SBML Level 3 Hierarchical Model Composition

Lucian Smith

COMBINE 2010

2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010

History

Possible

3 Submodels

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Version of November 27, 2000

Contents

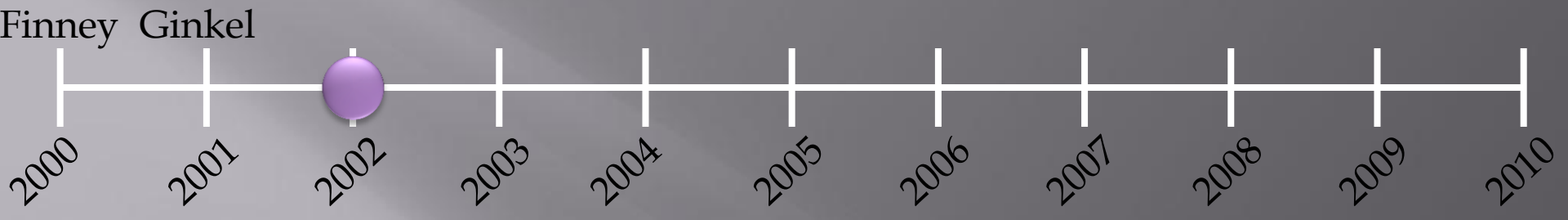
Finney

History

Modular Modeling of cellular systems

Martin Ginkel, Jörg Stelling
Max-Planck-Institute for Dynamics of complex technical Systems
Magdeburg, Germany

1st June 2001



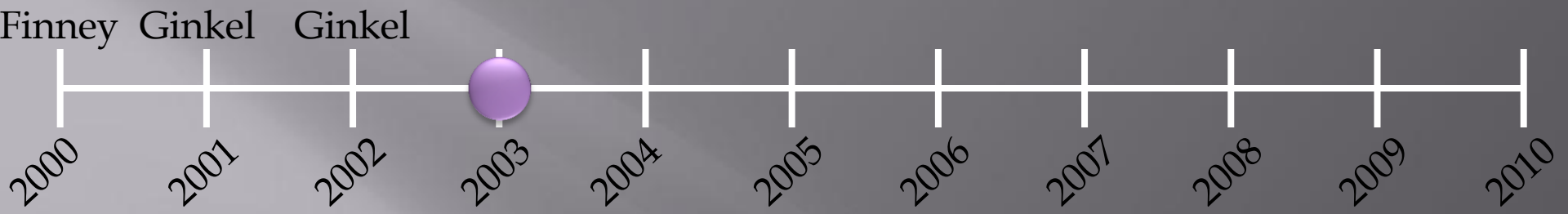
History

Modular SBML

Proposal for an Extension of SBML towards level 2

Martin Ginkel
Max-Planck-Institute Dynamics of complex technical Systems,
Magdeburg, Germany
ginkel@mpi-magdeburg.mpg.de

10th June 2002



History

spod-central.org/~lpsmith/Webb/compose.html

BioSpice MDL Model Composition and Libraries

This document describes a set of capabilities supporting the construction of models from components and the collection of those components in libraries. Since BioSpice is currently using SBML as the MDL, this presentation is slanted toward describing extensions to SBML.

Please note this is work in progress. A number of sections are incomplete and we are looking for feedback on the general approach being proposed.

Model Composition

Models of realistic systems will be large. We presume there will be recurrent structures within models of a given system and between models of different and possibly related

Finney Ginkel Ginkel Webb

2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010

History

www.mpi-magdeburg.mpg.de/zlocal/martins/sbml-comp

HOME Contact Local Impressum

MAX-PLANCK-GESELLSCHAFT

Max-Planck-Institut
für Dynamik komplexer
technischer Systeme

About the Institute
Research
Public Relations
Library

Model Composition SIG of the SBML-Forum

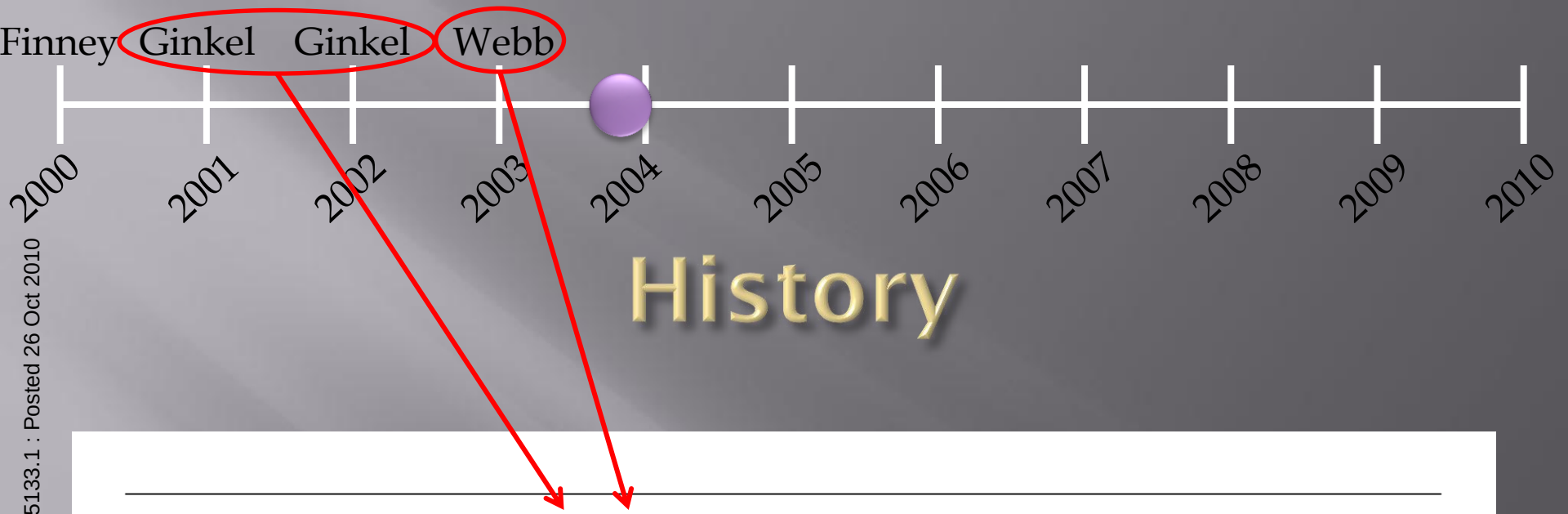
Model Composition SIG of the SBML-Forum

At this place some material is placed for the development of a
Model Composition Extension
of SBML (Systems Biology Markup Language)

- The (preliminary) Charter describes mission and ideas of this approach
- Here the members of the group are listed

The rest of the page are collected documents and talks:

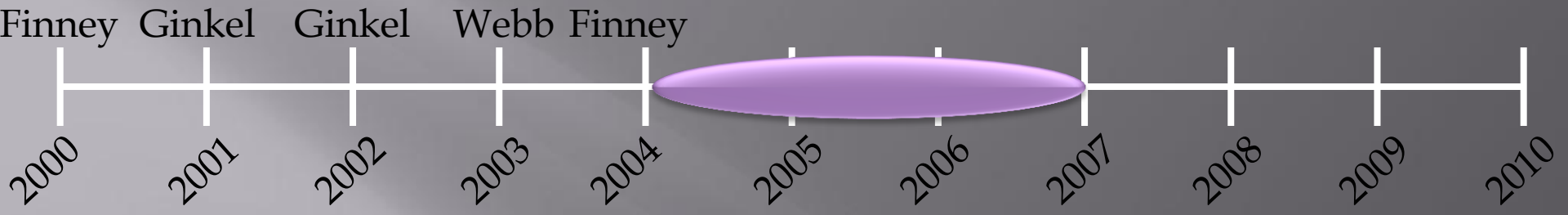
Name	Description	Size
sbml-modular-talk-1.pdf	Modular Modeling in SBML (Martin Ginkel at 3rd Workshop)	(164182 Bytes)
sbml-modular-talk-2.pdf	Modular Modeling in SBML (Martin Ginkel at 5th Workshop)	(309625 Bytes)
model-composition.pdf	Model Composition Proposal (Andrew Finney at 7th Workshop)	(156095 Bytes)



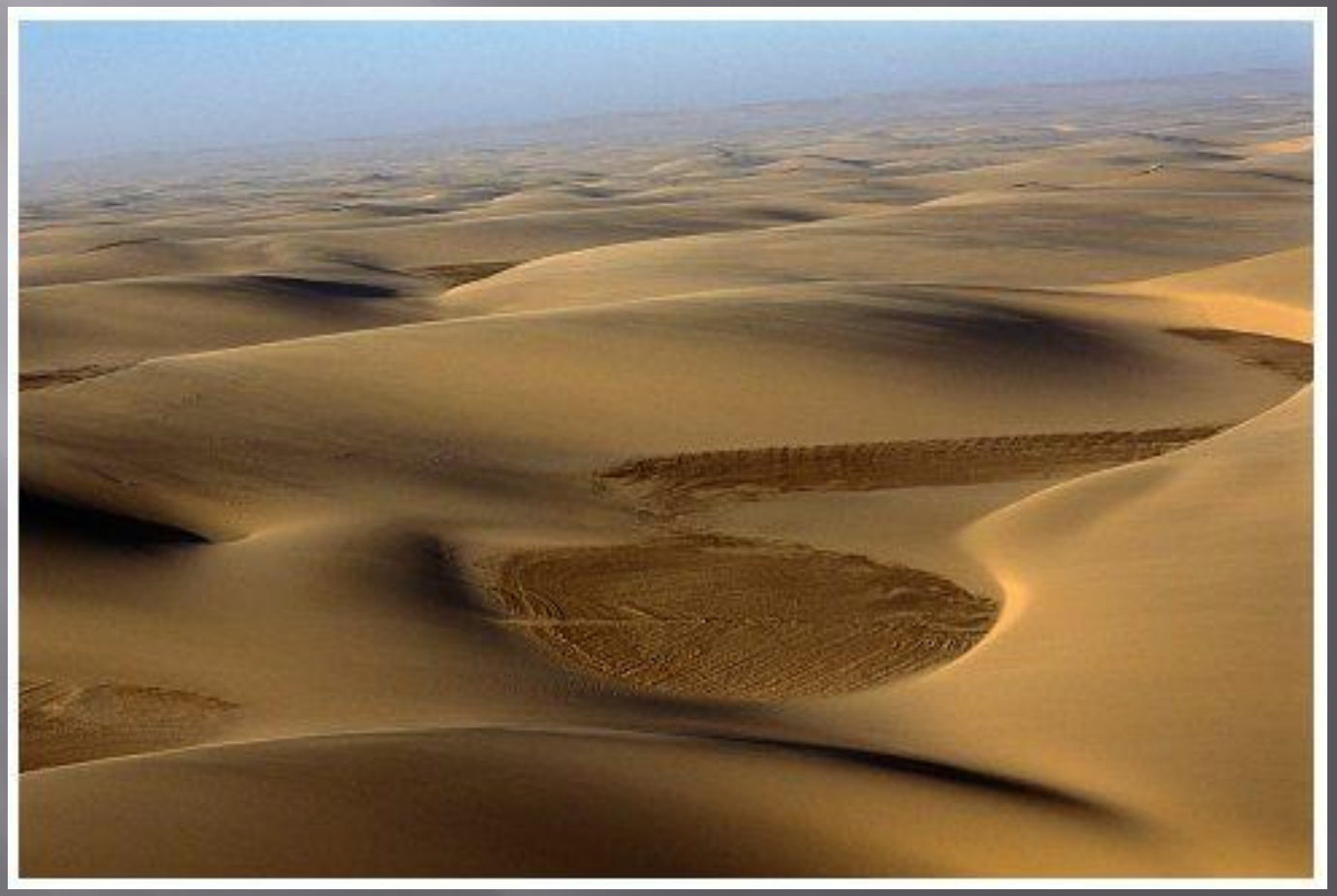
Systems Biology Markup Language (SBML) Level 3 Proposal: Model Composition Features

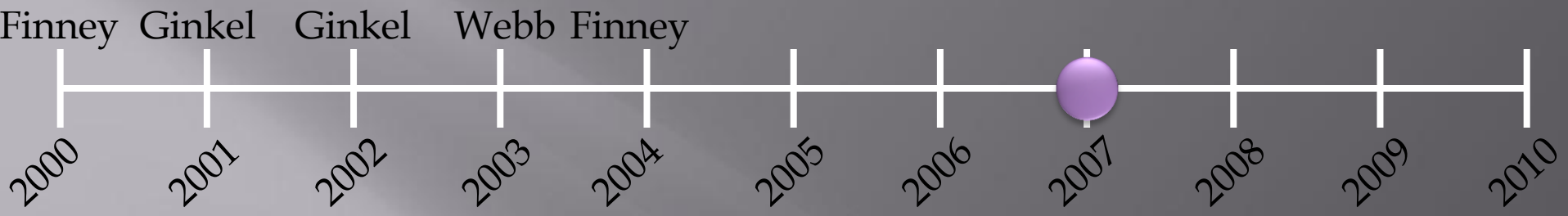
Andrew Finney
afinney@cds.caltech.edu

October 31, 2003



History





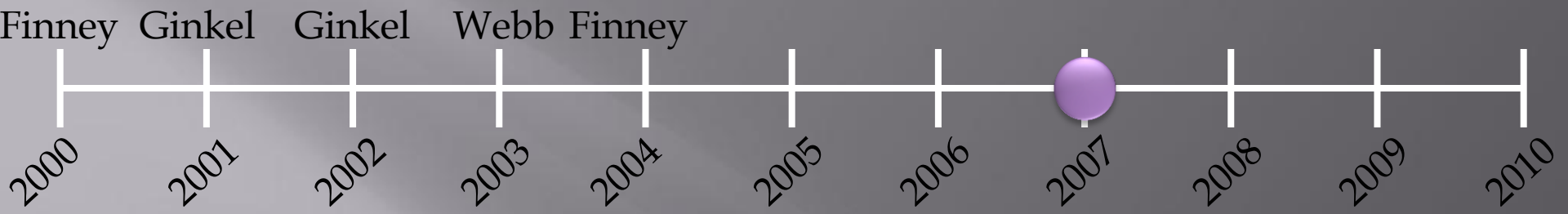
History

The 5th SBML Hackathon

SBML Composition Workshop 2007

University of Connecticut Health Center, Farmington, CT, USA, 9-10 September 2007

Model composition refers to the ability to include models as submodels inside other models. This requires defining the interfaces between the models and protocols for connecting parts of models together. One of the anticipated extensions for SBML Level 3 is to support model composition.



