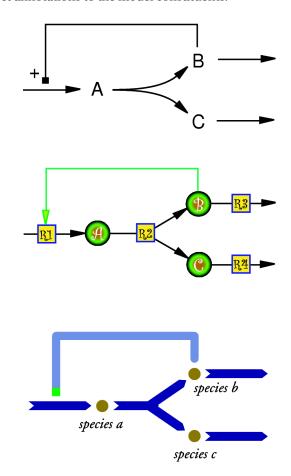


Figure 1: Illustration of different renderings of the same layout.

The layout of a reaction network diagram should be described as graphical representations of species and reactions (and not as arbitrary drawing or graph). This means that existing languages for the description of vector drawings (SVG) or general graphs cannot be used. While it may seem unnecessary to invent a new language when an existing one like SVG could in principle be used to describe the layout of a reaction network, there are good reasons to have a language tailored specifically for the layout of SBML models.

Presumably, most programs that will use this SBML extension are primarily programs dealing with biochemi-

Section 2 Background and context

15

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cal models. Internally, they will have data structures for species and reactions, so it will be natural for them to describe the layout of the reaction network also in terms of species and reactions (and not in terms of polygons or splines). Thus the layout object has a similar structure like the SBML model object and contains lists of graphical representations of compartments, species, and reactions (called compartmentGlyph, speciesGlyph, and reactionGlyph respectively). Additional layout elements and relationships can be represented by using the graphicalObject and generalGlyph elements.

Another important question is the level of detail that the description should provide. For simplicity, only the layout (i.e., the position of the different graphical objects) of the diagram is encoded, not the details of how it should be rendered. That is left to the SBML Level 3 Render package.

Figure 1 illustrates this distinction. All three diagrams could be renderings of the same layout and would be described by identical SBML files. No information about colors, line styles, fonts, etc., is present in the layout description.

The next question is how the relation between the model and the layout should be established. There seems to be consensus that one model element can be represented by several layout elements. For example, it can be useful to have several representations of one species in the layout to avoid crossing lines. This can be accomplished if every layout element has a field that refers to the id of a model element.

There are also cases where a layout element does not correspondent to exactly one model element. One example would be if a layout shows a simplified version of the model where one reaction in the layout corresponds to several reactions and intermediate species in the model. This is the reason why the field in the layout elements that refers to the model elements is optional, allowing layout objects that do not have a specific counterpart in the SBML model.

The result of all this is a way to describe a graphical layout of a reaction network in biochemical terms. This layout can be closely tied to the biochemical model. A graphical model editor for example would typically create a layout that is closely connected (by a one-to-several relation from the model elements to the layout elements) to the model.

A more general layout design program could also create a layout that is not so closely tied to the model, for example, it could create a layout that shows a simplified version of the model.

3 Package syntax and semantics

In this section, we define the syntax and semantics of the Layout package for SBML Level 3 Version 1. We expound on the various data types and constructs defined in this package, then in Section 4 on page 22, we provide complete examples of using the constructs in an example SBML model.

3.1 Namespace URI and other declarations necessary for using this package

Every SBML Level 3 package is identified uniquely by an XML namespace URI. For an SBML document to be able to use a given SBML Level 3 package, it must declare the use of that package by referencing its URI. The following is the namespace URI for this version of the Layout package for SBML Level 3 Version 1:

```
"http://www.sbml.org/sbml/level3/version1/layout/version1"
```

In addition, SBML documents using a given package must indicate whether understanding the package is required for complete mathematical interpretation of a model, or whether the package is optional. This is done using the attribute required on the <sbml> element in the SBML document. For the Layout Package, the value of this attribute must be set to "false".

The following fragment illustrates the beginning of a typical SBML model using SBML Level 3 Version 1 and this version of the Layout package:

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level3/version1/core" level="3" version="1"
    xmlns:layout="http://www.sbml.org/sbml/level3/version1/layout/version1" layout:required="false">
```

Historically, the layout package has also been used to encode the layout of SBML Level 2 models, there the following namespace is to be used within an annotation:

```
"http://projects.eml.org/bcb/sbml/level2"
```

A minimal example would look like this:

3.2 Coordinate System and Size

All size information given for layout objects are understood to be in Point (pt), which is defined to be 1/72 of an inch (0.3527777778 mm) as in postscript.

The layout extension uses a Cartesian coordinate system. The origin of the coordinate system will be in the upper left corner of the screen. The positive x-axis runs from left to right, the positive y-axis run from top to bottom and the positive z-axis points into the screen. The reason for having the origin in the upper left corner of the screen is that most 2D packages do it that way. This coordinate system is also right handed just like the ones in OpenGL and Java3D, which should facilitate 3D implementations as well.

Section 3 Package syntax and semantics

12

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43

3.3 Primitive data types

Section 3.1 of the SBML Level 3 Version 1 Core specification defines a number of primitive data types and also uses a number of XML Schema 1.0 data types (Biron and Malhotra, 2000). Of the data types defined and referenced in SBML Level 3 Version 1 Core, we make use of integer, double, string, SId, SIdRef and IDREF. Additionally, the Layout package defines the SpeciesReferenceRole and uses the xsi:type from the XML Schema instance (XSI) namespace.

Figure 8 illustrates the interrelation between these entities.

The SId type is used as the data type for the identifiers of all layout classes. As such they have to be unique within the model and are not allowed to conflict with SIds from SBML elements or any package that use the same SId namespace.

3.3.1 Type SpeciesReferenceRole

The Layout package defines a new enumerated type **SpeciesReferenceRole** which represents the role that a species takes within a reaction. It can take only one of the following values:

substrate, product, sidesubstrate, sideproduct, modifier, activator, inhibitor undefined.

3.3.2 Type xsi:type

In order to easily differentiate between **LineSegment** and **CubicBezier** elements, the **xsi:type** attribute from the XML Schema instance (XSI) namespace is used. The namespace is:

"http://www.w3.org/2001/XMLSchema-instance"

For this purpose the xsi:type is set to the following fixed values: "LineSegment" for line segments and "CubicBezier" for splines.

3.4 General features

This section describes the common classes **Point**, **Dimensions** and **BoundingBox** that are used by all other classes of this package. It also describes the representation of curves.

3.4.1 The Point class

A point is specified via the required attributes \mathbf{x} , \mathbf{y} and an optional attribute \mathbf{z} , all of which are of type **double**. If the attribute \mathbf{z} is not specified, the object is a two dimensional object.

The **Point** class also has an optional attribute **id** of type **SId**. While not used in the Layout package, it can be used by programs to refer to the elements.

3.4.2 The Dimensions class

A dimension is specified via the required attributes width, height and an optional attribute depth, all of which are of type double. If the attribute depth is not specified, the object is a two dimensional object.

The width specifies the size of the object in the direction of the positive x axis, the height attribute specifies the size of the object along the positive y axis and the depth attribute specifies the size of the object along the positive z axis. All sizes for **Dimensions** objects are positive values, and so the attributes are not allowed to take negative values.

23

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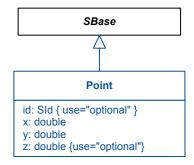


Figure 2: The definitions of the Point class.

The **Dimensions** class also has an optional attribute **id** of type **SId**. While not used in the Layout package, it can be used by programs to refer to the elements.

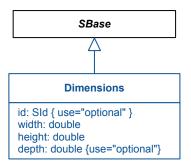


Figure 3: The definitions of the Dimensions class.

3.4.3 The BoundingBox class

A **BoundingBox** consists of the required elements **position** and **dimensions**.

The **BoundingBox** class also has an optional attribute **id** of type **SId**. While not used in the Layout package, it can be used by programs to refer to the elements.

The position element

The position always specifies the upper left corner of the bounding box. The position is of type Point.

The dimensions element

The dimensions element is required and of type **Dimensions**. It represents the size of the bounding box.

3.4.4 The Curve class

The curve class describes how to connect elements of the layout package. It is fully specified by a mandatory listOfCurveSegments element and is used in four places:

- SpeciesReferenceGlyph: Here it describes a curve from/to the center piece of the parent ReactionGlyph to/from the SpeciesGlyph it represents.
- **ReactionGlyph**: Here it describes a curve for the center piece of a reaction.

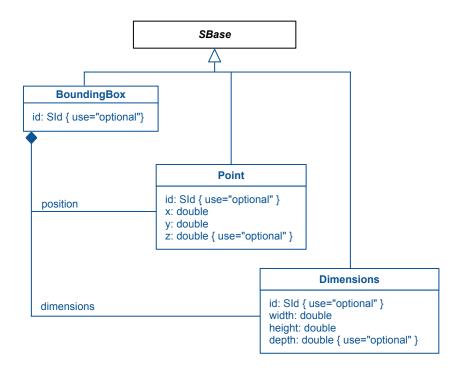


Figure 4: The definitions of the BoundingBox class.

- **ReferenceGlyph**: Here it describes a curve from/to the center piece of the parent **GeneralGlyph** to/from the glyph it represents.
- GeneralGlyph: Here it describes a curve for the center piece of an additional relationship.

In the above the *center piece* refers to either the **Curve** element of a **ReactionGlyph**, or its **BoundingBox**.

The listOfCurveSegments element

The listOfCurveSegments contains an arbitrary number of curve segments that can be either of type LineSegment or of type CubicBezier.

3.4.5 The LineSegment class

The **LineSegment** class consists of the mandatory attribute **xsi:type** and two elements of type **Point**. One is called **start** and represents the starting point of the line, the other is called **end** and represents the endpoint of the line.

The xsi:type attribute

For straight line segments, the attribute xsi:type must have the value set to:

"LineSegment"

Note that the xsi:type is from the xsi namespace:

"http://www.w3.org/2001/XMLSchema-instance"

3.4.6 The CubicBezier class

In order to be able to represent smooth curves the Layout package defines the class **CubicBezier**. It represents a Bezier curve (Wikipedia (2013)), as is readily available in most Graphic APIs.

The class **CubicBezier** is derived from **LineSegment**. It consists of four elements, the two inherited elements **start**

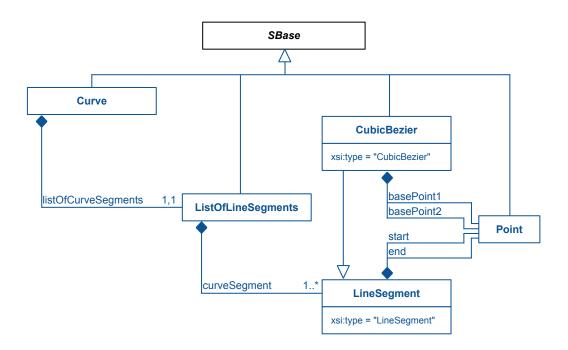


Figure 5: The definitions of the Curve class.

and end, that specify the starting point and the endpoint of the cubic bezier curve, and two elements basePoint1 and basePoint2 which specify the two additional base points that are needed to describe a cubic bezier curve.

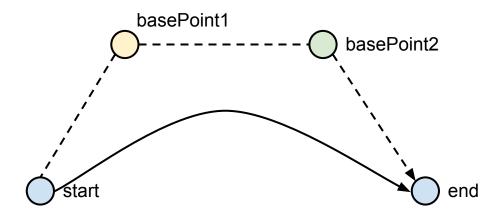


Figure 6: A depiction of a cubic bezier curve, including the points start, end as well as basePoint1 and basePoint2.

The basePoint1 element represents the base point closer to the start point and basePoint2 the base point closer to end point. This allows tools not able to render bezier curves to approximate them by directly connecting the four points (as visible in the dashed line in Figure 6).

The xsi:type attribute

For cubic bezier curves, the attribute xsi:type must have the value set to:

"CubicBezier"

Note that the xsi:type is from the xsi namespace:

"http://www.w3.org/2001/XMLSchema-instance"

3.5 The extended Model class

The **SBML Model** class is extended with the addition of one child the **listOfLayouts**. A **Model** may contain at most one such list.

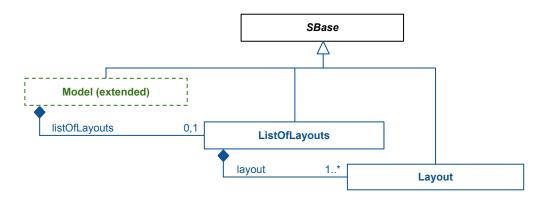


Figure 7: The definitions of the extended Model class.

The listOfLayouts class

As shown in Figure 7 the **ListOfLayouts** is derived from **SBase** and inherits the attributes **metaid** and **sboTerm**, as well as the subcomponents for **Annotation** and **Notes**. The **ListOfLayouts** must contain at least one Layout (defined in Section 3.6).

Should the Layout package be used in an **SBML** Level 2 model, the **ListOfLayouts** needs to be placed in an **Annotation** on the **Model** element. For a complete example that uses SBML Level 2 see Section 4.6 on page 30.

3.6 The Layout class

The layout class stores layout information for some or all elements of the SBML model as well as additional objects that need not be connected to the model.

The **Layout** has two attributes: **id** and **name**. Additionally a **Dimensions** element specifies the size of the layout. The actual layout elements are contained in several lists namely: a **ListOfCompartmentGlyphs**, a **ListOfSpeciesGlyphs**, a **ListOfReactionGlyphs**, a **ListOfTextGlyphs**, and a **ListOfAdditionalGraphicalObjects**. Each of these lists can only occur once, and, if present, is not allowed to be empty.

The id attribute

The id attributes takes a required value of type SId. The id which uniquely identifies the layout.

The name attribute

The name attributes takes an optional value of type String. It allows to specify a human readable name for the **Layout**.

20

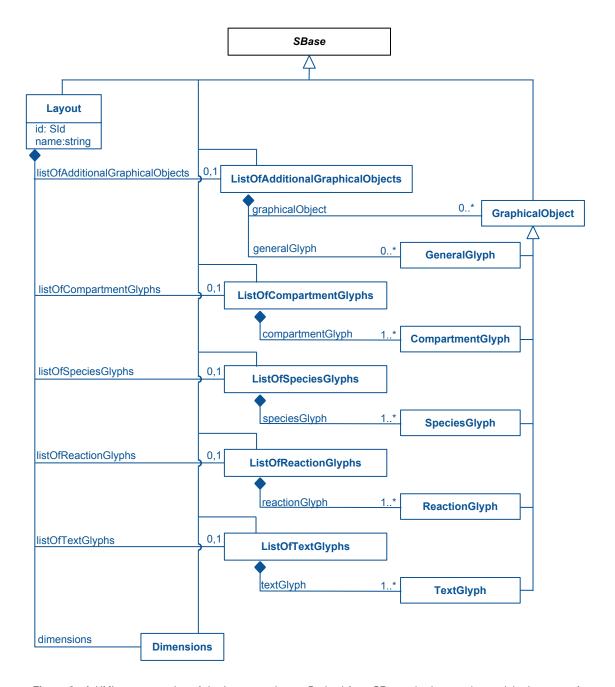


Figure 8: A UML representation of the Layout package. Derived from SBase, the Layout classes inherit support for constructs such as SBML Notes and Annotations. See Section 1.4 for conventions related to this figure. The individual classes are further discussed in the text.

The dimensions element

The **dimensions** element of type **Dimensions** specifies the dimensions of this layout. This element is required. It holds the dimensions of all layout elements (care should be taken when using cubic beziers (see Section 3.4.6), that the described curve also lies within the given dimensions).

The listOfCompartmentGlyphs element

The listOfCompartmentGlyphs, when present must contain one or more CompartmentGlyph elements.

Note that not all **Compartment** elements have to be represented by a **CompartmentGlyph**. In fact quite often the compartment is omitted in a layout for a uni-compartmental network. (In which case the **ListOfCompartment-Glyphs** would be ommitted altogether.)

The listOfSpeciesGlyphs element

The listOfSpeciesGlyphs, when present must contain one or more SpeciesGlyph elements. Just as with CompartmentGlyph elements, not every Species of the model has to have a representation in this list.

The listOfReactionGlyphs element

The listOfReactionGlyphs, when present must contain one or more ReactionGlyph elements. Again, not all reactions of the containing SBML model have to be included in the containing layout.

The listOfTextGlyphs element

The listOfTextGlyphs, when present, must contain one or more TextGlyph elements.

The listOfAdditionalGraphicalObjects element

Most objects for which layout information is to be included in an SBML file have a corresponding object in the SBML model. As there might be cases where the user wants to include object types in the layout that do fall in any of the other categories described below, we include a <code>listOfAdditionalGraphicalObjects</code> in each Layout object. This list holds an arbitrary number of <code>graphicalObject</code> elements. The <code>graphicalObject</code> only defines a bounding box in a specific place in the layout without giving additional information about its contents.

The listOfAdditionalGraphicalObjects, when present must contain one or more of the following elements: GraphicalObject, GeneralGlyph.

When using a **GraphicalObject** it is recommended that some form of meta information is provided. For additional relationships such as SBML events or rules, the **GeneralGlyph** can be used, see Section 3.11.

3.7 The GraphicalObject class

All the more specific layout elements (CompartmentGlyph, GeneralGlyph, SpeciesGlyph, ReactionGlyph, ReferenceGlyph, TextGlyph, and SpeciesReferenceGlyph) are derived from GraphicalObject.

Each GraphicalObject has a mandatory BoundingBox, which specifies the position and the size of the object.

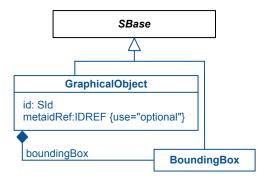


Figure 9: The definitions of the GraphicalObject class.

While **GraphicalObject** is the base class for most elements in the Layout package, it is **not** an abstract class. It can be instantiated when used in the **listOfAdditionalGraphicalObjects** to describe additional elements and relationships. Since it only describes a **BoundingBox**, programs are encouraged to add **Annotation** objects that

describe program specific graphical information.

The id attribute

The GraphicalObject has a mandatory id attribute of type SId through which it can be identified.

The metaidRef attribute

The **GraphicalObject** has an optional **metaidRef** attribute of type **IDREF** that allows the object to uniquely reference elements in the **Model**. Wherever possible it is preferred that the more specific reference mechanisms are used.

3.8 The CompartmentGlyph class

The **CompartmentGlyph** class is derived from **GraphicalObject** and inherits its attributes. Additionally, it has two optional attributes **compartment** and **order**. For an example see Section 4.1.

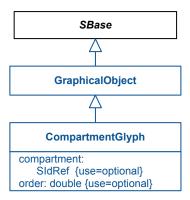


Figure 10: The definitions of the CompartmentGlyph class.

The compartment attribute

The compartment attribute is of type SIdRef. It is used to add a reference to the id of the corresponding compartment in the model. Since the compartment is optional, the user can specify compartments in the layout that are not part of the model.

If the compartment attribute is used together with the metaidRef they need to refer to the same object in the Model.

The order attribute

The **order** attribute is an optional attribute of type **double**. It is there to handle the case where compartments in a layout are overlapping, and tools would want to clearly disambiguate which **CompartmentGlyph** is on top of another one.

The **order** attribute follows the coordinate system. There the **z** dimension is pointing into the screen, thus an element with a **lower order** value will be **in front** of elements with a **higher** value.

If not specified, the **order** is undefined and tools are free to display the compartment glyphs in the order that best fits their needs.

Note: Usually the **order** attribute is only used for two dimensional layouts since in three dimensional layouts the **z** coordinate can be used to easily distinguish CompartmentGlyphs. However, there may be uses for having the same **z** coordinate in three dimensional layouts, in which case the **order** attribute will help to disambiguate the drawing order.

26

3.9 The SpeciesGlyph class

In addition to the attributes from **GraphicalObject**, the **SpeciesGlyph** object has an optional **species** attribute. For an example see Section 4.2.

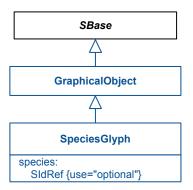


Figure 11: The definitions of the SpeciesGlyph class.

The species attribute

The species attribute of type SIdRef allows modelers to link the SpeciesGlyph to the id of the corresponding species object in the Model. The species attribute is optional to allow the program to specify species representations that do not have a direct correspondence in the model. This might be useful if some pathway has been collapsed, but is still treated by layout programs.

If the species attribute is used together with the metaidRef they need to refer to the same object in the Model.

3.10 The ReactionGlyph class

The **ReactionGlyph** is used to represent **Reaction** elements in the layout. Analogous to how a **Reaction** object has to at least have one reactant or product, the **ReactionGlyph** has to at least have one **SpeciesReferenceGlyph** stored in the **ListOfSpeciesReferenceGlyphs**.

The **ReactionGlyph** inherits from **GraphicalObject**. In addition to the attributes inherited from **GraphicalObject**, the **ReactionGlyph** is described by an attribute **reaction**, a **Curve** element and a **listOfSpeciesReferenceGlyphs** element.

The **Curve** describes the center section of a **ReactionGlyph**. The center section is frequently used by tools to separate the point where substrates arcs come together, from the point where product arcs split off. The **Curve** is optional, and when not present the dimensions of the inherited **BoundingBox** describes the center section, by storing its position and dimension.

For an example see Section 4.3.

The reaction attribute

The **reaction** attribute of type **SIdRef** is used to specify the **id** of the corresponding **Reaction** in the model. This reference is optional.

If the reaction attribute is used together with the metaidRef they need to refer to the same object in the Model.

The listOfSpeciesReferenceGlyphs element

Since a **Species** element can have several graphical representations in the layout there must be a way to specify which **SpeciesGlyph** should be connected to the **ReactionGlyph**. This is done using the **listOfSpeciesReference**-

Section 3 Package syntax and semantics

18

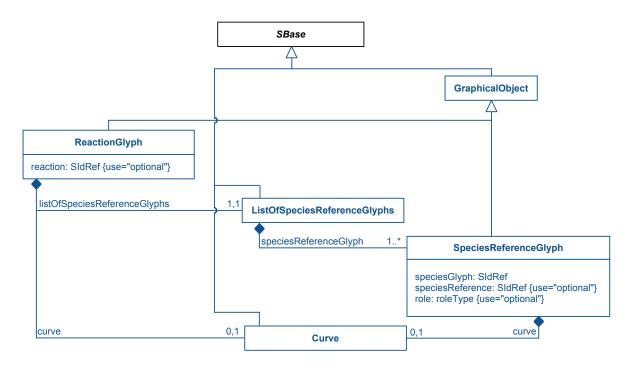


Figure 12: The definitions of the ReactionGlyph class.

Glyphs.

The ListOfSpeciesReferenceGlyphs is mandatory, since every Reaction has to have at least one reactant or product.

The curve element

The optional **Curve** element (Section 3.4.4) can be used to describe a curve representation for the **ReactionGlyph**. If a **ReactionGlyph** specifies a curve, the bounding box is to be ignored.

3.10.1 The SpeciesReferenceGlyph class

The speciesReferenceGlyph element describes the graphical connection between a SpeciesGlyph and a Reaction-Glyph (which would be an arrow or some curve in most cases).

As can be seen in the diagram Section 3.10, a **SpeciesReferenceGlyph** inherits from **GraphicalObject**. Additionally, it has a mandatory attribute **speciesGlyph** and two optional attributes **speciesReference** and **role**. Optionally, the **SpeciesReferenceGlyph** also has an element **curve**.

If the **curve** is specified, it overrides the inherited bounding box.

The speciesGlyph attribute

The **speciesGlyph** is of type **SIdRef**. It contains a reference to the **id** of a **SpeciesGlyph** object that is to be connected to the **ReactionGlyph**. This attribute is mandatory so as to ensure unambiguity about which SpeciesGlyph has to be connected with this ReactionGlyph.

The speciesReference attribute

The speciesReference is an optional attribute of type SIdRef that allows modelers to connect the SpeciesReference(or ModifierSpeciesReference) of the containing model.

If the speciesReference attribute is used together with the metaidRef they need to refer to the same object in

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the Model.

NOTE: The id on a SpeciesReference and ModifierSpeciesReference was only introduced in SBML Level 3 Version 1 Core, in order to successfully use the speciesReference in prior Levels of SBML, the corresponding species reference has to be annotated with an identifier. The annotation would look like this:

