

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

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

```
CREATED : 4th June 2002
```

```
LAST MODIFIED : 22nd July 2002
```

```
AUTHOR : Catherine Lloyd  
The Bioengineering Institute  
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.
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```
DESCRIPTION : This file contains a CellML description of a generic model of the TCA Cycle.
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CHANGES:
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```
22/07/2002 - CML - Added more metadata.
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```
<model name="the_TCA_cycle_model" pathway_editor:rendering_config_file="the_TCA cycle_cycle_0
```

```
<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="">
```

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<!--
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```
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>
```

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

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

```
<dcterms:W3CDTF>2002-06-04</dcterms:W3CDTF>
```

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

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```
The Last Modified Date metadata. This is the date on which
```

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    the model was last changed.
-->
<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>2002-07-22</dcterms:W3CDTF>
  </dcterms:modified>
</cmeta:modification>

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

<!--
  The following metadata refers to the model itself, as indicated by the
  reference to the ID "the_TCA_cycle_model", which is declared on the
  <model> element.
-->
<rdf:Description rdf:about="#the_TCA_cycle_model">
  <!-- A human readable name for the model. -->
  <dc:title>A Generic Model Of The TCA Cycle</dc:title>

  <!-- A comment regarding the model. -->
  <cmeta:comment rdf:parseType="Resource">
    <rdf:value>
      Below is a CellML description of a general model of the metabolic
      tricarboxylic acid (TCA) cycle. It is not based on a specific
      published mathematical model, but instead it is based on a textbook
      defined pathway. The general sequential structure and all the
      reactant, product and enzyme components are included.
      Michaelis-Menten enzyme kinetics are assumed.

      The purpose of this description is to illustrate how CellML can be
      used to model a general metabolic pathway.
    </rdf:value>
    <!-- The creator of the comment. -->
    <dc:creator>
      <vCard:FN>Catherine Lloyd</vCard:FN>
    </dc:creator>
  </cmeta:comment>

  <cmeta:species>Homo sapiens</cmeta:species>

  <!-- 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>

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    </dc:subject>
  </bqs:reference>

  <bqs:Book rdf:parseType="Resource">
    <dc:creator rdf:parseType="Resource">
      <bqs:Person rdf:parseType="Resource">
        <vCard:N rdf:parseType="Resource">
          <vCard:Family>Bronk</vCard:Family>
          <vCard:Given>J</vCard:Given>
          <vCard:Other>Ramsey</vCard:Other>
        </vCard:N>
      </bqs:Person>
    </dc:creator>
    <dc:title>Human Metabolism</dc:title>
    <dcterms:issued rdf:parseType="Resource">
      <dcterms:W3CDTF>1999</dcterms:W3CDTF>
    </dcterms:issued>
    <dc:publisher rdf:parseType="Resource">
      <bqs:Organisation>Addison Wesley Longman Limited</bqs:Organisation>
      <bqs:Property rdf:parseType="Resource">
        <bqs:property_type>location</bqs:property_type>
        <rdf:value>England</rdf:value>
      </bqs:Property>
    </dc:publisher>
  </bqs:Book>
</rdf:Description>
</rdf:RDF>

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

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```

<units name="micromolar">
  <unit prefix="micro" unit="mole" />
  <unit unit="litre" exponent="-1" />
</units>

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

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

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

<units name="third_order_rate_constant">
  <unit unit="micromolar" exponent="-2" />
  <unit unit="second" exponent="-1" />
</units>

<units name="forth_order_rate_constant">
  <unit unit="micromolar" exponent="-3" />

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    <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 metabolites - both reactants and
products - involved in the TCA cycle.
-->

<component name="Phosphoenolpyruvate" cmeta:id="Phosphoenolpyruvate">
  <variable name="Phosphoenolpyruvate" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Phosphoenolpyruvate_rxn11" public_interface="in" units="flux" />
  <variable name="delta_Phosphoenolpyruvate_rxn0" 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>Phosphoenolpyruvate</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_Phosphoenolpyruvate_rxn11</ci>
        <ci>delta_Phosphoenolpyruvate_rxn0</ci>
      </apply>
    </math>
</component>

<component name="Pyruvate" cmeta:id="Pyruvate">
  <variable name="Pyruvate" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Pyruvate_rxn0" public_interface="in" units="flux" />
  <variable name="delta_Pyruvate_rxn1" public_interface="in" units="flux" />
  <variable name="delta_Pyruvate_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>Pyruvate</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_Pyruvate_rxn0</ci>
      </apply>
    </math>
</component>

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        <ci>delta_Pyruvate_rxn1</ci>
        <ci>delta_Pyruvate_rxn2</ci>
    </apply>
</apply>
</math>
</component>

<component name="Oxaloacetate" cmeta:id="Oxaloacetate">
    <variable name="Oxaloacetate" public_interface="out" initial_value="1.0" units="micromol" />
    <variable name="delta_Oxaloacetate_rxn1" public_interface="in" units="flux" />
    <variable name="delta_Oxaloacetate_rxn10" public_interface="in" units="flux" />
    <variable name="delta_Oxaloacetate_rxn3" public_interface="in" units="flux" />
    <variable name="delta_Oxaloacetate_rxn11" 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>Oxaloacetate</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_Oxaloacetate_rxn1</ci>
                <ci>delta_Oxaloacetate_rxn10</ci>
                <ci>delta_Oxaloacetate_rxn3</ci>
                <ci>delta_Oxaloacetate_rxn11</ci>
            </apply>
        </apply>
    </math>
</component>

<component name="Acetyl_coenzyme_A" cmeta:id="Acetyl_coenzyme_A">
    <variable name="Acetyl_coenzyme_A" public_interface="out" initial_value="1.0" units="micromol" />
    <variable name="delta_Acetyl_coenzyme_A_rxn2" public_interface="in" units="flux" />
    <variable name="delta_Acetyl_coenzyme_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>Acetyl_coenzyme_A</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_Acetyl_coenzyme_A_rxn2</ci>
                <ci>delta_Acetyl_coenzyme_A_rxn3</ci>
            </apply>
        </apply>
    </math>
</component>

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<component name="Citrate" cmeta:id="Citrate">
  <variable name="Citrate" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Citrate_rxn3" public_interface="in" units="flux" />
  <variable name="delta_Citrate_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>Citrate</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_Citrate_rxn3</ci>
        <ci>delta_Citrate_rxn4</ci>
      </apply>
    </apply>
  </math>
</component>

