Draft for Discussion: SBML Proposals for "*Revised Multi*", "*Simple Spatial*" and "*Multi-Spatial*" Extensions

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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

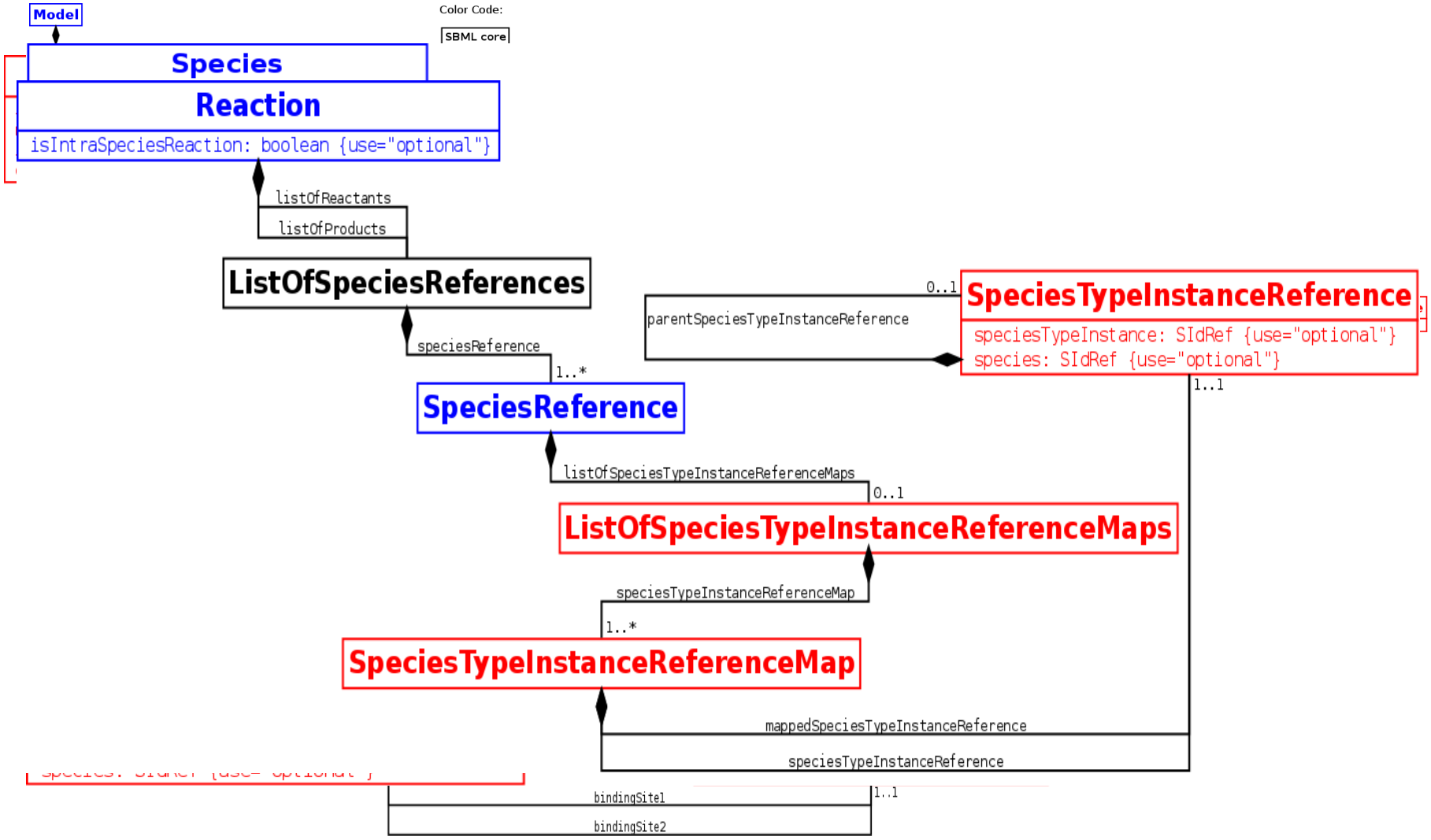
Discussion of Draft Specifications

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

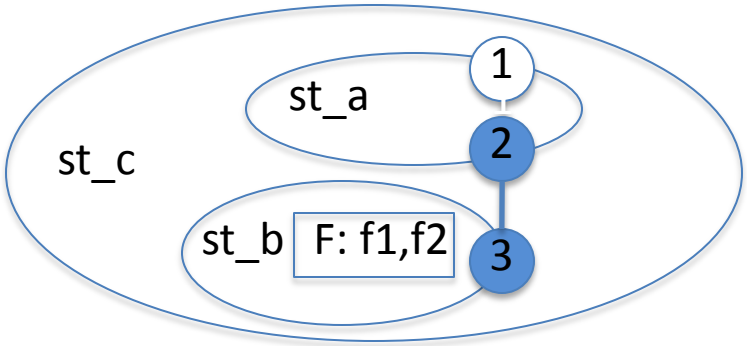
Comparison: “Multi” and “Revised Multi”

- 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