```
<annotation>
  <layoutId xmlns="http://projects.eml.org/bcb/sbml/level2" id="theId"/>
</annotation>
```

This **id** has to be unique within the global **SId** namespace of the SBML model and can thus be used to reference a given species reference. For a complete example see also Section 4.3.

The role attribute

The role attribute is of SpeciesReferenceRole (see Section 3.3.1) and is used to specify how the species reference should be displayed. Allowed values are substrate, product, sidesubstrate, sideproduct, modifier, activator, inhibitor and undefined.

This attribute is optional and should only be necessary if the optional **speciesReference** attribute is not given or if the respective information from the model needs to be overridden.

- The values **substrate** and **product** are used if the species reference is a main product or substrate in the reaction.
- sidesubstrate and sideproduct are used for simple chemicals like ATP, NAD+, etc. This allows programs to render them as side reactions.
- activator and inhibitor are modifiers where their influence on the reaction is known and modifier is a more general term if the influence is unknown or changes during the course of the simulation.

In order to specify more specific types of interactions it is recommended to use the **sboTerm** on the **SpeciesReference**. If both **role** and **sboTerm** are specified and conflicting, it is the **role** that takes precedence.

The curve element

The **curve** is an optional element of type **Curve**. When present the glyphs bounding box (as inherited from the **GraphicalObject**) is to be disregarded.

So as to make the drawing of these curves as easy as possible the line segments should be ordered depending on the role of the **SpeciesReferenceGlyph**. If no **role** attribute is defined the role to be assumed is taken from the role that the **SpeciesReference** referenced via the attribute **speciesReference** has, otherwise it is **undefined**.

- product, sideproduct, substrate, sidesubstrate, undefined: The line segments have their start element at the ReactionGlyph and their end element at the SpeciesGlyph.
- activator, inhibitor, modifier: The line segments have their start element at the SpeciesGlyph and their end element at the ReactionGlyph.

3.11 The GeneralGlyph class

The **GeneralGlyph** is used to facilitate the representation of elements other than **Compartment**, **Species** and **Reaction** and thus can be used for the display of relationships of **Rule** or elements defined by other SBML packages. It closely follows the structure of the **ReactionGlyph**.

The **GeneralGlyph** is defined via an optional attribute **reference** as well as the elements **curve**, **listOfReference**-Glyphs and **listOfSubGlyphs**.

For an example that uses the **GeneralGlyph** to represents a basic influence see Section 4.7.

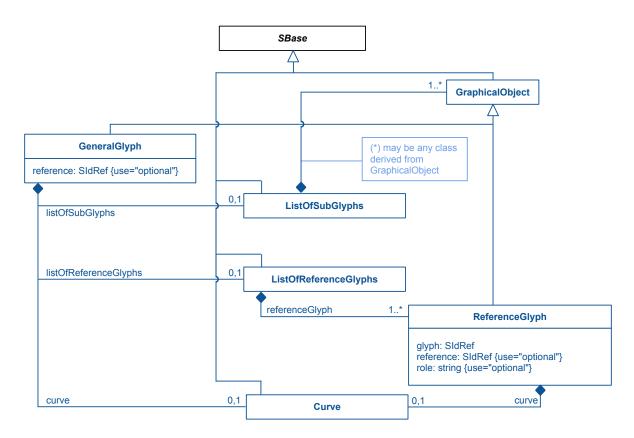


Figure 13: The definitions of the GeneralGlyph class.

The reference attribute

The optional **reference** attribute of type **SIdRef** that can be used to specify the **id** of the corresponding element in the model that is represented.

If the reference attribute is used together with the metaidRef they need to refer to the same object in the Model.

The listOfSubGlyphs element

The **ListOfSubGlyphs** is an optional list that can contain sub glyphs of the **GeneralGlyph**. One example of its use could be a sub-module, that contains species glyphs and reaction glyph, that are not necessarily part of the containing **Model**. Another example would be an **Event**, visualized with its **Trigger** and additional **GeneralGlyphs** for its **EventAssignments**. The **ListOfSubGlyphs** consists of **GraphicalObject** or derived classes. Thus, unlike the **ListOfAdditionalGraphicalObjects** (which may only contain **GraphicalObjects** or **GeneralGlyphs**), the **listOfSubGlyphs** may contain any derived class, such as for example **TextGlyph** elements.

When present the listOfSubGlyphs must contain at least one element.

The listOfReferenceGlyphs element

The **ListOfReferenceGlyphs** is optional, since conceivably the **GeneralGlyph** could just contain a number of sub glyphs. When present, it must include at least one **ReferenceGlyph**.

The curve element

The optional **Curve** element (Section 3.4.4) can be used to describe a curve representation for the **GeneralGlyph**. If a **GeneralGlyph** specifies a curve, the bounding box is to be ignored.

3.11.1 The ReferenceGlyph class

The **referenceGlyph** element describes the graphical connection between an arbitrary **GraphicalObject** (or derived element) and a **GeneralGlyph** (which would be an arrow or some curve in most cases).

As can be seen in the diagram Section 3.11, a **ReferenceGlyph** inherits from **GraphicalObject**. Additionally it has a mandatory attribute **glyph** and two optional attributes **reference** and **role**. Optionally the **ReferenceGlyph** also has an element **curve**.

The ReferenceGlyph should either contain a bounding box or a curve specification, if both are given, the bounding box should be ignored.

The glyph attribute

The glyph is of type SIdRef. It contains a reference to the id of a GraphicalObject (or derived) object that is to be connected to the GeneralGlyph.

This attribute is mandatory so as to ensure unambiguously which glyph has to be connected with this General-Glyph.

The reference attribute

The **reference** is an optional attribute of type **SIdRef** that is used to connect the **ReferenceGlyph** with a element of the containing SBML model.

The role attribute

The role attribute is of type string and is used to specify how the reference should be displayed.

While as **string**, the value of the **role** attribute is unconstraint, current implementations use the same values as specified in Section 3.3.1.

The curve element

The **curve** is an optional element of type **Curve**. When present the glyph's bounding box (as inherited from the **GraphicalObject**) is to be disregarded.

So as to make the drawing of these curves as easy as possible the line segments should be ordered depending on the role of the **ReferenceGlyph**:

- If the glyph represents a modification it should start at the glyph and end at the center of the **GeneralGlyph**.
- otherwise it should begin at the center section of the GeneralGlyph and end at the reference glyph.

3.12 The TextGlyph class

The **TextGlyph** class describes the position and dimension of text labels. It inherits from **GraphicalObject** and adds the attributes **graphicalObject**, **text** and **originOfText**.

For an example see Section 4.4.

The graphicalObject attribute

The attribute <code>graphicalObject</code> is of type <code>SIdRef</code>. It contains the <code>id</code> of any <code>GraphicalObject</code> and specifies that the <code>TextGlyph</code> should be considered to be a label to that object. This allows modelers to indicate that the label is to be moved together with the object.

If the **graphicalObject** attribute is used together with the **metaidRef** they need to refer to the same object in the **Layout**.

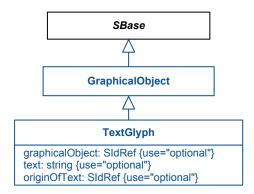


Figure 14: The definitions of the TextGlyph class.

The text attribute

The optional text attribute is of type string. It facilitates adding of independent text, like a title or a comment to the diagram.

The originOfText attribute

Additionally the optional attribute originOfText of type SIdRef can hold the id of an entity in the SBML model. If it is specified, the text to be displayed is taken from the name attribute of the referenced object.

If both attributes originOfText and text are specified, the text attribute overrides the originOfText.

4 Examples

4.1 CompartmentGlyph Example

Below a **CompartmentGlyph** is defined for the compartment Yeast. It is located at position x=5, y=5 and has dimensions width=390, height=220.

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2" level="2" version="1">
 <model id="TestModel_with_modifiers">
    <annotation>
     <listOfLayouts xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
              xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
      <layout id="Layout_1">
        <dimensions width="400" height="230"/>
        <listOfCompartmentGlyphs>
          <compartmentGlyph id="CompartmentGlyph_1" compartment="Yeast">
            <box><box<br/>d="bb1"></br>
              <position x="5" y="5"/>
              <dimensions width="390" height="220"/>
            </boundingBox>
          </compartmentGlyph>
        </listOfCompartmentGlyphs>
      </layout>
     </list0fLayouts>
    </annotation>
    <listOfCompartments>
      <compartment id="Yeast"/>
    </listOfCompartments>
  </model>
</sbml>
```

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4.2 SpeciesGlyph Example

Below a **SpeciesGlyph** is defined for the species **Glucose** at position x=105, y=20 with dimensions width=130, height=20.

The following defines a basic SpeciesGlyph.

Section 4 Examples Page 22 of 50

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4.3 ReactionGlyph Example

The following defines a **ReactionGlyph** for reaction **Hexokinase** containing only a center segment represented as straight line.

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2" level="2" version="1">
 <model id="TestModel_with_modifiers">
    <annotation>
    <listOfLayouts xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
             xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
      <layout id="Layout_1">
        <dimensions width="400" height="230"/>
        <listOfReactionGlyphs>
          <reactionGlyph id="glyph_Hexokinase" reaction="Hexokinase">
             <listOfCurveSegments>
               <curveSegment xsi:type="LineSegment">
                 <start x="170" y="100"/>
                 <end x="170" y="130"/>
               </curveSegment>
             </listOfCurveSegments>
           </curve>
           <listOfSpeciesReferenceGlyphs>
           </listOfSpeciesReferenceGlyphs>
          </reactionGlyph>
        </listOfReactionGlyphs>
     </layout>
    </list0fLayouts>
    </annotation>
```

Section 4 Examples Page 23 of 50

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The following adds a **SpeciesReferenceGlyph** and demonstrates adding an **id** to a **SpeciesReference** in SBML Level 2 Version 1.

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2" level="2" version="1">
 <model id="TestModel_with_modifiers">
     <listOfLayouts xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
              xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
      <layout id="Layout_1">
        <dimensions width="400" height="230">
        </dimensions>
        <listOfReactionGlyphs>
          <reactionGlyph id="glyph_Hexokinase" reaction="Hexokinase">
            <listOfSpeciesReferenceGlyphs>
              <speciesReferenceGlyph id="SpeciesReferenceGlyph_Glucose"</pre>
                   speciesReference="SpeciesReference_Glucose"
                   speciesGlyph="SpeciesGlyph_Glucose" role="substrate">
                <curve>
                  <listOfCurveSegments>
                    <curveSegment xsi:type="LineSegment">
                      <start x="170" y="100">
                      </start>
                      <end x="170" y="50">
                      </end>
                    </curveSegment>
                  </list0fCurveSegments>
                </curve>
              </speciesReferenceGlyph>
            </listOfSpeciesReferenceGlyphs>
          </reactionGlyph>
        </listOfReactionGlyphs>
      </layout>
     </list0fLayouts>
    </annotation>
    <listOfReactions>
      <reaction id="Hexokinase" reversible="false">
        <listOfReactants>
```

Section 4 Examples Page 24 of 50

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4.4 TextGlyph Example

The following defines a **TextGlyph** with **id=TextGlyph_Glucose** that is connected to a **SpeciesGlyph SpeciesGlyph_Glucose** and retrieves the text to display from the **Species** with **id="Glucose"**.