History

The 5th SBML Hackathon

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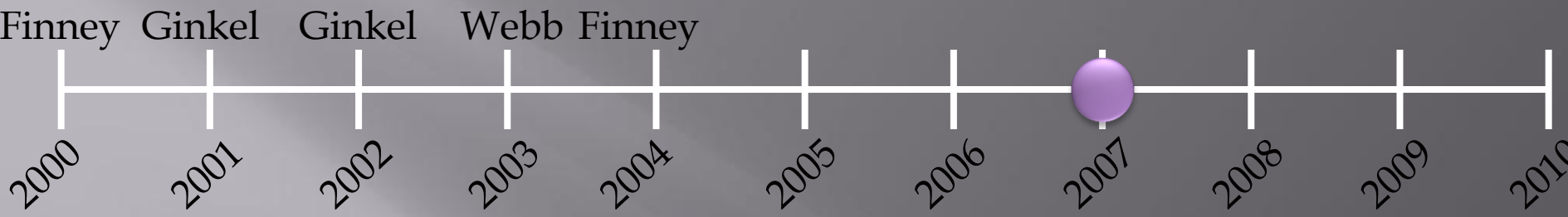
Martin Goals

1. General Goals
   - (UseCase? 1): Composing tool takes multiple traditional SBML changes to the original models.
   - (UseCase? 2): Modular modeling tool creates models from pre to be composed in the sense of software engineering.
   - (UseCase? 3): Analysis tools read and analyze (simulate, comp implementational effort
   - Important: Balance between complexity of storage format and
   - General question: Is it useful/necessary to make composition solved in general)
2. Goals for Composition Extension
   - Express multiple submodels or modules
   - Express instantiation
   - Create directed links



History

Object Oriented Modeling in Promot

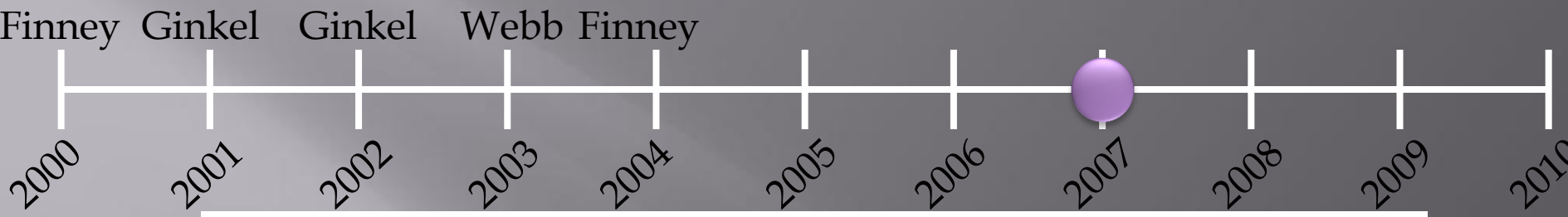
Motivation

- Structured Models are very common in other simulation descriptions
- Examples: **Simulink**, Dymola, **Modelica**, gProms, **CellML**
- Technical simulations naturally reflect the modular structure of the modeled systems (and there are still doubts about modules in biology)
- Learn from the experiences of other simulation fields.
- Promot was originally developed for process engineering
- It uses object-oriented models, composed from modules

Introductory Example

- EGF Model based on [Schoeberl 2002] implemented in Promot
- Model is constructed with modular structure, submodels are *designed to be composed*
- Modules for the major **specific functional networks** of the system
- Modules interact with their siblings by terminals (ports, interfaces)
- Modules are independently developed, tested and analyzed

◦ Create directed links



Andrew 2007 Comments about Model Composition

Folks

The following issues were raised which were not covered by the existing model comp
(despite the tone of the language I'm actually writing this for comments! - that inclu
if you have already thought these issues though ages ago

a) Explicit 'MustBeOverloaded' flag on ports

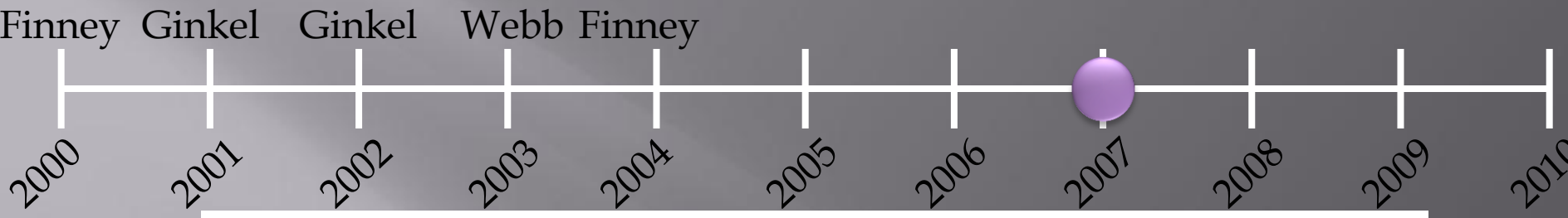
Currently ports (elements that are explictly part of a model's interface) by default ca
when the containing model is instantiated. Ports must have an additional flag 'MustB
that when true indicates that the port must be linked to. It is recommended that sim
containing, at the top level, ports with 'MustBeOverloaded' true values is simulated.

b) N to N links

(on links a 'from' reference overloads a 'to' reference) The syntax for links should be
and one or more 'to' object references. A link with zero 'from' references deletes the
more than one species or compartment 'from' references (otherwise you could split a
link to nothing is not allowed)

c) Reaction overloading

Reaction links should be allowed. Reaction overloading differs from species overloads
the reaction network bipartite graph the flattened model containing a link from one s
combines the edges from both models incident to both species e.g. model1: s1 -> s2



Andrew 2007 Comments about Model Composition

Folks

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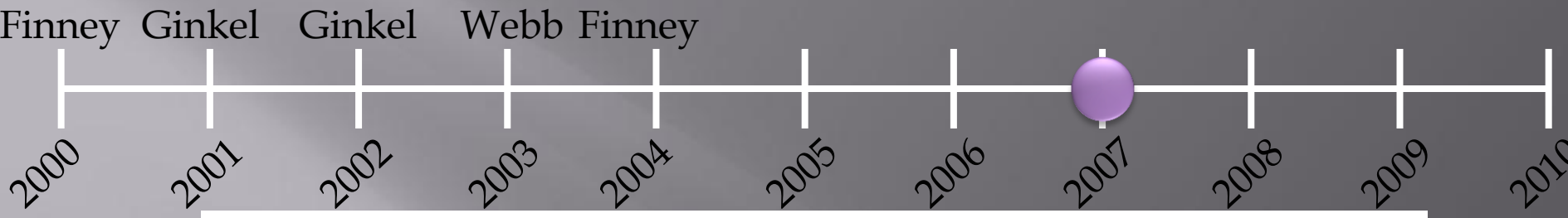
Model merging with semanticSBML

Wolfram Liebermeister, MPI-MG Berlin

Computational Systems Biology

SBML composition meeting

UCHC, September 9-10 2007



Andrew 2007 Comments about Model Composition

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Model merging with semanticSBML

Model Composition for Macromolecular Regulatory Networks

Ranjit Randhawa, Clifford A. Shaffer, *Senior Member, IEEE,* and John J. Tyson

split a

c) Reaction overloading

Reaction links should be allowed. Reaction overloading differs from species overloads
the reaction network bipartite graph the flattened model containing a link from one s
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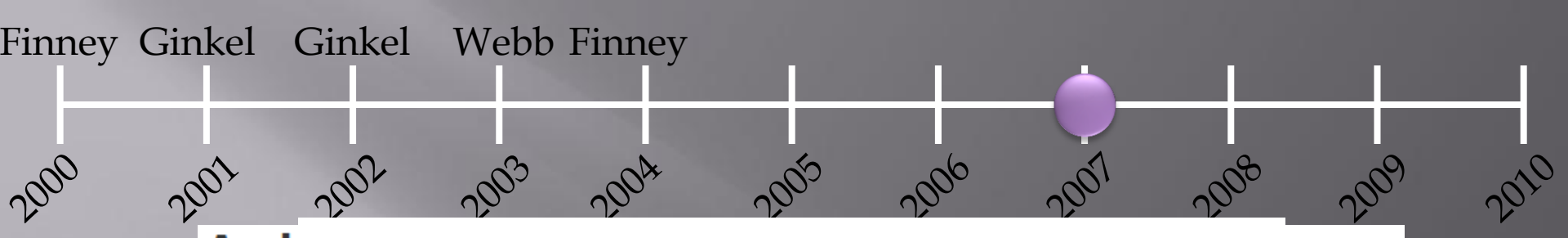


Issues To Address

The following are unresolved issues and questions that arose from th
videoconference discussions at UCHC during the SBML Composition r

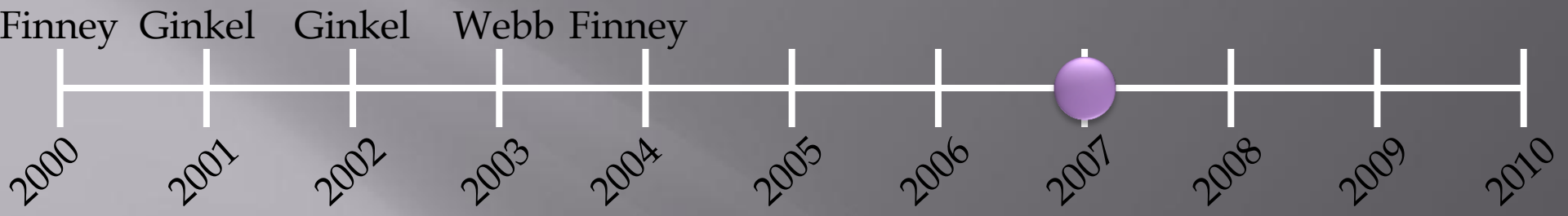
Before listing the issues, we articulate one starting requirement: wha
tool (e.g., libSBML) to unambiguously flatten an L3 "composed" mod
conflicts with some of the comments below, in which there are quest
below as they are, in order to describe the space of possibilities, but
model down to L2v3 is a desirable feature and should serve as a desi
interpreted immediately and transparently by software tools that use
adoption of the composition facility.

AF: This approach also simplifies the definition of some of the semar
model (in L3) is valid if the flattened L2 model is valid. This is not to
this way :).

[edit] Terminology

SBML **Inclusion**: Separating pieces of SBML into separate files and having a mechanism to include the external pieces into a given file.

SBML **Model Composition**: *composing* a model from submodels. AF suggests the following subdivisions within composition:



Hierarchical Model Composition (Hoops 2007)

[edit] Proposal title

Hierarchical Model Composition

[edit] Proposal authors

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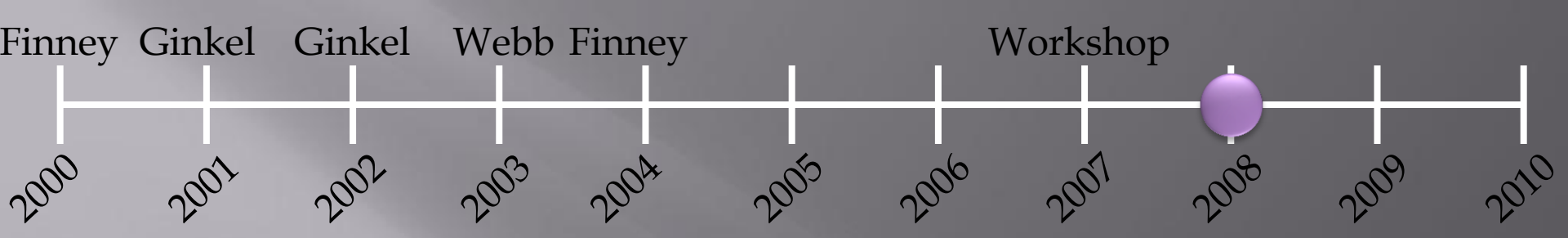
Virginia Bioinformatics Institute
Blacksburg, VA 24061, USA
Email: shoops at vbi.vt.edu

Nicolas Le Novère
European Bioinformatics Institute
Wellcome Trust Genome Campus
Hinxton, Cambridge CB10 1SD, UK
Email: lenov at ebi.ac.uk

Ion Moraru
Center for Cell Analysis and Modeling
University of Connecticut Health Center



Hierarchical Modeling

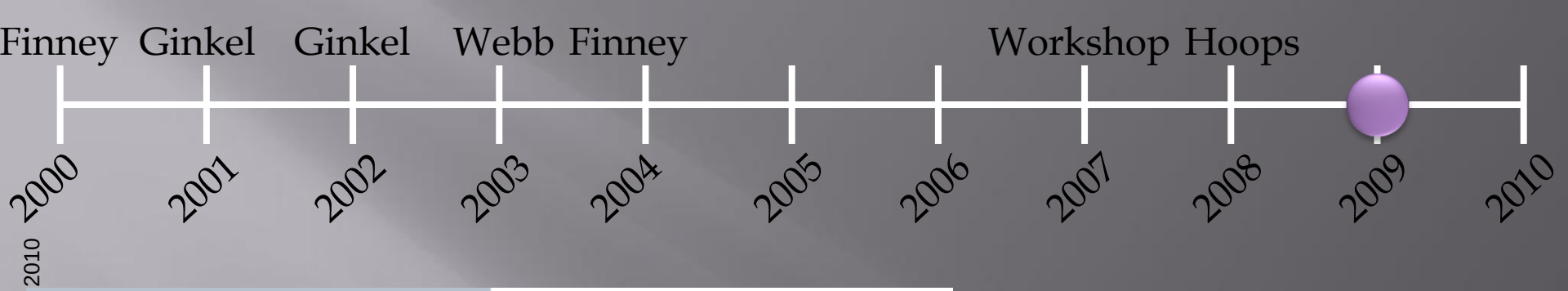
Ion Moraru
Stefan Hoops

SBML Workshop
Gotheburg
Sweden

VIRGINIA BIOINFORMATICS INSTITUTE AT VIRGINIA TECH

SBML Systems Biology Markup Language

NRCAM
National Resource for Cell Analysis and Modeling



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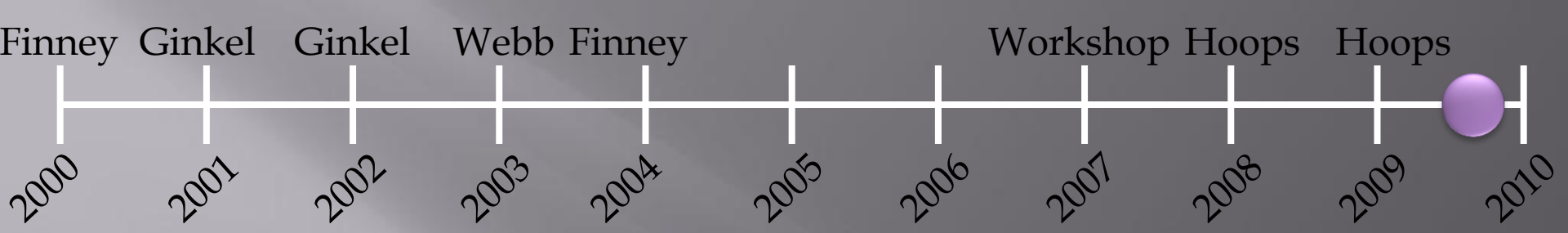

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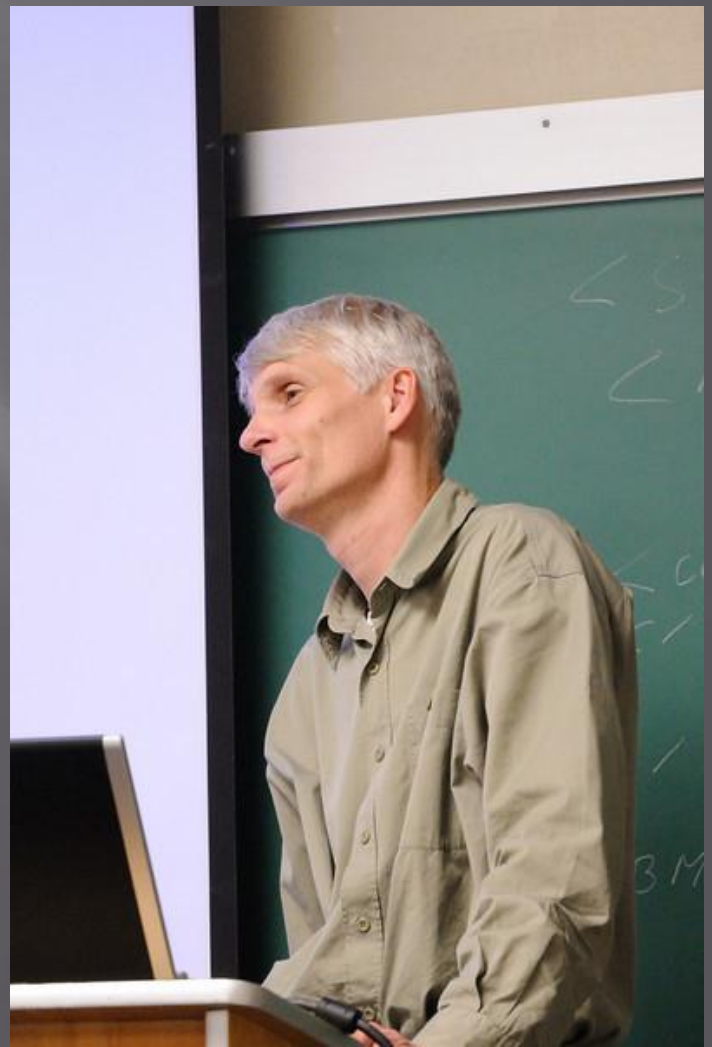
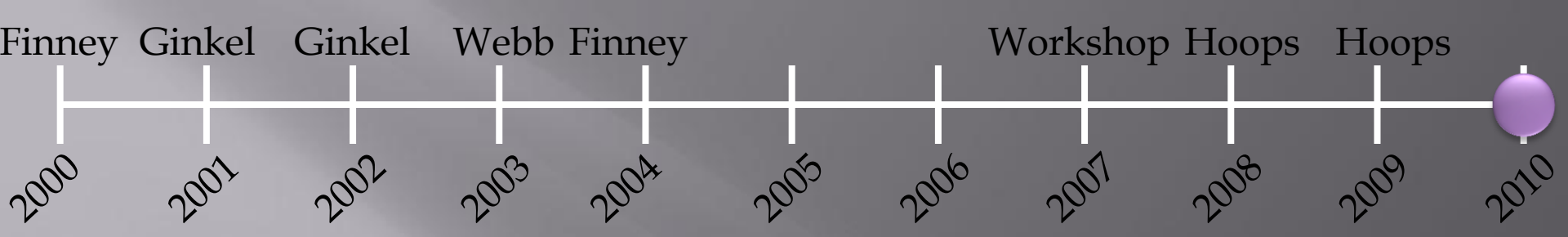
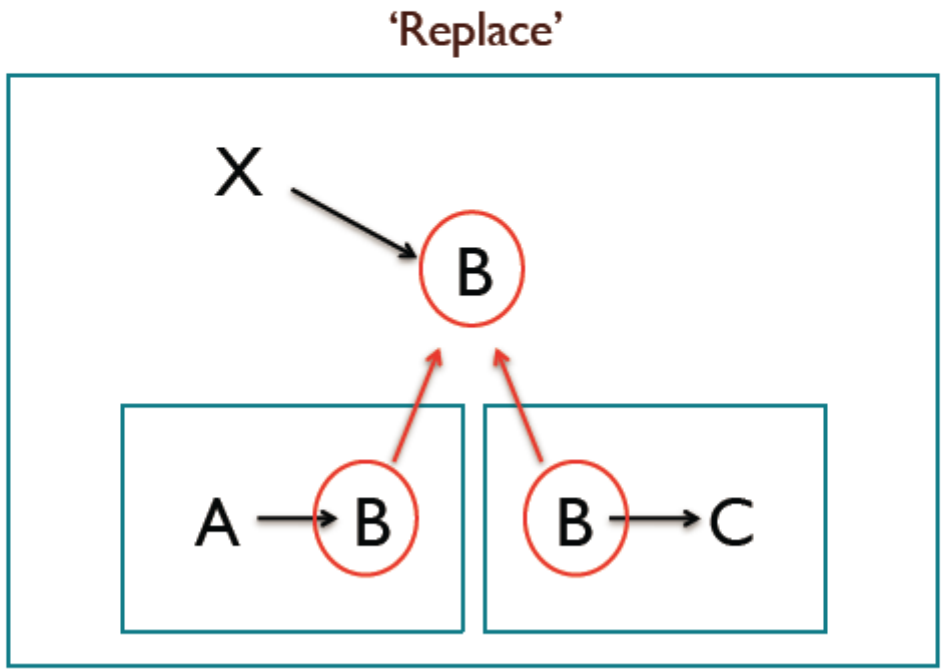
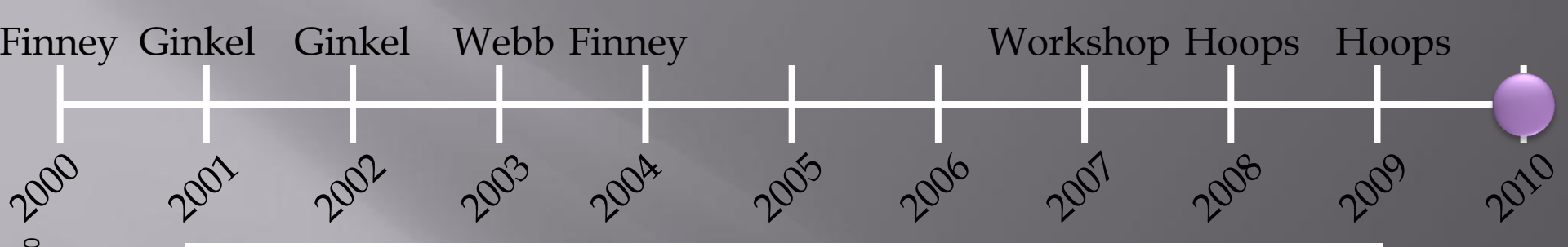




