



Visualising CellML models

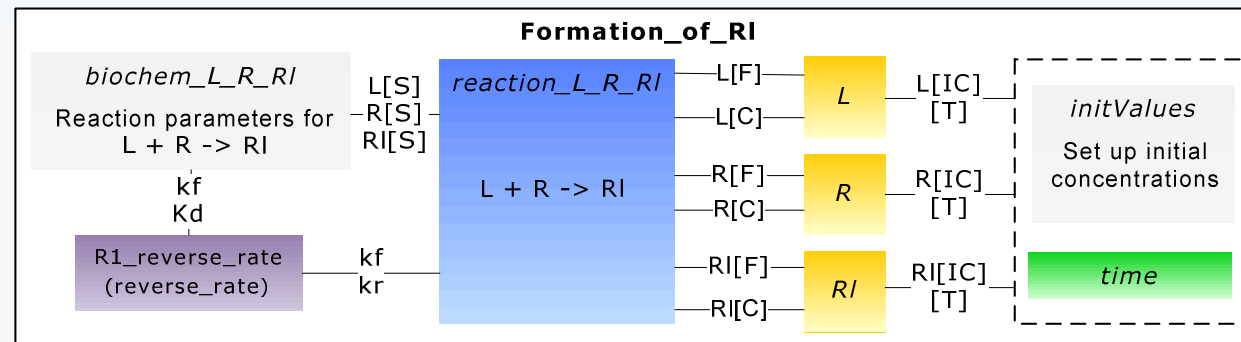
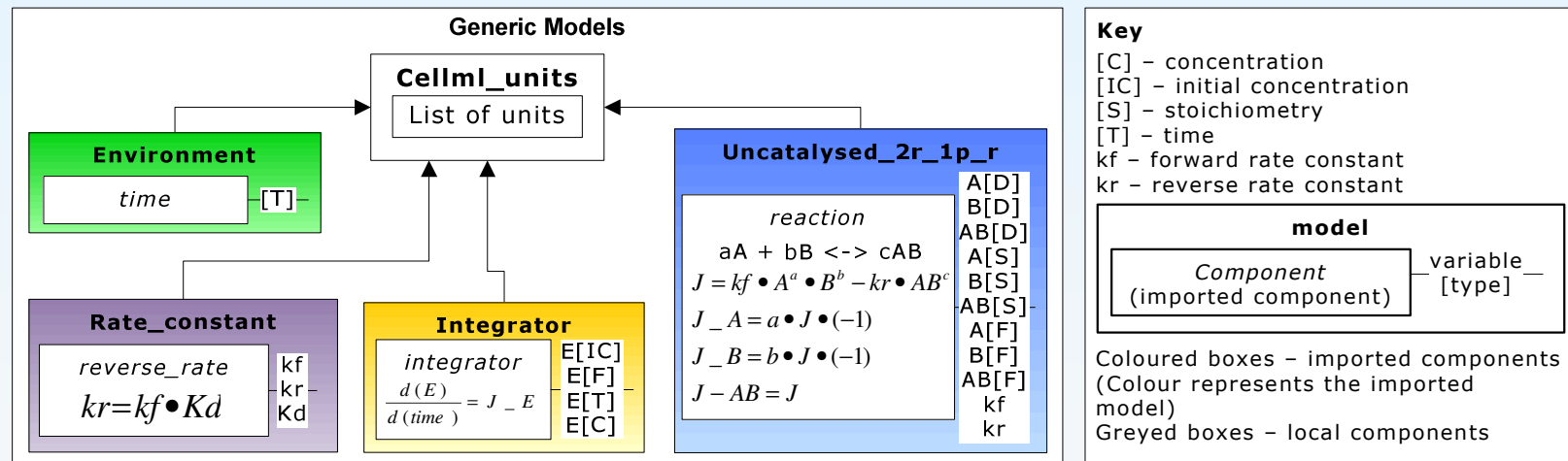


Sarala M. Wimalaratne

Modelling in CellML

- CellML focus on representing mathematical formulations of biological processes

A reaction modelled in CellML: $L+R \rightarrow RI$



CellML code

■ A reaction modelled in CellML: $L+R \rightarrow RI$

```
<model name="complex_formation" cmeta:id="complex_formation"
  xmlns="http://www.cellml.org/cellml/1.0#"
  xmlns:cellml="http://www.cellml.org/cellml/1.0#"
  xmlns:cmeta="http://www.cellml.org/metadata/1.0#"
  xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#"
  xmlns:dc="http://www.purl.org/dc/elements/1-1#"
  xmlns:biopaxbinding="http://www.sarala.bioeng.auckland.ac.nz/cellmlbiopaxbinding"
  <units name="micromolar">
    <unit units="mole" prefix="micro"/>
    <unit units="litre" exponent="-1"/>
  </units>
  <units name="flux">
    <unit units="micromolar"/>
    <unit units="second" exponent="-1"/>
  </units>
  <units name="second_order_rate_constant">
    <unit units="micromolar" exponent="-1"/>
    <unit units="second" exponent="-1"/>
  </units>
  <component name="environment">
    <variable name="time" units="second" public_interface="out"/>
  </component>
  <component name="L">
    <variable name="L" units="micromolar" initial_value="1" public_interface="out"/>
    <variable name="J_L" units="flux" public_interface="in"/>
    <variable name="time" units="second" public_interface="in"/>
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <eq>
          <apply>
            <diff/>
            <bvar>
              <ci>time</ci>
            </bvar>
            <ci>L</ci>
          </apply>
          <ci>J_L</ci>
        </eq>
      </apply>
    </math>
  </component>
  <component name="R">
    <variable name="R" units="micromolar" initial_value="1" public_interface="out"/>
    <variable name="J_R" units="flux" public_interface="in"/>
    <variable name="time" units="second" public_interface="in"/>
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <eq>
          <apply>
            <diff/>
            <bvar>
              <ci>time</ci>
            </bvar>
            <ci>R</ci>
          </apply>
          <ci>J_R</ci>
        </eq>
      </apply>
    </math>
  </component>
```

```
<component name="RI_complex">
  <variable name="RI_complex" units="micromolar" initial_value="1" public_interface="out"/>
  <variable name="J_RI" units="flux" public_interface="in"/>
  <variable name="time" units="second" public_interface="in"/>
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq>
        <apply>
          <diff/>
          <bvar>
            <ci>time</ci>
          </bvar>
          <ci>RI_complex</ci>
        </apply>
        <ci>J_RI</ci>
      </eq>
    </math>
  </component>
  <component name="reaction">
    <variable name="J_L" units="flux" public_interface="out"/>
    <variable name="J_R" units="flux" public_interface="out"/>
    <variable name="J_RI" units="flux" public_interface="out"/>
    <variable name="J" units="flux"/>
    <variable name="L" units="micromolar" public_interface="in"/>
    <variable name="R" units="micromolar" public_interface="in"/>
    <variable name="RI_complex" units="micromolar" public_interface="in"/>
    <variable name="time" units="second" public_interface="in"/>
    <variable name="k1" units="second_order_rate_constant" public_interface="in"/>
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <eq>
          <ci>J</ci>
          <apply>
            <times/>
            <ci>k1</ci>
            <ci>L</ci>
            <ci>R</ci>
          </apply>
        </eq>
      </apply>
    </math>
  </component>
```

```
<apply>
  <minus/>
  <cn cellml:units="dimensionless">1</cn>
</apply>
</apply>
</component>
<component name="rate_constant">
  <variable name="k1" units="second_order_rate_constant" initial_value="1" public_interface="out"/>
</component>
<connection>
  <map_components component_1="L" component_2="reaction"/>
  <map_variables variable_1="L" variable_2="L"/>
  <map_variables variable_1="J_L" variable_2="J_L"/>
</connection>
<connection>
  <map_components component_1="L" component_2="environment"/>
  <map_variables variable_1="time" variable_2="time"/>
</connection>
<connection>
  <map_components component_1="R" component_2="reaction"/>
  <map_variables variable_1="R" variable_2="R"/>
  <map_variables variable_1="J_R" variable_2="J_R"/>
</connection>
<connection>
  <map_components component_1="R" component_2="environment"/>
  <map_variables variable_1="time" variable_2="time"/>
</connection>
<connection>
  <map_components component_1="RI_complex" component_2="reaction"/>
  <map_variables variable_1="RI_complex" variable_2="RI_complex"/>
  <map_variables variable_1="J_RI" variable_2="J_RI"/>
</connection>
<connection>
  <map_components component_1="RI_complex" component_2="environment"/>
  <map_variables variable_1="time" variable_2="time"/>
</connection>
<connection>
  <map_components component_1="reaction" component_2="rate_constant"/>
  <map_variables variable_1="k1" variable_2="k1"/>
</connection>
<connection>
  <map_components component_1="reaction" component_2="environment"/>
  <map_variables variable_1="time" variable_2="time"/>
</model>
```

