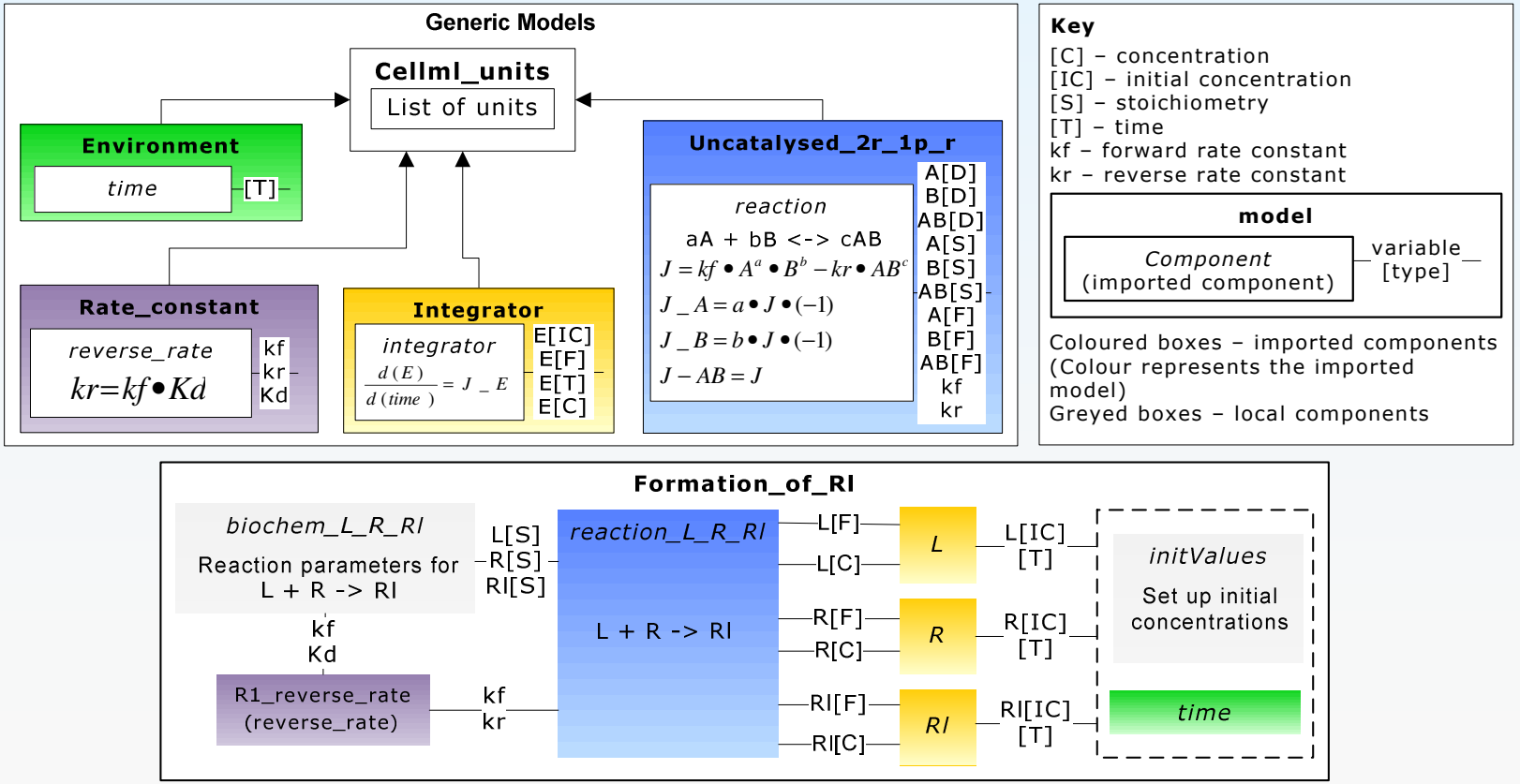
Visualising CellML models

Sarala M. Wimalaratne

Modelling in CellML

- CellML focus on representing mathematical formulations of biological processes

A reaction modelled in CellML: L+R -> RI



CellML code

- A reaction modelled in CellML: L+R -> 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/cellmlbiopaxbindin
  <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>
      </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>
      </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"/>
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          <diff/>
          <bvar>
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          </bvar>
          <ci>RI_complex</ci>
        </apply>
        <ci>J_RI</ci>
      </apply>
    </math>
  </component>
  <component name="reaction">
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    <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>
      <apply>
        <eq/>
        <ci>J_L</ci>
        <apply>
          <times/>
          <ci>J</ci>
          <apply>
            <minus/>
            <cn cellml:units="dimensionless">1</cn>
          </apply>
        </apply>
      </apply>
      <apply>
        <eq/>
        <ci>J_R</ci>
        <apply>
          <times/>
          <ci>J</ci>
```

```
          <apply>
            <minus/>
            <cn cellml:units="dimensionless">1</cn>
          </apply>
        </apply>
      </apply>
      <apply>
        <eq/>
        <ci>J_RI</ci>
        <apply>
          <times/>
          <ci>J</ci>
          <cn cellml:units="dimensionless">1</cn>
        </apply>
      </apply>
    </math>
  </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"/>
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  <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_formationOfRl">
      <variable name="J_L" units="flux" public_interface="out"/>
      <variable name="J_R" units="flux" public_interface="out"/>
      <variable name="J_Rl" units="flux" public_interface="out"/>
      <variable name="J" units="flux"/>
      <variable name="L" units="micromolar" pu                fa
      <variable name="R" units="micromolar" public_interface="in"/>
      <variable name="Rl_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>....
```

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_Rl">
      <variable name="J_L" units="flux" public_interface="out"/>
      <variable name="J_R" units="flux" public_interface="out"/>
      <variable name="J_Rl" 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="Rl_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>….
```

