SBML Spatial Extension

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libSBML Team

- **Frank Bergmann, Sarah Keating**

Agenda

- Overview of spatial extension proposal
- Application to Multicellular?

L3 Spatial Extension Proposal

- Defines spatial domains for compartments
  - Compartments mapped abstractly (topology)
  - Spatial Domains defined concretely (multiple geometric representations).

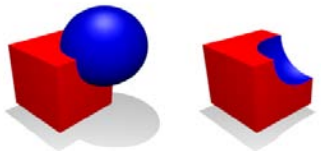
- Adds spatial attributes to species, reactions, parameters
  - Nonuniform Species/Parameter distributions
  - Localized Reaction and Transport processes
  - Defines a global coordinate system (e.g. x,y,z)

- Can represent spatial models modeling with
  - Reaction-Diffusion-Advection equations (e.g. **VCell**/JSim/CompuCell3D),
  - Particle Brownian Dynamics (e.g. **Smoldyn**/**VCell**/MCell/ChemCell/GridCell/ E-Cell, Meredys, CDS-Cellular Dynamics Simulator),
  - Next Subvolume Method (e.g. MesoRD, SmartCell),
  - Greens Function Reaction Dynamics (e.g. GFRD, E-Cell)

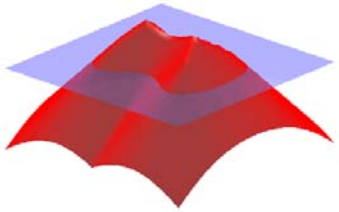
Some Geometric Descriptions

Segmented Image

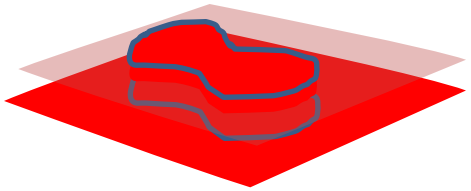
CSG (constructive solid geometry)



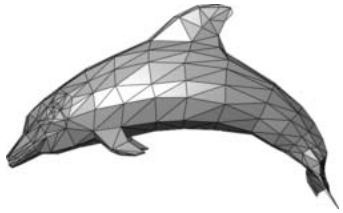
signed distance map



inside-outside function

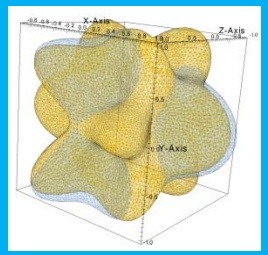


Polygonal Meshes



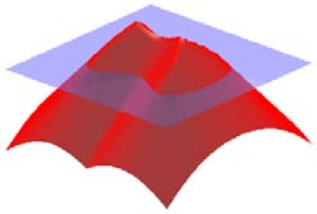
Spatial Applications / Geometry

FronTier

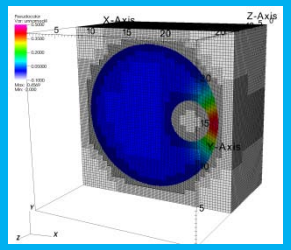


Wolgemuth
Level Set code

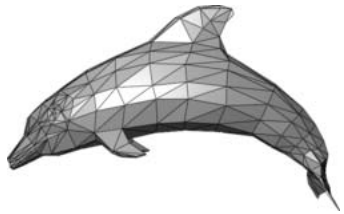
signed distance map



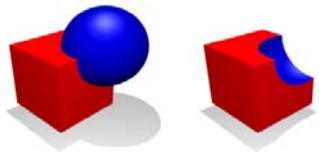
CHOMBO



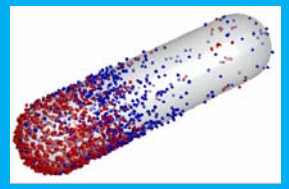
Polygonal Meshes



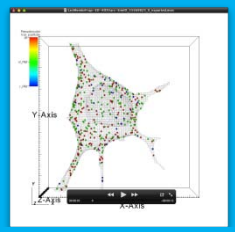
CSG (constructive
solid geometry)



