

**Draft for Discussion:
SBML Proposals for
“*Revised Multi*”, “*Simple Spatial*”
and “*Multi-Spatial*” Extensions
(COMBINE 2012, Toronto)**

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Background and Motivation

- Rule Based Modeling approaches
 - Bionetgen, Kappa, Simmune etc.
- Proposal of Multi
(Multistate and Multicomponent Species)
 - SBML.org: Proposal approved, Drafted Specification, libSBML not released
- Rule Based Spatial Models
 - Special features such as diffusion coefficient
 - Example: Simmune 2

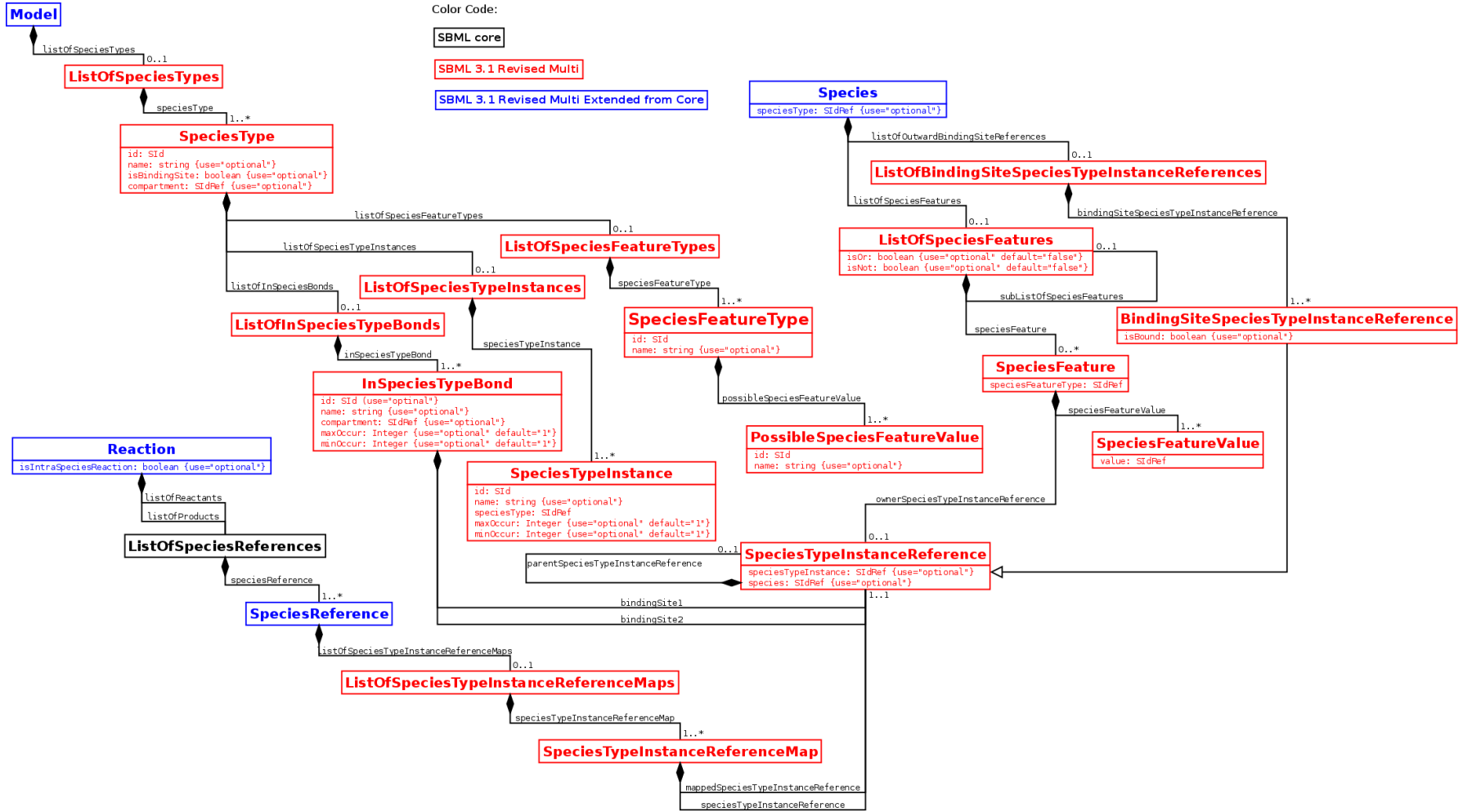
Discussion of Draft Specifications

- “Revised Multi”
 - Achieve goals described in the multi proposal in simpler manner
- “Simple Spatial”
 - Diffusion Coefficient
 - Multi Compartments
- “Multi-Spatial”

