

# **Things to fix in Level 2 Version 3 before it becomes the core package of Level 3**



- Inclusion (of material from different files)
- Unit of kineticLaw: event quantity per time unit
- Extension of MathML: vector, matrix, selector, sum, product etc.
- No mandatory orders based on dependencies
- Location of initialAssignments: Within the relevant element
- Modularisation of models



- The order of the listOf was supposed to reflect the dependencies
- This rationale disappeared when we created reaction's id that can be used in rules
  
- Similarly, the order of compartment's declarations should not depend on “outside” attribute



```
<listOfCompartments>
  <compartment id="A" size="" />
</listOfCompartments>
<listOfSpecies>
  <species id="B" initialXXX="" />
</listOfSpecies>
<listOfParameters>
  <parameter id="C" value="" />
</listOfParameters>
<listOfInitialAssignments>
  <initialAssignment symbol="A" />
  <initialAssignment symbol="B" />
  <initialAssignment symbol="C" />
</listOfInitialAssignments>
```



```
<listOfCompartments>
  <compartment id="A" size="" >
    <initialAssignment />
  </compartment>
</listOfCompartments>
<listOfSpecies>
  <species id="B" initialXXX="" >
    <initialAssignment />
  </species>
</listOfSpecies>
<listOfParameters>
  <parameter id="C" value="" >
    <initialAssignment />
  </parameter>
</listOfParameters>
```



- Ease of maintenance of large models
- Use of a given element (e.g. species) with different units in different contexts
- Provide a safe ground for hierarchical modelling etc.
- Improved interoperability with CellML



