Spatial Processes

James C. Schaff
schaff@neuron.uchc.edu
Center for Cell Analysis and Modeling
University of Connecticut
Farmington, Connecticut, US

Lucian P. Smith

lpsmith@u.washington.edu

Computing and Mathematical Sciences

California Institute of Technology

Seattle, Washington, US

Devin P. Sullivan

devin.sullivan@scilifelab.se
 Science for Life Laboratory

KTH-Royal Institute of Technology
 Stockholm, Sweden

Anu Lakshminarayana
anu@uchc.edu
Center for Cell Analysis and Modeling
University of Connecticut
Farmington, Connecticut, US

Frank Bergmann
fbergman@caltech.edu
BioQuant/Centre for Organismal Studies (COS)
University of Heidelberg
Heidelberg, Germany

Robert F. Murphy
murphy@cmu.edu
Computational Biology Department
Carnegie Mellon University
Pittsburgh, Pennsylvania, US

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This is a draft specification for the SBML Level 3 package called "spatial". It is not a normative document. Please send feedback to the Package Working Group mailing list at sbml-spatial@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/spatial

This release of the specification is available at

TBD



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1 Introduction

There is no better test of our understanding of a biological system than to create a mechanistic model of that system and show that it possesses all known properties of the system – i.e., that it is consistent with all measurements or observations of the system in hand. However, the creation of such models is even more useful when a system is not already understood, because the model may suggest mechanisms by which known behaviors are accomplished, or predict behaviors not previously expected. Extensive work has been done on the creation of methods for simulating biochemical systems (Andrews and Bray, 2004; Blinov et al., 2004; Hoops et al., 2006; Loew and Schaff, 2001; Stiles et al., 1998; Tomita et al., 1999), including the development of languages, such as the Systems Biology Markup Language (SBML), for saving and exchanging the definition of the system being simulated and the simulation parameters used (Hucka et al., 2003). Historically, most tools for biochemical simulations either did not consider possible spatial relationships or compartmentalization of system components, or used a compartmental modeling approach (Jacquez et al., 1985) in which spatial organization is approximated by a set of compartments (e.g. membrane-bound organelles in a cell) containing well-mixed populations of molecules. However, a growing number of modeling and simulation tools do permit specification of the size, shape and positions of compartments and the initial spatial distributions of components (typically referred to as a 'geometry' definition). While SBML Level 3 Core has explicit support for multi-compartmental modeling, it does not have a standardized mechanism to store or exchange these geometries. We address this deficit here through the definition of a package of extensions to SBML termed SBML spatial.

Saving geometries in a standardized way is useful to ensure that the definition is complete (which is important when, for example, provided as part of supplementary information for published studies), and to permit comparison of simulations of the same spatial system using different simulation tools, to enable simulations of a new biochemical model using the same geometry as a previous model (or vice versa). Historically, the creation of a geometry has been done (often through painstaking manual work) by the same investigators who defined a biochemical model and performed a simulation. The advent of SBML has permitted a partial division of this labor, by enabling databases of biochemical models, such as the BioModels database (Le Novere et al., 2006; Li et al., 2010), to be created. Building on this theme, having a mechanism to exchange geometries will enable a open access 'marketplace' in which some investigators focus on the creation of well-characterized geometries (and distribute them through databases or repositories) enabling others to focus on biochemical model creation and/or performance of simulations. These geometries, however, typically need to be more than raw images. To be most broadly useful across different modeling approaches, they need, for example, to define explicit watertight boundaries for cells and intracellular compartments and contain statistically accurate estimates of concentrations of components at various locations. This can be accomplished for individual images by hand segmentation (Loew and Schaff, 2001) or automated segmentation (Perez et al., 2014). An alternative is to produce synthetic geometries that are drawn from generative models of cell shape and organization learned from many images (Zhao and Murphy, 2007). In both cases, the availability of well-characterized geometries for examples of different cell types (and multiple cells of each type) can enhance the use of simulation methods.

Examples of simulations using biochemical models and geometries from different sources have already occurred using a preliminary version of the SBML spatial standard (Donovan et al., 2016; Sullivan et al., 2015). In these, cell geometries created using CellOrganizer and saved using the SBML spatial extension were combined with biochemical models created using BioNetGen and saved in SBML.

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Additional considerations when considering spatially-realistic simulations is that properties of molecules or reactions may be spatially varying, and that rates of transport between locations need to be specified.

In summary, the purpose of this SBML Level 3 extension is to meet the needs identified above by defining standardized ways of representing geometries, spatial mappings of species and reactions, and explicit species transport.

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1.1 Proposal corresponding to this package specification

This specification for Spatial in SBML Level 3 Version 1 is based on the proposal located at the following URL:

https://sbml.svn.sf.net/svnroot/sbml/trunk/specifications/sbml-level-3/version-1/spatial/proposal

The tracking number in the SBML issue tracking system (SBML Team, 2010) for Spatial package activities is 188 (http://sourceforge.net/p/sbml/sbml-specifications/188/).

1.2 Package dependencies

The Spatial package has no dependencies on other SBML Level 3 packages.

1.3 Document conventions

UML 1.0 (Unified Modeling Language; Eriksson and Penker 1998; Oestereich 1999) notation is used in this document to define the constructs provided by this package. Colors in the diagrams carry the following additional information for the benefit of those viewing the document on media that can display color:

- *Black*: Items colored black in the UML diagrams are components taken unchanged from their definition in the SBML Level 3 Core specification document.
- *Green*: Items colored green are components that exist in SBML Level 3 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 Core specification.
- *Red lines*: Classes with red lines in the corner are fully defined in a different figure.

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

AbstractClass: Abstract classes are never instantiated directly, but rather serve as parents of other classes. Their names begin with a capital letter and they are printed in a slanted, bold, sans-serif typeface. 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 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, sans-serif 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 Core specification.)

SomeThing, **otherThing**: Attributes of classes, data type names, literal XML, and tokens *other* than SBML class names, are printed in an upright typewriter typeface.

[elementName]: In some cases, an element may contain a child of any class inheriting from an abstract base class. In this case, the name of the element is indicated by giving the abstract base class name in brackets, meaning that the actual name of the element is the de-capitalized form of whichever subclass is used.

For other matters involving the use of UML and XML, this document follows the conventions used in the SBML Level 3 Core specification document.

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2 Background and context

2.1 Problems with current SBML approaches

There is no standard way of specifying spatial models in SBML short of introducing an explicit spatial discretization in the form of a large number of compartments with duplicate species and reactions and additional reactions for coupling due to transport. This approach hard-codes the numerical methods which destroys portability and is not practical beyond a few compartments. Tools have been forced to resort to proprietary extensions (e.g. MesoRD custom annotations) to encode geometry.

2.2 Past work on this problem or similar topics

There are many standards for the exchange of geometric information of engineered parts in Computer Aided Design and Manufacturing. These formats are designed for geometric shapes which are directly specified by a designer rather than the data driven, freeform biological structures encountered in cell biology.

There also exist standards for the representation of unstructured computational meshes that can encode these freeform biological structures more readily. However, it is important to note that while a computational mesh necessarily encodes an approximation to the shapes of geometric objects, the particular form will be algorithm dependent.

To ensure model interoperability, we must encode the geometric shapes in a way that is independent of the numerical methods and even the mathematical framework. The representation of a spatial model within SBML should be largely invariant of the particular encoding of the geometry definition within that model. For example, a spatial model represented in SBML that encodes geometry as a set of geometric primitives (e.g. spheres, cylinders) should be easily portable to a tool that only supports polygonal surface tessellation. It is expected that a geometry translation library will be very useful for interoperability the same way that libSBML greatly improved model interchange by solving similar implementation problems in a standard way.

2.3 Prior work

The first version of the Spatial proposal was written [fill in history]

Lucian: We probably do need something here.

3 Package syntax and semantics

This section contains a definition of the syntax and semantics of the Spatial package for SBML Level 3 Version 1 Core. The Spatial package involves several new object classes, and extends the existing **Model**, **Compartment**, **Species**, **Reaction**, and **Parameter** object class. Section 4 on page 44 contains complete examples of using the constructs in SBML models.

Lucian: Periodically when I have comments, I'll put them in sections that look like this-in red, with the pointy-hand icon off to the side. They tend to be design questions I had when creating this document for parts I thought were not clear, or are suggestions for changes that could be made.

3.1 Overview of spatial extension

The SBML Compartment, Reaction and Species, and molecular transport mechanisms (DiffusionCoefficient, AdvectionCoefficient, BoundaryCondition) are mapped to geometric domains to describe spatial models within SBML. The primary mechanism to accomplish this mapping is to simply map Compartments to collections of geometric Domains called DomainTypes. Each Domain is a contiguous patch of volumetric space or a contiguous surface patch that is ultimately described by a single system of equations (whichever mathematical framework is used). In analogy with initial conditions, the mathematical system defined within a domain often needs a definition of what happens at the domain boundary (e.g. boundary conditions) to complete the specification. Because of this, the boundaries between adjacent domains need to be identified so that appropriate boundary conditions can be specified. For compactness of representation, rather than map to each individual Domain, Compartments are mapped to DomainTypes, along with the corresponding Species and Reactions (with the new compartment attribute).

3.1.1 Geometry

The **Geometry** object within a model is completely modular and does not reference the rest of the model, promoting reuse of the same geometry in different models. The geometry separately defines a coordinate system, a list of domain types, a list of domains and their adjacency relationships, and a list of alternate geometric representations.

3.1.2 Alternative Geometry Definitions

Modeling and simulation tools will each natively support some subset (often just one) of the possible *GeometryDefinitions* (analytic, sampled field, constructive solid geometry, parametric, or mixed shapes). Interoperability will be enhanced if tools write as many geometry definitions as they are able. Upon reading the model, a tool will typically choose the most convenient geometry definition, i.e. the one that it natively supports. If a tool does not edit the geometry, it has the ability to preserve the alternate representations during model editing (because the mapping of the model to the geometry is not stored in the geometry).

There are two general classes of geometric representation specification: those that explicitly specify surfaces and those that implicitly specify surfaces. For example, a level set is a field where a specific isosurface of the field specifies a geometric surface. A geometry described using constructive solid geometry of geometric primitives (e.g. spheres, cylinders) specifies directly which points are "inside" an object. Alternatively, explicit surface representations explicitly declare the set of points belonging to surfaces (e.g. polygonal tessellations).

3.2 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 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 Spatial package for SBML Level 3 Version 1 Core:

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

In addition, SBML documents using a given package must indicate whether the package can be used to change the mathematical interpretation of a model. This is done using the attribute **required** on the **sbml** element in the SBML document. For the Spatial package, the value of this attribute must be "**true**", because the use of the Spatial package can change the mathematical meaning of a model.

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

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

3.3 Primitive data types

The Spatial package uses a number of the primitive data types described in Section 3.1 of the SBML Level 3 Version 1 Core specification, and adds several additional primitive types described below.

3.3.1 Type SpId

The type SpId is derived from SId (SBML Level 3 Version 1 Core specification Section 3.1.7) and has identical syntax. The SpId type is used as the data type for the identifiers of various objects in the Spatial Processes package. The purpose of having a separate type for such identifiers is to enable the space of possible spatial identifier values to be separated from the space of all other identifier values in SBML. The equality of SpId values is determined by an exact character sequence match; i.e., comparisons of these identifiers must be performed in a case-sensitive manner.

3.3.2 Type SpIdRef

Type <code>SpIdRef</code> is used for all attributes that refer to identifiers of type <code>SpId</code>. It is derived from <code>SpId</code>, but with the restriction that the value of an attribute having type <code>SpIdRef</code> must match the value of a <code>SpId</code> attribute in the relevant model; in other words, the value of the attribute must be an existing spatial identifier in the referenced model. As with <code>SpId</code>, the equality of <code>SpIdRef</code> values is determined by exact character sequence match; i.e., comparisons of these identifiers must be performed in a case-sensitive manner.

3.3.3 Type BoundaryConditionKind

The BoundaryConditionKind primitive data type is used in the definition of the BoundaryCondition class. It is derived from type string and its values are restricted to being one of the following possibilities: "Neumann", "Dirichlet", "Robin_valueCoefficient", "Robin_inwardNormalGradientCoefficient", and "Robin_sum". Attributes of type BoundaryConditionKind cannot take on any other values. The meaning of these values is discussed in the context of the BoundaryCondition class's definition in Section 3.12 on page 16.

3.3.4 Type CoordinateKind

The CoordinateKind primitive data type is used in the definition of the CoordinateComponent class. It is derived from type string and its values are restricted to being one of the following possibilities: "cartesianX", "cartesianY", and "cartesianZ". Attributes of type CoordinateKind cannot take on any other values. The meaning of these values is discussed in the context of the CoordinateComponent class's definition in Section 3.16 on page 20.

Other CoordinateKind types are held in reserve for future versions of this specification, and may include "spherical-Radius", "sphericalAzimuth", "sphericalElevation", "cylindricalRadius", "cylindricalAzimuth", "cylindricalHeight", "polarRadius", and "polarAzimuth".

3.3.5 Type DataKind

The DataKind primitive data type is used in the definition of the SampledField and ParametricGeometry classes. It is derived from type string and its values are restricted to being one of the following possibilities: "double", "float", "uint8", "uint16", and "uint32". Attributes of type DataKind cannot take on any other values. The meaning of these values is discussed in the context of the classes' definitions in Section 3.50 on page 41 and Section 3.44 on page 36.

3.3.6 Type DiffusionKind

The DiffusionKind primitive data type is used in the definition of the DiffusionCoefficient class. It is derived from type string and its values are restricted to being one of the following possibilities: "isotropic", "anisotropic", and "tensor". Attributes of type DiffusionKind cannot take on any other values. The meaning of these values is discussed in the context of the DiffusionCoefficient class's definition in Section 3.10 on page 15.

3.3.7 Type CompressionKind

The CompressionKind primitive data type is used in the definition of the SampledField and ParametricObject classes. It is derived from type string and its values are restricted to being one of the following possibilities: "uncompressed", and "deflated". Attributes of type CompressionKind cannot take on any other values. The meaning of these values is discussed in the context of the classes' definitions in Section 3.50 on page 41 and Section 3.46 on page 38.

3.3.8 Type FunctionKind

The FunctionKind primitive data type is used in the definition of the AnalyticVolume class. It is derived from type string and its values are restricted to being one of the single possibility "layered". Attributes of type FunctionKind cannot take on any other values. The meaning of these values is discussed in the context of the AnalyticVolume class's definition in Section 3.25 on page 26.

3.3.9 Type GeometryKind

The GeometryKind primitive data type is used in the definition of the Geometry class. It is derived from type string and its values are restricted to being the single possibility "cartesian". Other GeometryKind types are held in reserve for future versions of this specification, and may include "cylindrical", "spherical", and "polar". Attributes of type GeometryKind cannot take on any other values. The meaning of these values is discussed in the context of the Geometry class's definition in Section 3.15 on page 18.

3.3.10 Type InterpolationKind

The InterpolationKind primitive data type is used in the definition of the SampledField class. It is derived from type string and its values are restricted to being one of the following possibilities: "nearestNeighbor" and "linear". Attributes of type InterpolationKind cannot take on any other values. The meaning of these values is discussed in the context of the SampledField class's definition in Section 3.50 on page 41.

3.3.11 Type PolygonKind

The PolygonKind primitive data type is used in the definition of the ParametricObject class. It is derived from type string and its values are restricted to being one of the following possibilities: "triangle" and "quadrilateral". Attributes of type PolygonKind cannot take on any other values. The meaning of these values is discussed in the context of the ParametricObject class's definition in Section 3.46 on page 38.

3.3.12 Type PrimitiveKind

The PrimitiveKind primitive data type is used in the definition of the CSGPrimitive class. It is derived from type string and its values are restricted to being one of the following possibilities: "sphere", "cube", "cylinder", and

"cone", for three-dimensional CSGObject elements, and "circle", and "square", for two-dimensional CSGObject elements. Attributes of type PrimitiveKind cannot take on any other values. The meaning of these values is discussed in the context of the CSGPrimitive class's definition in Section 3.50 on page 41.

3.3.13 Type SetOperation

The SetOperation primitive data type is used in the definition of the CSGSetOperator class. It is derived from type string and its values are restricted to being one of the following possibilities: "union", "intersection", and "difference". Attributes of type SetOperation cannot take on any other values. The meaning of these values is discussed in the context of the CSGSetOperator class's definition in Section 3.35 on page 32.

3.3.14 Type doubleArray

The doubleArray primitive data type is a space-delimited list of double values in a single string.

3.3.15 Type arrayData

The arrayData primitive data type is used in the definition of the SampledField and ParametricObject classes. It consists of a possibly-compressed whitespace-and-semicolon-delimited list of numerical values in a single string. The meaning and possible content of these values is discussed in the context of the classes' definitions in Section 3.50 on page 41 and Section 3.44 on page 36.

3.4 The extended Model object

The **Model** object is extended in the spatial package to contain a new **Geometry** child, as seen in Figure 1. The **Geometry** element is contained in the Model element in the 'spatial' namespace. In order to specify a spatial geometry, some of the existing SBML elements need to be extended (**Compartment**, **Species**, **Parameter**, and **Reaction**). These extensions to the SBML elements are discussed in the sections that follow.

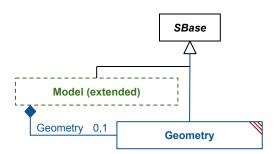


Figure 1: The definition of the extended **Model** object from the Spatial package. The **Geometry** object and its children are defined in their own sections.

