Multi-component multistate species in SBML

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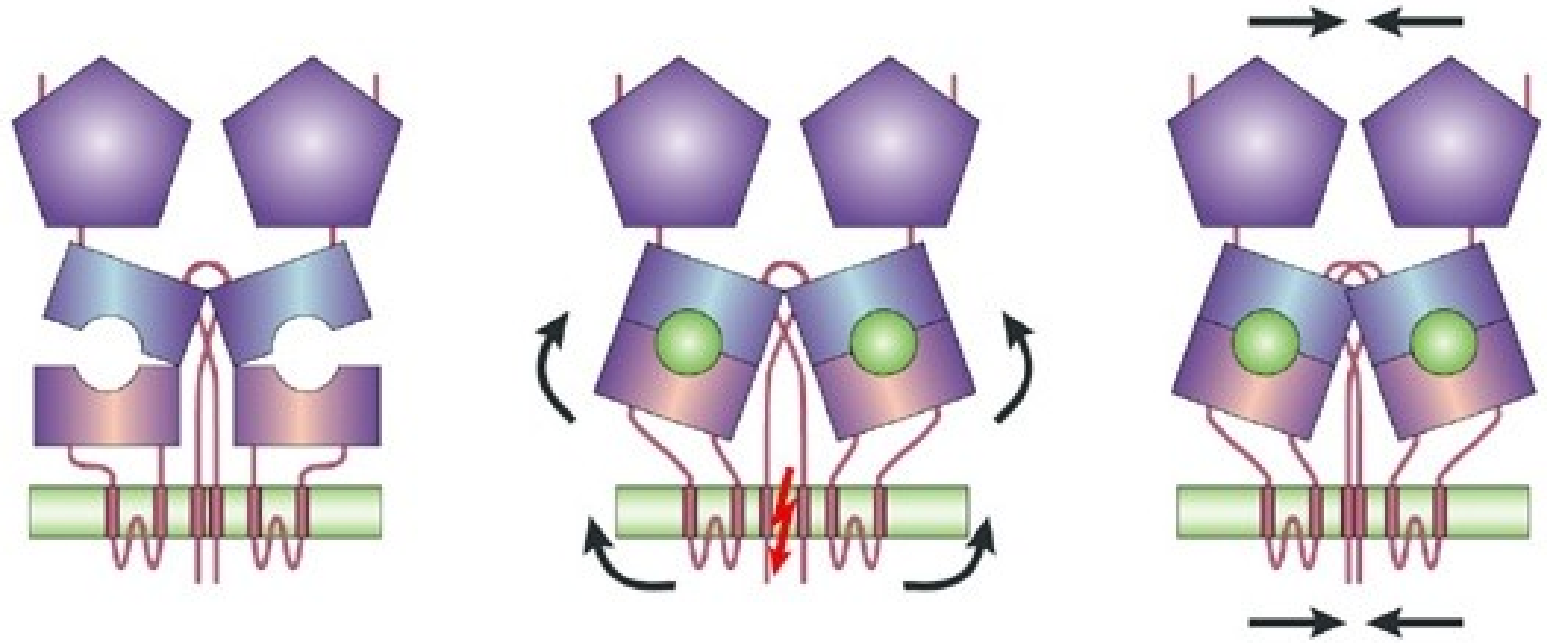
Anika Oellrich, Software Engineer
EBI, WT Genome Campus
Hinxton, Cambridge, U.K.

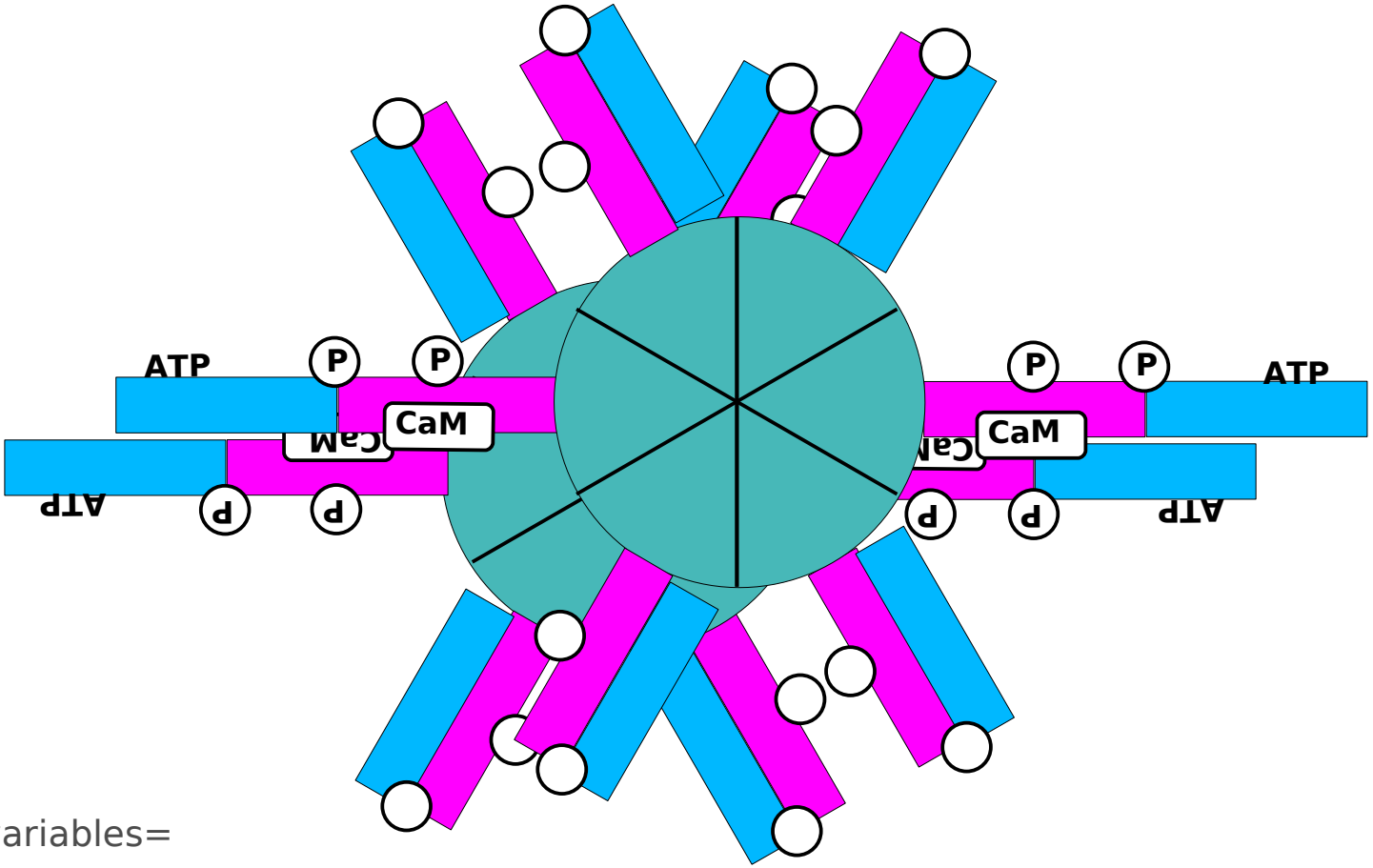
EMBL-EBI

Multistate multi-component species



- Multistate: different states characterised through features
- Multi-component: complex consisting of subunits