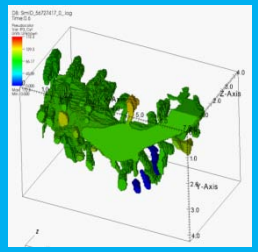
MesoRD



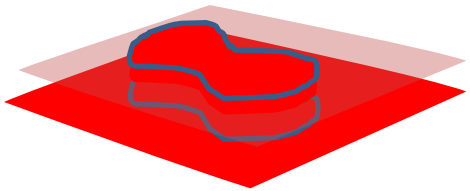
Smoldyn



VCell

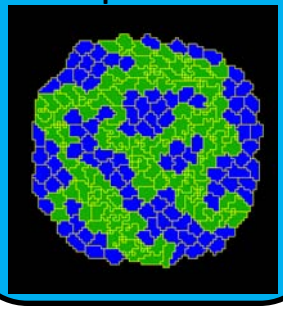


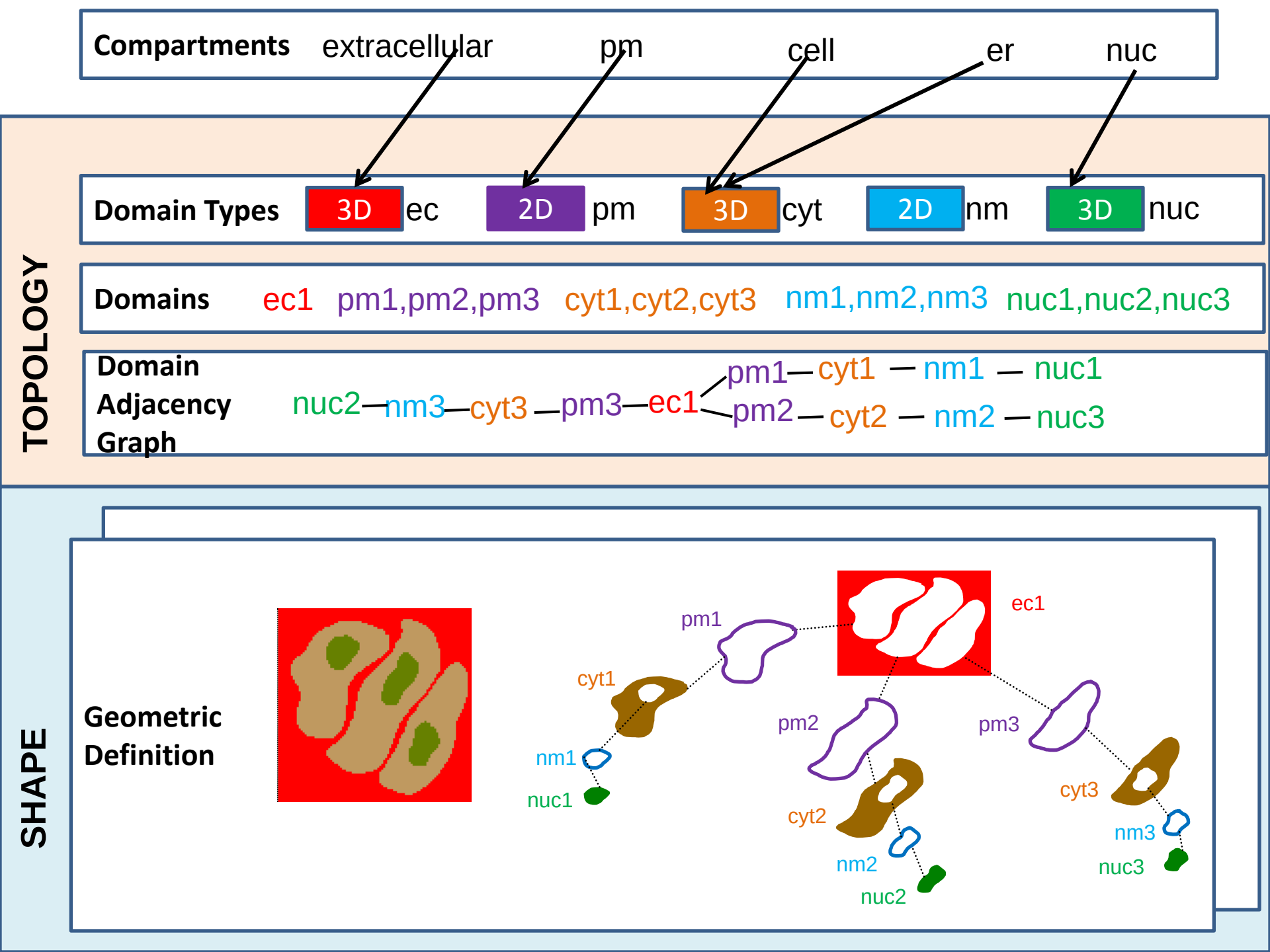
inside-outside function

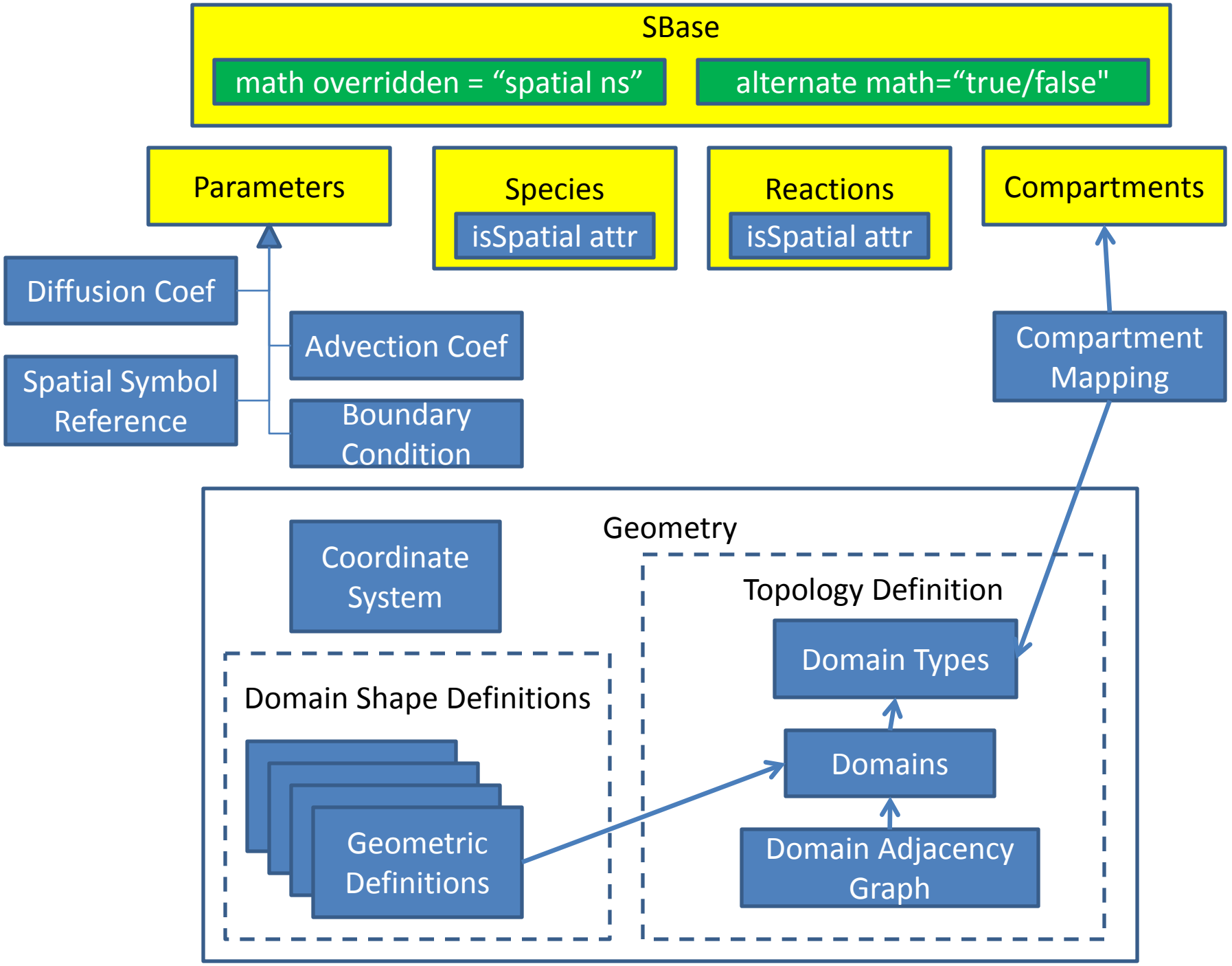


Segmented Images

CompuCell3D




Compartments
extracellular
pm
cell
er
nuc
TOPOLOGY
Domain Types
3D
ec
2D
pm
3D
cyt
2D
nm
3D
nuc
Domains
ec1
pm1,pm2,pm3
cyt1,cyt2,cyt3
nm1,nm2,nm3
nuc1,nuc2,nuc3
Domain Adjacency Graph
nuc2
nm3
cyt3
pm3
ec1
pm1
cyt1
nm1
nuc1
pm2
cyt2
nm2
nuc3
SHAPE
Geometric Definition
ec1
pm1
cyt1
nm1
nuc1
pm2
cyt2
nm2
nuc2
pm3
cyt3
nm3
nuc3


SBase
math overridden = “spatial ns”
alternate math=“true/false"
Parameters
Species
isSpatial attr
Reactions
isSpatial attr
Compartments
Diffusion Coef
Advection Coef
Spatial Symbol Reference
Boundary Condition
Compartment Mapping
Geometry
Coordinate System
Topology Definition
Domain Types
Domain Shape Definitions
Domains
Geometric Definitions
Domain Adjacency Graph