3.5 The extended Compartment object

The **Compartment** in the SBML core is extended while defining a spatial model. An SBML model with spatial geometry defines domain types (classes of domains that are anatomically and physiologically similar). These domain types need to be mapped to a compartment in the SBML model. **Compartments** are extended to define **CompartmentMappings** that map compartments to **DomainTypes** such that each corresponding **DomainType** is assigned the same biological and mathematical function. Within SBML L3 Core, the compartment Sid refers to the size of that compartment and is specified by the size attribute or may be set by a rule. For spatial models, the compartment size is calculated as the product of the unit size specified in the compartment mapping and the size of the current domain. The definition for the extension of the Compartment element is shown in Figure 2 on the next page.

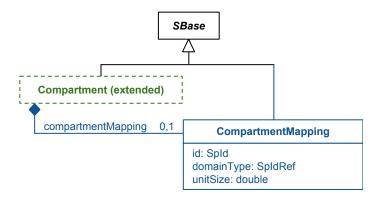


Figure 2: The definition of the extension to the Compartment element, and the definition of the CompartmentMapping class. The SBML core attributes of Compartment are not displayed.

The **Compartment** element has an optional **CompartmentMapping** child which indicates the **DomainType** to which the **Compartment** is mapped. If there is no **CompartmentMapping** for a **Compartment** in a spatial model, then that **Compartment** is excluded from the spatial version of the model. In the same way, if a **DomainType** is not mapped to one or more **Compartments**, then the corresponding **Domains** in the geometry have no assigned function.

3.6 The CompartmentMapping class

Each **Compartment** in a model that defines a spatial geometry may contain an optional **CompartmentMapping**. A **CompartmentMapping** is defined as part of the model rather than part of the geometry so that the geometry is modular and may be readily shared between models and reused. A **CompartmentMapping** maps a **Compartment** defined in the model to a **DomainType** defined in the geometry such that each corresponding **DomainType** is assigned the same biological and mathematical function described by the set of **Compartments** that are mapped to that **DomainType**.

This mapping need not be one-to-one. In fact, it is common to map er-lumen, er-membrane, and cytosol to the same cell interior volume or 3D **DomainType**. The **unitSize** attribute specifies the relative quantity of each **Compartment** that is mapped to the **DomainType**.

3.6.1 The id attribute

The id attribute is a mandatory attribute of type SpId that is used to uniquely identify a CompartmentMapping in the model. All identifiers of type SpId must be unique within the Geometry. The mathematical value of a CompartmentMapping is its unitSize attribute, and can be bound to a Parameter by using a SpatialSymbolReference.

3.6.2 The domainType attribute

The mandatory domainType attribute is of type SpIdRef that indicates a DomainType defined in the Geometry element.

3.6.3 The unitSize attribute

The unitSize attribute is of type double and represents the relative size of the Compartment with respect to the size of the Domains to which they are mapped. Thus for any infinitesimal subset of the Domains with size S, there exists an amount of $Compartment_i$ of size $(S^*unitSize_i)$ for i=1..N compartments mapped to that DomainType. For example, a 3D Compartment (and DomainType) which is mapped to a 3D DomainType has a unitSize which is a volume fraction of dimensionless unit. The total set of all such volume fractions mapped to a particular DomainType will typically sum to one.

If the spatialDimensions attribute of the parent Compartment is different than the spatialDimensions attribute

of referenced **DomainType**, the **unitSize** attribute is a conversion factor between the two. The most common example of this would be a 2D **Compartment** being mapped to a 3D **DomainType**, such as an ER-membrane being mapped to a volumetric cell interior. In this case, the **unitSize** is a surface-to-volume ratio.

If connected to a **Parameter** via a **SpatialSymbolReference**, an **InitialAssignment** may override the value of the **unitSize** attribute. It is theoretically possible to have this value change in time through the use of a **Rule** or **Event**, but some (if not all) software tools may not support this setup. If the value is set to change, and the dimensionality of the parent **Compartment** and referenced **DomainType** is the same, the other **CompartmentMapping** elements for the same **DomainType** will typically change in concert, so that they continue to sum to one. Also note that **Species** amounts are preserved in SBML, so a changing **unitSize** may induce a corresponding change in any correlated **Species** concentration.

Any bound **Parameter**'s units should be equivalent to the units of the parent **Compartment** divided by the units of the referenced **DomainType**.

Here is an example of a **Compartment** element extended to have spatial information:

```
<compartment id="Extracellular" spatialDimensions="3" constant="true">
  <spatial:compartmentMapping spatial:id="spatialExtracellular"
     spatial:domainType="Extracellular" spatial:unitSize="1"/>
  </compartment>
```

3.7 The extended Species object

The SBML core **Species** is extended when a spatial geometry is defined in the model with the addition of a single new required boolean "isSpatial" attribute. The extension to the **Species** element is shown in Figure 3.

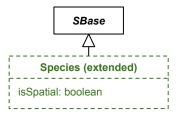


Figure 3: The extension to the Species element. The attributes of Species from SBML Level 3 Version 1 Core are not displayed.

3.7.1 The isSpatial attribute

The **isSpatial** attribute is of data type boolean. If it is set to true, the **Species** is spatially distributed in a possibly nonhomogeneous manner within the **Domains** of the same type as the mapped **DomainType**.

For continuous deterministic models (described by partial differential equations), a spatial **Species** will result in a concentration field described by a partial differential equation which incorporates contributions from **Reactions**, diffusion (**DiffusionCoefficient**) and advection (**AdvectionCoefficient**) and are subject to boundary conditions (**BoundaryCondition**) and initial conditions (**InitialAssignment** and **Rule**). All of these quantities can be explicit functions of the spatial coordinates as well as spatial and nonspatial **Parameters** and **Species**.

For stochastic models, the **Species** is represented as a collection of particles that are distributed throughout the **Domains** and are subject to reactions, diffusion and advection. Simulation algorithms either track individual particles (e.g. Particle-based methods) or use spatial discretization to track a large number of well stirred pools (e.g. Next-Subvolume Method).

The compartment of any Species set is Spatial = "true" must have a child Compartment Mapping: if it did not, its

compartment would not actually be a part of the spatial model.

3.8 The extended Parameter object

When an SBML model defines a spatial geometry, the SBML core **Parameter** is used to define the diffusion coefficient, transport velocity (advection) and boundary conditions for species and the coordinate components defined in the **Geometry**. One **Parameter** is created for each quantity, by adding a child **DiffusionCoefficient**, **AdvectionCoefficient**, or **BoundaryCondition**. Conversely, some elements defined in the spatial package may need to be referenced by mathematics in core constructs, or even have their value set by core constructs such as **InitialAssignment** or **Rule**. These spatial elements can be semantically linked to a **Parameter** by giving it a child **SpatialSymbolReference** pointing to that element.

A **Parameter** that has been extended for the Spatial package can have only one of the above listed objects. For example, if a **Parameter** is extended to represent the diffusion coefficient of a species, the existing attributes of the **Parameter** (id, name, value, units, constant) are defined according to SBML core specifications, along with a **DiffusionCoefficient** child that contains the information about the species it represents. **Figure 4** represents the extension to the **Parameter** element.

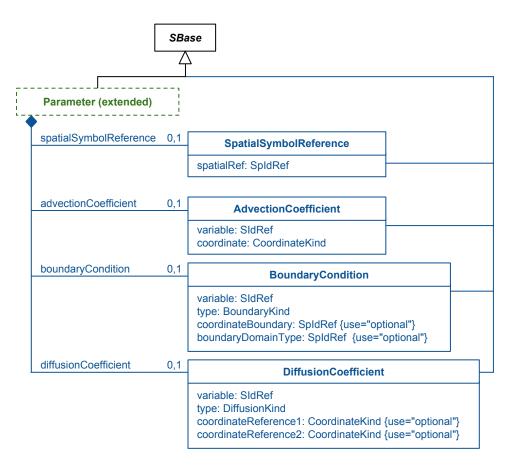


Figure 4: The Parameter element extension for spatial package, and the definitions of the SpatialSymbolReference, AdvectionCoefficient, BoundaryCondition, and DiffusionCoefficient classes. The SBML Level 3 Version 1 Core attributes for Parameter are not displayed in this figure.

3.9 The SpatialSymbolReference class

A **Parameter** is extended with a **SpatialSymbolReference** element, when a symbol from the defined spatial geometry (**id** of any element contained in **Geometry**) is required to be used in the SBML core model. Typically, the **SpatialSymbolReference** is used to represent the coordinate components defined in the **Geometry**'s listOfCoordinateComponents. For example, if the **Geometry** is defined in a 2-dimensional Cartesian coordinate system with X and Y defined as coordinate components, two **Parameters** (one each for **CoordinateComponents** X and Y) are created in the model. The value of the parameter is not required to be set. For each of these parameters, a **SpatialSymbolReference** object is created.

3.9.1 The spatialRef attribute

The spatialRef attribute of SpatialSymbolReference, is of type SpIdRef and refers to the SpId of any element defined in the Geometry of the model.

3.10 The DiffusionCoefficient class

When a species in a spatial model has a diffusion rate constant, a **Parameter** for this diffusion constant is created in the SBML model with a **DiffusionCoefficient** child, which is used to identify the **Species** whose diffusion rate the **Parameter** represents. The diffusion coefficient can then be set like any other variable: its initial value can be set using the **Parameter**'s **value** attribute or through an **InitialAssignment**, and if the diffusion coefficient changes in time, this can be defined with a **Rule** or **Event**. If set, the units of this **Parameter** should be length²/time. If left unset, the **DiffusionCoefficient** will inherit the model units of length²/time (typically cm²s⁻¹ or um²s⁻¹).

It is possible to define both diffusion and advection for the same **Species**.

3.10.1 The variable attribute

The required variable attribute of **DiffusionCoefficient** is of type **SIdRef** and is the **SId** of the **Species** or **Parameter** in the model whose diffusion coefficient is being set.

3.10.2 The type and coordinateReference attributes

The required type attribute of DiffusionCoefficient is of type DiffusionKind and indicates whether the diffusion coefficient is "isotropic" (i.e. applies equally in all dimensions/directions), "anisotropic" (i.e. applies only for a single coordinate), or "tensor" (i.e. applies only for a particular pair of coordinates). Coefficients of type "isotropic" may not have any coordinateReference attributes defined, since diffusion is defined for all axes. Coefficients of type "anisotropic" must define the coordinateReference1 attribute and not the coordinateReference2 attribute, and applies in the direction of that axis. Coefficients of type "tensor" must define both the attributes coordinateReference1 and coordinateReference2, defining diffusion in relation to the direction due to a gradient in the diagonal term of the diffusion tensor for the two coordinates. In no case may coordinateReference2 be defined but not coordinateReference1.

3.10.3 DiffusionCoefficient uniqueness

Only one **DiffusionCoefficient** may be defined per **Species** per axis or pair of valid axes in the **Compartment** in which it resides. Since isotropic diffusion is defined for all axes at once, this means that if an isotropic **DiffusionCoefficient** is defined for a **Species**, it may have no other diffusuion coefficients.

3.11 The AdvectionCoefficient class

The AdvectionCoefficient is the extension to Parameter in SBML core that is used to represent transport velocity of a species, if it exists. The transport velocity for the species is defined in a manner similar to the diffusion constant with a unit of length/time (regardless of the units of the corresponding Species' "compartment" attribute). A Parameter is created in SBML code for the velocity with an AdvectionCoefficient child to identify the Species whose velocity is

represented by the **Parameter**; its initial value is set either through the **value** attribute or an **InitialAssignment**. If the advection coefficient changes in time or space, this can be modeled with a **Rule** or **Event**.

If defined, the units of the parent **Parameter** should be in length/time; if not defined, it inherits from the model-wide units of length divided by the model-wide units of time.

It is possible to define both diffusion and advection for the same **Species**.

3.11.1 The variable attribute

The variable attribute of AdvectionCoefficient is of type SIdRef and is the SId of the Species or Parameter in the model whose advection coefficient (transport velocity) is being set.

3.11.2 The coordinate attribute

The coordinate is of type CoordinateKind and represents the coordinate component of the velocity. For example, if the Geometry is defined in the Cartesian coordinate system and is 2-dimensional, the species can have velocity terms for both X and Y. If the Parameter represents the transport velocity of the species in the X-coordinate, the coordinate attribute will take a value of "cartesianX", and if it represents the velocity in the Y-coordinate, the attribute will take a value of "cartesianY". Only one AdvectionCoefficient may be defined per Species per valid coordinate.

3.12 The BoundaryCondition class

A **Species** in a spatial model that has a diffusion rate or an advection velocity needs to have specified boundary conditions. A boundary condition is either the concentration of the species or the flux density of the species at a boundary. The boundary refers to either an internal membrane boundary or a face of the box defined by the minimum and maximum coordinates of the geometry (the geometries bounding box).

When creating a spatial SBML model, species boundary conditions are created as parameters, one for each boundary condition, by adding a child **BoundaryCondition** that points to the corresponding **Species** and boundary, depending on the coordinate system.

For Cartesian Geometries, there are two boundaries for every axis being modeled. For example, in a 2D cartesian geometry for the external boundaries, there could be up to four parameters or parameter sets created for each spatial **Species** whose **Compartments** abut the minimum and maximums of the X and Y axes).

For internal boundaries, one may either define a **BoundaryCondition** for a **Species** at that boundary, or one may define one or more transport reactions that describe how the physical entities that **Species** represent are moved (or converted) from one side of the boundary to the other. One may not define both a **BoundaryCondition** and a **Reaction** that describes the same phenomenon, as this would result in the equivalent of an overdetermined system, not dissimilar from the reason that the change in a **Species** may not be defined by both a **Reaction** and a **RateRule**. A **Species** set **boundaryCondition** = "true" may have a defined **BoundaryCondition** and also appear in a transport **Reaction**, but its change in time and space will only be determined by the **BoundaryCondition**.

If neither a **BoundaryCondition** nor a **Reaction** is defined for a particular **Species**/boundary pair, the flux of that **Species** at that boundary is zero.

The **Parameter**'s value is set either through the **value** attribute or an **InitialAssignment**. If the boundary condition changes in time, it can be set with a **Rule** or **Event**. If set, the **Parameter** unit must be equal to the appropriate unit for its **type** (see below). Only one **BoundaryCondition** may be defined per **Species** per boundary (regardless of type).

3.12.1 The variable attribute

The variable attribute of **BoundaryCondition** is of type **SIdRef** and is the SId of the **Species** or **Parameter** in the model whose boundary condition is being set.

3.12.2 The type attribute

The type attribute is of type BoundaryConditionKind and indicates the type of boundary condition. The boundary condition types come in three groups: for Neumann boundaries, "Neumann" (the inward normal flux) is used. For Dirichlet boundaries, "Dirichlet" (the value) is used. For Robin boundaries, three different Parameters must be defined, with BoundaryCondition elements of type "Robin_inwardNormalGradientCoefficient", "Robin_valueCoefficient", and "Robin_sum".

The unit of the boundary condition is determined by the type, and the unit for density and velocity. For "Dirichlet", the unit would be the unit of concentration. For "Neumann", the unit would be concentration*length/time. For Robin boundaries, for a variable "u" with an inward pointing normal vector "n", Robin value coefficient "a", Robin inward normal gradient coefficient "b", and Robin sum "g", the condition is defined by the equation "a*u + $b*inner_product(grad(u),n) = g$ ", with appropriate units. The suggested set of units that satisfy this condition is to have units of nondimensional for "a", 1/length for "b", and the same units as the referenced variable for "c".

3.12.3 The coordinateBoundary attribute

The coordinateBoundary attribute is of type SpIdRef and refers to the SpId of either the boundaryMin or the boundaryMax object of the CoordinateComponent defined in Geometry. This SpId indicates the boundary condition (minimum or maximum) in the CoordinateComponent. A Parameter that is extended with a BoundaryCondition object can only define the coordinateBoundary attribute or the boundaryDomainType attribute, but not both.

3.12.4 The boundaryDomainType attribute

The boundaryDomainType attribute is of type SpIdRef and refers to the SpId of the DomainType of the location of the species whose boundary condition is being defined. A Parameter that is extended with a BoundaryCondition object can only define the coordinateBoundary attribute or the boundaryDomainType attribute, but not both.

3.13 Extended Parameter examples

As an example, here are four examples of parameters that have been extended with spatial information. These four parameters are extended with the four different possible spatial extensions: the **SpatialSymbolReference** to allow the model to refer to the spatial id "x" as the SBML core id "x"; a **BoundaryCondition** to define the boundary condition for "s1_nuc" to be zero; a **DiffusionCoefficient** to define the diffusion coefficient for "s1_nuc" to be "0.1"; and an **AdvectionCoefficient** to define the advection coefficient for "s2_nuc" to be "0.13".

3.14 The extended Reaction object

The SBML core **Reaction** is extended when a spatial geometry is defined in the model with the addition of a single new required boolean **isLocal** attribute. Figure 5 on the following page displays the definition of the extension of the **Reaction** element.

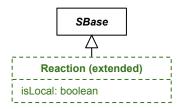


Figure 5: The extension to the Reaction element. The SBML Level 3 Version 1 Core attributes and children for Reaction are not displayed in the figure.

3.14.1 The isLocal attribute

The isLocal attribute for a Reaction is of type Boolean. The attribute is set to true if the reaction is to be considered a local description of the reaction in terms of concentration/time defined at each point in space rather than substance/time over an entire Compartment or "pool". Note that this means that the units of the KineticLaw are different depending on whether the Reaction is local or not.

If a **Reaction** is defined to be a local (having an **isLocal** value of "true"), the value of the **compartment** attribute of the **Reaction** must be defined. This is because the interpretation of the **Reaction** is very different if the reaction takes place at the boundary of the **Compartment** of the **Species** (where the reaction rate units are flux densities) than if it takes place within the interior of that **Compartment** (where the reaction rate units are concentration/time define throughout the volume). The first will give you gradients in the solution, while the other will not.

