

```
<?xml version="1.0"?>
```

```
<!-- FILE : PFK_1999.xml
```

```
CREATED : 4th March 2002
```

```
LAST MODIFIED : 9th April 2003
```

```
AUTHOR : Catherine Lloyd  
         Department of Engineering Science  
         The University of Auckland
```

```
MODEL STATUS : This model conforms to the CellML 1.0 Specification released on  
10th August 2001, and the 16/01/2002 CellML Metadata 1.0 Specification.
```

```
DESCRIPTION : This file contains a CellML description of the 1999 Mulquiney and  
Kuchel mathematical model of PFK in erythrocytes.
```

```
CHANGES:
```

```
18/07/2002 - CML - Added more metadata.
```

```
09/04/2003 - AAC - Added publication date information.
```

```
-->
```

```
<model name="PFK_1999" cmeta:id="PFK_1999" pathway_editor:rendering_config_file="PFK_1999_ce
```

```
<rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:bgs="http://www.cel
```

```
<!--
```

```
The following RDF block contains metadata that applies to this document  
as a whole, as indicated by the empty about attribute on the  
<rdf:Description> element.
```

```
-->
```

```
<rdf:Description rdf:about="">
```

```
<!--
```

```
The Model Builder Metadata. The Dublin Core "creator" element is used  
to indicate the person who translated the model into CellML.
```

```
-->
```

```
<dc:creator rdf:parseType="Resource">
```

```
<vCard:N rdf:parseType="Resource">
```

```
<vCard:Family>Lloyd</vCard:Family>
```

```
<vCard:Given>Catherine</vCard:Given>
```

```
<vCard:Other>May</vCard:Other>
```

```
</vCard:N>
```

```
<vCard:EMAIL rdf:parseType="Resource">
```

```
<rdf:value>c.lloyd@auckland.ac.nz</rdf:value>
```

```
<rdf:type rdf:resource="http://imc.org/vCard/3.0#internet" />
```

```
</vCard:EMAIL>
```

```
<vCard:ORG rdf:parseType="Resource">
```

```
<vCard:Orgname>The University of Auckland</vCard:Orgname>
```

```
<vCard:Orgunit>The Bioengineering Institute</vCard:Orgunit>
```

```
</vCard:ORG>
```

```
</dc:creator>
```

```
<!--
```

```
The Creation Date metadata. This is the date on which the model  
was translated into CellML.
```

```
-->
```

```
<dcterms:created rdf:parseType="Resource">
```

```
<dcterms:W3CDTF>2002-03-04</dcterms:W3CDTF>
```

```
</dcterms:created>
```

```

<!--
  The Modification History metadata. This lists the changes that have been
  made to the document, who made the changes, and when they were made.
-->
<cmeta:modification rdf:parseType="Resource">
  <rdf:value>
    Added publication date information.
  </rdf:value>
  <cmeta:modifier rdf:parseType="Resource">
    <vCard:N rdf:parseType="Resource">
      <vCard:Family>Cuellar</vCard:Family>
      <vCard:Given>Autumn</vCard:Given>
      <vCard:Other>A</vCard:Other>
    </vCard:N>
  </cmeta:modifier>
  <dcterms:modified rdf:parseType="Resource">
    <dcterms:W3CDTF>2003-04-09</dcterms:W3CDTF>
  </dcterms:modified>
</cmeta:modification>
<cmeta:modification rdf:parseType="Resource">
  <rdf:value>
    Added more metadata.
  </rdf:value>
  <cmeta:modifier rdf:parseType="Resource">
    <vCard:N rdf:parseType="Resource">
      <vCard:Family>Lloyd</vCard:Family>
      <vCard:Given>Catherine</vCard:Given>
      <vCard:Other>May</vCard:Other>
    </vCard:N>
  </cmeta:modifier>
  <dcterms:modified rdf:parseType="Resource">
    <dcterms:W3CDTF>2002-07-17</dcterms:W3CDTF>
  </dcterms:modified>
</cmeta:modification>

<!-- The Publisher metadata. -->
<dc:publisher>
  The University of Auckland, Bioengineering Research Group
</dc:publisher>
</rdf:Description>

<!--
  The following metadata refers to the model itself, as indicated by the
  reference to the ID "PFK_1999", which is declared on
  the <model> element.
-->
<rdf:Description rdf:about="#PFK_1999">
  <!-- A human readable name for the model. -->
  <dc:title>
    A model of PFK in human erythrocytes.
  </dc:title>

  <!-- A comment regarding the model. -->
  <cmeta:comment rdf:parseType="Resource">
    <rdf:value>
      This is the CellML description of Mulquiney and Kuchel's mathematical
      model of PFK in human erythrocytes (1999).
    </rdf:value>