Progress/Status

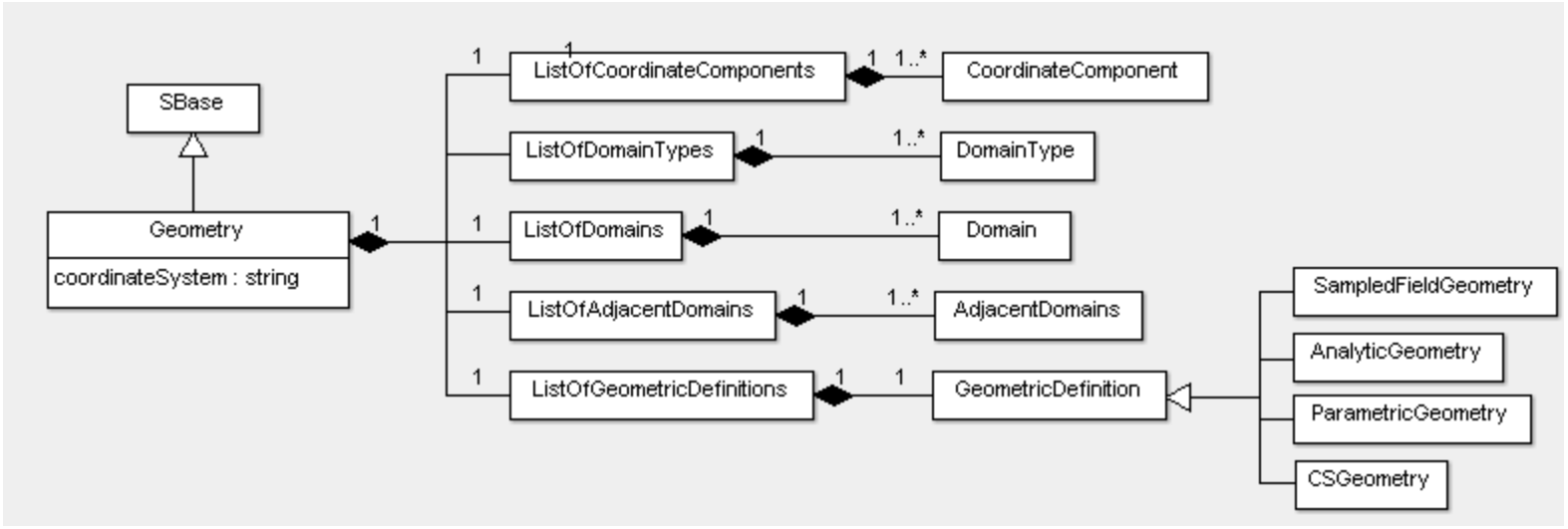
- Draft Proposal uploaded (http://sbml
- libSBML implementation available
  - http://sourceforge.net/projects/sbml/files/libsbml/5.0-packages-beta
  - download from libSBML site
  - New support for CSG Geometry (tested in VCell 5.1)
  - New support for Parametric Geometry (not tested).
- VCell 5.0 implementation (vcell.org)
  - Vcell 5.0 beta 14 released under MIT license
    - http://sourceforge.net/projects/vcell/files/VCell_5.0_beta_14.zip/download
  - Uses Java binding for libSBML (reads/writes)
  - Supports spatial models using image-based and analytic geometric descriptions
  - implements all compartment/domainType mappings.
  - Solves Reaction-Diffusion-Advection PDEs and Particle-based brownian dynamics (via Smoldyn).

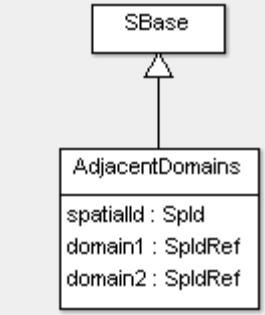
What's next?

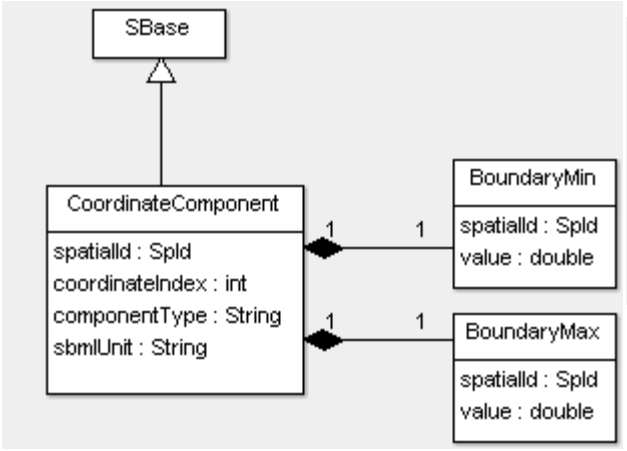
- complete L3 extension proposal (incomplete draft)
- Attempt model exchange and solicit input.
- write formal L3 extension specification
- finalize libSBML (validation, test cases)

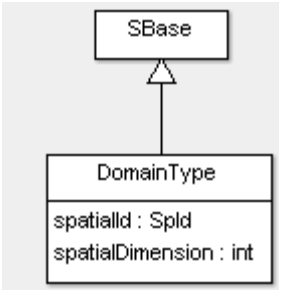
  - libSBML/Spatial build available on sf.net (sbml)
    - /svnroot/sbml/branches/libsbml-packages/spatial
  - Spatial extension development moved to vcell's sourceforge SVN (/svnroot/vcell/community/sbmlSpatial)

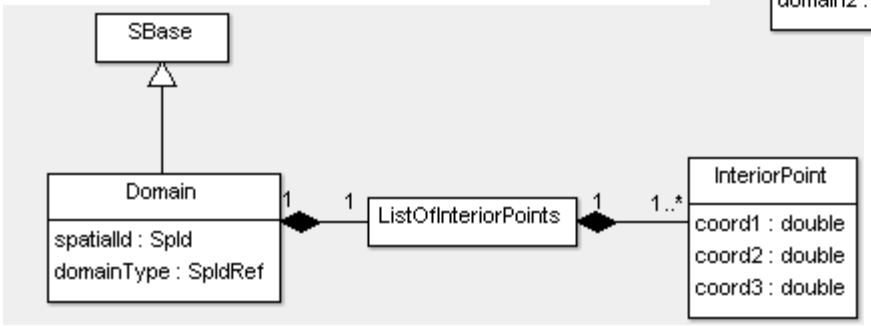
Geometry


SBase
Geometry
coordinateSystem : string
ListOfCoordinateComponents
CoordinateComponent
ListOfDomainTypes
DomainType
ListOfDomains
Domain
ListOfAdjacentDomains
AdjacentDomains
ListOfGeometricDefinitions
GeometricDefinition
SampledFieldGeometry
AnalyticGeometry
ParametricGeometry
CSGeometry