Combinatorial explosion

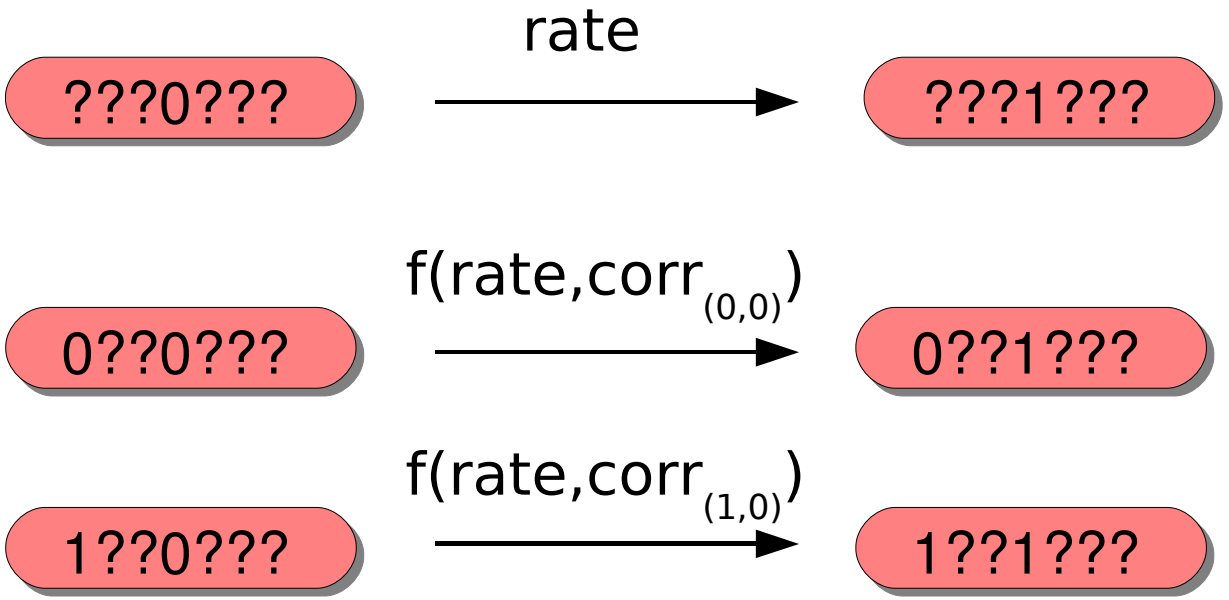


5x12 state variables=

1 152 900 000 000 000 000 states

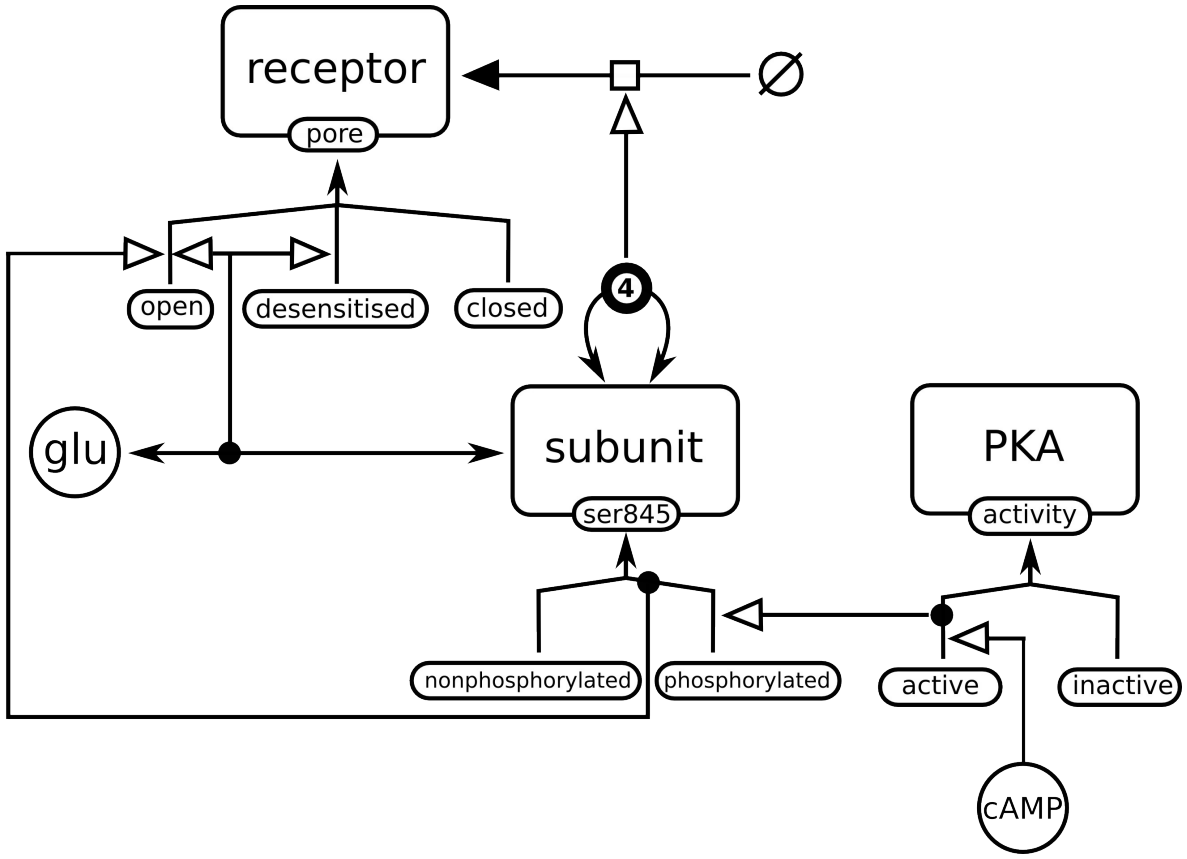
(1 billion of billion)