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2" level="2" version="1">
  <model id="TestModel_with_modifiers">
    <annotation>
     <listOfLayouts xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
               xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
      <layout id="Layout_1">
        <dimensions width="400" height="230"/>
        <listOfSpeciesGlyphs>
          <speciesGlyph id="SpeciesGlyph_Glucose" species="Glucose">
             <box><box id="bb2"></br>
               <position x="105" y="20"/>
<dimensions width="130" height="20"/>
             </boundingBox>
          </speciesGlyph>
        </listOfSpeciesGlyphs>
        <listOfTextGlyphs>
          <textGlyph id="TextGlyph_Glucose" graphicalObject="SpeciesGlyph_Glucose"</pre>
                      originOfText="Glucose">
             <box><box<br/>dingBox<br/>id="bbA"></br>
               <position x="115" y="20">
               <dimensions width="110" height="20">
               </dimensions>
             </boundingBox>
          </textGlyph>
        </listOfTextGlyphs>
      </layout>
     </list0fLayouts>
    </annotation>
```

Section 4 Examples Page 25 of 50

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4.5 Example using SBML Level 3 Version 1

Here a small complete example to illustrate and complement the paragraphs above. The model consists of the Hexokinase reaction.

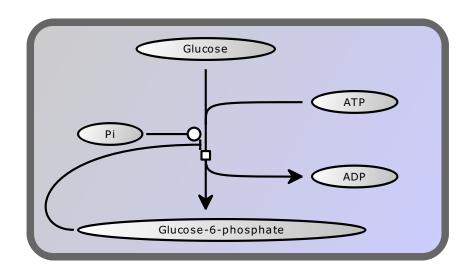


Figure 15: One possible rendering of the example layout.

This reaction has a feedback inhibition by glucose-6-phosphate and it is activated by free organic phosphate. These two relations are represented by species reference glyphs and a corresponding role attribute. We did not include any coordinates in the third dimension.

Section 4 Examples Page 26 of 50

```
</listOfUnits>
  </unitDefinition>
 <unitDefinition id="time">
    tofUnits>
      <unit kind="second" exponent="1" scale="0" multiplier="1"/>
    </listOfUnits>
  </unitDefinition>
</listOfUnitDefinitions>
<listOfCompartments>
  <compartment id="Yeast" spatialDimensions="3" units="volume" constant="true"/>
</listOfCompartments>
<listOfSpecies>
  <species id="Glucose" compartment="Yeast" substanceUnits="substance"</pre>
                                                                                                           13
 hasOnlySubstanceUnits="false" boundaryCondition="false" constant="false"/>
                                                                                                           14
  <species id="G6P" name="Glucose-6-phosphate" compartment="Yeast"</pre>
                                                                                                           15
  substanceUnits="substance" hasOnlySubstanceUnits="false"
                                                                                                           16
  boundaryCondition="false" constant="false"/>
  <species id="ATP" compartment="Yeast" substanceUnits="substance"</pre>
                                                                                                           18
 hasOnlySubstanceUnits="false" boundaryCondition="false" constant="false"/>
                                                                                                           19
  <species id="ADP" compartment="Yeast" substanceUnits="substance"</pre>
                                                                                                           20
 hasOnlySubstanceUnits="false" boundaryCondition="false" constant="false"/>
                                                                                                          21
  <species id="Pi" compartment="Yeast" substanceUnits="substance"</pre>
                                                                                                           22
 hasOnlySubstanceUnits="false" boundaryCondition="false" constant="false"/>
                                                                                                           23
</listOfSpecies>
                                                                                                           24
<reaction id="Hexokinase" reversible="false" fast="false">
                                                                                                           26
    listOfReactants>
                                                                                                           27
      <speciesReference id="SpeciesReference_Glucose" species="Glucose"</pre>
  stoichiometry="1" constant="true"/>
                                                                                                           29
      <speciesReference id="SpeciesReference_ATP" species="ATP"</pre>
                                                                                                           30
  stoichiometry="1" constant="true"/>
    </listOfReactants>
                                                                                                           32
    tofProducts>
                                                                                                          33
      <speciesReference id="SpeciesReference_G6P" species="G6P"</pre>
  stoichiometry="1" constant="true"/>
                                                                                                           35
      <speciesReference id="SpeciesReference_ADP" species="ADP"</pre>
                                                                                                           36
  stoichiometry="1" constant="true"/>
                                                                                                           37
    </listOfProducts>
                                                                                                           38
    listOfModifiers>
                                                                                                           39
      <modifierSpeciesReference id="ModifierSpeciesReference_G6P" species="G6P"/>
      <modifierSpeciesReference id="ModifierSpeciesReference_Pi" species="Pi"/>
                                                                                                           41
    </listOfModifiers>
                                                                                                           42
  </reaction>
                                                                                                           43
</listOfReactions>
                                                                                                           44
<layout:listOfLayouts xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"</pre>
xmlns:layout="http://www.sbml.org/sbml/level3/version1/layout/version1">
                                                                                                           46
  <layout:layout layout:id="Layout_1">
                                                                                                           47
    <layout:dimensions layout:width="400" layout:height="230"/>
    <layout:listOfCompartmentGlyphs>
                                                                                                           49
      <layout:compartmentGlyph layout:id="CompartmentGlyph_1" layout:compartment="Yeast">
                                                                                                           50
        <layout:boundingBox layout:id="bb1">
                                                                                                           51
          <layout:position layout:x="5" layout:y="5"/>
                                                                                                           52
          <layout:dimensions layout:width="390" layout:height="220"/>
                                                                                                           53
        </layout:boundingBox>
      </layout:compartmentGlyph>
                                                                                                           55
    </layout:listOfCompartmentGlyphs>
                                                                                                           56
    <layout:listOfSpeciesGlyphs>
      <layout:speciesGlyph layout:id="SpeciesGlyph_Glucose" layout:species="Glucose">
                                                                                                           58
        <layout:boundingBox layout:id="bb2">
                                                                                                           59
          <layout:position layout:x="105" layout:y="20"/>
          <layout:dimensions layout:width="130" layout:height="20"/>
                                                                                                           61
        </lavout:boundingBox>
                                                                                                           62
      </layout:speciesGlyph>
                                                                                                           63
      <layout:speciesGlyph layout:id="SpeciesGlyph_G6P" layout:species="G6P">
                                                                                                           64
        <layout:boundingBox layout:id="bb5">
                                                                                                           65
          <layout:position layout:x="50" layout:y="190"/>
```

Section 4 Examples Page 27 of 50

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```
<layout:dimensions layout:width="270" layout:height="20"/>
    </layout:boundingBox>
  </layout:speciesGlyph>
  <layout:speciesGlyph layout:id="SpeciesGlyph_ATP" layout:species="ATP">
    <layout:boundingBox layout:id="bb3">
      <layout:position layout:x="270" layout:y="70"/>
      <layout:dimensions layout:width="80" layout:height="20"/>
    </layout:boundingBox>
  </layout:speciesGlyph>
  <layout:speciesGlyph layout:id="glyph_ADP" layout:species="ADP">
    <layout:boundingBox layout:id="bb4">
      <layout:position layout:x="270" layout:y="140"/>
      <layout:dimensions layout:width="80" layout:height="20"/>
    </layout:boundingBox>
  </layout:speciesGlyph>
  <layout:speciesGlyph layout:id="SpeciesGlyph_Pi" layout:species="Pi">
    <layout:boundingBox layout:id="bb6">
      <layout:position layout:x="50" layout:y="100"/>
      <layout:dimensions layout:width="60" layout:height="20"/>
    </layout:boundingBox>
  </layout:speciesGlyph>
</layout:listOfSpeciesGlyphs>
<layout:listOfReactionGlyphs>
  <layout:reactionGlyph layout:id="glyph_Hexokinase" layout:reaction="Hexokinase">
    <layout:curve>
      <layout:listOfCurveSegments>
        <layout:curveSegment</pre>
  xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
 xsi:type="LineSegment">
          <layout:start layout:x="170" layout:y="100"/>
          <layout:end layout:x="170" layout:y="130"/>
        </layout:curveSegment>
      </layout:listOfCurveSegments>
    </layout:curve>
    <layout:listOfSpeciesReferenceGlyphs>
      <layout:speciesReferenceGlyph layout:id="SpeciesReferenceGlyph_Glucose"</pre>
layout:speciesReference="SpeciesReference_Glucose"
layout:speciesGlyph="SpeciesGlyph_Glucose"
layout:role="substrate">
        <layout:curve>
          <layout:listOfCurveSegments>
            <layout:curveSegment</pre>
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
    xsi:type="LineSegment">
              <layout:start layout:x="170" layout:y="100"/>
              <layout:end layout:x="170" layout:y="50"/>
            </layout:curveSegment>
          </layout:listOfCurveSegments>
        </layout:curve>
      </layout:speciesReferenceGlyph>
      <layout:speciesReferenceGlyph layout:id="SpeciesReferenceGlyph_ATP"</pre>
layout:speciesReference="SpeciesReference_ATP"
layout:speciesGlyph="SpeciesGlyph_ATP"
layout:role="sidesubstrate">
        <layout:curve>
          <layout:listOfCurveSegments>
            <layout:curveSegment</pre>
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
    xsi:type="CubicBezier">
              <layout:start layout:x="170" layout:y="100"/>
              <layout:end layout:x="260" layout:y="80"/>
              <layout:basePoint1 layout:x="170" layout:y="80"/>
              <layout:basePoint2 layout:x="170" layout:y="80"/>
            </layout:curveSegment>
          </layout:listOfCurveSegments>
        </layout:curve>
```

Section 4 Examples Page 28 of 50

```
</layout:speciesReferenceGlyph>
      <layout:speciesReferenceGlyph layout:id="SpeciesReferenceGlyph_G6P_1"</pre>
layout:speciesReference="SpeciesReference_G6P"
layout:speciesGlyph="SpeciesGlyph_G6P"
layout:role="product">
        <layout:curve>
          <layout:listOfCurveSegments>
            <layout:curveSegment</pre>
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
    xsi:type="LineSegment">
              <layout:start layout:x="170" layout:y="130"/>
              <layout:end layout:x="170" layout:y="180"/>
            </layout:curveSegment>
                                                                                                        13
          </layout:listOfCurveSegments>
                                                                                                        14
        </layout:curve>
                                                                                                        15
      </layout:speciesReferenceGlyph>
                                                                                                        16
      <layout:speciesReferenceGlyph layout:id="SpeciesReferenceGlyph_ADP"</pre>
layout:speciesReference="SpeciesReference_ADP"
                                                                                                        18
layout:speciesGlyph="glyph_ADP"
                                                                                                        19
layout:role="sideproduct">
                                                                                                        20
        <layout:curve>
                                                                                                        21
          <layout:listOfCurveSegments>
                                                                                                        22
            <layout:curveSegment</pre>
                                                                                                        23
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
                                                                                                        24
    xsi:type="CubicBezier">
              <layout:start layout:x="170" layout:y="130"/>
                                                                                                        26
              <layout:end layout:x="260" layout:y="150"/>
                                                                                                        27
              <layout:basePoint1 layout:x="170" layout:y="150"/>
              <layout:basePoint2 layout:x="170" layout:y="150"/>
                                                                                                        29
            </layout:curveSegment>
                                                                                                        30
          </layout:listOfCurveSegments>
                                                                                                        31
        </layout:curve>
                                                                                                        32
      </layout:speciesReferenceGlyph>
                                                                                                        33
      <layout:speciesReferenceGlyph layout:id="SpeciesReferenceGlyph_G6P_2"</pre>
                                                                                                        34
layout:speciesReference="ModifierSpeciesReference_G6P"
                                                                                                        35
layout:speciesGlyph="SpeciesGlyph_G6P"
                                                                                                        36
layout:role="inhibitor">
                                                                                                        37
        <lavout:curve>
                                                                                                        38
          <layout:listOfCurveSegments>
                                                                                                        39
            <layout:curveSegment</pre>
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
                                                                                                        41
    xsi:type="CubicBezier">
                                                                                                        42
              <layout:start layout:x="45" layout:y="200"/>
                                                                                                        43
              <layout:end layout:x="165" layout:y="120"/>
                                                                                                        44
              <layout:basePoint1 layout:x="0" layout:y="200"/>
              <layout:basePoint2 layout:x="0" layout:y="120"/>
                                                                                                        46
            </layout:curveSegment>
                                                                                                        47
          </layout:listOfCurveSegments>
        </layout:curve>
                                                                                                        49
      </layout:speciesReferenceGlyph>
                                                                                                        50
      <layout:speciesReferenceGlyph layout:id="SpeciesReferenceGlyph_PI"</pre>
                                                                                                        51
layout:speciesReference="ModifierSpeciesReference_Pi"
                                                                                                        52
layout:speciesGlyph="SpeciesGlyph_Pi"
                                                                                                        53
layout:role="activator">
        <layout:curve>
                                                                                                        55
          <layout:listOfCurveSegments>
                                                                                                        56
            <layout:curveSegment</pre>
                                                                                                        57
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
                                                                                                        58
    xsi:type="CubicBezier">
                                                                                                        59
              <layout:start layout:x="115" layout:y="110"/>
              <layout:end layout:x="165" layout:y="110"/>
                                                                                                        61
              <layout:basePoint1 layout:x="140" layout:y="110"/>
                                                                                                        62
              <layout:basePoint2 layout:x="140" layout:y="110"/>
                                                                                                        63
            </layout:curveSegment>
                                                                                                        64
          </layout:listOfCurveSegments>
                                                                                                        65
        </layout:curve>
```