<component name="Isocitrate" cmeta:id="Isocitrate">
  <variable name="Isocitrate" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Isocitrate_rxn4" public_interface="in" units="flux" />
  <variable name="delta_Isocitrate_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>Isocitrate</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_Isocitrate_rxn4</ci>
        <ci>delta_Isocitrate_rxn5</ci>
      </apply>
    </apply>
  </math>
</component>

<component name="Oxoglutarate_2" cmeta:id="Oxoglutarate_2">
  <variable name="Oxoglutarate_2" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Oxoglutarate_2_rxn5" public_interface="in" units="flux" />
  <variable name="delta_Oxoglutarate_2_rxn6" public_interface="in" units="flux" />
  <variable name="delta_Oxoglutarate_2_rxn12" 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 />

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        <bvar>
          <ci>time</ci>
        </bvar>
        <ci>Oxoglutarate_2</ci>
      </apply>
    <apply>
      <plus />
      <ci>delta_Oxoglutarate_2_rxn5</ci>
      <ci>delta_Oxoglutarate_2_rxn6</ci>
      <ci>delta_Oxoglutarate_2_rxn12</ci>
    </apply>
  </apply>
</math>
</component>

<component name="Glutamate" cmeta:id="Glutamate">
  <variable name="Glutamate" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Glutamate_rxn12" 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>Glutamate</ci>
      </apply>
      <ci>delta_Glutamate_rxn12</ci>
    </apply>
  </math>
</component>

<component name="Succinyl_CoA" cmeta:id="Succinyl_CoA">
  <variable name="Succinyl_CoA" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Succinyl_CoA_rxn6" public_interface="in" units="flux" />
  <variable name="delta_Succinyl_CoA_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>Succinyl_CoA</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_Succinyl_CoA_rxn6</ci>
        <ci>delta_Succinyl_CoA_rxn7</ci>
      </apply>
    </apply>
  </math>
</component>

<component name="Succinate" cmeta:id="Succinate">

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<variable name="Succinate" public_interface="out" initial_value="1.0" units="micromolar" />
<variable name="delta_Succinate_rxn7" public_interface="in" units="flux" />
<variable name="delta_Succinate_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>Succinate</ci>
    </apply>
    <apply>
      <plus />
      <ci>delta_Succinate_rxn7</ci>
      <ci>delta_Succinate_rxn8</ci>
    </apply>
  </apply>
</math>
</component>

<component name="Fumarate" cmeta:id="Fumarate">
  <variable name="Fumarate" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Fumarate_rxn8" public_interface="in" units="flux" />
  <variable name="delta_Fumarate_rxn9" 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>Fumarate</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_Fumarate_rxn8</ci>
        <ci>delta_Fumarate_rxn9</ci>
      </apply>
    </apply>
  </math>
</component>

<component name="NADH" cmeta:id="NADH">
  <variable name="NADH" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_NADH_rxn2" public_interface="in" units="flux" />
  <variable name="delta_NADH_rxn5" public_interface="in" units="flux" />
  <variable name="delta_NADH_rxn6" public_interface="in" units="flux" />
  <variable name="delta_NADH_rxn10" public_interface="in" units="flux" />
  <variable name="delta_NADH_rxn12" 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>

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        <diff />
        <bvar>
            <ci>time</ci>
        </bvar>
        <ci>NADH</ci>
    </apply>
    <apply>
        <plus />
        <ci>delta_NADH_rxn2</ci>
        <ci>delta_NADH_rxn5</ci>
        <ci>delta_NADH_rxn6</ci>
        <ci>delta_NADH_rxn10</ci>
        <ci>delta_NADH_rxn12</ci>
    </apply>
</apply>
</math>
</component>

<component name="NAD" cmeta:id="NAD">
    <variable name="NAD" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_NAD_rxn12" public_interface="in" units="flux" />
    <variable name="delta_NAD_rxn2" public_interface="in" units="flux" />
    <variable name="delta_NAD_rxn5" public_interface="in" units="flux" />
    <variable name="delta_NAD_rxn6" public_interface="in" units="flux" />
    <variable name="delta_NAD_rxn10" 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>NAD</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_NAD_rxn12</ci>
                <ci>delta_NAD_rxn2</ci>
                <ci>delta_NAD_rxn5</ci>
                <ci>delta_NAD_rxn6</ci>
                <ci>delta_NAD_rxn10</ci>
            </apply>
        </apply>
    </math>
</component>

<component name="H" cmeta:id="H">
    <variable name="H" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_H_rxn0" public_interface="in" units="flux" />
    <variable name="delta_H_rxn2" public_interface="in" units="flux" />
    <variable name="delta_H_rxn3" public_interface="in" units="flux" />
    <variable name="delta_H_rxn10" public_interface="in" units="flux" />
    <variable name="delta_H_rxn12" public_interface="in" units="flux" />
    <variable name="time" public_interface="in" units="second" />
    <math xmlns="http://www.w3.org/1998/Math/MathML">
        <apply>
            <eq />

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    <apply>
      <diff />
      <bvar>
        <ci>time</ci>
      </bvar>
      <ci>H</ci>
    </apply>
    <apply>
      <plus />
      <ci>delta_H_rxn0</ci>
      <ci>delta_H_rxn2</ci>
      <ci>delta_H_rxn3</ci>
      <ci>delta_H_rxn10</ci>
      <ci>delta_H_rxn12</ci>
    </apply>
  </apply>
</math>
</component>

<component name="GTP" cmeta:id="GTP">
  <variable name="GTP" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_GTP_rxn7" public_interface="in" units="flux" />
  <variable name="delta_GTP_rxn11" 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>GTP</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_GTP_rxn7</ci>
        <ci>delta_GTP_rxn11</ci>
      </apply>
    </apply>
  </math>
</component>

<component name="GDP" cmeta:id="GDP">
  <variable name="GDP" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_GDP_rxn11" public_interface="in" units="flux" />
  <variable name="delta_GDP_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>GDP</ci>
      </apply>
    </apply>
  </math>
</component>

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        <plus />
        <ci>delta_GDP_rxn11</ci>
        <ci>delta_GDP_rxn7</ci>
    </apply>
</apply>
</math>
</component>

<component name="Pi" cmeta:id="Pi">
    <variable name="Pi" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_Pi_rxn1" public_interface="in" units="flux" />
    <variable name="delta_Pi_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>Pi</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_Pi_rxn1</ci>
                <ci>delta_Pi_rxn7</ci>
            </apply>
        </apply>
    </math>
</component>