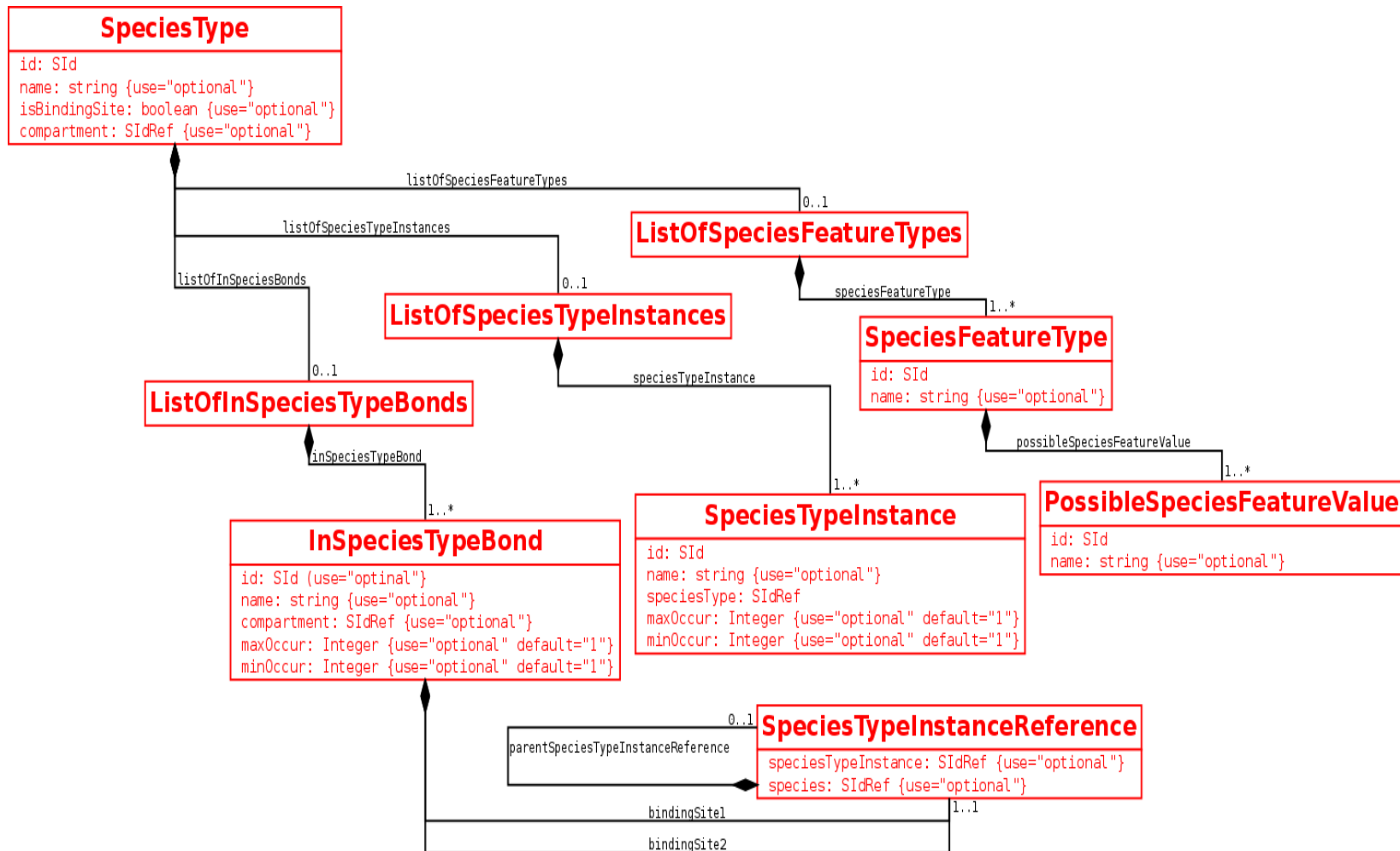
Comparison: “Multi” and “Revised Multi”

- Both: Add “[SpeciesType](#)” (Not in SBML L3V1 core)
- Similar in handling [multistate](#).
 - Multi: “[StateFeature](#)”
 - Revised Multi: “[SpeciesFeatureType](#)” and “[SpeciesFeature](#)”
- Major differences:
 - Multi:
 - [Selectors](#)
 - [Extra components](#) in “Rule”, “Reaction” and “Event”, etc
 - Revised Multi:
 - Extend “[Species](#)”
 - [Reference](#) to “SpeciesType” (functions as ‘template’ for species, internal bonds)
 - [States](#): “ListOfSpeciesFeatures”
 - [Binding status](#) of outward binding sites: “ListOfBindingSiteSpeciesTypeInstanceReferences”
 - [No extra components](#) in “Rule”, “Reaction” and “Event”, etc