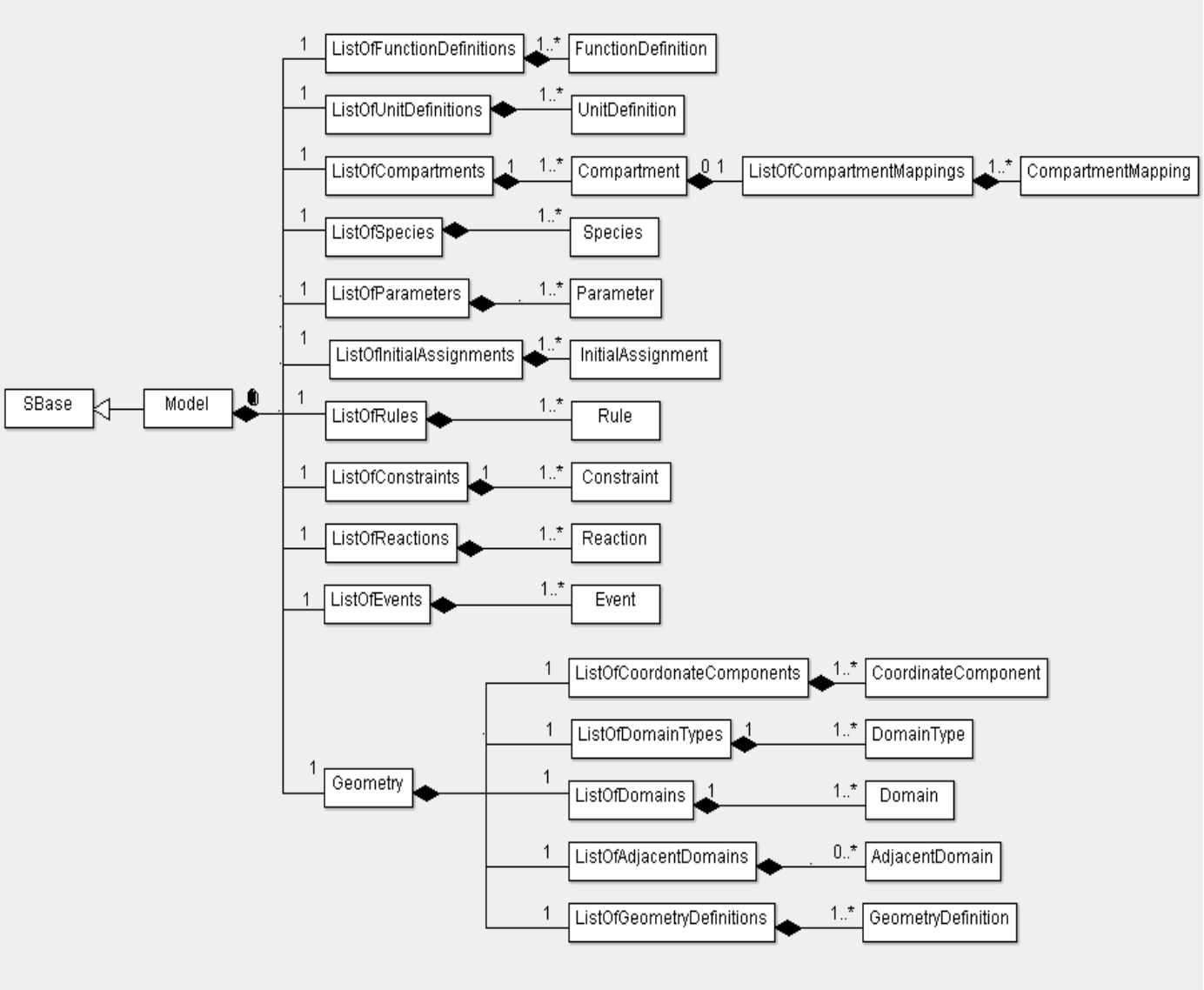

SBase
AdjacentDomains
spatialId : SpId
domain1 : SpIdRef
domain2 : SpIdRef


SBase
CoordinateComponent
spatialId : SpId
coordinateIndex : int
componentType : String
sbmlUnit : String
BoundaryMin
spatialId : SpId
value : double
BoundaryMax
spatialId : SpId
value : double