```

```

<!-- The creator of the comment. -->
<dc:creator rdf:parseType="Resource">
  <vCard:FN>Catherine Lloyd</vCard:FN>
</dc:creator>
</cmeta:comment>

<!-- The model is relevant to human erythrocytes. -->
<cmeta:species>Homo Sapiens</cmeta:species>

<!-- This model is specific to erythrocytes. -->
<cmeta:bio_entity>erythrocyte</cmeta:bio_entity>

<!-- Keyword(s) -->
<bqs:reference rdf:parseType="Resource">
  <dc:subject rdf:parseType="Resource">
    <bqs:subject_type>keyword</bqs:subject_type>
    <rdf:value>metabolism</rdf:value>
  </dc:subject>
</bqs:reference>

<!--
The CellML Metadata Specification recommends that bibliographic metadata
is used to provide information about the original model reference. The
"identifier" attribute on the "BibliographicReference" class provides an
elegant way to identify a cited reference using a database identifier
date, etc can be looked up on the database.
-->
<bqs:reference rdf:parseType="Resource">
  <bqs:Pubmed_id>10477269</bqs:Pubmed_id>
  <bqs:JournalArticle rdf:parseType="Resource">
    <dc:creator>
      <rdf:Seq>
        <rdf:li rdf:parseType="Resource">
          <bqs:Person rdf:parseType="Resource">
            <vCard:N rdf:parseType="Resource">
              <vCard:Family>Mulquiney</vCard:Family>
              <vCard:Given>Peter</vCard:Given>
              <vCard:Other>J</vCard:Other>
            </vCard:N>
          </bqs:Person>
        </rdf:li>
        <rdf:li rdf:parseType="Resource">
          <bqs:Person rdf:parseType="Resource">
            <vCard:N rdf:parseType="Resource">
              <vCard:Family>Kuchel</vCard:Family>
              <vCard:Given>Philip</vCard:Given>
              <vCard:Other>W</vCard:Other>
            </vCard:N>
          </bqs:Person>
        </rdf:li>
      </rdf:Seq>
    </dc:creator>
    <dc:title>
      Model of 2,3-bisphosphoglycerate metabolism in the human erythrocyte
      refinement
    </dc:title>
    <dcterms:issued rdf:parseType="Resource">
      <dcterms:W3CDTF>1999-09-15</dcterms:W3CDTF>
    </dcterms:issued>
  </bqs:JournalArticle>
</bqs:reference>

```

such

```

    <bqs:Journal rdf:parseType="Resource">
      <dc:title>Biochemical Journal</dc:title>
    </bqs:Journal>
    <bqs:volume>342</bqs:volume>
    <bqs:first_page>581</bqs:first_page>
    <bqs:last_page>596</bqs:last_page>
  </bqs:JournalArticle>
</bqs:reference>
</rdf:Description>
</rdf:RDF>

<!--
  We start the model definition with a definition of some named
  sets of units for use throughout the model.
-->

<units name="molar">
  <unit units="mole" />
  <unit units="litre" exponent="-1" />
</units>

<units name="millimolar">
  <unit prefix="milli" units="molar" />
</units>

<units name="flux">
  <unit prefix="milli" units="mole" />
  <unit units="second" exponent="-1" />
</units>

<units name="first_order_rate_constant">
  <unit units="second" exponent="-1" />
</units>

<units name="second_order_rate_constant">
  <unit units="molar" exponent="-1" />
  <unit units="second" exponent="-1" />
</units>

<!--
  The following component is defined for modelling convenience. It contains
  all the universal variables, in this case, only time.
-->
<component name="global_variables">
  <variable name="time" public_interface="out" units="second" />
</component>

<!--
  The following components describe all the substrates, enzymes,
  enzyme-substrate complexes and products in PFK.
-->

<component name="E" cmeta:id="E">
  <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:dc="http://purl.
    <rdf:Description rdf:about="E">
      <dc:title>E</dc:title>
      <dcterms:alternative>free PFK</dcterms:alternative>
    </rdf:Description>
  </rdf:RDF>

```

```

<variable name="E" public_interface="out" units="millimolar" />
<variable name="delta_E_rxn5" public_interface="in" units="flux" />
<variable name="delta_E_rxn0" public_interface="in" units="flux" />
<variable name="delta_E_rxn1" public_interface="in" units="flux" />
<variable name="delta_E_rxn4" public_interface="in" units="flux" />
<variable name="time" public_interface="in" units="second" />
<math xmlns="http://www.w3.org/1998/Math/MathML">
  <apply>
    <eq />
    <apply>
      <diff />
      <bvar>
        <ci>time</ci>
      </bvar>
      <ci>E</ci>
    </apply>
    <apply>
      <plus />
      <ci>delta_E_rxn5</ci>
      <ci>delta_E_rxn0</ci>
      <ci>delta_E_rxn1</ci>
      <ci>delta_E_rxn4</ci>
    </apply>
  </apply>
</math>
</component>

