Including Layout Information in SBML Files

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Introduction

With 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 [1, 2, 3]. Since SBML had no means of storing layout information for reaction networks, we developed an extension to SBML that would allow us to store this layout information in SBML files. Fortunately, SBML already provides a very flexible way of extending the specification through <annotations> tags which is a container for arbitrary XML data.

Programs that use this means of extending the SBML specification should place those extensions in a separate unique namespace to avoid interference with extensions of other programs. There already exists an extension to SBML by Herbert M. Sauro that deals with layout information in SBML files [5] well tailored to his program JDesigner [4]. However, in order to provide generality, our specification tries to limit the extensions to just specifying information that concerns the placement of the objects and leaves the rendering to the application.

This extension can equally well be applied to SBML Level 2 files. One notable difference would be the <SpeciesReference> tags in the <listOfModifiers>. The kind of information would probably be the same as for substrates and products, but the interpretation might be different. Where substrates and products get connected to the two pseudo nodes of a reactions, the modifier would probably rather be connected to the midpoint of the connection of those two pseudo nodes. To deduce wether a modifiers is an activator or an inhibitor is up to the application so far, putting this kind of information with the render information of the modifier would be an option. The handling of resulting inconsistencies with information given in the kinetic a the reaction would have to be handled by the application. Since simulation programs should only use the information given in the kinetics of the reactions, this should not be a major issue. In the worst case, the reaction is displayed incorrectly.

Since we only add layout information the SBML specification, our extensions are few and simple. After we have received so much valuable feedback from the SBML discussion list, we updated this document to include layout information in the third dimension. All layout information now has an optional z coordinate as well as depth information where appropriate. This information is optional and all the values default to 0.0 if no value is given in the sbml file.

1 Namespace

For the extensions we use a separate namespace of the following form
xmlns:sl="http://projects.eml.org/bcb/sbml/level1". A SBML file that would
utilize the extension could have the following form:

```
<?xml version="1.0" encoding="UTF-8"?>
   <sbml xmlns="http://www.sbml.org/sbml/level1" level="1" version="1"
         xmlns:sl="http://projects.eml.org/bcb/sbml/level1"
         xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
         xsi:schemaLocation="http://projects.eml.org/bcb/sbml/level1
         http://projects.eml.org/bcb/sbml/level1/layout.xsd">
```

<Compartment> Layout Information

For compartments we just specify a layout tag that hold the location of the
compartment as x, y and z coordinates and the size as width, height and
depth. All values are of type double and the origin is in the upper left to
facilitate the implementation. The z and depth value are optional and their
value defaults to 0.0 if not specified otherwise.

XML Schema representation:

```
<xsd:element name="layout">
  <xsd:complexType>
    <xsd:attribute name="x" type="xsd:double"/>
    <xsd:attribute name="y" type="xsd:double"/>
    <xsd:attribute name="z" type="xsd:double" use="optional" default="0.0"/>
    <xsd:attribute name="w" type="xsd:double"/>
    <xsd:attribute name="h" type="xsd:double"/>
    <xsd:attribute name="d" type="xsd:double" use="optional" default="0.0"/>
  </xsd:complexType>
</xsd:element>
```

example:

```
<compartment ...>
        .
        .
        .
  <annotation>
    <sl:layout x="3.0" y="20.0" w="40.0" h="30.0"/>
  </annotation>
</compartment>
```

\<Specie\> Layout Information

Since an sbml document can contain species that don't appear in any reaction a species can have zero or more representations on screen which are grouped in a \<listOfNodes\> tag. Each representation has a unique id which consists of a unique unsigned integer value and is referenced in the corresponding SpecieReference object (see below). The actual layout information is given as x, y and z coordinates as well as width, height and depth. As in the compartment layout, the z coordiante and the depth value are optional. They default to 0.0 if not specified.