<component name="CO2" cmeta:id="CO2">
    <variable name="CO2" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_CO2_rxn2" public_interface="in" units="flux" />
    <variable name="delta_CO2_rxn5" public_interface="in" units="flux" />
    <variable name="delta_CO2_rxn6" public_interface="in" units="flux" />
    <variable name="delta_CO2_rxn11" public_interface="in" units="flux" />
    <variable name="delta_CO2_rxn1" 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>CO2</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_CO2_rxn2</ci>
                <ci>delta_CO2_rxn5</ci>
                <ci>delta_CO2_rxn6</ci>
                <ci>delta_CO2_rxn11</ci>
                <ci>delta_CO2_rxn1</ci>
            </apply>
        </apply>
    </math>
</component>

```

```

</math>
</component>

<component name="H2O" cmeta:id="H2O">
  <variable name="H2O" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_H2O_rxn2" public_interface="in" units="flux" />
  <variable name="delta_H2O_rxn12" public_interface="in" units="flux" />
  <variable name="delta_H2O_rxn3" public_interface="in" units="flux" />
  <variable name="delta_H2O_rxn9" 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>H2O</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_H2O_rxn2</ci>
        <ci>delta_H2O_rxn12</ci>
        <ci>delta_H2O_rxn3</ci>
        <ci>delta_H2O_rxn9</ci>
      </apply>
    </apply>
  </math>
</component>

<component name="NH4" cmeta:id="NH4">
  <variable name="NH4" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_NH4_rxn12" 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>NH4</ci>
      </apply>
      <ci>delta_NH4_rxn12</ci>
    </apply>
  </math>
</component>

<component name="ATP" cmeta:id="ATP">
  <variable name="ATP" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_ATP_rxn0" public_interface="in" units="flux" />
  <variable name="delta_ATP_rxn1" 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>ATP</ci>
    </apply>
    <apply>
        <plus />
        <ci>delta_ATP_rxn0</ci>
        <ci>delta_ATP_rxn1</ci>
    </apply>
</math>
</component>

<component name="ADP" cmeta:id="ADP">
    <variable name="ADP" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_ADP_rxn1" public_interface="in" units="flux" />
    <variable name="delta_ADP_rxn0" 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>ADP</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_ADP_rxn1</ci>
                <ci>delta_ADP_rxn0</ci>
            </apply>
        </apply>
    </math>
</component>

<component name="CoA_SH" cmeta:id="CoA_SH">
    <variable name="CoA_SH" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_CoA_SH_rxn3" public_interface="in" units="flux" />
    <variable name="delta_CoA_SH_rxn7" public_interface="in" units="flux" />
    <variable name="delta_CoA_SH_rxn2" public_interface="in" units="flux" />
    <variable name="delta_CoA_SH_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>CoA_SH</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_CoA_SH_rxn3</ci>

```

```

        <ci>delta_CoA_SH_rxn7</ci>
        <ci>delta_CoA_SH_rxn2</ci>
        <ci>delta_CoA_SH_rxn6</ci>
    </apply>
</apply>
</math>
</component>

<component name="FAD" cmeta:id="FAD">
    <variable name="FAD" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_FAD_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>FAD</ci>
            </apply>
            <ci>delta_FAD_rxn8</ci>
        </apply>
    </math>
</component>

<component name="FADH2" cmeta:id="FADH2">
    <variable name="FADH2" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_FADH2_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>FADH2</ci>
            </apply>
            <ci>delta_FADH2_rxn8</ci>
        </apply>
    </math>
</component>

<component name="Malate" cmeta:id="Malate">
    <variable name="Malate" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_Malate_rxn9" public_interface="in" units="flux" />
    <variable name="delta_Malate_rxn10" 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>
            </apply>
        </math>
    </component>

```

```

        <ci>Malate</ci>
    </apply>
    <apply>
        <plus />
        <ci>delta_Malate_rxn9</ci>
        <ci>delta_Malate_rxn10</ci>
    </apply>
</apply>
</math>
</component>

<!--
The following components describe all the enzymes involved in the TCA cycle.
-->

<component name="Citrate_synthase" cmeta:id="Citrate_synthase">
    <variable name="Citrate_synthase" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="time" public_interface="in" units="second" />
</component>

<component name="Aconitase" cmeta:id="Aconitase">
    <variable name="Aconitase" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="time" public_interface="in" units="second" />
</component>

<component name="Isocitrate_dehydrogenase" cmeta:id="Isocitrate_dehydrogenase">
    <variable name="Isocitrate_dehydrogenase" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="time" public_interface="in" units="second" />
</component>

<component name="Oxoglutarate_2_dehydrogenase" cmeta:id="Oxoglutarate_2_dehydrogenase">
    <variable name="Oxoglutarate_2_dehydrogenase" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="time" public_interface="in" units="second" />
</component>

<component name="Succinyl_CoA_synthetase" cmeta:id="Succinyl_CoA_synthetase">
    <variable name="Succinyl_CoA_synthetase" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="time" public_interface="in" units="second" />
</component>

<component name="Succinate_dehydrogenase" cmeta:id="Succinate_dehydrogenase">
    <variable name="Succinate_dehydrogenase" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="time" public_interface="in" units="second" />
</component>

<component name="Fumarate_hydratase" cmeta:id="Fumarate_hydratase">
    <variable name="Fumarate_hydratase" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="time" public_interface="in" units="second" />
</component>

<component name="Malate_dehydrogenase" cmeta:id="Malate_dehydrogenase">
    <variable name="Malate_dehydrogenase" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="time" public_interface="in" units="second" />
</component>

<component name="Pyruvate_kinase" cmeta:id="Pyruvate_kinase">
    <variable name="Pyruvate_kinase" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="time" public_interface="in" units="second" />
</component>

```

```

<component name="Pyruvate_dehydrogenase" cmeta:id="Pyruvate_dehydrogenase">
  <variable name="Pyruvate_dehydrogenase" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="time" public_interface="in" units="second" />
</component>

<component name="Pyruvate_carboxylase" cmeta:id="Pyruvate_carboxylase">
  <variable name="Pyruvate_carboxylase" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="time" public_interface="in" units="second" />
</component>

<component name="Phosphoenolpyruvate_carboxykinase" cmeta:id="Phosphoenolpyruvate_carboxykinase">
  <variable name="Phosphoenolpyruvate_carboxykinase" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="time" public_interface="in" units="second" />
</component>

<component name="Glutamate_dehydrogenase" cmeta:id="Glutamate_dehydrogenase">
  <variable name="Glutamate_dehydrogenase" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="time" public_interface="in" units="second" />
</component>

<!--
  The following components represent the reaction steps of the TCA cycle.
-->