If the referenced **Species** come from multiple compartments, the **compartment** of the **Reaction** must be a **Compartment** that makes physical sense for the individual **Species** to meet.

3.15 The Geometry class

A single geometry must be defined within the model if the spatial extension is to be used. Figure 6 on the next page shows the definition of the **Geometry** element.

3.15.1 The id attribute

The **id** attribute is of type **SpId**, uniquely identifies the **Geometry** element, and is optional. It has no mathematical meaning, and cannot be connected to a **Parameter** via a **SpatialSymbolReference** element.

3.15.2 The coordinateSystem attribute

The coordinateSystem attribute is a required attribute and is of type GeometryKind. It represents the coordinate system used by the Geometry. A value of "cartesian" indicates that the geometry is a cartesian coordinate system, with the coordinate components corresponding to the x, y, and z components of that system (which could be 1-, 2-, or 3-dimensional). This is the only coordinate system defined in this version of the specification—in the future, if necessary, "cylendrical", "spherical", and "polar" may be added as possibilities, along with n-dimensional cartesian modeling, should there be interest in the modeling community to exchange these types of models.

3.15.3 The listOf container classes

The **Geometry** has listOfCoordinateComponents, listOfDomainTypes, listOfDomains, listOfAdjacentDomains, listOfGeometryDefinitions, and listOfSampledFields that help define the geometry. The **ListOfCoordinateComponents** is a list of **CoordinateComponent** objects, the **ListOfDomainTypes** is a list of **DomainType** objects, the **ListOfDomains** is a list of **Domain** objects, **ListOfAdjacentDomains** is a list of **AdjacentDomains** objects, the **ListOfGeometryDefinitions** is a list of alternative **GeometryDefinitions** (**ParametricGeometry**, **CSGeometry**, **SampledFieldGeometry**, **Analytic-Geometry**, and **MixedGeometry**), and the **ListOfSampledFields** is a list of **SampledField** objects. Of these, only the **ListOfCoordinateComponents** is required, but, if present, none of them may be empty.

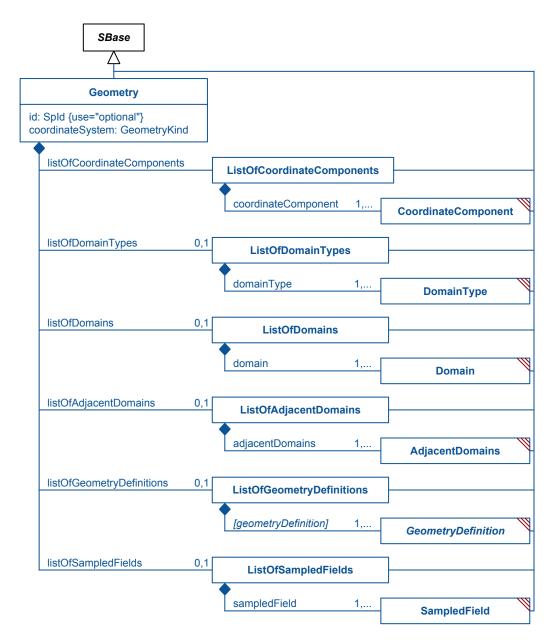


Figure 6: The definition of the Geometry, ListOfCoordinateComponents, ListOfDomainTypes, ListOfDomains, ListOfAdjacentDomains, ListOfGeometryDefinitions, and ListOfSampledFields classes from the Spatial package. The various children of the ListOf- classes are defined in their own sections.

Note that the children of the **ListOfGeometryDefinitions** object are not called **geometryDefinition** but rather take the name of the derived class, decapitalized. Thus, they may be called **analyticGeometry**, **csGeometry**, parametricGeometry, sampledFieldGeometry, or mixedGeometry.

The **ListOfCoordinateComponents** is unique in that it defines the dimensions of the **Geometry**. Thus, every **Geometry** must have a child **ListOfCoordinateComponents** with exactly one, two, or three children. When there is one child, it must be of type cartesianX; when there are two, they must be of type cartesianX and cartesianY, and when there are three, they must be of types cartesianX, cartesianY, and cartesianZ.

3.16 The CoordinateComponent class

A **CoordinateComponent** object explicitly defines a coordinate component of the coordinate axes and gives them names, units, and formally associates them with a coordinate system. The **CoordinateComponent** also defines the minimum and maximum values of the coordinate axis it represents. The definition of **CoordinateComponent** is shown in Figure 7.

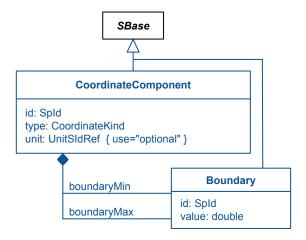


Figure 7: The CoordinateComponent and Boundary object definitions. One or more instances of CoordinateComponent objects in a ListOfCoordinateComponents can be present in Geometry.

3.16.1 The id attribute

A **CoordinateComponent** is identified with the **id** attribute which is of type **SpId**. The mathematical value of a **CoordinateComponent** is its coordinate value **unitSize** attribute, and can be bound to a **Parameter** by using a **SpatialSymbolReference**.

Because a **CoordinateComponent** represents an entire axis, it is not appropriate, should it be connected to a **Parameter** via a **SpatialSymbolReference**, for that **Parameter** to be set via an **InitialAssignment** or **Rule**. Rather, it is treated like the SBML core **csymbol** "time", and can be used as an independent variable in other calculations.

3.16.2 The type attribute

The type attibute of type CoordinateKind represents the type of the coordinate component, and may take one of a subset of all possible CoordinateKind values depending on its parent Geometry, as defined in Table 1 on the next page. For Cartesian geometries, one-dimensional geometries must be defined by having a single "cartesianX" CoordinateComponent; two-dimensional geometries must be defined by having exactly two CoordinateComponent children with type values of "cartesianX" and "cartesianY", and three-dimensional geometries must be defined by having exactly three CoordinateComponent children with type values of "cartesianX", "cartesianY", and "cartesianZ". No Geometry may have two CoordinateComponent children with the same type.

3.16.3 The unit attribute

The unit of a **CoordinateComponent** is represented by the **unit** attribute, of type **UnitSIdRef**. If not specified, the unit of a **CoordinateComponent** inherits from the **lengthUnits** attribute of the **Model** object, and if that in turn is not specified, the **CoordinateComponent** units cannot be determined.

GeometryKind	Dimensions	CoordinateKinds
cartesian	1	"cartesianX" (coord1)
cartesian	2	"cartesianX" (coord1) and "cartesianY" (coord2)
cartesian	3	"cartesianX" (coord1), "cartesianY" (coord2), and "cartesianZ" (coord3)

Table 1: Correspondance between the type of a **Geometry** and the possible types of its child **CoordinateComponent** elements. Also noted is the corresponding attribute (coord1, coord2, or coord3) corresponding to each axis when defining **InteriorPoint** elements (see Section 3.20 on page 23).

3.17 The Boundary class

The minimum and the maximum for a **CoordinateComponent** represent the bounds in each coordinate. For example, for three dimensional Cartesian coordinate system with x, y, and z coordinates, the minimum and maximum limits for each coordinates define planes orthogonal to each coordinate axis and passing through the minimum or maximum. If max-min is the same for each x,y,z then the bounds on the geometry is a cube. The **Boundary** class interacts with the **BoundaryCondition** class, allowing modelers to define how model elements behave at the boundary of the model. For species defined within volumes adjacent to these surfaces, **BoundaryCondition** elements must be introduced.

The minimum limit of a **CoordinateComponent** is represented by the **boundaryMin** object and the maximum limit is represented by the **boundaryMax** object, and apply to **CoordinateComponent** elements. Both are **Boundary** objects, and have the following attributes:

3.17.1 The id attribute

The **id** attribute of the **Boundary** object identifies the object. The attribute is required and is of type **SpId**. This attribute is used when specifying the **BoundaryCondition** for a species as an extension of an SBML core **Parameter**. The mathematical value of a **Boundary** is its **value** attribute, and can be bound to a **Parameter** by using a **SpatialSymbolReference**. The units are the same as its parent **CoordinateComponent**, and are not set separately.

3.17.2 The value attribute

The **value** attribute is of type **double**. In a **boundaryMin** object, it represents the minimum limit of the **Coordinate-Component**. In a **boundaryMax** object, it represents the maximum limit of the **CoordinateComponent**.

If connected to a **Parameter** via a **SpatialSymbolReference**, this **value** may be overridden by an **InitialAssignment**. However, the **Parameter** must be set **constant**="true", because it may not change over the course of the simulation.

3.17.3 A CoordinateComponent example

In this example, a **CoordinateComponent** is used to define an X axis that goes from 0 to 10 um.

```
<spatial:coordinateComponent spatial:id="x" spatial:type="cartesianX" spatial:unit="um">
        <spatial:boundaryMin spatial:id="Xmin" spatial:value="0"/>
        <spatial:boundaryMax spatial:id="Xmax" spatial:value="10"/>
        </spatial:coordinateComponent>
```

3.18 The DomainType class

A **DomainType** is a class of domains that are identified as being anatomically and physiologically similar. For example, a **DomainType** "cytosol" may be defined in a **Geometry** as identifying the structure and function of the cell interior. If there is one cell, then there is one domain, if there are multiple cells, then there are multiple disjoint domains ("cytosol1", "cytosol2", etc.) identified with the **DomainType** "cytosol". **CompartmentMappings**, defined as an extension to an SBML core **Compartment**, map compartments to domain types such that each corresponding domain is assigned the same biological and mathematical function. Figure 8 on the following page shows the

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DomainType object.

Each SBML **Compartment** maps to a single **DomainType**, meaning that the initial condition of each **Species** in each **Compartment** will be the same across all **Domains** that map to a given **DomainType**. If those **Species** are spatially distributed, they will subsequently evolve independently from each other. However, if modeling two **Domains** that are similar but whose **Species** have different initial conditions, those **Domains** should be modeled as separate **DomainTypes**.

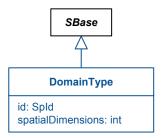


Figure 8: The definition of the DomainType class. One or more instances of DomainType in a ListOfDomainTypes instance can be present in a Geometry object.

3.18.1 The id attribute

Each **DomainType** is identified with a **id** of type **SpId**. The mathematical value of a **CompartmentMapping** is the sum of the sizes of all domains associated with this **DomainType**, and can be bound to a **Parameter** by using a **SpatialSymbolReference**.

As a derived quantity, if connected to a **Parameter** via a **SpatialSymbolReference**, this value may *not* be overridden by an **InitialAssignment**, nor by the use of a **Rule** or **Event**. Its value is always connected to the size of its component **Domains** instead. The units of a **DomainType** are the units of the corresponding base units of the SBML **Model** for length (for one-dimensional domains), area (for two-dimensional domains), or volume (for three-dimensional domains). It is required to define the corresponding base units for every **DomainType** in the **Model**.

3.18.2 The spatialDimensions attribute

The **spatialDimensions** attribute of the **DomainType** is of type **int** and can take on a value of 0, 1, 2, or 3. The spatial dimension is specified for a **DomainType**, rather than being repeated for each **Domain** that is represented by the **DomainType**.

If the spatialDimensions attribute of a **DomainType** is a lower dimensionality than the **Geometry** to which it refers (via the **Domain**), it is considered to describe the surface of that **Geometry** in the 3D case, or the perimeter of that **Geometry** in the 2D case. Since there is no defined perimeter of a 3D object, it is illegal to have a **DomainType** with a spatialDimensions of "1" where the corresponding **Geometry** is three-dimensional.

3.19 The Domain class

Domains represent contiguous regions identified by the same **DomainType**. One, two and three dimensional domains are contiguous linear regions, surface regions, and volume regions (respectively), bounded by the limits of the coordinate system (e.g. min/max of x,y,z) and adjacent domains corresponding to different domain types. **Domain** is shown in Figure 9 on the next page.

3.19.1 The id attribute

A **Domain** is identified with an **id** attribute of type **SpId**. This **id** may be used within a **SpatialSymbolReference** object that is extended from an SBML core **Parameter** and can be used in an expression. The mathematical value

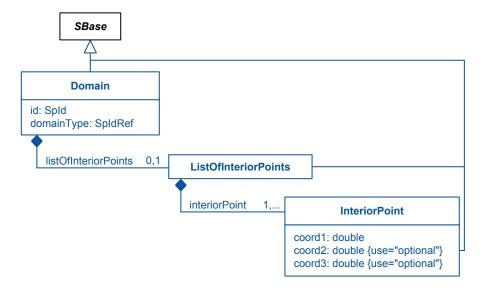


Figure 9: The definition of the **Domain**, **ListOfInteriorPoints**, and **InteriorPoint** classes. A **ListOfDomains** instance in **Geometry** can contain one or more **Domain** object instances.

of a **Domain** is the absolute size of that domain as used by the simulator (the meshed size), and can be bound to a **Parameter** by using a **SpatialSymbolReference**.

As a derived quantity, if connected to a **Parameter** via a **SpatialSymbolReference**, this value may *not* be overridden by an **InitialAssignment**, nor by the use of a **Rule** or **Event**. Its value is always connected to the size of the corresponding **Geometry** instead. The units of the **Domain** are the same as the units of the corresponding **DomainType**.

3.19.2 The domainType attribute

The domainTpe attribute refers to the SpId of the DomainType that describes the anatomy and physiology of this domain. The attribute is of type SpIdRef. It is through this association that compartments, and hence the whole SBML model, gets mapped to the individual domains.

3.20 The InteriorPoint class

Each **Domain** can contain a **ListOfInteriorPoints**. The list of spatial points for a domain is interior to that domain. This list is optional for a **Domain** if it is the only **Domain** defined for its **DomainType**, but is required otherwise.

For those geometric descriptions that can describe multiple disjoint domains belonging to the same domainType, these interior points allow unambiguous identification of each domain. Formally, a single point would suffice, but in practice some tools (e.g. Smoldyn) require multiple points to handle non-convex volumes bounded by explicit surfaces. For discontinuous surfaces with the same domainType, the interior point identifies which domain is associated with which surface patch defined in the geometry definition.

Each InteriorPoint has three attributes: coord1, coord2, and coord3.

3.20.1 The coord1, coord2, and coord3 attributes

An InteriorPoint element represents a single point within the defined coordinate system and should be in the interior of the domain that contains it. It has three attributes, coord1, coord2, and coord3, of type double, representing the position along each of the up to three coordinate axes defined by the CoordinateComponents (with type "cartesianX", "cartesianY", and "cartesianZ", respectively, for each coord_ attribute; see Table 1 on page 21).

Each InteriorPoint must define the same number of attributes as there are dimensions of the corresponding **Geometry** to which it belongs.

In the case of surfaces, interior points are sometimes required to make unambiguous identification of multiple surfaces (e.g multiple plasma membranes for multiple cells present in a geometry). Due to roundoff error and finite word lengths, it is difficult to find a three dimensional point that lies on a surface. In this case, the distance from the surface will be used to provide unambiguous identification.

3.21 The AdjacentDomains class

AdjacentDomains (or domain adjacencies) captures the topological relationships within the **Geometry**. Consider that the **Domains** are nodes in a graph. The **AdjacentDomains** objects are the edges that specify the spatial connectivity of these nodes. Armed with the topology and the domain sizes, one can readily perform a compartmental approximation. Figure 10 shows the definition of the **AdjacentDomains** object.

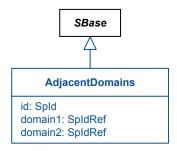


Figure 10: The definition of the AdjacentDomains class. Geometry can contain one instance of ListOfAdjacentDomains that can have one or more instances of AdjacentDomains objects.

3.21.1 The id attribute

This attribute identifies an **AdjacentDomains** object. The attribute is of type **SpId**. It has no mathematical meaning, and cannot be connected to a **Parameter** via a **SpatialSymbolReference** element.

3.21.2 The domain1 and domain2 attributes

The domain1 and domain2 attributes, of type SpIdRef, are required attributes. They are the SpId's of two domains that touch each other (spatially adjacent). These are typically surface-volume contacts.

3.22 Domain example

The following is an example of a set of **Domain**, **DomainType**, and **AdjacentDomains** objects.

```
<spatial:listOfDomainTypes>
  <spatial:domainType spatial:id="Cytosol" spatial:spatialDimensions="3"/>
  <spatial:domainType spatial:id="Nucleus" spatial:spatialDimensions="3"/>
</spatial:listOfDomainTypes>
<spatial:listOfDomains>
  <spatial:domain spatial:id="Cytosol0" spatial:domainType="Cytosol">
    <spatial:listOfInteriorPoints>
      <spatial:interiorPoint spatial:coord1="2.4" spatial:coord2="2.4" spatial:coord3="0.5"/>
    </spatial:listOfInteriorPoints>
  </spatial:domain>
  <spatial:domain spatial:id="Nucleus0" spatial:domainType="Nucleus">
    <spatial:listOfInteriorPoints>
      <spatial:interiorPoint spatial:coord1="4.8" spatial:coord2="4.8" spatial:coord3="0.5"/>
    </spatial:listOfInteriorPoints>
  </spatial:domain>
</spatial:listOfDomains>
<spatial:listOfAdjacentDomains>
```

3.23 The Geometry Definition class

A **Geometry** can specify a list of **GeometryDefinitions**. The **GeometryDefinition** is an abstract class that is the general term for the container which defines the concrete geometric constructs represented by the **Geometry**. Four types of **GeometryDefinitions** have been identified - **AnalyticGeometry**, **SampledFieldGeometry**, **ParametricGeometry**, **CSGeometry** (Constructed Solid Geometry) - and are elaborated in the following sections. The definition of the **GeometryDefinition** element is displayed in Figure 11. The spatial dimension of the **GeometryDefinition** must match the **spatialDimensions** of the **DomainType** defined for the associated **Domain**.