Physical data

```
<component name="complexFormationReaction_formationOfRI">
  <variable name="J_L" units="flux" public_interface="out"/>
  <variable name="J_R" units="flux" public_interface="out"/>
  <variable name="J_RI" units="flux" public_interface="out"/>
  <variable name="J" units="flux"/>
  <variable name="L" units="micromolar" public_interface="fa" />
  <variable name="R" units="micromolar" public_interface="in"/>
  <variable name="RI_complex" units="micromolar" public_interface="in"/>
  <variable name="time" units="second" public_interface="in"/>
  <variable name="k1" units="second_order_rate_constant" public_interface="in"/>
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq/>
      <ci>J</ci>
      <apply>
        <times/>
        <ci>k1</ci>
        <ci>L</ci>
        <ci>R</ci>
      </apply>
    </apply>....
  </math>
</component>
```

Concentration

Reaction kinetics for a second order, forward reaction with two reactants, a first order reverse reaction, reversible mass action kinetics action, and a continuous scheme

Biological data

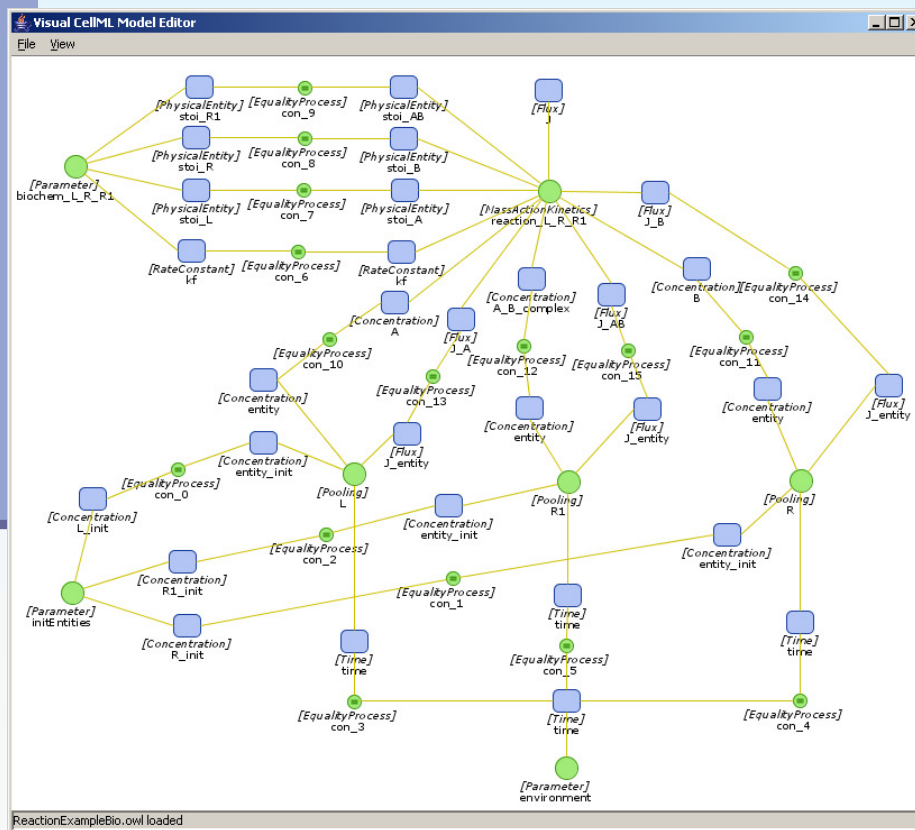
```
<component name="reaction_L_R_RI">
  <variable name="J_L" units="flux" public_interface="out"/>
  <variable name="J_R" units="flux" public_interface="out"/>
  <variable name="J_RI" units="flux" public_interface="out"/>
  <variable name="J" units="flux"/>
  <variable name="L" units="micromolar" public_interface="in"/>
  <variable name="R" units="micromolar" public_interface="in"/>
  <variable name="RI_complex" units="micromolar" public_interface="in"/>
  <variable name="time" units="second" public_interface="in"/>
  <variable name="k1" units="second_order_rate_constant" public_interface="in"/>
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq/>
      <ci>J</ci>
      <apply>
        <times/>
        <ci>k1</ci>
        <ci>L</ci>
        <ci>R</ci>
      </apply>
    </apply>....
```

Complex formation

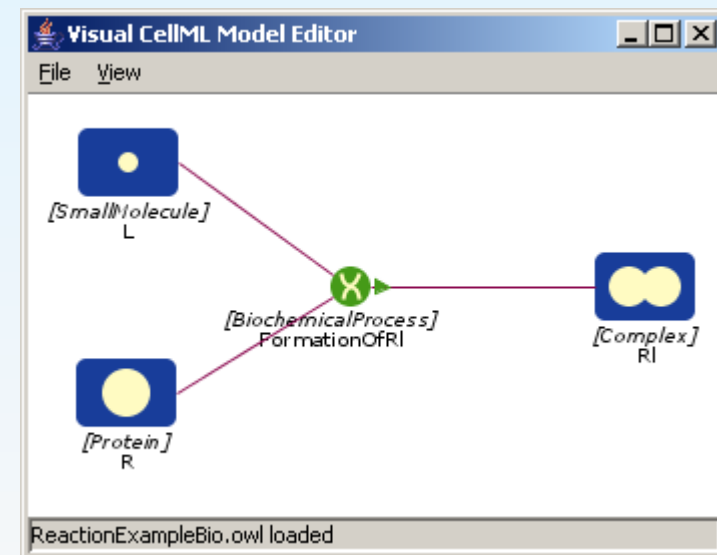
Complex

Visualising CellML models

CellML structure (Physical View)