Number of reactions



- only 4 states instead of 128
- only 2 reactions instead of 64

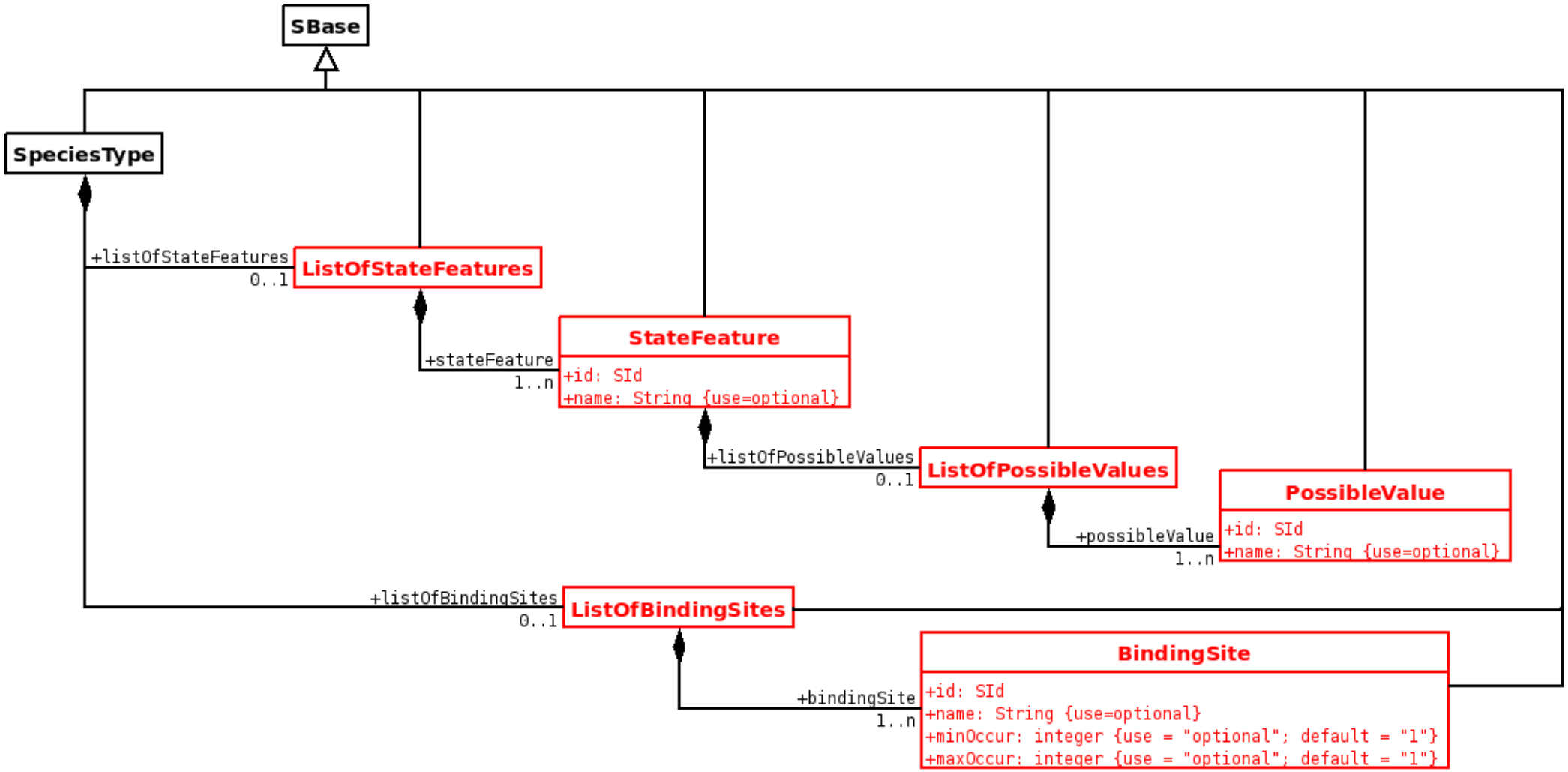
Example we will use throughout the presentation



L3M – General overview

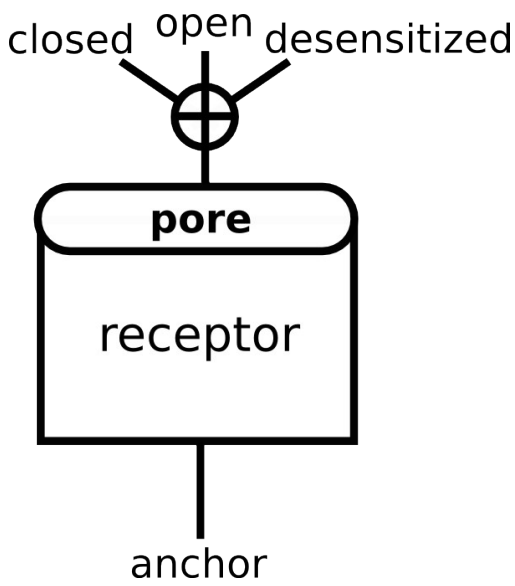
```
<sbml xmlns="http://www.sbml.org/sbml/level3/version1"
      xmlns:l3m="http://www.sbml.org/sbml/extension/multi/version1" >

  <listOfSpeciesTypes>
    <speciesType id="X" >
      <l3m:listOfStateFeatures />
      <l3m:listOfBindingSites />
    </speciesType>
  </listOfSpeciesTypes>

  <l3m:listOfSelectors>
    <l3m:selector id="Y">
      <l3m:listOfSpeciesTypeStates />
      <l3m:listOfBonds />
      <l3m:listOfUnboundBindingSites />
    </l3m:selector>
  </l3m:listOfSelectors>

    <listOfSpecies>
      <species id="X1" speciesType="X>
        <l3m:listOfInitialSpeciesInstances />
      </species>
    </listOfSpecies>

    <listOfReactions>
      <reaction id="R">
        <listOfReactants />
        <listOfProducts />
        <listOfModifiers />
        <kineticLaw />
        <l3m:listOfReactionRules />
      </reaction>
    </listOfReactions>
</sbml>
```