Hierarchical Model Composition





1: Separate the concepts of 'replacement' and 'deletion' into parallel elements: ListOfReplacements/Replacement, and ListOfDeletions/Deletion

2: Annotate the Deletions with a list of conceptual replacements for those elements.

3. Let ConversionFactors be non-const; possibly make them required instead of optional.

4. Loosen reliance on xpointers by allowing ObjectRefs to reference by metaID and/or by increasing the number of elements with SIDs.

5. Separate model definitions from model instantiations.

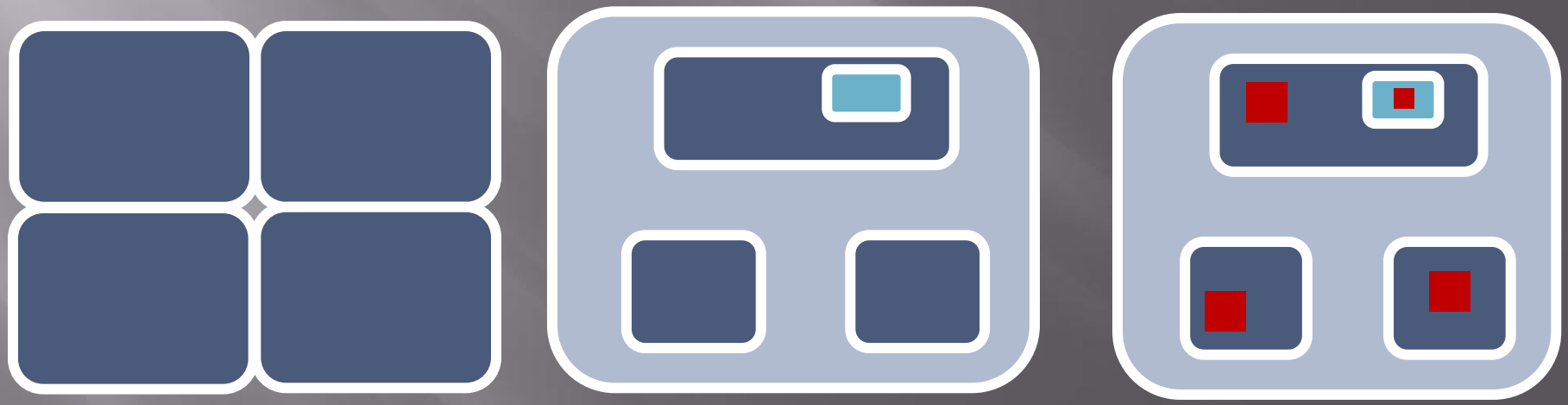
6. Turn 'Ports' into annotations. (this one is not my proposal, but a proposal 'from the floor', as it were).

7. The spec should be written in such a way as to explicitly accommodate packages in general, without needing to refer to particular packages.