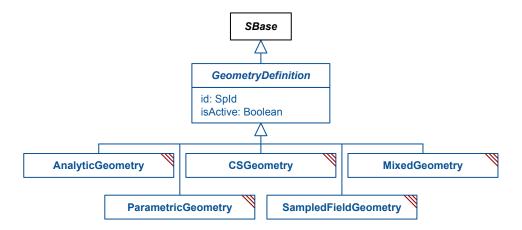


Figure 11: The GeometryDefinition element. Geometry contains one instance of listOfGeometryDefinitions that can contain one or more instances of GeometryDefinition (one of AnalyticGeometry, SampledFieldGeometry, CSGeometry, ParametricGeometry, or MixedGeometrydefined below).

3.23.1 The id attribute

The id attribute is common to all the *GeometryDefinition* types and is used to uniquely identify the *GeometryDefinition*. The attribute is of type SpId. It has no mathematical meaning, and cannot be connected to a **Parameter** via a SpatialSymbolReference element.

3.23.2 The isActive attribute

The isActive attribute that is common to all the *GeometryDefinition* types is used to identify the *GeometryDefinition* that is considered the active *GeometryDefinition* for the document. When multiple *GeometryDefinition* elements define the same underlying geometry, each may set their isActive attribute to "true". At least one *GeometryDefinition* in a Model must have an isActive attribute of "true", and any other *GeometryDefinition* that does not describe that same underlying physical geometry must have an isActive value of "false".

3.24 The AnalyticGeometry class

The **AnalyticGeometry** is a class of **GeometryDefinition** where the geometry of each domain is defined by an analytic expression. An **AnalyticGeometry** is defined as a collection of **AnalyticVolumes**, one **AnalyticVolume** for each volumetric domain in the geometry. In this representation, the surfaces are treated as the boundaries between dissimilar **AnalyticVolumes**. The **AnalyticGeometry** object contains a **ListOfAnalyticVolumes**. Figure 12 on the next page shows the definition of the **AnalyticGeometry** object.

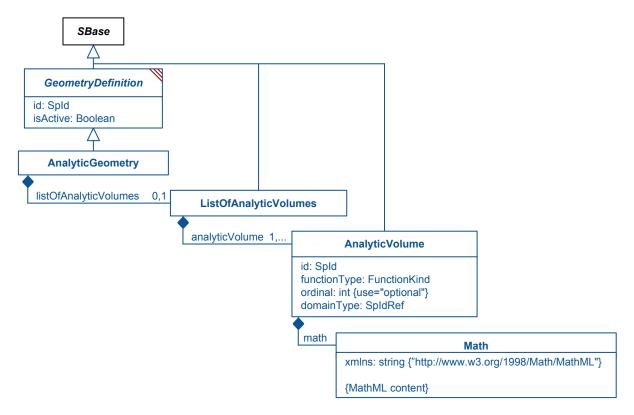


Figure 12: The definition of the AnalyticGeometry, ListOfAnalyticVolumes, and AnalyticVolume classes.

3.25 The Analytic Volume class

The **AnalyticVolume** is used to specify the analytic expression of a volumetric (3-dimensional) domain. The analytic expression for the **AnalyticVolume** is defined in the Math element.

3.25.1 The id attribute

The **id** attribute uniquely identifies the **AnalyticVolume**. The attribute is required and is of type **SpId**. It has no mathematical meaning, and cannot be connected to a **Parameter** via a **SpatialSymbolReference** element.

3.25.2 The functionType attribute

The functionType attribute is of type FunctionKind and is currently limited to just "layered" (a possibility for future versions of the specification is to allow the value "R-function"). A "layered" function type implies that the Math child element contains an inequality in the spatial dimensions (e.g. x,y,z) such that evaluation to "true" indicates that the point (x,y,z) is within that shape, and "false" indicates that it is not covered by that shape.

3.25.3 The domainType attribute

The domainType attribute of type SpIdRef is a required attribute. It represents the SpId of the DomainType of the Domain that is represented by this AnalyticVolume.

3.25.4 The ordinal attribute

The **ordinal** attribute is of type **int**, and is required. It is used to represent the order of the **AnalyticVolume**. The **ordinal** is useful while reconstructing the geometry in the specific software tool - it represents the order in which the **AnalyticVolumes** representing geometric domains have to be evaluated.

Rather than struggle with the task of preventing overlapping regions of space from different **AnalyticVolumes**, the **AnalyticVolumes** are to be considered to be evaluated in the reverse order of their ordinals. In this way, any **AnalyticVolumes** that have already been processed will cover those with a smaller ordinal, thus resolving any ambiguities and removing the constraint that all **AnalyticVolumes** be disjoint and cover the entire geometric domain. The **AnalyticVolume** with **ordinal** 0 can be the "background" layer (typically the extracellular space).

No two **AnalyticVolume** elements should have the same **ordinal** value, even if they should not overlap, because some tools may not calculate the geometries to the same level of precision as other tools, and may end up with overlap due to rounding errors, and will still need to resolve the ambiguity for their own purposes. If a software tool discovers two overlapping **AnalyticVolume** elements with the same **ordinal** value, it may resolve the situation however it sees fit.

3.26 The Math class

The Math element is a required element for an **AnalyticVolume**. The Math element contains a MathML expression that defines the analytic expression for the **AnalyticVolume** referencing the coordinate components that are specified in the **ListOfCoordinateComponents** in the **Geometry**, according to the **functionType**.

3.27 AnalyticGeometry example

The following is an example of an analytic geometry, with a single volume described by the formula " $8 * (x-1)^2 + 8 * (y-1)^2 + 8 * (z-1)^2 < 1$ " (the formula for a sphere).

3.28 The SampledFieldGeometry class

SampledFieldGeometry is a type of *GeometryDefinition* that defines a sampled image-based geometry or a geometry based on samples from a level set. **SampledFieldGeometry** is defined by referencing a **SampledField** from the **ListOf-SampledFields** on the **Geometry** element that specifies the sampled image, together with a a list of **SampledVolumes** that represent the volumetric domains as sampled image regions. Figure 13 on the following page shows the definition of the **SampledFieldGeometry** object. It may be used for geometries of any dimension.

3.28.1 The sampledField attribute

The **sampledField** attribute is of type SpIdRef, and must reference a **SampledField** from the same **Geometry**. That referenced field is to be used to set up the different spatial areas in the geometry of the **Model**, according to the **SampledVolume** child elements.

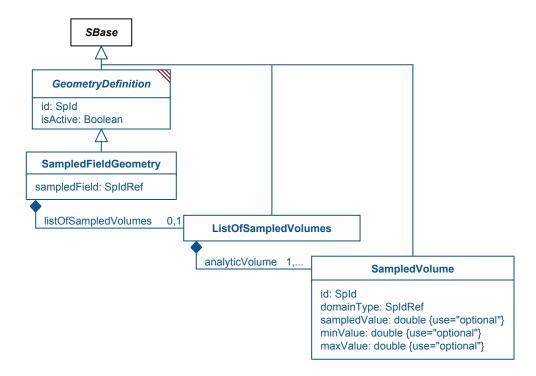


Figure 13: The definition of the SampledFieldGeometry, ListOfSampledVolumes, and SampledVolume classes.

3.29 The SampledVolume class

A SampledVolume represents an interval of the sampled field that constitutes one or more contiguous regions. A SampledVolume is defined for each volumetric (3-dimensional) Domain in the Geometry. Volumes are defined as regions within the referenced image that match a particular pixel value (sampledValue) or that match a range of pixel values (minValue and maxValue). A given SampledVolume must define for itself either a single value or a range of values to which it applies, but not both. Within a ListOfSampledVolumes, there must be at most one SampledVolume that corresponds to any given pixel value. That is, any given pixel value may only appear as the sampledVolume of a single SampledVolume, or be between the minValue and maxValue (inclusive) of a single SampledVolume. It has the following attributes:

3.29.1 The id attribute

The id attribute identifies a **SampledVolume** object. The attribute is of type **SpId** and is required when specifying a **SampledVolume**. It has no mathematical meaning, and cannot be connected to a **Parameter** via a **SpatialSymbol-Reference** element.

3.29.2 The domainType attribute

The required domainType attribute is of type SpIdRef. It is the SpId of the DomainType that represents this class of anatomical features. If there are more than one contiguous regions, then more than one domain will be defined corresponding to each SampledVolume.

3.29.3 The sampledValue attribute

The optional sampledValue attribute is of type double. It represents the pixel value of a SampledVolume. When used, all pixels with this particular value are to be assigned to this SampledVolume, and no pixel without this value is assigned to the SampledVolume. It is illegal to define a sampledValue attribute for a SampledVolume that also has a minValue and maxValue defined.

3.29.4 The minValue attribute

The optional minValue attribute is of type double. It represents the minimum of the pixel value (sampledValue) range to be assigned to this SampledVolume. If a minValue attribute is defined, a maxValue attribute must also be defined, and the sampledValue attribute must not be defined. Areas in the SampledField with exactly this value are to be included in this SampledVolume.

3.29.5 The maxValue attribute

The optional maxValue attribute is of type double. It represents the maximum of the pixel value (sampledValue) range to be assigned to this SampledVolume. If a maxValue attribute is defined, a minValue attribute must also be defined, and the sampledValue attribute must not be defined. Areas in the SampledField with *exactly* this value are to be excluded from this SampledVolume.

Having the minValue be included and the maxValue be excluded allows modelers to define adjacent volumes without ambiguity at the boundaries. One **SampledVolume** may be defined from 0 to 100, and a second volume defined from 100 to 200, and any location with a **SampledField** value of exactly 100 is only assigned to the first **SampledVolume**, and every location with a value close to 100 is included in exactly one **SampledVolume**.

3.30 SampledFieldGeometry example

The following is an example of a sampled field geometry with three volumes. The referenced **SampledField** (defined in Section 3.50 on page 41) is also included (though truncated).

```
<spatial:listOfGeometryDefinitions>
  <spatial:sampledFieldGeometry spatial:isActive="true" spatial:sampledField="imgvals">
    <spatial:listOfSampledVolumes>
      <spatial:sampledVolume spatial:id="Extracellular2" spatial:domainType="Extracellular"</pre>
      spatial:minValue="0" spatial:maxValue="64"/>
<spatial:sampledVolume spatial:id="Cytosol2" spatial:domainType="Cytosol2"
                               spatial:minValue="64" spatial:maxValue="192"
      <spatial:sampledVolume spatial:id="Nucleus2" spatial:domainType="Nucleus"</pre>
                               spatial:minValue="192" spatial:maxValue="256"/>
    </spatial:listOfSampledVolumes>
  </spatial:sampledFieldGeometry>
</spatial:listOfGeometryDefinitions>
<spatial:listOfSampledFields>
  <spatial:sampledField spatial:id="imgvals" spatial:dataType="uint8" spatial:numSamples1="51"</pre>
                         spatial:numSamples2="59" spatial:numSamples3="23"
                         spatial:interpolationType="linear" spatial:compression="uncompressed"
                         spatial:samplesLength="1255">
                                120 218 237 [...] 131 28 215
  </spatial:sampledField>
</spatial:listOfSampledFields>
```

3.31 The CSGeometry class

CSGeometry (Constructed Solid Geometry) is a type of *GeometryDefinition* that defines a combined, solid, volumetric object from a number of primitive solid volumes by the application of set operations such as union, intersection and difference and affine transformations such as rotation, scaling, translation, etc. The **CSGeometry** element is defined by a listOfCSGObjects element that contains a collection of **CSGObjects**. Figure 14 on the following page shows the definition of the **CSGeometry** object.

3.32 The CSGObject class

Each **CSGObject** is a scene graph representing a particular geometric object using constructed solid geometry. A node in a tree (scene graph) is made up of **CSGPrimitives**, **CSGSetOperators**, and **CSGTransformations**. Note that

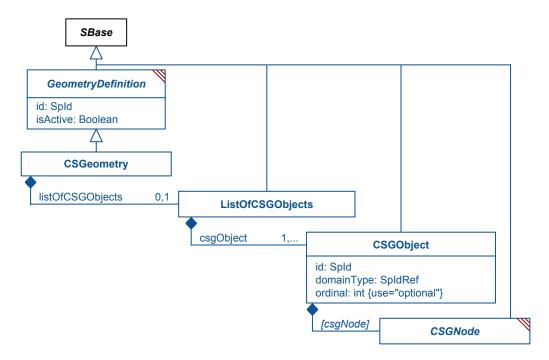


Figure 14: The definition of the CSGeometry, ListOfCSGObjects, and CSGObject classes.

the **CSGOP**imitives are always leaves in this tree. The **CSGOP**iect is analogous to an **AnalyticVolume** element in the sense that it is a constructed geometry (from primitives) used to specify a volumetric (3-dimensional) domain. The **CSGOP**iect element has three attributes: **id**, **domainType** and **ordinal**. The definition of the **CSGOP**iect is completed by defining a **CSGNode** which is the root of the **CSGOP**iect scene graph.

3.32.1 The id attribute

The **id** attribute uniquely identifies the **CSGObject** element. The attribute is required and is of type **SpId**. It has no mathematical meaning, and cannot be connected to a **Parameter** via a **SpatialSymbolReference** element.

3.32.2 The domainType attribute

The domainType attribute is of type SpIdRef and is a required attribute. It is a reference to the id of the DomainType that this CSGObject represents.

All InteriorPoints of the corresponding DomainType must be points inside the geometry this CSGObject describes.

3.32.3 The ordinal attribute

The **ordinal** attribute is of type **int**. It is used to represent the order of the **CSGObject**. The **ordinal** is useful while reconstructing the geometry in the specific software tool - it represents the order in which the **CSGObjects** representing geometric domains have to be placed.

No two **CSGObject** elements should have the same **ordinal** value, even if they should not overlap, because some tools may not calculate the geometries to the same level of precision as other tools, and may end up with overlap due to rounding errors, and will still need to resolve the ambiguity for their own purposes. If a software tool discovers two overlapping **CSGObject** elements with the same **ordinal** value, it may resolve the situation however it sees fit.

3.32.4 The [csgNode] child

The child [csgNode] element represents the geometry that is to be linked to the domainType of the CSGObject. Note that the child of the CSGObject element is not called "csgNode" but rather takes the name of the derived class,

decapitalized. Thus, a **CSGObject** may have a csgPrimitive, csgSetOperator, csgTranslation, csgRotation, csgScale, or csgHomogeneousTransformation child.

3.33 The CSGNode class

The operators and operands used to construct a constructed solid geometry are generalized as a *CSGNode*, defined in Figure 15 as an abstract base class. The classes that inherit from *CSGNode* can be one of the following: *CSGSetOperator*, *CSGTransformation* (operators; itself another abstract base class), or *CSGPrimitive* (operands). The *CSGNode* has one attribute: id. The *CSGObject* contains a *CSGNode* object which is the root of the *CSGObject* scene graph (representing one constructed solid geometry domain).

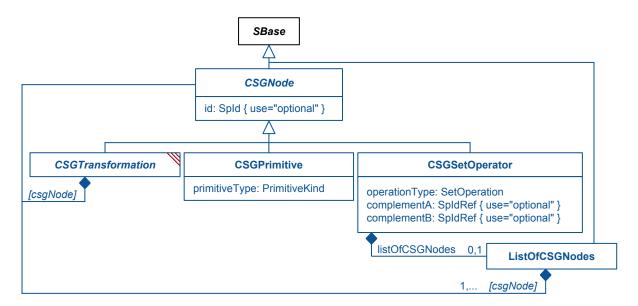


Figure 15: The definition of the abstract base class CSGNode, and its subclasses CSGPrimitive, and CSGSetOperator. The abstract base class CSGTransformation (also a subclass of CSGNode) is defined in Section 3.37 on page 33.

3.33.1 The id attribute

The **id** attribute uniquely identifies the *CSGNode* element. The attribute is optional and is of type SpId. It has no mathematical meaning, and cannot be connected to a **Parameter** via a **SpatialSymbolReference** element.

3.34 The CSGPrimitive class

CSGPrimitive element represents the primitive geometric shapes that can be represented by the **CSGeometry**. These shapes are defined in Table 2 on the following page with a predefined orientation and fitting within the unit cube (+/-1 in x, y, and z) or unit square (+/-1 in x and y). This element has one required attribute: **primitiveType** of type **PrimitiveKind**.

3.34.1 The primitiveType attribute

The **primitiveType** attribute is a required attribute that is of type **PrimitiveKind**. It represents one of the predefined primitive shapes. The meaning and definition of those types is listed in Table 2 on the next page.

PrimitiveKind	Dimensions	Definition
sphere	3	A sphere with radius 1, centered at the origin.
cube	3	A cube with sides of length 2, centered at the origin.
cylinder	3	A cylinder with a base circle of radius 1, centered at $(0,0,-1)$, and top circle of radius 1, centered at $(0,0,1)$. The height is 2.
cone	3	A cone with a base circle of radius 1, centered at (0,0,-1), and top vertex at (0,0,1).
circle	2	A circle with radius 1, centered at the origin.
square	2	A square with sides of length 2, centered at the origin

Table 2: Definitions of the possible values of the primitiveType attribute of the CSGPrimitive class.

3.35 The CSGSetOperator class

The **CSGSetOperator** element represents the set operations (union, intersection, difference) that can be performed on a set of primitive geometric shapes (**CSGPrimitives**) or on a set of **CSGNodes** (a transformation or set operation on one or a set of **CSGPrimitives**). This element has one attribute of type **string**. It also contains a required child **ListOfCSGNodes** that represents the set of nodes on which the set operation is performed.