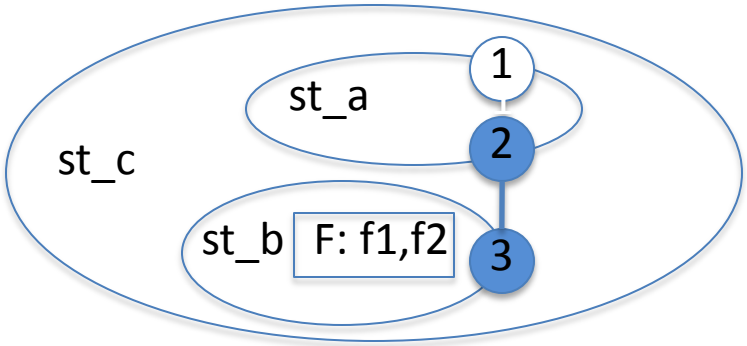


Revised Multi Example: SpeciesType



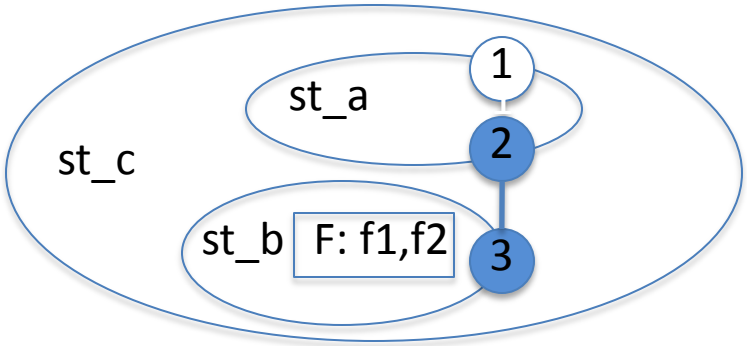

```
<sbml xmlns="http://www.sbml.org/sbml/level3/version1/core" level="3" version="1”
xmlns:multi=http://www.sbml.org/sbml/level3/version1/revised_multi/version1 >
...
<multi:speciesType multi:id="1" multi:isBindingSite="true" />
<multi:speciesType multi:id=“2" multi:isBindingSite="true" />
<multi:speciesType 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



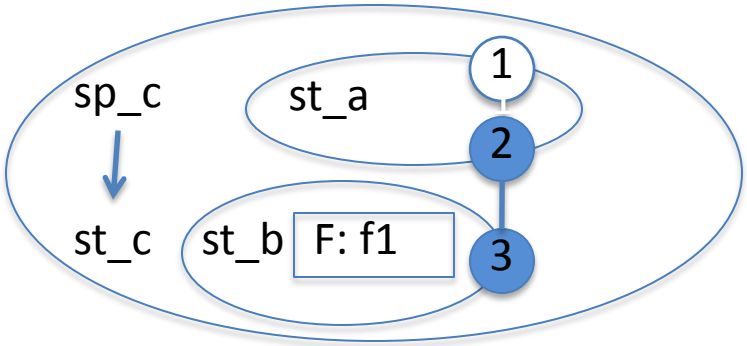