```

```

<component name="A" cmeta:id="A">
  <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:dc="http://purl.org/dc/terms/">
    <rdf:Description rdf:about="A">
      <dc:title>A</dc:title>
      <dcterms:alternative>MgATP</dcterms:alternative>
    </rdf:Description>
  </rdf:RDF>
  <variable name="A" public_interface="out" units="millimolar" />
  <variable name="delta_A_rxn0" public_interface="in" units="flux" />
  <variable name="delta_A_rxn3" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq />
      <apply>
        <diff />
        <bvar>
          <ci>time</ci>
        </bvar>
        <ci>A</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_A_rxn0</ci>
        <ci>delta_A_rxn3</ci>
      </apply>
    </apply>
  </math>
</component>

```

```

<component name="EA">
  <variable name="EA" public_interface="out" units="millimolar" />

```

```

<variable name="delta_EA_rxn0" public_interface="in" units="flux" />
<variable name="delta_EA_rxn2" public_interface="in" units="flux" />
<variable name="time" public_interface="in" units="second" />
<math xmlns="http://www.w3.org/1998/Math/MathML">
  <apply>
    <eq />
    <apply>
      <diff />
      <bvar>
        <ci>time</ci>
      </bvar>
      <ci>EA</ci>
    </apply>
    <apply>
      <plus />
      <ci>delta_EA_rxn0</ci>
      <ci>delta_EA_rxn2</ci>
    </apply>
  </apply>
</math>
</component>

```

```

<component name="B" cmeta:id="B">
  <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:dc="http://purl.org/dc/terms/">
    <rdf:Description rdf:about="B">
      <dc:title>B</dc:title>
      <dcterms:alternative>Fru6P</dcterms:alternative>
    </rdf:Description>
  </rdf:RDF>
  <variable name="B" public_interface="out" units="millimolar" />
  <variable name="delta_B_rxn1" public_interface="in" units="flux" />
  <variable name="delta_B_rxn2" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq />
      <apply>
        <diff />
        <bvar>
          <ci>time</ci>
        </bvar>
        <ci>B</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_B_rxn1</ci>
        <ci>delta_B_rxn2</ci>
      </apply>
    </apply>
  </math>
</component>

```

```

<component name="EB">
  <variable name="EB" public_interface="out" units="millimolar" />
  <variable name="delta_EB_rxn1" public_interface="in" units="flux" />
  <variable name="delta_EB_rxn3" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>

```

```

    <eq />
    <apply>
      <diff />
      <bvar>
        <ci>time</ci>
      </bvar>
      <ci>EB</ci>
    </apply>
    <apply>
      <plus />
      <ci>delta_EB_rxn1</ci>
      <ci>delta_EB_rxn3</ci>
    </apply>
  </math>
</component>

```

```

<component name="EAB">
  <variable name="EAB" public_interface="out" units="millimolar" />
  <variable name="delta_EAB_rxn2" public_interface="in" units="flux" />
  <variable name="delta_EAB_rxn3" public_interface="in" units="flux" />
  <variable name="delta_EAB_rxn7" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq />
      <apply>
        <diff />
        <bvar>
          <ci>time</ci>
        </bvar>
        <ci>EAB</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_EAB_rxn2</ci>
        <ci>delta_EAB_rxn3</ci>
        <ci>delta_EAB_rxn7</ci>
      </apply>
    </math>
  </component>

```

```

<component name="Q" cmeta:id="Q">
  <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:dc="http://purl.org/dc/terms/">
    <rdf:Description rdf:about="Q">
      <dc:title>Q</dc:title>
      <dcterms:alternative>MgADP</dcterms:alternative>
    </rdf:Description>
  </rdf:RDF>
  <variable name="Q" public_interface="out" units="millimolar" />
  <variable name="delta_Q_rxn4" public_interface="in" units="flux" />
  <variable name="delta_Q_rxn6" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq />
      <apply>
        <diff />

```

```

        <bvar>
          <ci>time</ci>
        </bvar>
        <ci>Q</ci>
      </apply>
    <apply>
      <plus />
      <ci>delta_Q_rxn4</ci>
      <ci>delta_Q_rxn6</ci>
    </apply>
  </apply>
</math>
</component>