3.35.1 The operationType attribute

The operationType attribute is of type SetOperation and represents an operation that can be performed on a set of *CSGNodes*. The possible values that the operationType attribute can take are "union", "intersection", or "relativeComplement". The values "union" and "intersection" are n-ary, meaning they are defined for any number of child nodes of this CSGSetOperator. The intersection or union of the empty set (zero children) is defined as the empty set, and the intersection or union of a single child is defined as that child. The union of multiple sets is defined as including any element that appears in any of those component sets, and the intersection of multiple sets is defined as including only those elements that appear in all of the component sets.

The value "relativeComplement" is binary, meaning that it must have exactly two children. Its meaning is defined according to the complement attributes, below.

3.35.2 The complementA and complementB attributes

The complement attributes are of type SpIdRef. If the operationType of the CSGSetOperator has the value "relativeComplement", they both must be set to indicate the order in which the complement is to be carried out, and must refer, respectively, to the two csgNode children of this CSGSetOperator. The relative complement of the children (and thus the meaning of this node) is defined as the set of elements in complementB, but not in complementA.

If the operationType of the CSGSetOperator is not "relativeComplement", neither complement attribute may be set.

3.36 The ListOfCSGNodes class

The **ListOfCSGNodes** must contain one or more **csgNode** children that are to be combined according to the set operation of the parent **CSGSetOperator**. While having a single child is legal, this is semantically equivalent to simply putting that child in the model instead of the **CSGSetOperator**, and therefore has limited modeling benefit. Note that the children of the **ListOfCSGNodes** object are not called **csgNode** but rather take the name of the derived class, decapitalized. Thus, they may be called **csgPrimitive**, **csgSetOperator**, **csgTranslation**, **csgRotation**, **csgScale**, or **csgHomogeneousTransformation**.

3.37 The CSGTransformation class

The *CSGTransformation* represents a generalization for the type of transformation that can be performed on a primitive geometric shape (*CSGPrimitive*) or on a *CSGNode* (a transformation or set operation on one or a set of *CSGPrimitives*). The types of possible transformations are 'rotation', 'translation', 'scaling', and 'homogeneous transformation', defined below. The *CSGTransformation* element contains a *CSGNode* element upon which the transformation is performed.

Each transformation is performed directly on its child *CSGNode*, with any transformation or set operation from that node already performed. This essentially defines a 'bottom-up' approach, where the tips of the XML tree children of a *CSGObject* are all *CSGPrimitive* objects, that are progressively transformed or combined with other *CSGPrimitive* objects by each successive node moving rootward through the XML. For an example, see Section 3.43 on page 36.

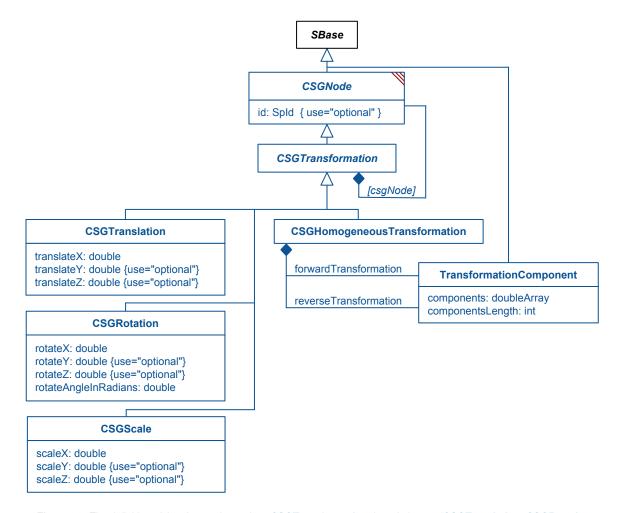


Figure 16: The definition of the abstract base class CSGTransformation, its subclasses (CSGTranslation, CSGRotation, CSGScale, and CSGHomogeneousTransformation), and the TransformationComponent class.

3.37.1 The csgNode child

The child csgNode element represents the geometry that is to be transformed by the *CSGTransformation* element. Note that this child is not called csgNode but rather takes the name of the derived class, decapitalized. Thus, it may be called csgPrimitive, csgSetOperator, csgTranslation, csgRotation, csgScale, or csgHomogeneousTransformation.

3.38 The CSGTranslation class

The **CSGTranslation** element represents a translation transformation on a **CSGNode** (a transformation or set operation on one or a set of **CSGPrimitives**) or a **CSGPrimitive** along the axes defined in the **Geometry**. This element has 3 attributes:

3.38.1 The translateX attribute

The translateX required attribute is of type double. It represents the translation of the *CSGNode* along the x-axis (the CoordinateComponent with the type of "cartesianX").

3.38.2 The translateY attribute

The translateY attribute is of type double. It represents the translation of the *CSGNode* along the y-axis (the CoordinateComponent with the type of "cartesianY"). This attribute must not be defined if no such Coordinate-Component is present in the parent Geometry, and is required otherwise.

3.38.3 The translateZ attribute

The translateZ attribute is of type double. It represents the translation of the *CSGNode* along the z-axis (the CoordinateComponent with the type of "cartesianZ"). This attribute must not be defined if no such Coordinate-Component is present in the parent Geometry, and is required otherwise.

3.39 The CSGRotation class

The **CSGRotation** element represents a rotation transformation on a *CSGNode* (a transformation or set operation on one or a set of **CSGPrimitives**) or a **CSGPrimitive** about the axes defined in the **Geometry**. This element has 4 attributes:

3.39.1 The rotateX, rotateY, and rotateZ attributes

The rotate attributes are of type double, and must be defined for the same number of CoordinateComponents as are present in the parent Geometry. If all three are defined, they define a point in space that determines the vector (from the origin) of the axis about which the rotation is to occur in three-dimensional space. They must therefore not all be equal to zero. If two are defined (rotateX and rotateY), they define the point in two-dimensional space about which the rotation is to occur. (In this case, (0,0) would be legal.) Nothing can be rotated in 1-dimensional space, and therefore defining only rotateX is meaningless.

3.39.2 The rotateAngleInRadians attribute

The **rotateAngleInRadians** attribute is of type **double**. It represents the rotation angle of the *CSGNode*, in radians, along the defined axis. In three-dimensional space, this rotation is defined as counterclockwise from the perspective of the origin, viewing the constructed vector. In two-dimensional space, this rotation is defined the same way, as a counterclockwise rotation along the *Z* axis emerging from the defined point. From the perspective of the surface of the shape, this view looks down the negative side of the *Z* axis, appearing as a clockwise rotation.

Overall, the rotate attributes define where the rotation is to occur, and the rotateAngleInRadians define how much rotation is to take place. A rotateAngleInRadians value of "0" would therefore define a CSGRotation that left the shape fixed in space.

3.40 The CSGScale class

The **CSGScale** element represents a scale transformation on a *CSGNode* (a transformation or set operation on one or a set of **CSGPrimitives**) or a **CSGPrimitive** along the axes defined in the **Geometry**. All scaling occurs collectively for the component primitive shapes, and the expansion occurs from the geometrical center of the object, i.e. the center of the smallest bounding box that would contain the current volume of the object. This means, for example,

that if the child of the **CSGScale** object is a hemisphere, defined as the intersection of a sphere and a cube, the bounding box would be half the size of a box that would have included the original entire sphere.

This element has 3 attributes:

3.40.1 The scaleX attribute

The **scaleX** required attribute is of type **double**. It represents the amount of scaling of the **CSGNode** along the x-axis (the **CoordinateComponent** with the **type** of "cartesianX").

3.40.2 The scaleY attribute

The scaleY attribute is of type double. It represents the amount of scaling of the *CSGNode* along the y-axis (the CoordinateComponent with the type of "cartesianY"). This attribute must not be defined if no such Coordinate-Component is present in the parent Geometry, and is required otherwise.

3.40.3 The scaleZ attribute

The scaleZ attribute is of type double. It represents the amount of scaling of the *CSGNode* along the z-axis (the CoordinateComponent with the type of "cartesianZ"). This attribute must not be defined if no such Coordinate-Component is present in the parent Geometry, and is required otherwise.

The amount of scaling for all three attributes is relative to the original size of the object. In other words, if a **CSGScale** object has a **scaleX** value of "**1.0**", is it not scaled along the X axis at all, with "**0.5**" halving it, "**2.0**" doubling it, and "**0.0**" making the entire object disappear completely. Negative values produce effective inversions of the object, e.g. inverting a unit cone by giving it a **scaleZ** scaling factor of "-1".

3.41 The CSGHomogeneousTransformation class

The **CSGHomogeneousTransformation** element represents a homogeneous transformation on a **CSGNode**: a transformation or set operation on one or more **CSGPrimitives**. This element contains two **TransformationComponent** elements: a **forwardTransformation** and a **reverseTransformation**, both of type **TransformationComponent**.

Lucian: Still trying to track down whether anyone has implemented 'reverseTransformation'. If not, we'll remove it from the spec as unnecessary, and just leave 'forwardTransformation'.

3.42 The TransformationComponent class

The **TransformationComponent** element represents an affine transformation that can be applied to a *CSGNode*. This element has the following two attributes:

3.42.1 The components attribute

The **components** attribute is of type **doubleArray**, whose values represent the affine transformation. This attribute is required.

An affine transformation is essentially a method to transform a shape's scale, rotation, and translation all at once instead of breaking it down into its component tranformations.

Lucian: If someone can concisely explain the algorithm at work here, and can send it to me, I will put it into the spec, because despite reading up on affine transformations on Wikipedia, I don't understand it well enough to explain how you get from a vector of components to a transformed shape.

3.42.2 The componentsLength attribute

The componentsLength attribute is of type int and is required. It represents the array length of the components attribute (number of values in the components array).

3.43 CSGObject examples

The following is an example of a **CSGObject** which has been scaled, rotated, and translated:

The manipulations can be read from the inside out: at the base level, we have the **CSGPrimitive** sphere: a sphere with radius 1.0, centered at the origin. It's then scaled such that it is compressed along each axis by different amounts: along the X axis to 7.5833%, along the Y axis to 8.0451%, and along the Z axis to 2.9583%. Then the scaled figure is rotated around a vector with its origin at (0,0,0) and its point at (2.4391, 1.5373, 0.58404), by 0.9104 radians. Finally, it is translated by 5.439 along the X axis, 5.88 along the Y axis, and 1.078 along the Z axis.

In this second example, a hemisphere is created through the intersection of a primitive sphere and translated cube:

3.44 The ParametricGeometry class

ParametricGeometry is a type of *GeometryDefinition* that parametrically defines geometric strucutures/domains. The ParametricGeometry element is defined with a SpatialPoints object and a listOfParametricObjects that is a collection of ParametricObjects. Each point in the SpatialPoints list is given an index, and those indices are used in the creation of each ParametricObject. There may be points whose indices are never used; this does not affect the ParametricGeometry. Figure 17 on the next page shows the definition of the ParametricGeometry object.

3.45 The SpatialPoints class

The **SpatialPoints** element represents the set of points to be used as vertices in the **ParametricGeometry**. In essence, the **SpatialPoints** defines a lattice on which each **ParametricObject** is to be drawn. There may be unused points in the list if no **ParametricObject** ever uses that index to draw its shape.

3.45.1 The compression attribute

The required **compression** attribute is of type **CompressionKind**. It is used to specify the compression used when encoding the data, and can have the value "**uncompressed**" if no compression was used, or "**deflated**" if the deflation algorithm was used to compress the text version of the data.

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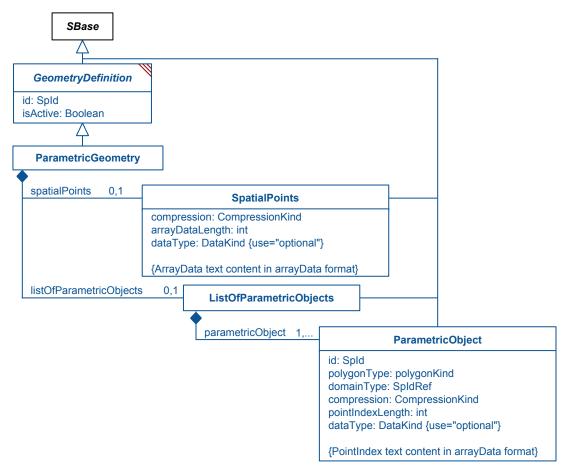


Figure 17: The definition of the ParametricGeometry, SpatialPoints, ListOfParametricObjects, and ParametricObject classes.

3.45.2 The arrayDataLength attribute

The arrayDataLength attribute is of type int and is required. It represents the array length of the arrayData text child of this node. If uncompressed, this will equal the total number of coordinates, but if compressed, this will equal the new compressed length of the array, not including any added whitespace. It is included for convenience and validation purposes.

3.45.3 The dataType attribute

The dataType attribute is of type DataKind and is optional. It is used to specify the type of the data being stored. The value "double" is used to indicate double-precision (64-bit) floating point values; "float" to indicate single-precision (32-bit) floating point values, and "uint8", "uint16", and "uint32" to indicate 8-bit, 16-bit, and 32-bit unsigned integer values, respectively. This attribute is required so that the compressed data can be properly uncompressed.

3.45.4 The ArrayData text child

The ArrayData text child of the **SpatialPoints** is in arrayData format, and represents an ordered list of sets of coordinates that will be used as the vertices of **ParametricObject** elements in this **ParametricGeometry**, with "0" representing the first such coordinate, "1" the second, etc. The list will define vertexes with as many values as there are **CoordinateComponent** children of the parent **Geometry**: three values for representing the X, Y, and Z coordinates (respectively) of 3-dimensional geometries, or two values for representing the X and Y coordinates (respectively) of

2-dimensional geometries. (**ParametricGeometry** elements cannot be created in 1-dimensional geometries.) It is suggested, but not required, that if the data is uncompressed, that the grouped points be separated from each other with the use of a semicolon. If the data is compressed, a semicolon is not to be used.

3.46 The ParametricObject class

The **ParametricObject** element represents a single parametric geometry object. It contains a list of point indices from the parent **ParametricGeometry**'s **SpatialPoints**, which collectively define the faces of the object.

3.46.1 The id attribute

The **id** attribute is a required attribute of type **SpId**. It uniquely identifies the **ParametricObject** element. It has no mathematical meaning, and cannot be connected to a **Parameter** via a **SpatialSymbolReference** element.

3.46.2 The polygonType attribute

The polygonType attribute is of type PolygonKind and is a required attribute. It represents the type of polygon that describes the ParametricObject. ParametricObject elements of type "triangle" have three points, and those of type "quadrilateral" have four.

3.46.3 The domainType attribute

The domainType attribute is of type SpIdRef and is a required attribute. It is a reference to the id of the DomainType that this ParametricObject represents.

3.46.4 The compression attribute

The required **compression** attribute is of type **CompressionKind**. It is used to specify the compression used when encoding the data, and can have the value "**uncompressed**" if no compression was used, or "**deflated**" if the deflation algorithm was used to compress the text version of the data.

3.46.5 The pointIndexLength attribute

The pointIndexLength attribute is of type int and is required. It represents the array length of the arrayData text child of this node. If uncompressed, this will equal the number of referenced indices, but if compressed, this will equal the new compressed length of the array, not including any added whitespace. It is included for convenience and validation purposes.

3.46.6 The dataType attribute

The dataType attribute is of type DataKind and is optional. It is used to specify the type of the data being stored. Because all of the data will be indexes into the ArrayData of the SpatialPoints element, the allowed formats are "uint8", "uint16", and "uint32" to indicate 8-bit, 16-bit, and 32-bit unsigned integer values, respectively. The values "double" and "float" are not to be used. This attribute is required so that the compressed data can be properly uncompressed.

3.46.7 The PointIndex text child

The PointIndex text child of the ParametricObject is in arrayData format, and represents an ordered list of indices that refer to elements in the SpatialPoints array and are interpreted by considering the polygonType attribute of the ParametricObject with a value of "triangle" indicating that the data is to be grouped in sets of three, and a value of "quadrilateral" indicating that the data is to be grouped in sets of four. The sequence of indices must follow adjacent edges, with an implied edge between the first and last vertex. Additionally, the order of that sequence should be consistently clockwise or counter-clockwise for any contiguous surface. This can be accomplished by ensuring that when an edge is used for two different faces, the order of that edge is reversed for the second face. It is

suggested, but not required, that if the data is uncompressed, that the grouped points be separated from each other with the use of a semicolon. If the data is compressed, a semicolon is not to be used. Each set of indices that define a polygon face should each refer to a different location. This means that one should not re-use index values with a single polygon face, nor should one use two index values in the same face that are mapped to the same location.

3.47 A ParametricGeometry example

As an example, if the **SpatialPoints** element in a three-dimensional **Geometry** is:

```
<spatialPoints compression="uncompressed" arrayDataLength="24">
     0 0 0; 0 0 1; 0 1 0; 1 0 0; 0 1 1; 1 0 1; 1 1 0; 1 1 1
</spatialPoints>
```

This defines eight points, with point '0' at coordinates [0, 0, 0], point '1' at coordinates [0, 0, 1], etc., that happen to form the vertexes of a cube. These point indexes are then used in the following **ParametricObject**:

This defines a pyramid with four triangular faces. The first triangle is defined by points [0,0,0], [0,1,0], and [0,1,1]; the second triangle by points [0,0,0], [1,1,0], and [0,1,0]; the third by [0,0,0], [0,1,1], and [1,1,0]; and the fourth by [0,1,0], [1,1,0], and [0,1,1]. Note also that the order of the faces is consistent, defining each face in a counter-clockwise order, as observed from 'outside' the pyramid. This can be seen, for example, in the last two faces defined, where the shared edge is defined in the order '5 6' in the first face, but '6 5' in the second.