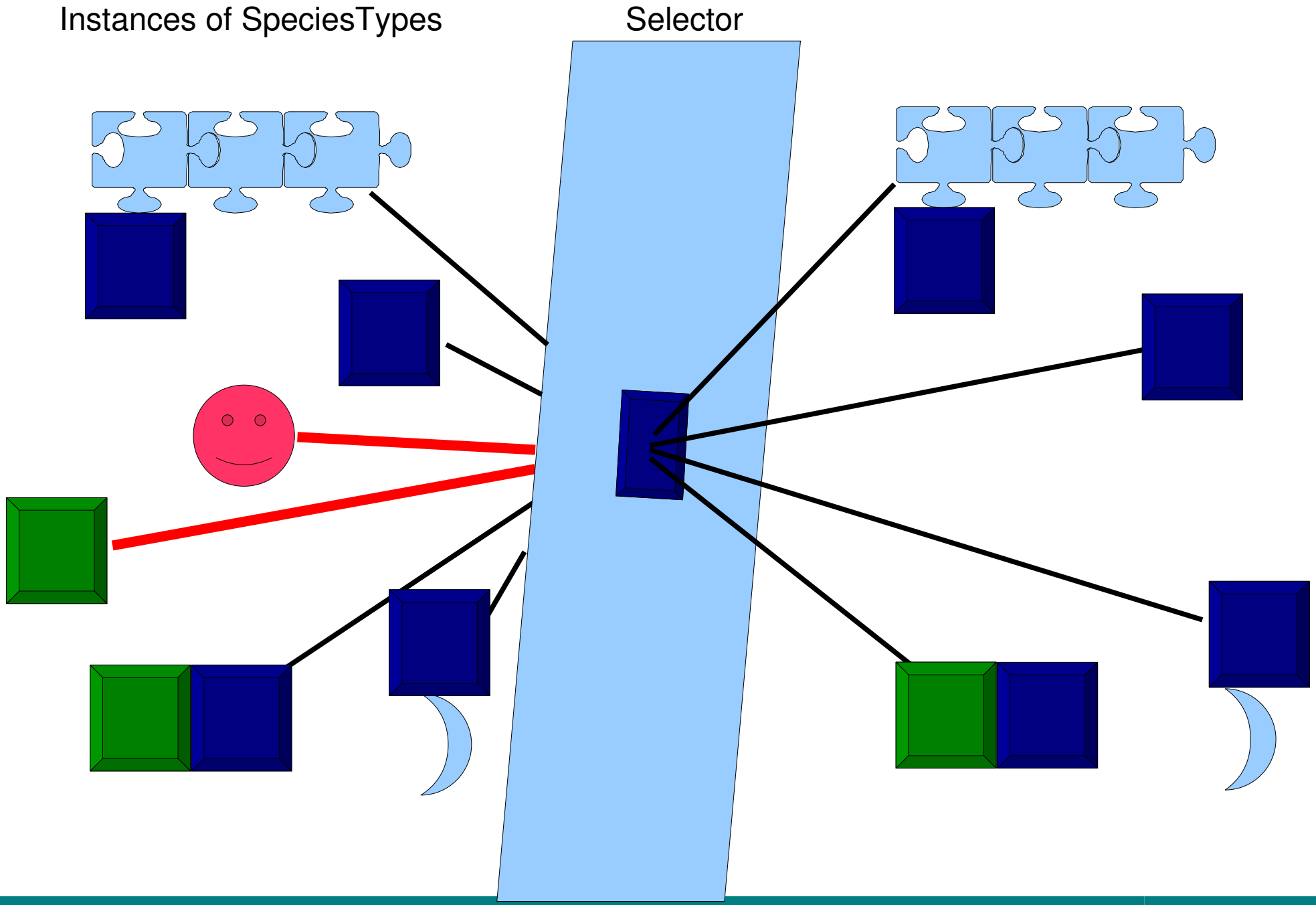
SpeciesType



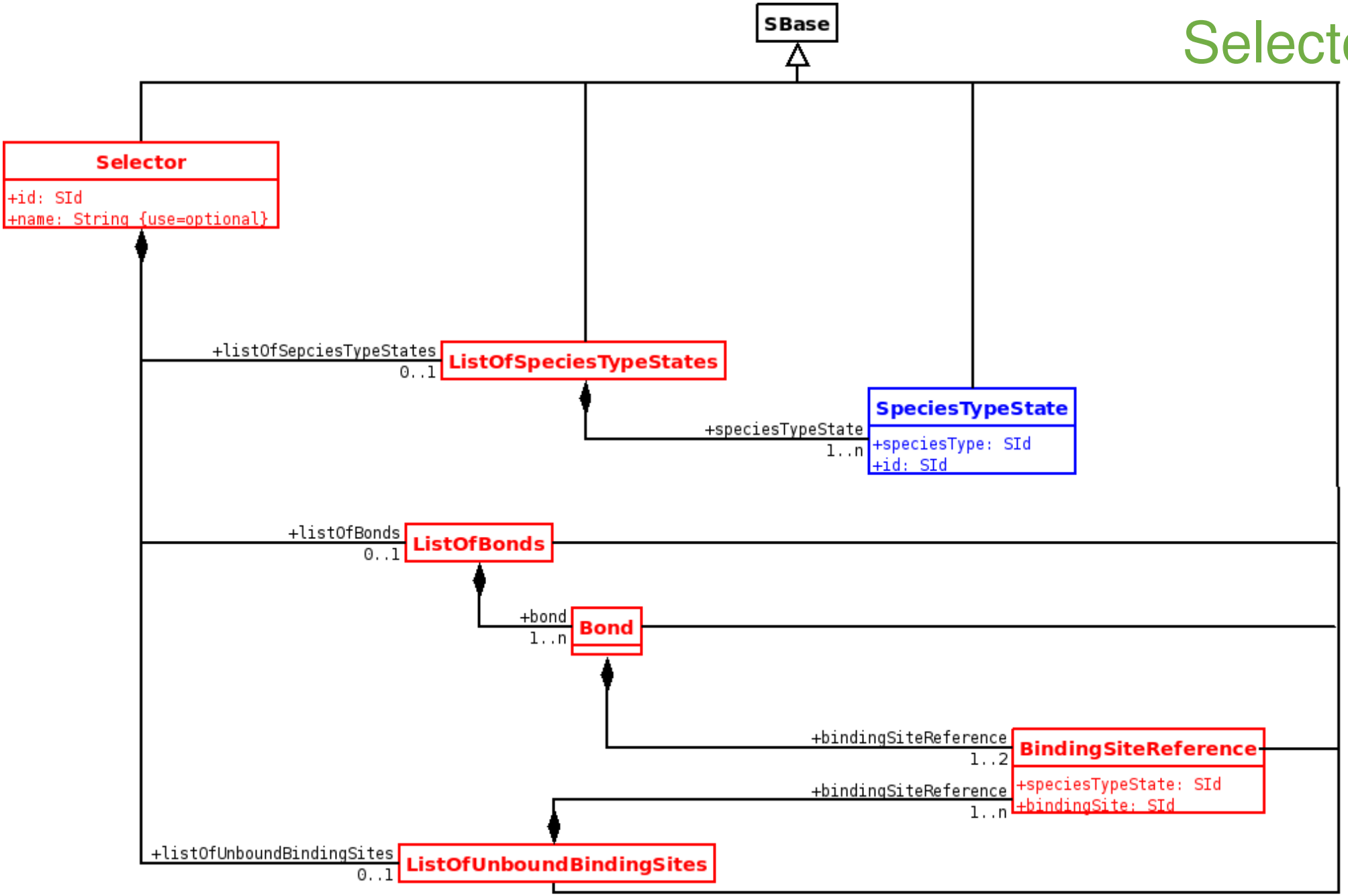
SpeciesType - example

```
<speciesType id="st_receptor" name="glutamate receptor">
  <l3m:listOfStateFeatures>
    <l3m:stateFeature id="pore">
      <l3m:listOfPossibleValues>
        <l3m:possibleValue id="closed" />
        <l3m:possibleValue id="open" />
        <l3m:possibleValue id="desensitized" />
      </l3m:listOfPossibleValues>
    </l3m:stateFeature>
  </l3m:listOfStateFeatures>
  <l3m:listOfBindingSites>
    <l3m:bindingSite id="anchor" name="scaffolding binding site" />
  </l3m:listOfBindingSites>
</speciesType>
```