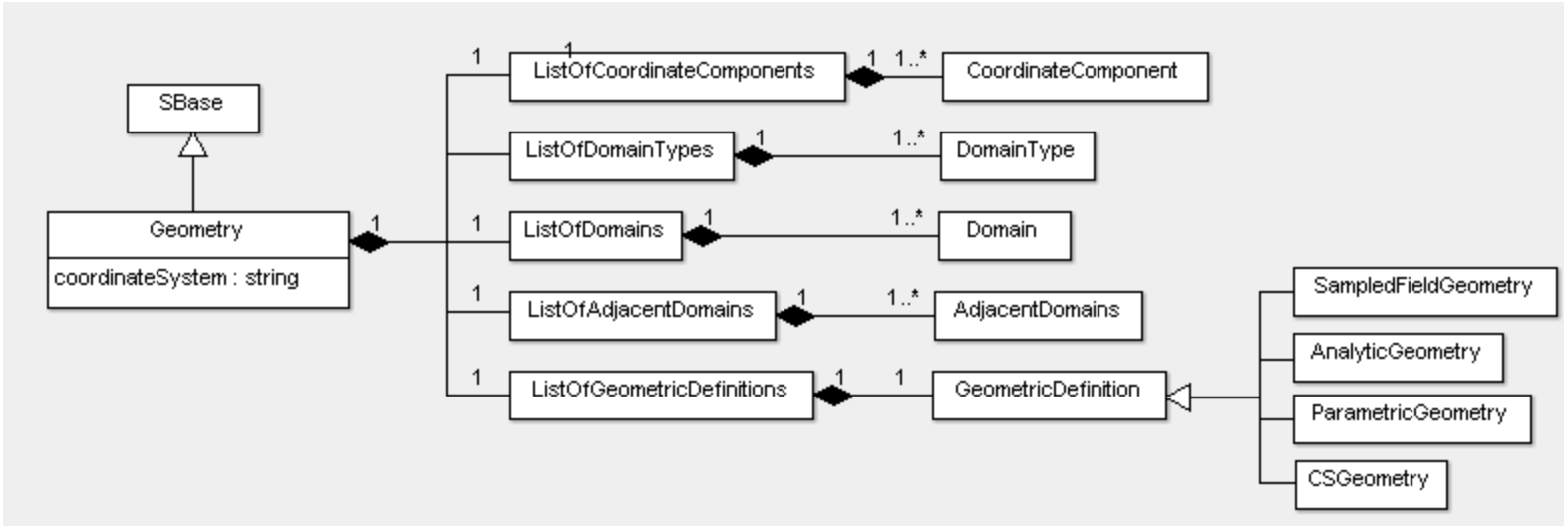

SBase
DomainType
spatialId : SpId
spatialDimension : int

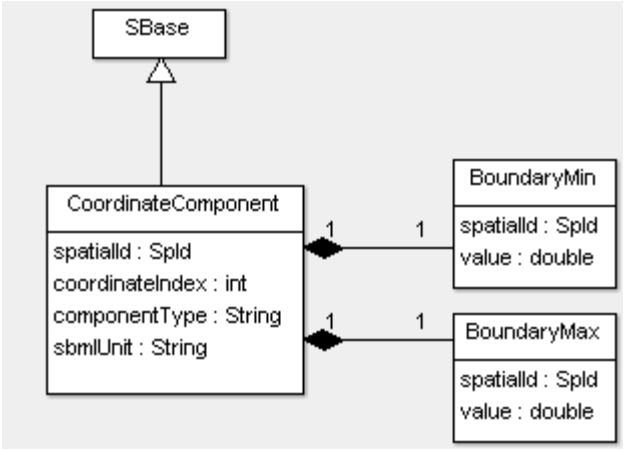

SBase
Domain
spatialId : SpId
domainType : SpIdRef
ListOfInteriorPoints
InteriorPoint
coord1 : double
coord2 : double
coord3 : double

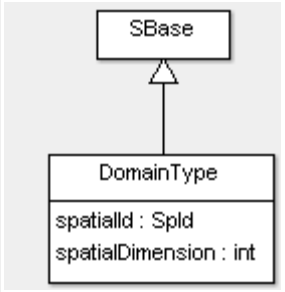
Model structure

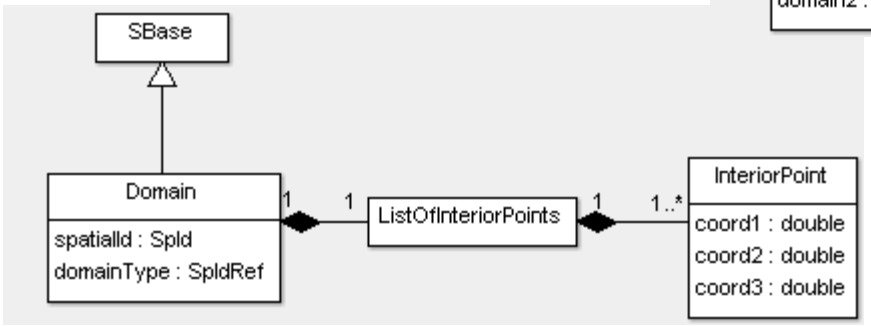


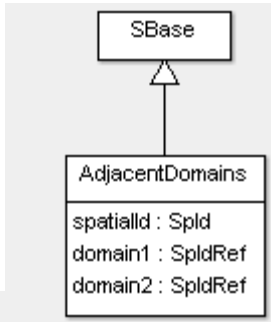
Geometry (self contained)