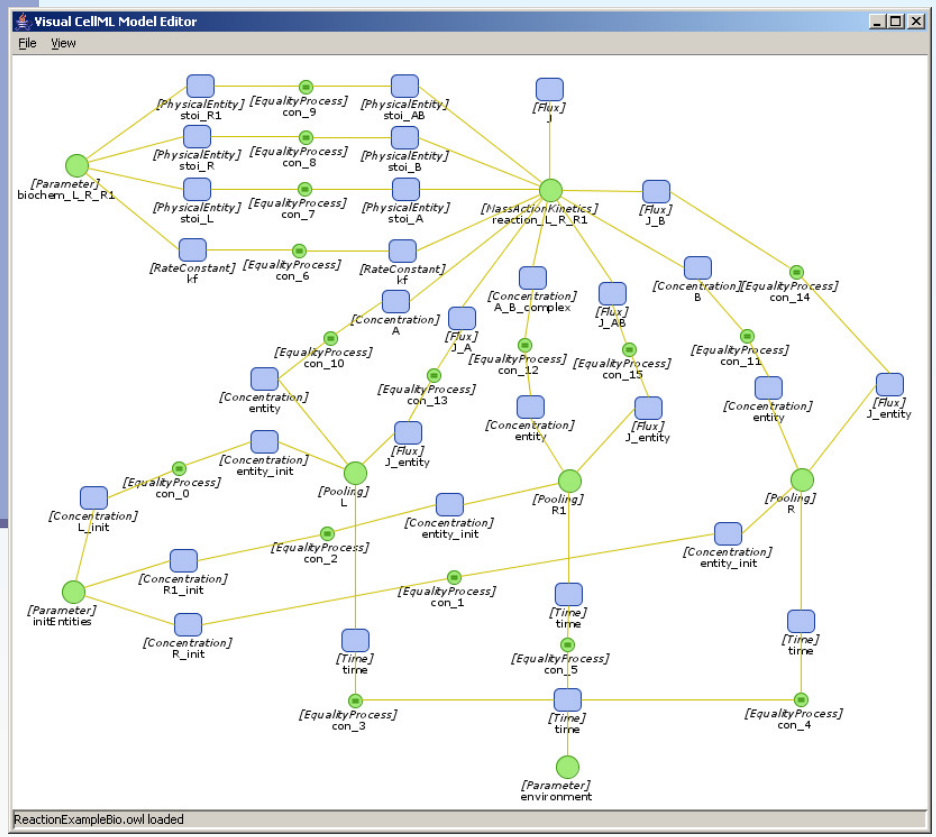
Complex formation

Complex

Visualising CellML models

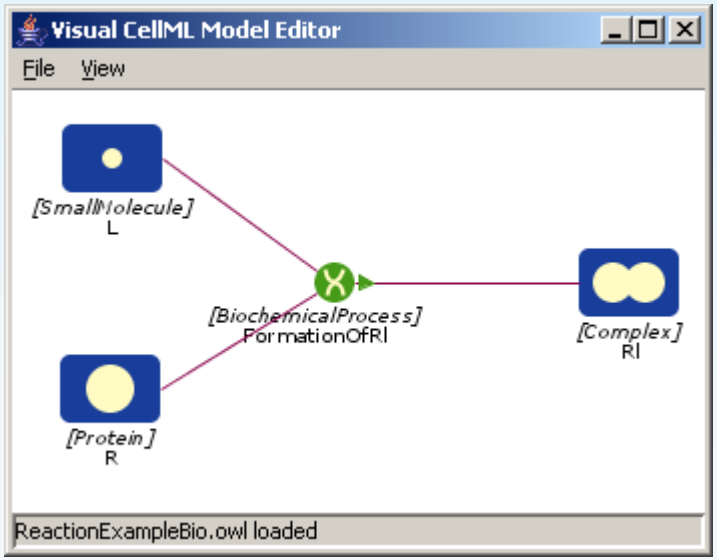
CellML structure

(Physical View)



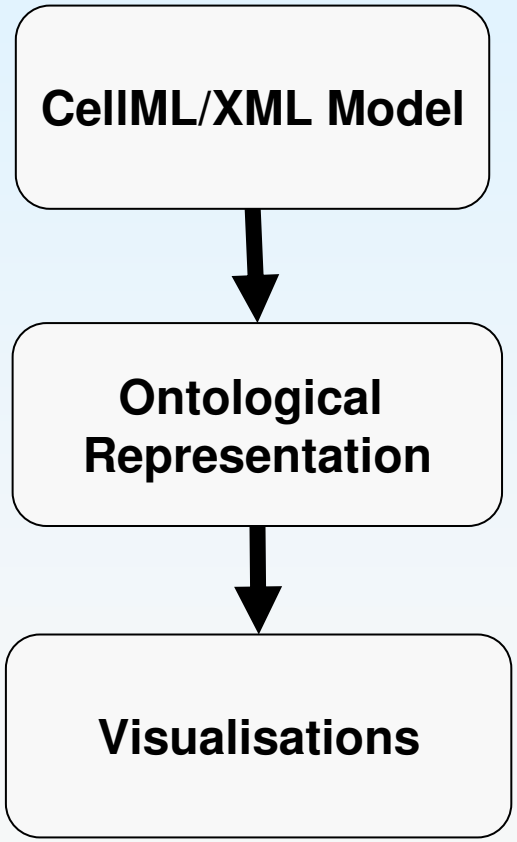
Underlying biology

(Biological View)