8. Function Definitions must only apply to the model they are a member of. Do we want a more general list as well?

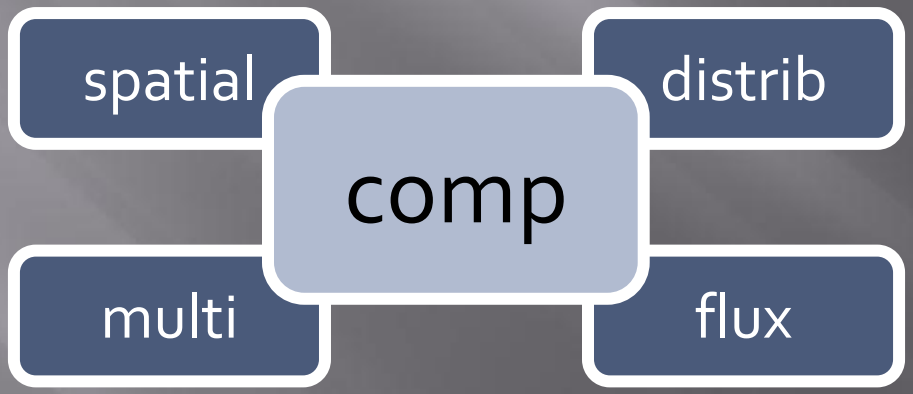
Design Goals

- Aggregation, Composition, or Black Box



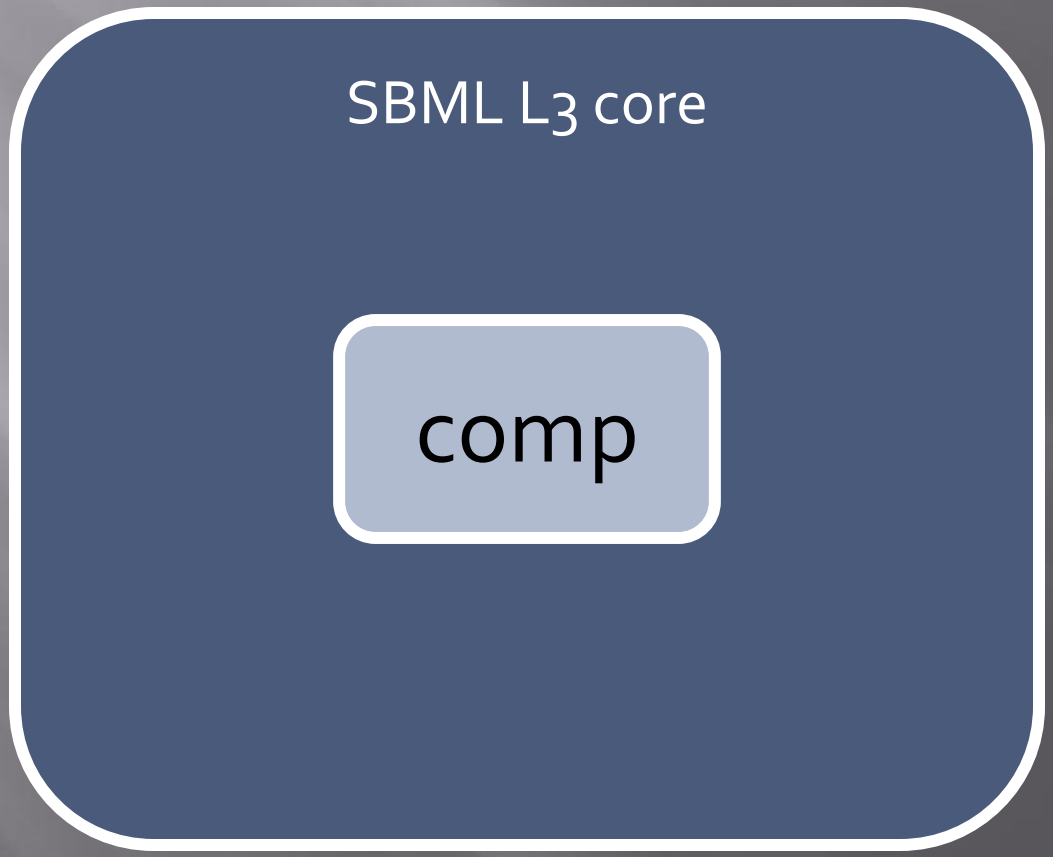
Design Goals

- Interact cleanly with other packages



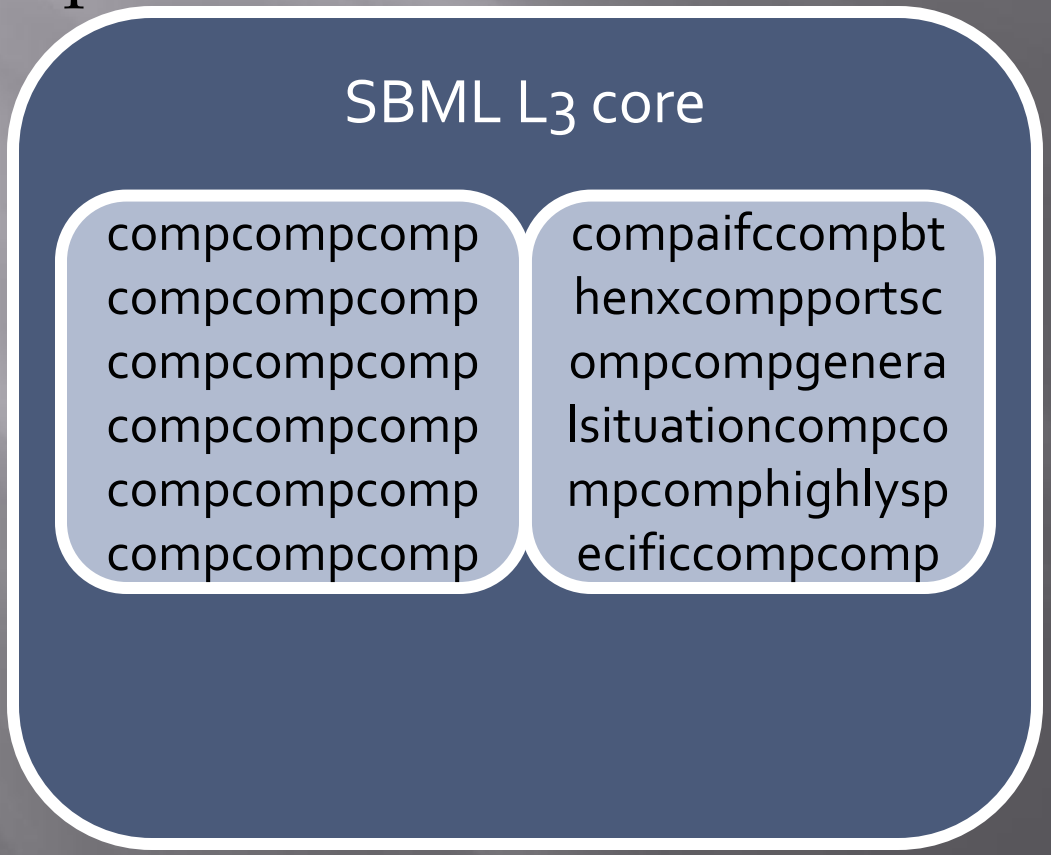
Design Goals

- Core still valid without comp constructs



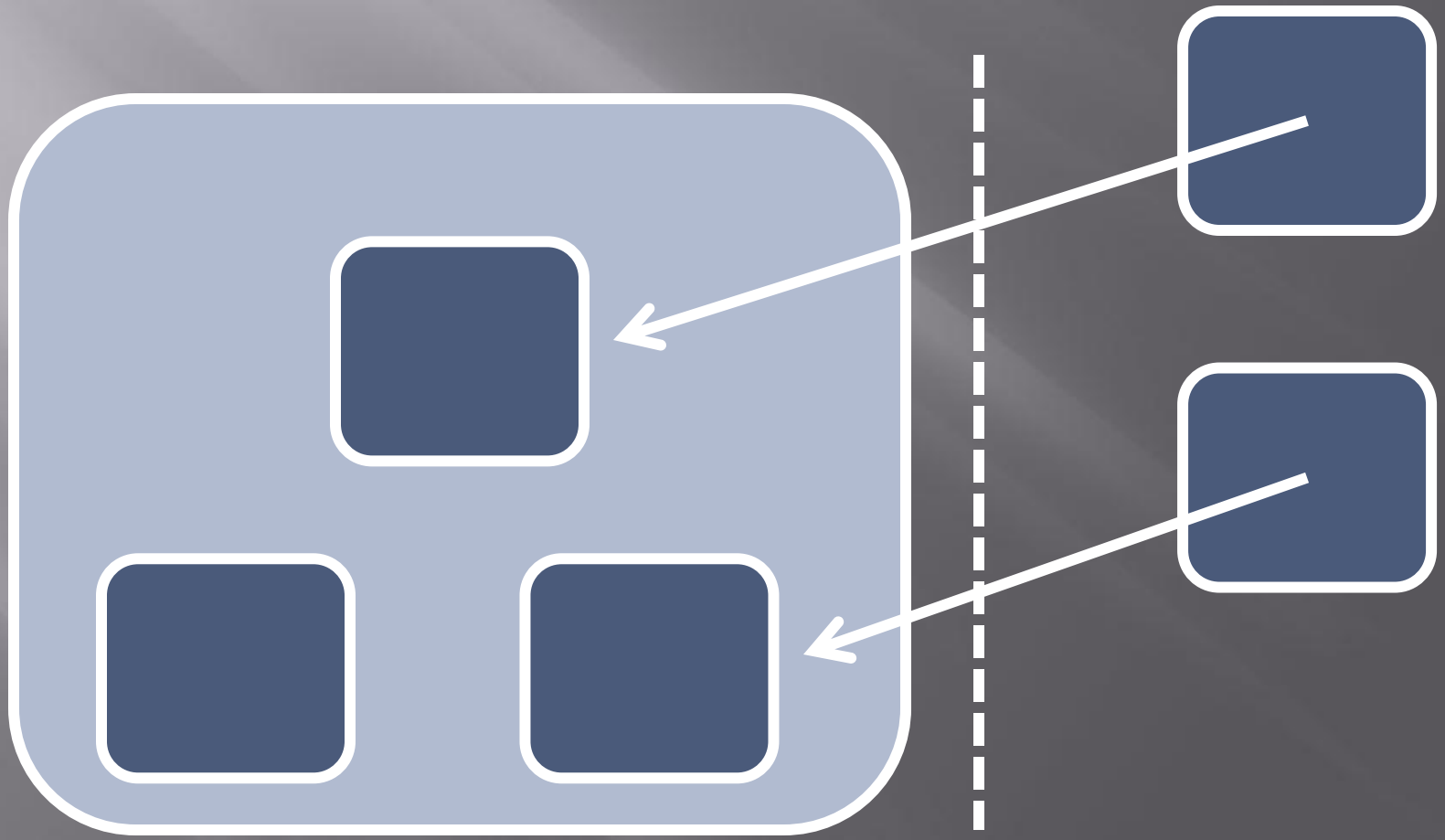
Design Goals

- Ignore verbosity of model, but don't over-complicate



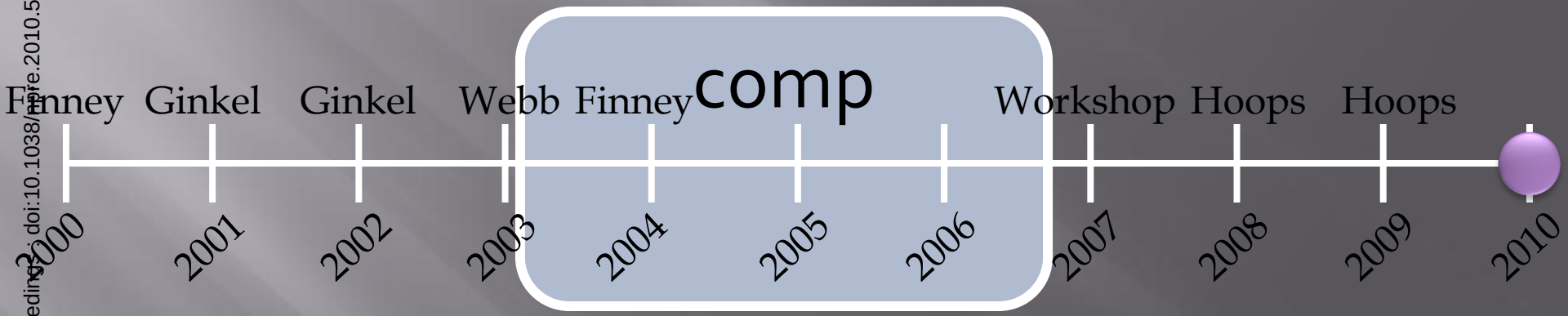
Design Goals

- Allow modular access by reference

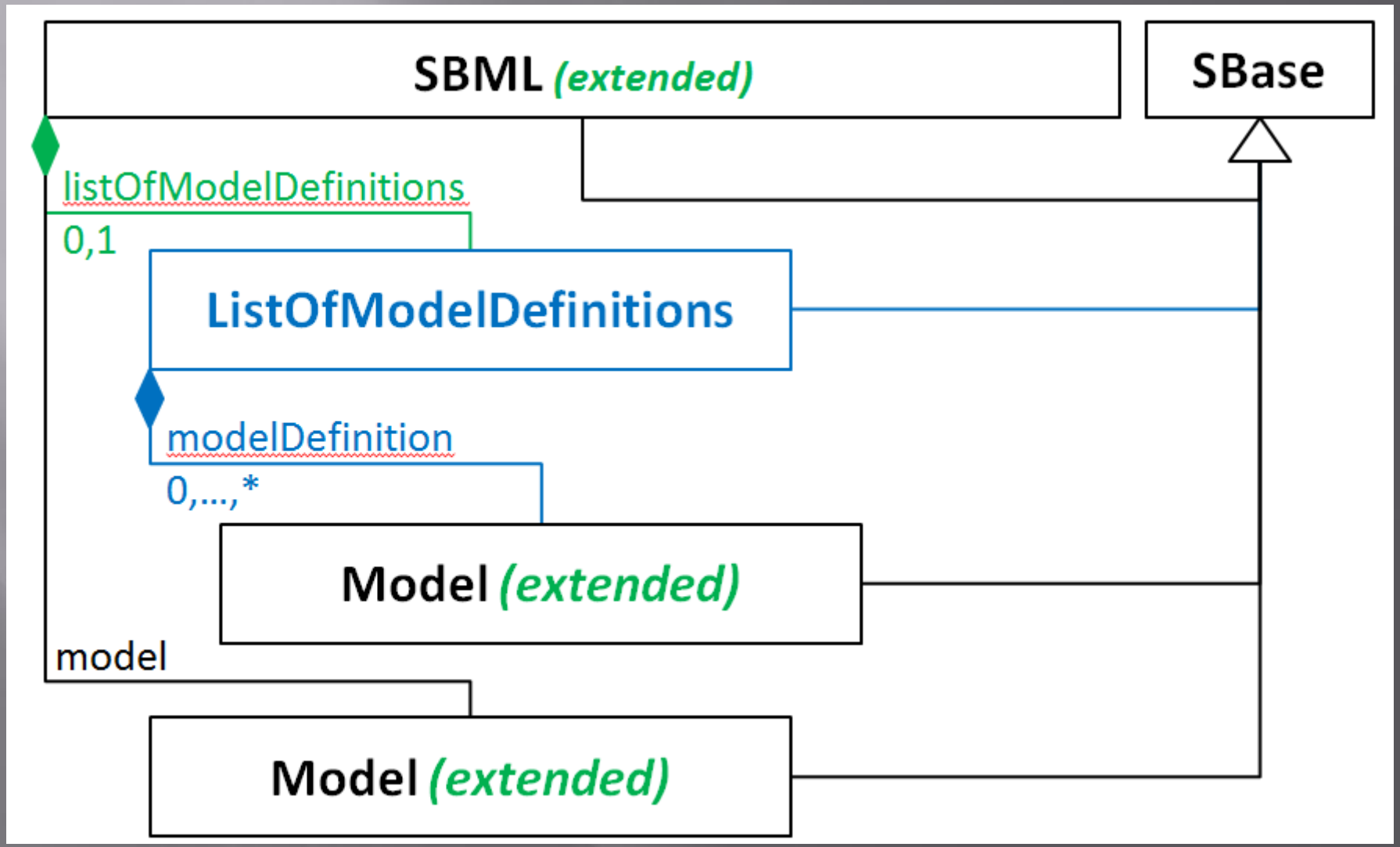


Design Goals

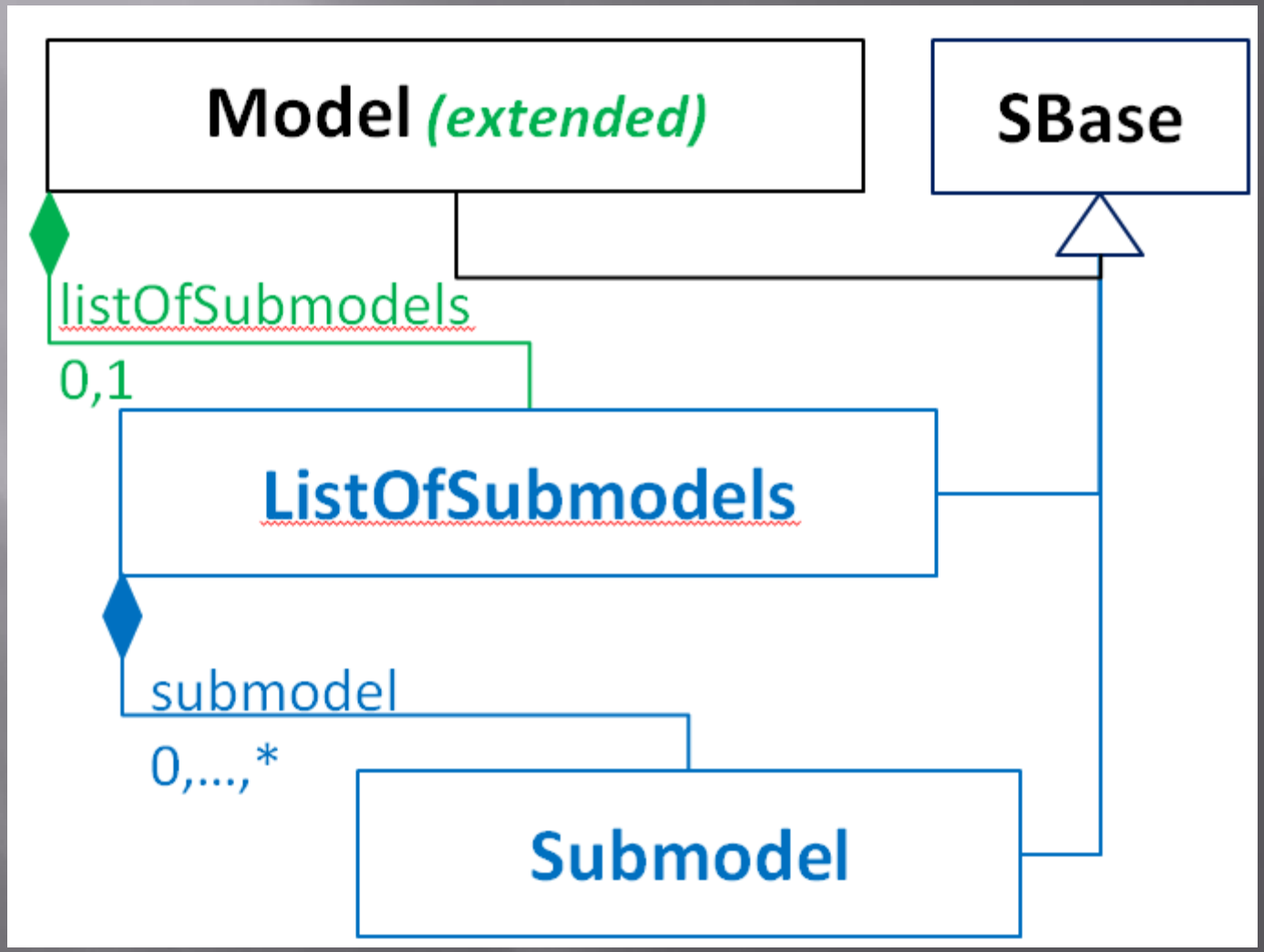
- Incorporate past design goals



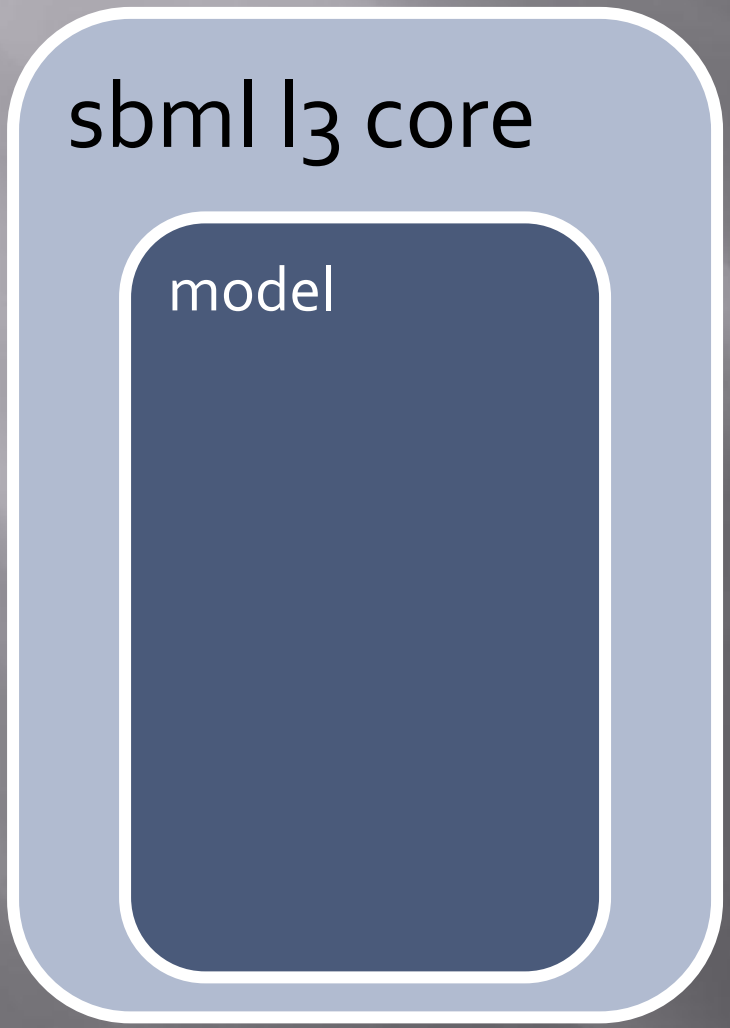
Basic structure: Definitions and Submodels



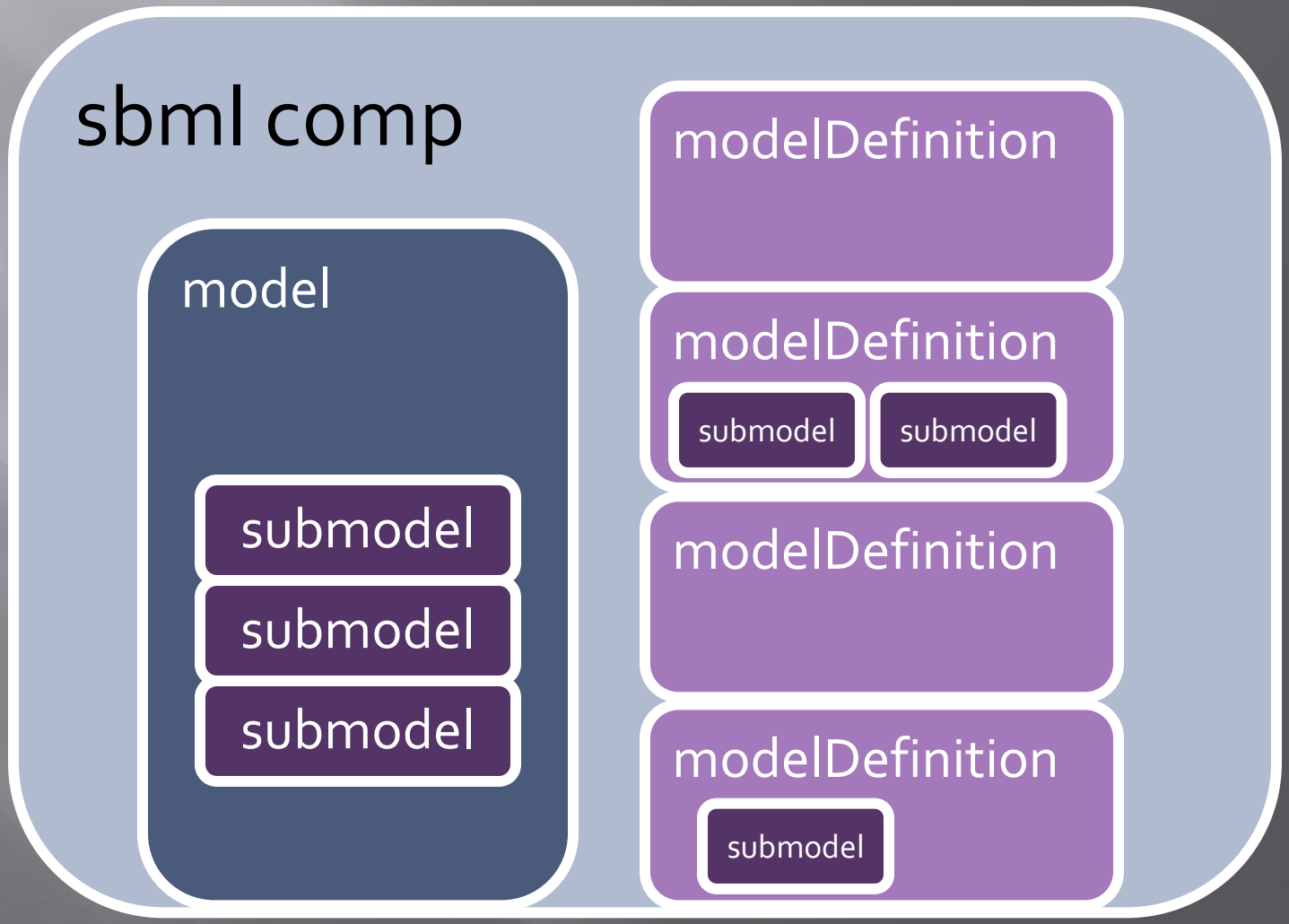
Basic structure: Definitions and Submodels



