

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

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

```
CREATED : 30th October 2002
```

```
LAST MODIFIED : 5th April 2003
```

```
AUTHOR : Catherine Lloyd  
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.
```

```
DESCRIPTION : This file contains a CellML description of Vojtek and Der's 1998 analysis of a
```

```
CHANGES:
```

```
05/04/2003 - AAC - Changed the model name so the model loads in the database  
easier.
```

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-->
```

```
<model name="Ras_cascade_1998" cmeta:id="Ras_cascade" xmlns="http://www.cellml.org/cellml/1.0" >  
<rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:bgs="http://www.cellml.org/cellml/1.0" >
```

```
<!--
```

```
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>
```

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<!--
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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>2002-10-30</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>
    Changed the model name so the model loads in the database easier.
  </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>2003-04-05</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 "Ras_cascade", which is declared on the
  <model> element.
-->
<rdf:Description rdf:about="#Ras_cascade">
  <!-- A human readable name for the model. -->
  <dc:title>
    Vojtek and Der's 1998 analysis of a Ras signalling pathway.
  </dc:title>

  <!-- A comment regarding the model. -->
  <cmeta:comment rdf:parseType="Resource">
    <rdf:value>
      This is the CellML description of Vojtek and Der's 1998 analysis of a
      Ras signalling pathway.
    </rdf:value>
    <!-- The creator of the comment. -->
    <dc:creator rdf:parseType="Resource">
      <vCard:FN>Catherine Lloyd</vCard:FN>
    </dc:creator>
  </cmeta:comment>

  <!-- Keyword(s) -->
  <bqs:reference rdf:parseType="Resource">
    <dc:subject rdf:parseType="Resource">
      <bqs:subject_type>keyword</bqs:subject_type>
      <rdf:value>signal transduction</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 such as Pubmed. All associated data such as author, journal title, date, etc can be looked up on the database.

-->