<component name="reaction0">
  <variable name="ADP" public_interface="in" units="micromolar" />
  <variable name="Phosphoenolpyruvate" public_interface="in" units="micromolar" />
  <variable name="H" public_interface="in" units="micromolar" />
  <variable name="ATP" public_interface="in" units="micromolar" />
  <variable name="Pyruvate" public_interface="in" units="micromolar" />
  <variable name="Pyruvate_kinase" public_interface="in" units="micromolar" />
  <variable name="delta_ADP_rxn0" public_interface="out" units="flux" />
  <variable name="delta_Phosphoenolpyruvate_rxn0" public_interface="out" units="flux" />
  <variable name="delta_H_rxn0" public_interface="out" units="flux" />
  <variable name="delta_ATP_rxn0" public_interface="out" units="flux" />
  <variable name="delta_Pyruvate_rxn0" public_interface="out" units="flux" />
  <variable name="vmax0" initial_value="1.0" units="third_order_rate_constant" />
  <variable name="km0" initial_value="1.0" units="micromolar" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="ADP">
      <role role="reactant" delta_variable="delta_ADP_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Phosphoenolpyruvate">
      <role role="reactant" delta_variable="delta_Phosphoenolpyruvate_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="H">
      <role role="reactant" delta_variable="delta_H_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="ATP">
      <role role="product" delta_variable="delta_ATP_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Pyruvate">
      <role role="product" delta_variable="delta_Pyruvate_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Pyruvate_kinase">
      <role role="catalyst" />
    </variable_ref>
  </reaction>
</component>

```

```

<variable_ref variable="rate">
  <role role="rate">
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <eq />
        <ci>rate</ci>
        <apply><divide />
          <apply><times />
            <ci>vmax0</ci>
            <ci>ADP</ci>
            <ci>Phosphoenolpyruvate</ci>
            <ci>H</ci>
          </apply>
        <apply><plus />
          <ci>km0</ci>
          <ci>ADP</ci>
          <ci>Phosphoenolpyruvate</ci>
          <ci>H</ci>
        </apply>
      </apply>
    </math>
  </role>
</variable_ref>
</reaction>
</component>

```

```

<component name="reaction1">
  <variable name="ATP" public_interface="in" units="micromolar" />
  <variable name="CO2" public_interface="in" units="micromolar" />
  <variable name="Pyruvate" public_interface="in" units="micromolar" />
  <variable name="ADP" public_interface="in" units="micromolar" />
  <variable name="Oxaloacetate" public_interface="in" units="micromolar" />
  <variable name="Pi" public_interface="in" units="micromolar" />
  <variable name="Pyruvate_carboxylase" public_interface="in" units="micromolar" />
  <variable name="delta_ATP_rxn1" public_interface="out" units="flux" />
  <variable name="delta_CO2_rxn1" public_interface="out" units="flux" />
  <variable name="delta_Pyruvate_rxn1" public_interface="out" units="flux" />
  <variable name="delta_ADP_rxn1" public_interface="out" units="flux" />
  <variable name="delta_Oxaloacetate_rxn1" public_interface="out" units="flux" />
  <variable name="delta_Pi_rxn1" public_interface="out" units="flux" />
  <variable name="km1" initial_value="1.0" units="micromolar" />
  <variable name="vmax1" initial_value="1.0" units="third_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="ATP">
      <role role="reactant" delta_variable="delta_ATP_rxn1" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="CO2">
      <role role="reactant" delta_variable="delta_CO2_rxn1" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Pyruvate">
      <role role="reactant" delta_variable="delta_Pyruvate_rxn1" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="ADP">
      <role role="product" delta_variable="delta_ADP_rxn1" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Oxaloacetate">
      <role role="product" delta_variable="delta_Oxaloacetate_rxn1" stoichiometry="1" />
    </variable_ref>
  </reaction>

```

```

</variable_ref>
<variable_ref variable="Pi">
  <role role="product" delta_variable="delta_Pi_rxn1" stoichiometry="1" />
</variable_ref>
<variable_ref variable="Pyruvate_carboxylase">
  <role role="catalyst" />
</variable_ref>
<variable_ref variable="rate">
  <role role="rate">
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <eq />
        <ci>rate</ci>
        <apply>
          <divide />
          <apply>
            <times />
            <ci>ATP</ci>
            <ci>CO2</ci>
            <ci>Pyruvate</ci>
            <ci>vmax1</ci>
          </apply>
          <apply>
            <plus />
            <ci>km1</ci>
            <ci>ATP</ci>
            <ci>CO2</ci>
            <ci>Pyruvate</ci>
          </apply>
        </apply>
      </math>
    </role>
  </variable_ref>
</reaction>
</component>

<component name="reaction2">
  <variable name="CoA_SH" public_interface="in" units="micromolar" />
  <variable name="Pyruvate" public_interface="in" units="micromolar" />
  <variable name="NAD" public_interface="in" units="micromolar" />
  <variable name="H" public_interface="in" units="micromolar" />
  <variable name="H2O" public_interface="in" units="micromolar" />
  <variable name="CO2" public_interface="in" units="micromolar" />
  <variable name="NADH" public_interface="in" units="micromolar" />
  <variable name="Acetyl_coenzyme_A" public_interface="in" units="micromolar" />
  <variable name="Pyruvate_dehydrogenase" public_interface="in" units="micromolar" />
  <variable name="delta_CoA_SH_rxn2" public_interface="out" units="flux" />
  <variable name="delta_Pyruvate_rxn2" public_interface="out" units="flux" />
  <variable name="delta_NAD_rxn2" public_interface="out" units="flux" />
  <variable name="delta_H_rxn2" public_interface="out" units="flux" />
  <variable name="delta_H2O_rxn2" public_interface="out" units="flux" />
  <variable name="delta_CO2_rxn2" public_interface="out" units="flux" />
  <variable name="delta_NADH_rxn2" public_interface="out" units="flux" />
  <variable name="delta_Acetyl_coenzyme_A_rxn2" public_interface="out" units="flux" />
  <variable name="km2" initial_value="1.0" units="micromolar" />
  <variable name="vmax2" initial_value="1.0" units="forth_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">

```