```

```

<component name="EQ">
  <variable name="EQ" public_interface="out" units="millimolar" />
  <variable name="delta_EQ_rxn4" public_interface="in" units="flux" />
  <variable name="delta_EQ_rxn8" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq />
      <apply>
        <diff />
        <bvar>
          <ci>time</ci>
        </bvar>
        <ci>EQ</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_EQ_rxn4</ci>
        <ci>delta_EQ_rxn8</ci>
      </apply>
    </apply>
  </math>
</component>

```

```

<component name="P" cmeta:id="P">
  <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:dc="http://purl.org/dc/terms/">
    <rdf:Description rdf:about="P">
      <dc:title>P</dc:title>
      <dcterms:alternative>Fru(1,6)P2</dcterms:alternative>
    </rdf:Description>
  </rdf:RDF>
  <variable name="P" public_interface="out" units="millimolar" />
  <variable name="delta_P_rxn5" public_interface="in" units="flux" />
  <variable name="delta_P_rxn8" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq />
      <apply>
        <diff />
        <bvar>
          <ci>time</ci>
        </bvar>
        <ci>P</ci>
      </apply>
    </math>
  </component>

```

```

    <apply>
      <plus />
      <ci>delta_P_rxn5</ci>
      <ci>delta_P_rxn8</ci>
    </apply>
  </apply>
</math>
</component>

<component name="EP">
  <variable name="EP" public_interface="out" units="millimolar" />
  <variable name="delta_EP_rxn6" public_interface="in" units="flux" />
  <variable name="delta_EP_rxn5" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq />
      <apply>
        <diff />
        <bvar>
          <ci>time</ci>
        </bvar>
        <ci>EP</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_EP_rxn6</ci>
        <ci>delta_EP_rxn5</ci>
      </apply>
    </apply>
  </math>
</component>

<component name="EPQ">
  <variable name="EPQ" public_interface="out" units="millimolar" />
  <variable name="delta_EPQ_rxn7" public_interface="in" units="flux" />
  <variable name="delta_EPQ_rxn6" public_interface="in" units="flux" />
  <variable name="delta_EPQ_rxn8" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>
      <eq />
      <apply>
        <diff />
        <bvar>
          <ci>time</ci>
        </bvar>
        <ci>EPQ</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_EPQ_rxn7</ci>
        <ci>delta_EPQ_rxn6</ci>
        <ci>delta_EPQ_rxn8</ci>
      </apply>
    </apply>
  </math>
</component>

```

```
<!--
```

```
The following components represent the individual reaction steps.
```

```
-->
```

```
<component name="reaction0">
  <variable name="A" public_interface="in" units="millimolar" />
  <variable name="E" public_interface="in" units="millimolar" />
  <variable name="EA" public_interface="in" units="millimolar" />
  <variable name="delta_A_rxn0" public_interface="out" units="flux" />
  <variable name="delta_E_rxn0" public_interface="out" units="flux" />
  <variable name="delta_EA_rxn0" public_interface="out" units="flux" />
  <variable name="k0" initial_value="82200.0" units="second_order_rate_constant" />
  <variable name="k0_" initial_value="5.5896" units="first_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="yes">
    <variable_ref variable="A">
      <role role="reactant" direction="forward" delta_variable="delta_A_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="E">
      <role role="reactant" direction="forward" delta_variable="delta_E_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="EA">
      <role role="product" direction="forward" delta_variable="delta_EA_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <plus />
              <apply>
                <times />
                <ci>k0</ci>
                <ci>A</ci>
                <ci>E</ci>
              </apply>
              <apply>
                <minus />
                <apply>
                  <times />
                  <ci>k0_</ci>
                  <ci>EA</ci>
                </apply>
              </apply>
            </apply>
          </math>
        </role>
      </variable_ref>
    </reaction>
  </component>

  <component name="reaction1">
    <variable name="E" public_interface="in" units="millimolar" />
    <variable name="B" public_interface="in" units="millimolar" />
    <variable name="EB" public_interface="in" units="millimolar" />
    <variable name="delta_E_rxn1" public_interface="out" units="flux" />
```

```

<variable name="delta_B_rxn1" public_interface="out" units="flux" />
<variable name="delta_EB_rxn1" public_interface="out" units="flux" />
<variable name="k1" initial_value="82200.0" units="second_order_rate_constant" />
<variable name="k1_" initial_value="6.165" units="first_order_rate_constant" />
<variable name="rate" units="flux" />
<reaction reversible="yes">
  <variable_ref variable="E">
    <role role="reactant" direction="forward" delta_variable="delta_E_rxn1" stoichiometric_coefficient="1" />
  </variable_ref>
  <variable_ref variable="B">
    <role role="reactant" direction="forward" delta_variable="delta_B_rxn1" stoichiometric_coefficient="1" />
  </variable_ref>
  <variable_ref variable="EB">
    <role role="product" direction="forward" delta_variable="delta_EB_rxn1" stoichiometric_coefficient="1" />
  </variable_ref>
  <variable_ref variable="rate">
    <role role="rate">
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <apply>
          <eq />
          <ci>rate</ci>
          <apply>
            <plus />
            <apply>
              <times />
              <ci>k1</ci>
              <ci>E</ci>
              <ci>B</ci>
            </apply>
            <apply>
              <minus />
              <apply>
                <times />
                <ci>k1_</ci>
                <ci>EB</ci>
              </apply>
            </apply>
          </apply>
        </math>
      </role>
    </variable_ref>
  </reaction>
</component>

<component name="reaction2">
  <variable name="EA" public_interface="in" units="millimolar" />
  <variable name="B" public_interface="in" units="millimolar" />
  <variable name="EAB" public_interface="in" units="millimolar" />
  <variable name="delta_EA_rxn2" public_interface="out" units="flux" />
  <variable name="delta_B_rxn2" public_interface="out" units="flux" />
  <variable name="delta_EAB_rxn2" public_interface="out" units="flux" />
  <variable name="k2" initial_value="82200.0" units="second_order_rate_constant" />
  <variable name="k2_" initial_value="6.165" units="first_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="yes">
    <variable_ref variable="EA">
      <role role="reactant" direction="forward" delta_variable="delta_EA_rxn2" stoichiometric_coefficient="1" />
    </variable_ref>
  </reaction>
</component>