```
...
<multi:speciesType multi:id="st_b">
  <multi:listOfSpeciesTypeInstances>
    <multi:speciesTypeInstance multi:id="sti_b_3" multi:speciesType="3" />
  </multi:listOfSpeciesTypeInstances>
  <multi:listOfSpeciesFeatureTypes>
    <multi:speciesFeatureType multi:id="F">
      <multi:possibleSpeciesFeatureValue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

Revised Multi Example: SpeciesType



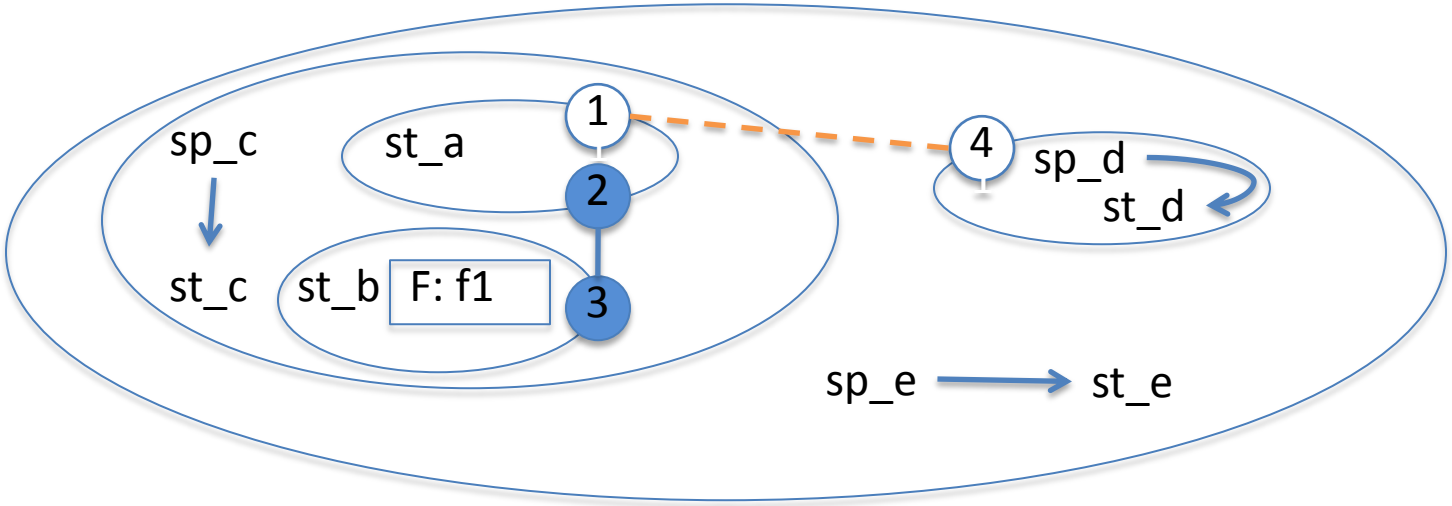

```
...
<multi:speciesType multi:id="st_c">
  <multi:listOfSpeciesTypeInstances>
    <multi:speciesTypeInstance multi:id="sti_c_a" multi:speciesType="st_a" />
    <multi:speciesTypeInstance multi:id="sti_c_b" multi:speciesType="st_b" />
  </multi:listOfSpeciesTypeInstances>
  <multi:listOfInSpeciesTypeBonds>
    <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>
```