```

<variable_ref variable="CoA_SH">
  <role role="reactant" delta_variable="delta_CoA_SH_rxn2" stoichiometry="1" />
</variable_ref>
<variable_ref variable="Pyruvate">
  <role role="reactant" delta_variable="delta_Pyruvate_rxn2" stoichiometry="1" />
</variable_ref>
<variable_ref variable="NAD">
  <role role="reactant" delta_variable="delta_NAD_rxn2" stoichiometry="1" />
</variable_ref>
<variable_ref variable="H2O">
  <role role="reactant" delta_variable="delta_H2O_rxn2" stoichiometry="1" />
</variable_ref>
<variable_ref variable="H">
  <role role="product" delta_variable="delta_H_rxn2" stoichiometry="1" />
</variable_ref>
<variable_ref variable="CO2">
  <role role="product" delta_variable="delta_CO2_rxn2" stoichiometry="1" />
</variable_ref>
<variable_ref variable="NADH">
  <role role="product" delta_variable="delta_NADH_rxn2" stoichiometry="1" />
</variable_ref>
<variable_ref variable="Acetyl_coenzyme_A">
  <role role="product" delta_variable="delta_Acetyl_coenzyme_A_rxn2" stoichiometry="1" />
</variable_ref>
<variable_ref variable="Pyruvate_dehydrogenase">
  <role role="catalyst" />
</variable_ref>
<variable_ref variable="rate">
  <role role="rate">
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <eq />
        <ci>rate</ci>
        <apply>
          <divide />
          <apply>
            <times />
            <ci>CoA_SH</ci>
            <ci>Pyruvate</ci>
            <ci>NAD</ci>
            <ci>H2O</ci>
            <ci>vmax2</ci>
          </apply>
          <apply>
            <plus />
            <ci>km2</ci>
            <ci>CoA_SH</ci>
            <ci>Pyruvate</ci>
            <ci>NAD</ci>
            <ci>H2O</ci>
          </apply>
        </apply>
      </math>
    </role>
  </variable_ref>
</reaction>
</component>

```

```

<component name="reaction3">
  <variable name="Acetyl_coenzyme_A" public_interface="in" units="micromolar" />
  <variable name="Oxaloacetate" public_interface="in" units="micromolar" />
  <variable name="H2O" public_interface="in" units="micromolar" />
  <variable name="CoA_SH" public_interface="in" units="micromolar" />
  <variable name="Citrate" public_interface="in" units="micromolar" />
  <variable name="H" public_interface="in" units="micromolar" />
  <variable name="Citrate_synthase" public_interface="in" units="micromolar" />
  <variable name="delta_Acetyl_coenzyme_A_rxn3" public_interface="out" units="flux" />
  <variable name="delta_Oxaloacetate_rxn3" public_interface="out" units="flux" />
  <variable name="delta_H2O_rxn3" public_interface="out" units="flux" />
  <variable name="delta_CoA_SH_rxn3" public_interface="out" units="flux" />
  <variable name="delta_Citrate_rxn3" public_interface="out" units="flux" />
  <variable name="delta_H_rxn3" public_interface="out" units="flux" />
  <variable name="km3" initial_value="1.0" units="micromolar" />
  <variable name="vmax3" initial_value="1.0" units="third_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="Acetyl_coenzyme_A">
      <role role="reactant" delta_variable="delta_Acetyl_coenzyme_A_rxn3" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Oxaloacetate">
      <role role="reactant" delta_variable="delta_Oxaloacetate_rxn3" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="H2O">
      <role role="reactant" delta_variable="delta_H2O_rxn3" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="CoA_SH">
      <role role="product" delta_variable="delta_CoA_SH_rxn3" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Citrate">
      <role role="product" delta_variable="delta_Citrate_rxn3" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="H">
      <role role="product" delta_variable="delta_H_rxn3" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Citrate_synthase">
      <role role="catalyst" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <divide />
              <apply>
                <times />
                <ci>Acetyl_coenzyme_A</ci>
                <ci>Oxaloacetate</ci>
                <ci>H2O</ci>
                <ci>vmax3</ci>
              </apply>
            </apply>
            <plus />
            <ci>km3</ci>
            <ci>Acetyl_coenzyme_A</ci>
            <ci>Oxaloacetate</ci>
          </math>

```

```

        <ci>H2O</ci>
      </apply>
    </apply>
  </apply>
</math>
</role>
</variable_ref>
</reaction>
</component>

<component name="reaction4">
  <variable name="Citrate" public_interface="in" units="micromolar" />
  <variable name="Isocitrate" public_interface="in" units="micromolar" />
  <variable name="Aconitase" public_interface="in" units="micromolar" />
  <variable name="delta_Citrate_rxn4" public_interface="out" units="flux" />
  <variable name="delta_Isocitrate_rxn4" public_interface="out" units="flux" />
  <variable name="km4" initial_value="1.0" units="micromolar" />
  <variable name="vmax4" initial_value="1.0" units="first_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="Citrate">
      <role role="reactant" delta_variable="delta_Citrate_rxn4" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Isocitrate">
      <role role="product" delta_variable="delta_Isocitrate_rxn4" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Aconitase">
      <role role="catalyst" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <divide />
              <apply>
                <times />
                <ci>Citrate</ci>
                <ci>vmax4</ci>
              </apply>
              <apply>
                <plus />
                <ci>km4</ci>
                <ci>Citrate</ci>
              </apply>
            </apply>
          </math>
        </role>
      </variable_ref>
    </reaction>
  </component>

<component name="reaction5">
  <variable name="Isocitrate" public_interface="in" units="micromolar" />
  <variable name="NAD" public_interface="in" units="micromolar" />
  <variable name="CO2" public_interface="in" units="micromolar" />

```

```

<variable name="NADH" public_interface="in" units="micromolar" />
<variable name="Isocitrate_dehydrogenase" public_interface="in" units="micromolar" />
<variable name="Oxoglutarate_2" public_interface="in" units="micromolar" />
<variable name="delta_Isocitrate_rxn5" public_interface="out" units="flux" />
<variable name="delta_NAD_rxn5" public_interface="out" units="flux" />
<variable name="delta_CO2_rxn5" public_interface="out" units="flux" />
<variable name="delta_NADH_rxn5" public_interface="out" units="flux" />
<variable name="delta_Oxoglutarate_2_rxn5" public_interface="out" units="flux" />
<variable name="km5" initial_value="1.0" units="micromolar" />
<variable name="vmax5" initial_value="1.0" units="second_order_rate_constant" />
<variable name="rate" units="flux" />
<reaction reversible="no">
  <variable_ref variable="Isocitrate">
    <role role="reactant" delta_variable="delta_Isocitrate_rxn5" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="NAD">
    <role role="reactant" delta_variable="delta_NAD_rxn5" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="CO2">
    <role role="product" delta_variable="delta_CO2_rxn5" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="NADH">
    <role role="product" delta_variable="delta_NADH_rxn5" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="Oxoglutarate_2">
    <role role="product" delta_variable="delta_Oxoglutarate_2_rxn5" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="Isocitrate_dehydrogenase">
    <role role="catalyst" direction="forward" />
  </variable_ref>
  <variable_ref variable="rate">
    <role role="rate">
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <apply>
          <eq />
          <ci>rate</ci>
          <apply>
            <divide />
            <apply>
              <times />
              <ci>Isocitrate</ci>
              <ci>NAD</ci>
              <ci>vmax5</ci>
            </apply>
            <apply>
              <plus />
              <ci>km5</ci>
              <ci>Isocitrate</ci>
              <ci>NAD</ci>
            </apply>
          </apply>
        </math>
      </role>
    </variable_ref>
  </reaction>
</component>