Section 4 Examples Page 29 of 50

18

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```
</layout:speciesReferenceGlyph>
            </layout:listOfSpeciesReferenceGlyphs>
          </layout:reactionGlyph>
        </layout:listOfReactionGlyphs>
        <layout:listOfTextGlyphs>
          <layout:textGlyph layout:id="TextGlyph_Glucose"</pre>
      layout:originOfText="Glucose"
      layout:graphicalObject="SpeciesGlyph_Glucose">
            <layout:boundingBox layout:id="bbA">
              <layout:position layout:x="115" layout:y="20"/>
              <layout:dimensions layout:width="110" layout:height="20"/>
            </layout:boundingBox>
          </layout:textGlyph>
          <layout:textGlyph layout:id="TextGlyph_G6P"</pre>
      layout:originOfText="G6P"
      layout:graphicalObject="SpeciesGlyph_G6P">
            <layout:boundingBox layout:id="bbD">
              <layout:position layout:x="60" layout:y="190"/>
              <layout:dimensions layout:width="250" layout:height="20"/>
            </layout:boundingBox>
          </layout:textGlyph>
          <layout:textGlyph layout:id="TextGlyph_ATP"</pre>
      layout:originOfText="ATP"
      layout:graphicalObject="SpeciesGlyph_ATP">
            <layout:boundingBox layout:id="bbB">
              <layout:position layout:x="280" layout:y="70"/>
              <layout:dimensions layout:width="60" layout:height="20"/>
            </layout:boundingBox>
          </layout:textGlyph>
          <layout:textGlyph layout:id="TextGlyph_ADP"</pre>
      layout:originOfText="ADP"
      layout:graphicalObject="glyph_ADP">
            <layout:boundingBox layout:id="bbC">
              <layout:position layout:x="280" layout:y="140"/>
              <layout:dimensions layout:width="60" layout:height="20"/>
            </layout:boundingBox>
          </layout:textGlyph>
          <layout:textGlyph layout:id="TextGlyph_PI"</pre>
      layout:originOfText="Pi"
      layout:graphicalObject="SpeciesGlyph_Pi">
            <layout:boundingBox layout:id="bbE">
              <layout:position layout:x="60" layout:y="100"/>
              <layout:dimensions layout:width="40" layout:height="20"/>
            </layout:boundingBox>
          </layout:textGlyph>
        </layout:listOfTextGlyphs>
      </layout:layout>
    </layout:listOfLayouts>
  </model>
</sbml>
```

4.6 Example using SBML Level 2 Version 1

As mentioned before, the Layout package has been used since 2003 in **SBML** Level 2 documents. Wheras the previous example used the Level 3 package, here Here we repeat the previous example again using the **SBML** annotations.

In order to use the Layout package in **SBML** Level 2 documents, all that is needed is to use the Level 2 Namespace (see Section 3.1) and move the **ListOfLayouts** into the **Model annotation** element.

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2" level="2" version="1">
```

Section 4 Examples Page 30 of 50

14

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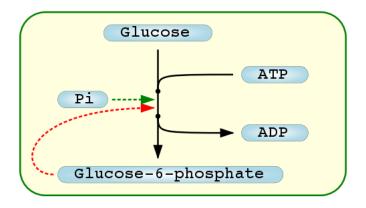


Figure 16: Another possible rendering of the example layout.

```
<model id="TestModel_with_modifiers">
  <annotation>
   <listOfLayouts xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
             xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
    <layout id="Layout_1">
      <dimensions width="400" height="230"/>
      <listOfCompartmentGlyphs>
        <compartmentGlyph id="CompartmentGlyph_1" compartment="Yeast">
           <box><box<br/>d="bb1"></br>
             <position x="5" y="5"/>
             <dimensions width="390" height="220"/>
           </boundingBox>
        </compartmentGlyph>
      </listOfCompartmentGlyphs>
      <listOfSpeciesGlyphs>
        <speciesGlyph id="SpeciesGlyph_Glucose" species="Glucose">
           <box><box<br/>id="bb2"></br>
             <position x="105" y="20"/>
             <dimensions width="130" height="20"/>
           </boundingBox>
        </speciesGlyph>
        <speciesGlyph id="SpeciesGlyph_G6P" species="G6P">
           <box><box<br/>dingBox<br/>id="bb5"></br>
             <position x="50" y="190"/>
             <dimensions width="270" height="20"/>
          </boundingBox>
        </speciesGlyph>
        <speciesGlyph id="SpeciesGlyph_ATP" species="ATP">
           <box><box<br/>dingBox<br/>id="bb3"></br>
             <position x="270" y="70"/>
             <dimensions width="80" height="20"/>
          </boundingBox>
        </speciesGlyph>
        <speciesGlyph id="glyph_ADP" species="ADP">
           <boundingBox id="bb4">
             <position x="270" y="140"/>
             <dimensions width="80" height="20"/>
          </boundingBox>
        </speciesGlyph>
        <speciesGlyph id="SpeciesGlyph_Pi" species="Pi">
           <body><br/><br/>dingBox id="bb6"></br>
             <position x="50" y="100"/>
<dimensions width="60" height="20"/>
          </boundingBox>
        </speciesGlyph>
      </listOfSpeciesGlyphs>
      <listOfReactionGlyphs>
```

Section 4 Examples Page 31 of 50

14

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```
<reactionGlyph id="glyph_Hexokinase" reaction="Hexokinase">
  <curve>
    <listOfCurveSegments>
      <curveSegment xsi:type="LineSegment">
        <start x="170" y="100"/>
        <end x="170" y="130"/>
      </curveSegment>
    </list0fCurveSegments>
  </curve>
  <listOfSpeciesReferenceGlyphs>
    <speciesReferenceGlyph id="SpeciesReferenceGlyph_Glucose"</pre>
                  speciesReference="SpeciesReference_Glucose"
                  speciesGlyph="SpeciesGlyph_Glucose" role="substrate">
      <curve>
        <listOfCurveSegments>
          <curveSegment xsi:type="LineSegment">
            <start x="170" y="100"/>
            <end x="170" y="50"/>
          </curveSegment>
        </listOfCurveSegments>
      </curve>
    </speciesReferenceGlyph>
    <speciesReferenceGlyph id="SpeciesReferenceGlyph_ATP"</pre>
                  speciesReference="SpeciesReference_ATP"
                  speciesGlyph="SpeciesGlyph_ATP" role="sidesubstrate">
      <curve>
        <listOfCurveSegments>
          <curveSegment xsi:type="CubicBezier">
            <start x="170" y="100"/>
            <end x="260" y="80"/>
            <basePoint1 x="170" y="80"/>
            <basePoint2 x="170" y="80"/>
          </curveSeament>
        </list0fCurveSegments>
      </curve>
    </speciesReferenceGlyph>
    <speciesReferenceGlyph id="SpeciesReferenceGlyph_G6P_1"</pre>
                    speciesReference="SpeciesReference_G6P"
                    speciesGlyph="SpeciesGlyph_G6P" role="product">
      <curve>
        <listOfCurveSegments>
          <curveSegment xsi:type="LineSegment">
            <start x="170" y="130"/>
            <end x="170" y="180"/>
          </curveSegment>
        </list0fCurveSegments>
      </curve>
    </speciesReferenceGlyph>
    <speciesReferenceGlyph id="SpeciesReferenceGlyph_ADP"</pre>
                  speciesReference="SpeciesReference_ADP"
                  speciesGlyph="glyph_ADP" role="sideproduct">
      <curve>
        <listOfCurveSegments>
          <curveSegment xsi:type="CubicBezier">
            <start x="170" y="130"/>
            <end x="260" y="150"/>
            <basePoint1 x="170" y="150"/>
            <basePoint2 x="170" y="150"/>
          </curveSegment>
        <le></listOfCurveSegments>
      </curve>
    </speciesReferenceGlvph>
    <speciesReferenceGlyph id="SpeciesReferenceGlyph_G6P_2"</pre>
            speciesReference="ModifierSpeciesReference_G6P"
            speciesGlyph="SpeciesGlyph_G6P" role="inhibitor">
      <curve>
```

Section 4 Examples Page 32 of 50

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```
<listOfCurveSegments>
                <curveSegment xsi:type="CubicBezier">
                  <start x="45" y="200"/>
                  <end x="165" y="120"/>
                  <basePoint1 x="0" y="200"/>
                  <basePoint2 x="0" y="120"/>
                </curveSegment>
              </list0fCurveSegments>
           </curve>
         </speciesReferenceGlyph>
         <speciesReferenceGlyph id="SpeciesReferenceGlyph_PI"</pre>
                speciesReference="ModifierSpeciesReference_Pi"
                speciesGlyph="SpeciesGlyph_Pi" role="activator">
              <listOfCurveSegments>
                <curveSegment xsi:type="CubicBezier">
                  <start x="115" y="110"/>
                  <end x="165" y="110"/>
                  <basePoint1 x="140" y="110"/>
<basePoint2 x="140" y="110"/>
                </curveSegment>
              </list0fCurveSegments>
            </curve>
         </speciesReferenceGlyph>
       </listOfSpeciesReferenceGlyphs>
     </reactionGlyph>
   </listOfReactionGlyphs>
   <listOfTextGlyphs>
     <textGlyph id="TextGlyph_Glucose" graphicalObject="SpeciesGlyph_Glucose"</pre>
                 originOfText="Glucose">
       <box><box<br/>dingBox<br/>id="bbA"></br>
         <position x="115" y="20"/>
         <dimensions width="110" height="20"/>
       </boundingBox>
     </textGlyph>
     <textGlyph id="TextGlyph_G6P" graphicalObject="SpeciesGlyph_G6P"</pre>
                 originOfText="G6P">
       <body><br/><boundingBox id="bbD"></br>
         <position x="60" y="190"/>
         <dimensions width="250" height="20"/>
       </boundingBox>
     </textGlyph>
     <textGlyph id="TextGlyph_ATP" graphicalObject="SpeciesGlyph_ATP"</pre>
                 originOfText="ATP">
       <box><box<br/>id="bbB"></br>
         <position x="280" y="70"/>
         <dimensions width="60" height="20"/>
       </boundingBox>
     </textGlyph>
     <textGlyph id="TextGlyph_ADP" graphicalObject="glyph_ADP"</pre>
                 originOfText="ADP">
       <box><box<br/>id="bbC"></br>
         <position x="280" y="140"/>
         <dimensions width="60" height="20"/>
       </boundingBox>
     </textGlyph>
     <textGlyph id="TextGlyph_PI" graphicalObject="SpeciesGlyph_Pi"</pre>
                 originOfText="Pi">
       <box><box<br/>dingBox<br/>id="bbE"></br>
         <position x="60" y="100"/>
         <dimensions width="40" height="20"/>
       </boundingBox>
     </textGlyph>
   </listOfTextGlyphs>
  </layout>
</list0fLayouts>
```

Section 4 Examples Page 33 of 50

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```
</annotation>
    <listOfCompartments>
      <compartment id="Yeast"/>
    </listOfCompartments>
    Species>
      <species id="Glucose" compartment="Yeast"/>
      <species id="G6P" name="Glucose-6-phosphate" compartment="Yeast"/>
      <species id="ATP" compartment="Yeast"/>
      <species id="ADP" compartment="Yeast"</pre>
      <species id="Pi" compartment="Yeast"/>
    </listOfSpecies>
    listOfReactions>
      <reaction id="Hexokinase" reversible="false">
        <listOfReactants>
          <speciesReference species="Glucose">
            <annotation>
              <layoutId xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
                        id="SpeciesReference_Glucose"/>
            </annotation>
          </speciesReference>
          <speciesReference species="ATP">
            <annotation>
              <layoutId xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
                        id="SpeciesReference_ATP"/>
            </annotation>
          </speciesReference>
        </list0fReactants>
        <speciesReference species="G6P">
            <annotation>
              <layoutId xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
                        id="SpeciesReference_G6P"/>
            </annotation>
          </speciesReference>
          <speciesReference species="ADP">
            <annotation>
              <layoutId xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
                        id="SpeciesReference_ADP"/>
            </annotation>
          </speciesReference>
        </list0fProducts>
        <listOfModifiers>
          <modifierSpeciesReference species="G6P">
            <annotation>
              <layoutId xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
                        id="ModifierSpeciesReference_G6P"/>
            </annotation>
          </modifierSpeciesReference>
          <modifierSpeciesReference species="Pi">
            <annotation>
              <layoutId xmlns="http://projects.eml.org/bcb/sbml/level2"</pre>
                        id="ModifierSpeciesReference_Pi"/>
            </annotation>
          </modifierSpeciesReference>
        </listOfModifiers>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

4.7 Example using the GeneralGlyph

Here a small complete example that shows how to draw a basic influence diagram, where Node0 negatively influences Node1.