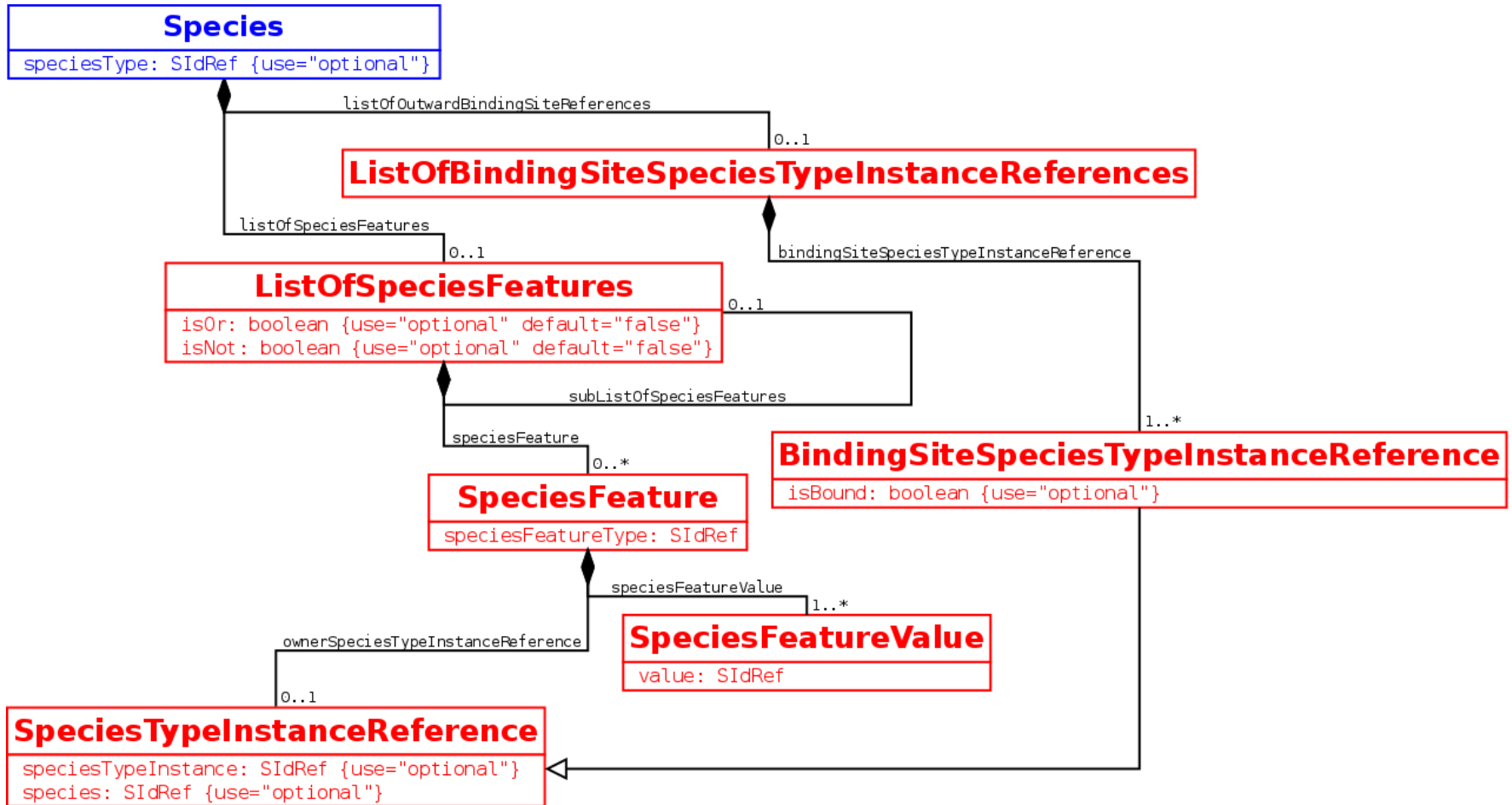
Revised Multi: UML



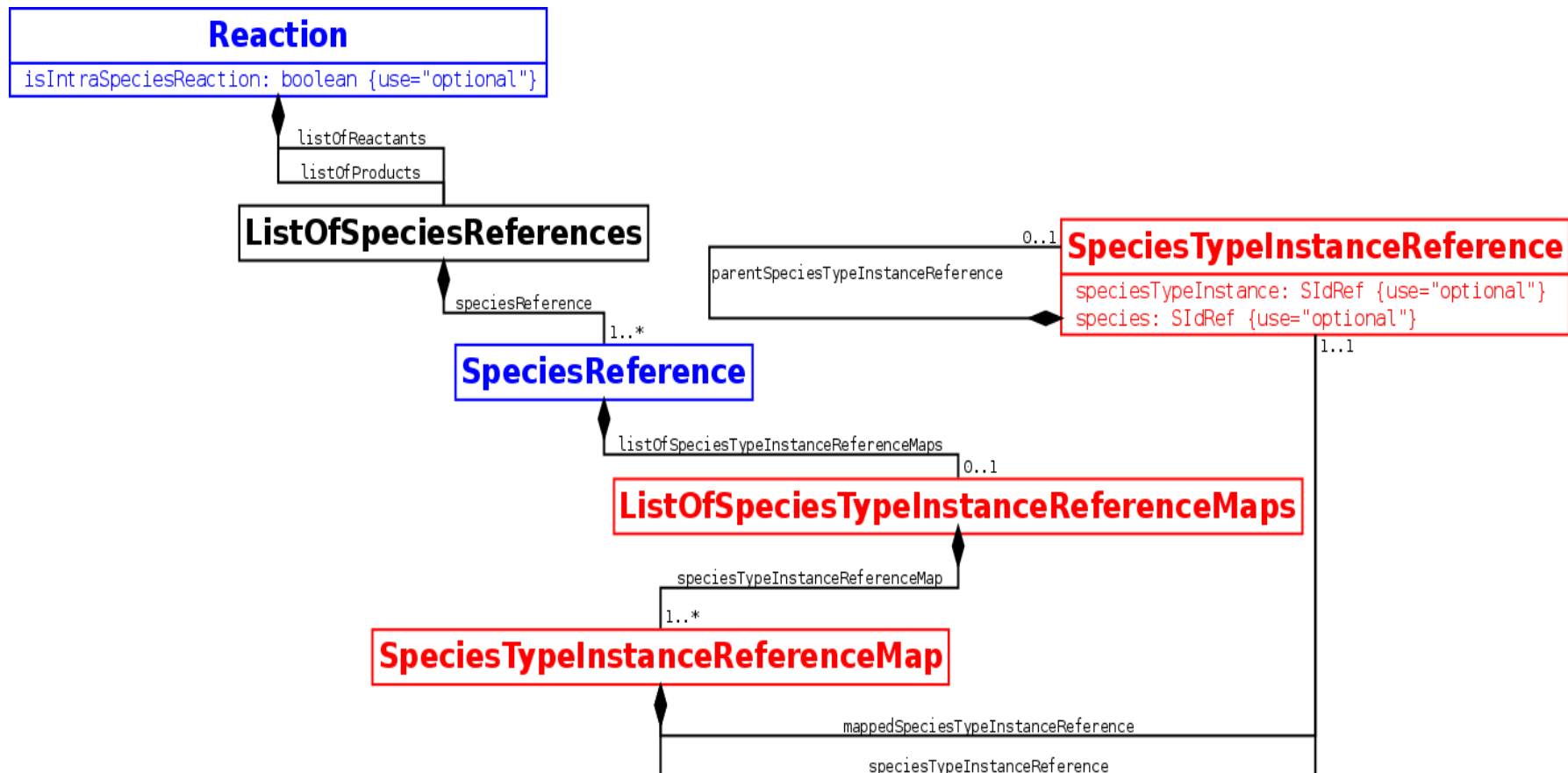
Revised Multi: UML



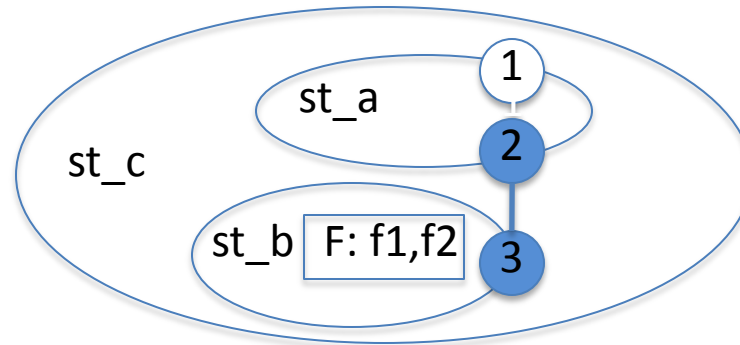
Revised Multi: UML



Revised Multi: UML



Revised Multi Example: SpeciesType



```
<sbml xmlns="http://www.sbml.org/sbml/level3/version1/core" level="3" version="1"
xmlns:multi=http://www.sbml.org/sbml/level3/version1/revised_multi/version1 >
```

```
...
```

```
<multi:speciesType multi:id="1" multi:isBindingSite="true" />