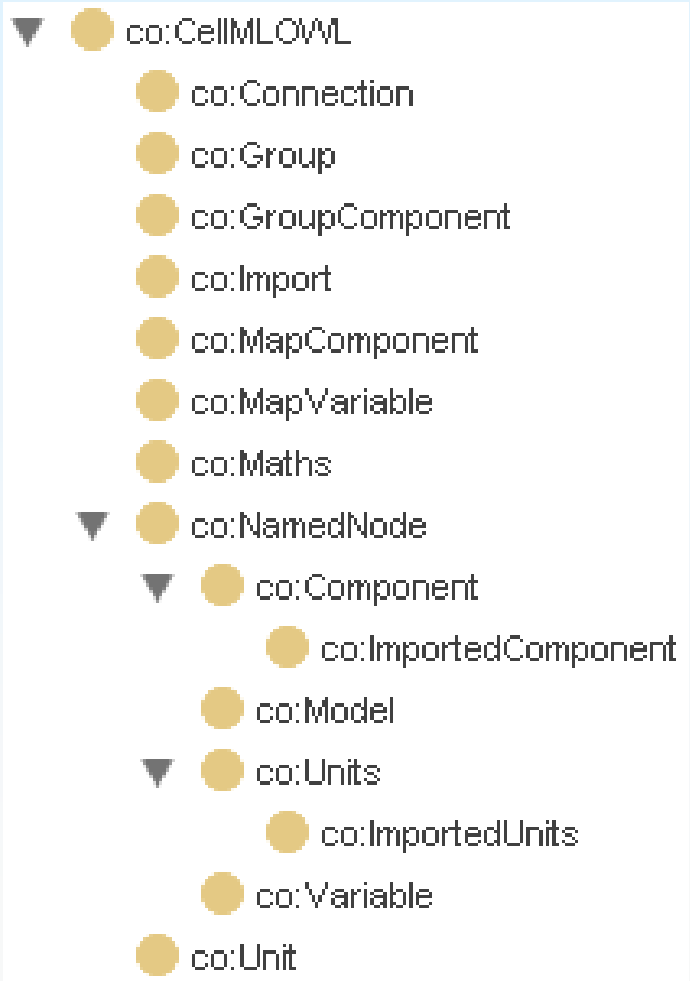
Ontology

- 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

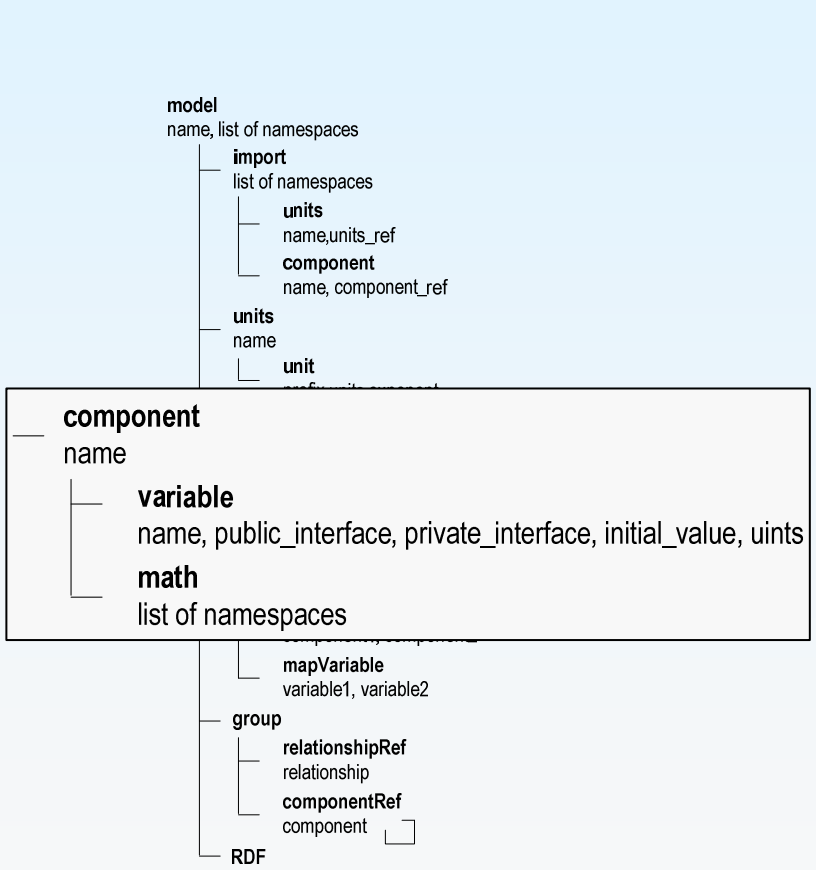


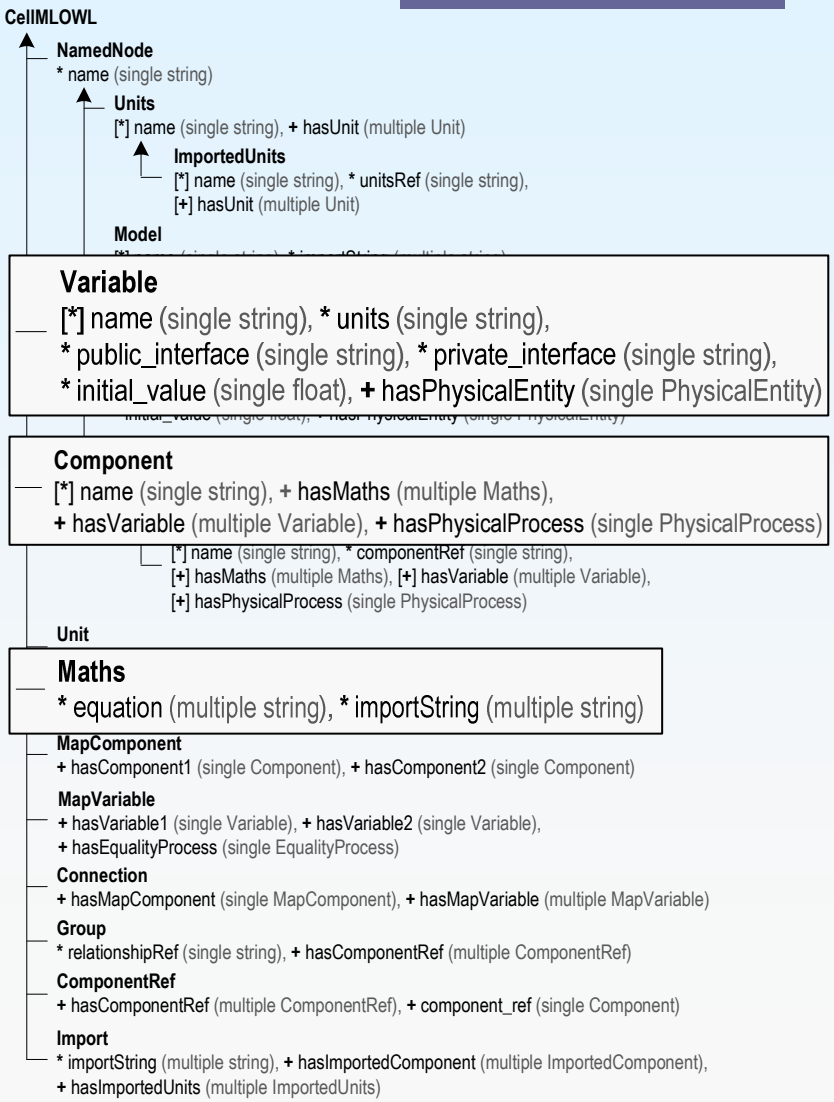
CellML/OWL ontology

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



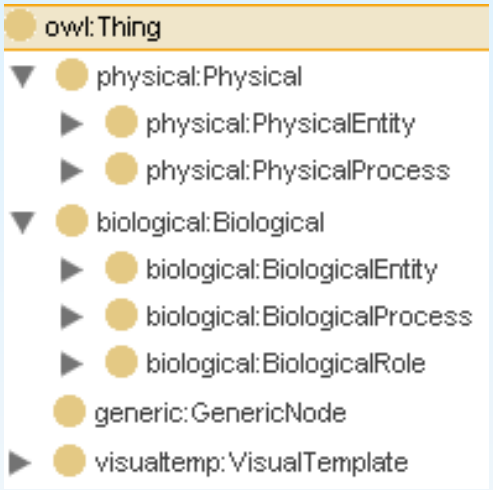
CellML/OWL ontology





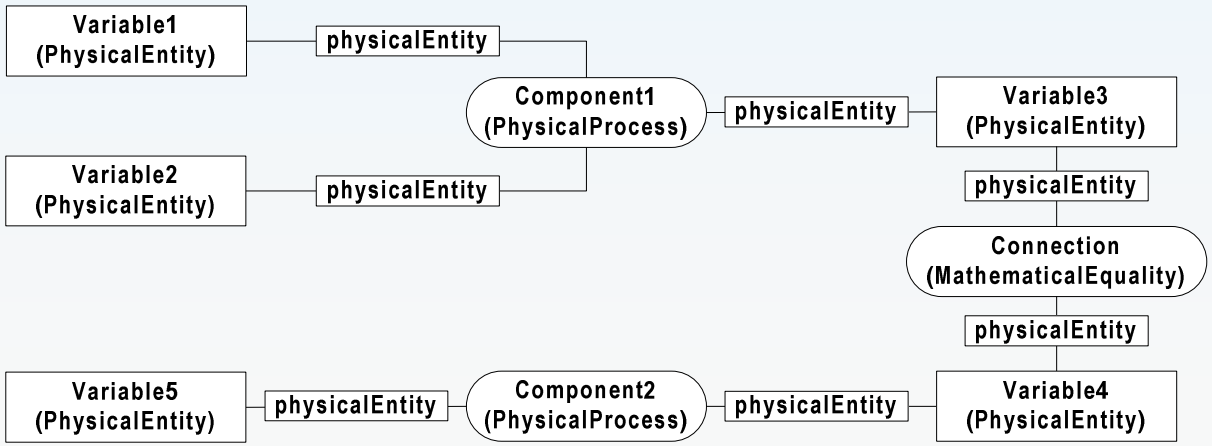
CellMLBiophysical/OWL ontology

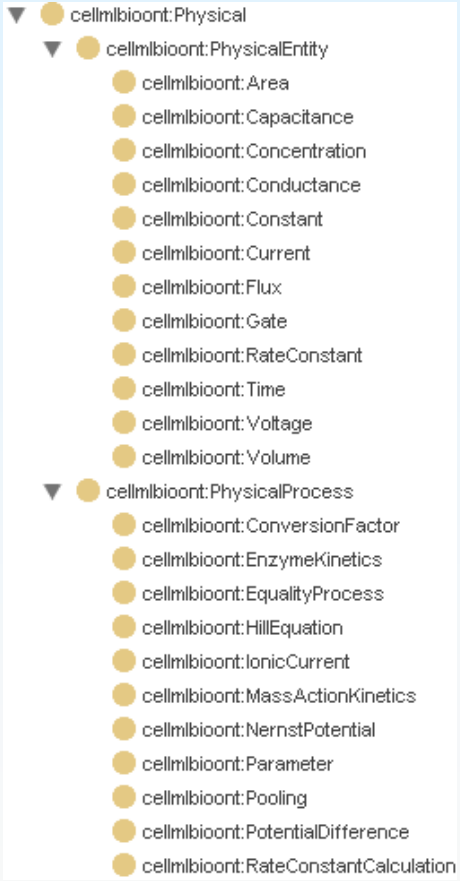