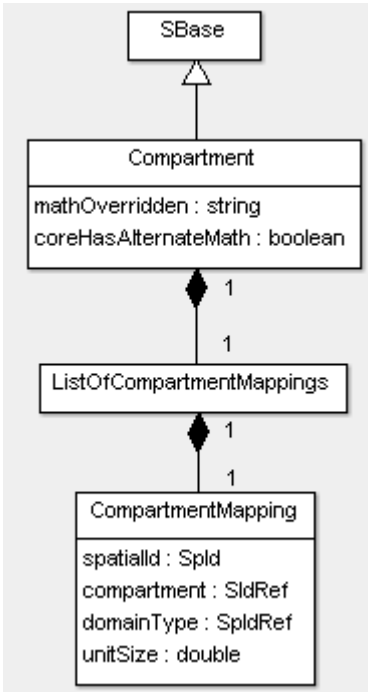


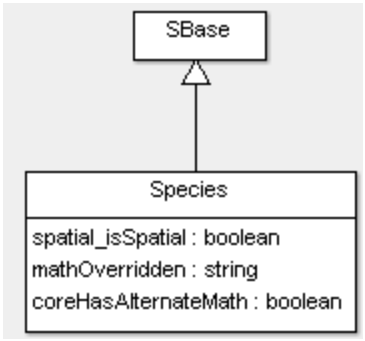


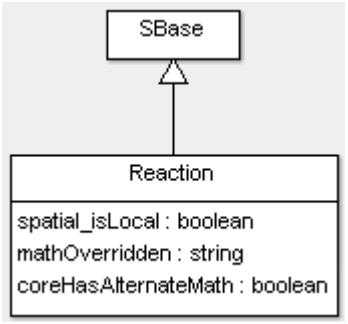


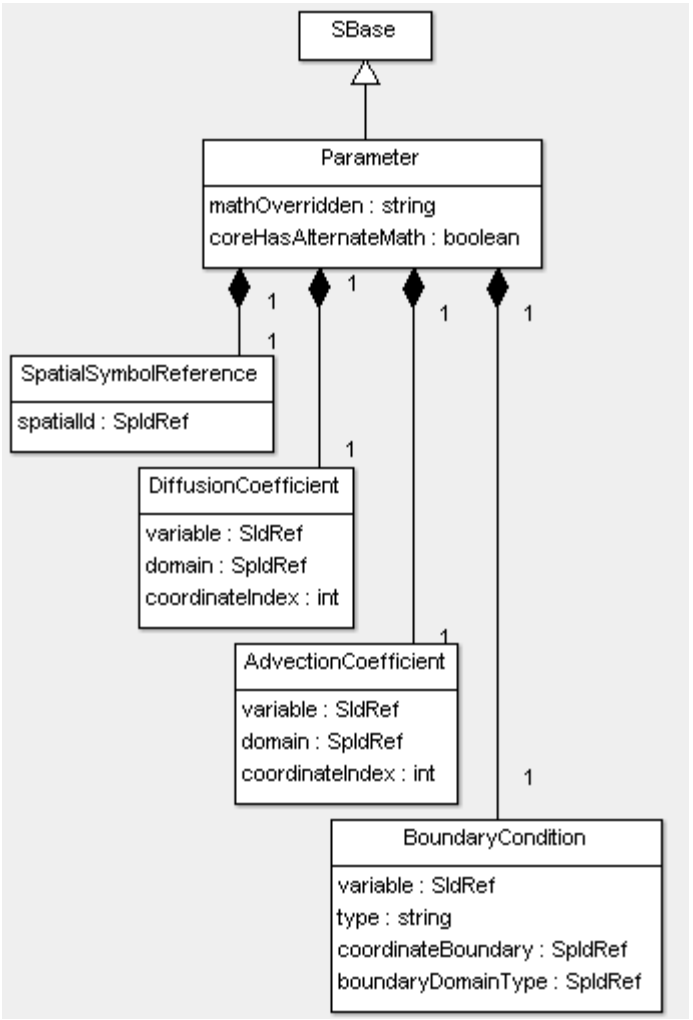


Additions to SBML Core

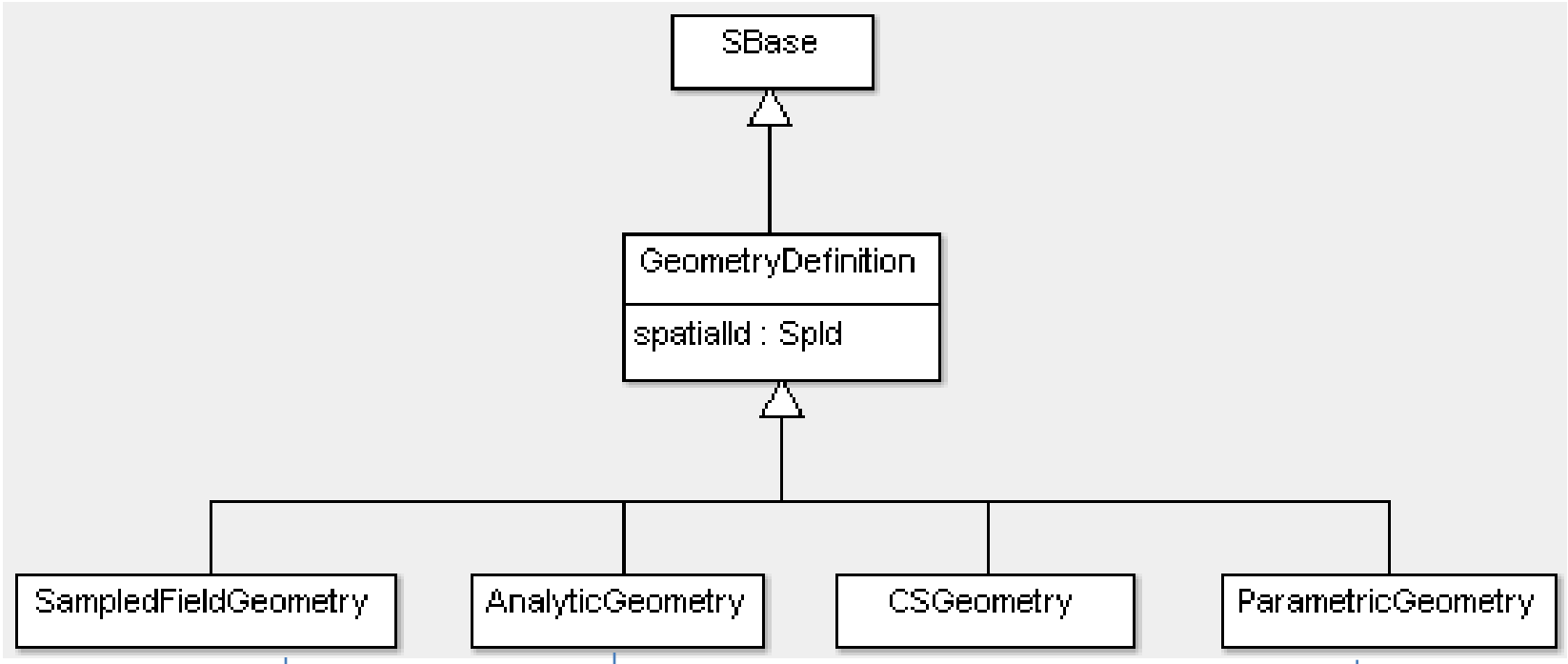


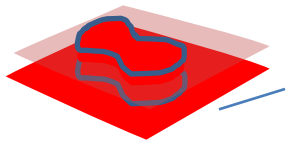




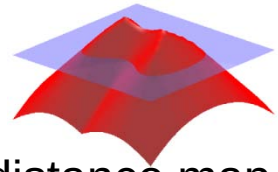


Geometry Definitions Overview



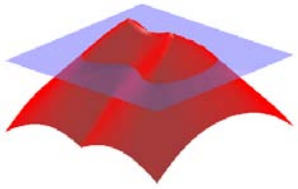


discrete valued (uncertain)

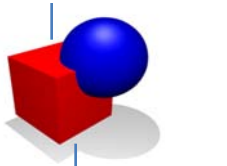


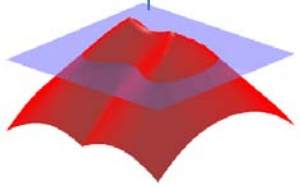
distance map

f(x)