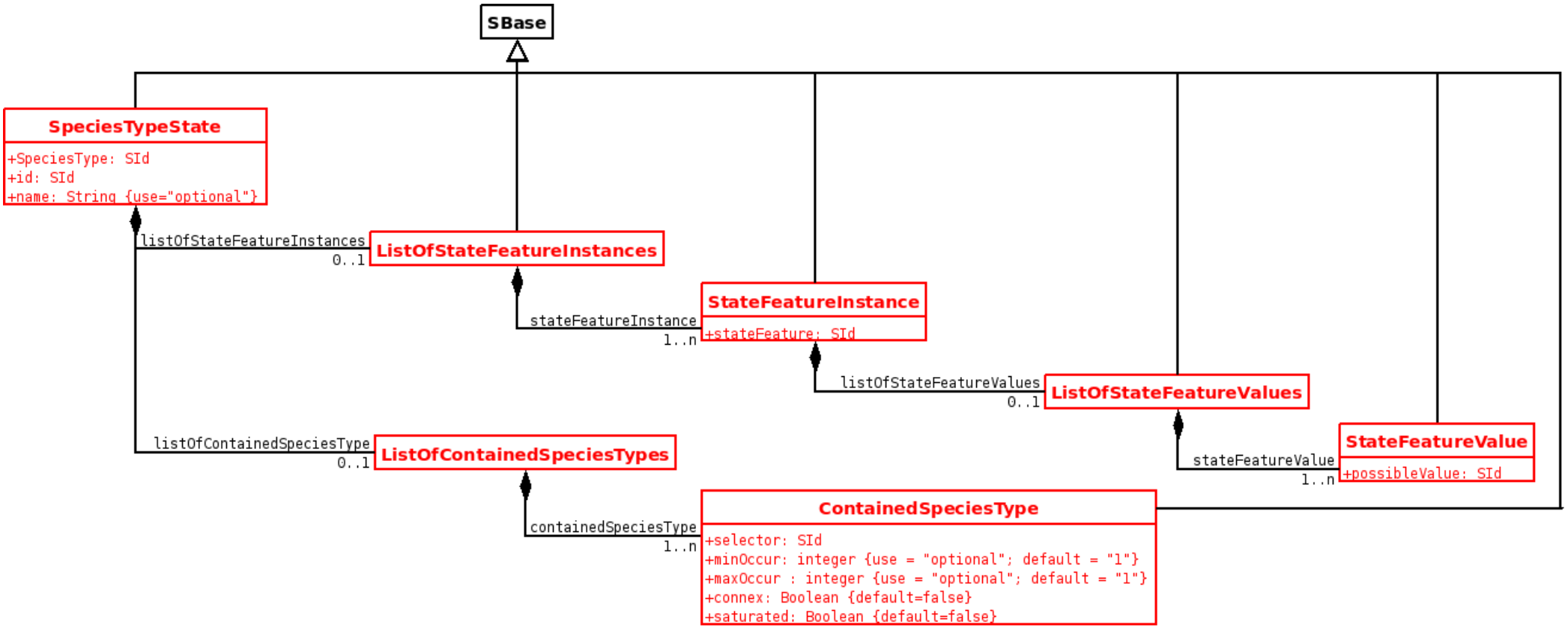



Instances of SpeciesTypes
Selector

Selector

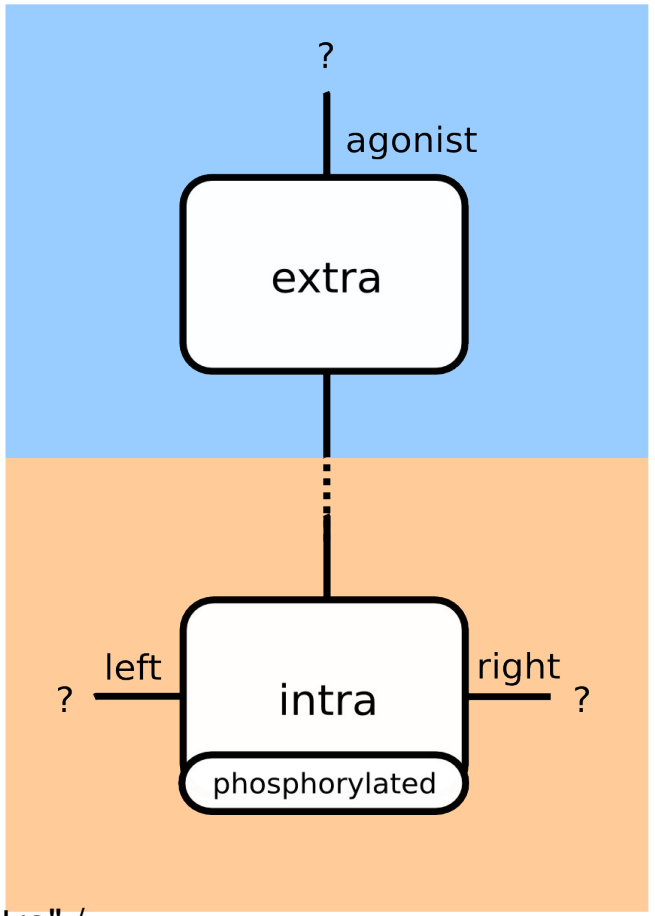

SBase
Selector
+id: SId
+name: String {use=optional}
+listOfSepciesTypeStates
0..1
ListOfSpeciesTypeStates
+speciesTypeState
1..n
SpeciesTypeState
+speciesType: SId
+id: SId
+listOfBonds
0..1
ListOfBonds
+bond
1..n
Bond
+bindingSiteReference
1..2
BindingSiteReference
+speciesTypeState: SId
+bindingSite: SId
+bindingSiteReference
1..n
+listOfUnboundBindingSites
0..1
ListOfUnboundBindingSites

SpeciesTypeState



Selector – multicompartment example

```
<l3m:selector id="sel_subunitP">
  <l3m:listOfSpeciesTypeStates>
    <l3m:speciesTypeState id="extra" speciesType="st_extra" />
    <l3m:speciesTypeState id="intra" speciesType="st_intra">
      <l3m:listOfStateFeatureInstances>
        <l3m:featureStateInstance stateFeature="ser845">
          <l3m:listOfStateFeatureValues>
            <l3m:stateFeatureValue possibleValue="phosphorylated" />
          </l3m:listOfStateFeatureValues>
        </l3m:featureStateInstance>
      </l3m:listOfStateFeatureInstances>
    </l3m:speciesTypeState>
  </l3m:listOfSpeciesTypeStates>
  <l3m:listOfBonds>
    <l3m:bond>
      <l3m:bindingSiteReference speciesTypeState="extra" bindingSite="toIntra" />
      <l3m:bindingSiteReference speciesTypeState="intra" bindingSite="toExtra" />
    </l3m:bond>
  </l3m:listOfBonds>`
</l3m:selector>
```