- integrates 3 ontologies
  - Physical
  - Biological
  - VisualTemplate



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

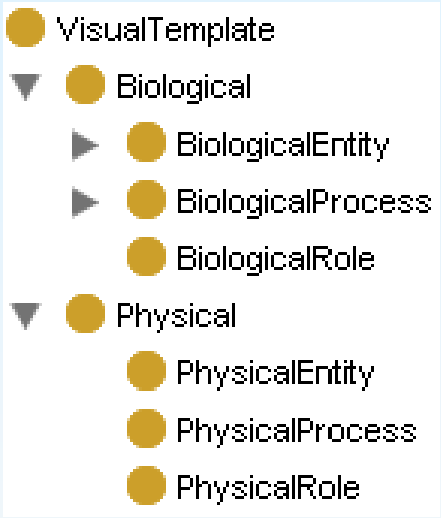
CellML/OWL	CellMLBiophysical/OWL (Physical)
Component	PhysicalProcess
Variable	PhysicalEntity
Connection	MathematicalEquality

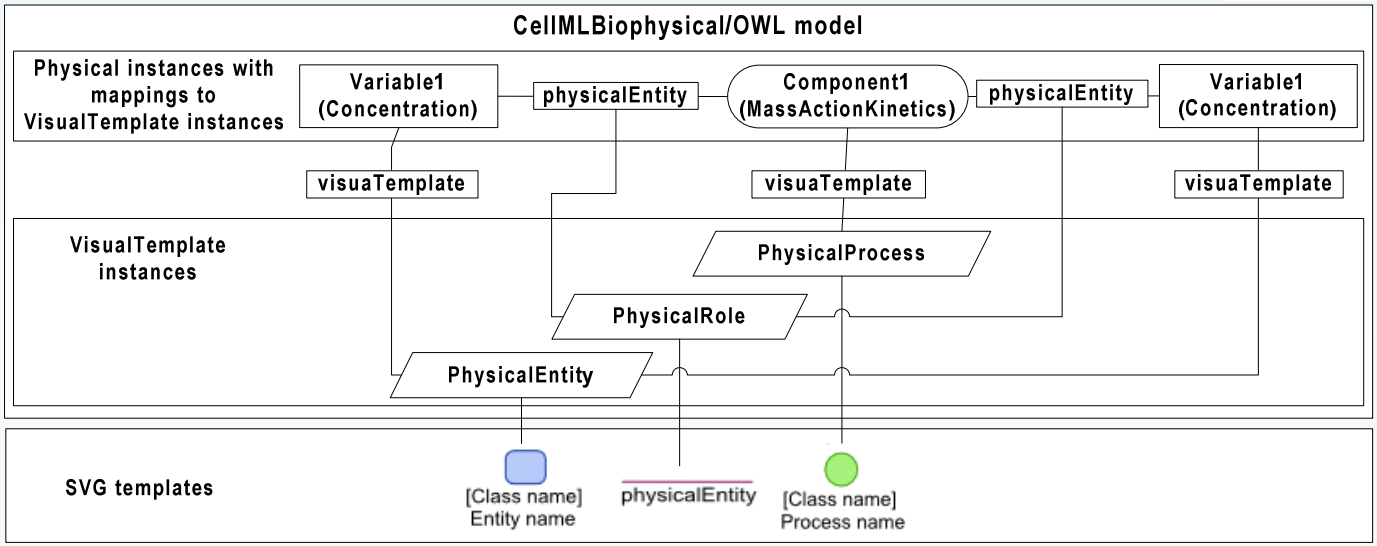




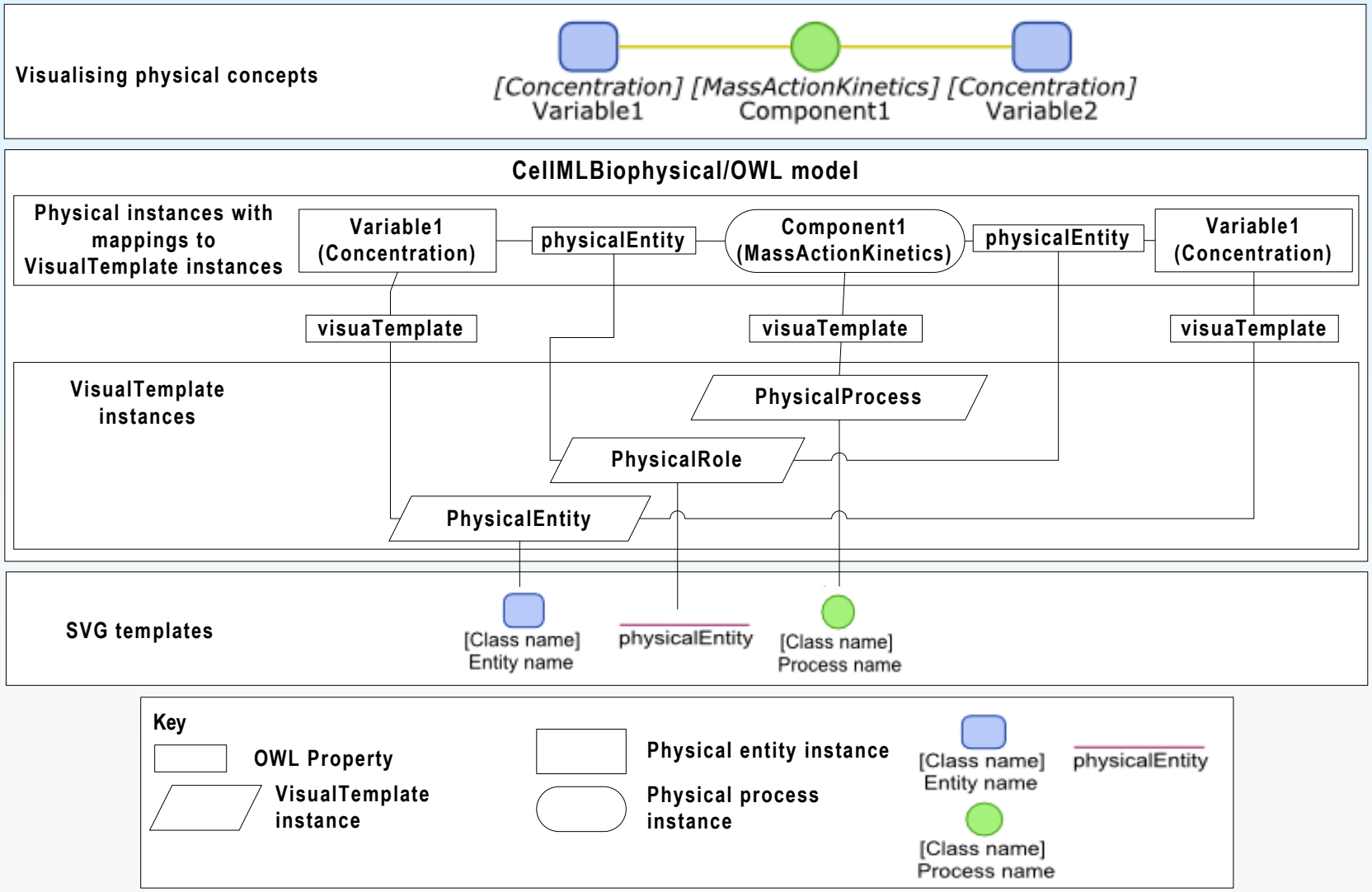
Mapping between Physical and VisualTemplate instances