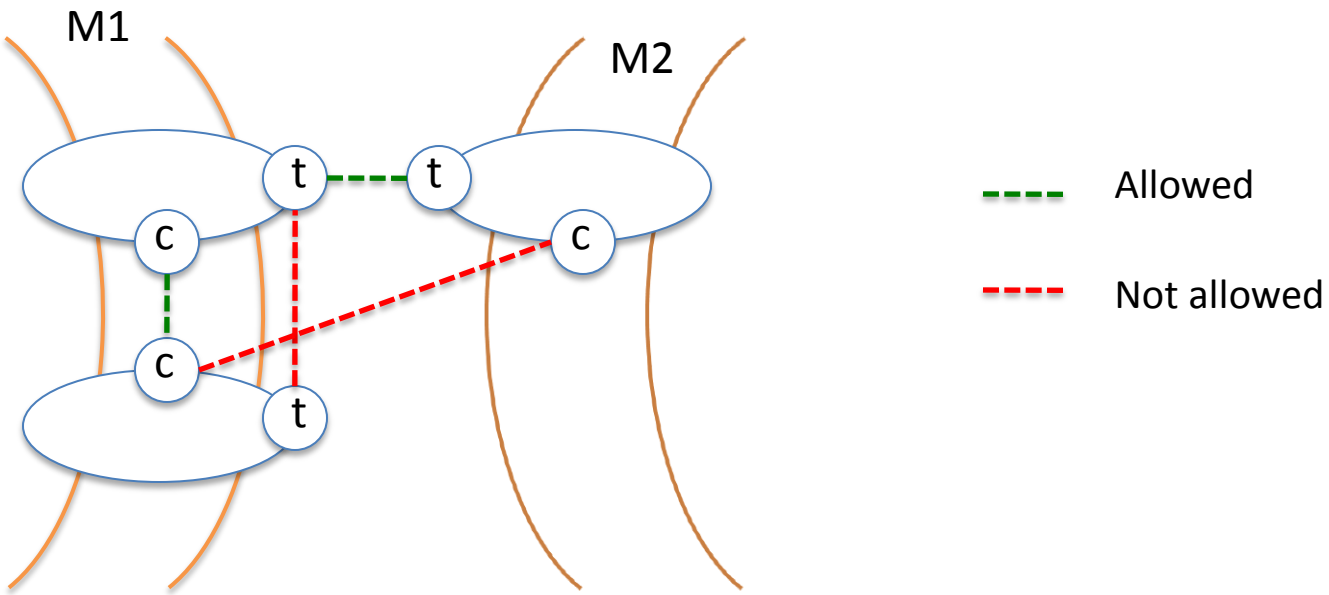
Revised Multi Example: Reaction



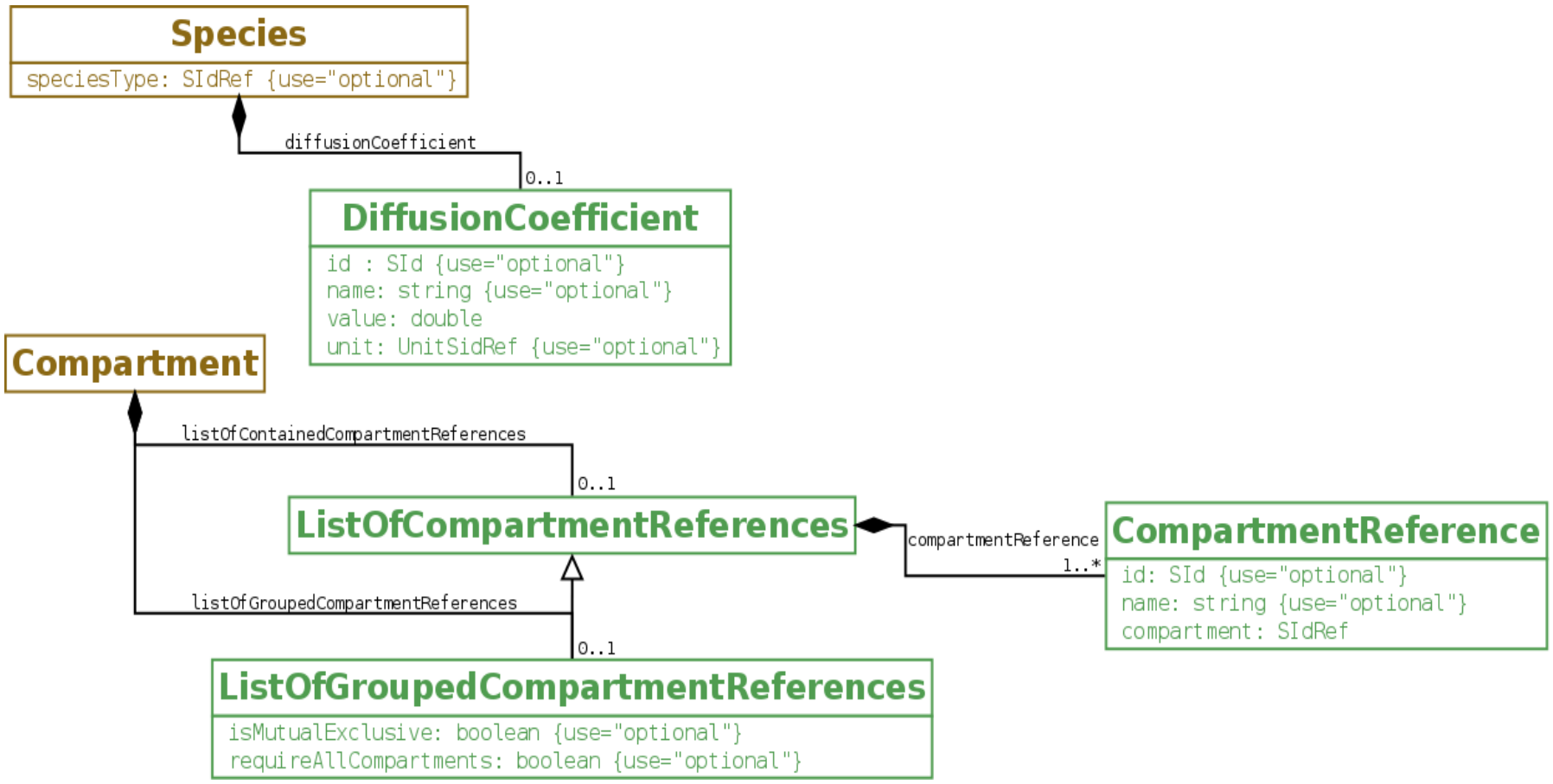

```
<reaction id="reaction1">
  <listOfReactants>
    <speciesReference species="sp_c" />
    <speciesReference species="sp_d" />
  <listOfReactants>