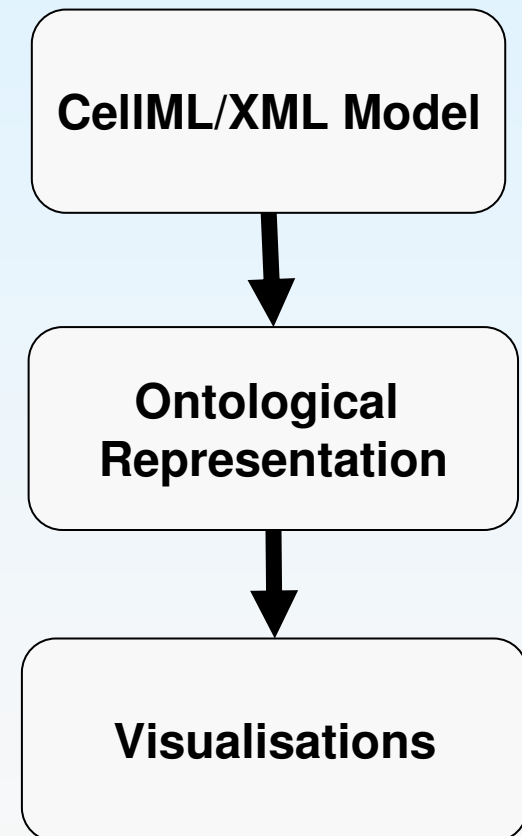


Underlying biology (Biological View)



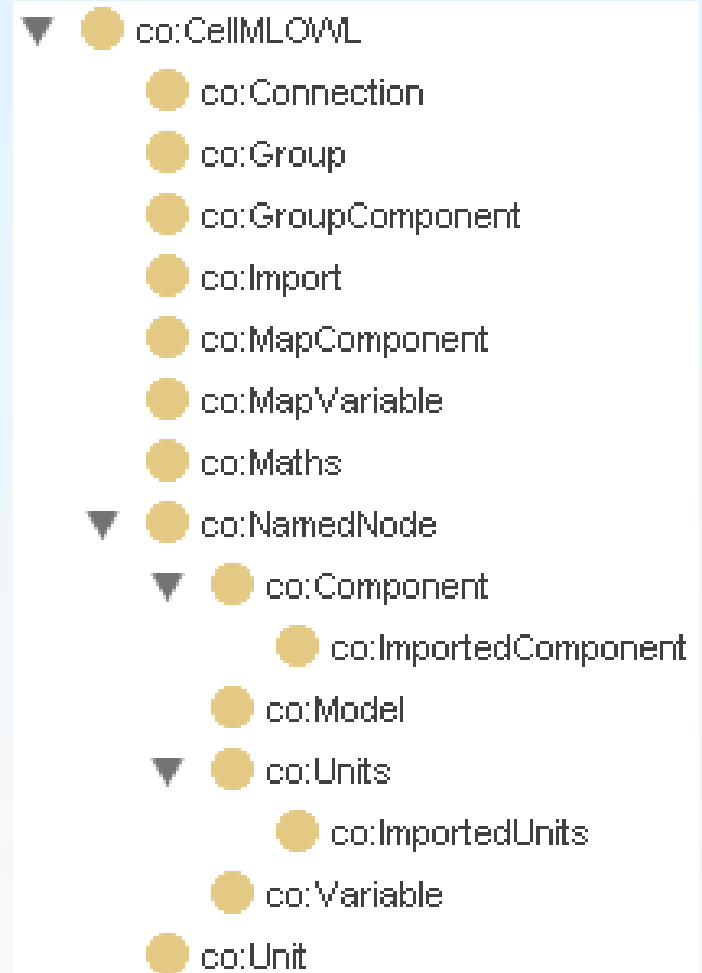
Ontology

- A formal and machine interpretable specification of concepts and relations between the concepts within a domain of knowledge
- Defines a common vocabulary and set of rules to unambiguously represent information

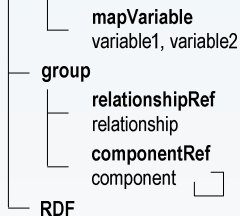
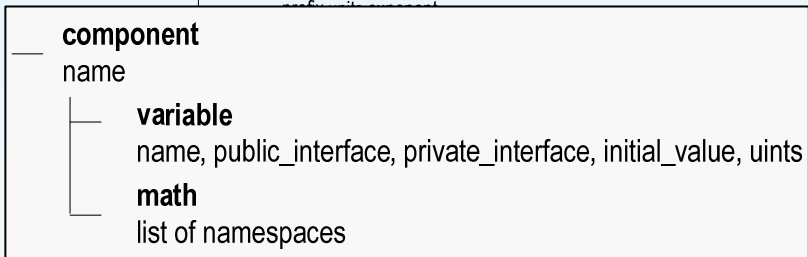
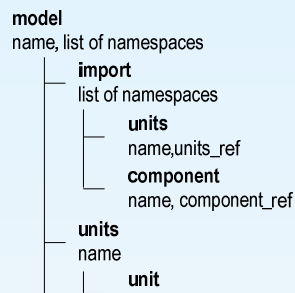


CellML/OWL ontology

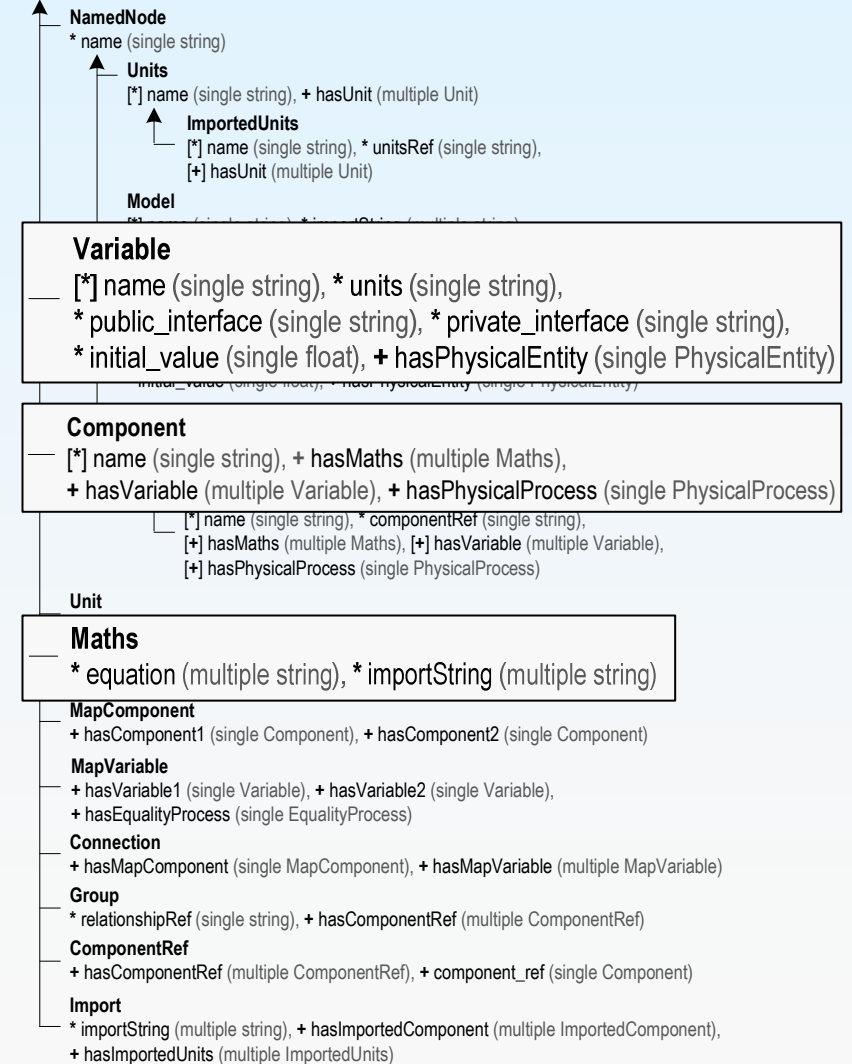
- Captures CellML/XML structure in Web Ontology Language format (OWL)