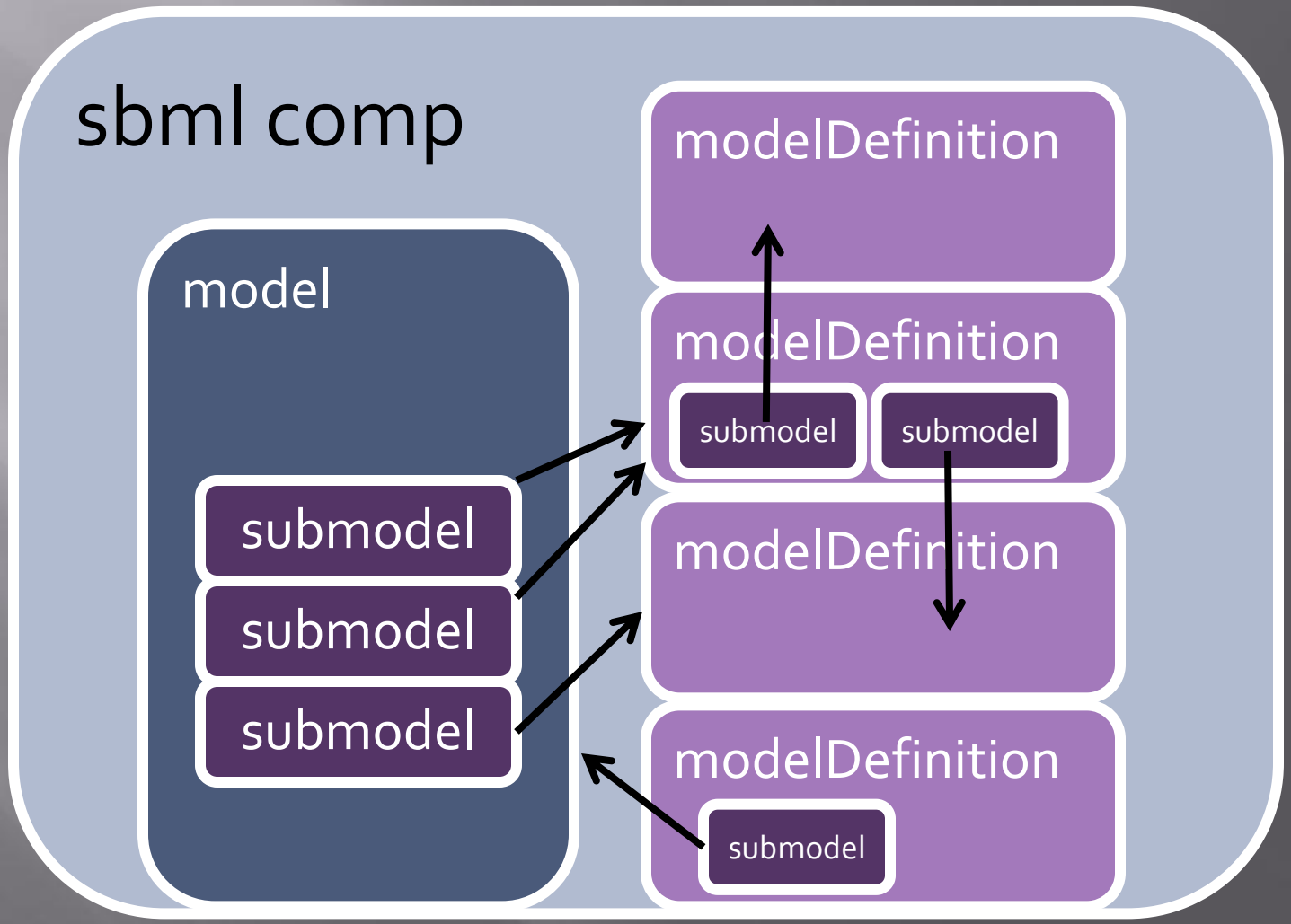
Basic structure: Definitions and Submodels



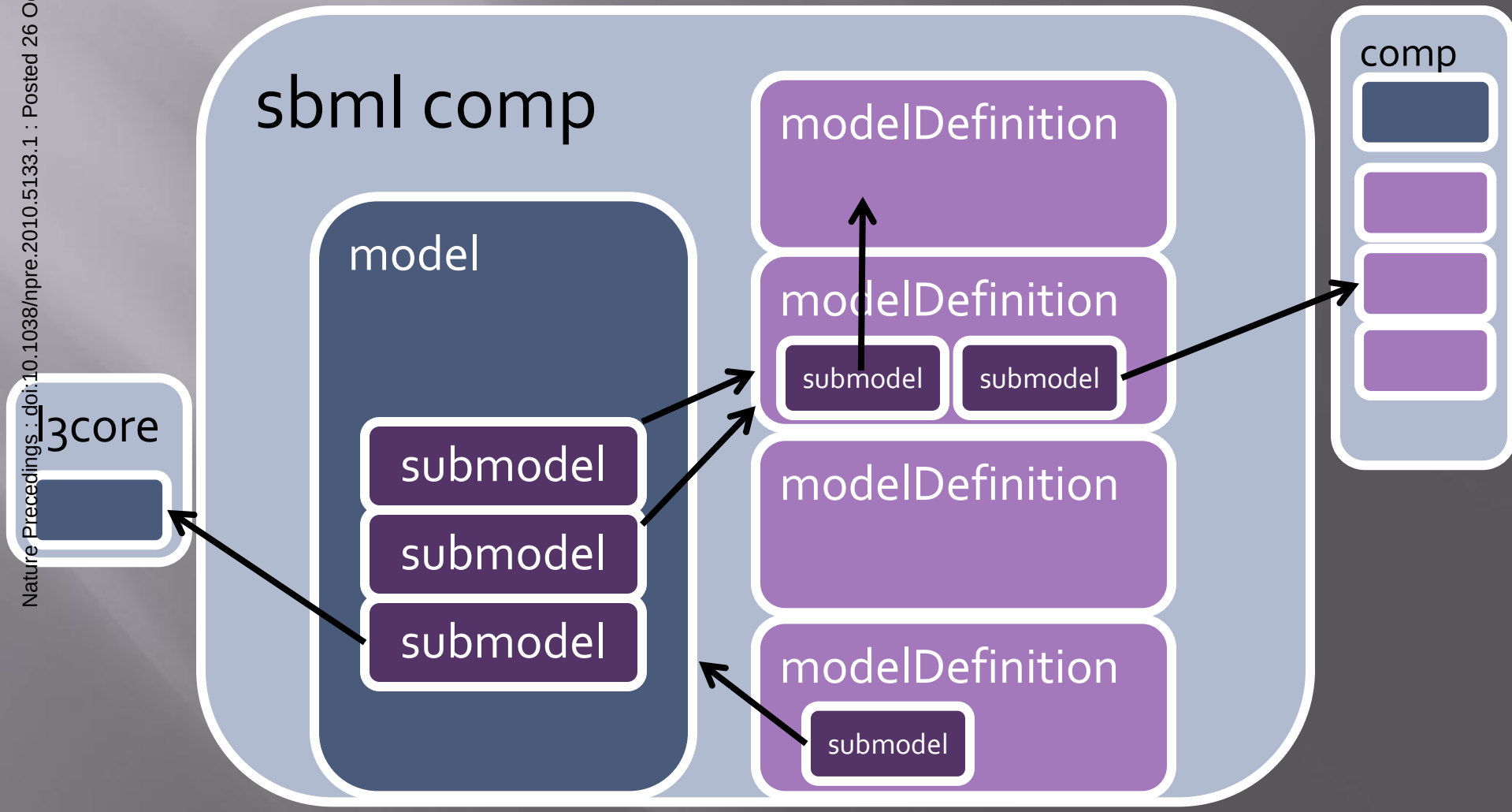
Basic structure: Definitions and Submodels



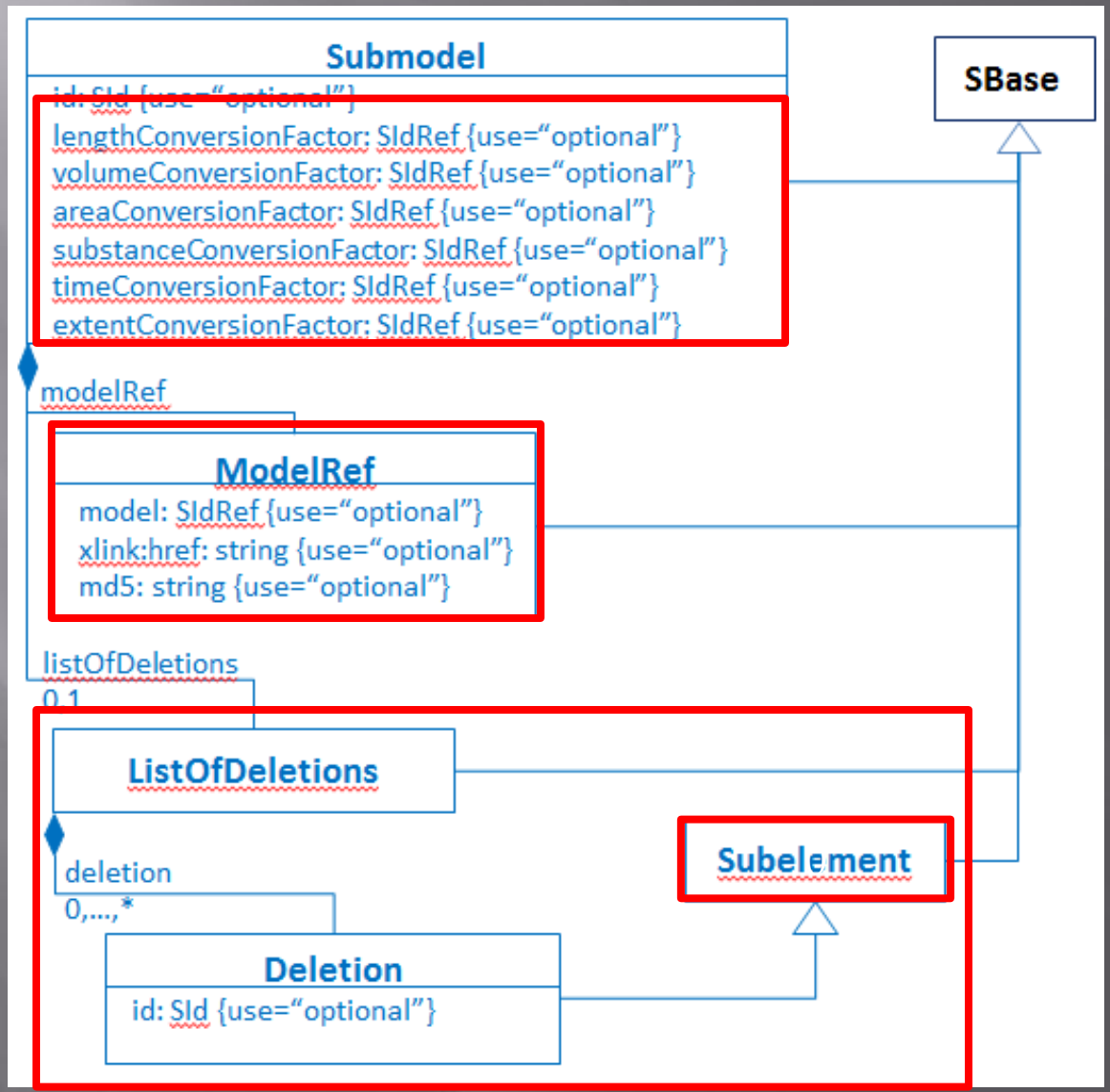
Basic structure: Definitions and Submodels



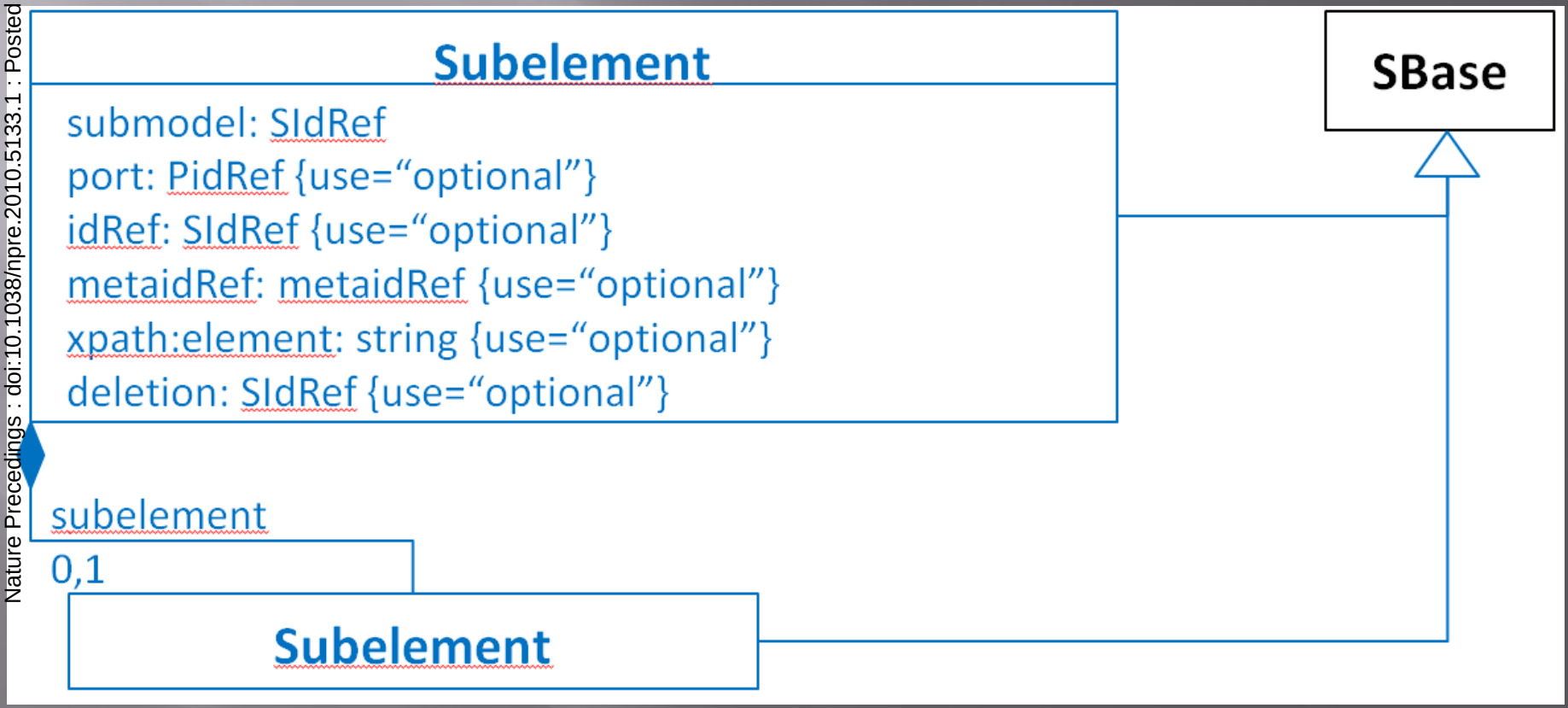
Basic structure: Definitions and Submodels



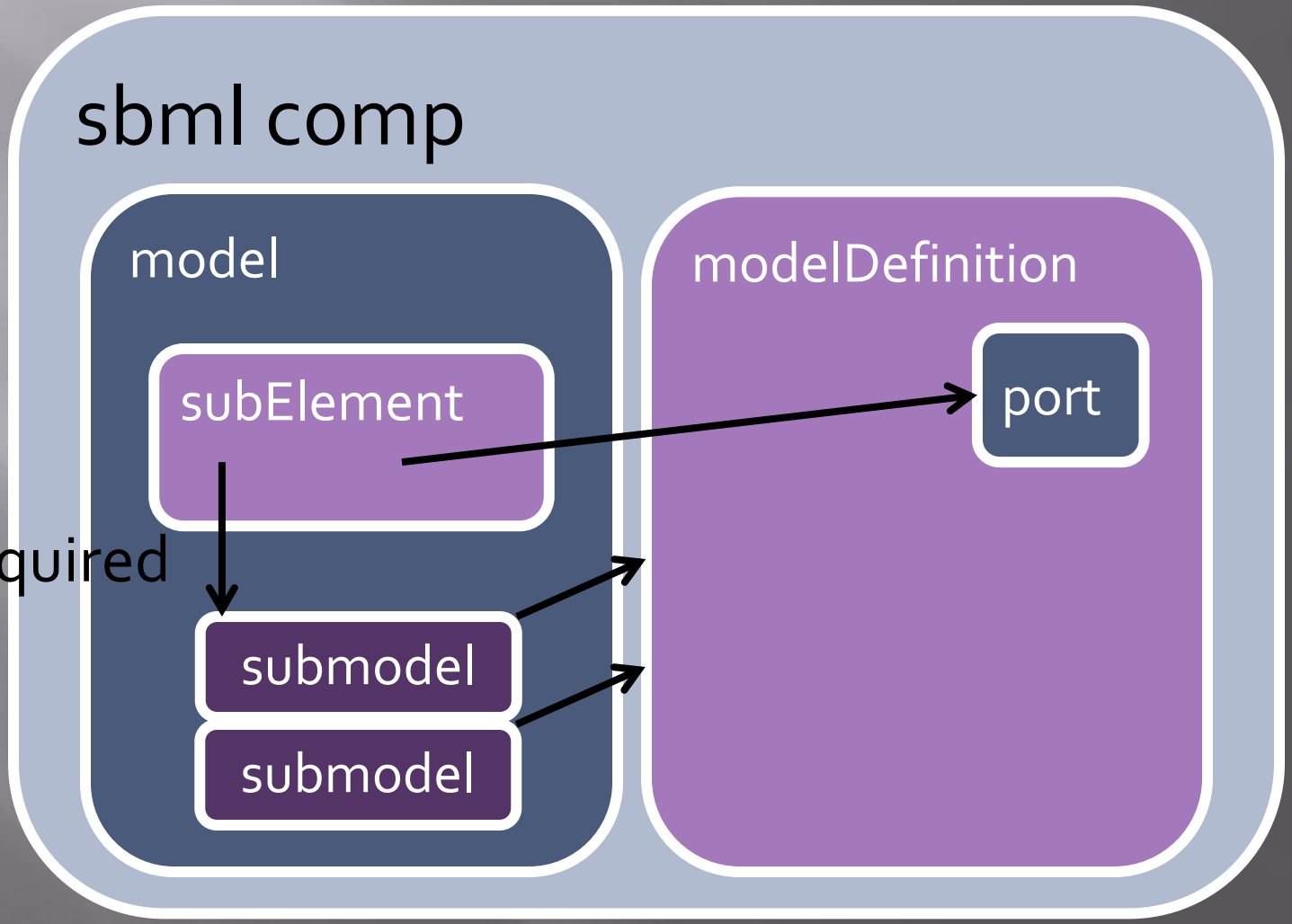
Basic structure: Definitions and Submodels