```
<bqs:reference rdf:parseType="Resource">
  <bqs:Pubmed_id>9685325</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>Vojtek</vCard:Family>
              <vCard:Given>Anne</vCard:Given>
              <vCard:Other>B</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>Der</vCard:Family>
              <vCard:Given>Channing</vCard:Given>
              <vCard:Other>J</vCard:Other>
            </vCard:N>
          </bqs:Person>
        </rdf:li>
      </rdf:Seq>
    </dc:creator>
    <dc:title>
      Increasing Complexity of the Ras Signaling Pathway
    </dc:title>
    <dcterms:issued rdf:parseType="Resource">
      <dcterms:W3CDTF>1998-08-07</dcterms:W3CDTF>
    </dcterms:issued>
    <bqs:Journal rdf:parseType="Resource">
      <dc:title>The Journal of Biological Chemistry</dc:title>
    </bqs:Journal>
    <bqs:volume>273</bqs:volume>
    <bqs:first_page>19925</bqs:first_page>
    <bqs:last_page>19928</bqs:last_page>
  </bqs:JournalArticle>
</bqs:reference>
</rdf:Description>
</rdf:RDF>
```

<!--

Below, we define some additional units for association with variables and constants within the model. The identifiers are fairly self-explanatory.

-->

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

<units name="flux">
```

```

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

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

<!--
  The "environment" component is used to declare variables that are used by
  all or most of the other components, in this case just "time".
-->

<component name="environment">
    <variable name="time" public_interface="out" units="second" />
</component>

<!--
  The following components describe all the reactants, products, enzymes,
  activators and inhibitors involved in the reactions.
-->

<component name="TRK" cmeta:id="TRK">
    <variable name="TRK" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_TRK_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>TRK</ci>
            </apply>
            <ci>delta_TRK_rxn0</ci>
        </apply>
    </math>
</component>

<component name="EGF" cmeta:id="EGF">
    <variable name="EGF" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_EGF_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>

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```

        <diff />
        <bvar>
            <ci>time</ci>
        </bvar>
        <ci>EGF</ci>
    </apply>
    <ci>delta_EGF_rxn0</ci>
</apply>
</math>
</component>

<component name="EGF_TRK_complex" cmeta:id="EGF_TRK_complex">
    <variable name="EGF_TRK_complex" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_EGF_TRK_complex_rxn0" public_interface="in" units="flux" />
    <variable name="delta_EGF_TRK_complex_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>EGF_TRK_complex</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_EGF_TRK_complex_rxn0</ci>
                <ci>delta_EGF_TRK_complex_rxn1</ci>
            </apply>
        </apply>
    </math>
</component>

<component name="Phosphate" cmeta:id="Phosphate">
    <variable name="Phosphate" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_Phosphate_rxn1" public_interface="in" units="flux" />
    <variable name="delta_Phosphate_rxn6" public_interface="in" units="flux" />
    <variable name="delta_Phosphate_rxn7" public_interface="in" units="flux" />
    <variable name="delta_Phosphate_rxn8" public_interface="in" units="flux" />
    <variable name="delta_Phosphate_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>Phosphate</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_Phosphate_rxn1</ci>
                <ci>delta_Phosphate_rxn6</ci>
                <ci>delta_Phosphate_rxn7</ci>
                <ci>delta_Phosphate_rxn8</ci>
            </apply>
        </math>
    </component>

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        <ci>delta_Phosphate_rxn9</ci>
    </apply>
</apply>
</math>
</component>

<component name="Phosphorylated_receptor_complex" cmeta:id="Phosphorylated_receptor_compl
    <variable name="Phosphorylated_receptor_complex" public_interface="out" initial_value=
    <variable name="delta_Phosphorylated_receptor_complex_rxn1" public_interface="in" units
    <variable name="delta_Phosphorylated_receptor_complex_rxn2" public_interface="in" units
    <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>Phosphorylated_receptor_complex</ci>
            </apply>
            <apply>
                <plus />
                <ci>delta_Phosphorylated_receptor_complex_rxn1</ci>
                <ci>delta_Phosphorylated_receptor_complex_rxn2</ci>
            </apply>
        </apply>
    </math>
</component>

<component name="GRB2" cmeta:id="GRB2">
    <variable name="GRB2" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_GRB2_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>GRB2</ci>
            </apply>
            <ci>delta_GRB2_rxn2</ci>
        </apply>
    </math>
</component>

<component name="SOS" cmeta:id="SOS">
    <variable name="SOS" public_interface="out" initial_value="1.0" units="micromolar" />
    <variable name="delta_SOS_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>

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        <ci>time</ci>
      </bvar>
      <ci>SOS</ci>
    </apply>
    <ci>delta_SOS_rxn2</ci>
  </apply>
</math>
</component>

<component name="Ras_GDP" cmeta:id="Ras_GDP">
  <variable name="Ras_GDP" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Ras_GDP_rxn3" public_interface="in" units="flux" />
  <variable name="delta_Ras_GDP_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>Ras_GDP</ci>
      </apply>
      <apply>
        <plus />
        <ci>delta_Ras_GDP_rxn3</ci>
        <ci>delta_Ras_GDP_rxn4</ci>
      </apply>
    </apply>
  </math>
</component>

<component name="active_receptor_complex" cmeta:id="active_receptor_complex">
  <variable name="active_receptor_complex" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_active_receptor_complex_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>active_receptor_complex</ci>
      </apply>
      <ci>delta_active_receptor_complex_rxn2</ci>
    </apply>
  </math>
</component>

<component name="Ras_GTP" cmeta:id="Ras_GTP">
  <variable name="Ras_GTP" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_Ras_GTP_rxn4" public_interface="in" units="flux" />
  <variable name="delta_Ras_GTP_rxn3" public_interface="in" units="flux" />
  <variable name="time" public_interface="in" units="second" />
  <math xmlns="http://www.w3.org/1998/Math/MathML">
    <apply>

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```

    <eq />
    <apply>
      <diff />
      <bvar>
        <ci>time</ci>
      </bvar>
      <ci>Ras_GTP</ci>
    </apply>
    <apply>
      <plus />
      <ci>delta_Ras_GTP_rxn4</ci>
      <ci>delta_Ras_GTP_rxn3</ci>
    </apply>
  </math>
</component>

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

<component name="inactive_Raf" cmeta:id="inactive_Raf">
  <variable name="inactive_Raf" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_inactive_Raf_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>inactive_Raf</ci>
      </apply>
      <ci>delta_inactive_Raf_rxn5</ci>
    </apply>
  </math>
</component>

<component name="active_Raf" cmeta:id="active_Raf">
  <variable name="active_Raf" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_active_Raf_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>active_Raf</ci>
      </apply>
      <ci>delta_active_Raf_rxn5</ci>
    </apply>
  </math>
</component>

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<component name="inactive_MEK" cmeta:id="inactive_MEK">
  <variable name="inactive_MEK" public_interface="out" initial_value="1.0" units="micromol">
  <variable name="delta_inactive_MEK_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>inactive_MEK</ci>
      </apply>
      <ci>delta_inactive_MEK_rxn6</ci>
    </apply>
  </math>
</component>

<component name="active_MEK" cmeta:id="active_MEK">
  <variable name="active_MEK" public_interface="out" initial_value="1.0" units="micromol">
  <variable name="delta_active_MEK_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>active_MEK</ci>
      </apply>
      <ci>delta_active_MEK_rxn6</ci>
    </apply>
  </math>
</component>

<component name="inactive_ERK" cmeta:id="inactive_ERK">
  <variable name="inactive_ERK" public_interface="out" initial_value="1.0" units="micromol">
  <variable name="delta_inactive_ERK_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>inactive_ERK</ci>
      </apply>
      <ci>delta_inactive_ERK_rxn7</ci>
    </apply>
  </math>
</component>

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