CellML/OWL ontology

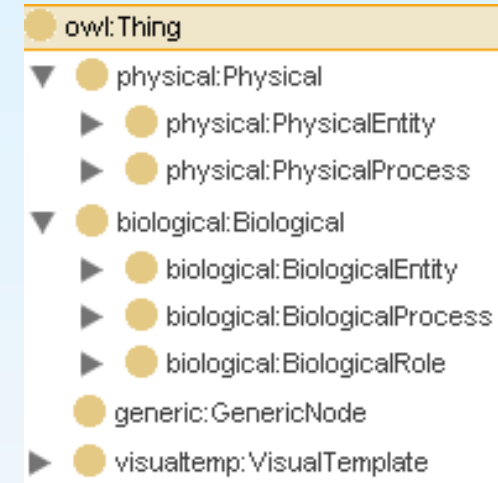


CellMLOWL



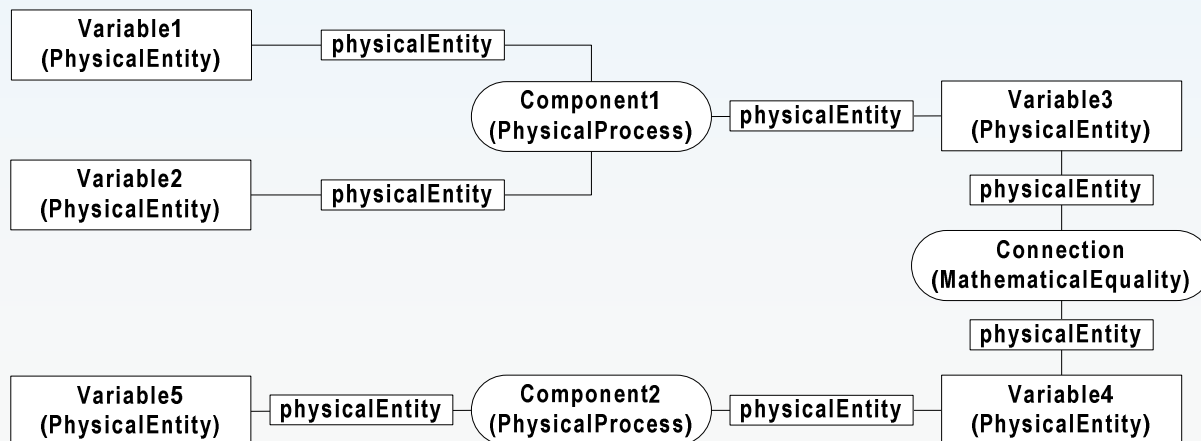
CellMLBiophysical/OWL ontology

- integrates 3 ontologies
 - Physical
 - Biological
 - VisualTemplate



Mapping between CellML/OWL and CellMLBiophysical/OWL (Physical) instances

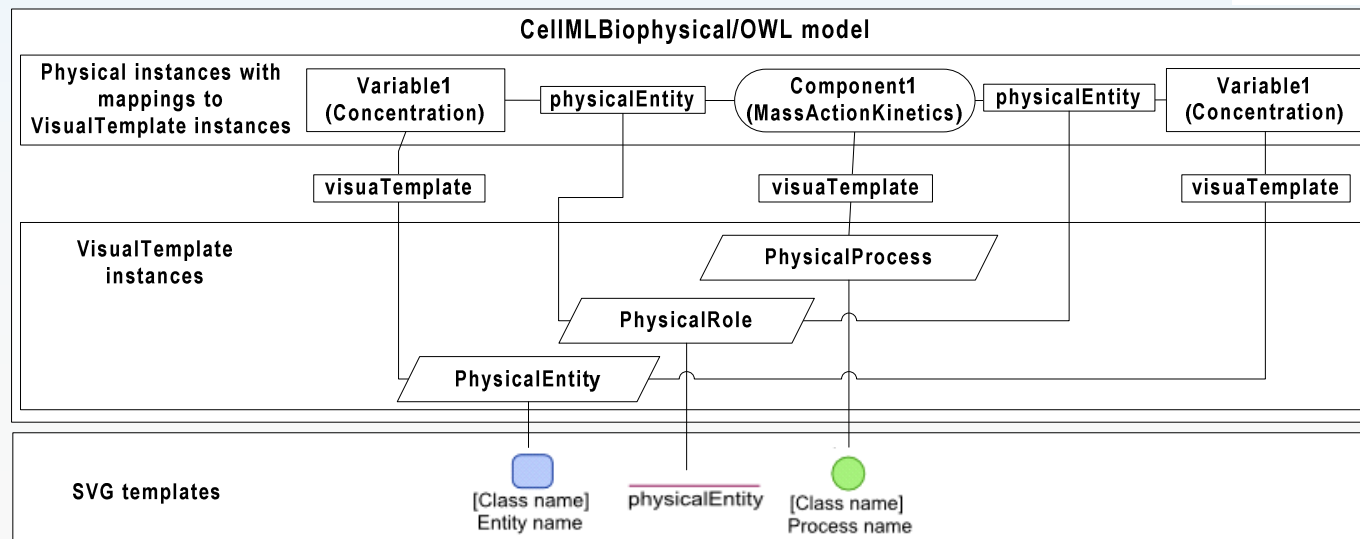
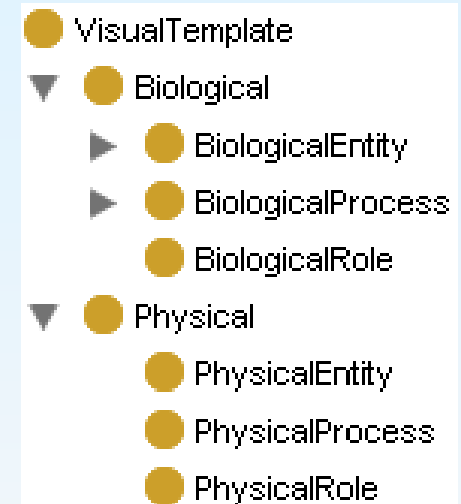
CellML/OWL	CellMLBiophysical/OWL (Physical)
Component	PhysicalProcess
Variable	PhysicalEntity
Connection	MathematicalEquality