```

```
<multi:speciesType multi:id="2" multi:isBindingSite="true" />
```

```
<multi:speciesType multi:id="3" multi:isBindingSite="true" />
```

```
<multi:speciesType multi:id="st_a">
```

```
  <multi:listOfSpeciesTypeInstances>
```

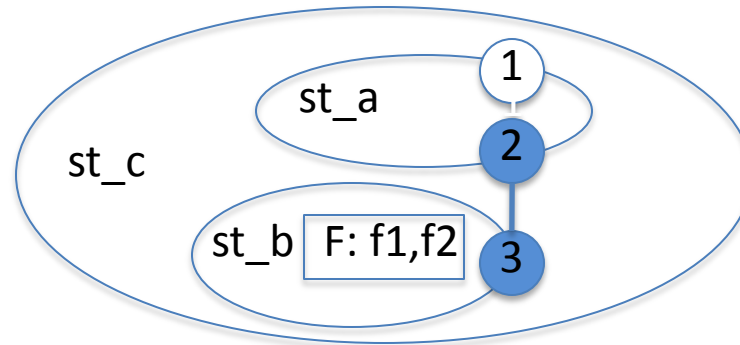
```
    <multi:speciesTypeInstance multi:id="sti_a_1" multi:speciesType="1" />
```

```
    <multi:speciesTypeInstance multi:id="sti_a_2" multi:speciesType="2" />
```

```
  </multi:listOfSpeciesTypeInstances>
```