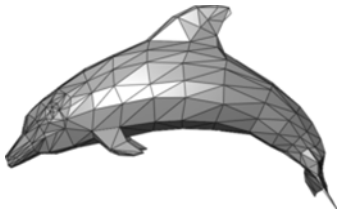


R-functions

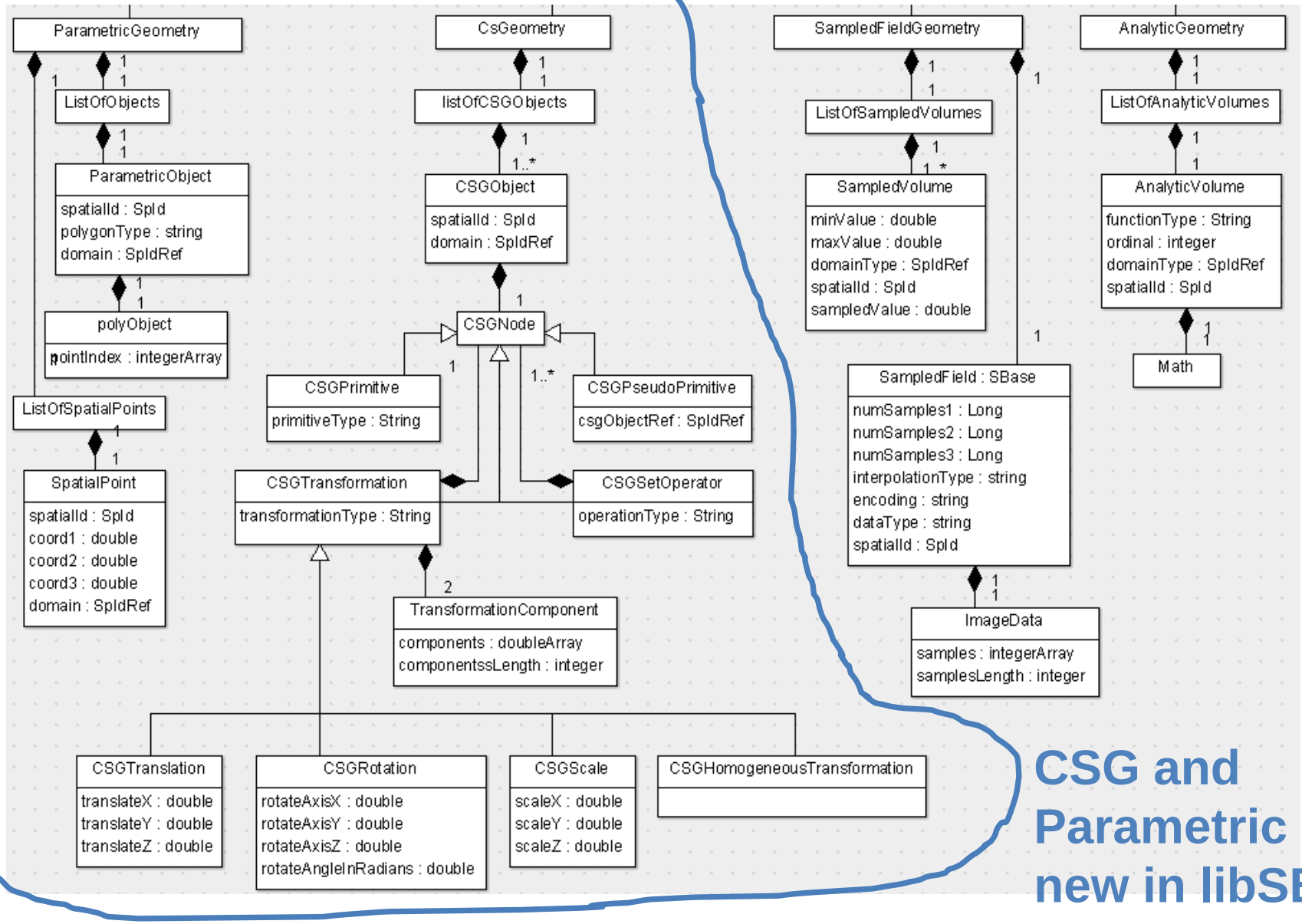




R-functions

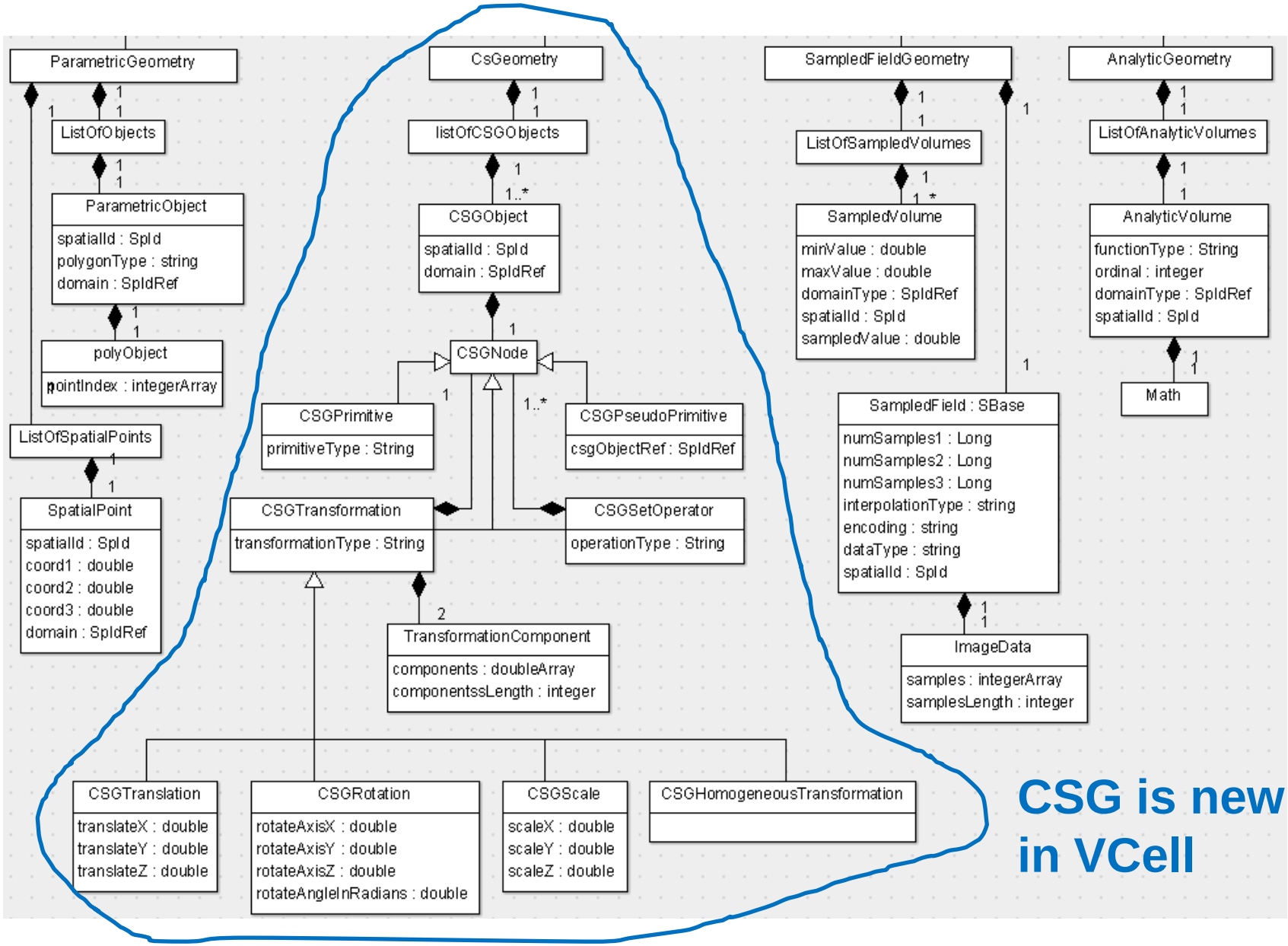


Geometry Definitions (Detail)