```

```

<variable_ref variable="B">
  <role role="reactant" direction="forward" delta_variable="delta_B_rxn2" stoichiometric_coefficient="1" />
</variable_ref>
<variable_ref variable="EAB">
  <role role="product" direction="forward" delta_variable="delta_EAB_rxn2" stoichiometric_coefficient="1" />
</variable_ref>
<variable_ref variable="rate">
  <role role="rate">
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <eq />
        <ci>rate</ci>
        <apply>
          <plus />
          <apply>
            <times />
            <ci>k2</ci>
            <ci>EA</ci>
            <ci>B</ci>
          </apply>
          <apply>
            <minus />
            <apply>
              <times />
              <ci>k2_</ci>
              <ci>EAB</ci>
            </apply>
          </apply>
        </apply>
      </math>
    </role>
  </variable_ref>
</reaction>
</component>

<component name="reaction3">
  <variable name="A" public_interface="in" units="millimolar" />
  <variable name="EB" public_interface="in" units="millimolar" />
  <variable name="EAB" public_interface="in" units="millimolar" />
  <variable name="delta_A_rxn3" public_interface="out" units="flux" />
  <variable name="delta_EB_rxn3" public_interface="out" units="flux" />
  <variable name="delta_EAB_rxn3" public_interface="out" units="flux" />
  <variable name="k3" initial_value="82200.0" units="second_order_rate_constant" />
  <variable name="k3_" initial_value="5.5896" units="first_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="yes">
    <variable_ref variable="A">
      <role role="reactant" direction="forward" delta_variable="delta_A_rxn3" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="EB">
      <role role="reactant" direction="forward" delta_variable="delta_EB_rxn3" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="EAB">
      <role role="product" direction="forward" delta_variable="delta_EAB_rxn3" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">

```

```

    <apply>
      <eq />
      <ci>rate</ci>
      <apply>
        <plus />
        <apply>
          <times />
          <ci>k3</ci>
          <ci>A</ci>
          <ci>EB</ci>
        </apply>
        <apply>
          <minus />
          <apply>
            <times />
            <ci>k3_</ci>
            <ci>EAB</ci>
          </apply>
        </apply>
      </apply>
    </math>
  </role>
</variable_ref>
</reaction>
</component>

<component name="reaction4">
  <variable name="E" public_interface="in" units="millimolar" />
  <variable name="Q" public_interface="in" units="millimolar" />
  <variable name="EQ" public_interface="in" units="millimolar" />
  <variable name="delta_E_rxn4" public_interface="out" units="flux" />
  <variable name="delta_Q_rxn4" public_interface="out" units="flux" />
  <variable name="delta_EQ_rxn4" public_interface="out" units="flux" />
  <variable name="k4" initial_value="3600.0" units="first_order_rate_constant" />
  <variable name="k4_" initial_value="6.67" units="second_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="yes">
    <variable_ref variable="E">
      <role role="reactant" direction="forward" delta_variable="delta_E_rxn4" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="Q">
      <role role="product" direction="forward" delta_variable="delta_Q_rxn4" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="EQ">
      <role role="product" direction="forward" delta_variable="delta_EQ_rxn4" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <plus />
              <apply>
                <times />
                <ci>k4</ci>
                <ci>E</ci>
              </apply>
            </apply>
          </math>
        </role>
      </variable_ref>
    </reaction>
  </component>