A more realistic example can be found below, though most of the values are elided for reasons of space:

```
<spatial:parametricGeometry spatial:id="id051101043048054" spatial:isActive="true">
  <spatial:spatialPoints spatial:compression="uncompressed" spatial:arrayDataLength="179901">
        -0.472894296 -0.4420042305 -0.457890447 [...]
        0.830988196507629 0.857225748552666 0.827138489800772
  </spatial:spatialPoints>
  <spatial:listOfParametricObjects>
    <spatial:parametricObject spatial:id="nucObj" spatial:polygonType="triangle"</pre>
                              spatial:domainType="nuc" spatial:pointIndexLength="24414"
                              spatial:compression="uncompressed">
        69 225 253 247 217 24 181 451 452 [...] 732 2417 3925
    </spatial:parametricObject>
    <spatial:parametricObject spatial:id="cellObj" spatial:polygonType="triangle"</pre>
                              spatial:domainType="cell" spatial:pointIndexLength="46242"
                              spatial:compression="uncompressed">
        423 8 418 2240 439 180 187 97 299 [...] 8197 1262 3043
    </spatial:parametricObject>
  </spatial:listOfParametricObjects>
</spatial:parametricGeometry>
```

Here, an array of 179901 values is defined in the **SpatialPoints** object. Because this is a model with 3D geometry (described elsewhere in the model), the points are grouped in threes, with the first value representing the X value for the first point, the second value the Y of the first point, and the third the Z value of the first point. The next value (elided) would be the X value of the second point, etc., until the final three values encode the final point, for a total of 59967 points (179901/3). The first point (-0.472894296, -0.4420042305, -0.457890447) is referenced by its index of "0", the second by its index of "1", etc., through (0.830988196507629, 0.857225748552666, 0.827138489800772) for the point with index 59966.

These points are then used as in two meshes: one for the nucObj, and one for the cellObj. Because both have the polygonType "triangle", the list of points are intrepreted in groups of three: (69, 225, 253) being the three vertices

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of the first triangle of "nuc0bj", (245, 217, 24) the vertices of the second, etc. Similarly, (423, 8, 418) is the first defined triangle for "cel10bj", and (8197, 1262, 3043) the last.

Because so many values were included, a decision was made to omit the optional ";" characters, which would have principally served to increase the file size.

3.48 The MixedGeometry class

A MixedGeometry defines a Geometry constructed from a collection of various GeometryDefinition objects that together define the complete geometry for the Model. It has a child ListOfGeometryDefinitions object that behaves exactly the same as the ListOfGeometryDefinitions child of the Geometry, but instead of that collection of geometry definitions defining alternate geometries, or alternate ways to define one geometry, the collection of geometry definitions in a MixedGeometry together define a single space. For example, a MixedGeometry may contain a ParametricGeometry that defines the contours of a cell membrane, plus a CSGeometry that defines a sphere that models the nucleus of that cell. The definition of a MixedGeometry is shown in Figure 18. Its OrdinalMapping children define how those geometries overlap one another.

Note that every child *GeometryDefinition* of a **MixedGeometry** must have an **isActive** value of "false". 'Active' geometries are a concept that applies only to the **Model** and its direct children, not to component geometries of a **MixedGeometry**.

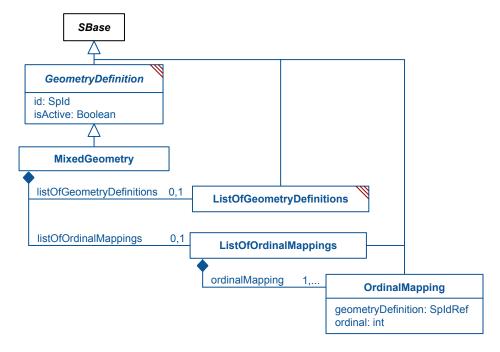


Figure 18: The definition of the MixedGeometry, ListOfOrdinalMappings, and OrdinalMapping classes from the Spatial package. The ListOfGeometryDefinitions class is defined in Section 3.15 on page 18

3.49 The Ordinal Mapping class

A **OrdinalMapping** defines an ordinal level for the various geometries that comprised this **MixedGeometry**. In this way, the overlap between them can be resolved cleanly. There must be exactly one **OrdinalMapping** for each child **GeometryDefinition** of a **MixedGeometry**.

Lucian: Or we could make that a 'should'? 'ordinal' is required in the other places it is used, so 'must' is parallel to that.

3.49.1 The geometryDefinition attribute

The tokengeometryDefinition attribute is of type SpIdRef, and is required. It must reference a direct child *GeometryDefinition* of this MixedGeometry. The ordinal value is then taken to refer to that geometry.

3.49.2 The ordinal attribute

The **ordinal** attribute is of type **int**, and is required. It is used to represent the order of the corresponding **GeometryDefinition** within this **MixedGeometry**. The **ordinal** is useful while reconstructing the geometry in the specific software tool - it represents the order in which each **GeometryDefinition** have to be evaluated.

Rather than struggle with the task of preventing overlapping regions of space from each different *GeometryDefinition*, they are to be considered to be evaluated in the reverse order of their ordinals. In this way, any *GeometryDefinition* that has already been processed will cover those with a smaller ordinal, thus resolving any ambiguities and removing the constraint that each *GeometryDefinition* be disjoint and cover the entire geometric domain. The *GeometryDefinition* with ordinal 0 can be the "background" layer (typically the extracellular space).

No two *GeometryDefinition* elements should have the same ordinal value, even if they should not overlap, because some tools may not calculate the geometries to the same level of precision as other tools, and may end up with overlap due to rounding errors, and will still need to resolve the ambiguity for their own purposes. If a software tool discovers two overlapping *GeometryDefinition* elements with the same ordinal value, it may resolve the situation however it sees fit.

Note that these ordinals only apply at the level of the immediate parent MixedGeometry. Any ordinal attribute from any AnalyticVolume or CSGObject applies only at the level of those volumes or objects, and serve to distinguish within-GeometryDefinition layout order, not between-GeometryDefinition layout order, defined here. Likewise, if a GeometryDefinition child of a MixedGeometry it itself a MixedGeometry, those ordinals also only apply at the level of that MixedGeometry, and not at the level of the parent MixedGeometry.

3.50 The SampledField class

A **SampledField** is a sampled scalar field such as an image or samples from a level set. The attributes of **SampledField** represent the specification of a sample dataset (the number of samples in x, y, z coordinates, data type of the sample representation, etc.) and the text child of the **SampledField** is the actual sampled data, defined in **Figure 19**. The purpose of a **SampledField** is to fill the **Geometry** with values that can be used in math and/or in **SampledFieldGeometry** elements. Values are defined at lattice points within the **Geometry**, and are interpolated to fill the remainder of all off-lattice locations.

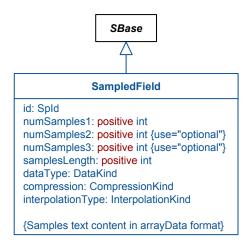


Figure 19: The definition of the SampledField class from the Spatial package.

3.50.1 The id attribute

The id attribute identifies a **SampledField**. It is of type **SpId** and is a required attribute. The mathematical value of a **SampledField** is the value and dimensionality of the field itself, and can be bound to a **Parameter** by using a **SpatialSymbolReference**. If used in conjunction with the SBML Level 3 "arrays" package, it can be used and manipulated as if it was an array of the appropriate dimensions, even though its *meaning* is the value of the field at all points within its borders, not just those at the lattice points. However, even without the use of the "arrays" package, it can be used in SBML Level 3 Version 1 Core MathML to set the value of a spatially-distributed SBML symbol such as a **Species** or **Parameter**, such as through an **InitialAssignment**, **Rule**, or **EventAssignment**.

The size of the field is assumed to match the axes (the CoordinateComponent children) of the parent Geometry, and is assumed to be regularly spaced in each dimension, but is not required to be spaced the same way in all dimensions. In other words, if the Geometry defines a 10 cm by 10 cm square, and a SampledField is a 10x5 array, the "[0,0]" entry in the array will correspond to the point "0 cm, 0 cm" in the Geometry, and the "[10,5]" entry in the array will correspond to the point "10 cm, 10 cm" in the Geometry. Off-latice points (such as the value at "9 cm, 9 cm" in this example) have no direct corresponding value in the SampledField, and are determined according to the interpolationType attribute, defined below.

When tied to a **SpatialSymbolReference**, regardless of its useage, each **SampledField** still must represent values across the entire **Geometry**. If used in an **InitialAssignment** to assign values to a **Species** that only exists in a particular **DomainType** within the **Geometry**, entries in the **SampledField** that correspond to areas of space not covered by that **DomainType** will simply be ignored. Those values may be set to zero, or could be used in other contexts. For example, a **SampledField** could represent 'the concentration of ATP in the Geometry', and one **InitialAssignment** could be used to apply the field to the species 'ATP in the cytosol' and a second **InitialAssignment** could be used to apply the same field to the species 'ATP in the nucleus', with different values being examined and used in each case.

When used in a **SampledFieldGeometry**, again, the values of the field are interpolated to all off-lattice points to determine whether or not any arbitrary location within the **Geometry** is part of a given **SampledVolume** or not.

3.50.2 The interpolationType attribute

The required interpolationType attribute is type InterpolationKind. It is used to specify how values at off-lattice locations are to be calculated. A value of "nearestNeighbor" means that the nearest lattice point value is to be returned. A value of "linear" means that the value to be returned is the linear interpolation from nearby lattice points, either simple linear in the case of one-dimensional interpolation, bilinear in the case of two-dimensional interpolation.

3.50.3 The numSamples1, numSamples2, numSamples3 attributes

The numSamples1, numSamples2, and numSamples3 attributes represent the number of samples in each of the coordinate components. (e.g. numX, numY, numZ) in an image dataset. These attributes are of type positive int and are required to specify the SampledField. The samples are assumed to be uniformly sampled. It is required to have as many numSamples attributes as there are CoordinateComponent elements in the Geometry, with numSamples1 defined if there is a cartesianX element; numSamples2 defined if there is a cartesianY element, and numSamples3 defined if there is a cartesianZ element, each attribute corresponding to the CoordinateComponent with the respective type.

3.50.4 The compression attribute

The required **compression** attribute is of type **CompressionKind**. It is used to specify the compression used when encoding the data, and can have the value "**uncompressed**" if no compression was used, or "**deflated**" if the deflation algorithm was used to compress the text version of the data.

3.50.5 The samplesLength attribute

The samplesLength attribute is of type positive int and is required. It represents the array length of the arrayData text child of this node. If uncompressed, this will equal the product of the numSamples* attributes, but if compressed, this will equal the new compressed length of the array, not including any added whitespace. It is included for convenience and validation purposes.

3.50.6 The dataType attribute

The dataType attribute is of type DataKind and is optional. It is used to specify the type of the data being stored. The value "double" is used to indicate double-precision (64-bit) floating point values; "float" to indicate single-precision (32-bit) floating point values, and "uint8", "uint16", and "uint32" to indicate 8-bit, 16-bit, and 32-bit unsigned integer values, respectively.

3.50.7 The Samples text child

The Samples text child of the SampledField is where the data for the SampledField resides. It is of type arrayData, which is defined as whitespace-delimited, possibly-compressed numerical values. Whether or not the data is compressed (and how, if so) is stated with the compression attribute, and the type of numerical values included is stated in the dataType attribute. The total number of entries in the array can be derived from the numSamples attributes, by multiplying them together (if present). It is suggested, but not required, that if the data is uncompressed, that the grouped points be separated from each other with the use of a semicolon. If the data is compressed, a semicolon is not to be used.

3.50.8 A SampledField example

Here are snippets of an example in which a **SampledField** element is used in an initial assignment, where the field's value inside the nucleus ("img") is used in a formula to compute the ATP level:

```
<species id="ATP_nuc" compartment="Nucleus" hasOnlySubstanceUnits="false"</pre>
           boundaryCondition="false" constant="false" spatial:isSpatial="true"/>
 <parameter id="img" constant="false">
    <spatial:spatialSymbolReference spatial:spatialRef="imgvals"/>
 </parameter>
 <initialAssignment symbol="ATP_nuc">
    <math xmlns="http://www.w3.org/1998/Math/MathML">
        <plus/>
        <apply>
          <divide/>
          <ci> img </ci>
          <cn type="integer"> 2 </cn>
        </apply>
        <cn type="integer"> 3 </cn>
      </apply>
    </initialAssignment>
[...]
  <spatial:sampledField spatial:id="imgvals" spatial:dataType="uint8"</pre>
           spatial:numSamples1="51" spatial:numSamples2="59"
spatial:numSamples3="23" spatial:interpolationType="linear"
           spatial:compression="uncompressed" spatial:samplesLength="1255">
    120 218 237 221 235 114 219 48 [...]
  </spatial:sampledField>
```

4 Examples

Several models have been created to demonstrate the basic capabilities of the 'spatial' package. Most of the smaller examples in this specification are snippets from these models.

- https://sourceforge.net/p/sbml/code/HEAD/tree/trunk/specifications/sbml-level-3/version-1/spatial/specification/examples/analytic_3d.xml: An example that uses the **AnalyticGeometry** construct to define spatial domains by the application of mathematical formulas.
- https://sourceforge.net/p/sbml/code/HEAD/tree/trunk/specifications/sbml-level-3/version-1/ spatial/specification/examples/csg0nly.xml: An example that uses the CSGeometry construct to define spatial domains through building elements based on primitive shapes.
- https://sourceforge.net/p/sbml/code/HEAD/tree/trunk/specifications/sbml-level-3/version-1/ spatial/specification/examples/parametric_1dom.xml: An example that uses the ParametricGeometry construct to define spatial domains through building a mesh that defines a surface.
- https://sourceforge.net/p/sbml/code/HEAD/tree/trunk/specifications/sbml-level-3/version-1/spatial/specification/examples/parametric_2dom.xml: A slightly more complicated ParametricGeometry example that defines three nested three-dimensional domains, with two-dimensional domains at the boundaries.
- https://sourceforge.net/p/sbml/code/HEAD/tree/trunk/specifications/sbml-level-3/version-1/spatial/specification/examples/sampledfield_3d.xml: An example that uses the SampledFieldGeometry construct to define spatial domains through assigning different values in a field (such as those produced in an image) to different domains.
- https://sourceforge.net/p/sbml/code/HEAD/tree/trunk/specifications/sbml-level-3/version-1/spatial/specification/examples/sampledfield_asnt.xml: The same SampledFieldGeometry example extended to use the SampledField values in an initial assignment for a species.

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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 Spatial Processes. 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 Spatial Processes 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 Spatial Processes 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 Spatial Processes package.

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

General rules about this package

- spatial-10101

 ✓ To conform to the Spatial Processes specification for SBML Level 3 Version 1, an SBML document must declare "http://www.sbml.org/sbml/level3/version1/spatial/version1" as the XMLNamespace to use for elements of this package. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1 Section 3.2 on page 8.)
- spatial-10102
 ✓ Wherever they appear in an SBML document, elements and attributes from the Spatial Processes must use the "http://www.sbml.org/sbml/level3/version1/spatial/version1" namespace, declaring so either explicitly or implicitly. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1 Section 3.2 on page 8.)

General rules about identifiers

- spatial-10301
 ✓ (Extends validation rule #10301 in the SBML Level 3 Version 1 Core specification. TO DO list scope of ids) (Reference: SBML Level 3 Version 1 Core, Section 3.1.7.)
- spatial-10302 ✓ The value of a spatial:id must conform to the syntax of the SBML data type SId (Reference: SBML Level 3 Version 1 Core, Section 3.1.7.)

Rules for the extended SBML class

- spatial-20101 ☑ In all SBML documents using the Spatial Processes, the SBML object must have the spatial:-required attribute. (Reference: SBML Level 3 Version 1 Core, Section 4.1.2.)
- spatial-20102

 ✓ The value of attribute spatial:required on the SBML object must be of data type boolean. (Reference: SBML Level 3 Version 1 Core, Section 4.1.2.)
- spatial-20103 ✓ The value of attribute spatial:required on the SBML object must be set to "true". (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1 Section 3.2 on page 8.)

Rules for extended Model object

spatial-20201 ✓ A Model object may contain one and only one instance of the Geometry element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.4 on page 11.)

Rules for extended Compartment object

spatial-20301

✓ A Compartment object may contain one and only one instance of the CompartmentMapping element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a Compartment object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.5 on page 11.)

Rules for extended Species object

- spatial-20401 ✓ A Species object may have the optional attribute spatial:isSpatial. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a Species object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.7 on page 13.)
- spatial-20402

 ✓ The attribute spatial:isSpatial on a Species must have a value of data type boolean. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.7 on page 13.)

Rules for extended Parameter object

spatial-20501 ✓ A Parameter object may contain one and only one instance of each of the SpatialSymbolReference, AdvectionCoefficient, BoundaryCondition and DiffusionCoefficient elements. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a Parameter object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.8 on page 14.)

Rules for extended Reaction object

- spatial-20601 ✓ A Reaction object must have the required attribute spatial:isLocal. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a Reaction object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.14 on page 17.)
- spatial-20602 ☑ The attribute spatial:isLocal on a Reaction must have a value of data type boolean. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.14 on page 17.)