SBML

model

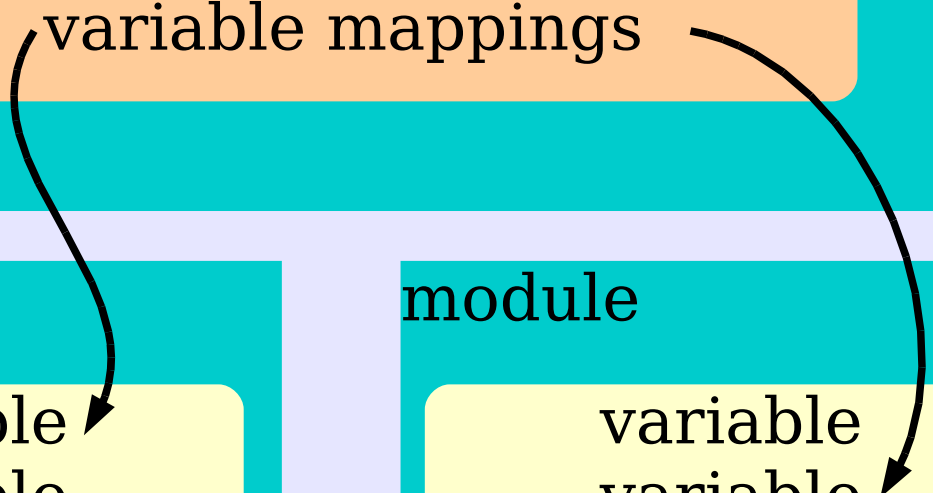
variable mappings

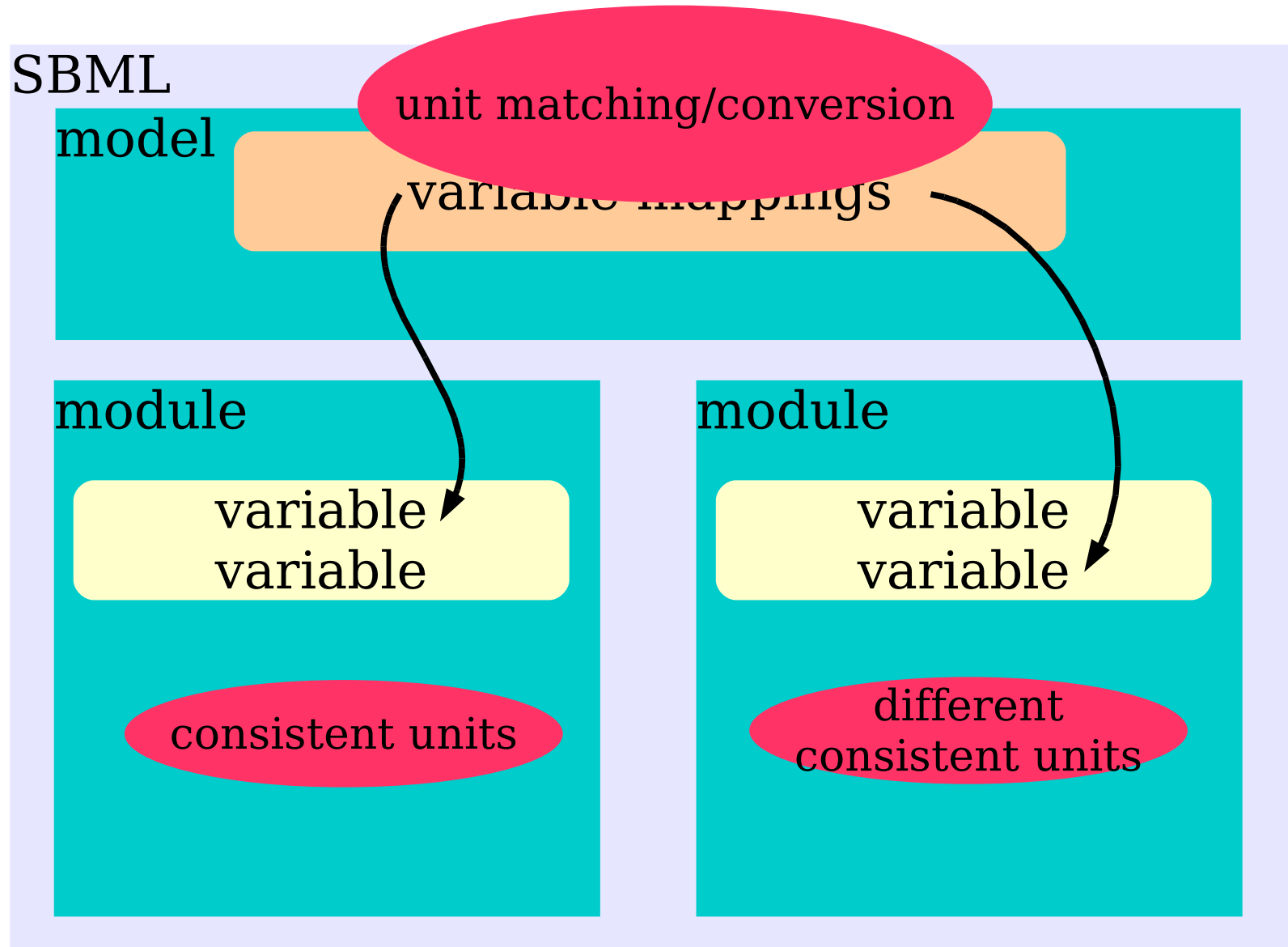
module

variable  
variable

module

variable  
variable





SBML

model

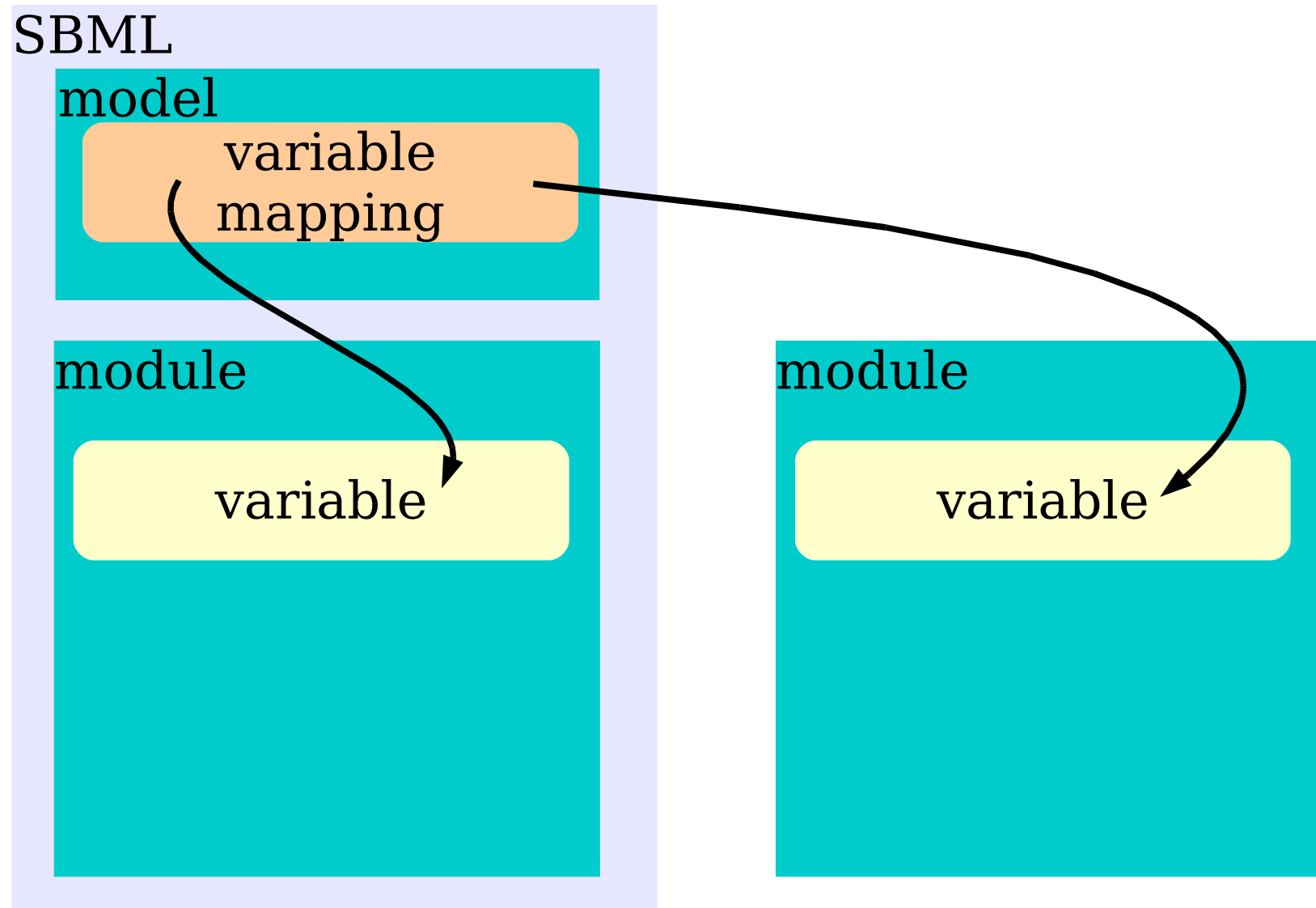
variable  
mapping

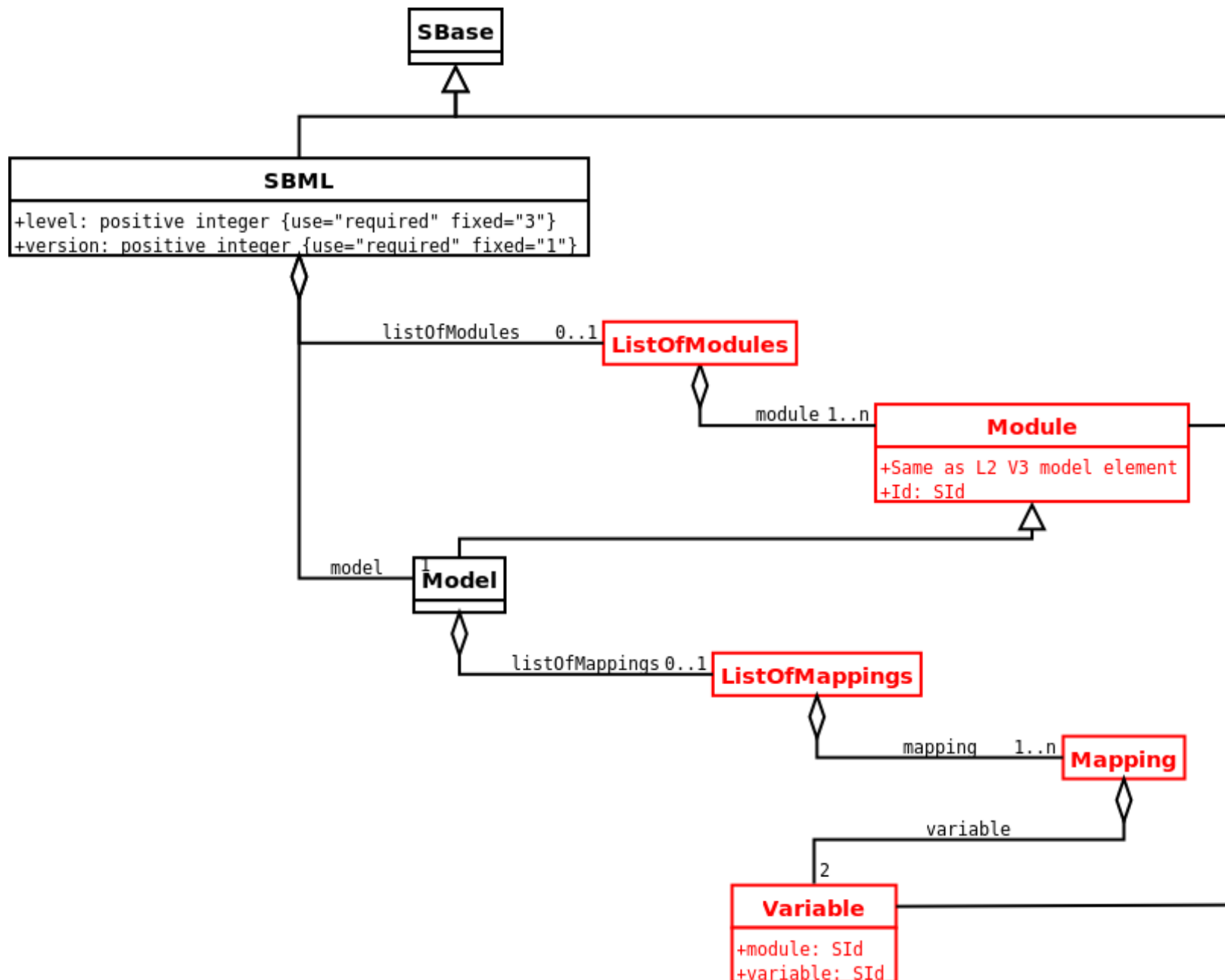
module

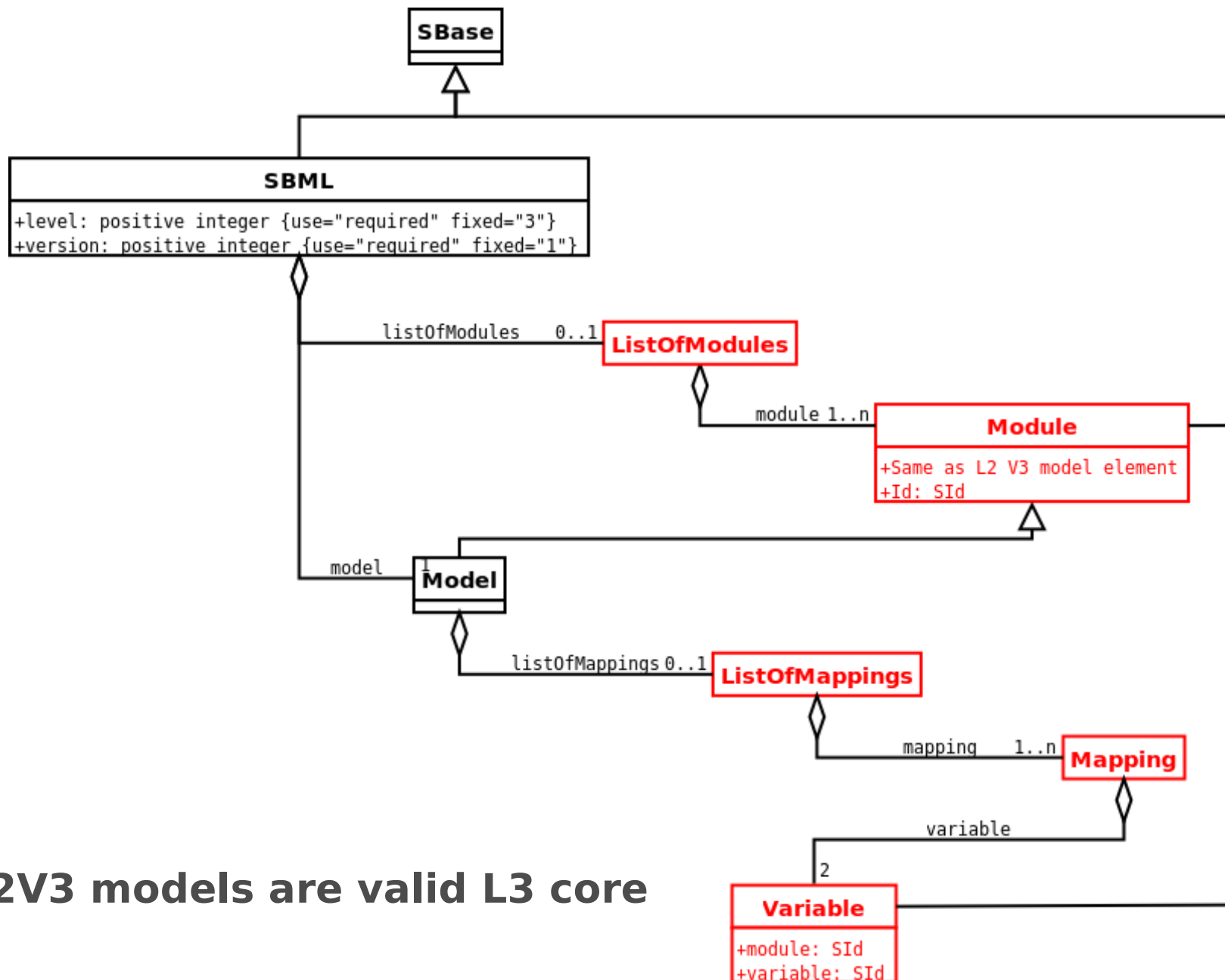