Selector - example

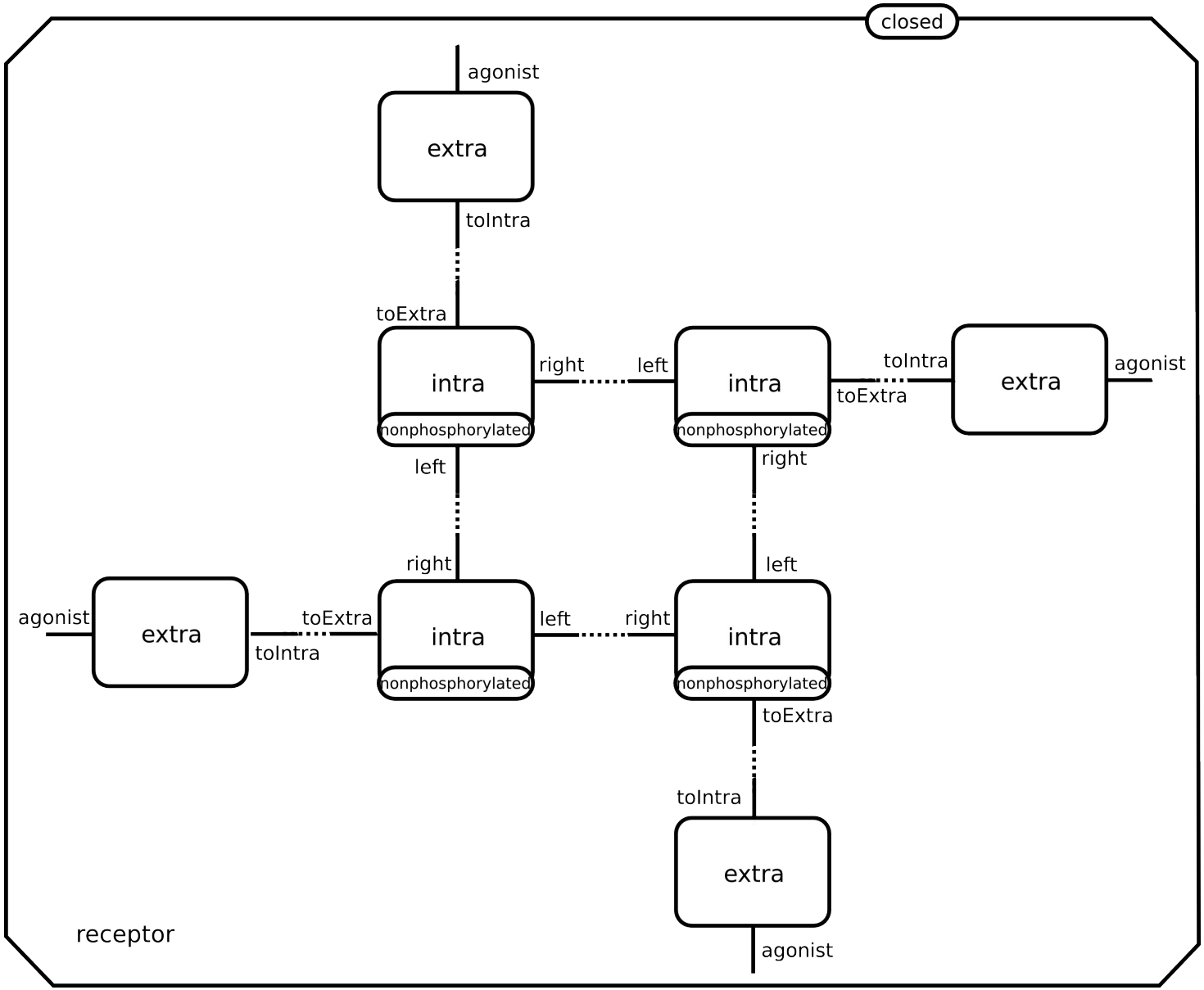
```
<l3m:selector id="sel_receptor">
  <l3m:listOfSpeciesTypeStates>
    <l3m:speciesTypeState id="extra" speciesType="st_extra" />
    <l3m:speciesTypeState id="intra" speciesType="st_intra">
      <l3m:listOfStateFeatureInstances>
        <l3m:featureStateInstance stateFeature="ser845">
          <l3m:listOfStateFeatureValues>
            <l3m:stateFeatureValue possibleValue="nonphosphorylated" />
          </l3m:listOfStateFeatureValues>
        </l3m:featureStateInstance>
      </l3m:listOfStateFeatureInstances>
    </l3m:speciesTypeState>
    <l3m:speciesTypeState id="receptor" speciesType="st_receptor">
      <l3m:listOfStateFeatureInstances>
        <l3m:featureStateInstance stateFeature="pore">
          <l3m:listOfStateFeatureValues>
            <l3m:stateFeatureValue possibleValue="closed" />
          </l3m:listOfStateFeatureValues>
        </l3m:featureStateInstance>
      </l3m:listOfStateFeatureInstances>
      <l3m:listOfContainedSpeciesTypes>
        <l3m:containedSpeciesType selector="extra" minOccur="4" maxOccur="4" connex="true" saturated="true" />
        <l3m:containedSpeciesType selector="intra" minOccur="4" maxOccur="4" connex="true" saturated="true" />
      </l3m:listOfContainedSpeciesTypes>
    </l3m:speciesTypeState>
  </l3m:listOfSpeciesTypeStates>
```

Selector - example

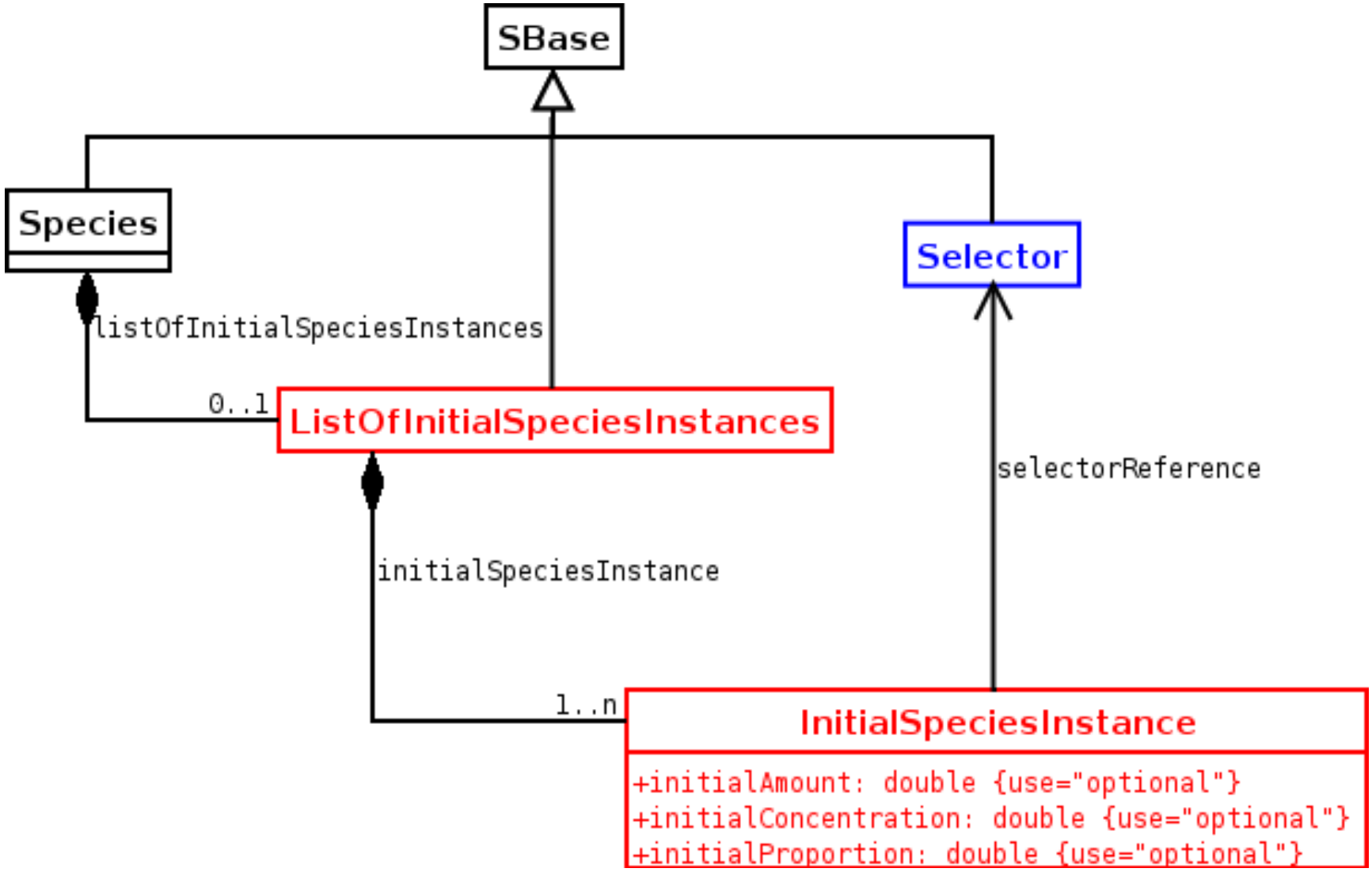
```
    <l3m:listOfBonds>
    <l3m:bond>
      <l3m:bindingSiteReference speciesTypeState="intra" bindingSite="right" />
      <l3m:bindingSiteReference speciesTypeState="intra" bindingSite="left" />
    </l3m:bond>
    <l3m:bond>
      <l3m:bindingSiteReference speciesTypeState="extra" bindingSite="toIntra" />
      <l3m:bindingSiteReference speciesTypeState="intra" bindingSite="toExtra" />
    </l3m:bond>
  </l3m:listOfBonds>
  <l3m:listOfUnboundBindingSites>
    <l3m:bindingSiteReference speciesTypeState="receptor" bindingSite="anchor" />
    <l3m:bindingSiteReference speciesTypeState="intra" bindingSite="agonist" />
  </l3m:listOfUnboundBindingSites>
</l3m:selector>
```