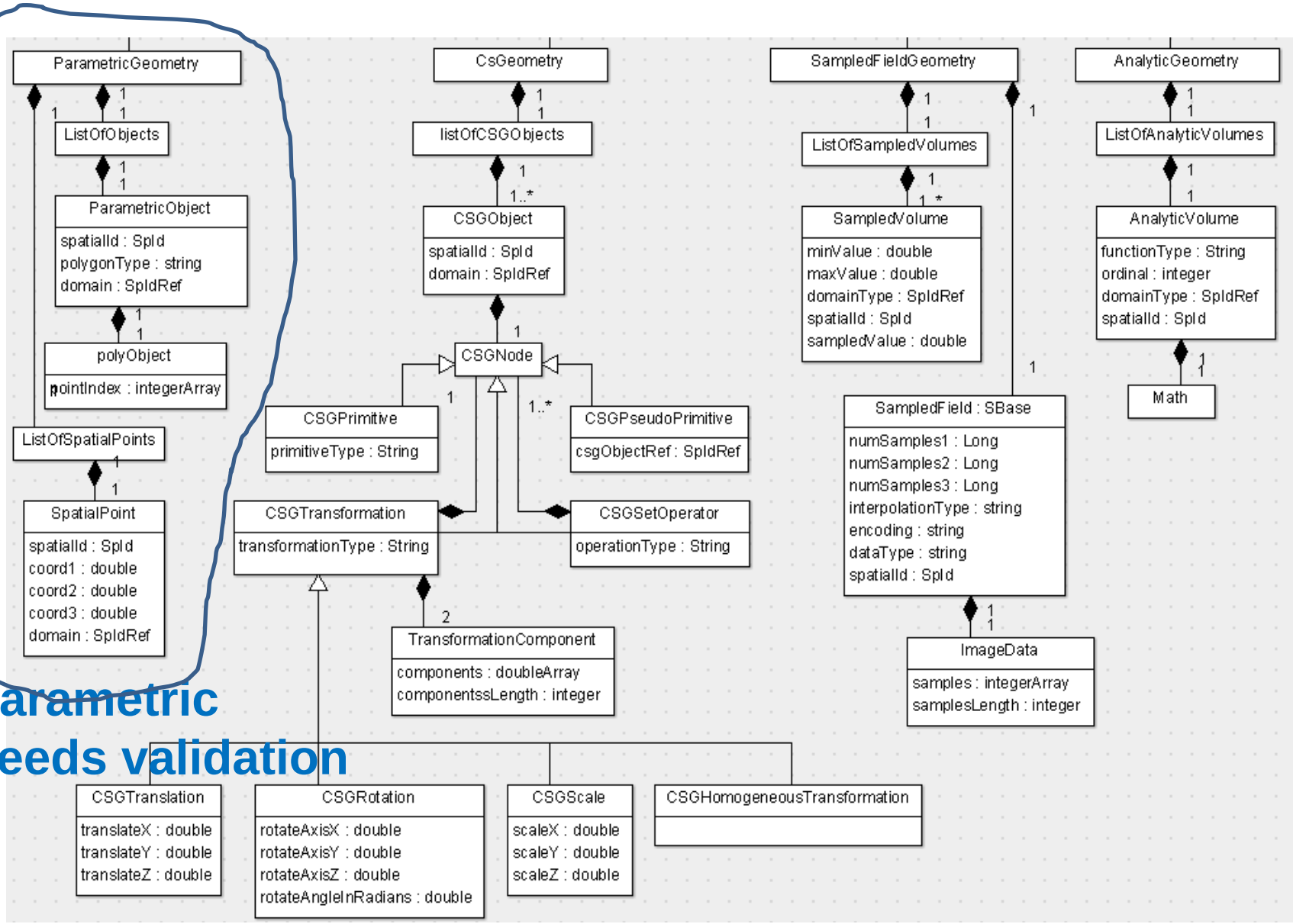


CSG and Parametric are new in libSBML

Geometry Definitions (Detail)



Geometry Definitions (Detail)



Parametric needs validation

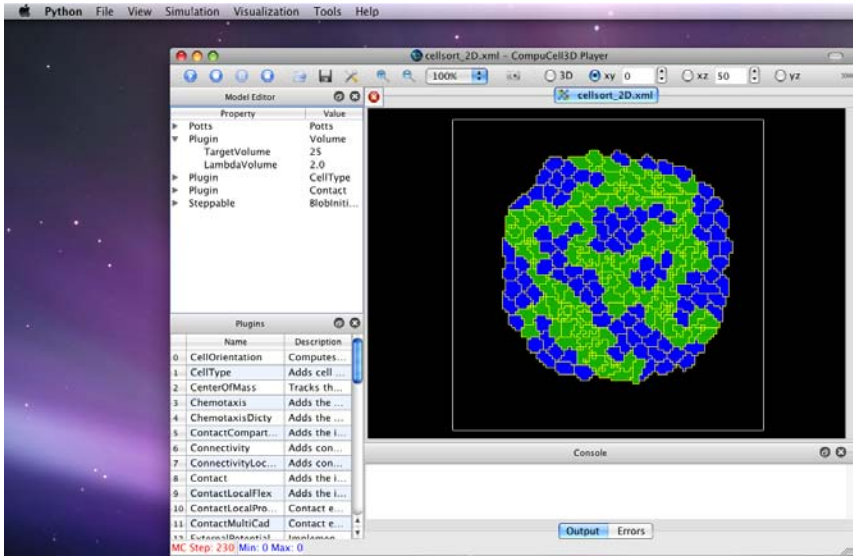
Agenda

- Overview of spatial extension proposal
- Application to Multicellular?

Beyond L3 Spatial – Multicellular?

ICSB 2011 Workshop 5:
Standardized Model Description Language for Multi-Cellular Simulations
Heidelberg, September 1 - 2, 2011

Cell Behavior Model Specification Language (CBMSL)
(or one or more SBML extensions)



Population (>100) discrete cells move, deform, adhere, divide, change internal state, communicate directly and via "fields" (e.g. concentration)

Could leverage SBML – but there are challenges

- SBML L3 Spatial Representation (overkill?, need flexible "fields")
- SBML Core (too "ODE-centric"?)

Multiple mathematical frameworks

- Lattice models (Cellular Potts – energy functionals → transition probability)
- Off-lattice agent-based models (Voronoi or discrete parametric shapes)
- PDEs for fields

Multicellular spatial support

Initial Spatial Definition (defined by Spatial Extension):

- **Cell Identity** (each cell is a single spatial::Domains).
- **Cell-Cell contact** (spatial Domain-Domain adjacency graph)
- **Cell shape** (parameterized in GeometryDefinition)
- **Extracellular Concentration and Velocity Fields** defined everywhere (overlapping spatial::Domain).

Useful concepts for Spatial Dynamics:

- **Cell instances** enumerated by list of "cellular" domains.
- **Dynamic Cell-Cell contact relationships** represented in dynamic adjacency graph.
- **Cell creation and destruction events** (adds/removes Domains, changes adjacency graph, edits geometry representation)
- **Cell Collisions/Separation** (changes adjacency graph, geometric representation).
- **Cell Shape changes, motion** (via parameterization of Geometry Definition).

Multicellular Mathematical Framework operates directly its **GeometryDefinition (extensible)**

- **Lattice-based modeling (CompuCell3D)** - (discrete pixel values are dynamic) – **Sampled Data "segmented image"**
- **Off-lattice (Voronoi)** – (cell center and shape parameters are dynamic) **– Parametric - Voronoi**
- **Off-lattice (CSG, meshed objects)** - parametric (object location, shape parameters are dynamic) – **Parametric**

Summary

- Simulators free to use any internal representation during runtime.
- Model Description could use SBML Spatial to enumerate cells, describe contact relationships, and parameterize motion, describe fields
- Topological changes or cell creation/destruction could spawn events or and influence behavior.