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

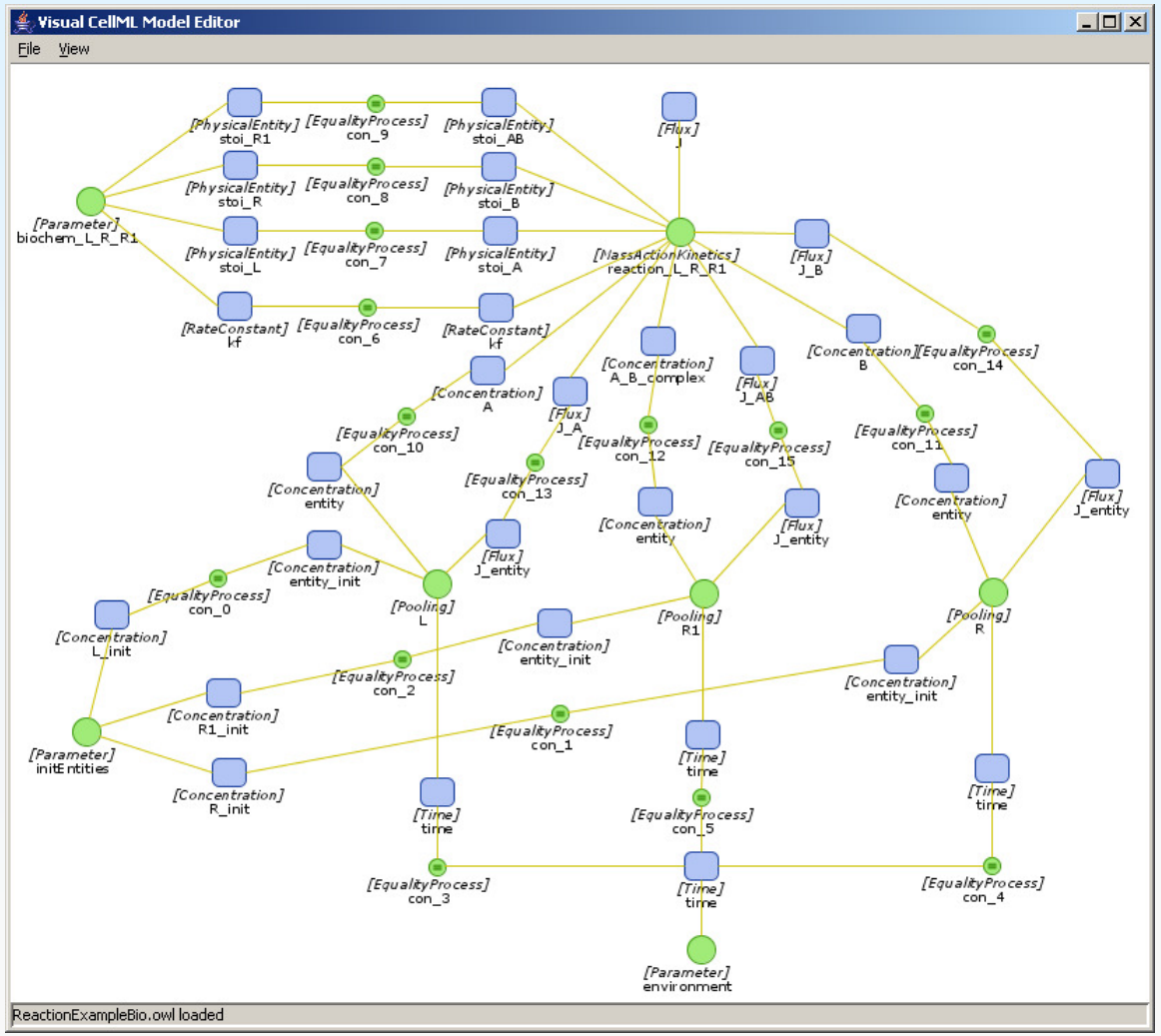




Generating a physical view

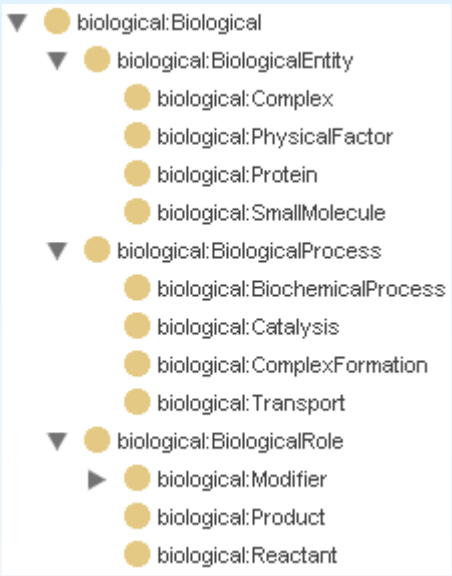


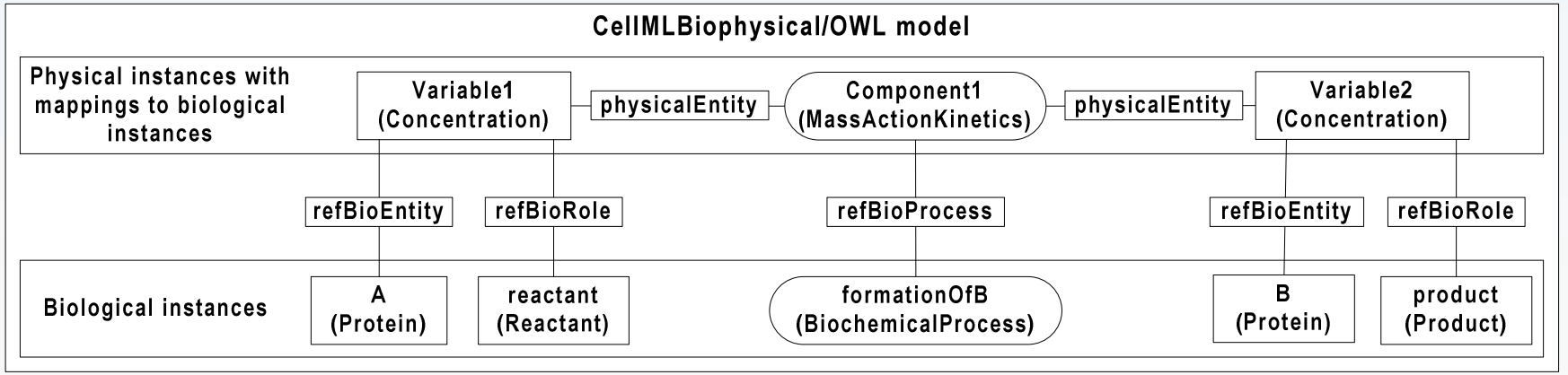
Physical view of the reaction: R+L->Rl