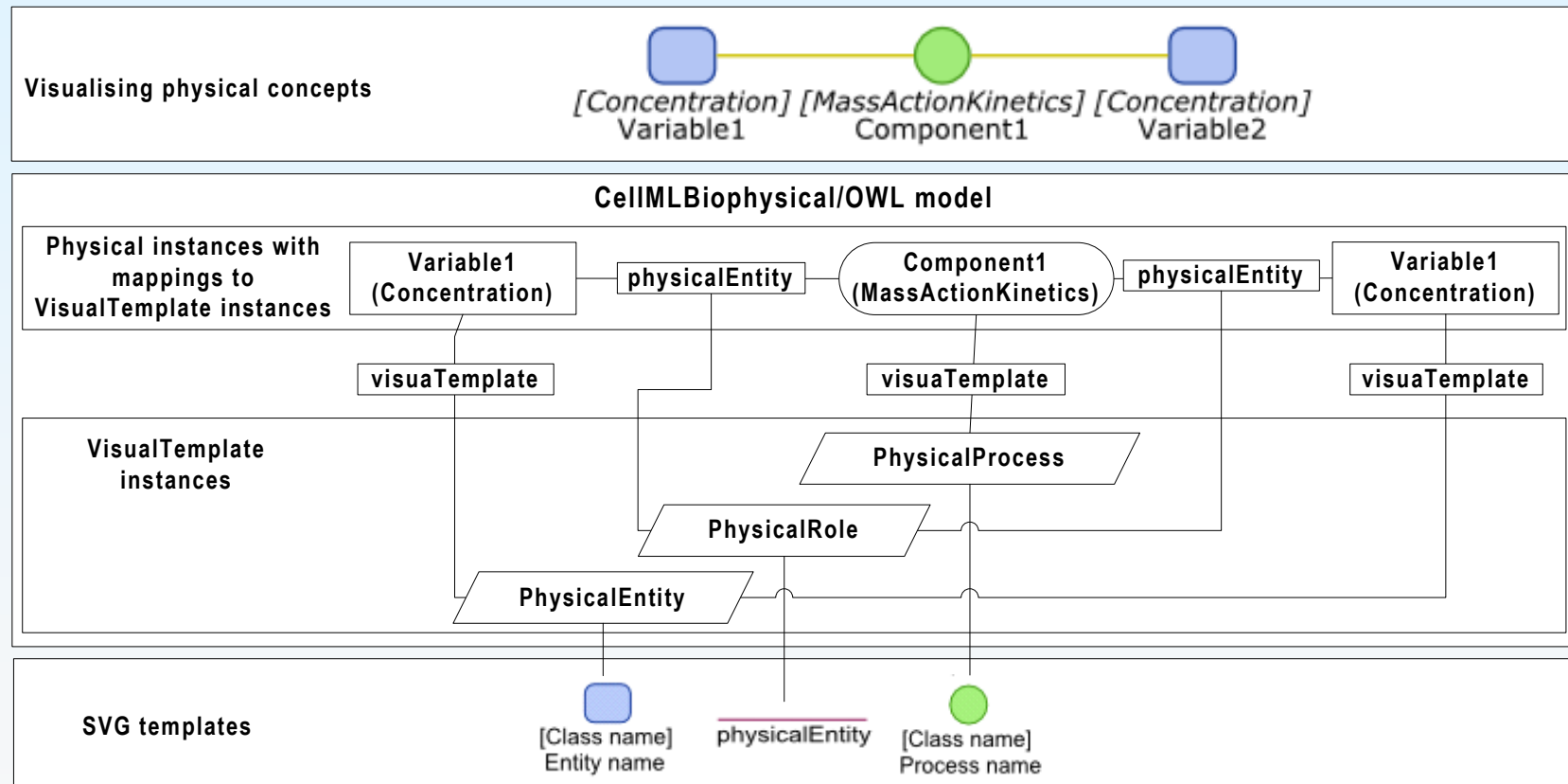
- ▼ ● cellmlbioont:Physical
- ▼ ● cellmlbioont:PhysicalEntity
 - cellmlbioont:Area
 - cellmlbioont:Capacitance
 - cellmlbioont:Concentration
 - cellmlbioont:Conductance
 - cellmlbioont:Constant
 - cellmlbioont:Current
 - cellmlbioont:Flux
 - cellmlbioont:Gate
 - cellmlbioont:RateConstant
 - cellmlbioont:Time
 - cellmlbioont:Voltage
 - cellmlbioont:Volume
- ▼ ● cellmlbioont:PhysicalProcess
 - cellmlbioont:ConversionFactor
 - cellmlbioont:EnzymeKinetics
 - cellmlbioont:EqualityProcess
 - cellmlbioont:HillEquation
 - cellmlbioont:IonicCurrent
 - cellmlbioont:MassActionKinetics
 - cellmlbioont:NernstPotential
 - cellmlbioont:Parameter
 - cellmlbioont:Pooling
 - cellmlbioont:PotentialDifference
 - cellmlbioont:RateConstantCalculation

Mapping between Physical and VisualTemplate instances

CellMLBiophysical/OWL (Physical)	CellMLBiophysical/OWL (VisualTemplate)
PhysicalProcess	PhysicalProcess
PhysicalEntity	PhysicalEntity