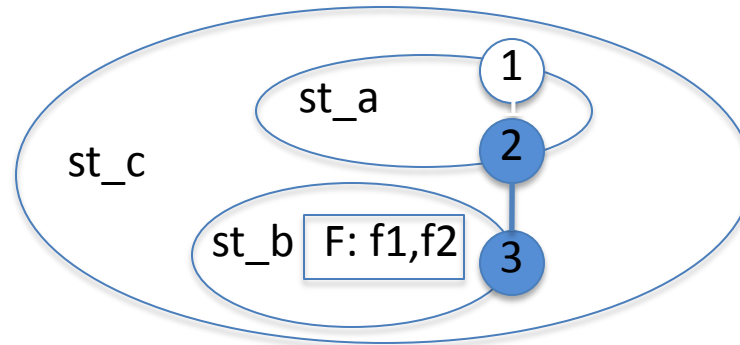
```
</multi:speciesType>
```

Revised Multi Example: SpeciesType



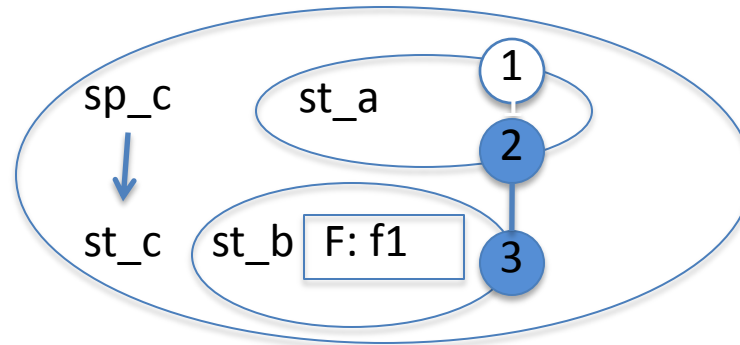
```
...  
<multi:speciesType multi:id="st_b">  
  <multi:listOfSpeciesTypeInstances>  
    <multi:speciesTypeInstance multi:id="sti_b_3" multi:speciesType="3" />  
  </multi:listOfSpeciesTypeInstances>  
  <multi:listOfSpeciesFeatureTypes>  
    <multi:speciesFeatureType multi:id="F">  
      <multi:possibleSpeciesFeatureValue multi:id="f1" />  
      <multi:possibleSpeciesFeatureValue multi:id="f2" />  
    </multi:speciesFeatureType>  
  </multi:listOfSpeciesFeatureTypes>  
</multi:speciesType>
```

Revised Multi Example: SpeciesType



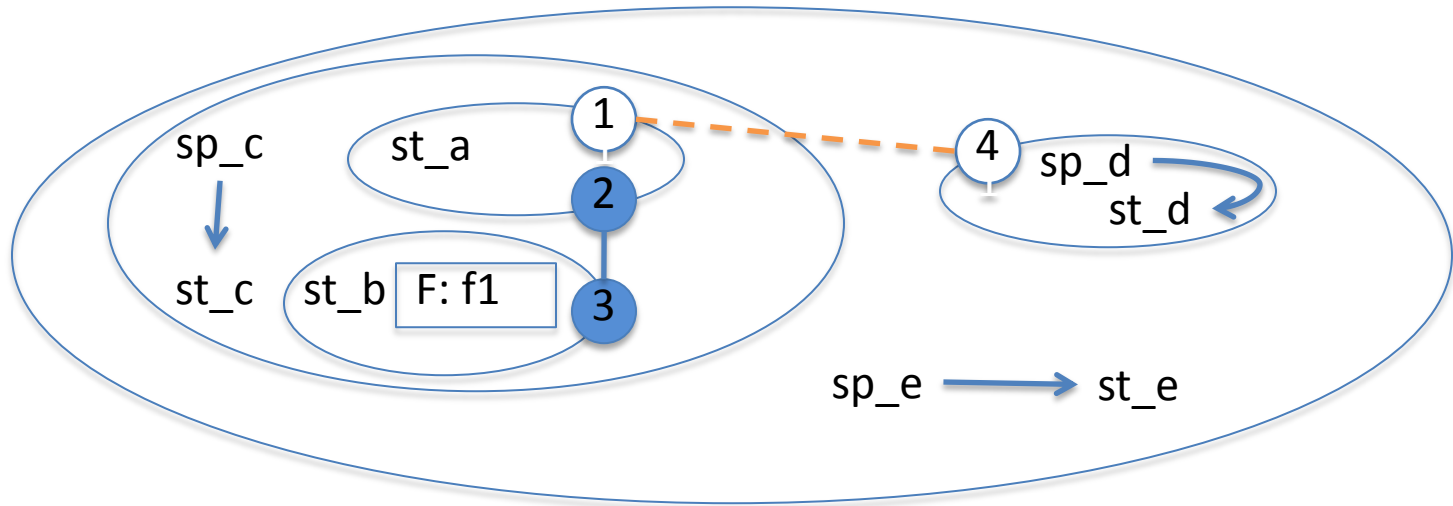
```
...  
<multi:speciesType multi:id="st_c">  
  <multi:listOfSpeciesTypeInstances>  
    <multi:speciesTypeInstance multi:id="sti_c_a" multi:speciesType="st_a" />  
    <multi:speciesTypeInstance multi:id="sti_c_b" multi:speciesType="st_b" />  
  </multi:listOfSpeciesTypeInstances>  
  <multi:listOfInSpeciesTypeBonds>  
    <multi:inSpeciesTypeBond>  
      <multi:bindingSite1 multi:speciesTypeInstance="sti_a_2"/>  
      <multi:bindingSite2 multi:speciesTypeInstance="sti_b_3" />  
    </multi:inSpeciesTypeBond>  
  </multi:listOfInSpeciesTypeBonds>  
</multi:speciesType>
```