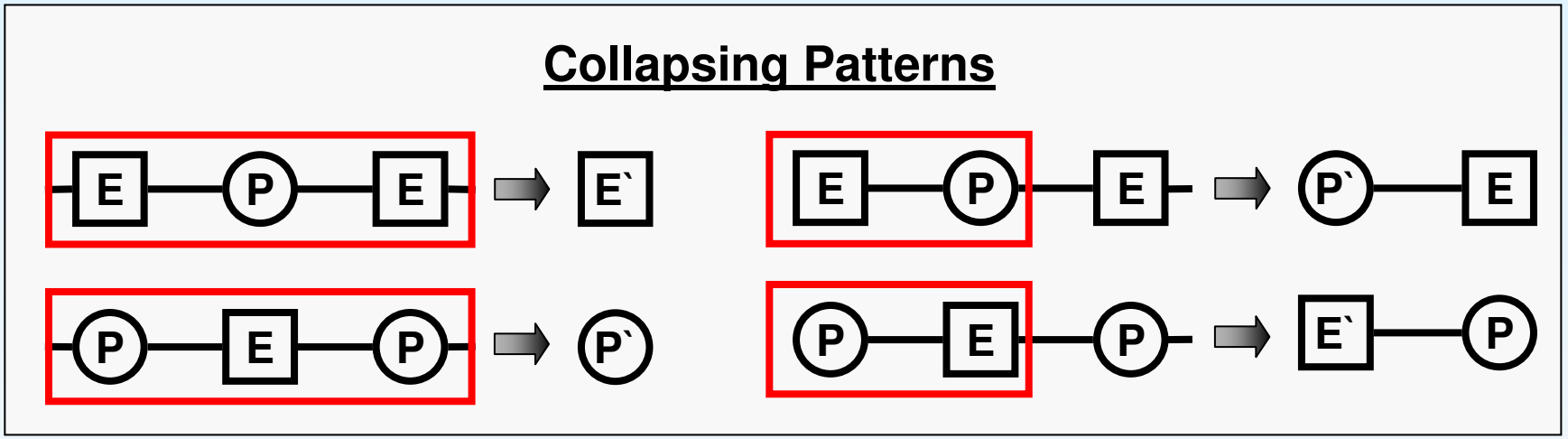
Mapping between Physical and Biological instances

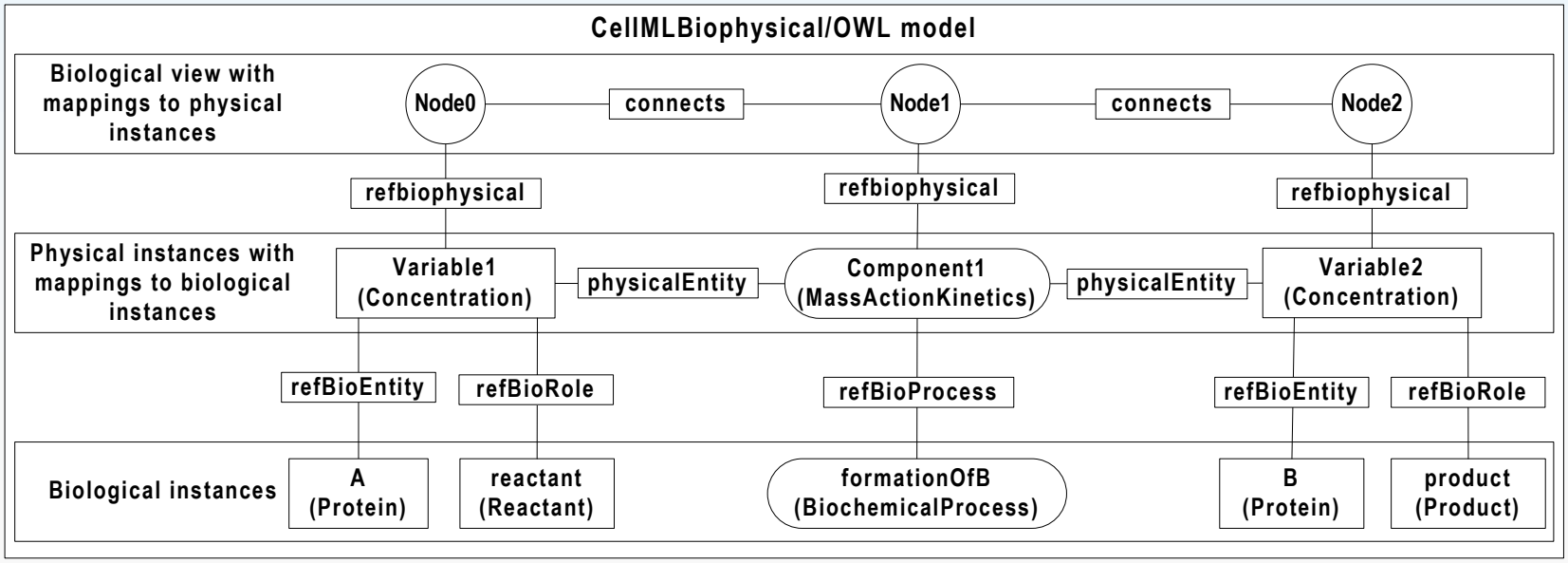
CellMLBiophysical/OWL (Physical)	CellMLBiophysical/OWL (Biological)
PhysicalProcess	BiologicalProcess
PhysicalEntity	BiologicalEntity/ BiologicalRole