```

```

        </apply>
        <apply>
            <minus />
            <apply>
                <times />
                <ci>k4</ci>
                <ci>Q</ci>
                <ci>EQ</ci>
            </apply>
        </apply>
    </apply>
</math>
</role>
</variable_ref>
</reaction>
</component>

<component name="reaction5">
    <variable name="EP" public_interface="in" units="millimolar" />
    <variable name="E" public_interface="in" units="millimolar" />
    <variable name="P" public_interface="in" units="millimolar" />
    <variable name="delta_EP_rxn5" public_interface="out" units="flux" />
    <variable name="delta_E_rxn5" public_interface="out" units="flux" />
    <variable name="delta_P_rxn5" public_interface="out" units="flux" />
    <variable name="k5" initial_value="3600.0" units="first_order_rate_constant" />
    <variable name="k5_" initial_value="7.2" units="second_order_rate_constant" />
    <variable name="rate" units="flux" />
    <reaction reversible="yes">
        <variable_ref variable="EP">
            <role role="reactant" direction="forward" delta_variable="delta_EP_rxn5" stoichiome
        </variable_ref>
        <variable_ref variable="E">
            <role role="product" direction="forward" delta_variable="delta_E_rxn5" stoichiome
        </variable_ref>
        <variable_ref variable="P">
            <role role="product" direction="forward" delta_variable="delta_P_rxn5" stoichiome
        </variable_ref>
        <variable_ref variable="rate">
            <role role="rate">
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                    <apply>
                        <eq />
                        <ci>rate</ci>
                        <apply>
                            <plus />
                            <apply>
                                <times />
                                <ci>k5</ci>
                                <ci>EP</ci>
                            </apply>
                            <apply>
                                <minus />
                                <apply>
                                    <times />
                                    <ci>k5_</ci>
                                    <ci>E</ci>
                                    <ci>P</ci>
                                </apply>
                            </apply>
                        </apply>
                    </math>
                </role>
            </variable_ref>
        </reaction>
    </component>

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```

        </apply>
      </apply>
    </apply>
  </math>
</role>
</variable_ref>
</reaction>
</component>

<component name="reaction6">
  <variable name="EPQ" public_interface="in" units="millimolar" />
  <variable name="Q" public_interface="in" units="millimolar" />
  <variable name="EP" public_interface="in" units="millimolar" />
  <variable name="delta_EPQ_rxn6" public_interface="out" units="flux" />
  <variable name="delta_Q_rxn6" public_interface="out" units="flux" />
  <variable name="delta_EP_rxn6" public_interface="out" units="flux" />
  <variable name="k6" initial_value="3600.0" units="first_order_rate_constant" />
  <variable name="k6_" initial_value="6.67" units="second_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="yes">
    <variable_ref variable="EPQ">
      <role role="reactant" direction="forward" delta_variable="delta_EPQ_rxn6" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Q">
      <role role="product" direction="forward" delta_variable="delta_Q_rxn6" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="EP">
      <role role="product" direction="forward" delta_variable="delta_EP_rxn6" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <plus />
              <apply>
                <times />
                <ci>k6</ci>
                <ci>EPQ</ci>
              </apply>
              <apply>
                <minus />
                <apply>
                  <times />
                  <ci>k6.</ci>
                  <ci>Q</ci>
                  <ci>EP</ci>
                </apply>
              </apply>
            </apply>
          </math>
        </role>
      </variable_ref>
    </reaction>
  </component>