Generating a physical view




Key


 OWL Property

 VisualTemplate instance

 Physical entity instance

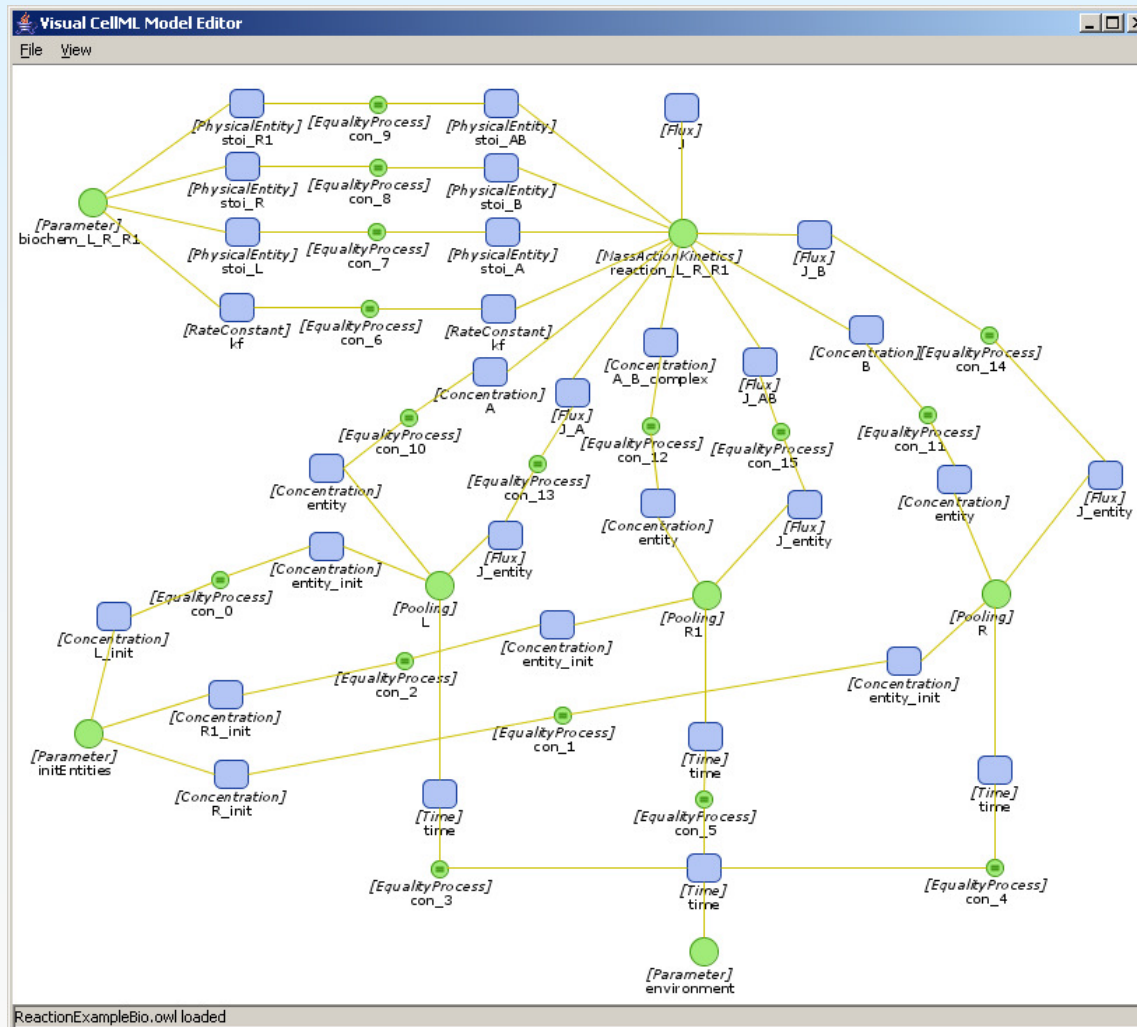
 Physical process instance

 [Class name] Entity name

 physicalEntity

 [Class name] Process name

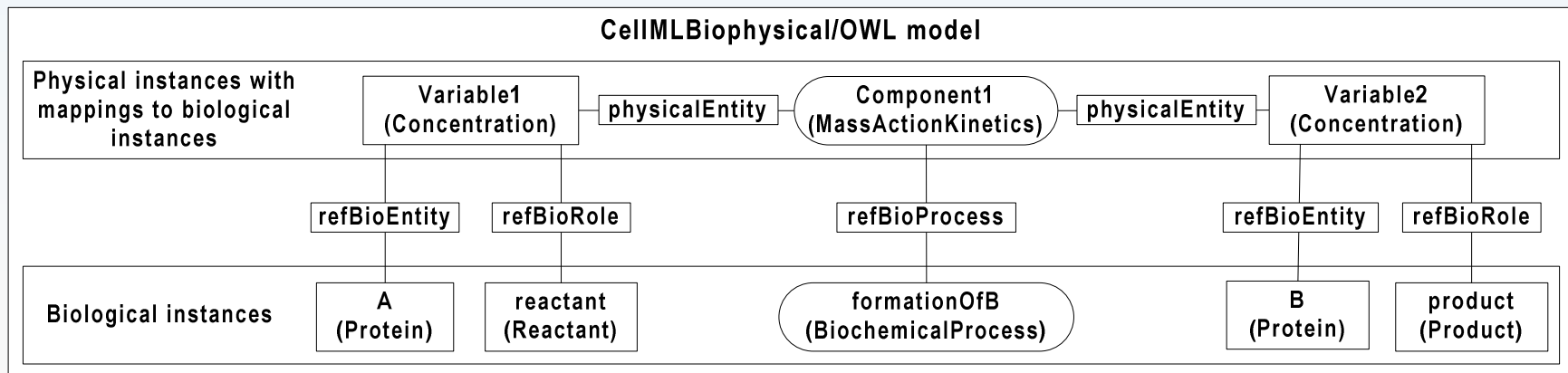
Physical view of the reaction: $R+L \rightarrow RL$



Mapping between Physical and Biological instances

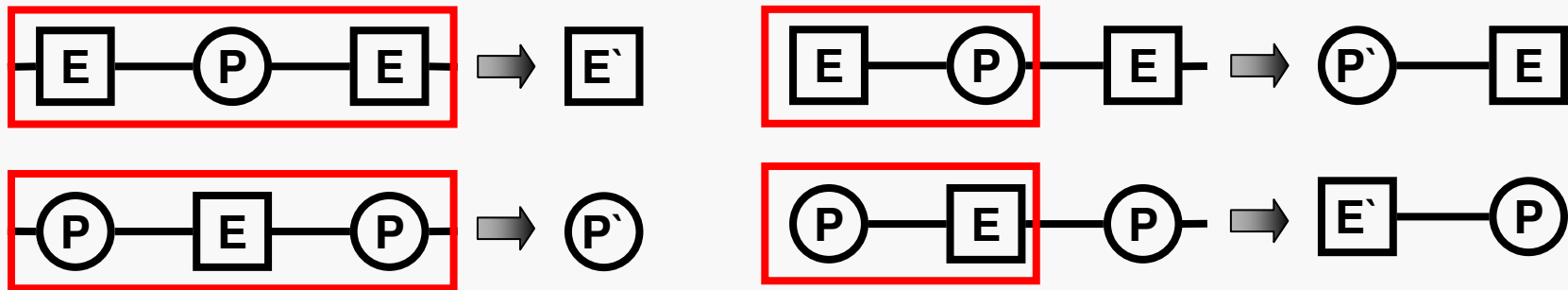
CellMLBiophysical/OWL (Physical)	CellMLBiophysical/OWL (Biological)
PhysicalProcess	BiologicalProcess
PhysicalEntity	BiologicalEntity/ BiologicalRole

- ▼ ● biological:Biological
 - ▼ ● biological:BiologicalEntity
 - biological:Complex
 - biological:PhysicalFactor
 - biological:Protein
 - biological:SmallMolecule
 - ▼ ● biological:BiologicalProcess
 - biological:BiochemicalProcess
 - biological:Catalysis
 - biological:ComplexFormation
 - biological:Transport
 - ▼ ● biological:BiologicalRole
 - ▶ ● biological:Modifier
 - biological:Product
 - biological:Reactant