Section 4 Examples Page 34 of 50

18

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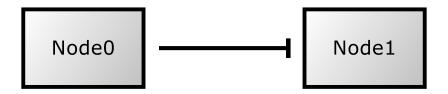


Figure 17: One possible rendering of an influence diagram.

In this example we have a simple SBML model that contains two species, Node0 and Node1. For both of them there are species glyph elements and associated Text labels. A **GeneralGlyph** then represents the influence.

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level3/version1/core"</pre>
              xmlns:layout="http://www.sbml.org/sbml/level3/version1/layout/version1"
         level="3" version="1" layout:required="false" >
    <model id="GeneralGlyphExample" >
    <listOfCompartments>
              <compartment id="compartment"</pre>
         spatialDimensions="3" size="1" constant="true"/>
         </listOfCompartments>
    tofSpecies>
              <species sboTerm="SBO:0000395" id="Node0"</pre>
              \verb|compartment| = \verb|compartment| = \verb|initialConcentration| = \verb|volume| = | oultiment| = oultiment| =
             hasOnlySubstanceUnits="false" boundaryCondition="false" constant="false"/>
              <species sboTerm="SBO:0000395" id="Node1"</pre>
              compartment="compartment" initialConcentration="0"
             hasOnlySubstanceUnits="false" boundaryCondition="false" constant="false"/>
         </listOfSpecies>
         <layout:listOfLayouts</pre>
           xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
           xmlns:layout="http://www.sbml.org/sbml/level3/version1/layout/version1">
              <layout:layout layout:id="example">
                  <layout:dimensions layout:width="239.037328720093" layout:height="76.5"/>
         <layout:listOfSpeciesGlyphs>
                       <layout:speciesGlyph layout:id="sGlyph_0" layout:species="Node0" >
                            <layout:boundingBox>
                                <layout:position layout:x="16" layout:y="18"/>
                                <layout:dimensions layout:width="62" layout:height="40"/>
                            </layout:boundingBox>
                       </layout:speciesGlyph>
                       <layout:speciesGlyph layout:id="sGlyph_1" layout:species="Node1" >
                            <layout:boundingBox>
                                <layout:position layout:x="161" layout:y="18"/>
                                <layout:dimensions layout:width="62" layout:height="40"/>
                            </layout:boundingBox>
                       </layout:speciesGlyph>
                  </layout:listOfSpeciesGlyphs>
         <layout:listOfAdditionalGraphicalObjects>
                       <layout:generalGlyph layout:id="rGlyph_0" reference="sGlyph_0">
                  <!-- unused bounding box -->
                            <layout:boundingBox>
                                <layout:position layout:x="0" layout:y="0"/>
                                <layout:dimensions layout:width="0" layout:height="0"/>
                            </layout:boundingBox>
                            <layout:listOfReferenceGlyphs>
```

Section 4 Examples Page 35 of 50

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```
<!-- reference glyph representing the inhibited species -->
              <layout:referenceGlyph</pre>
            layout:id="SpeciesReference_J0_0"
          layout:reference="Node1"
          layout:glyph="sGlyph_1"
          layout:role="inhibitor">
                <layout:curve>
                  <layout:listOfCurveSegments>
                    <layout:curveSegment</pre>
            xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
            xsi:type="LineSegment">
                      <layout:start layout:x="86" layout:y="38"/>
                      <layout:end layout:x="153" layout:y="38"/>
                    </layout:curveSegment>
                   </layout:listOfCurveSegments>
                </layout:curve>
              </layout:referenceGlyph>
            </layout:listOfReferenceGlyphs>
          </layout:generalGlyph>
        </layout:listOfAdditionalGraphicalObjects>
    <layout:listOfTextGlyphs>
          <layout:textGlyph layout:id="tGlyph_0" layout:text="Node0"</pre>
           layout:graphicalObject="sGlyph_0">
            <layout:boundingBox>
              <layout:position layout:x="16" layout:y="18"/>
              <layout:dimensions layout:width="62" layout:height="40"/>
            </layout:boundingBox>
          </layout:textGlyph>
          <layout:textGlyph layout:id="tGlyph_1" layout:text="Node1"</pre>
                        layout:graphicalObject="sGlyph_1">
            <layout:boundingBox>
              <layout:position layout:x="161" layout:y="18"/>
              <layout:dimensions layout:width="62" layout:height="40"/>
            </layout:boundingBox>
          </layout:textGlyph>
        </layout:listOfTextGlyphs>
      </layout:layout>
    </layout:listOfLayouts>
  </model>
</sbml>
```

Section 4 Examples Page 36 of 50

A Validation of SBML documents

A.1 Validation and consistency rules

This section summarizes all the conditions that must (or in some cases, at least *should*) be true of an SBML Level 3 Version 1 model that uses the Layout package. We use the same conventions as are used in the SBML Level 3 Version 1 Core specification document. In particular, there are different degrees of rule strictness. Formally, the differences are expressed in the statement of a rule: either a rule states that a condition *must* be true, or a rule states that it *should* be true. Rules of the former kind are strict SBML validation rules—a model encoded in SBML must conform to all of them in order to be considered valid. Rules of the latter kind are consistency rules. To help highlight these differences, we use the following three symbols next to the rule numbers:

- ✓ A checked box indicates a *requirement* for SBML conformance. If a model does not follow this rule, it does not conform to the Layout specification. (Mnemonic intention behind the choice of symbol: "This must be checked.")
- A triangle indicates a *recommendation* for model consistency. If a model does not follow this rule, it is not considered strictly invalid as far as the Layout specification is concerned; however, it indicates that the model contains a physical or conceptual inconsistency. (Mnemonic intention behind the choice of symbol: "This is a cause for warning.")
- ★ A star indicates a strong recommendation for good modeling practice. This rule is not strictly a matter of SBML encoding, but the recommendation comes from logical reasoning. As in the previous case, if a model does not follow this rule, it is not strictly considered an invalid SBML encoding. (Mnemonic intention behind the choice of symbol: "You're a star if you heed this.")

The validation rules listed in the following subsections are all stated or implied in the rest of this specification document. They are enumerated here for convenience. Unless explicitly stated, all validation rules concern objects and attributes specifically defined in the Layout package.

For convenience and brevity, we use the shorthand "layout:x" to stand for an attribute or element name x in the namespace for the Layout package, using the namespace prefix layout. In reality, the prefix string may be different from the literal "layout" used here (and indeed, it can be any valid XML namespace prefix that the modeler or software chooses). We use "layout:x" because it is shorter than to write a full explanation everywhere we refer to an attribute or element in the Layout package namespace.

General rules about this package

layout-10101 ☑ To conform to the Layout package specification for SBML Level 3 Version 1, an SBML document must declare the use of the following XML Namespace:

"http://www.sbml.org/sbml/level3/version1/layout/version1".

(References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.1 on page 7.)

Wherever they appear in an SBML document, elements and attributes from the Layout package must be declared either implicitly or explicitly to be in the XML namespace "http://www.sbml.org/sbml/level3/version1/layout/version1".

(References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.1 on page 7.)

General rules about identifiers

layout-10301

✓ (Extends validation rule #10301 in the SBML Level 3 Version 1 Core specification.) Within a Model the values of the attributes id and layout:id on every instance of the following classes of objects must be unique across the set of all id and layout:id attribute values of all such objects in a model: the Model itself, plus all contained FunctionDefinition, Compartment, Species, Reaction, SpeciesReference, ModifierSpeciesReference, Event, and Parame-

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ter objects, plus the BoundingBox, CompartmentGlyph, GeneralGlyph, GraphicalObject, Layout, SpeciesGlyph, SpeciesReferenceGlyph, ReactionGlyph, ReferenceGlyph, and TextGlyph objects defined by the Layout package. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.3 on page 8.)

Rules for the extended SBML class

- layout-20101 ✓ In all SBML documents using the Layout package, the SBML object must include a value for the attribute layout:required attribute. (References: SBML Level 3 Version 1 Core, Section 4.1.2.)
- layout-20102

 ✓ The value of attribute layout:required on the SBML object must be of the data type boolean. (References: SBML Level 3 Version 1 Core, Section 4.1.2.)
- layout-20103

 ✓ The value of attribute layout:required on the SBML object must be set to "false". (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.1 on page 7.)

Rules for extended Model object

- layout-20201 ✓ There may be at most one instance of ListOfLayouts element within a Model object using Layout. No other elements from the Layout package are allowed. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.5 on page 12.)
- layout-20202 ☑ The ListOfLayouts within a Model object is optional, but if present, these it object must not be empty. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.5 on page 12.)
- layout-20203
 ✓ Apart from the general notes and annotation subobjects permitted on all SBML objects, a

 ListOfLayouts container object may only contain Layout objects. (References: SBML Level 3

 Package Specification for Layout, Version 1, Section 3.5 on page 12.)
- layout-20204 ✓ A ListOfLayouts object may have the optional metaid and sboTerm defined by SBML Level 3 Core. No other attributes from the SBML Level 3 Core namespace or the Layout namespace are permitted on a ListOfLayouts object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.5 on page 12.)

Rules for the Layout object

- layout-20301
 ✓ A Layout object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a Layout. (References: SBML Level 3 Version 1 Core, Section 3.2.)
- layout-20302
 ✓ A Layout object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a Layout. (References: SBML Level 3 Version 1 Core, Section 3.2.)
- Iayout-20303

 ✓ There may be at most one instance of each of the following kinds of objects within a Layout object: Dimensions, ListOfCompartmentGlyphs, ListOfSpeciesGlyphs, ListOfReactionGlyphs, ListOfTextGlyphs, ListOfAdditionalGraphicalObjects. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.6 on page 12.)
- Iayout-20304 ✓ The various ListOf— subobjects within a Layout object are optional, but if present, these container object must not be empty. Specifically, if any of the following classes of objects are present on the Layout, it must not be empty: ListOfCompartmentGlyphs, ListOfSpecies-Glyphs, ListOfReactionGlyphs, ListOfTextGlyphs, ListOfAdditionalGraphicalObjects. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.6 on page 12.)

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layout-20305
✓ A Layout object must have the required attribute layout:id and may have the optional attribute layout:name. No other attributes from the SBML Level 3 Layout namespace are permitted on a Layout object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.6 on page 12.) layout-20306

✓ The attribute layout:name of a Layout must be of the data type string. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.6 on page 12.) A ListOfCompartmentGlyphs object may have the optional metaid and sboTerm defined by SBML Level 3 Core. No other attributes from the SBML Level 3 Core namespace or the Layout namespace are permitted on a **ListOfCompartmentGlyphs** object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.6 on page 13.) layout-20308

✓ Apart from the general notes and annotation subobjects permitted on all SBML objects, a ListOfCompartmentGlyphs container object may only contain CompartmentGlyph objects. 12 (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.6 on page 13.) A ListOfSpeciesGlyphs object may have the optional metaid and sboTerm defined by SBML Level 3 Core. No other attributes from the SBML Level 3 Core namespace or the Layout namespace are permitted on a ListOfSpeciesGlyphs object. (References: SBML Level 3 Pack-16 age Specification for Layout, Version 1, Section 3.6 on page 14.) Apart from the general notes and annotation subobjects permitted on all SBML objects, a layout-20310 ✓ ListOfSpeciesGlyphs container object may only contain SpeciesGlyph objects. (References: 19 SBML Level 3 Package Specification for Layout, Version 1, Section 3.6 on page 14.) 20 layout-20311 ✓ A ListOfReactionGlyphs object may have the optional metaid and sboTerm defined by SBML Level 3 Core. No other attributes from the SBML Level 3 Core namespace or the Layout 22 namespace are permitted on a ListOfReactionGlyphs object. (References: SBML Level 3 Pack-23 age Specification for Layout, Version 1, Section 3.6 on page 14.) Apart from the general notes and annotation subobjects permitted on all SBML objects, a 25 ListOfReactionGlyphs container object may only contain ReactionGlyph objects. (References: 26 SBML Level 3 Package Specification for Layout, Version 1, Section 3.6 on page 14.) layout-20313 A ListOfAdditionalGraphicalObjects object may have the optional metaid and sboTerm de-28 fined by SBML Level 3 Core. No other attributes from the SBML Level 3 Core namespace or the Layout namespace are permitted on a ListOfAdditionalGraphicalObjects object. (Refer-30 ences: SBML Level 3 Package Specification for Layout, Version 1, Section 3.6 on page 14.) layout-20314 **☑** Apart from the general notes and annotation subobjects permitted on all SBML objects, a ListOfAdditionalGraphicalObjects container object may only contain GeneralGlyph and GraphicalObject objects. (References: SBML Level 3 Package Specification for Layout, Ver-34 sion 1, Section 3.6 on page 14.) 35 A Layout object must contain exactly one **Dimensions** object. (References: SBML Level 3 Packlayout-20315 🗹 age Specification for Layout, Version 1, Section 3.6 on page 12.) Rules for the GraphicalObject class layout-20401

A GraphicalObject object may have the optional SBML Level 3 Core subobjects for notes and 39 annotations. No other elements from the SBML Level 3 Core namespace are permitted on a **GraphicalObject**. (References: SBML Level 3 Version 1 Core, Section 3.2.) A GraphicalObject object may have the optional SBML Level 3 Core attributes metaid and

sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a

GraphicalObject. (References: SBML Level 3 Version 1 Core, Section 3.2.)