Revised Multi Example: Species



```
<species id="sp_c" multi:speciesType ="st_c">  
  <multi:listOfOutwardBindingSiteReferences>  
    <multi:bindingSiteSpeciesTypeInstanceReference  
      multi:speciesTypeInstance="sti_s_1" multi:isBound="false" />  
  </multi:listOfOutwardBindingSiteReferences>  
  <multi:listOfSpeciesFeatures>  
    <multi:speciesFeature multi:speciesFeatureType="F">  
      <multi:speciesFeatureValue multi:value="f1" />  
    </multi:speciesFeature>  
  </multi:listOfSpeciesFeatures>  
</species>
```

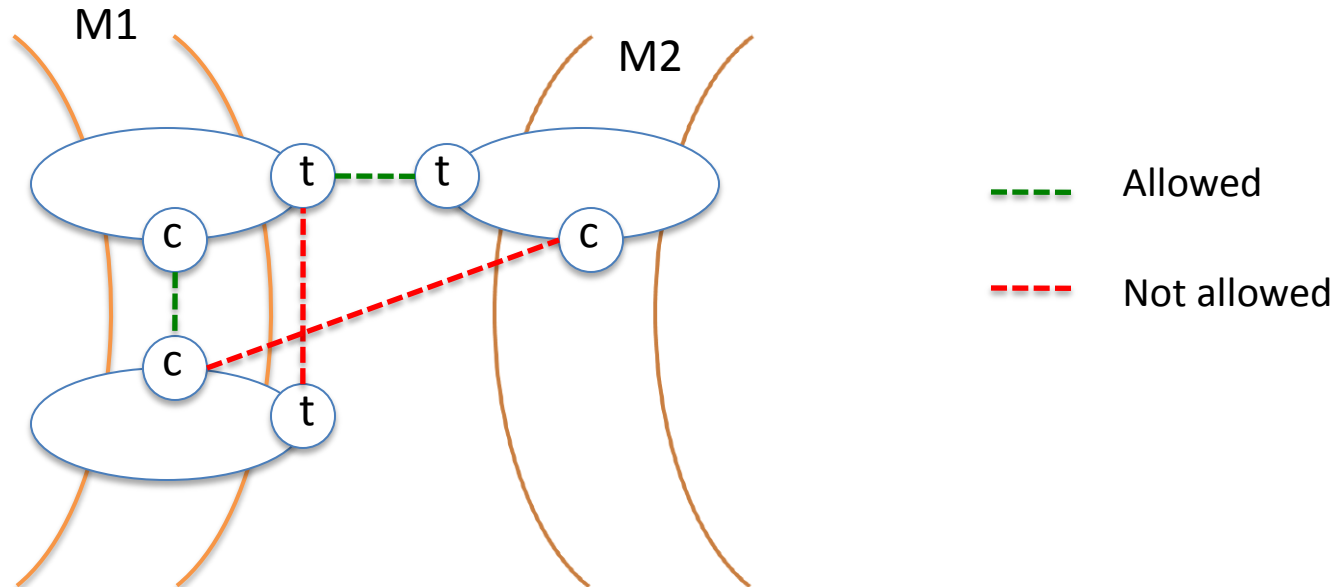
Revised Multi Example: Reaction



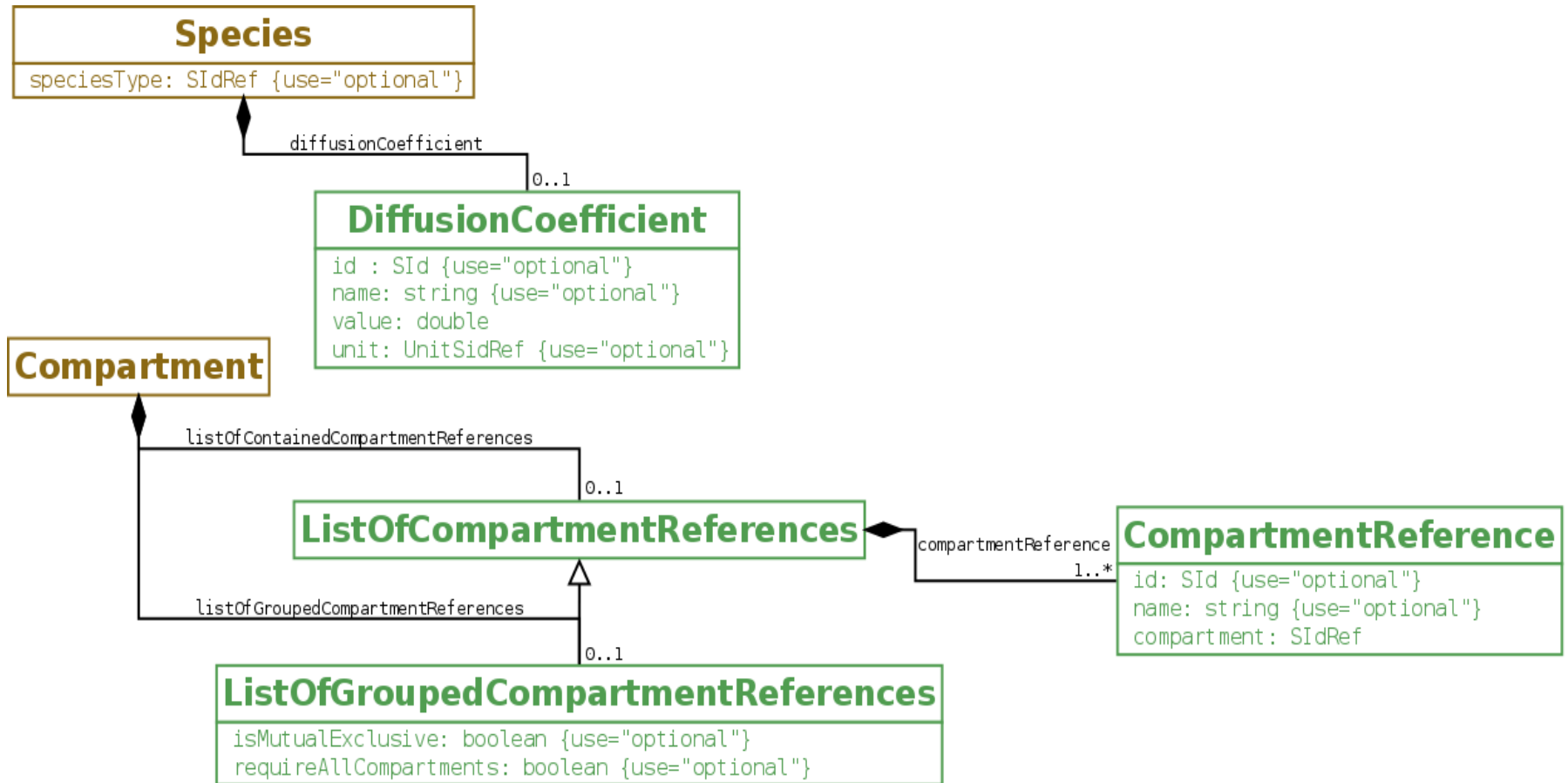
```
<reaction id="reaction1">
  <listOfReactants>
    <speciesReference species="sp_c" />
    <speciesReference species="sp_d" />
  </listOfReactants>
  <listOfProducts>
    <speciesReference species="sp_e" />
  </listOfProducts>
  ...
</reaction>
```

Simple Spatial

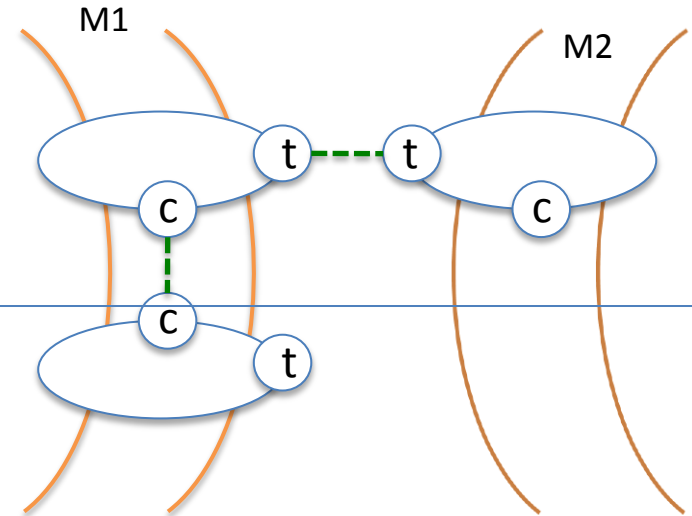
- Diffusion Coefficient
- Same species in multiple compartments
 - Example: Ecad model