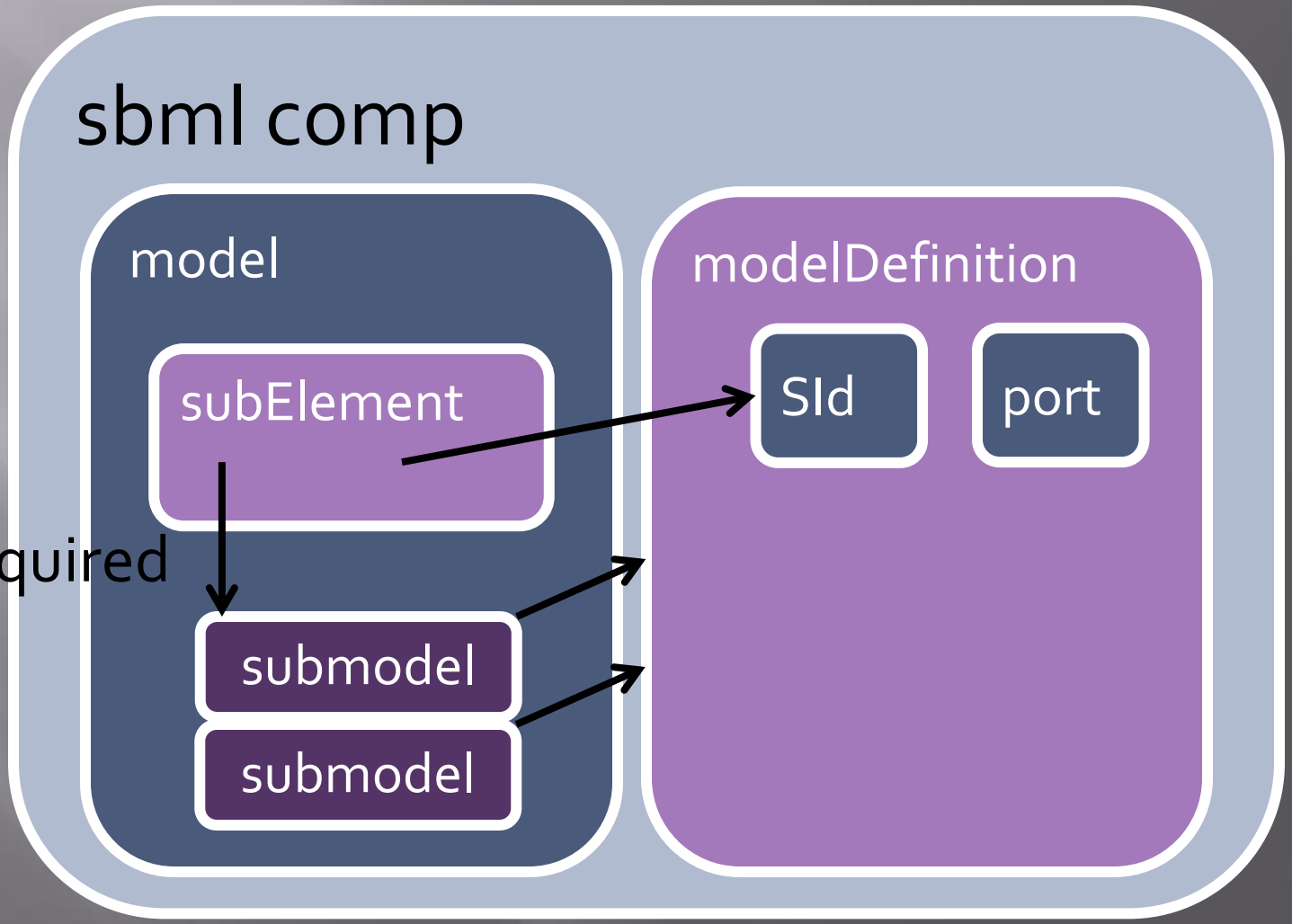
Subelements: ways to refer to submodel elements