variable

module

variable





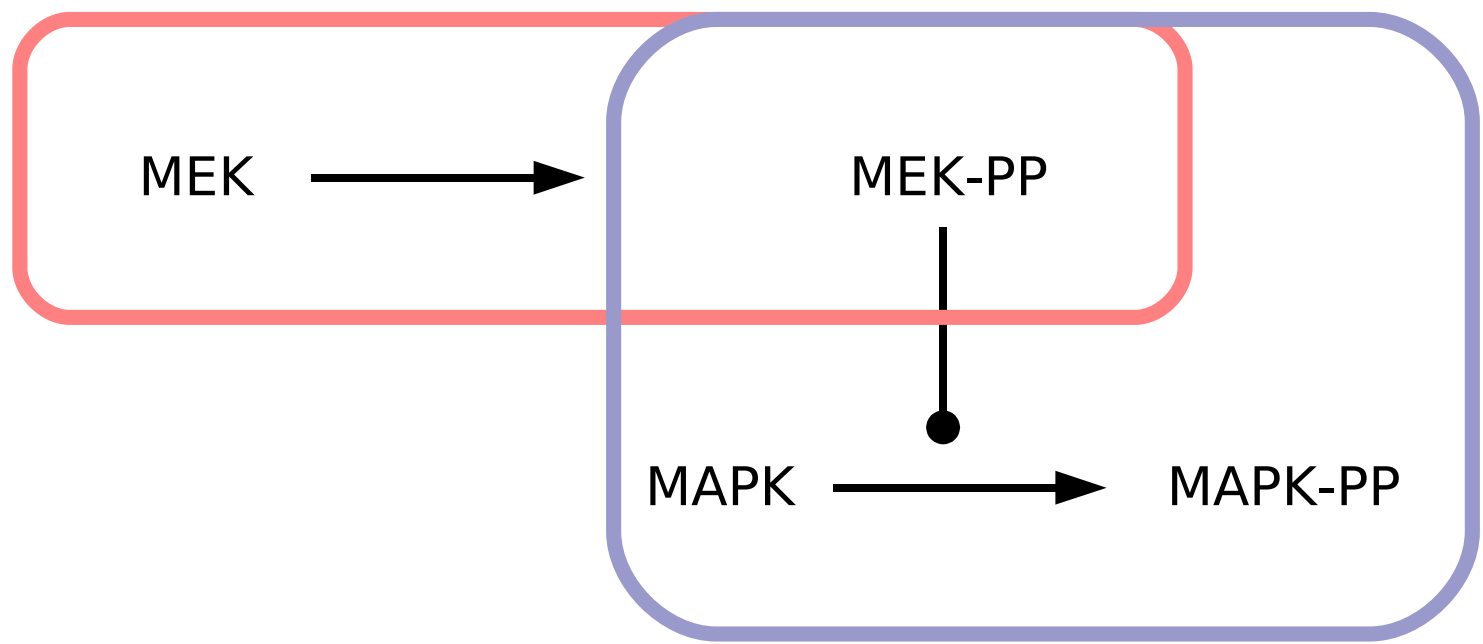


all L2V3 models are valid L3 core



```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level3" level="3" version="1">
  <model>
    <listOfMappings>
      ...
    </listOfMappings>
    <listOfCompartments>
      ...
    </listOfCompartments>
  </model>
  <listOfModules>
    <module id="A">
      <listOfSpecies>
        ...
      </listOfSpecies>
      ...
      <listOfReactions>
        ...
      </listOfReactions>
    </module>
    <module id="B">
      ...
    </module>
  </listOfModules>
</sbml>
```





```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level3" level="3" version="1">
  <model>
    <listOfMappings>
      <mapping> <!-- THIS MAPPING SAYS THAT THE VARIABLE A.MEKPP
                    and B.MAPKKPP REPRESENT THE SAME ENTITY -->
        <variable module="A" variable="MEKPP" />
        <variable module="B" variable="MAPKKPP" />
      </mapping>
    </listOfMappings>
    <listOfCompartments>
      <!-- THIS COMPARTMENT WILL BE KNOWN BY EVERY MODULES -->
      <compartment id="cell" size="1"/>
    </listOfCompartments>
  </model>
  <listOfModules>
    <module id="A"><!-- ... --></module>
    <module id="B"><!-- ... --></module>
  </listOfModules>
</sbml>
```