```

```

<variable name="active_ERK_i" public_interface="out" initial_value="1.0" units="micromol" />
<variable name="delta_active_ERK_i_rxn7" public_interface="in" units="flux" />
<variable name="delta_active_ERK_i_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>active_ERK_i</ci>
    </apply>
    <apply>
      <plus />
      <ci>delta_active_ERK_i_rxn7</ci>
      <ci>delta_active_ERK_i_rxn10</ci>
    </apply>
  </apply>
</math>
</component>

<component name="inactive_Mnk" cmeta:id="inactive_Mnk">
  <variable name="inactive_Mnk" public_interface="out" initial_value="1.0" units="micromol" />
  <variable name="delta_inactive_Mnk_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>inactive_Mnk</ci>
      </apply>
      <ci>delta_inactive_Mnk_rxn8</ci>
    </apply>
  </math>
</component>

<component name="active_Mnk" cmeta:id="active_Mnk">
  <variable name="active_Mnk" public_interface="out" initial_value="1.0" units="micromol" />
  <variable name="delta_active_Mnk_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>active_Mnk</ci>
      </apply>
      <ci>delta_active_Mnk_rxn8</ci>
    </apply>
  </math>

```

</component>

```
<component name="active_ERK_n" cmeta:id="active_ERK_n">
  <variable name="active_ERK_n" public_interface="out" initial_value="1.0" units="micromol" />
  <variable name="delta_active_ERK_n_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>active_ERK_n</ci>
      </apply>
      <ci>delta_active_ERK_n_rxn10</ci>
    </apply>
  </math>
</component>
```

```
<component name="inactive_Elk_1" cmeta:id="inactive_Elk_1">
  <variable name="inactive_Elk_1" public_interface="out" initial_value="1.0" units="micromol" />
  <variable name="delta_inactive_Elk_1_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>inactive_Elk_1</ci>
      </apply>
      <ci>delta_inactive_Elk_1_rxn9</ci>
    </apply>
  </math>
</component>
```

```
<component name="active_Elk_1" cmeta:id="active_Elk_1">
  <variable name="active_Elk_1" public_interface="out" initial_value="1.0" units="micromol" />
  <variable name="delta_active_Elk_1_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>active_Elk_1</ci>
      </apply>
      <ci>delta_active_Elk_1_rxn9</ci>
    </apply>
  </math>
</component>
```

```

<component name="DNA" cmeta:id="DNA">
  <variable name="DNA" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_DNA_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>DNA</ci>
      </apply>
      <ci>delta_DNA_rxn11</ci>
    </apply>
  </math>
</component>

<component name="mRNA" cmeta:id="mRNA">
  <variable name="mRNA" public_interface="out" initial_value="1.0" units="micromolar" />
  <variable name="delta_mRNA_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>mRNA</ci>
      </apply>
      <ci>delta_mRNA_rxn11</ci>
    </apply>
  </math>
</component>

<!--
  The following components describe the reactions of the model.
-->

<component name="reaction0">
  <variable name="TRK" public_interface="in" units="micromolar" />
  <variable name="EGF" public_interface="in" units="micromolar" />
  <variable name="EGF_TRK_complex" public_interface="in" units="micromolar" />
  <variable name="delta_TRK_rxn0" public_interface="out" units="flux" />
  <variable name="delta_EGF_rxn0" public_interface="out" units="flux" />
  <variable name="delta_EGF_TRK_complex_rxn0" public_interface="out" units="flux" />
  <variable name="k0" initial_value="1.0" units="second_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="TRK">
      <role role="reactant" delta_variable="delta_TRK_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="EGF">
      <role role="reactant" delta_variable="delta_EGF_rxn0" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="EGF_TRK_complex">