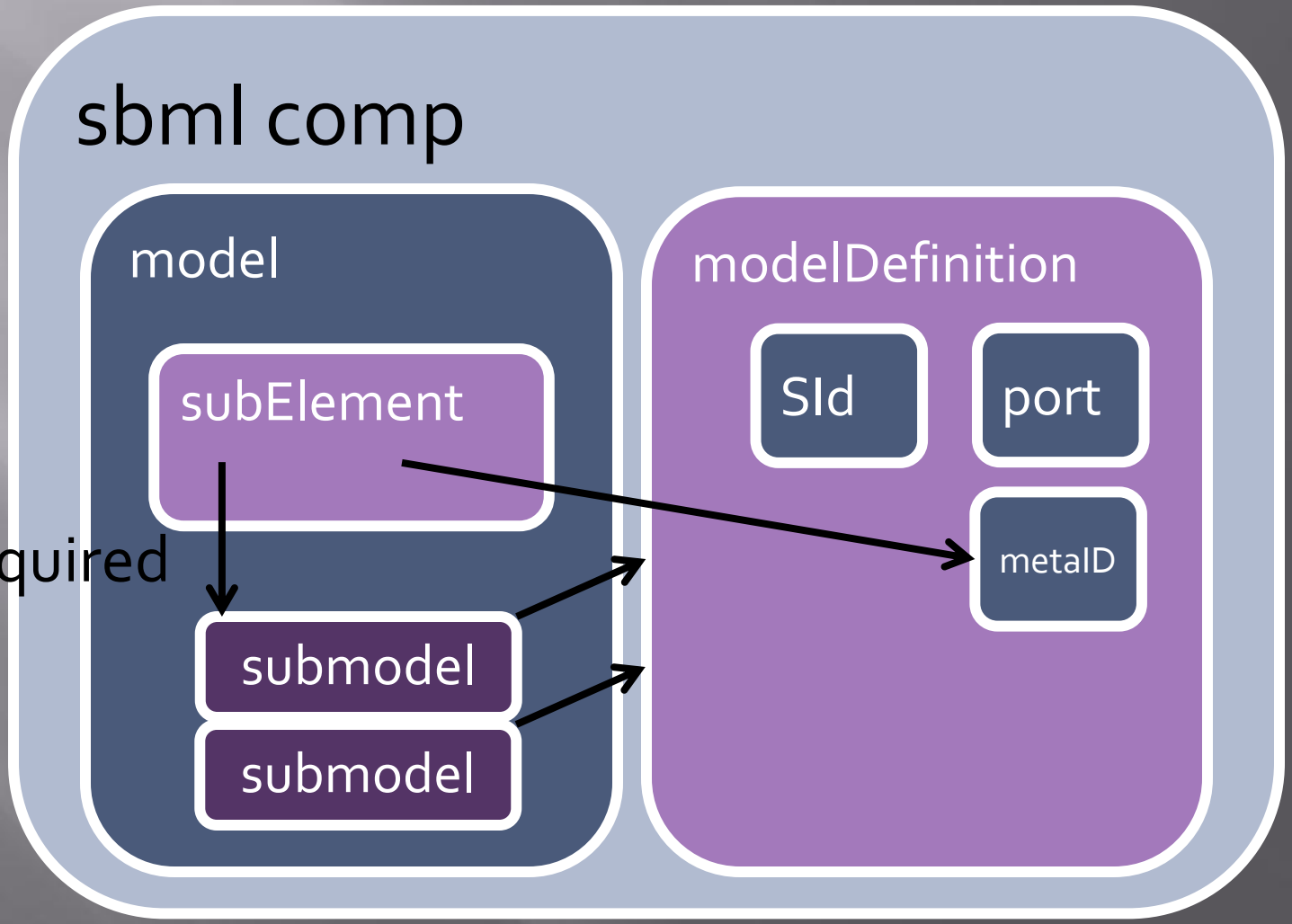
Subelements: ways to refer to objects



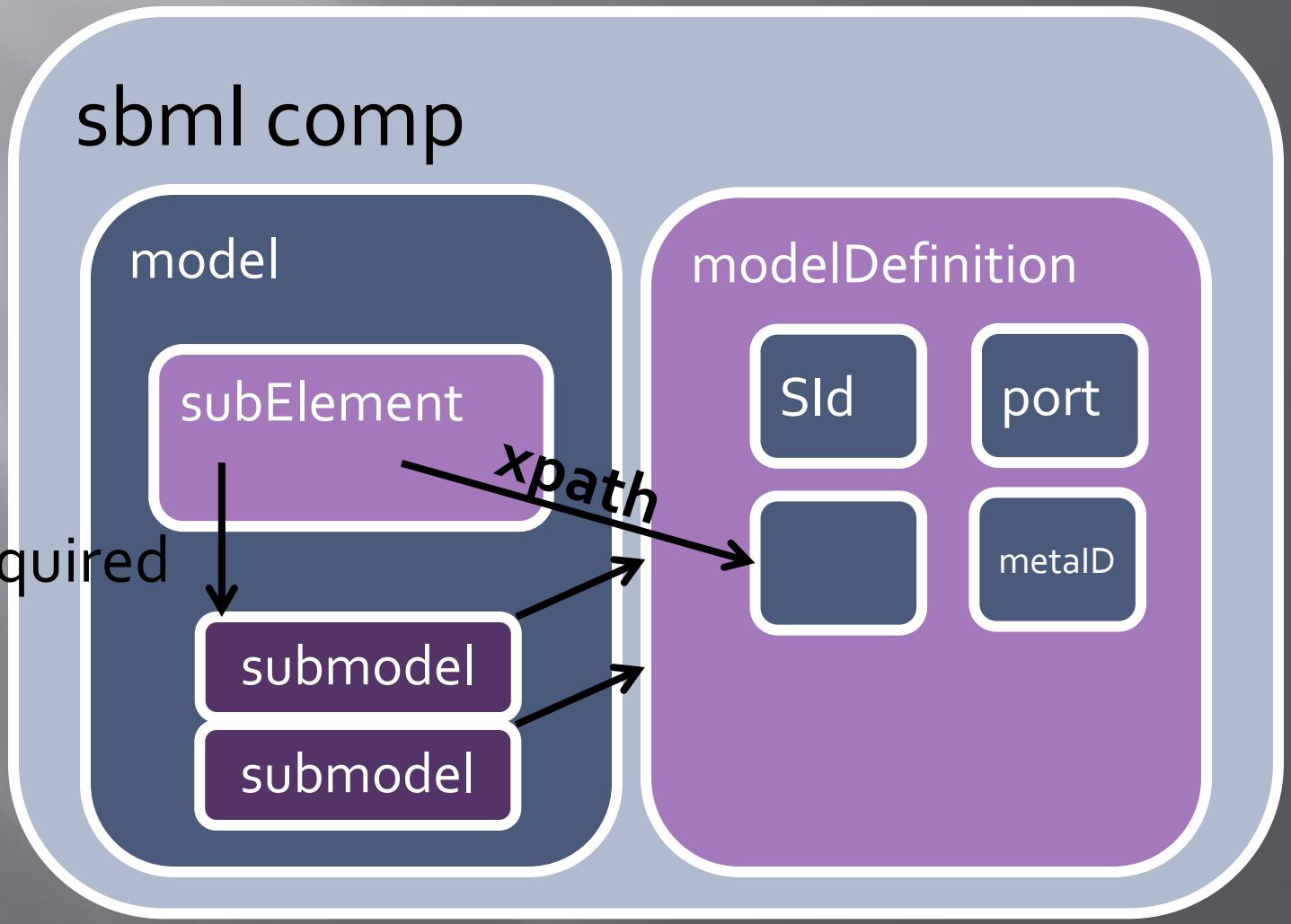
Subelements: ways to refer to objects



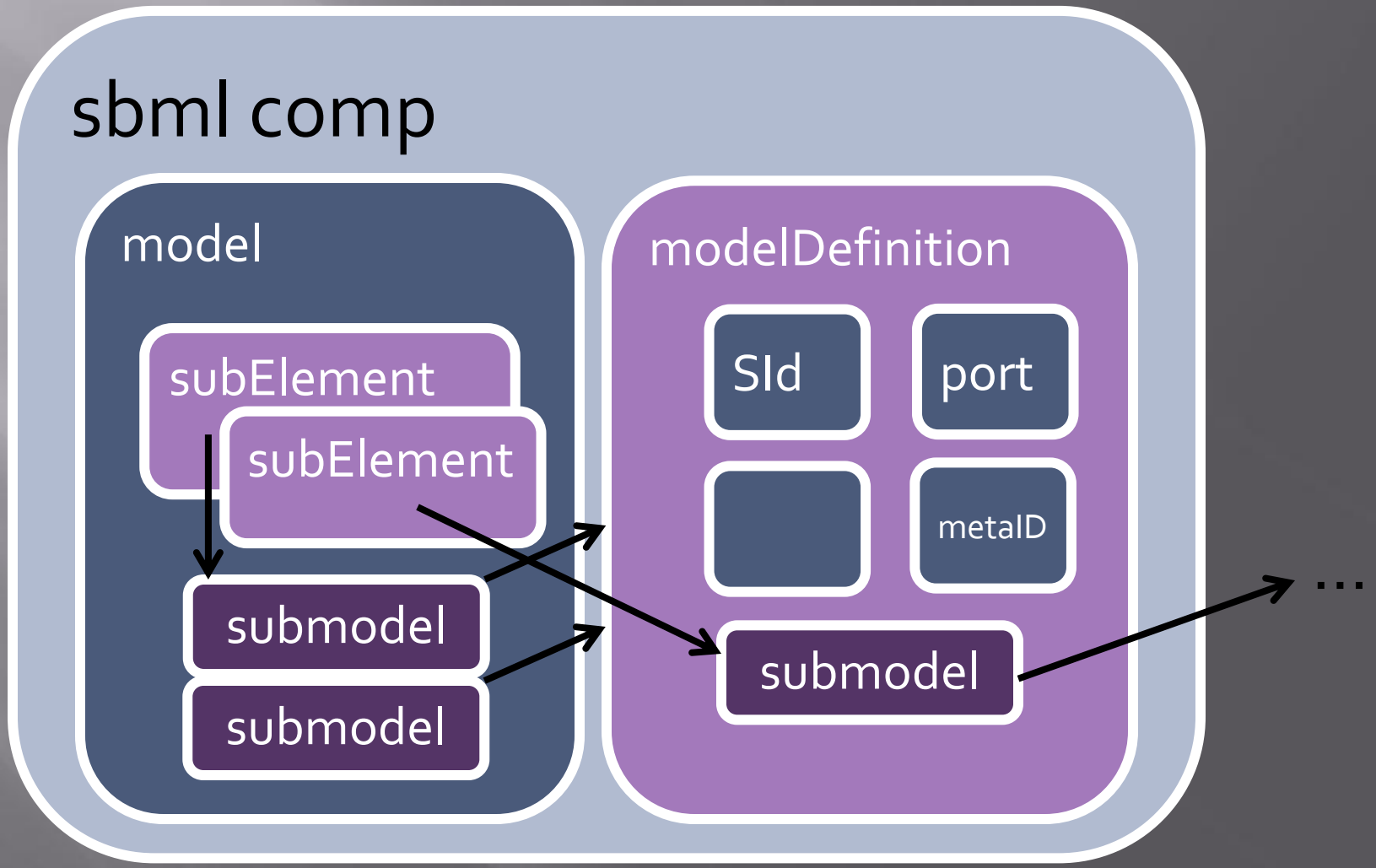
Subelements: ways to refer to objects



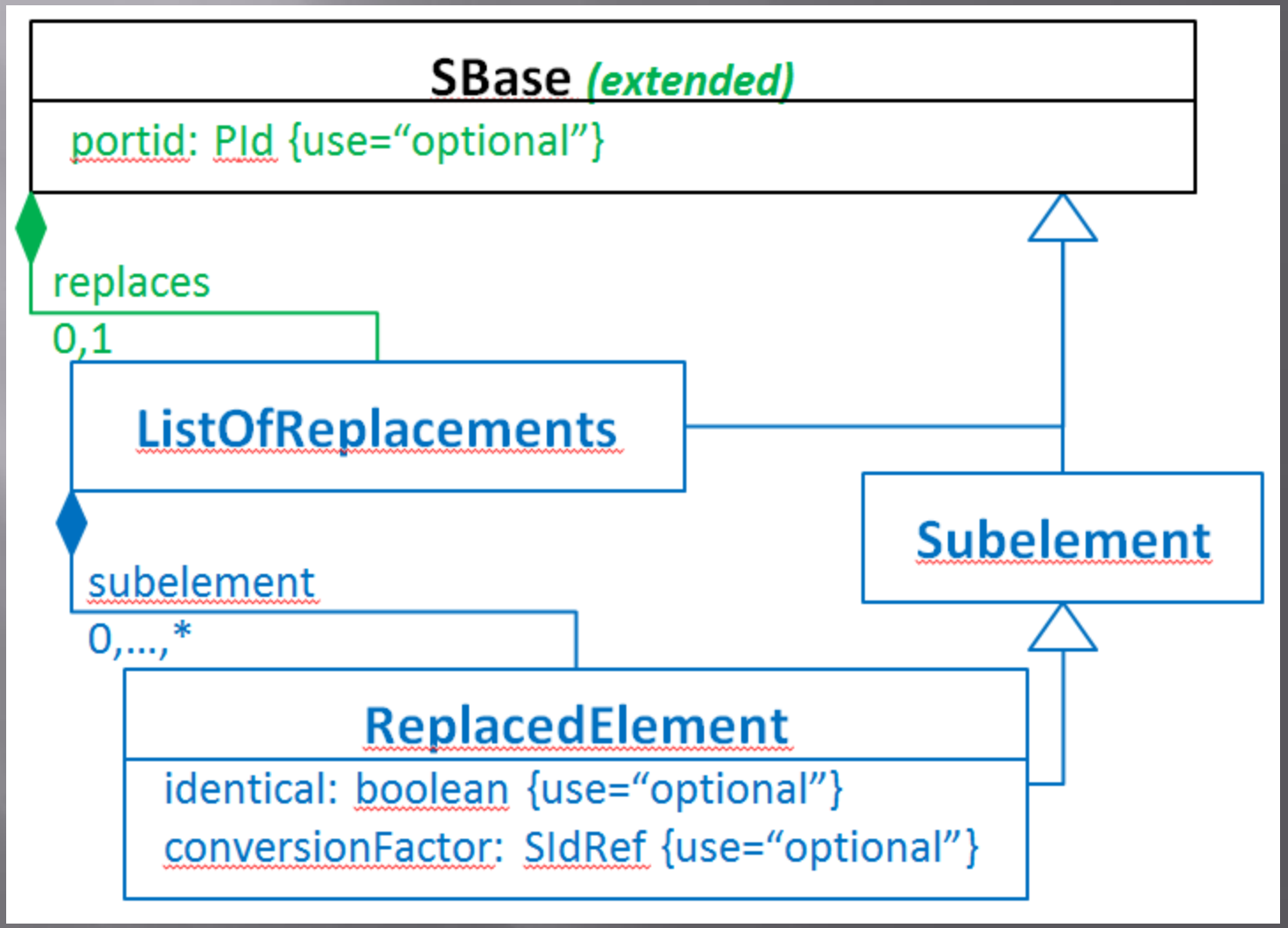
Subelements: ways to refer to objects



Subelements: ways to refer to objects



Ports and Replacements



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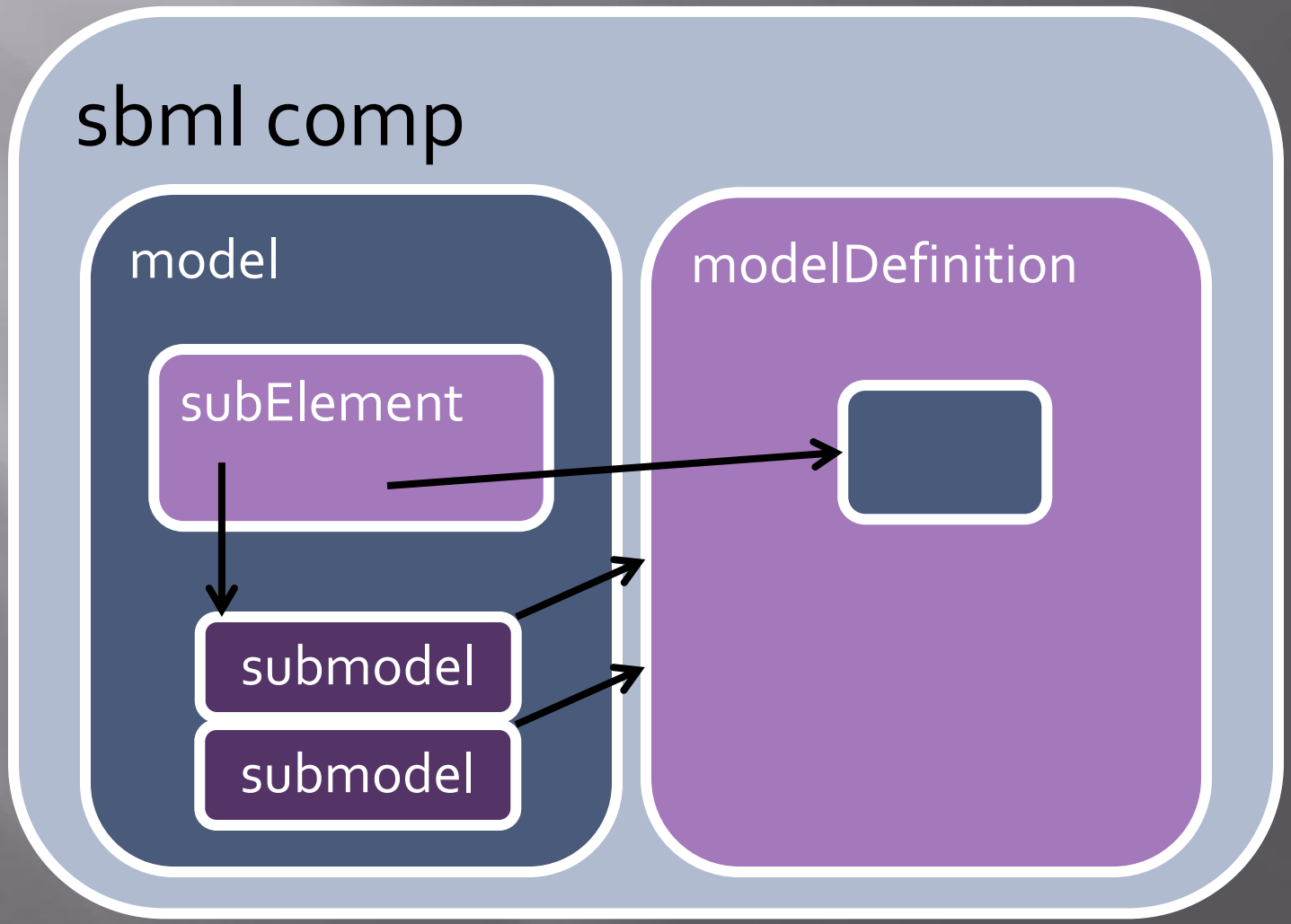

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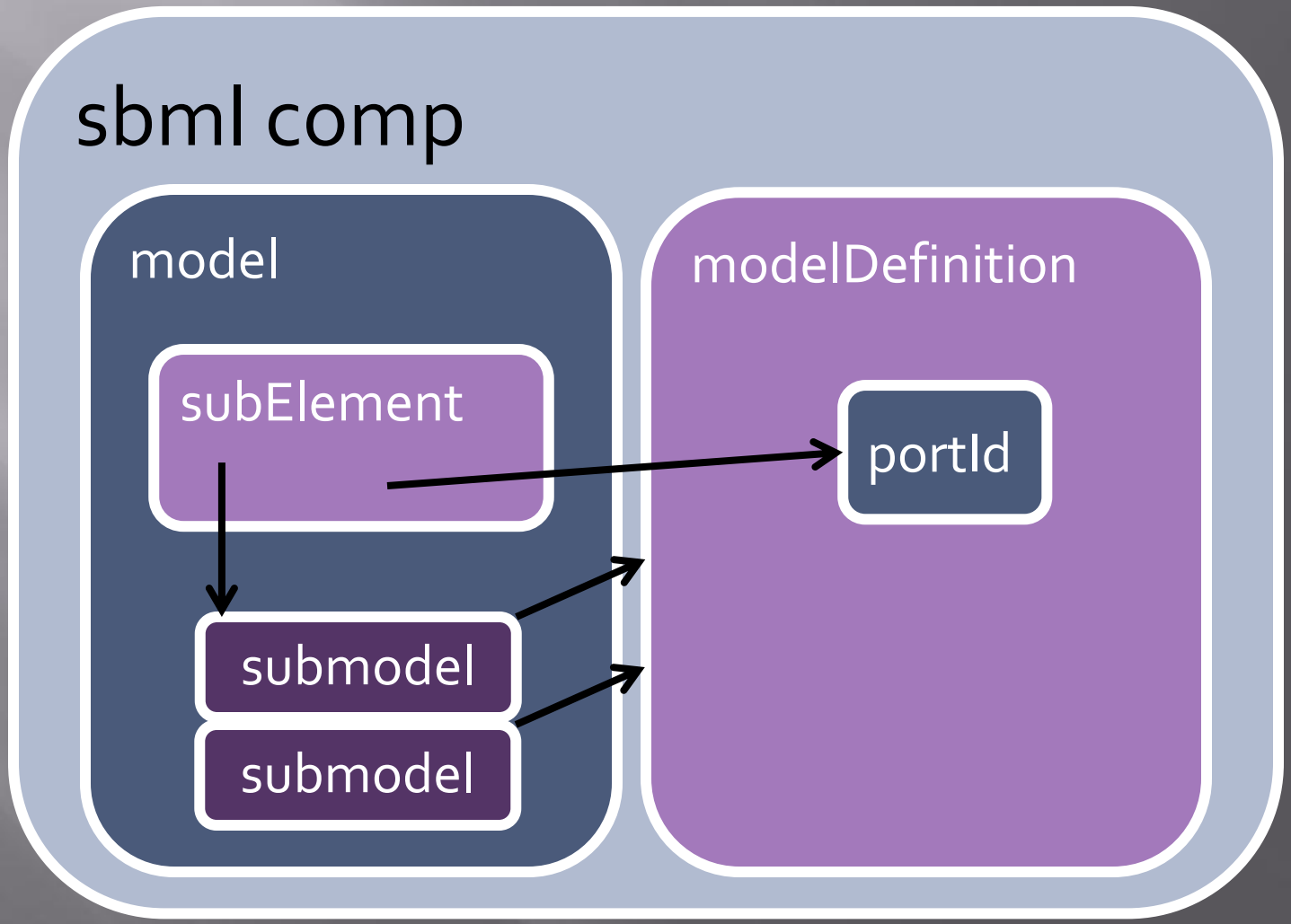

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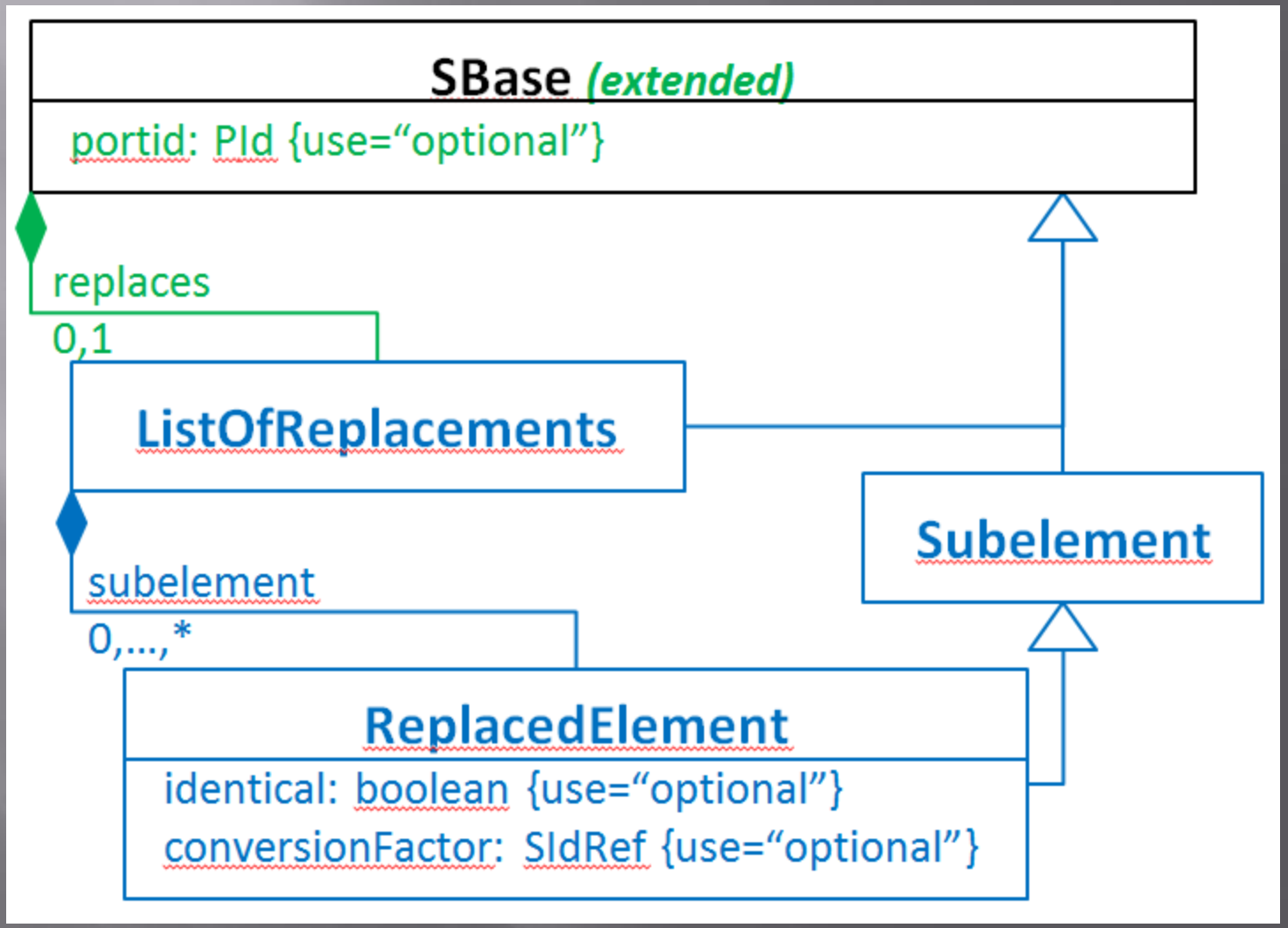