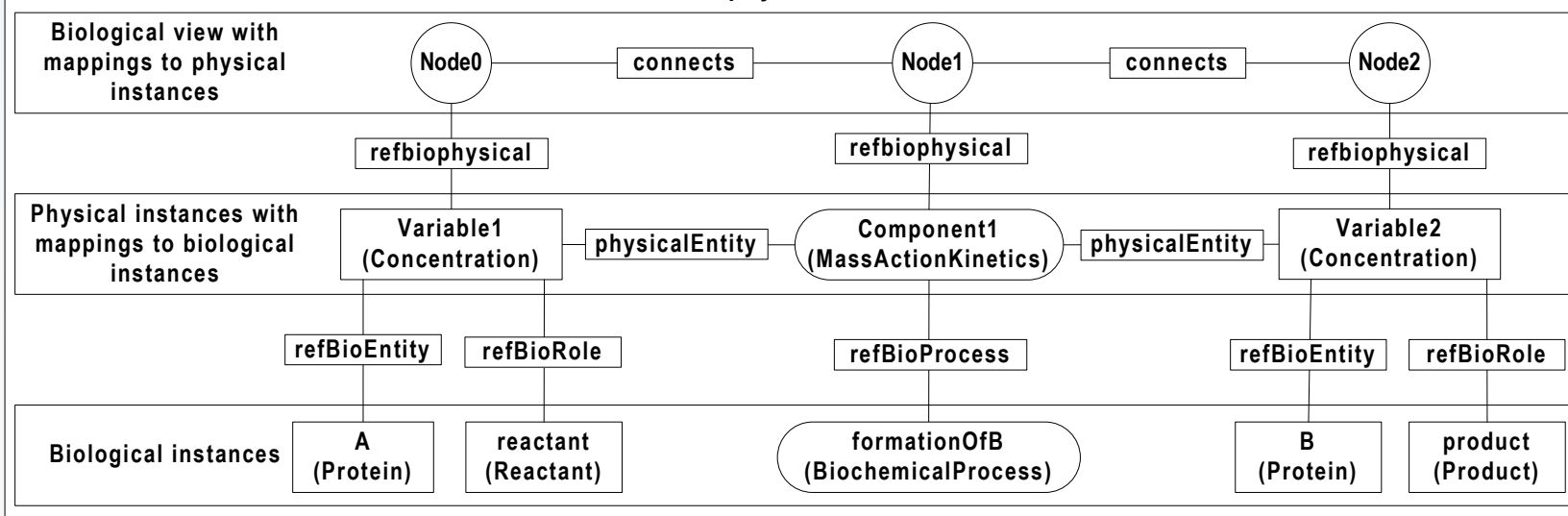


Reducing the complexity

Collapsing Patterns

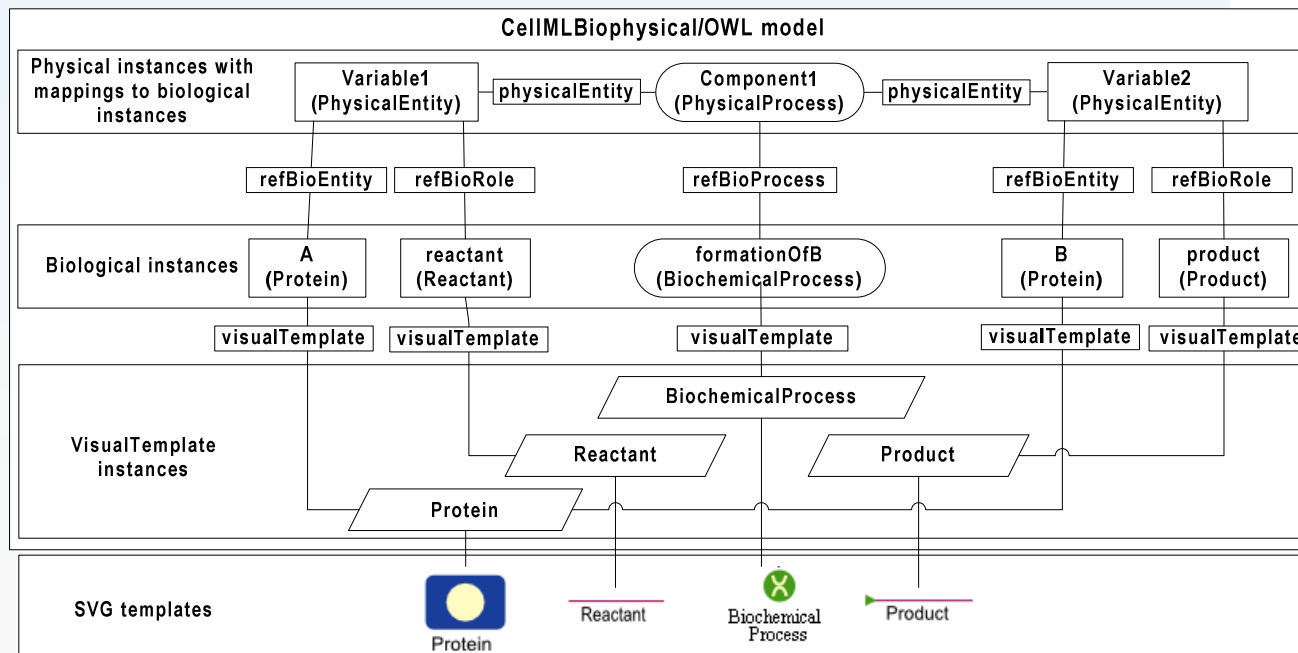
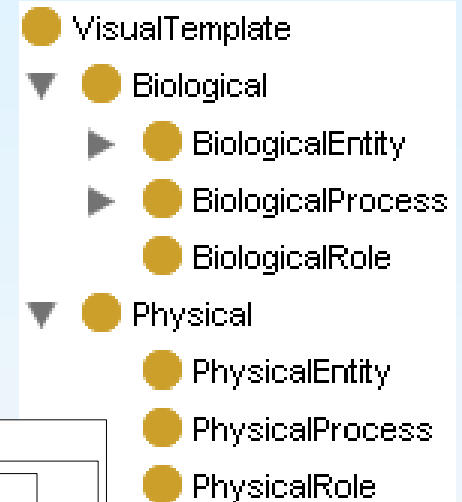