```

```

<component name="reaction7">
  <variable name="EAB" public_interface="in" units="millimolar" />
  <variable name="EPQ" public_interface="in" units="millimolar" />
  <variable name="delta_EAB_rxn7" public_interface="out" units="flux" />
  <variable name="delta_EPQ_rxn7" public_interface="out" units="flux" />
  <variable name="k7" initial_value="822.0" units="first_order_rate_constant" />
  <variable name="k7_" initial_value="36.0" units="first_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="yes">
    <variable_ref variable="EAB">
      <role role="reactant" direction="forward" delta_variable="delta_EAB_rxn7" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="EPQ">
      <role role="product" direction="forward" delta_variable="delta_EPQ_rxn7" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <plus />
              <apply>
                <times />
                <ci>k7</ci>
                <ci>EAB</ci>
              </apply>
              <apply>
                <minus />
                <apply>
                  <times />
                  <ci>k7_</ci>
                  <ci>EPQ</ci>
                </apply>
              </apply>
            </apply>
          </math>
        </role>
      </variable_ref>
    </reaction>
  </component>

<component name="reaction8">
  <variable name="EPQ" public_interface="in" units="millimolar" />
  <variable name="P" public_interface="in" units="millimolar" />
  <variable name="EQ" public_interface="in" units="millimolar" />
  <variable name="delta_EPQ_rxn8" public_interface="out" units="flux" />
  <variable name="delta_P_rxn8" public_interface="out" units="flux" />
  <variable name="delta_EQ_rxn8" public_interface="out" units="flux" />
  <variable name="k8" initial_value="3600.0" units="first_order_rate_constant" />
  <variable name="k8_" initial_value="7.2" units="second_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="yes">
    <variable_ref variable="EPQ">
      <role role="reactant" direction="forward" delta_variable="delta_EPQ_rxn8" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="P">
      <role role="reactant" direction="forward" delta_variable="delta_P_rxn8" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="EQ">
      <role role="product" direction="forward" delta_variable="delta_EQ_rxn8" stoichiometric_coefficient="1" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <plus />
              <apply>
                <times />
                <ci>k8</ci>
                <ci>EPQ</ci>
              </apply>
              <apply>
                <times />
                <ci>k8_</ci>
                <ci>P</ci>
                <ci>EQ</ci>
              </apply>
            </apply>
          </math>
        </role>
      </variable_ref>
    </reaction>
  </component>

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    <role role="product" direction="forward" delta_variable="delta_P_rxn8" stoichiome
</variable_ref>
<variable_ref variable="EQ">
    <role role="product" direction="forward" delta_variable="delta_EQ_rxn8" stoichion
</variable_ref>
<variable_ref variable="rate">
    <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
                <eq />
                <ci>rate</ci>
                <apply>
                    <plus />
                    <apply>
                        <times />
                        <ci>k8</ci>
                        <ci>EPQ</ci>
                    </apply>
                    <apply>
                        <minus />
                        <apply>
                            <times />
                            <ci>k8_</ci>
                            <ci>P</ci>
                            <ci>EQ</ci>
                        </apply>
                    </apply>
                </apply>
            </math>
        </role>
    </variable_ref>
</reaction>
</component>

<connection>
    <map_components component_1="E" component_2="reaction5" />
    <map_variables variable_1="E" variable_2="E" />
    <map_variables variable_1="delta_E_rxn5" variable_2="delta_E_rxn5" />
</connection>

<connection>
    <map_components component_1="E" component_2="reaction0" />
    <map_variables variable_1="E" variable_2="E" />
    <map_variables variable_1="delta_E_rxn0" variable_2="delta_E_rxn0" />
</connection>

<connection>
    <map_components component_1="E" component_2="reaction1" />
    <map_variables variable_1="E" variable_2="E" />
    <map_variables variable_1="delta_E_rxn1" variable_2="delta_E_rxn1" />
</connection>

<connection>
    <map_components component_1="E" component_2="reaction4" />
    <map_variables variable_1="E" variable_2="E" />
    <map_variables variable_1="delta_E_rxn4" variable_2="delta_E_rxn4" />
</connection>