XML Schema representation:

```
<xsd:element name="listOfNodes">
  <xsd:complexType>
    <xsd:sequence>
      <xsd:element name="node"
          minOccurs="1" maxOccurs="unbounded">
        <xsd:complexType>
          <xsd:attribute name="x"  type="xsd:double"/>
          <xsd:attribute name="y"  type="xsd:double"/>
          <xsd:attribute name="z"  type="xsd:double" use="optional" default="0.0
          <xsd:attribute name="w"  type="xsd:double"/>
          <xsd:attribute name="h"  type="xsd:double"/>
          <xsd:attribute name="d"  type="xsd:double" use="optional" default="0.0
          <xsd:attribute name="id" type="xsd:unsignedInt"/>
        </xsd:complexType>
      </xsd:element>
    </xsd:sequence>
  </xsd:complexType>
</xsd:element>
```

example:

```
<specie>
    .
    .
    .
  <annotation>
    <sl:listOfNodes>
      <sl:node id="23" x="123.0" y="200.0" w="42.0" h="10.0"/>
```

```
      <sl:node id="45" x="45.0 y=23.0" w="30.0" h="10.0"/>
    </sl:listOfNodes>
  </annotation>
</specie>
```

\<Reaction\> Layout Information

The reaction layout consists of two pseudo nodes. One that connects to the substrates and one that connects to the products of the reaction. We use a \<connector\> tag which contains the coordinates for the two pseudo nodes. Each pseudo node has a x, y and z coordinate which are named x1,y1,z1 and x2,y2,z2 respectively. The z1 and z2 coordinate are optional and they default to 0.0. We suggest connecting the two pseudo nodes by a straight line, but this is up to the application programmer.

XML Schema representation:

```
<xsd:element name="connector">
   <xsd:complexType>
     <xsd:attribute name="x1" type="xsd:double"/>
     <xsd:attribute name="y1" type="xsd:double"/>
     <xsd:attribute name="z1" type="xsd:double" use="optional" default="0.0"/>
     <xsd:attribute name="x2" type="xsd:double"/>
     <xsd:attribute name="y2" type="xsd:double"/>
     <xsd:attribute name="z1" type="xsd:double" use="optional" default="0.0"/>
   </xsd:complexType>
</xsd:element>
```

example:

```
<reaction>
     .
     .
     .
  <annotation>
    <sl:connector x1="111.0" y1="192.0" x2="110.0" y2="217.0"/>
  </annotation>
</reaction>
```

<SpecieReference> Layout Information

The layout information for SpecieReference objects consists of a reference to the corresponding representational node which has been defined in the <listOfNodes> for the Specie object (see above) and optionally a <listOf-Basepoints> tag which holds one or more base-points which define the path of the arrow that connects the SpecieReference representation object to one of the pseudo nodes of the reaction object. Each basepoint has attributes for its x, y and z coordinates. Again, specifying the z coordinate is optional and it defaults to 0.0 if not given. The order of base-points is very important since changing the order changes the appearance of the path. The base-points can either be interpreted as a polygon or as a smooth curve that goes through all base-points. Alternatively the base-points can be ignored; in this case the graphical representation for the SpecieReference is connected to the pseudo node of the reaction via a straight line. The same holds if the listOfBasepoints is absent.

XML Schema representation:

```
<xsd:element name="edge">
  <xsd:complexType>
    <xsd:sequence>
      <xsd:element name="listOfBasepoints"
                 minOccurs="0" maxOccurs="1">
        <xsd:complexType>
          <xsd:sequence>
            <xsd:element name="bp"
             minOccurs="1" maxOccurs="unbounded">
              <xsd:complexType>
                <xsd:attribute name="x" type="xsd:double"/>
                <xsd:attribute name="y" type="xsd:double"/>
                <xsd:attribute name="z" type="xsd:double" use="optional" default=
              </xsd:complexType>
            </xsd:element>
          </xsd:sequence>
        </xsd:complexType>
      </xsd:element>
    </xsd:sequence>
    <xsd:attribute name="nodeRef" type="xsd:unsignedInt"/>
  </xsd:complexType>
</xsd:element>
```

example:

```
<reaction ...>
    .
    .
    .
  <specieReference ...>
        .
        .
        .
    <annotation>
        <sl:edge nodeRef="23">
            <sl:listOfBasepoints>
                <sl:bp x="23.0" y="45.0"/>
                <sl:bp x="16.0" y="24.0"/>
            </sl:listOfBasepoints>
        </sl:edge>
    </annotation>
  </specieReference>
    .
    .
    .
</reaction>
```

Further Plans

The extensions so far leave the rendering of the objects to the application. So each application has to come up with an extension of its own to store rendering information. In the future we hope to come up with a general way for specifying rendering information as well. This document is a work in progress and can be subject to changes any time. We are glad for any suggestions, corrections or hints to further improve these extensions. Hopefully with some help we could come up with a set of extensions that would suite the needs of many applications developed in this area.