Rules for DomainType object spatial-20701 \(\text{\sqrt{2}} \) A DomainType object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a **DomainType**. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-20702 A DomainType object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a **DomainType.** (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-20703 ✓ A DomainType object must have the required attributes spatial:id and spatial:spatialDimensions. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a DomainType object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.18 on page 21.) **spatial-20704** ✓ The attribute **spatial:spatialDimensions** on a **DomainType** must have a value of data type integer. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.18 on page 21.) Rules for Domain object spatial-20801 \(\vec{v} \) A Domain object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a Domain. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-20802 \(\text{A Domain} \) A Domain object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a **Domain**. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) **spatial-20803** ✓ A **Domain** object must have the required attributes **spatial:id** and **spatial:domainType**. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a Domain object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.19 on page 22.) spatial-20804 \(\vec{V} \) A Domain object may contain one and only one instance of the ListOfInteriorPoints element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a **Domain** object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.19 on page 22.) spatial-20805 \(\text{The value of the attribute spatial:domainType of a Domain object must be the identifier of an existing object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.19 on page 22.) Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfInteriorPoints container object may only contain InteriorPoint objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.19 on page 22.) spatial-20807 & ListOfInteriorPoints object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfInteriorPoints object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.19 on page 22.) Rules for InteriorPoint object spatial-20901 \(\vec{v} \) An Interior Point object may have the optional SBML Level 3 Core attributes metaid and **sboTerm**. No other attributes from the SBML Level 3 Core namespaces are permitted on

an InteriorPoint. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)

spatial-20902

✓ An Interior Point object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on an **InteriorPoint**. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) An InteriorPoint object must have the required attribute spatial:coordOne, and may have the optional attributes spatial:coordTwo and spatial:coordThree. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on an Interior Point object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.20 on page 23.) **spatial-20904** ✓ The attribute **spatial:coordOne** on an **InteriorPoint** must have a value of data type **double**. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.20 on page 23.) spatial-20905 ✓ The attribute spatial:coordTwo on an InteriorPoint must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.20 on page 23.) **spatial-20906** ✓ The attribute **spatial:coordThree** on an **InteriorPoint** must have a value of data type **double**. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.20 on page 23.) Rules for Boundary object spatial-21001

A Boundary object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a **Boundary**. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21002
A Boundary object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a **Boundary**. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21003 \(\text{A Boundary} \) A Boundary object must have the required attributes spatial:id and spatial:value. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a Boundary object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.17 on page 21.) spatial-21004 The attribute spatial:value on a Boundary must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.17 on page 21.) Rules for AdjacentDomains object spatial-21101 \(\text{ An AdjacentDomains} \) object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on an AdjacentDomains. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21102 ✓ An AdjacentDomains object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on an AdjacentDomains. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21103
An AdjacentDomains object must have the required attributes spatial:id, spatial:domainOne and spatial:domainTwo. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on an AdjacentDomains object. (Reference: SBML Level 3 Package speci-

fication for Spatial Processes, Version 1, Section 3.21 on page 24.)

- spatial-21104 ✓ The value of the attribute spatial:domainOne of an AdjacentDomains object must be the identifier of an existing Domain object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.21 on page 24.)

 spatial-21105 ✓ The value of the attribute spatial:domainTwo of an AdjacentDomains object must be the
- spatial-21105 ✓ The value of the attribute spatial:domainTwo of an AdjacentDomains object must be the identifier of an existing Domain object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.21 on page 24.)

Rules for GeometryDefinition object

- spatial-21201 ✓ A *GeometryDefinition* object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a *GeometryDefinition*. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-21202 ☑ A *GeometryDefinition* object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a *GeometryDefinition*. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-21203 ✓ A *GeometryDefinition* object must have the required attributes spatial:id and spatial:isActive. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a *GeometryDefinition* object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.23 on page 25.)
- spatial-21204

 ✓ The attribute spatial:isActive on a *GeometryDefinition* must have a value of data type boolean. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.23 on page 25.)

Rules for CompartmentMapping object

- spatial-21301 ☑ A CompartmentMapping object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a CompartmentMapping. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-21302 ✓ A CompartmentMapping object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CompartmentMapping. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-21303
 A CompartmentMapping object must have the required attributes spatial:id, spatial:domainType and spatial:unitSize. No other attributes from the SBML Level 3 Spatial
 Processes namespaces are permitted on a CompartmentMapping object. (Reference: SBML
 Level 3 Package specification for Spatial Processes, Version 1, Section 3.6 on page 12.)
- spatial-21304 ✓ The value of the attribute spatial:domainType of a CompartmentMapping object must be the identifier of an existing DomainType object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.6 on page 12.)
- spatial-21305

 ✓ The attribute spatial:unitSize on a CompartmentMapping must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.6 on page 12.)

Rules for CoordinateComponent object

- spatial-21401 ✓ A CoordinateComponent object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a CoordinateComponent. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-21402 🗹 A CoordinateComponent object may have the optional SBML Level 3 Core subobjects for notes

and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CoordinateComponent. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21403 \(\text{ A CoordinateComponent} \) object must have the required attributes spatial:id and spatial:type, and may have the optional attribute spatial:unit. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a **CoordinateComponent** object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.16 on page 20.) spatial-21404 \(\vec{v} \) A CoordinateComponent object must contain one and only one instance of each of the Boundary and Boundary elements. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a CoordinateComponent object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.16 on page 20.) spatial-21405 ✓ The value of the attribute spatial:type of a CoordinateComponent object must conform to the syntax of SBML data type coordinateKind and may only take on the allowed values of coordinateKind defined in SBML; that is, the value must be one of the following: 'cartesianX', 'cartesianY' or 'cartesianZ'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.16 on page 20.) spatial-21406
✓ The value of the attribute spatial:unit on a CoordinateComponent must have a taken from the following: the identifier of a **UnitDefinition** object in the enclosing **Model**, or one of the base units in SBML. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.16 on page 20.) Rules for SampledFieldGeometry object spatial-21501 \(\times \) A SampledFieldGeometry object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a SampledFieldGeometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21502 \(\text{2}}}}} \ext{\ti}\text{\texitile}}\text{\texi}\tint{\text{\text{\text{\text{\text{\texi}\tinz{\text{\texi}\tint{\text{\text{\texit{\text{\text{\texi}\text{\text{\text{\text{\te notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a SampledFieldGeometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21503

✓ A SampledFieldGeometry object must have the required attribute spatial:sampledField. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a SampledFieldGeometry object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.28 on page 27.) spatial-21504 \(\text{ A SampledFieldGeometry} \) object may contain one and only one instance of the ListOfSampled-Volumes element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a SampledFieldGeometry object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.28 on page 27.) spatial-21505 \(\text{T}\) The value of the attribute spatial:sampledField of a SampledFieldGeometry object must be the identifier of an existing SampledField object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.28 on page 27.)

spatial-21506
✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a

ListOfSampledVolumes container object may only contain **SampledVolume** objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.28 on

page 27.)

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spatial-21507 ✓ A ListOfSampledVolumes object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfSampledVolumes object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.28 on page 27.)

Rules for SampledField object

- spatial-21601 ✓ A SampledField object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a SampledField. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-21602 ☑ A SampledField object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a SampledField. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-21603 ✓ A SampledField object must have the required attributes spatial:id, spatial:dataType, spatial:numSamplesOne, spatial:interpolationType, spatial:compression, spatial:-samples and spatial:samplesLength, and may have the optional attributes spatial:-numSamplesTwo and spatial:numSamplesThree. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a SampledField object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.50 on page 41.)
- spatial-21604 ✓ The value of the attribute spatial:dataType of a SampledField object must conform to the syntax of SBML data type dataKind and may only take on the allowed values of dataKind defined in SBML; that is, the value must be one of the following: 'double', 'float', 'uint8', 'uint16' or 'uint32'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.50 on page 41.)
- spatial-21605 ☑ The attribute spatial:numSamplesOne on a SampledField must have a value of data type integer. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.50 on page 41.)
- spatial-21606 ✓ The value of the attribute spatial:interpolationType of a SampledField object must conform to the syntax of SBML data type interpolationKind and may only take on the allowed values of interpolationKind defined in SBML; that is, the value must be one of the following: 'nearestNeighbor' or 'linear'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.50 on page 41.)
- spatial-21607

 ✓ The value of the attribute spatial:compression of a SampledField object must conform to the syntax of SBML data type compressionKind and may only take on the allowed values of compressionKind defined in SBML; that is, the value must be one of the following: 'uncompressed' or 'deflated'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.50 on page 41.)
- spatial-21608 ✓ The value of the attribute spatial:samples of a SampledField object must be an array of values of type Int. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.50 on page 41.)
- spatial-21609 ☑ The attribute spatial:samplesLength on a SampledField must have a value of data type integer. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.50 on page 41.)
- spatial-21610 ☑ The attribute spatial:numSamplesTwo on a SampledField must have a value of data type integer. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.50 on page 41.)

spatial-21611
✓ The attribute spatial:numSamplesThree on a SampledField must have a value of data type integer. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.50 on page 41.) Rules for SampledVolume object spatial-21701 \(\text{Y} \) A SampledVolume object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a **SampledVolume.** (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21702

A SampledVolume object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a **Sampled Volume.** (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21703 ✓ A SampledVolume object must have the required attributes spatial:id, spatial:domainType and spatial:sampledValue, and may have the optional attributes spatial:minValue and spatial:maxValue. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a SampledVolume object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.29 on page 28.) spatial-21704 of the value of the attribute spatial:domainType of a SampledVolume object must be the identifier of an existing **DomainType** object defined in the enclosing **Model** object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.29 on page 28.) spatial-21705

✓ The attribute spatial:sampledValue on a SampledVolume must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.29 on page 28.) **spatial-21706** ✓ The attribute **spatial:minValue** on a **SampledVolume** must have a value of data type **double**. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.29 on page 28.) **spatial-21707** In the attribute **spatial:maxValue** on a **SampledVolume** must have a value of data type **double**. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.29 on page 28.) Rules for AnalyticGeometry object spatial-21801 \(\text{\ti}}\text{\tetx{\text{\tetx{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\texi}\text{\text{\text{\text{\text{\texi}\text{\text{\text{\text{\texi}\text{\text{\text{\tet{\text{\text{\text{\text{\text{\texi}\text{\text{\text{\text{\te sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on an AnalyticGeometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21802 \(\text{ An AnalyticGeometry} \) object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on an AnalyticGeometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.) spatial-21803 🗹 An AnalyticGeometry object may contain one and only one instance of the ListOfAnalyticVolumes element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on an AnalyticGeometry object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.24 on page 25.) spatial-21804
Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfAnalyticVolumes container object may only contain AnalyticVolume objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.24 on page 25.)

spatial-21805 \(\text{A ListOfAnalyticVolumes} \) object may have the optional SBML Level 3 Core attributes metaid

and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on

a **ListOfAnalyticVolumes** object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.24 on page 25.)

Rules for AnalyticVolume object

- spatial-21901 ✓ An AnalyticVolume object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on an AnalyticVolume. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-21902 ✓ An AnalyticVolume object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on an AnalyticVolume. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-21903 ✓ An AnalyticVolume object must have the required attributes spatial:id, spatial:functionType and spatial:domainType, and may have the optional attribute spatial:ordinal. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on an AnalyticVolume object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.25 on page 26.)
- spatial-21904 ✓ An AnalyticVolume object may contain one and only one instance of the ASTNode element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on an AnalyticVolume object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.25 on page 26.)
- spatial-21905

 ✓ The value of the attribute spatial: functionType of an AnalyticVolume object must conform to the syntax of SBML data type functionKind and may only take on the allowed values of functionKind defined in SBML; that is, the value must be one of the following: 'layered'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.25 on page 26.)
- spatial-21906 ✓ The value of the attribute spatial:domainType of an AnalyticVolume object must be the identifier of an existing DomainType object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.25 on page 26.)
- spatial-21907 ☑ The attribute spatial:ordinal on an Analytic Volume must have a value of data type integer. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.25 on page 26.)

Rules for ParametricGeometry object

- spatial-22001 ✓ A ParametricGeometry object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ParametricGeometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22002 ✓ A ParametricGeometry object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a ParametricGeometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22003 ✓ A ParametricGeometry object may contain one and only one instance of each of the Spatial-Points and ListOfParametricObjects elements. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a ParametricGeometry object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.44 on page 36.)
- spatial-22004 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfParametricObjects container object may only contain ParametricObject objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.44 on page 36.)

spatial-22005 ✓ A ListOfParametricObjects object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfParametricObjects object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.44 on page 36.)

Rules for ParametricObject object

- spatial-22101 ☑ A ParametricObject object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ParametricObject. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22102
 ✓ A ParametricObject object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a ParametricObject. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22103 ✓ A ParametricObject object must have the required attributes spatial:id, spatial:polygonType, spatial:domainType, spatial:pointIndex, spatial:pointIndexLength and spatial:-compression, and may have the optional attribute spatial:dataType. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a ParametricObject object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.46 on page 38.)
- spatial-22104 ✓ The value of the attribute spatial:polygonType of a ParametricObject object must conform to the syntax of SBML data type polygonKind and may only take on the allowed values of polygonKind defined in SBML; that is, the value must be one of the following: 'triangle' or 'quadrilateral'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.46 on page 38.)
- spatial-22105

 ✓ The value of the attribute spatial:domainType of a ParametricObject object must be the identifier of an existing DomainType object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.46 on page 38.)
- spatial-22106

 ✓ The value of the attribute spatial:pointIndex of a ParametricObject object must be an array of values of type Int. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.46 on page 38.)
- spatial-22107 ✓ The attribute spatial:pointIndexLength on a ParametricObject must have a value of data type integer. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.46 on page 38.)
- spatial-22108

 ✓ The value of the attribute spatial:compression of a ParametricObject object must conform to the syntax of SBML data type compressionKind and may only take on the allowed values of compressionKind defined in SBML; that is, the value must be one of the following: 'uncompressed' or 'deflated'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.46 on page 38.)
- spatial-22109

 ✓ The value of the attribute spatial:dataType of a ParametricObject object must conform to the syntax of SBML data type dataKind and may only take on the allowed values of dataKind defined in SBML; that is, the value must be one of the following: 'double', 'float', 'uint8', 'uint16' or 'uint32'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.46 on page 38.)

Rules for CSGeometry object

spatial-22201 ☑ A CSGeometry object may have the optional SBML Level 3 Core attributes metaid and sboTerm.

No other attributes from the SBML Level 3 Core namespaces are permitted on a CSGeometry.

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

- spatial-22202
 ✓ A CSGeometry object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CSGeometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22203 ✓ A CSGeometry object may contain one and only one instance of the ListOfCSGObjects element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGeometry object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.31 on page 29.)
- spatial-22204 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfCSGObjects container object may only contain CSGObject objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.31 on page 29.)
- spatial-22205 ✓ A ListOfCSGObjects object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfCSGObjects object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.31 on page 29.)

Rules for CSGObject object

- spatial-22301 ✓ A CSGObject object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a CSGObject. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22302 ✓ A CSGObject object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CSGObject. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22303 ✓ A CSGObject object must have the required attributes spatial:id and spatial:domainType, and may have the optional attribute spatial:ordinal. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGObject object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.32 on page 29.)
- spatial-22304 ✓ A CSGObject object must contain one and only one instance of the CSGNode element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGObject object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.32 on page 29.)
- spatial-22305

 ✓ The value of the attribute spatial:domainType of a CSGObject object must be the identifier of an existing DomainType object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.32 on page 29.)
- spatial-22306

 ✓ The attribute spatial:ordinal on a CSGObject must have a value of data type integer.

 (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.32 on page 29.)

Rules for CSGNode object

- spatial-22401 ✓ A *CSGNode* object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a *CSGNode*. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22402 ✓ A *CSGNode* object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a *CSGNode*. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)

spatial-22403 ✓ A CSGNode object may have the optional attribute spatial:id. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGNode object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.33 on page 31.)

Rules for CSGTransformation object

spatial-22501 ✓ A CSGTransformation object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a CSGTransformation. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)

spatial-22502 ✓ A CSGTransformation object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CSGTransformation. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)

spatial-22503 ✓ A *CSGTransformation* object may contain one and only one instance of the CSGNode element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a *CSGTransformation* object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.37 on page 33.)

Rules for CSGTranslation object

- spatial-22601 ✓ A CSGTranslation object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a CSGTranslation. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22602 ☑ A CSGTranslation object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CSGTranslation. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22603 ✓ A CSGTranslation object must have the required attribute spatial:translateX, and may have the optional attributes spatial:translateY and spatial:translateZ. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGTranslation object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.38 on page 34.)
- spatial-22604

 ✓ The attribute spatial:translateX on a CSGTranslation must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.38 on page 34.)
- spatial-22605 ☑ The attribute spatial:translateY on a CSGTranslation must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.38 on page 34.)
- spatial-22606 ✓ The attribute spatial:translateZ on a CSGTranslation must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.38 on page 34.)