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There may be at most one instance of an **BoundingBox** object on a **GraphicalObject**, no other elements from the Layout namespace are permitted on a GraphicalObject. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) layout-20404 V A GraphicalObject object must have the required attribute layout:id and may have the optional attribute layout:metaidRef. No other attributes from the SBML Level 3 Layout namespace are permitted on a GraphicalObject object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) The attribute layout:metaidRef of a GraphicalObject must be of the data type IDREF. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) layout-20406

✓ The value of a layout:metaidRef of a GraphicalObject must be of the metaid of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) layout-20407

✓ A Graphical Object object must contain exactly one Bounding Box object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) Rules for the CompartmentGlyph object layout-20501
✓ A CompartmentGlyph object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a CompartmentGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.) layout-20502

✓ A CompartmentGlyph object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a CompartmentGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.) layout-20503

✓ There may be at most one instance of an **BoundingBox** object on a **CompartmentGlyph**, no other elements from the Layout namespace are permitted on a CompartmentGlyph. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.8 on page 15.) layout-20504

✓ A CompartmentGlyph object must have the required attribute layout:id and may have the optional attributes layout:metaidRef, layout:compartment or layout:order. No other attributes from the SBML Level 3 Layout namespace are permitted on a CompartmentGlyph object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.8 on page 15.) layout-20505

✓ The attribute layout:metaidRef of a CompartmentGlyph must be of the data type IDREF. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) layout-20506

✓ The value of a layout: metaidRef of a CompartmentGlyph must be of the metaid of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) layout-20507

✓ The attribute layout: compartment of a CompartmentGlyph must be of the data type SIdRef. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.8 on page 15.) layout-20508 V The value of a layout:compartment of a CompartmentGlyph must be of the id of an existing Compartment in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.8 on page 15.) layout-20509 V If both attributes layout:compartment and layout:metaidRef are specified on a **Compartment Glyph** they have to reference the same **Compartment** of the **Model**. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.8 on page 15.) The attribute layout: order of a CompartmentGlyph must be of the data type double. (Ref-

erences: SBML Level 3 Package Specification for Layout, Version 1, Section 3.8 on page 15.)

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Rules for the SpeciesGlyph object

- layout-20601 ✓ A SpeciesGlyph object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a SpeciesGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.)
- layout-20602 ✓ A SpeciesGlyph object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a SpeciesGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.)
- layout-20603 ✓ There may be at most one instance of an BoundingBox object on a SpeciesGlyph, no other elements from the Layout namespace are permitted on a SpeciesGlyph. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.9 on page 16.)
- layout-20604 ✓ A SpeciesGlyph object must have the required attribute layout:id and may have the optional attribute layout:metaidRef or layout:species. No other attributes from the SBML Level 3 Layout namespace are permitted on a SpeciesGlyph object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.9 on page 16.)
- layout-20605

 ✓ The attribute layout:metaidRef of a SpeciesGlyph must be of the data type IDREF. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.)
- layout-20606

 ✓ The value of a layout:metaidRef of a SpeciesGlyph must be of the metaid of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.)
- layout-20607

 The attribute layout: species of a SpeciesGlyph must be of the data type SIdRef. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.9 on page 16.)
- layout-20608 ✓ The value of a layout: species of a SpeciesGlyph must be of the id of an existing Species in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.9 on page 16.)
- layout-20609
 ✓ If both attributes layout: species and layout: metaidRef are specified on a SpeciesGlyph they have to reference the same Species of the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.9 on page 16.)

Rules for the ReactionGlyph object

- layout-20701 ✓ A ReactionGlyph object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a ReactionGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.)
- layout-20702 ✓ A ReactionGlyph object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a ReactionGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.)
- There may be at most one instance of each of the following kinds of objects within a **Reaction-Glyph** object: **BoundingBox**, **Curve**, **ListOfSpeciesReferenceGlyphs**, no other elements from the Layout namespace are permitted on a **ReactionGlyph**. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10 on page 16.)
- layout-20704 ✓ A ReactionGlyph object must have the required attribute layout:id and may have the optional attribute layout:metaidRef or layout:reaction. No other attributes from the SBML Level 3 Layout namespace are permitted on a ReactionGlyph object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10 on page 16.)

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layout-20705 ✓ The attribute layout:metaidRef of a ReactionGlyph must be of the data type IDREF. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) The value of a layout:metaidRef of a ReactionGlyph must be of the metaid of an existing layout-20706

✓ element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) layout-20707

✓ The attribute layout:reaction of a ReactionGlyph must be of the data type SIdRef. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10 on page 16.) The value of a layout:reaction of a ReactionGlyph must be of the id of an existing Reaction in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10 on page 16.) If both attributes layout:reaction and layout:metaidRef are specified on a Reaction-Glyph they have to reference the same Reaction of the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10 on page 16.) Apart from the general notes and annotation subobjects permitted on all SBML objects, a layout-20710 🗹 ListOfSpeciesReferenceGlyphs container object may only contain SpeciesReferenceGlyph objects. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10 on page 16.) layout-20711 ✓ A ListOfSpeciesReferenceGlyphs object may have the optional metaid and sboTerm defined by SBML Level 3 Core. No other attributes from the SBML Level 3 Core namespace or the Layout namespace are permitted on a ListOfSpeciesReferenceGlyphs object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10 on page 16.) Rules for the GeneralGlyph object layout-20801
✓ A GeneralGlyph object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a **GeneralGlyph.** (References: SBML Level 3 Version 1 Core, Section 3.2.) layout-20802

✓ A GeneralGlyph object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a GeneralGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.) There may be at most one instance of each of the following kinds of objects within a General-Glyph object: BoundingBox, Curve, ListOfReferenceGlyphs and ListOfSubGlyphs, no other elements from the Layout namespace are permitted on a GeneralGlyph. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11 on page 18.) layout-20804

✓ A GeneralGlyph object must have the required attribute layout:id and may have the optional attribute layout:metaidRef or layout:reference. No other attributes from the SBML Level 3 Layout namespace are permitted on a **GeneralGlyph** object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11 on page 18.) layout-20805 V The attribute layout:metaidRef of a GeneralGlyph must be of the data type IDREF. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) layout-20806 V The value of a layout:metaidRef of a GeneralGlyph must be of the metaid of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.)

The attribute layout:reference of a GeneralGlyph must be of the data type SIdRef. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11 on page 18.)

layout-20807

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layout-20708 ✓	The value of a layout:reference of a GeneralGlyph must be of the id of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11 on page 18.)	1 2 3
layout-20809 ✓	If both attributes layout:reference and layout:metaidRef are specified on a General-	4
•	Glyph they have to reference the same element of the Model. (References: SBML Level 3	5
	Package Specification for Layout, Version 1, Section 3.11 on page 18.)	6
layout-20810	Apart from the general notes and annotation subobjects permitted on all SBML objects, a	7
	ListOfReferenceGlyphs container object may only contain ReferenceGlyph objects. (Refer-	8
	ences: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11 on page 18.)	9
layout-20811	A ListOfReferenceGlyphs object may have the optional metaid and sboTerm defined by SBML	10
	Level 3 Core. No other attributes from the SBML Level 3 Core namespace or the Layout	11
	namespace are permitted on a ListOfReferenceGlyphs object. (References: SBML Level 3	12
	Package Specification for Layout, Version 1, Section 3.11 on page 18.)	13
layout-20812	Apart from the general notes and annotation subobjects permitted on all SBML objects, a	14
	ListOfSubGlyphs container object may only contain CompartmentGlyph, SpeciesGlyph,	15
	ReactionGlyph, GeneralGlyph, GraphicalObject, TextGlyph,	16
	SpeciesReferenceGlyph and ReferenceGlyph objects. (References: SBML Level 3 Package	17
	Specification for Layout, Version 1, Section 3.11 on page 18.)	18
layout-20813 ✓	A ListOfSubGlyphs object may have the optional metaid and	19
	sboTerm defined by SBML Level 3 Core. No other attributes from the SBML Level 3 Core	20
	namespace or the Layout namespace are permitted on a ListOfSubGlyphs object.	21
	(References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11 on page 18.)	22
Rules for the Tex	ctGlyph object	23
layout-20901	A TextGlyph object may have the optional SBML Level 3 Core subobjects for notes and an-	24
	notations. No other elements from the SBML Level 3 Core namespace are permitted on a	25
	TextGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.)	26
layout-20902	A TextGlyph object may have the optional SBML Level 3 Core attributes metaid and sboTerm.	27
	No other attributes from the SBML Level 3 Core namespace are permitted on a TextGlyph.	28
	(References: SBML Level 3 Version 1 Core, Section 3.2.)	29
layout-20903 ✓	A TextGlyph object must contain exactly one BoundingBox object, no other elements from	30
	the Layout namespace are permitted on a TextGlyph. (References: SBML Level 3 Package	31
	Specification for Layout, Version 1, Section 3.12 on page 20.)	32
layout-20904 ✓	A TextGlyph object must have the required attribute layout:id and may have the optional	33
•	attributes layout:metaidRef, layout:graphicalObject, layout:text and	34
	layout:originOfText. No other attributes from the SBML Level 3 Layout namespace are	35
	permitted on a TextGlyph object. (References: SBML Level 3 Package Specification for Layout,	36
	Version 1, Section 3.12 on page 20.)	37
layout-20905 ✓	The attribute layout:metaidRef of a TextGlyph must be of the data type IDREF. (References:	38
-	SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.)	39
Invest 00000 -	The relice of a largest material De Code Tout Ohn to see the of the second of the seco	
layout-20906 ✓	The value of a layout:metaidRef of a TextGlyph must be of the metaid of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1,	40
	Section 3.7 on page 14.)	41
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layout-20907
✓ The attribute layout:originOfText of a TextGlyph must be of the data type SIdRef. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.12 on page 20.) layout-20908

✓ The value of a layout:originOfText of a TextGlyph must be of the id of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.12 on page 20.) If both attributes layout:originOfText and layout:metaidRef are specified on a Text-Glyph they have to reference the same element of the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.12 on page 20.) layout-20910 ✓ The attribute layout: graphicalObject of a TextGlyph must be of the data type SIdRef. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.12 on page 20.) layout-20911 ✓ The value of a layout:graphicalObject of a TextGlyph must be of the id of an existing GraphicalObject (or derived) element in the Layout. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.12 on page 20.) layout-20912 ✓ The attribute layout:text of a TextGlyph must be of the data type string. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.12 on page 20.) Rules for the SpeciesReferenceGlyph object layout-21001 ✓ A SpeciesReferenceGlyph object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a SpeciesReferenceGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.) A SpeciesReferenceGlyph object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a SpeciesReferenceGlyph. (References: SBML Level 3 Version 1 Core, Section 3.2.) A SpeciesReferenceGlyph may have at most one instance of a BoundingBox and Curve object, no other elements from the Layout namespace are permitted on a SpeciesReference-Glyph. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10.1 on page 17.) layout-21004 🗹 A Species Reference Glyph object must have the required attributes layout: id and layout: speciesGlyph and may have the optional attribute layout:metaidRef or layout:species-Reference and layout:role. No other attributes from the SBML Level 3 Layout namespace are permitted on a SpeciesReferenceGlyph object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10.1 on page 17.) The attribute layout:metaidRef of a SpeciesReferenceGlyph must be of the data type IDREF. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) layout-21006

✓ The value of a layout:metaidRef of a SpeciesReferenceGlyph must be of the metaid of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) The attribute layout: speciesReference of a SpeciesReferenceGlyph must be of the data type SIdRef. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10.1 on page 17.) layout-21008