<component name="reaction6">

```

```

<variable name="Oxoglutarate_2" public_interface="in" units="micromolar" />
<variable name="NAD" public_interface="in" units="micromolar" />
<variable name="CoA_SH" public_interface="in" units="micromolar" />
<variable name="NADH" public_interface="in" units="micromolar" />
<variable name="CO2" public_interface="in" units="micromolar" />
<variable name="Succinyl_CoA" public_interface="in" units="micromolar" />
<variable name="Oxoglutarate_2_dehydrogenase" public_interface="in" units="micromolar" />
<variable name="delta_Oxoglutarate_2_rxn6" public_interface="out" units="flux" />
<variable name="delta_NAD_rxn6" public_interface="out" units="flux" />
<variable name="delta_CoA_SH_rxn6" public_interface="out" units="flux" />
<variable name="delta_NADH_rxn6" public_interface="out" units="flux" />
<variable name="delta_CO2_rxn6" public_interface="out" units="flux" />
<variable name="delta_Succinyl_CoA_rxn6" public_interface="out" units="flux" />
<variable name="km6" initial_value="1.0" units="micromolar" />
<variable name="vmax6" initial_value="1.0" units="third_order_rate_constant" />
<variable name="rate" units="flux" />
<reaction reversible="no">
  <variable_ref variable="Oxoglutarate_2">
    <role role="reactant" delta_variable="delta_Oxoglutarate_2_rxn6" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="NAD">
    <role role="reactant" delta_variable="delta_NAD_rxn6" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="CoA_SH">
    <role role="reactant" delta_variable="delta_CoA_SH_rxn6" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="NADH">
    <role role="product" delta_variable="delta_NADH_rxn6" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="CO2">
    <role role="product" delta_variable="delta_CO2_rxn6" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="Succinyl_CoA">
    <role role="product" delta_variable="delta_Succinyl_CoA_rxn6" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="Oxoglutarate_2_dehydrogenase">
    <role role="catalyst" direction="forward" />
  </variable_ref>
  <variable_ref variable="rate">
    <role role="rate">
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <apply>
          <eq />
          <ci>rate</ci>
          <apply>
            <divide />
            <apply>
              <times />
              <ci>Oxoglutarate_2</ci>
              <ci>NAD</ci>
              <ci>CoA_SH</ci>
              <ci>vmax6</ci>
            </apply>
          </apply>
          <plus />
          <ci>km6</ci>
          <ci>Oxoglutarate_2</ci>
          <ci>NAD</ci>
          <ci>CoA_SH</ci>
        </math>
      </role>
    </variable_ref>
  </reaction>

```

```

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

<component name="reaction7">
  <variable name="GDP" public_interface="in" units="micromolar" />
  <variable name="Pi" public_interface="in" units="micromolar" />
  <variable name="Succinyl_CoA" public_interface="in" units="micromolar" />
  <variable name="Succinate" public_interface="in" units="micromolar" />
  <variable name="GTP" public_interface="in" units="micromolar" />
  <variable name="CoA_SH" public_interface="in" units="micromolar" />
  <variable name="Succinyl_CoA_synthetase" public_interface="in" units="micromolar" />
  <variable name="delta_GDP_rxn7" public_interface="out" units="flux" />
  <variable name="delta_Pi_rxn7" public_interface="out" units="flux" />
  <variable name="delta_Succinyl_CoA_rxn7" public_interface="out" units="flux" />
  <variable name="delta_Succinate_rxn7" public_interface="out" units="flux" />
  <variable name="delta_GTP_rxn7" public_interface="out" units="flux" />
  <variable name="delta_CoA_SH_rxn7" public_interface="out" units="flux" />
  <variable name="km7" initial_value="1.0" units="micromolar" />
  <variable name="vmax7" initial_value="1.0" units="third_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="GDP">
      <role role="reactant" delta_variable="delta_GDP_rxn7" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Pi">
      <role role="reactant" delta_variable="delta_Pi_rxn7" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Succinyl_CoA">
      <role role="reactant" delta_variable="delta_Succinyl_CoA_rxn7" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Succinate">
      <role role="product" delta_variable="delta_Succinate_rxn7" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="GTP">
      <role role="product" delta_variable="delta_GTP_rxn7" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="CoA_SH">
      <role role="product" delta_variable="delta_CoA_SH_rxn7" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Succinyl_CoA_synthetase">
      <role role="catalyst" direction="forward" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <divide />
              <apply>
                <times />
                <ci>GDP</ci>
              </apply>
            </apply>
          </math>

```



```

        <ci>Succinate</ci>
        <ci>vmax8</ci>
    </apply>
    <apply>
        <plus />
        <ci>km8</ci>
        <ci>FAD</ci>
        <ci>Succinate</ci>
    </apply>
</apply>
</math>
</role>
</variable_ref>
</reaction>
</component>

<component name="reaction9">
    <variable name="H2O" public_interface="in" units="micromolar" />
    <variable name="Fumarate" public_interface="in" units="micromolar" />
    <variable name="Malate" public_interface="in" units="micromolar" />
    <variable name="Fumarate_hydratase" public_interface="in" units="micromolar" />
    <variable name="delta_H2O_rxn9" public_interface="out" units="flux" />
    <variable name="delta_Fumarate_rxn9" public_interface="out" units="flux" />
    <variable name="delta_Malate_rxn9" public_interface="out" units="flux" />
    <variable name="km9" initial_value="1.0" units="micromolar" />
    <variable name="vmax9" initial_value="1.0" units="second_order_rate_constant" />
    <variable name="rate" units="flux" />
    <reaction reversible="no">
        <variable_ref variable="H2O">
            <role role="reactant" delta_variable="delta_H2O_rxn9" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="Fumarate">
            <role role="reactant" delta_variable="delta_Fumarate_rxn9" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="Malate">
            <role role="product" delta_variable="delta_Malate_rxn9" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="Fumarate_hydratase">
            <role role="catalyst" direction="forward" />
        </variable_ref>
        <variable_ref variable="rate">
            <role role="rate">
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                    <apply>
                        <eq />
                        <ci>rate</ci>
                    <apply>
                        <divide />
                        <apply>
                            <times />
                            <ci>H2O</ci>
                            <ci>Fumarate</ci>
                            <ci>vmax9</ci>
                        </apply>
                    <apply>
                        <plus />
                        <ci>km9</ci>
                        <ci>H2O</ci>
                    </apply>
                </math>
            </role>
        </variable_ref>
    </reaction>

```