Simple Spatial UML



Simple Spatial Example

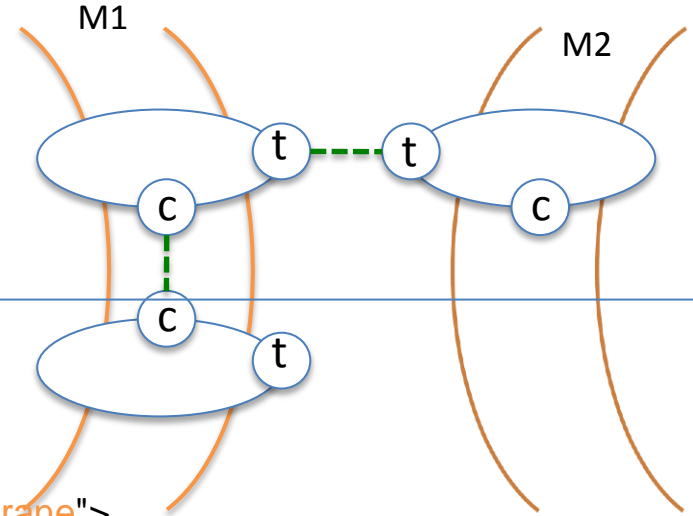


```
<compartment id="M1" />
<compartment id="M2" />

<compartment id="M_single" >
  <spatial:listOfGroupedCompartmentReferences
    multi:isMutualExclusive="true">
    <spatial:compartmentReference compartment="M1" />
    <spatial:compartmentReference compartment="M2" />
  </spatial:listOfGroupedCompartmentReferences>
</compartment>

<compartment id="inter_membrane">
  <spatial:listOfGroupedCompartmentReferences
    multi:requireAllCompartments="true">
    <spatial:compartmentReference compartment="M1" />
    <spatial:compartmentReference compartment="M2" />
  </spatial:listOfGroupedCompartmentReferences>
</compartment>
```


Simple Spatial Example



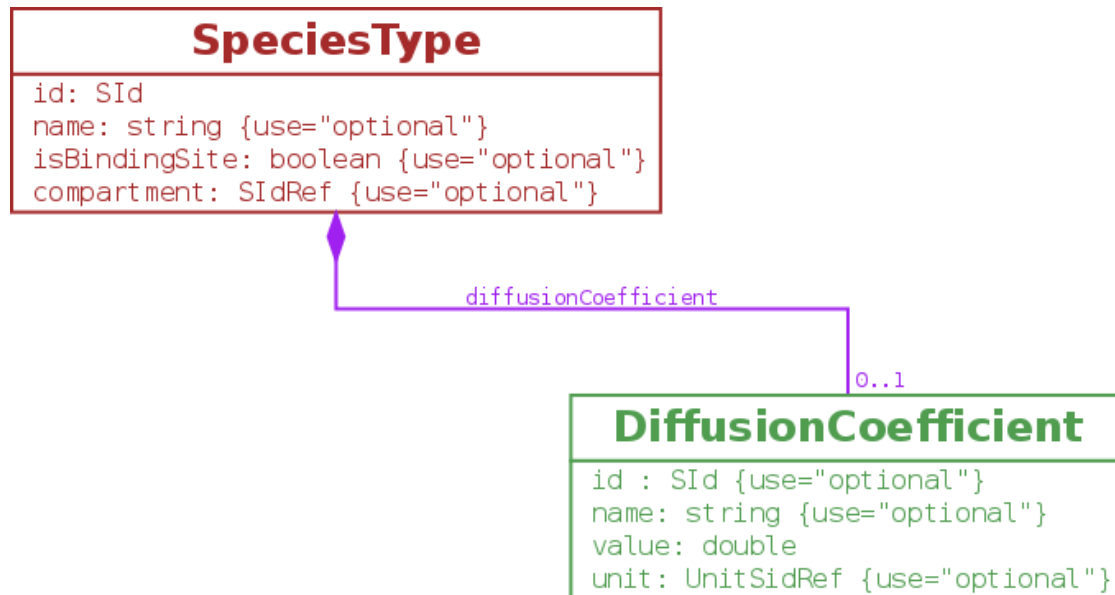
```

...
<species id="sp_Ecad" multi:speciesType="st_Ecad"
  compartment="membrane_single" >
...
<reaction id="rc_trans_association" compartment="inter_membrane">
  <listOfReactants>
    <speciesReference species="sp_Ecad" stoichiometry="2" />
  </listOfReactants>
...
</reaction>
...
<reaction id="rc_cis_association" compartment="single_membrane">
  <listOfReactants>
    <speciesReference species="sp_Ecad" stoichiometry="2" />
  </listOfReactants>
...
</reaction>

```

Multi-Spatial

- Require both “Revised Multi” and “Simple Spatial”
- Enable *SpeciesType* to have *DiffusionCoefficient* component



Development Status

- Complete working draft **specifications** for “Revised Multi”, “Simple Spatial” and “Multi-Spatial” extensions
- Complete examples:
 - 3 examples from “**multi**” proposal
 - 2 examples from **Simmune**
 - 1 example from **Bionetgen** Manual
- **libSBML** extension
 - Under development: output multi examples

Acknowledge

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 - Computational Biology Group
 - Martin Meier-Schellersheim
 - Bastian Angermann
 - All members at LSB/NIAID/NIH
- SBML and Multi editors, community

Question?

- You may also send comment/suggestion to
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