  <listOfProducts>
    <speciesReference species="sp_e" />
  </listOfProducts>
  ...
</reaction>
```

Simple Spatial

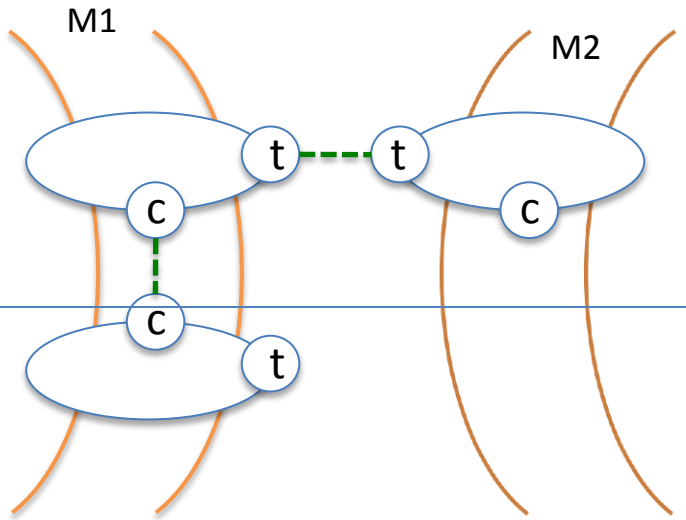
- Diffusion Coefficient
- Same species in multiple compartments
  - Example: Ecad model