Rules for CSGRotation object

- spatial-22701
 ✓ A CSGRotation object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a CSGRotation. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22702 ✓ A CSGRotation object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CSGRotation. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)

spatial-22703 ✓	A CSGRotation object must have the required attributes spatial:rotateX and spatial:rotateAngleInRadians, and may have the optional attributes spatial:rotateY and spatial:rotateZ. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGRotation object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.39 on page 34.)	1 2 3 4 5
spatial-22704 🗹	The attribute spatial:rotateX on a CSGRotation must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.39 on page 34.)	6 7 8
spatial-22705 ✓	The attribute spatial:rotateAngleInRadians on a CSGRotation must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.39 on page 34.)	9 10 11
spatial-22706	The attribute spatial:rotateY on a CSGRotation must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.39 on page 34.)	12 13 14
spatial-22707 🗹	The attribute spatial:rotateZ on a CSGRotation must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.39 on page 34.)	15 16 17
Rules for CSGSc	ale object	18
spatial-22801 ✓	A CSGScale object may have the optional SBML Level 3 Core attributes metaid and sboTerm . No other attributes from the SBML Level 3 Core namespaces are permitted on a CSGScale . (Reference: SBML Level 3 Version 1 Core, Section 3.2.)	19 20 21
spatial-22802 ✓	A CSGScale object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CSGScale . (Reference: SBML Level 3 Version 1 Core, Section 3.2.)	22 23 24
spatial-22803 ✓	A CSGScale object must have the required attribute spatial:scaleX , and may have the optional attributes spatial:scaleY and spatial:scaleZ . No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGScale object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.40 on page 34.)	25 26 27 28
spatial-22804	The attribute spatial: scaleX on a CSGScale must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.40 on page 34.)	29 30 31
spatial-22805 ✓	The attribute spatial:scaleY on a CSGScale must have a value of data type double . (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.40 on page 34.)	32 33 34
spatial-22806	The attribute spatial: scaleZ on a CSGScale must have a value of data type double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.40 on page 34.)	35 36 37
Rules for CSGHo	omogeneousTransformation object	38
spatial-22901 ✓	A CSGHomogeneousTransformation object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a CSGHomogeneousTransformation . (Reference: SBML Level 3 Version 1 Core, Section 3.2.)	39 40 41 42

- spatial-22902

 ✓ A CSGHomogeneousTransformation object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CSGHomogeneousTransformation. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-22903 ✓ A CSGHomogeneousTransformation object must contain two child TransformationComponent elements, one with the name 'forwardTransformation' and the other with the name 'reverseTransformation'. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGHomogeneousTransformation object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.41 on page 35.)

Rules for TransformationComponent object

- spatial-23001 ✓ A TransformationComponent object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a TransformationComponent. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23002 ✓ A TransformationComponent object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a TransformationComponent. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23003 ☑ A TransformationComponent object must have the required attributes spatial:components and spatial:componentsLength. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a TransformationComponent object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.42 on page 35.)
- spatial-23004 ✓ The value of the attribute spatial:components of a TransformationComponent object must be an array of values of type Double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.42 on page 35.)
- spatial-23005 ☑ The attribute spatial:componentsLength on a TransformationComponent must have a value of data type integer. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.42 on page 35.)

Rules for CSGPrimitive object

- spatial-23101 ✓ A CSGPrimitive object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a CSGPrimitive. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23102 ☑ A CSGPrimitive object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CSGPrimitive. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23103 ✓ A CSGPrimitive object must have the required attribute spatial:primitiveType. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGPrimitive object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.34 on page 31.)
- spatial-23104 ✓ The value of the attribute spatial:primitiveType of a CSGPrimitive object must conform to the syntax of SBML data type primitiveKind and may only take on the allowed values of primitiveKind defined in SBML; that is, the value must be one of the following: 'sphere', 'cube', 'cylinder', 'cone', 'circle' or 'square'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.34 on page 31.)

Rules for CSGSetOperator object

- spatial-23201 ☑ A CSGSetOperator object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a CSGSetOperator. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23202 ✓ A CSGSetOperator object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a CSGSetOperator. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23203
 ✓ A CSGSetOperator object must have the required attribute spatial:operationType, and may have the optional attributes spatial:complementA and spatial:complementB. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGSetOperator object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.35 on page 32.)
- spatial-23204 ✓ A CSGSetOperator object may contain one and only one instance of the ListOfCSGNodes element. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a CSGSetOperator object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.35 on page 32.)
- spatial-23205

 ✓ The value of the attribute spatial:operationType of a CSGSetOperator object must conform to the syntax of SBML data type setOperation and may only take on the allowed values of setOperation defined in SBML; that is, the value must be one of the following: 'union', 'intersection' or 'relativeComplement'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.35 on page 32.)
- spatial-23206

 ✓ The value of the attribute spatial:complementA of a CSGSetOperator object must be the identifier of an existing *CSGNode* object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.35 on page 32.)
- spatial-23207 ✓ The value of the attribute spatial:complementB of a CSGSetOperator object must be the identifier of an existing *CSGNode* object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.35 on page 32.)
- spatial-23208 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfCSGNodes container object may only contain *CSGNode* objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.36 on page 32.)
- spatial-23309 ✓ A ListOfCSGNodes object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfCSGNodes object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.36 on page 32.)

Rules for SpatialSymbolReference object

- spatial-23301 ✓ A SpatialSymbolReference object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a SpatialSymbolReference. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23302 ☑ A SpatialSymbolReference object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a SpatialSymbolReference. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23303

 ✓ A SpatialSymbolReference object must have the required attribute spatial: spatialRef. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a

	SpatialSymbolReference object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.9 on page 15.)		
spatial-23304	The value of the attribute spatial:spatialRef of a SpatialSymbolReference object must be the identifier of an existing Geometry object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.9 on page 15.)		
Rules for DiffusionCoefficient object			
spatial-23401 ✓	A DiffusionCoefficient object may have the optional SBML Level 3 Core attributes metaid and sboTerm . No other attributes from the SBML Level 3 Core namespaces are permitted on a DiffusionCoefficient . (Reference: SBML Level 3 Version 1 Core, Section 3.2.)		
spatial-23402 ✓	A DiffusionCoefficient object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a DiffusionCoefficient . (Reference: SBML Level 3 Version 1 Core, Section 3.2.)		
spatial-23403 ✓	A DiffusionCoefficient object must have the required attributes spatial:variable and spatial:-type , and may have the optional attributes spatial:coordinateReferenceOne and spatial:-coordinateReferenceTwo . No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a DiffusionCoefficient object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.10 on page 15.)		
spatial-23404 ✓	The value of the attribute spatial:variable of a DiffusionCoefficient object must be the identifier of an existing Species object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.10 on page 15.)		
spatial-23405 ✓	The value of the attribute spatial:type of a DiffusionCoefficient object must conform to the syntax of SBML data type diffusionKind and may only take on the allowed values of diffusionKind defined in SBML; that is, the value must be one of the following: 'isotropic', 'anisotropic' or 'tensor'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.10 on page 15.)		
spatial-23406 ✓	The value of the attribute spatial:coordinateReferenceOne of a DiffusionCoefficient object must conform to the syntax of SBML data type coordinateKind and may only take on the allowed values of coordinateKind defined in SBML; that is, the value must be one of the following: 'cartesianX', 'cartesianY' or 'cartesianZ'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.10 on page 15.)		
spatial-23407 ✓	The value of the attribute spatial:coordinateReferenceTwo of a DiffusionCoefficient object must conform to the syntax of SBML data type coordinateKind and may only take on the allowed values of coordinateKind defined in SBML; that is, the value must be one of the following: 'cartesianX', 'cartesianY' or 'cartesianZ'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.10 on page 15.)		
Rules for Advect	ionCoefficient object		
spatial-23501 ✓	An AdvectionCoefficient object may have the optional SBML Level 3 Core attributes metaid and sboTerm . No other attributes from the SBML Level 3 Core namespaces are permitted on an AdvectionCoefficient . (Reference: SBML Level 3 Version 1 Core, Section 3.2.)		
spatial-23502	An AdvectionCoefficient object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on an AdvectionCoefficient . (Reference: SBML Level 3 Version 1 Core, Section 3.2.)		
spatial-23503 🇹	An AdvectionCoefficient object must have the required attributes spatial:variable and		

spatial:coordinate. No other attributes from the SBML Level 3 Spatial Processes names-

- paces are permitted on an **AdvectionCoefficient** object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.11 on page 15.)
- spatial-23504 ✓ The value of the attribute spatial:variable of an AdvectionCoefficient object must be the identifier of an existing Species object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.11 on page 15.)
- spatial-23505

 ✓ The value of the attribute spatial:coordinate of an AdvectionCoefficient object must conform to the syntax of SBML data type coordinateKind and may only take on the allowed values of coordinateKind defined in SBML; that is, the value must be one of the following: 'cartesianX', 'cartesianY' or 'cartesianZ'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.11 on page 15.)

Rules for BoundaryCondition object

- spatial-23601 ☑ A BoundaryCondition object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a BoundaryCondition. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23602 ✓ A BoundaryCondition object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a BoundaryCondition. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23603 ✓ A BoundaryCondition object must have the required attributes spatial:variable and spatial:type, and may have the optional attributes spatial:coordinateBoundary and spatial:boundaryDomainType. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a BoundaryCondition object. (Reference: SBML Level 3 Package
 specification for Spatial Processes, Version 1, Section 3.12 on page 16.)
- spatial-23604 ✓ The value of the attribute spatial:variable of a BoundaryCondition object must be the identifier of an existing Species object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.12 on page 16.)
- spatial-23605 ☑ The value of the attribute spatial:type of a BoundaryCondition object must conform to the syntax of SBML data type boundaryConditionKind and may only take on the allowed values of boundaryConditionKind defined in SBML; that is, the value must be one of the following: 'Robin_valueCoefficient', 'Robin_inwardNormalGradientCoefficient', 'Robin_sum', 'Neumann' or 'Dirichlet'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.12 on page 16.)
- spatial-23606 ✓ The value of the attribute spatial:coordinateBoundary of a BoundaryCondition object must be the identifier of an existing Boundary object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.12 on page 16.)
- spatial-23607

 ✓ The value of the attribute spatial:boundaryDomainType of a BoundaryCondition object must be the identifier of an existing DomainType object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.12 on page 16.)

Rules for Geometry object

spatial-23701 ✓ A Geometry object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a Geometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)

- spatial-23702 ✓ A Geometry object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a Geometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23703 ✓ A Geometry object must have the required attribute spatial:coordinateSystem, and may have the optional attribute spatial:id. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a Geometry object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23704 ✓ A Geometry object may contain one and only one instance of each of the ListOfCoordinate-Components, ListOfDomainTypes, ListOfDomains, ListOfAdjacentDomains, ListOfGeometry-Definitions and ListOfSampledFields elements. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a Geometry object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23705 ✓ The value of the attribute spatial:coordinateSystem of a Geometry object must conform to the syntax of SBML data type geometryKind and may only take on the allowed values of geometryKind defined in SBML; that is, the value must be one of the following: 'cartesian'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23706 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfCoordinateComponents container object may only contain CoordinateComponent objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23707 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfDomainTypes container object may only contain DomainType objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23708 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a

 ListOfDomains container object may only contain Domain objects. (Reference: SBML Level 3

 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23709 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a List-OfAdjacentDomains container object may only contain AdjacentDomains objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23710 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfGeometryDefinitions container object may only contain *GeometryDefinition* objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23711 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfSampledFields container object may only contain SampledField objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23712 ✓ A ListOfCoordinateComponents object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfCoordinateComponents object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23713 ✓ A ListOfDomainTypes object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfDomainTypes object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)

- spatial-23714 ✓ A ListOfDomains object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfDomains object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23715 ✓ A ListOfAdjacentDomains object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfAdjacentDomains object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23716 ✓ A ListOfGeometryDefinitions object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfGeometryDefinitions object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23717 ✓ A ListOfSampledFields object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfSampledFields object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)

Rules for MixedGeometry object

- spatial-23801 ✓ A MixedGeometry object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a MixedGeometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23802 ✓ A MixedGeometry object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a MixedGeometry. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23803 ✓ A MixedGeometry object may contain one and only one instance of each of the ListOfGeometryDefinitions and ListOfOrdinalMappings elements. No other elements from the SBML Level 3 Spatial Processes namespaces are permitted on a MixedGeometry object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.48 on page 40.)
- spatial-23804 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfGeometryDefinitions container object may only contain *GeometryDefinition* objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23805 ✓ Apart from the general notes and annotations subobjects permitted on all SBML objects, a ListOfOrdinalMappings container object may only contain OrdinalMapping objects. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.48 on page 40.)
- spatial-23806 A ListOfGeometryDefinitions object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfGeometryDefinitions object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.15 on page 18.)
- spatial-23807 ✓ A ListOfOrdinalMappings object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a ListOfOrdinalMappings object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.48 on page 40.)

Rules for Ordinal Mapping object

- spatial-23901 ☑ An OrdinalMapping object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on an OrdinalMapping. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23902 ✓ An OrdinalMapping object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on an OrdinalMapping. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-23903 ✓ An OrdinalMapping object must have the required attributes spatial:geometryDefinition and spatial:ordinal. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on an OrdinalMapping object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.49 on page 40.)
- spatial-23904

 ✓ The value of the attribute spatial:geometryDefinition of an OrdinalMapping object must be the identifier of an existing *GeometryDefinition* object defined in the enclosing Model object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.49 on page 40.)
- spatial-23905

 ✓ The attribute spatial:ordinal on an OrdinalMapping must have a value of data type integer.

 (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.49 on page 40.)

Rules for SpatialPoints object

- spatial-24001 ☑ A SpatialPoints object may have the optional SBML Level 3 Core attributes metaid and sboTerm. No other attributes from the SBML Level 3 Core namespaces are permitted on a SpatialPoints. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-24002 A SpatialPoints object may have the optional SBML Level 3 Core subobjects for notes and annotations. No other elements from the SBML Level 3 Core namespaces are permitted on a SpatialPoints. (Reference: SBML Level 3 Version 1 Core, Section 3.2.)
- spatial-24003 ✓ A SpatialPoints object must have the required attributes spatial:id, spatial:compression, spatial:arrayData and spatial:arrayDataLength, and may have the optional attribute spatial:dataType. No other attributes from the SBML Level 3 Spatial Processes namespaces are permitted on a SpatialPoints object. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.45 on page 36.)
- spatial-24004 ✓ The value of the attribute spatial:compression of a SpatialPoints object must conform to the syntax of SBML data type compressionKind and may only take on the allowed values of compressionKind defined in SBML; that is, the value must be one of the following: 'uncompressed' or 'deflated'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.45 on page 36.)
- spatial-24005

 ✓ The value of the attribute spatial:arrayData of a SpatialPoints object must be an array of values of type Double. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.45 on page 36.)
- spatial-24006 ☑ The attribute spatial:arrayDataLength on a SpatialPoints must have a value of data type integer. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.45 on page 36.)
- spatial-24007

 ✓ The value of the attribute spatial:dataType of a SpatialPoints object must conform to the syntax of SBML data type dataKind and may only take on the allowed values of dataKind

defined in SBML; that is, the value must be one of the following: 'double', 'float', 'uint8', 'uint16' or 'uint32'. (Reference: SBML Level 3 Package specification for Spatial Processes, Version 1, Section 3.45 on page 36.)

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References

Andrews, S. S. and Bray, D. (2004). Stochastic simulation of chemical reactions with spatial resolution and single molecule detail. *Physical biology*, 1(3):137.

Blinov, M. L., Faeder, J. R., Goldstein, B., and Hlavacek, W. S. (2004). Bionetgen: software for rule-based modeling of signal transduction based on the interactions of molecular domains. *Bioinformatics*, 20(17):3289–3291.

Donovan, R. M., Tapia, J.-J., Sullivan, D. P., Faeder, J. R., Murphy, R. F., Dittrich, M., and Zuckerman, D. M. (2016). Unbiased rare event sampling in spatial stochastic systems biology models using a weighted ensemble of trajectories. *PLoS computational biology*, 12(2):e1004611.

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

Hoops, S., Sahle, S., Gauges, R., Lee, C., Pahle, J., Simus, N., Singhal, M., Xu, L., Mendes, P., and Kummer, U. (2006). CopasiŮa complex pathway simulator. *Bioinformatics*, 22(24):3067–3074.

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 Novère, 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., and Wang, J. (2003). The Systems Biology Markup Language (SBML): A medium for representation and exchange of biochemical network models. *Bioinformatics*, 19(4):524–531.

Jacquez, J. A. et al. (1985). Compartmental analysis in biology and medicine, volume 2. JSTOR.

Le Novere, N., Bornstein, B., Broicher, A., Courtot, M., Donizelli, M., Dharuri, H., Li, L., Sauro, H., Schilstra, M., Shapiro, B., et al. (2006). Biomodels database: a free, centralized database of curated, published, quantitative kinetic models of biochemical and cellular systems. *Nucleic acids research*, 34(suppl_1):D689–D691.

Li, C., Donizelli, M., Rodriguez, N., Dharuri, H., Endler, L., Chelliah, V., Li, L., He, E., Henry, A., Stefan, M. I., et al. (2010). Biomodels database: An enhanced, curated and annotated resource for published quantitative kinetic models. *BMC systems biology*, 4(1):92.

Loew, L. M. and Schaff, J. C. (2001). The virtual cell: a software environment for computational cell biology. *TRENDS in Biotechnology*, 19(10):401–406.

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

Perez, A. J., Seyedhosseini, M., Deerinck, T. J., Bushong, E. A., Panda, S., Tasdizen, T., and Ellisman, M. H. (2014). A workflow for the automatic segmentation of organelles in electron microscopy image stacks. *Frontiers in neuroanatomy*, 8.

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

Stiles, J. R., Bartol Jr, T. M., Salpeter, E. E., and Salpeter, M. M. (1998). Monte carlo simulation of neuro-transmitter release using mcell, a general simulator of cellular physiological processes. In *Computational neuroscience*, pages 279–284. Springer.

Sullivan, D. P., Arepally, R., Murphy, R. F., Tapia, J.-J., Faeder, J. R., Dittrich, M., and Czech, J. (2015). Design automation for biological models: a pipeline that incorporates spatial and molecular complexity. In *Proceedings of the 25th edition on Great Lakes Symposium on VLSI*, pages 321–323. ACM.

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Tomita, M., Hashimoto, K., Takahashi, K., Shimizu, T., Matsuzaki, Y., Miyoshi, F., Saito, K., Tanida, S., Yugi, K., Venter, J. C., and Hutchison, C. (1999). E-Cell: Software environment for whole cell simulation. *Bioinformatics*, 15(1):72–84.

Zhao, T. and Murphy, R. F. (2007). Automated learning of generative models for subcellular location: building blocks for systems biology. *Cytometry Part A*, 71(12):978–990.

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