Selector - example

```
 <l3m:listOfBonds>
  <l3m:bond>
   <l3m:bindingSiteReference speciesTypeState="intra" bindingSite="right" />
   <l3m:bindingSiteRefe
  </l3m:bond>
  <l3m:bond>
   <l3m:bindingSiteRefe
   <l3m:bindingSiteRefe
  </l3m:bond>
 </l3m:listOfBonds>
 <l3m:listOfUnboundBinc
  <l3m:bindingSiteRefer
  <l3m:bindingSiteRefer
 </l3m:listOfUnboundBin
</l3m:selector>
```

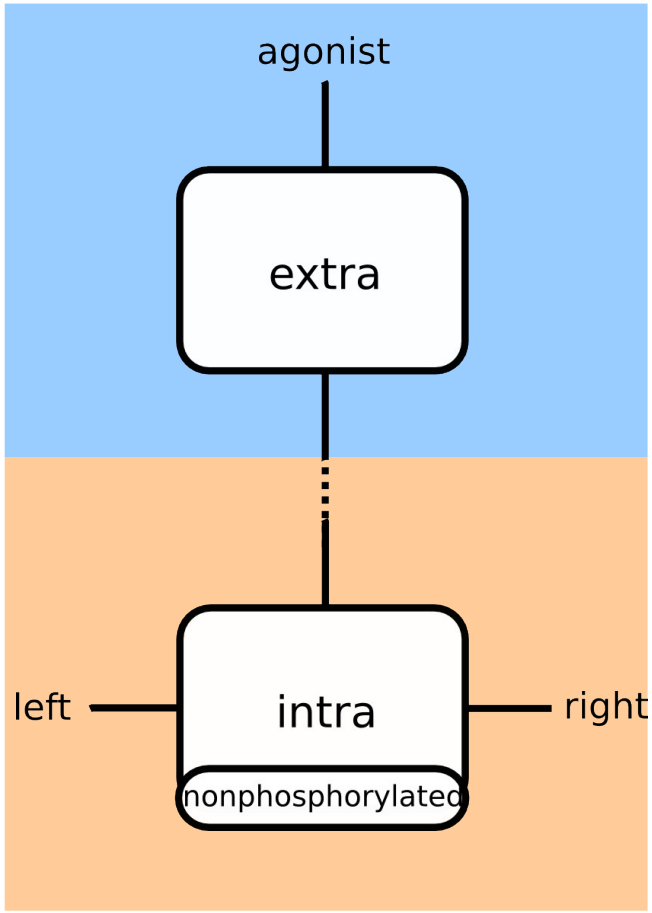


Species

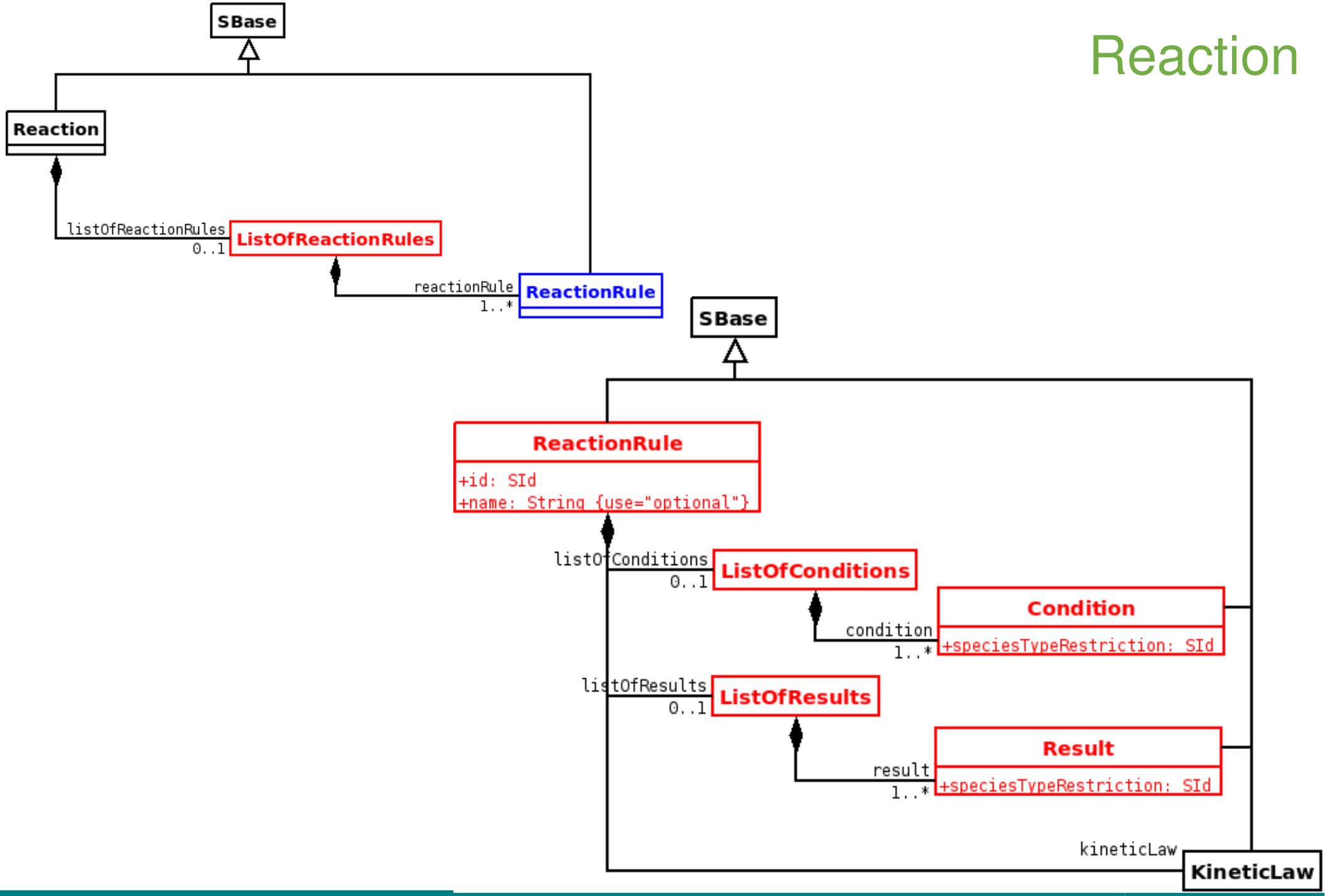

SBase
Species
Selector
listOfInitialSpeciesInstances
0..1
ListOfInitialSpeciesInstances
selectorReference
initialSpeciesInstance
1..n
InitialSpeciesInstance
+initialAmount: double {use="optional"}
+initialConcentration: double {use="optional"}
+initialProportion: double {use="optional"}