Simple Spatial UML

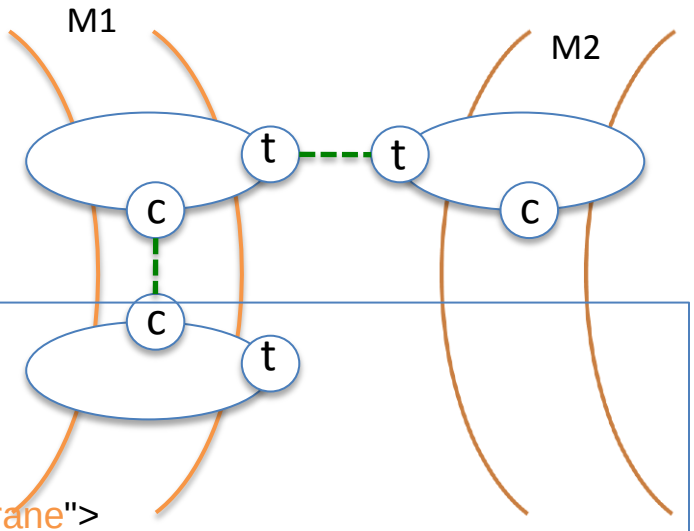


Simple Spatial Example




```
<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>
```

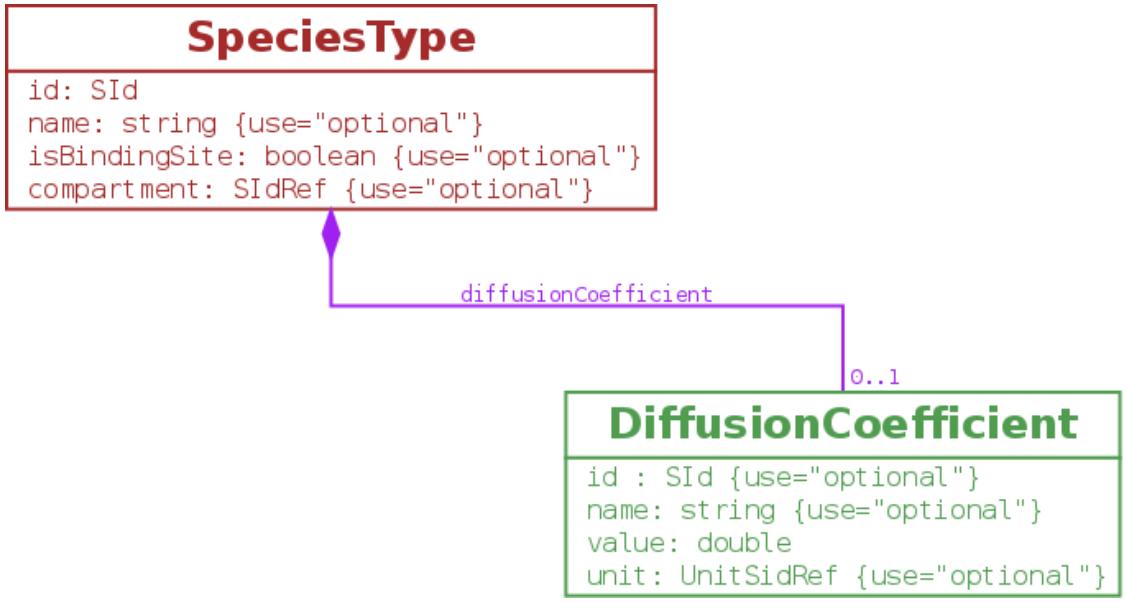
Simple Spatial Example




```
...
<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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