✓ The value of a layout: speciesReference of a SpeciesReferenceGlyph must be of the id of an existing **SpeciesReference** in the **Model**. (References: SBML Level 3 Package Specification

for Layout, Version 1, Section 3.10.1 on page 17.)

layout-21009 ✓	If both attributes layout: speciesReference and layout:metaidRef are specified on a SpeciesReferenceGlyph they have to reference the same SpeciesReference of the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10.1 on page 17.)	1 2 3
layout-21010 ✓	The attribute layout:speciesGlyph of a SpeciesReferenceGlyph must be of the data type SIdRef.	4 5
	(References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10.1 on page 17.)	6 7
layout-21011 ✓	The value of a layout:speciesGlyph of a SpeciesReferenceGlyph must be of the id of an existing SpeciesGlyph in the Layout. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10.1 on page 17.)	8 9 10
layout-21012 ✓	The attribute layout:role of a SpeciesReferenceGlyph must be of the data type Species-ReferenceRole. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10.1 on page 17.)	11 12 13
layout-21013	The value of a layout:role of a SpeciesReferenceGlyph must be one of: substrate, product, sidesubstrate, sideproduct, modifier, activator, inhibitor or undefined. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.10.1 on page 17.)	14 15 16
Rules for the Rei	ferenceGlyph object	17
layout-21101 ☑	A ReferenceGlyph object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a ReferenceGlyph . (References: SBML Level 3 Version 1 Core, Section 3.2.)	18 19 20
layout-21102 ✓	A ReferenceGlyph object may have the optional SBML Level 3 Core attributes metaid and sboTerm . No other attributes from the SBML Level 3 Core namespace are permitted on a ReferenceGlyph . (References: SBML Level 3 Version 1 Core, Section 3.2.)	21 22 23
layout-21103 ✓	There may be at most one instance of an BoundingBox and Curve object on a Reference-Glyph , no other elements from the Layout namespace are permitted on a ReferenceGlyph . (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11.1 on page 20.)	24 25 26 27
layout-21104	A ReferenceGlyph object must have the required attributes layout:id and layout:glyph and may have the optional attribute layout:metaidRef or layout:reference and layout:role. No other attributes from the SBML Level 3 Layout namespace are permitted on a ReferenceGlyph object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11.1 on page 20.)	28 29 30 31
layout-21105 ✓	The attribute layout:metaidRef of a ReferenceGlyph must be of the data type IDREF. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.)	33 34
layout-21106 ✓	The value of a layout:metaidRef of a ReferenceGlyph must be of the metaid of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.)	35 36 37
layout-21107 ☑	The attribute layout:reference of a ReferenceGlyph must be of the data type SIdRef. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11.1 on page 20.)	38
layout-21108 ✓	The value of a layout:reference of a ReferenceGlyph must be of the id of an existing element in the Model. (References: SBML Level 3 Package Specification for Layout, Version 1,	40 41

Section 3.11.1 on page 20.)

layout: reference and layout: metaidRef are specified on a Reference-Glyph they have to reference the same element of the Model. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11.1 on page 20.) layout-21110 **☑** The attribute layout:glyph of a ReferenceGlyph must be of the data type SIdRef. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11.1 on page 20.) The value of a layout: glyph of a ReferenceGlyph must be of the id of an existing Graphical-Object (or derived) element in the Layout. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11.1 on page 20.) The attribute layout:role of a ReferenceGlyph must be of the data type string. (Referlayout-21112 ences: SBML Level 3 Package Specification for Layout, Version 1, Section 3.11.1 on page 20.) Rules for the Point class layout-21201
✓ A Point object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core or Layout namespace are permitted on a Point. (References: SBML Level 3 Version 1 Core, Section 3.2.) layout-21202
✓ A Point object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a Point . (References: SBML Level 3 Version 1 Core, Section 3.2.) A **Point** object must have the required attributes **layout:** x and **layout:** y and may have the optional attributes layout:id and layout:z. No other attributes from the SBML Level 3 Layout namespace are permitted on a Point object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.1 on page 8.) The attributes layout:x, layout:y and layout:z of a Point element must be of the data layout-21204 🗹 type double. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.1 on page 8.) Rules for the Dimensions class layout-21201
✓ A Dimensions object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core or Layout namespace are permitted on a **Dimensions**. (References: SBML Level 3 Version 1 Core, Section 3.2.) A Dimensions object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a **Dimensions.** (References: SBML Level 3 Version 1 Core, Section 3.2.) layout-21203 A Dimensions object must have the required attributes layout:width and layout:height and may have the optional attributes layout:id and layout:depth. No other attributes from the SBML Level 3 Layout namespace are permitted on a Dimensions object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.2 on page 8.) layout-21204 🗹 The attributes layout:width, layout:height and layout:depth of a Dimensions object must be of the data type double. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.2 on page 8.)

Rules for the BoundingBox class

layout-21301 ☑ A BoundingBox object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a BoundingBox. (References: SBML Level 3 Version 1 Core, Section 3.2.)

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layout-21302

✓ A BoundingBox object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a **BoundingBox**. (References: SBML Level 3 Version 1 Core, Section 3.2.) There must be exactly one instance of a Point and a Dimensions object on a BoundingBox, no layout-21303 🗹 other elements from the Layout namespace are permitted on a **BoundingBox**. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.3 on page 9.) layout-21304 ✓ A **BoundingBox** object must have the optional attribute **layout:id**. No other attributes from the SBML Level 3 Layout namespace are permitted on a **BoundingBox** object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.3 on page 9.) layout-21305 ✓ If the layout: z attribute of a Point element on a BoundingBox is not specified, the attribute layout: depth of its Dimensions object must also not be specified. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.7 on page 14.) Rules for the Curve class layout-21401 ✓ A Curve object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a Curve. (References: SBML Level 3 Version 1 Core, Section 3.2.) layout-21402 ✓ A Curve object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a Curve. (References: SBML Level 3 Version 1 Core, Section 3.2.) layout-21403

✓ There must be exactly one instance of a **ListOfCurveSegments** object on a **Curve**, no other elements from the Layout namespace are permitted on a Curve. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.4 on page 9.) layout-21407
✓ A ListOfCurveSegments object may have the optional metaid and sboTerm defined by SBML Level 3 Core. No other attributes from the SBML Level 3 Core namespace or the Layout namespace are permitted on a ListOfCurveSegments object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.4 on page 10.) Apart from the general notes and annotation subobjects permitted on all SBML objects, a layout-21408 🗹 ListOfCurveSegments container object may only contain LineSegment and CubicBezier objects. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.4 on page 10.) The ListOfCurveSegments container object may not be emtpy. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.4 on page 10.) Rules for the LineSegment class layout-21501 ✓ A LineSegment object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a **LineSegment**. (References: SBML Level 3 Version 1 Core, Section 3.2.) layout-21502 🗹 A LineSegment object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespace are permitted on a

LineSegment. (References: SBML Level 3 Version 1 Core, Section 3.2.)

Specification for Layout, Version 1, Section 3.4.5 on page 10.)

A LineSegment must specify the two Point elements start and end. No other elements from

the Layout namespace are permitted on a LineSegment. (References: SBML Level 3 Package

layout-21503

layout-21504 ✓	A LineSegment object must have the required attribute xsi:type. No other attributes from the SBML Level 3 Layout namespace are permitted on a LineSegment object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.5 on page 10.)		
layout-21505 ✓	The attribute xsi:type of a LineSegment must be of the data type string. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.5 on page 10.)		
layout-21506 ✓	The value of a xsi:type of a LineSegment must be LineSegment. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.5 on page 10.)		
Rules for the CubicBezier class			
layout-21601 ✓	A CubicBezier object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespace are permitted on a CubicBezier . (References: SBML Level 3 Version 1 Core, Section 3.2.)		
layout-21602 ✓	A CubicBezier object may have the optional SBML Level 3 Core attributes metaid and sboTerm . No other attributes from the SBML Level 3 Core namespace are permitted on a CubicBezier . (References: SBML Level 3 Version 1 Core, Section 3.2.)		
layout-21603 ✓	A CubicBezier must specify the four Point elements start , basePoint1 , basePoint2 and end . No other elements from the Layout namespace are permitted on a CubicBezier . (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.6 on page 10.)		
layout-21604 ✓	A CubicBezier object must have the required attribute xsi:type . No other attributes from the SBML Level 3 Layout namespace are permitted on a CubicBezier object. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.6 on page 10.)		
layout-21605 ☑	The attribute xsi:type of a CubicBezier must be of the data type string. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.6 on page 10.)		
layout-21606 ✓	The value of a xsi:type of a CubicBezier must be CubicBezier. (References: SBML Level 3 Package Specification for Layout, Version 1, Section 3.4.6 on page 10.)		

17

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Section B Acknowledgments

References

Bergmann, F. T. and Sauro, H. M. (2006). SBW - a modular framework for systems biology. In *Proceedings of the 38th conference on Winter simulation*, WSC '06, pages 1637–1645. Winter Simulation Conference.

Biron, P. V. and Malhotra, A. (2000). XML Schema part 2: Datatypes (W3C candidate recommendation 24 October 2000). Available via the World Wide Web at http://www.w3.org/TR/xmlschema-2/.

Deckard, A., Bergmann, F. T., and Sauro, H. M. (2006). Supporting the sbml layout extension. *Bioinformatics*, 22(23):2966–2967.

Eriksson, H.-E. and Penker, M. (1998). UML Toolkit. John Wiley & Sons, New York.

Fallside, D. C. (2000). XML Schema part 0: Primer (W3C candidate recommendation 24 October 2000). Available via the World Wide Web at http://www.w3.org/TR/xmlschema-0/.

Gauges, R., Rost, U., Sahle, S., and Wegner, K. (2006). A model diagram layout extension for sbml. *Bioinformatics*, 22(15):1879–1885.

Hucka, M., Bergmann, F. T., Hoops, S., Keating, S. M., Sahle, S., and Wilkinson, D. J. (2011). Available via the World Wide Web at http://sbml.org/Documents/Specifications.

Hucka, M., Finney, A., Sauro, H., Bolouri, H., Doyle, J., Kitano, H., Arkin, A., Bornstein, B., Bray, D., Cornish-Bowden, A., Cuellar, A., Dronov, S., Gilles, E., Ginkel, M., Gor, V., Goryanin, I., Hedley, W., Hodgman, T., Hofmeyr, J., Hunter, P., Juty, N., Kasberger, J., Kremling, A., Kummer, U., Novère, N. L., Loew, L., Lucio, D., Mendes, P., Minch, E., Mjolsness, E., Nakayama, Y., Nelson, M., Nielsen, P., Sakurada, T., Schaff, J., Shapiro, B., shimizu, T., Spence, H., Stelling, J., Takahashi, K., Tomita, M., Wagner, J., and Wang, J. (2003). The Systems Biology Markup Language (SBML): a medium for representation and exchange of biochemical network models. *Bioinformatics*, 19(4):524–31.

Oestereich, B. (1999). *Developing Software with UML: Object-Oriented Analysis and Design in Practice*. Addison-Wesley.

Sahle, S., Gauges, R., Pahle, J., Simus, N., Kummer, U., Hoops, S., Lee, C., Singhal, M., Xu, L., and Mendes, P. (2006). Simulation of biochemical networks using copasi: a complex pathway simulator. In *Proceedings of the 38th conference on Winter simulation*, WSC '06, pages 1698–1706. Winter Simulation Conference.

SBML Team (2010). The SBML Issue Tracker. Available via the World Wide Web at http://sbml.org/issue-tracker.

SBML Team (2012). System biology markup language. Available via the World Wide Web at http://www.sbml.org/.

Thompson, H. S., Beech, D., Maloney, M., and Mendelsohn, N. (2000). XML Schema part 1: Structures (W3C candidate recommendation 24 October 2000). Available online via the World Wide Web at the address http://www.w3.org/TR/xmlschema-1/.

Wegner, K. and Kummer, U. (2005). A new dynamical layout algorithm for complex biochemical reaction networks. *BMC Bioinformatics*, 6(1):212.

Wikipedia (2013). Bèzier curve — Wikipedia, the free encyclopedia. Available via the World Wide Web at http://en.wikipedia.org/wiki/B%C3%A9zier_curve. [Online; accessed 5-May-2013].

13

16

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