```

```
<connection>
  <map_components component_1="A" component_2="reaction0" />
  <map_variables variable_1="A" variable_2="A" />
  <map_variables variable_1="delta_A_rxn0" variable_2="delta_A_rxn0" />
</connection>

<connection>
  <map_components component_1="A" component_2="reaction3" />
  <map_variables variable_1="A" variable_2="A" />
  <map_variables variable_1="delta_A_rxn3" variable_2="delta_A_rxn3" />
</connection>

<connection>
  <map_components component_1="EA" component_2="reaction0" />
  <map_variables variable_1="EA" variable_2="EA" />
  <map_variables variable_1="delta_EA_rxn0" variable_2="delta_EA_rxn0" />
</connection>

<connection>
  <map_components component_1="EA" component_2="reaction2" />
  <map_variables variable_1="EA" variable_2="EA" />
  <map_variables variable_1="delta_EA_rxn2" variable_2="delta_EA_rxn2" />
</connection>

<connection>
  <map_components component_1="B" component_2="reaction1" />
  <map_variables variable_1="B" variable_2="B" />
  <map_variables variable_1="delta_B_rxn1" variable_2="delta_B_rxn1" />
</connection>

<connection>
  <map_components component_1="B" component_2="reaction2" />
  <map_variables variable_1="B" variable_2="B" />
  <map_variables variable_1="delta_B_rxn2" variable_2="delta_B_rxn2" />
</connection>

<connection>
  <map_components component_1="EB" component_2="reaction1" />
  <map_variables variable_1="EB" variable_2="EB" />
  <map_variables variable_1="delta_EB_rxn1" variable_2="delta_EB_rxn1" />
</connection>

<connection>
  <map_components component_1="EB" component_2="reaction3" />
  <map_variables variable_1="EB" variable_2="EB" />
  <map_variables variable_1="delta_EB_rxn3" variable_2="delta_EB_rxn3" />
</connection>

<connection>
  <map_components component_1="EAB" component_2="reaction2" />
  <map_variables variable_1="EAB" variable_2="EAB" />
  <map_variables variable_1="delta_EAB_rxn2" variable_2="delta_EAB_rxn2" />
</connection>

<connection>
  <map_components component_1="EAB" component_2="reaction3" />
  <map_variables variable_1="EAB" variable_2="EAB" />
  <map_variables variable_1="delta_EAB_rxn3" variable_2="delta_EAB_rxn3" />
</connection>
```

```
<connection>
  <map_components component_1="EAB" component_2="reaction7" />
  <map_variables variable_1="EAB" variable_2="EAB" />
  <map_variables variable_1="delta_EAB_rxn7" variable_2="delta_EAB_rxn7" />
</connection>

<connection>
  <map_components component_1="Q" component_2="reaction4" />
  <map_variables variable_1="Q" variable_2="Q" />
  <map_variables variable_1="delta_Q_rxn4" variable_2="delta_Q_rxn4" />
</connection>

<connection>
  <map_components component_1="Q" component_2="reaction6" />
  <map_variables variable_1="Q" variable_2="Q" />
  <map_variables variable_1="delta_Q_rxn6" variable_2="delta_Q_rxn6" />
</connection>

<connection>
  <map_components component_1="EQ" component_2="reaction4" />
  <map_variables variable_1="EQ" variable_2="EQ" />
  <map_variables variable_1="delta_EQ_rxn4" variable_2="delta_EQ_rxn4" />
</connection>

<connection>
  <map_components component_1="EQ" component_2="reaction8" />
  <map_variables variable_1="EQ" variable_2="EQ" />
  <map_variables variable_1="delta_EQ_rxn8" variable_2="delta_EQ_rxn8" />
</connection>

<connection>
  <map_components component_1="P" component_2="reaction5" />
  <map_variables variable_1="P" variable_2="P" />
  <map_variables variable_1="delta_P_rxn5" variable_2="delta_P_rxn5" />
</connection>

<connection>
  <map_components component_1="P" component_2="reaction8" />
  <map_variables variable_1="P" variable_2="P" />
  <map_variables variable_1="delta_P_rxn8" variable_2="delta_P_rxn8" />
</connection>

<connection>
  <map_components component_1="EP" component_2="reaction6" />
  <map_variables variable_1="EP" variable_2="EP" />
  <map_variables variable_1="delta_EP_rxn6" variable_2="delta_EP_rxn6" />
</connection>

<connection>
  <map_components component_1="EP" component_2="reaction5" />
  <map_variables variable_1="EP" variable_2="EP" />
  <map_variables variable_1="delta_EP_rxn5" variable_2="delta_EP_rxn5" />
</connection>

<connection>
  <map_components component_1="EPQ" component_2="reaction7" />
  <map_variables variable_1="EPQ" variable_2="EPQ" />
  <map_variables variable_1="delta_EPQ_rxn7" variable_2="delta_EPQ_rxn7" />
</connection>
```

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</connection>

<connection>
  <map_components component_1="EPQ" component_2="reaction6" />
  <map_variables variable_1="EPQ" variable_2="EPQ" />
  <map_variables variable_1="delta_EPQ_rxn6" variable_2="delta_EPQ_rxn6" />
</connection>

<connection>
  <map_components component_1="EPQ" component_2="reaction8" />
  <map_variables variable_1="EPQ" variable_2="EPQ" />
  <map_variables variable_1="delta_EPQ_rxn8" variable_2="delta_EPQ_rxn8" />
</connection>

<connection>
  <map_components component_1="E" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

<connection>
  <map_components component_1="A" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

<connection>
  <map_components component_1="EA" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

<connection>
  <map_components component_1="B" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

<connection>
  <map_components component_1="EB" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

<connection>
  <map_components component_1="EAB" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

<connection>
  <map_components component_1="P" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

<connection>
  <map_components component_1="EP" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

<connection>
  <map_components component_1="Q" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>
```

```
<connection>
  <map_components component_1="EQ" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

<connection>
  <map_components component_1="EPQ" component_2="global_variables" />
  <map_variables variable_1="time" variable_2="time" />
</connection>

</model>
```