```

```

    <role role="product" delta_variable="delta_EGF_TRK_complex_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>
            <times />
            <ci>k0</ci>
            <ci>TRK</ci>
            <ci>EGF</ci>
          </apply>
        </apply>
      </math>
    </role>
  </variable_ref>
</reaction>
</component>

<component name="reaction1">
  <variable name="EGF_TRK_complex" public_interface="in" units="micromolar" />
  <variable name="Phosphate" public_interface="in" units="micromolar" />
  <variable name="Phosphorylated_receptor_complex" public_interface="in" units="micromolar" />
  <variable name="delta_EGF_TRK_complex_rxn1" public_interface="out" units="flux" />
  <variable name="delta_Phosphate_rxn1" public_interface="out" units="flux" />
  <variable name="delta_Phosphorylated_receptor_complex_rxn1" public_interface="out" units="flux" />
  <variable name="k1" initial_value="1.0" units="second_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="EGF_TRK_complex">
      <role role="reactant" delta_variable="delta_EGF_TRK_complex_rxn1" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Phosphate">
      <role role="reactant" delta_variable="delta_Phosphate_rxn1" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Phosphorylated_receptor_complex">
      <role role="product" delta_variable="delta_Phosphorylated_receptor_complex_rxn1" 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>
              <times />
              <ci>k1</ci>
              <ci>EGF_TRK_complex</ci>
              <ci>Phosphate</ci>
            </apply>
          </apply>
        </math>
      </role>
    </variable_ref>
  </reaction>
</component>

```

```

<component name="reaction2">
  <variable name="Phosphorylated_receptor_complex" public_interface="in" units="micromolar" />
  <variable name="GRB2" public_interface="in" units="micromolar" />
  <variable name="SOS" public_interface="in" units="micromolar" />
  <variable name="active_receptor_complex" public_interface="in" units="micromolar" />
  <variable name="delta_Phosphorylated_receptor_complex_rxn2" public_interface="out" units="flux" />
  <variable name="delta_GRB2_rxn2" public_interface="out" units="flux" />
  <variable name="delta_SOS_rxn2" public_interface="out" units="flux" />
  <variable name="delta_active_receptor_complex_rxn2" public_interface="out" units="flux" />
  <variable name="k2" initial_value="1.0" units="third_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="Phosphorylated_receptor_complex">
      <role role="reactant" delta_variable="delta_Phosphorylated_receptor_complex_rxn2" />
    </variable_ref>
    <variable_ref variable="GRB2">
      <role role="reactant" delta_variable="delta_GRB2_rxn2" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="SOS">
      <role role="reactant" delta_variable="delta_SOS_rxn2" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="active_receptor_complex">
      <role role="product" delta_variable="delta_active_receptor_complex_rxn2" 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>
              <times />
              <ci>k2</ci>
              <ci>Phosphorylated_receptor_complex</ci>
              <ci>GRB2</ci>
              <ci>SOS</ci>
            </apply>
          </apply>
        </math>
      </role>
    </variable_ref>
  </reaction>
</component>