```

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

<component name="reaction10">
  <variable name="Malate" public_interface="in" units="micromolar" />
  <variable name="NAD" public_interface="in" units="micromolar" />
  <variable name="Oxaloacetate" public_interface="in" units="micromolar" />
  <variable name="NADH" public_interface="in" units="micromolar" />
  <variable name="H" public_interface="in" units="micromolar" />
  <variable name="Malate_dehydrogenase" public_interface="in" units="micromolar" />
  <variable name="delta_Malate_rxn10" public_interface="out" units="flux" />
  <variable name="delta_NAD_rxn10" public_interface="out" units="flux" />
  <variable name="delta_Oxaloacetate_rxn10" public_interface="out" units="flux" />
  <variable name="delta_NADH_rxn10" public_interface="out" units="flux" />
  <variable name="delta_H_rxn10" public_interface="out" units="flux" />
  <variable name="km10" initial_value="1.0" units="micromolar" />
  <variable name="vmax10" initial_value="1.0" units="second_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="Malate">
      <role role="reactant" delta_variable="delta_Malate_rxn10" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="NAD">
      <role role="reactant" delta_variable="delta_NAD_rxn10" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Oxaloacetate">
      <role role="product" delta_variable="delta_Oxaloacetate_rxn10" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="NADH">
      <role role="product" delta_variable="delta_NADH_rxn10" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="H">
      <role role="product" delta_variable="delta_H_rxn10" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Malate_dehydrogenase">
      <role role="catalyst" direction="forward" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <divide />
              <apply>
                <times />
                <ci>Malate</ci>
                <ci>NAD</ci>
                <ci>vmax10</ci>
              </apply>
            </apply>
          </math>
        </role>
      </variable_ref>
    </reaction>
  </component>

```

```

        <plus />
        <ci>km10</ci>
        <ci>Malate</ci>
        <ci>NAD</ci>
    </apply>
</apply>
</apply>
</math>
</role>
</variable_ref>
</reaction>
</component>

<component name="reaction11">
  <variable name="Oxaloacetate" public_interface="in" units="micromolar" />
  <variable name="GTP" public_interface="in" units="micromolar" />
  <variable name="Phosphoenolpyruvate" public_interface="in" units="micromolar" />
  <variable name="GDP" public_interface="in" units="micromolar" />
  <variable name="CO2" public_interface="in" units="micromolar" />
  <variable name="Phosphoenolpyruvate_carboxykinase" public_interface="in" units="micromolar" />
  <variable name="delta_Oxaloacetate_rxn11" public_interface="out" units="flux" />
  <variable name="delta_GTP_rxn11" public_interface="out" units="flux" />
  <variable name="delta_Phosphoenolpyruvate_rxn11" public_interface="out" units="flux" />
  <variable name="delta_GDP_rxn11" public_interface="out" units="flux" />
  <variable name="delta_CO2_rxn11" public_interface="out" units="flux" />
  <variable name="km11" initial_value="1.0" units="micromolar" />
  <variable name="vmax11" initial_value="1.0" units="second_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="Oxaloacetate">
      <role role="reactant" delta_variable="delta_Oxaloacetate_rxn11" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="GTP">
      <role role="reactant" delta_variable="delta_GTP_rxn11" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Phosphoenolpyruvate">
      <role role="product" delta_variable="delta_Phosphoenolpyruvate_rxn11" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="GDP">
      <role role="product" delta_variable="delta_GDP_rxn11" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="CO2">
      <role role="product" delta_variable="delta_CO2_rxn11" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Phosphoenolpyruvate_carboxykinase">
      <role role="catalyst" direction="forward" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <divide />
              <apply>
                <times />
                <ci>Oxaloacetate</ci>
                <ci>GTP</ci>

```

```

        <ci>vmax11</ci>
    </apply>
    <apply>
        <plus />
        <ci>km11</ci>
        <ci>Oxaloacetate</ci>
        <ci>GTP</ci>
    </apply>
</apply>
</math>
</variable_ref>
</reaction>
</component>

<component name="reaction12">
    <variable name="H" public_interface="in" units="micromolar" />
    <variable name="NADH" public_interface="in" units="micromolar" />
    <variable name="NH4" public_interface="in" units="micromolar" />
    <variable name="Oxoglutarate_2" public_interface="in" units="micromolar" />
    <variable name="Glutamate" public_interface="in" units="micromolar" />
    <variable name="H2O" public_interface="in" units="micromolar" />
    <variable name="NAD" public_interface="in" units="micromolar" />
    <variable name="Glutamate_dehydrogenase" public_interface="in" units="micromolar" />
    <variable name="delta_H_rxn12" public_interface="out" units="flux" />
    <variable name="delta_NADH_rxn12" public_interface="out" units="flux" />
    <variable name="delta_NH4_rxn12" public_interface="out" units="flux" />
    <variable name="delta_Oxoglutarate_2_rxn12" public_interface="out" units="flux" />
    <variable name="delta_Glutamate_rxn12" public_interface="out" units="flux" />
    <variable name="delta_H2O_rxn12" public_interface="out" units="flux" />
    <variable name="delta_NAD_rxn12" public_interface="out" units="flux" />
    <variable name="km12" initial_value="1.0" units="micromolar" />
    <variable name="vmax12" initial_value="1.0" units="forth_order_rate_constant" />
    <variable name="km12_" initial_value="1.0" units="micromolar" />
    <variable name="vmax12_" initial_value="1.0" units="third_order_rate_constant" />
    <variable name="rate" units="flux" />
    <reaction reversible="yes">
        <variable_ref variable="H">
            <role role="reactant" direction="forward" delta_variable="delta_H_rxn12" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="NADH">
            <role role="reactant" direction="forward" delta_variable="delta_NADH_rxn12" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="NH4">
            <role role="reactant" direction="forward" delta_variable="delta_NH4_rxn12" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="Oxoglutarate_2">
            <role role="reactant" direction="forward" delta_variable="delta_Oxoglutarate_2_rxn12" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="Glutamate">
            <role role="product" direction="forward" delta_variable="delta_Glutamate_rxn12" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="H2O">
            <role role="product" direction="forward" delta_variable="delta_H2O_rxn12" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="NAD">
            <role role="product" direction="forward" delta_variable="delta_NAD_rxn12" stoichiometry="1" />
        </variable_ref>
    </reaction>

```