CellMLBiophysical/OWL model

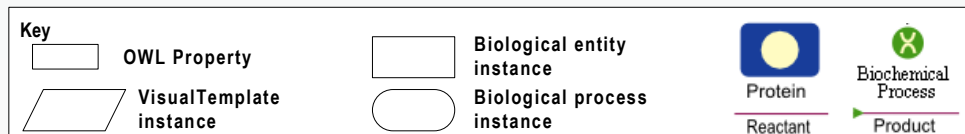
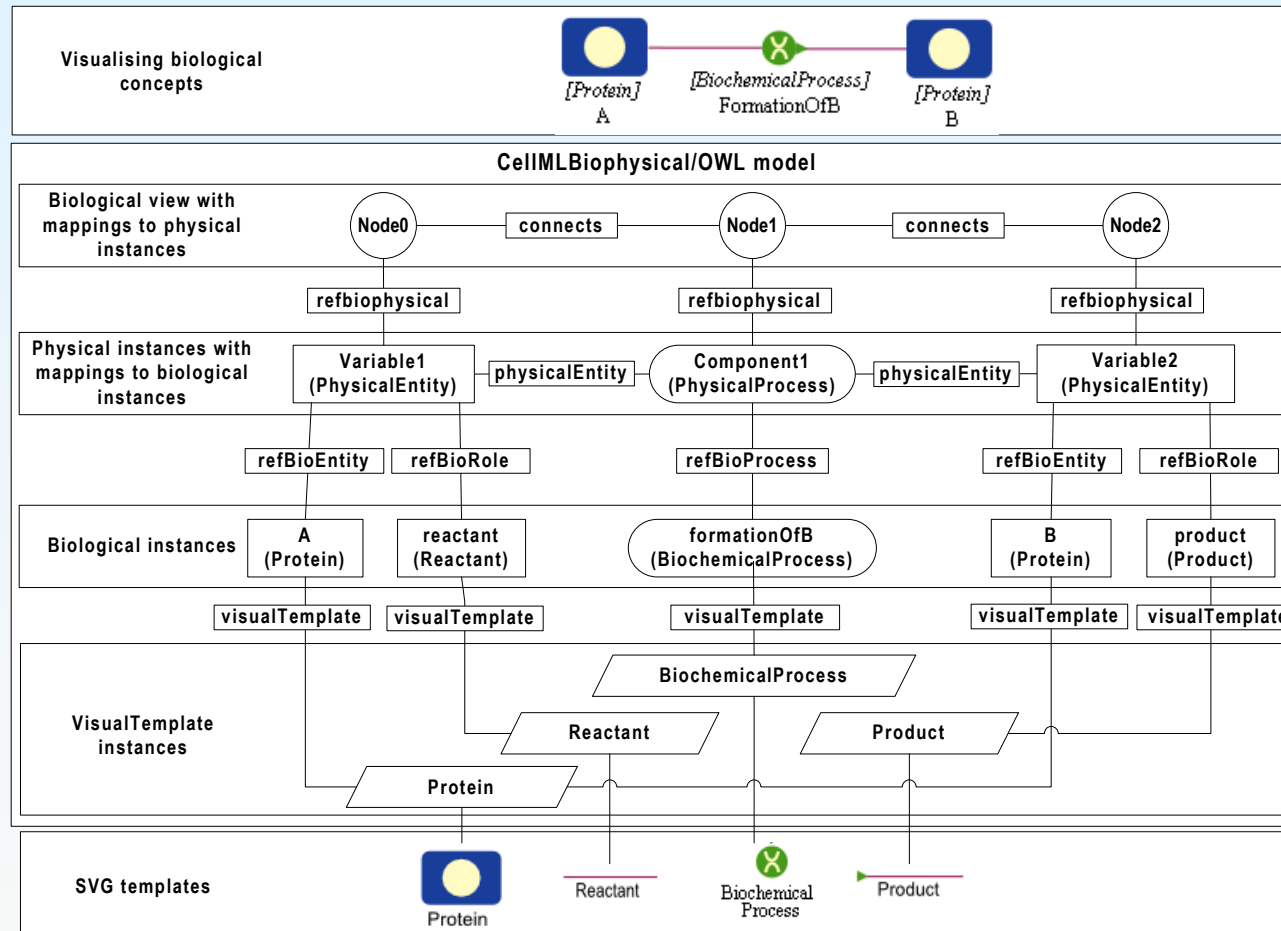


Mapping between Biological and VisualTemplate instances

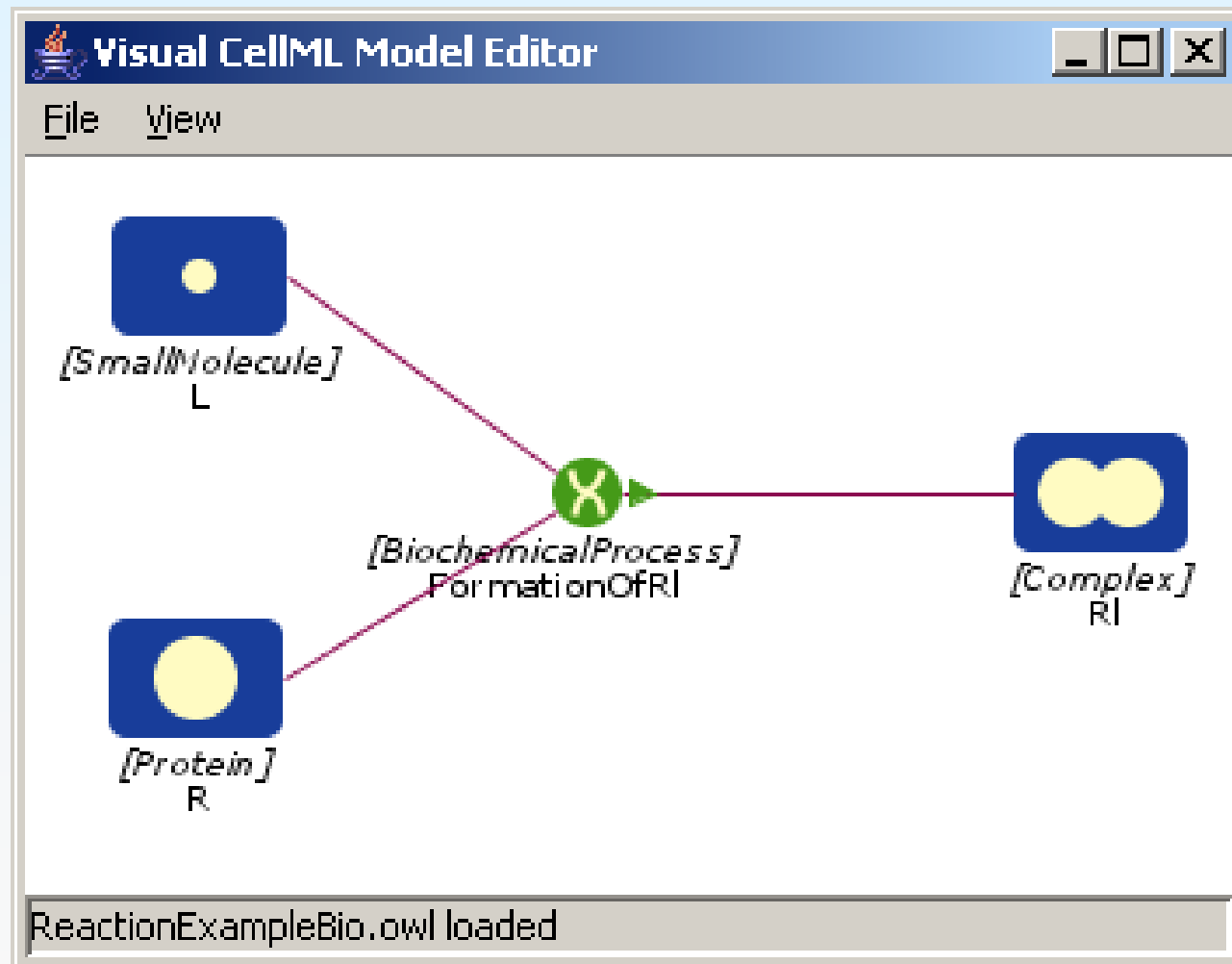
CellMLBiophysical/OWL (Biological)	CellMLBiophysical/OWL (VisualTemplate)
BiologicalProcess	BiologicalProcess
BiologicalEntity	BiologicalEntity
BiologicalRole	BiologicalRole



Generating a biological view



Biological view of the reaction: $R+L \rightarrow RI$



Summary