```

```

<component name="reaction3">
  <variable name="Ras_GTP" public_interface="in" units="micromolar" />
  <variable name="Ras_GDP" public_interface="in" units="micromolar" />
  <variable name="GAP" public_interface="in" units="micromolar" />
  <variable name="delta_Ras_GTP_rxn3" public_interface="out" units="flux" />
  <variable name="delta_Ras_GDP_rxn3" public_interface="out" units="flux" />
  <variable name="km3" initial_value="1.0" units="micromolar" />
  <variable name="vmax3" initial_value="1.0" units="flux" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="Ras_GTP">
      <role role="reactant" delta_variable="delta_Ras_GTP_rxn3" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Ras_GDP">
      <role role="product" delta_variable="delta_Ras_GDP_rxn3" stoichiometry="1" />
    </variable_ref>
  </reaction>
</component>

```

```

</variable_ref>
<variable_ref variable="GAP">
  <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>Ras_GTP</ci>
            <ci>vmax3</ci>
          </apply>
          <apply>
            <plus />
            <ci>km3</ci>
            <ci>Ras_GTP</ci>
          </apply>
        </apply>
      </math>
    </role>
  </variable_ref>
</reaction>
</component>

<component name="reaction4">
  <variable name="Ras_GDP" public_interface="in" units="micromolar" />
  <variable name="Ras_GTP" public_interface="in" units="micromolar" />
  <variable name="active_receptor_complex" public_interface="in" units="micromolar" />
  <variable name="delta_Ras_GDP_rxn4" public_interface="out" units="flux" />
  <variable name="delta_Ras_GTP_rxn4" public_interface="out" units="flux" />
  <variable name="k4" initial_value="1.0" units="first_order_rate_constant" />
  <variable name="km4" initial_value="1.0" units="micromolar" />
  <variable name="vmax4" initial_value="1.0" units="flux" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="Ras_GDP">
      <role role="reactant" delta_variable="delta_Ras_GDP_rxn4" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Ras_GTP">
      <role role="product" delta_variable="delta_Ras_GTP_rxn4" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="active_receptor_complex">
      <role role="activator" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <apply>
            <eq />
            <ci>rate</ci>
            <apply>
              <times />
              <ci>k4</ci>
            </apply>
          </math>
        </role>
      </variable_ref>
    </reaction>
  </component>

```

```

    <ci>Ras_GDP</ci>
    <apply>
      <plus />
      <cn cellml:units="dimensionless">1.0</cn>
    <apply>
      <times />
      <apply>
        <minus />
        <ci>vmax4</ci>
        <cn cellml:units="dimensionless">1.0</cn>
      </apply>
    <apply>
      <minus />
      <cn cellml:units="dimensionless">1.0</cn>
    <apply>
      <exp />
      <apply>
        <minus />
        <apply>
          <divide />
          <ci>active_receptor_complex</ci>
          <ci>km4</ci>
        </apply>
      </apply>
    </apply>
  </apply>
</math>
</role>
</variable_ref>
</reaction>
</component>

```

```

<component name="reaction5">
  <variable name="inactive_Raf" public_interface="in" units="micromolar" />
  <variable name="active_Raf" public_interface="in" units="micromolar" />
  <variable name="Ras_GTP" public_interface="in" units="micromolar" />
  <variable name="delta_inactive_Raf_rxn5" public_interface="out" units="flux" />
  <variable name="delta_active_Raf_rxn5" public_interface="out" units="flux" />
  <variable name="k5" initial_value="1.0" units="first_order_rate_constant" />
  <variable name="km5" initial_value="1.0" units="micromolar" />
  <variable name="vmax5" initial_value="1.0" units="flux" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="inactive_Raf">
      <role role="reactant" delta_variable="delta_inactive_Raf_rxn5" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="active_Raf">
      <role role="product" delta_variable="delta_active_Raf_rxn5" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Ras_GTP">
      <role role="activator" />
    </variable_ref>
    <variable_ref variable="rate">
      <role role="rate">
        <math xmlns="http://www.w3.org/1998/Math/MathML">