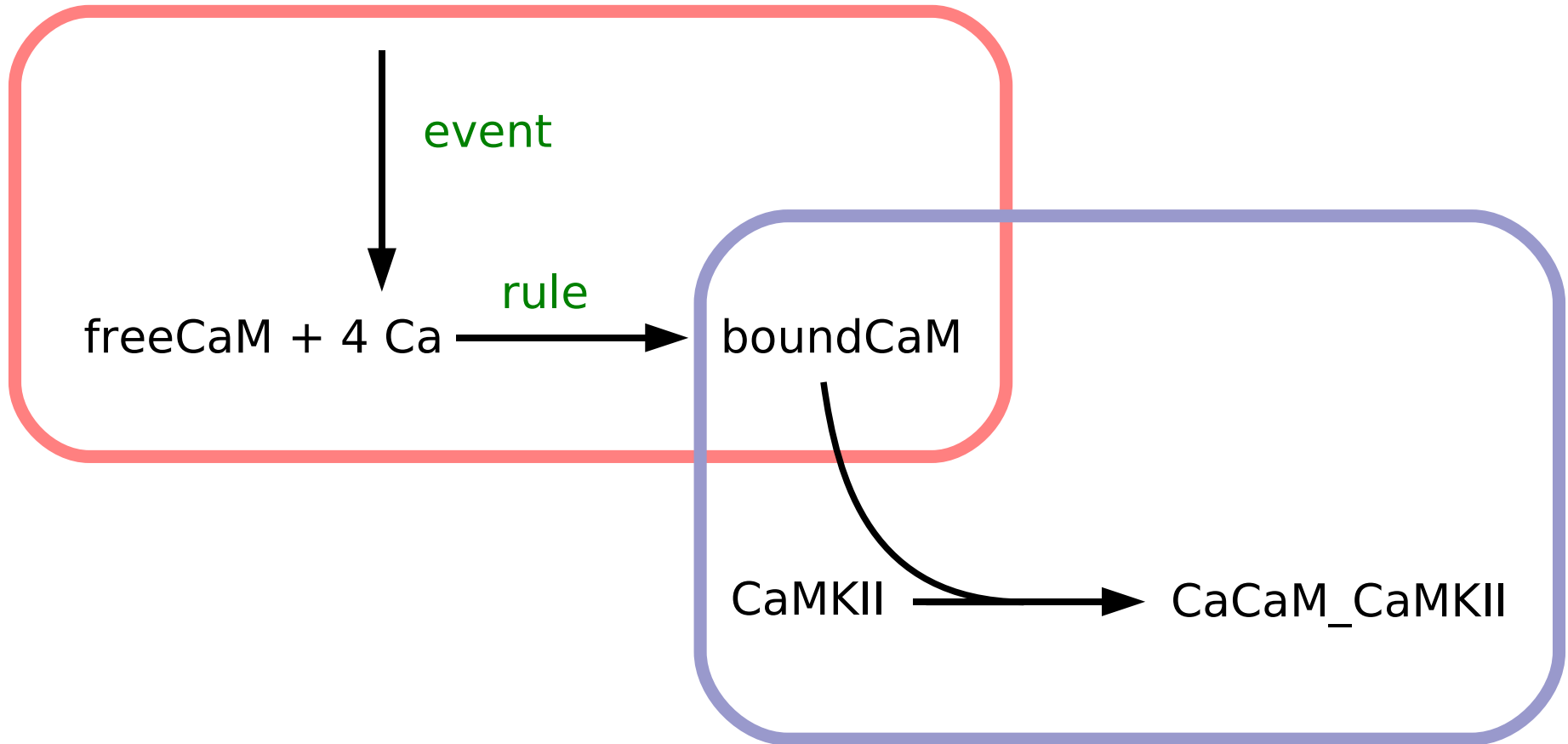


```
<module id="A">
  <listOfSpecies> <!-- NOTE THAT UNITS ARE NOT DEFINED.
                   SBML BUILT-IN UNITS ARE USED -->
    <species id="MEK" compartment="cell" initialConcentration="1e-5" />
    <species id="MEKPP" compartment="cell" initialConcentration="1e-5" />
  </listOfSpecies>
  <listOfParameters>
    <parameter id="Vmax" />
    <parameter id="Km" />
  </listOfParameters>
  <listOfReactions>
    <listOfReactants>
      <speciesReference species="MEK"/>
    </listOfReactants>
    <listOfProducts>
      <speciesReference species="MEKPP" />
    </listOfProducts>
    <kineticLaw>
<!--      ... Vmax * MEK / (Km + MEK) * cell      -->
    </kineticLaw>
  </listOfReactions>
</module>
```



```
<module id="B">
  <listOfUnitDefinitions> <!-- DEFAULT SUBSTANCE UNIT IS REDEFINED TO MICROMOLE -->
    <unitDefinition id="substance" name="micromole">
      <listOfUnits>
        <unit kind="mole" scale="-6" />
      </listOfUnits>
    </unitDefinition>
  </listOfUnitDefinitions>
  <listOfSpecies>
    <species id="MAPKKPP" compartment="cell" initialConcentration="0" />
    <!-- THIS INITIALCONCENTRATION OVERRIDE THE ONE DECLARED IN MODULE A -->
    <species id="MAPK" compartment="cell" initialConcentration="1" />
    <species id="MAPKPP" compartment="cell" initialConcentration="0" />
  </listOfSpecies>
  <listOfParameters>
    <parameter id="kcat" />
    <parameter id="Km" />
  </listOfParameters>
  <listOfReactions>
    <listOfReactants>
      <speciesReference species="MAPK" />
    </listOfReactants>
    <listOfProducts>
      <speciesReference species="MAPKPP" />
    </listOfProducts>
    <listOfModifiers>
      <speciesReference species="MAKKPP" />
    </listOfModifiers>
    <kineticLaw>
<!--          ... kcat * MAKKPP * MAPK / (Km + MAPK) * cell -->
    </kineticLaw>
  </listOfReactions>
</module>
```





```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level3" level="3" version="1">
  <model>
    <listOfMappings>
      <mapping>
        <variable module="Ca" variable="boundCaM" />
        <variable module="KII" variable="CaCaM" />
      </mapping>
      <mapping>
        <variable module="Ca" variable="cell" />
        <variable module="KII" variable="cell" />
      </mapping>
    </listOfMappings>
  </model>
  <listOfModules>
    <module id="Ca"><!-- ... --></module>
    <module id="KII"><!-- ... --></module>
  </listOfModules>
</sbml>
```



```
<module id="Ca">
  <listOfCompartments>
    <compartment id="cell" size="1"/>