```

<variable_ref variable="Glutamate_dehydrogenase">
  <role role="catalyst" direction="forward" />
</variable_ref>
<variable_ref variable="rate">
  <role role="rate">
    <math xmlns="http://www.w3.org/1998/Math/MathML">
      <apply>
        <eq />
        <ci>rate</ci>
        <apply>
          <divide />
          <apply>
            <minus />
            <apply>
              <times />
              <ci>vmax12</ci>
              <apply>
                <divide />
                <apply>
                  <times />
                  <ci>H</ci>
                  <ci>NADH</ci>
                  <ci>NH4</ci>
                  <ci>Oxoglutarate_2</ci>
                </apply>
              </apply>
            </apply>
          </apply>
          <times />
          <ci>vmax12_</ci>
          <apply>
            <divide />
            <apply>
              <times />
              <ci>Glutamate</ci>
              <ci>H2O</ci>
              <ci>NAD</ci>
            </apply>
          </apply>
        </apply>
      </math>
    </role>
  </variable_ref>
  <plus />
  <cn cellml:units="dimensionless">1.0</cn>
  <apply>
    <divide />
    <apply>
      <times />
      <ci>H</ci>
      <ci>NADH</ci>
      <ci>NH4</ci>
      <ci>Oxoglutarate_2</ci>
    </apply>
  </apply>
  <ci>km12</ci>
</apply>
</variable_ref>
</math>

```

```

        <apply>
            <times />
            <ci>Glutamate</ci>
            <ci>H2O</ci>
            <ci>NAD</ci>
        </apply>
        <ci>km12.</ci>
    </apply>
</apply>
</apply>
</apply>
</math>
</role>
</variable_ref>
</reaction>
</component>

<connection>
    <map_components component_1="Phosphoenolpyruvate" component_2="reaction11" />
    <map_variables variable_1="Phosphoenolpyruvate" variable_2="Phosphoenolpyruvate" />
    <map_variables variable_1="delta_Phosphoenolpyruvate_rxn11" variable_2="delta_Phosphoenolpyruvate_rxn11" />
</connection>

<connection>
    <map_components component_1="Phosphoenolpyruvate" component_2="reaction0" />
    <map_variables variable_1="Phosphoenolpyruvate" variable_2="Phosphoenolpyruvate" />
    <map_variables variable_1="delta_Phosphoenolpyruvate_rxn0" variable_2="delta_Phosphoenolpyruvate_rxn0" />
</connection>

<connection>
    <map_components component_1="Pyruvate" component_2="reaction0" />
    <map_variables variable_1="Pyruvate" variable_2="Pyruvate" />
    <map_variables variable_1="delta_Pyruvate_rxn0" variable_2="delta_Pyruvate_rxn0" />
</connection>

<connection>
    <map_components component_1="Pyruvate" component_2="reaction1" />
    <map_variables variable_1="Pyruvate" variable_2="Pyruvate" />
    <map_variables variable_1="delta_Pyruvate_rxn1" variable_2="delta_Pyruvate_rxn1" />
</connection>

<connection>
    <map_components component_1="Pyruvate" component_2="reaction2" />
    <map_variables variable_1="Pyruvate" variable_2="Pyruvate" />
    <map_variables variable_1="delta_Pyruvate_rxn2" variable_2="delta_Pyruvate_rxn2" />
</connection>

<connection>
    <map_components component_1="Oxaloacetate" component_2="reaction1" />
    <map_variables variable_1="Oxaloacetate" variable_2="Oxaloacetate" />
    <map_variables variable_1="delta_Oxaloacetate_rxn1" variable_2="delta_Oxaloacetate_rxn1" />
</connection>

<connection>
    <map_components component_1="Oxaloacetate" component_2="reaction10" />
    <map_variables variable_1="Oxaloacetate" variable_2="Oxaloacetate" />
    <map_variables variable_1="delta_Oxaloacetate_rxn10" variable_2="delta_Oxaloacetate_rxn10" />
</connection>

```

```
<connection>
  <map_components component_1="Oxaloacetate" component_2="reaction3" />
  <map_variables variable_1="Oxaloacetate" variable_2="Oxaloacetate" />
  <map_variables variable_1="delta_Oxaloacetate_rxn3" variable_2="delta_Oxaloacetate_rxn3" />
</connection>

<connection>
  <map_components component_1="Oxaloacetate" component_2="reaction11" />
  <map_variables variable_1="Oxaloacetate" variable_2="Oxaloacetate" />
  <map_variables variable_1="delta_Oxaloacetate_rxn11" variable_2="delta_Oxaloacetate_rxn11" />
</connection>

<connection>
  <map_components component_1="Acetyl_coenzyme_A" component_2="reaction2" />
  <map_variables variable_1="Acetyl_coenzyme_A" variable_2="Acetyl_coenzyme_A" />
  <map_variables variable_1="delta_Acetyl_coenzyme_A_rxn2" variable_2="delta_Acetyl_coenzyme_A_rxn2" />
</connection>

<connection>
  <map_components component_1="Acetyl_coenzyme_A" component_2="reaction3" />
  <map_variables variable_1="Acetyl_coenzyme_A" variable_2="Acetyl_coenzyme_A" />
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<connection>
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<connection>
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  <map_components component_1="Isocitrate_dehydrogenase" component_2="global_variables" />
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<connection>
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<connection>
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<connection>
  <map_components component_1="Malate_dehydrogenase" component_2="reaction10" />
  <map_variables variable_1="Malate_dehydrogenase" variable_2="Malate_dehydrogenase" />
</connection>

<connection>
  <map_components component_1="Phosphoenolpyruvate_carboxykinase" component_2="reaction11" />
  <map_variables variable_1="Phosphoenolpyruvate_carboxykinase" variable_2="Phosphoenolpyruvate_carboxykinase" />
</connection>

<connection>
  <map_components component_1="Glutamate_dehydrogenase" component_2="reaction12" />
  <map_variables variable_1="Glutamate_dehydrogenase" variable_2="Glutamate_dehydrogenase" />
</connection>

</model>
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