```

```

    <apply>
      <eq />
      <ci>rate</ci>
      <apply>
        <times />
        <ci>k5</ci>
        <ci>inactive_Raf</ci>
        <apply>
          <plus />
          <cn cellml:units="dimensionless">1.0</cn>
          <apply>
            <times />
            <apply>
              <minus />
              <ci>vmax5</ci>
              <cn cellml:units="dimensionless">1.0</cn>
            </apply>
          </apply>
          <apply>
            <minus />
            <cn cellml:units="dimensionless">1.0</cn>
          </apply>
          <apply>
            <exp />
            <apply>
              <minus />
              <apply>
                <divide />
                <ci>Ras_GTP</ci>
                <ci>km5</ci>
              </apply>
            </apply>
          </apply>
        </apply>
      </apply>
    </math>
  </role>
</variable_ref>
</reaction>
</component>

<component name="reaction6">
  <variable name="inactive_MEK" public_interface="in" units="micromolar" />
  <variable name="Phosphate" public_interface="in" units="micromolar" />
  <variable name="active_MEK" public_interface="in" units="micromolar" />
  <variable name="active_Raf" public_interface="in" units="micromolar" />
  <variable name="delta_inactive_MEK_rxn6" public_interface="out" units="flux" />
  <variable name="delta_active_MEK_rxn6" public_interface="out" units="flux" />
  <variable name="delta_Phosphate_rxn6" public_interface="out" units="flux" />
  <variable name="km6" initial_value="1.0" units="micromolar" />
  <variable name="vmax6" initial_value="1.0" units="flux" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="inactive_MEK">
      <role role="reactant" delta_variable="delta_inactive_MEK_rxn6" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Phosphate">
      <role role="reactant" delta_variable="delta_Phosphate_rxn6" stoichiometry="1" />
    </variable_ref>
  </reaction>
</component>

```

```

</variable_ref>
<variable_ref variable="active_MEK">
  <role role="product" delta_variable="delta_active_MEK_rxn6" stoichiometry="1" />
</variable_ref>
<variable_ref variable="active_Raf">
  <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>inactive_MEK</ci>
            <ci>Phosphate</ci>
            <ci>vmax6</ci>
          </apply>
          <apply>
            <plus />
            <ci>km6</ci>
            <ci>inactive_MEK</ci>
            <ci>Phosphate</ci>
          </apply>
        </apply>
      </math>
    </role>
  </variable_ref>
</reaction>
</component>

<component name="reaction7">
  <variable name="inactive_ERK" public_interface="in" units="micromolar" />
  <variable name="Phosphate" public_interface="in" units="micromolar" />
  <variable name="active_ERK_i" public_interface="in" units="micromolar" />
  <variable name="active_MEK" public_interface="in" units="micromolar" />
  <variable name="delta_inactive_ERK_rxn7" public_interface="out" units="flux" />
  <variable name="delta_active_ERK_i_rxn7" public_interface="out" units="flux" />
  <variable name="delta_Phosphate_rxn7" public_interface="out" units="flux" />
  <variable name="km7" initial_value="1.0" units="micromolar" />
  <variable name="vmax7" initial_value="1.0" units="flux" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="inactive_ERK">
      <role role="reactant" delta_variable="delta_inactive_ERK_rxn7" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Phosphate">
      <role role="reactant" delta_variable="delta_Phosphate_rxn7" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="active_ERK_i">
      <role role="product" delta_variable="delta_active_ERK_i_rxn7" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="active_MEK">
      <role role="catalyst" />
    </variable_ref>
  </reaction>

```

```

<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>inactive_ERK</ci>
            <ci>Phosphate</ci>
            <ci>vmax7</ci>
          </apply>
          <apply>
            <plus />
            <ci>km7</ci>
            <ci>inactive_ERK</ci>
            <ci>Phosphate</ci>
          </apply>
        </apply>
      </math>
    </role>
  </variable_ref>
</reaction>
</component>