Example File

Last but not least, we include a small sample file to illustrate and complement the paragraphs above. The model consists of two reactions. Which are the first reaction of glycolysis where glucose is converted to glucose-6-phosphate

(G6P) and the reverse reaction of gluconeogenesis where glucose-6-phosphate is hydrolyzed to glucose. We did not include any coordinates in the third dimension, since we are only working in 2D space so far. As can be seen in the screenshot, the glucose SpecieReference has two representational objects on screen whereas glucose-6-phosphate only has one. This difference is reflected in the file where the glucose specie has two nodes in the listOfNodes whereas G6P only has one.
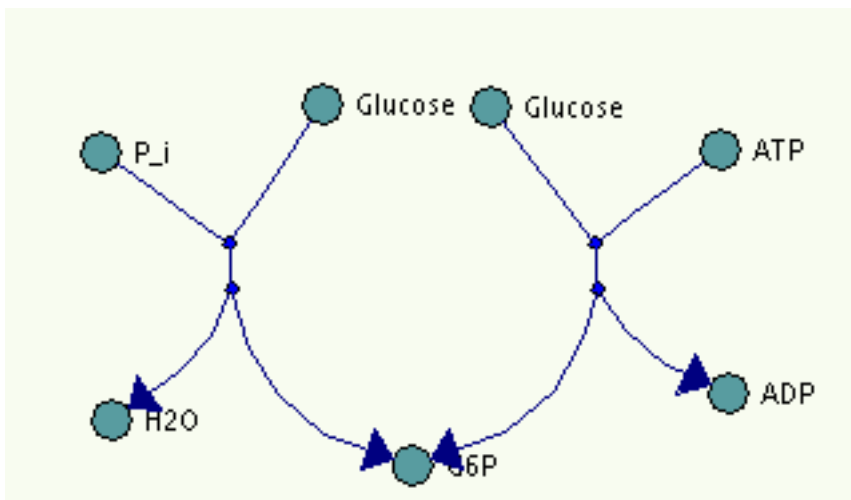

Figure 1: Partial screenshot from SimViz ReactionLayouter showing sample file.

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level1" level="1" version="1"
      xmlns:sl="http://projects.eml.org/bcb/sbml/level1"
      xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
      xsi:schemaLocation="http://projects.eml.org/bcb/sbml/level1
              http://projects.eml.org/bcb/sbml/level1/layout.xsd">

  <model name="Untitled">
    <listOfCompartments>
      <compartment name="compartment" volume="1">
        <annotations>
          <sl:layout x="10.0" y="10.0" w="60" h="50"/>
        </annotations>
      </compartment>
    </listOfCompartments>
    <listOfSpecies>
      <specie name="ATP" compartment="compartment" initialAmount="0">
        <annotations>
          <sl:listOfNodes>
```

```
              <sl:node x="295.0" y="123.0" w="16.0" h="16.0" id="15"/>
            </sl:listOfNodes>
          </annotations>
      </specie>
      <specie name="P_i" compartment="compartment" initialAmount="0">
          <annotations>
            <sl:listOfNodes>
              <sl:node x="63.0" y="124.0" w="16.0" h="16.0" id="2"/>
            </sl:listOfNodes>
          </annotations>
      </specie>
      <specie name="Glucose" compartment="compartment" initialAmount="0">
          <annotations>
            <sl:listOfNodes>
              <sl:node x="146.0" y="106.0" w="16.0" h="16.0" id="29"/>
              <sl:node x="209.0" y="107.0" w="16.0" h="16.0" id="31"/>
            </sl:listOfNodes>
          </annotations>
      </specie>
      <specie name="ADP" compartment="compartment" initialAmount="0">
          <annotations>
            <sl:listOfNodes>
              <sl:node x="298.0" y="214.0" w="16.0" h="16.0" id="17"/>
            </sl:listOfNodes>
          </annotations>
      </specie>
      <specie name="H2O" compartment="compartment" initialAmount="0">
          <annotations>
            <sl:listOfNodes>
              <sl:node x="67.0" y="224.0" w="16.0" h="16.0" id="4"/>
            </sl:listOfNodes>
          </annotations>
      </specie>
      <specie name="G6P" compartment="compartment" initialAmount="0">
          <annotations>
            <sl:listOfNodes>
              <sl:node x="180.0" y="241.0" w="15.0" h="16.0" id="28"/>
            </sl:listOfNodes>
          </annotations>
      </specie>
</listOfSpecies>
<listOfReactions>
      <reaction name="reaction_0" reversible="false">
          <annotations>
            <sl:connector x1="119.0" y1="166.0" x2="120.0" y2="183.0"/>
          </annotations>
          <listOfReactants>
             <specieReference specie="P_i" stoichiometry="1">
                <annotations>
```