Species - example

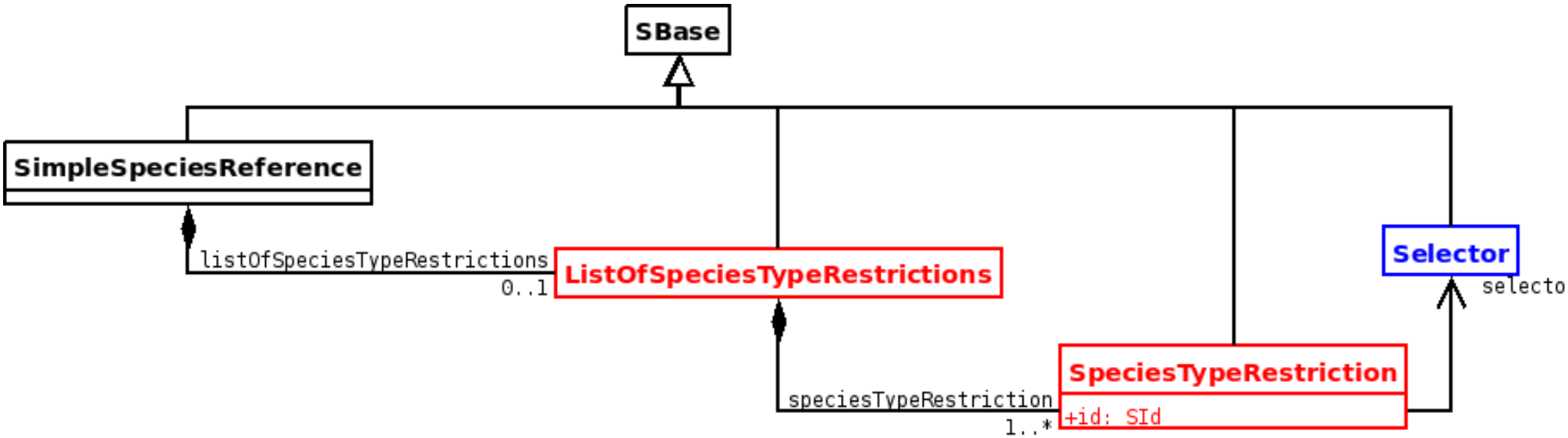
```
<species id="sp_extra" speciesType="st_extra" compartment="extracellular" initialAmount="100" >
  <l3m:listOfInitialSpeciesInstances>
    <l3m:initialSpeciesInstance id="initialSubunit" initialProportion="1" selector="sel_freeMonomerNonGNonP"/>
  </l3m:listOfInitialSpeciesInstances>
 </species>
```



Reaction


SBase
Reaction
listOfReactionRules
0..1
ListOfReactionRules
reactionRule
1..*
ReactionRule
SBase
ReactionRule
+id: SId
+name: String {use="optional"}
listOfConditions
0..1
ListOfConditions
condition
1..*
Condition
+speciesTypeRestriction: SId
listOfResults
0..1
ListOfResults
result
1..*
Result
+speciesTypeRestriction: SId
kineticLaw
KineticLaw

SimpleSpeciesReference

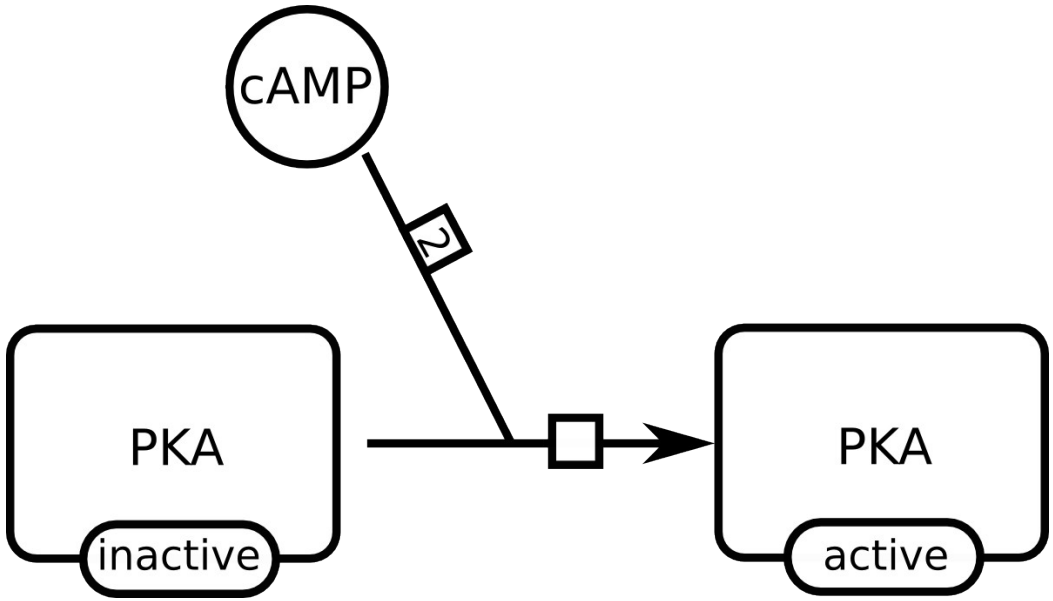


Reaction - example

```
<reaction id="PKAactivation">
  <listOfReactants>
    <speciesReference species="PKA" stoichiometry="1">
      <listOfSpeciesTypeRestrictions>
        <speciesTypeRestriction id="res_inactivePKA" selector="sel_inactivePKA" />
      </listOfSpeciesTypeRestrictions>
    </speciesReference>
    <speciesReference species="cAMP" stoichiometry="2" />
  </listOfReactants>
  <listOfProducts>
    <speciesReference species="PKA">
      <listOfSpeciesTypeRestrictions>
        <speciesTypeRestriction id="res_activePKA" selector="sel_activePKA" />
      </listOfSpeciesTypeRestrictions>
    </speciesReference>
  </listOfProducts>
  <kineticLaw>
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <cn>0</cn>
    </math>
  </kineticLaw>
```

Reaction - example

```
<listOfReactionRules>
  <reactionRule id="activationRule">
    <listOfConditions>
      <condition speciesTypeRestriction="res_inactivePKA" />
    </listOfConditions>
    <listOfResults>
      <result speciesTypeRestriction="res_activePKA" />
    </listOfResults>
    <kineticLaw>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <apply>
          <times />
          <ci>kon</ci>
          <ci>res_inactivePKA</ci>
          <apply>
            <power/>
            <ci>cAMP</ci>
            <cn type="integer">2</cn>
          </apply>
        </apply>
      </math>
      <listOfParameters>
        <parameter id="kon" value="1" />
      </listOfParameters>
    </kineticLaw>
  </reactionRule>
</listOfReactionRules>
</reaction>
```



Thanks for your attention!