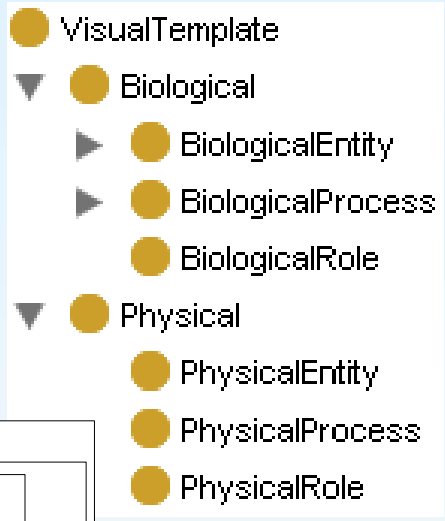
Reducing the complexity

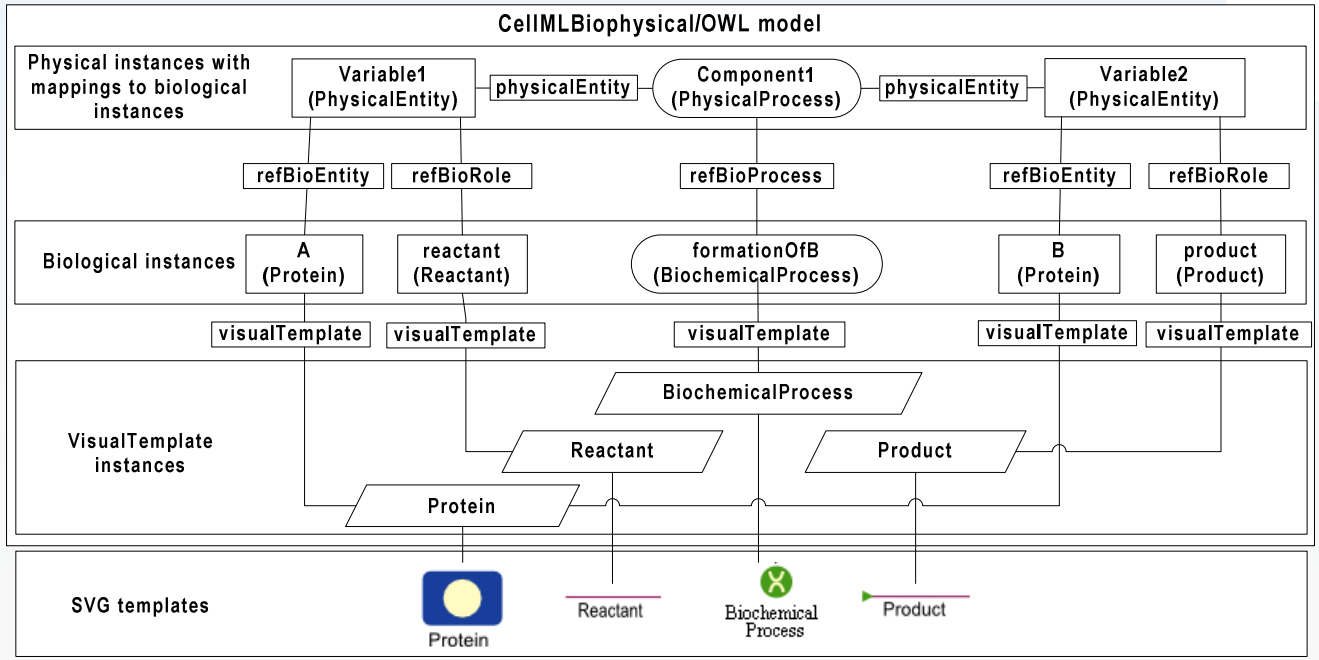




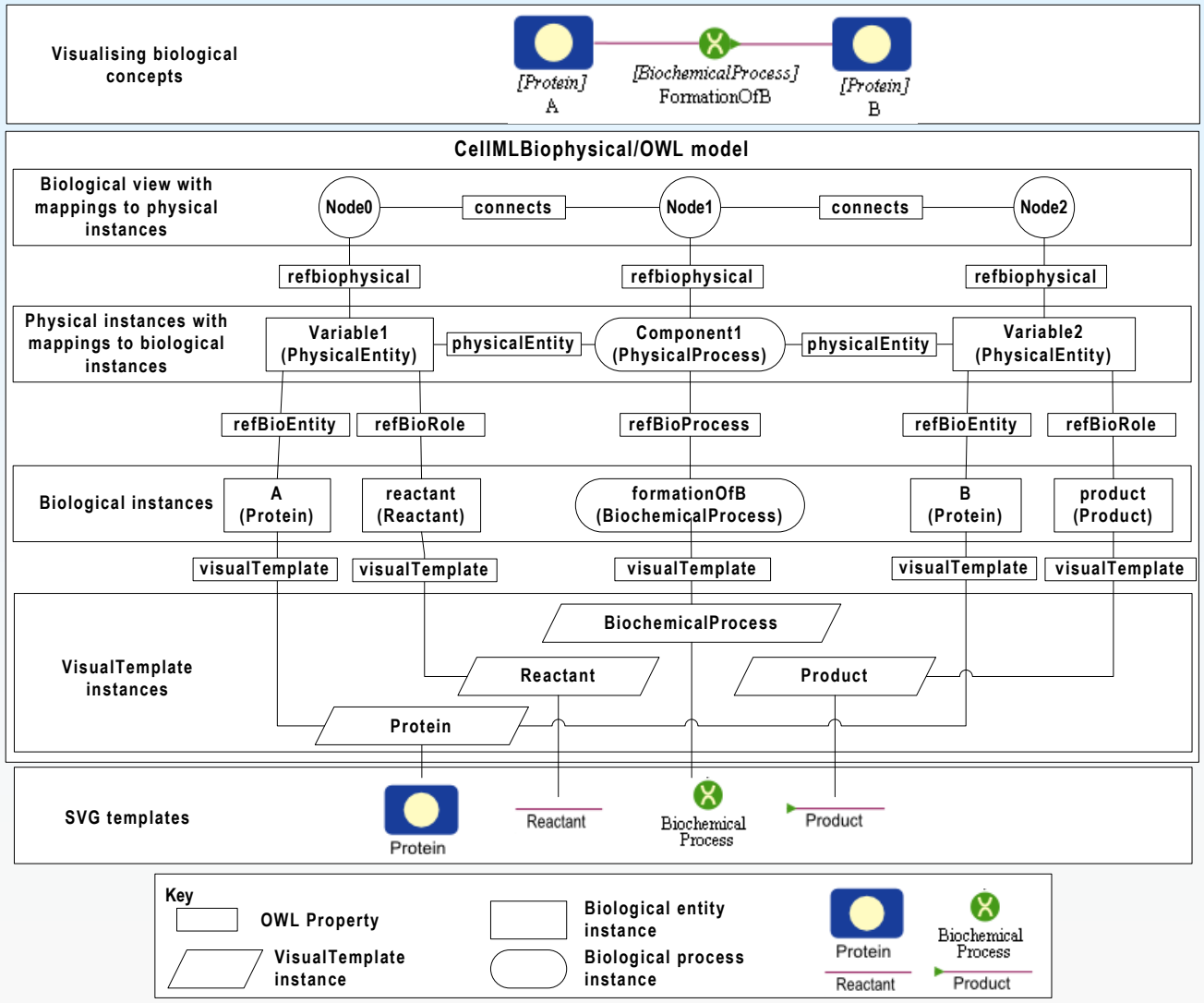
Mapping between Biological and VisualTemplate instances