```
                  <sl:edge nodeRef="2"/>
               </annotations>
         </specieReference>
         <specieReference specie="Glucose" stoichiometry="1">
               <annotations>
                  <sl:edge nodeRef="29"/>
               </annotations>
         </specieReference>
      </listOfReactants>
      <listOfProducts>
         <specieReference specie="H2O" stoichiometry="1">
               <annotations>
                  <sl:edge nodeRef="4">
                    <sl:listOfBasepoints>
                       <sl:bp x="99.104" y="214.471"/>
                       <sl:bp x="112.305" y="200.627"/>
                    </sl:listOfBasepoints>
                  </sl:edge>
               </annotations>
         </specieReference>
         <specieReference specie="G6P" stoichiometry="1">
               <annotations>
                  <sl:edge nodeRef="28">
                    <sl:listOfBasepoints>
                       <sl:bp x="154.176" y="237.283"/>
                       <sl:bp x="137.835" y="222.150"/>
                       <sl:bp x="126.535" y="205.056"/>
                    </sl:listOfBasepoints>
                  </sl:edge>
               </annotations>
         </specieReference>
      </listOfProducts>
</reaction>
<reaction name="reaction_1" reversible="false">
   <annotations>
     <sl:connector x1="256.0" y1="166.0" x2="257.0" y2="183.0"/>
   </annotations>
   <listOfReactants>
         <specieReference specie="ATP" stoichiometry="1">
               <annotations>
                  <sl:edge nodeRef="15"/>
               </annotations>
         </specieReference>
         <specieReference specie="Glucose" stoichiometry="1">
               <annotations>
                  <sl:edge nodeRef="31"/>
               </annotations>
         </specieReference>
      </listOfReactants>
```

```
            <listOfProducts>
                <specieReference specie="ADP" stoichiometry="1">
                    <annotations>
                      <sl:edge nodeRef="17">
                        <sl:listOfBasepoints>
                          <sl:bp x="282.165" y="211.213"/>
                          <sl:bp x="267.633" y="198.442"/>
                        </sl:listOfBasepoints>
                      </sl:edge>
                    </annotations>
                </specieReference>
                <specieReference specie="G6P" stoichiometry="1">
                    <annotations>
                      <sl:edge nodeRef="28">
                        <sl:listOfBasepoints>
                          <sl:bp x="222.632" y="236.283"/>
                          <sl:bp x="240.185" y="221.209"/>
                          <sl:bp x="251.826" y="201.056"/>
                        </sl:listOfBasepoints>
                      </sl:edge>
                    </annotations>
                </specieReference>
            </listOfProducts>
        </reaction>
      </listOfReactions>
   </model>
</sbml>
```

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References

[1] System Biology Markup Language Level 1 Website (*http://www.sbml.org/sbml/docs/index.html*)

[2] Michael Hucka, Andrew Finney, Herbert Sauro, Hamid Bolouri: Systems Biology Markup Language (SBML) Level 1: Structures and Facilities for Basic Model Definitions (*http://www.sbml.org/sbml/docs/papers/sbml-level-1/html/sbml-level-1.html*)

[3] Hucka M., Finney A., Sauro H.M., Bolouri H., Doyle J.C., Kitano H., Arkin A.P., Bornstein B.J., Bray D., Cornish-Bowden A., Cuellar A.A., Dronov S., Gilles E.D., Ginkel M., Gor V., Goryanin I.I., Hedley W.J., Hodgman T.C., Hofmeyr J.H., Hunter P.J., Juty N.S., Kasberger J.L., Kremling A., Kummer U., Le Novere N.,

Loew L.M., Lucio D., Mendes P., Minch E., Mjolsness E.D., Nakayama Y., Nelson M.R., Nielsen P.F., Sakurada T., Schaff J.C., Shapiro B.E., Shimizu T.S., Spence H.D., Stelling J., Takahashi K., Tomita M., Wagner J., Wang J. (2003) The systems biology markup language (SBML): a medium for representation and exchange of biochemical network models, *Bioinformatics*, **19**, 524-31.

[4] JDesigner Website (*http://www.cds.caltech.edu/ hsauro/JDesigner.htm*)

[5] Herbert Sauro: JDesigner SBML Annotation (*http://www.cds.caltech.edu/ hsauro/JDSBMLEx.pdf*)