  </listOfCompartments>
  <listOfSpecies>
    <species id="freeCaM" initialConcentration="1" compartment="cell">
    <species id="boundCaM" initialConcentration="0" compartment="cell">
  </listOfSpecies>
  <listOfParameters>
    <parameter id="ca" value="0" />
    <parameter id="Kd" value="1" />
    <parameter id="T" value="10" />
  </listOfParameters>
  <listOfRules>
    <assignmentRule variable="boundCaM">
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <apply>
          <times/>
          <ci> freeCaM </ci>
          <apply>
            <power>
              <apply>
                <divide/>
                <ci> ca </ci>
              </apply>
              <plus/><ci> Kd </ci><ci> ca </ci>
            </apply>
          </apply>
          <cn type="integer"> 4 </cn>
        </apply>
      </math>
    </assignmentRule>
  </listOfRules>
</module>
```



```
<listOfEvents>
  <event id="caEntry">
    <trigger>
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <apply>
          <gt/>
          <csymbol encoding="text"
            definitionURL="http://www.sbml.org/sbml/symbols/time">
            time
          </csymbol>
          <ci> T </ci>
        </apply>
      </math>
    </trigger>
    <listOfEventAssignments>
      <eventAssignment variable="ca">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <cn> 1 </cn>
        </math>
      </eventAssignment>
    </listOfEventAssignments>
  </event>
</listOfEvents>
</module>
```



```
<module id="KII">
  <listOfCompartments>
    <compartment id="cell" size="1"/>
  </listOfCompartments>
  <listOfSpecies>
    <species id="CaCaM" initialConcentration="0" compartment="cell">
    <species id="CaMKII" initialConcentration="1" compartment="cell">
    <species id="CaCaM_CaMKII" initialConcentration="0" compartment="cell">
  </listOfSpecies>
  <listOfReactions>
    <reaction id="bindingCaM">
      <listOfReactants>
        <speciesReference species="CaMKII">
        <speciesReference species="CaCaM">
      </listOfReactants>
      <listOfProducts>
        <speciesReference species="CaCaM_CaMKII">
      </listOfProducts>
      <kineticLaw>
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <times/>
            <ci> CaCaM </ci>
            <ci> CaMKII </ci>
            <ci> kon </ci>
            <ci> cell </ci>
          </apply>
        </math>
        <listOfParameters>
          <parameter id="kon" value="1"/>
        </listOfParameters>
      </kineticLaw>
    </reaction>
  </listOfReactions>
</module>
```