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

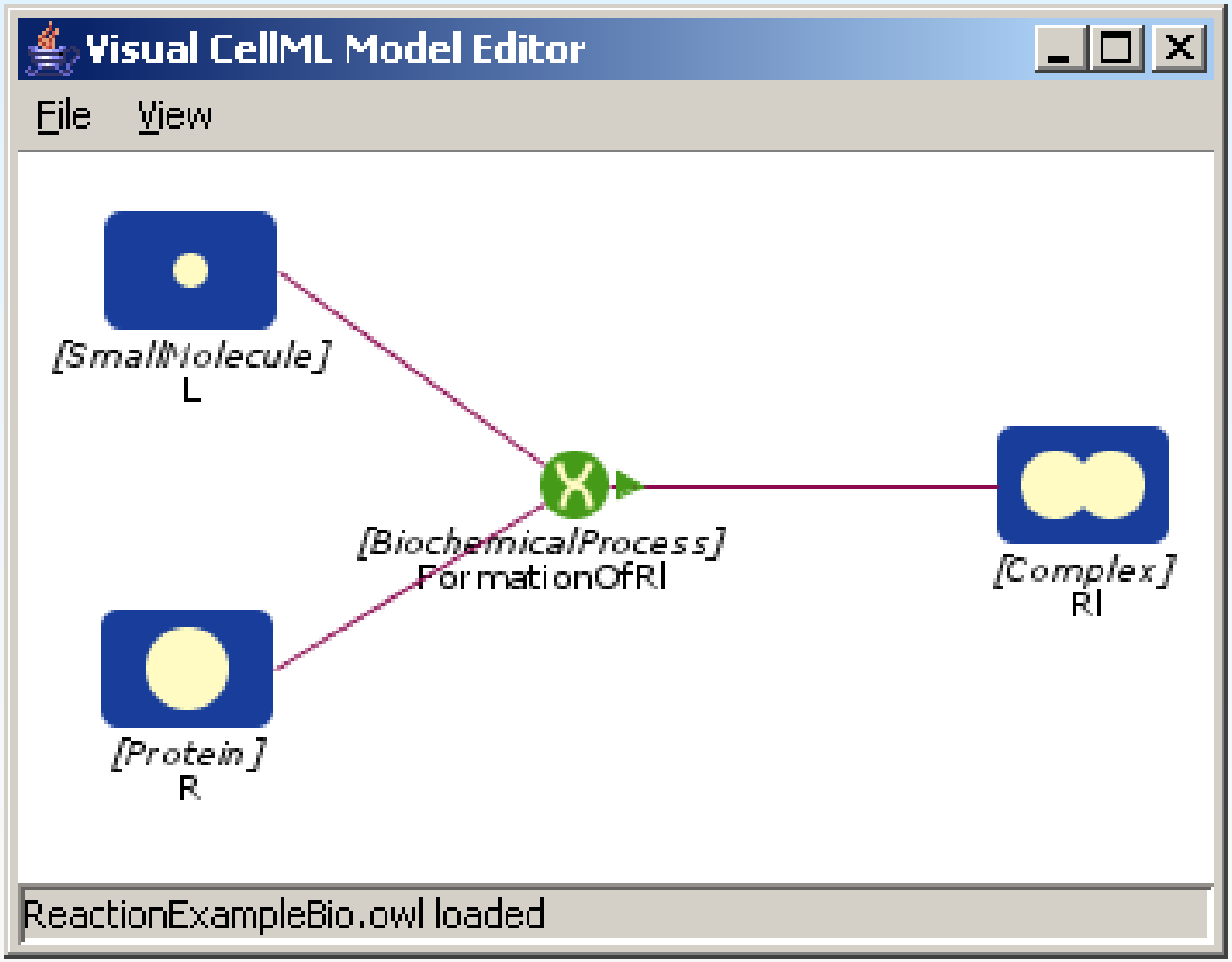




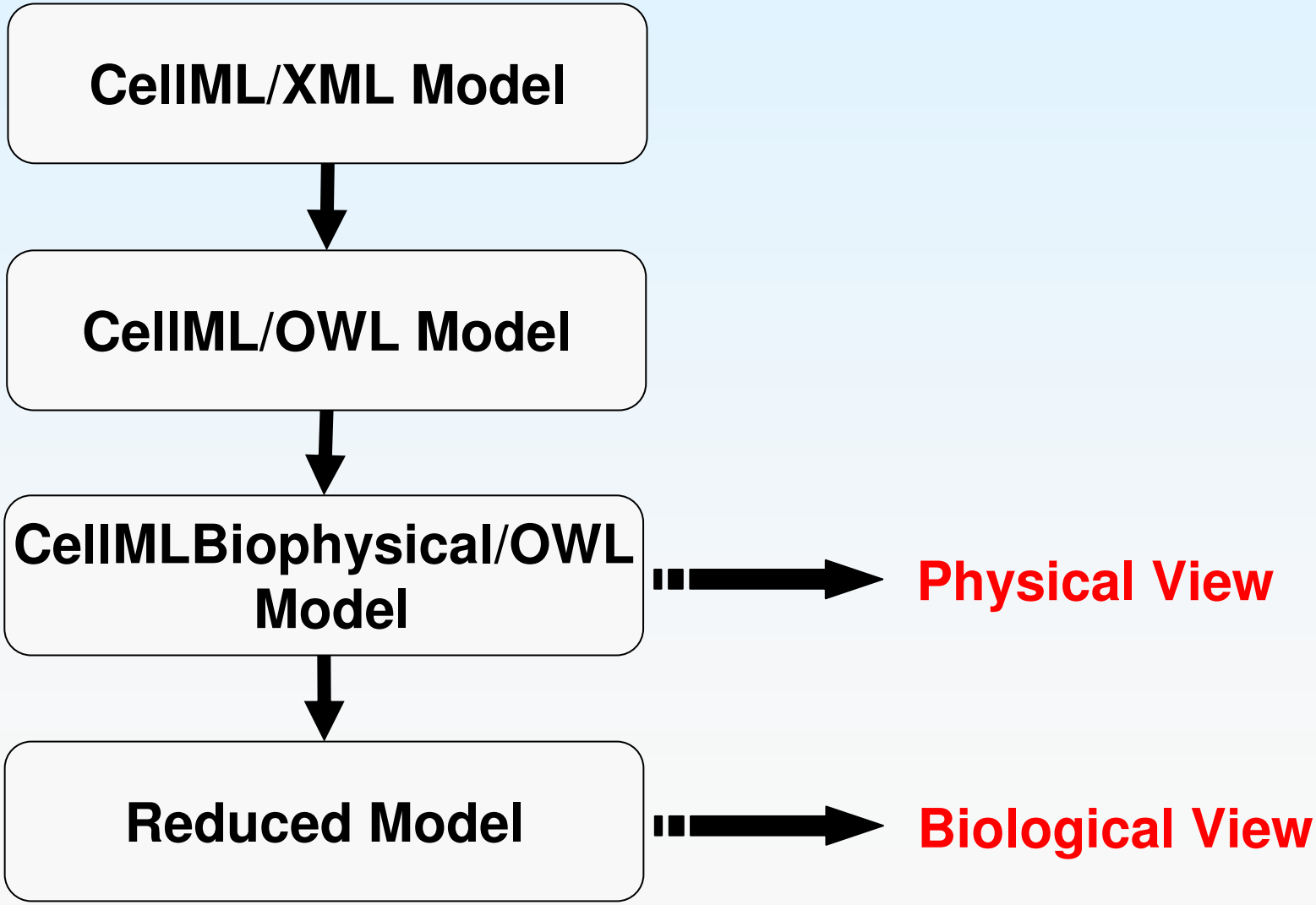
Generating a biological view



Biological view of the reaction: R+L->Rl



Summary


CellML/XML Model
CellML/OWL Model
CellMLBiophysical/OWL Model
Physical View
Reduced Model
Biological View