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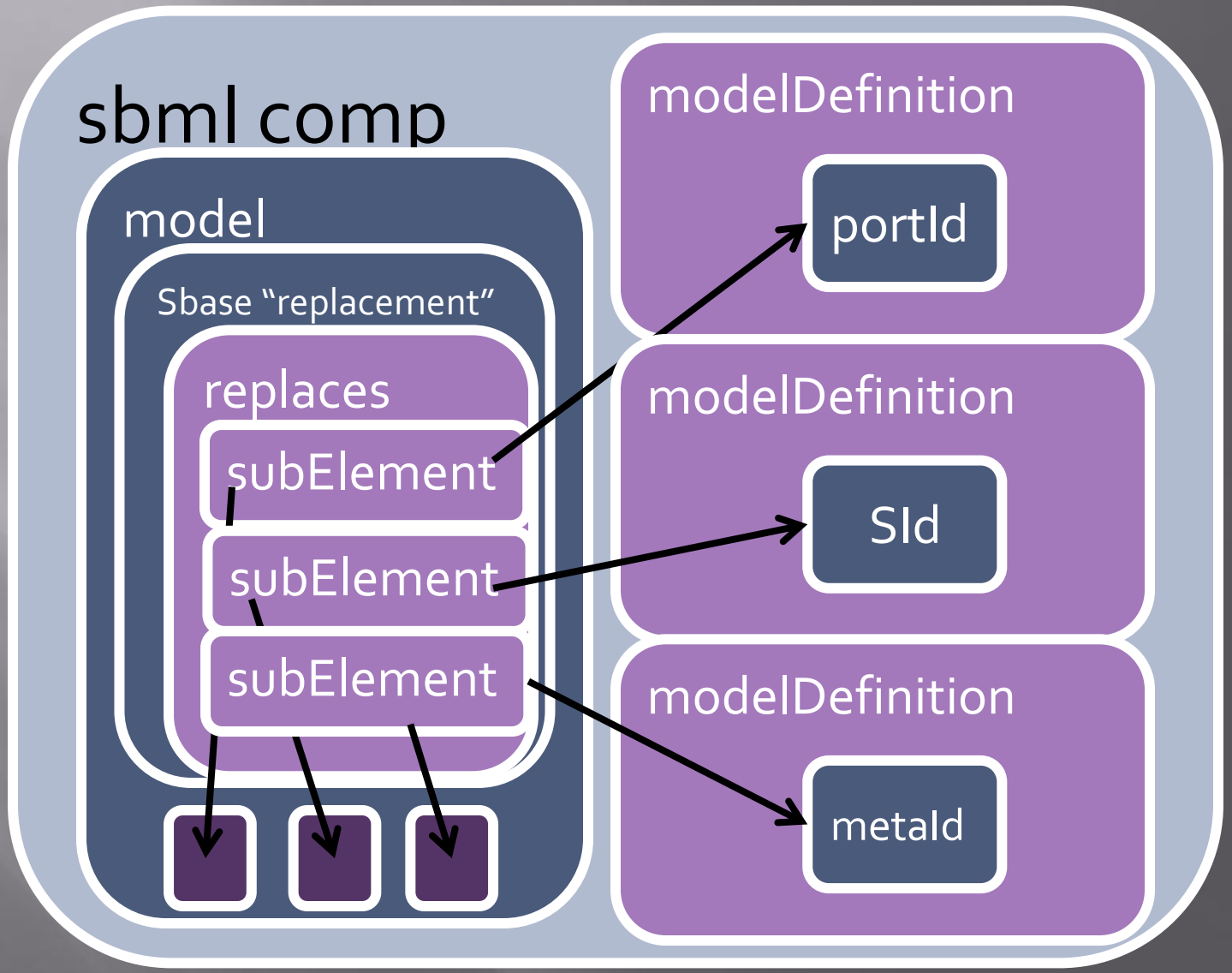
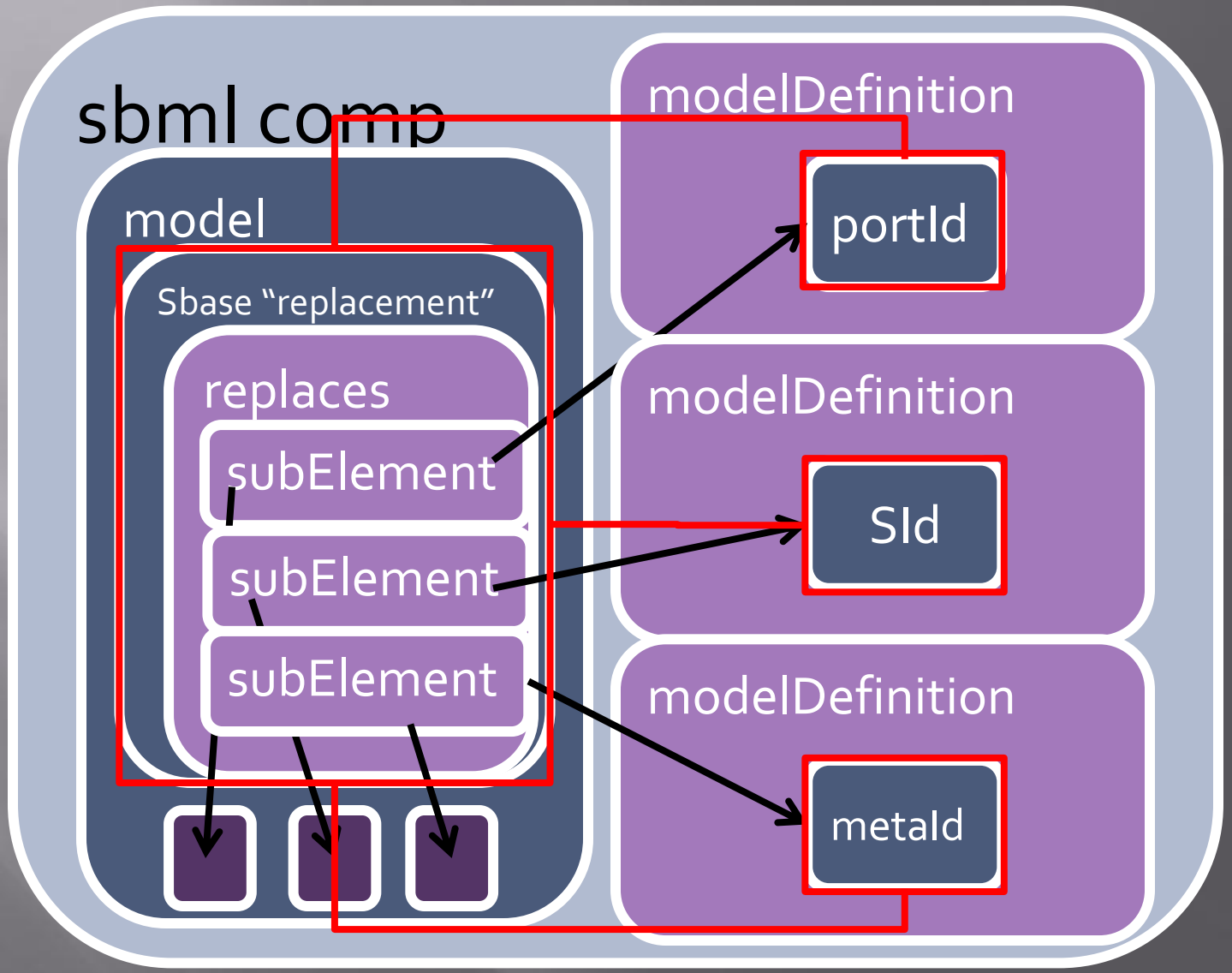


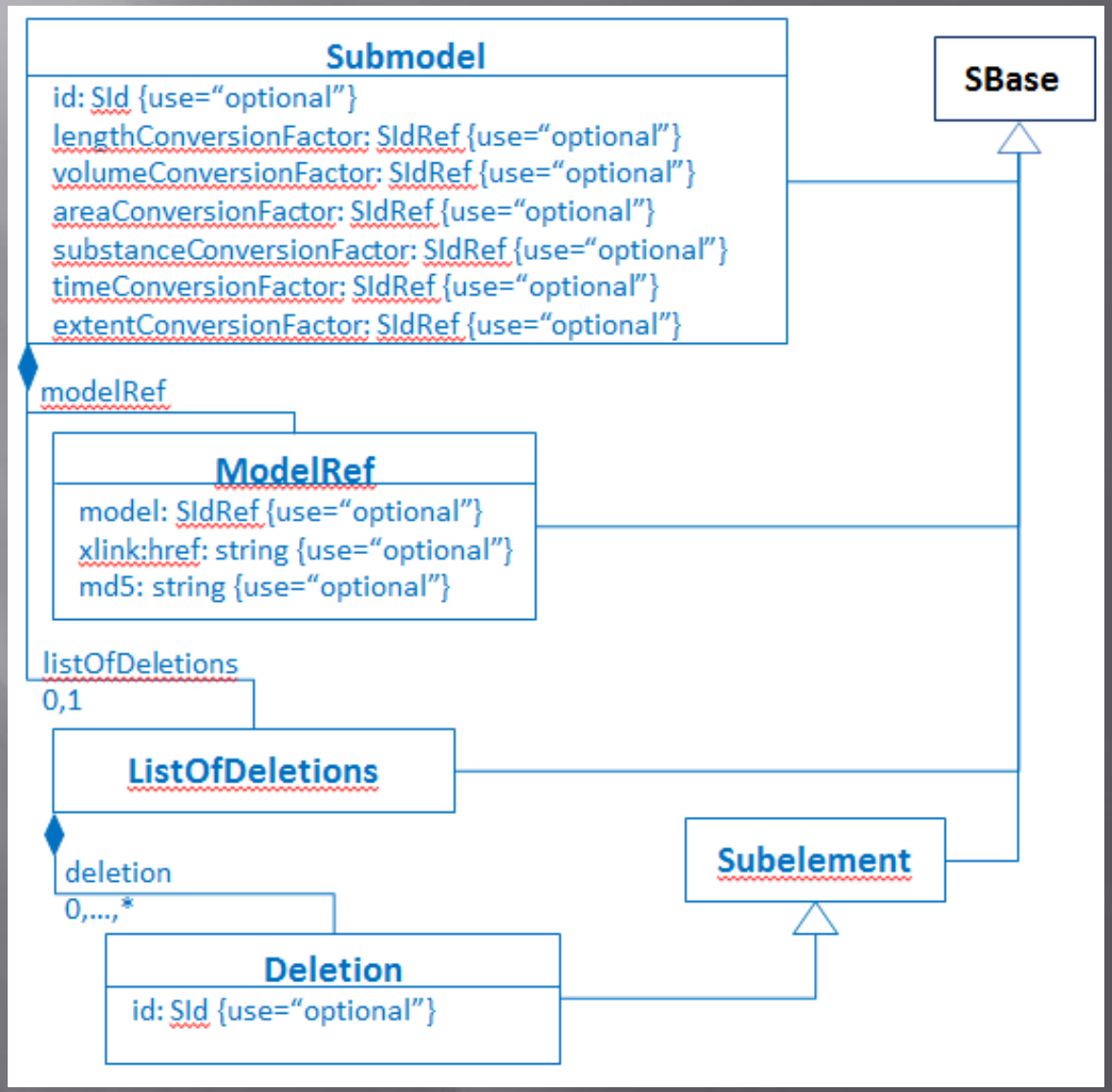
Ports and Replacements



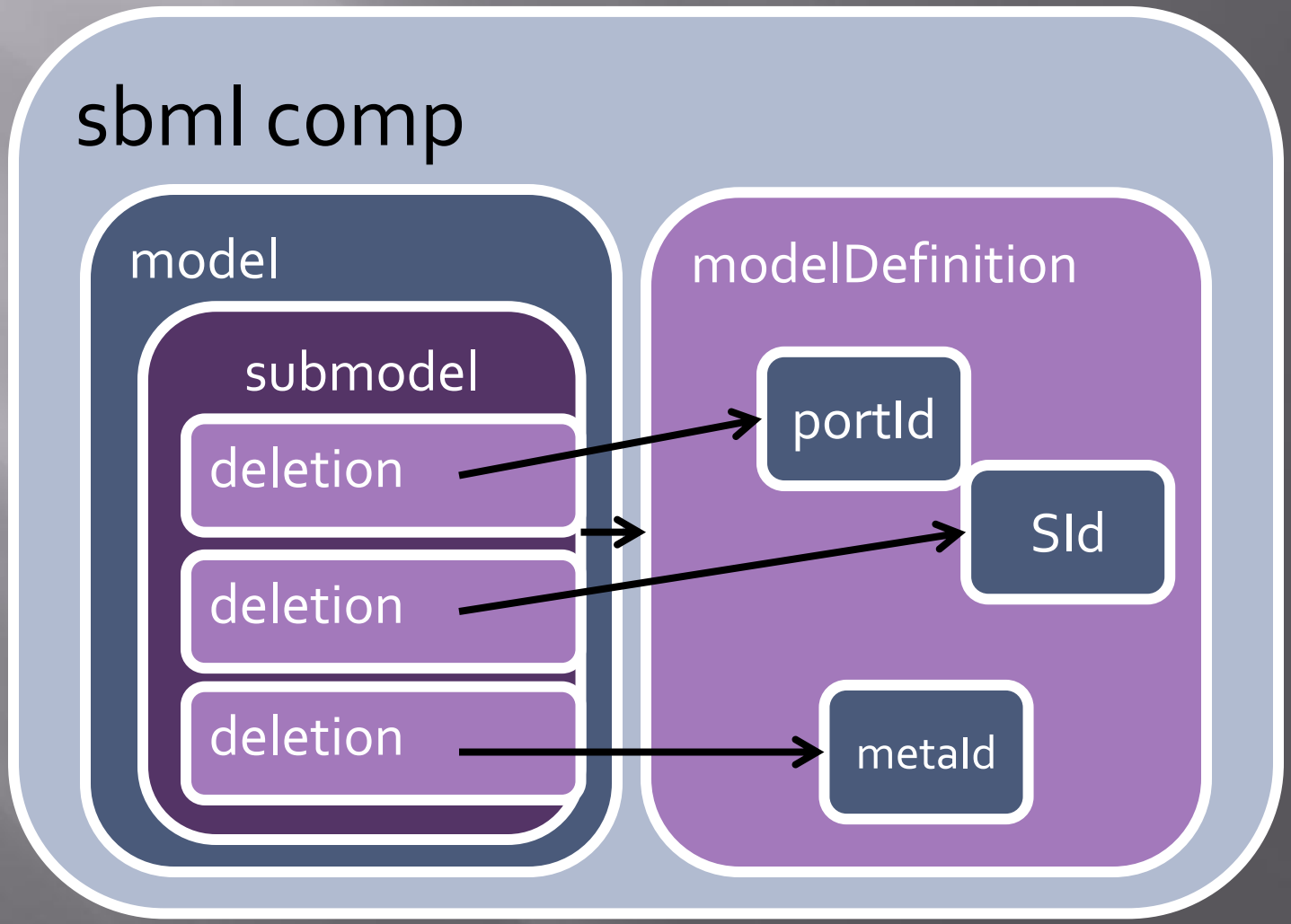
Replacement Rules

- Any old reference to a replaced element's SId now refers to the new element.
- Any old reference to a replaced element's metaId now refers to the new element.
- All old math must use conversionFactors from Replacement elements, if defined, or the Submodel's conversionFactors, if defined and relevant.
- If flagged 'identical=true', the replacing element must be identical to what it replaces.

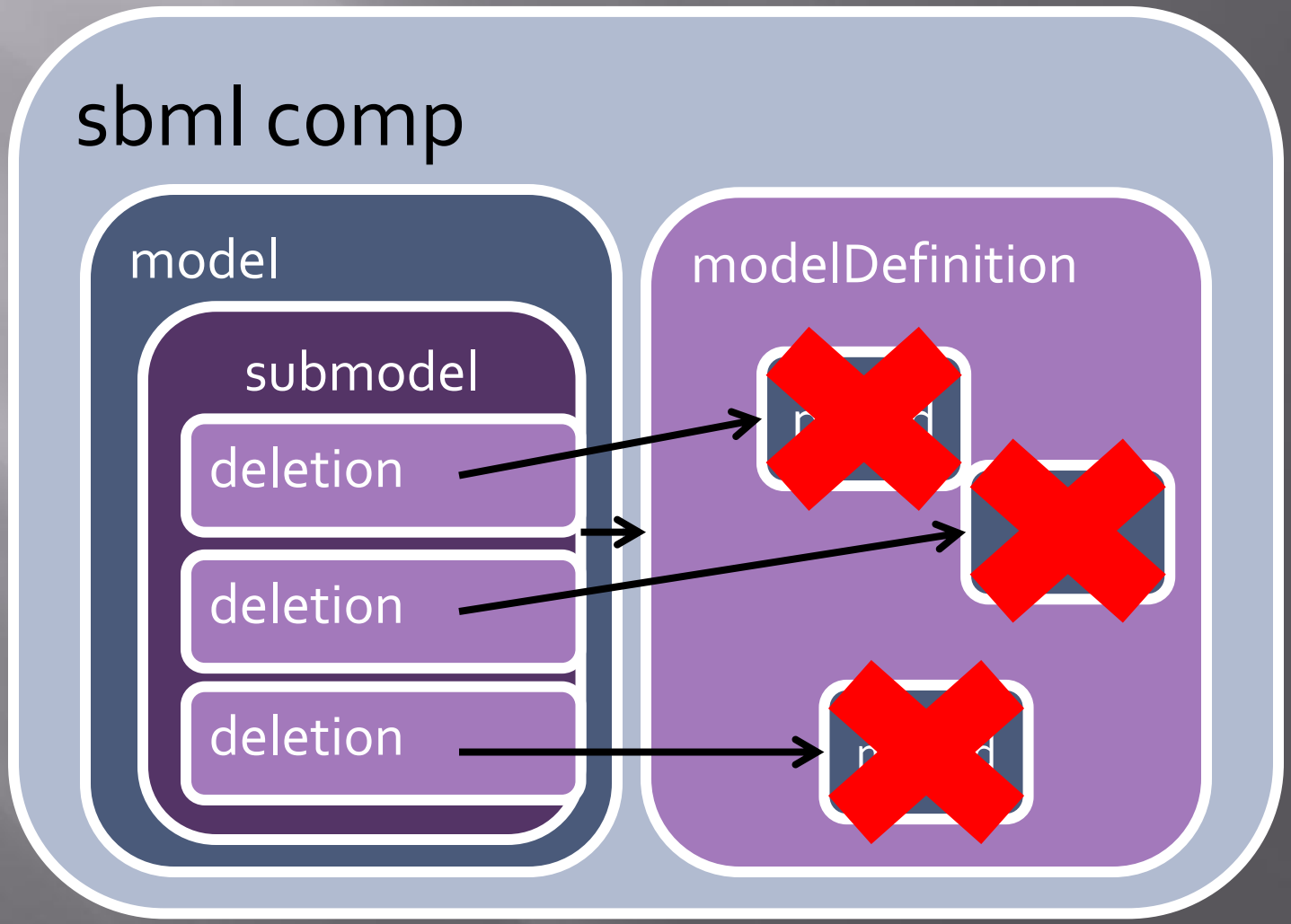
Deletions revisited



Deletions Revisited



Deletions Revisited



Validation

- Determine if the deletion/replacement rules can be followed.
- Determine if following the rules results in a valid ‘flat’ model.
- That’s it! (no type checking!)

conversionFactors

- If a conversionFactor is defined for a replacement, that takes precedence.
- If not, relevant conversionFactors are applied to **all** remaining subelements in the submodel.

What does 'relevant conversionFactor' mean?

- If an element has a unit type, it can be converted by the corresponding conversionFactor.
- Example: A compartment with spatialDimension=3 : areaConversionFactor
- Example 2: A species with 'hasOnlySubstanceUnits=true in a 3D comp: substanceConversionFactor/areaConversionFactor
- Species that replace species with different values for 'hasOnlySubstanceUnits' use the value of compartment in their conversion.

Acknowledgements

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