```

```

<component name="reaction8">
  <variable name="inactive_Mnk" public_interface="in" units="micromolar" />
  <variable name="Phosphate" public_interface="in" units="micromolar" />
  <variable name="active_Mnk" public_interface="in" units="micromolar" />
  <variable name="active_ERK_i" public_interface="in" units="micromolar" />
  <variable name="delta_inactive_Mnk_rxn8" public_interface="out" units="flux" />
  <variable name="delta_active_Mnk_rxn8" public_interface="out" units="flux" />
  <variable name="delta_Phosphate_rxn8" public_interface="out" units="flux" />
  <variable name="km8" initial_value="1.0" units="micromolar" />
  <variable name="vmax8" initial_value="1.0" units="flux" />
  <variable name="rate" units="flux" />
  <reaction reversible="no">
    <variable_ref variable="inactive_Mnk">
      <role role="reactant" delta_variable="delta_inactive_Mnk_rxn8" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="Phosphate">
      <role role="reactant" delta_variable="delta_Phosphate_rxn8" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="active_Mnk">
      <role role="product" delta_variable="delta_active_Mnk_rxn8" stoichiometry="1" />
    </variable_ref>
    <variable_ref variable="active_ERK_i">
      <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>
        </math>
      </role>
    </variable_ref>
  </reaction>

```

```

        <divide />
        <apply>
            <times />
            <ci>inactive_Mnk</ci>
            <ci>Phosphate</ci>
            <ci>vmax8</ci>
        </apply>
    </apply>
    <apply>
        <plus />
        <ci>km8</ci>
        <ci>inactive_Mnk</ci>
        <ci>Phosphate</ci>
    </apply>
</apply>
</math>
</role>
</variable_ref>
</reaction>
</component>

<component name="reaction9">
    <variable name="inactive_Elk_1" public_interface="in" units="micromolar" />
    <variable name="active_Elk_1" public_interface="in" units="micromolar" />
    <variable name="Phosphate" public_interface="in" units="micromolar" />
    <variable name="active_ERK_n" public_interface="in" units="micromolar" />
    <variable name="delta_inactive_Elk_1_rxn9" public_interface="out" units="flux" />
    <variable name="delta_active_Elk_1_rxn9" public_interface="out" units="flux" />
    <variable name="delta_Phosphate_rxn9" public_interface="out" units="flux" />
    <variable name="km9" initial_value="1.0" units="micromolar" />
    <variable name="vmax9" initial_value="1.0" units="flux" />
    <variable name="rate" units="flux" />
    <reaction reversible="no">
        <variable_ref variable="inactive_Elk_1">
            <role role="reactant" delta_variable="delta_inactive_Elk_1_rxn9" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="Phosphate">
            <role role="reactant" delta_variable="delta_Phosphate_rxn9" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="active_Elk_1">
            <role role="product" delta_variable="delta_active_Elk_1_rxn9" stoichiometry="1" />
        </variable_ref>
        <variable_ref variable="active_ERK_n">
            <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>inactive_Elk_1</ci>
                                <ci>Phosphate</ci>
                                <ci>vmax9</ci>
                            </apply>
                        </apply>
                    </math>
                </role>
            </variable_ref>
        </reaction>
    </component>

```

```

        <apply>
          <plus />
          <ci>km9</ci>
          <ci>inactive_Elk_1</ci>
          <ci>Phosphate</ci>
        </apply>
      </apply>
    </apply>
  </math>
</role>
</variable_ref>
</reaction>
</component>

<component name="reaction10">
  <variable name="active_ERK_i" public_interface="in" units="micromolar" />
  <variable name="active_ERK_n" public_interface="in" units="micromolar" />
  <variable name="delta_active_ERK_i_rxn10" public_interface="out" units="flux" />
  <variable name="delta_active_ERK_n_rxn10" public_interface="out" units="flux" />
  <variable name="k10" initial_value="1.0" units="first_order_rate_constant" />
  <variable name="k10_" initial_value="1.0" units="first_order_rate_constant" />
  <variable name="rate" units="flux" />
  <reaction reversible="yes">
    <variable_ref variable="active_ERK_i">
      <role role="reactant" direction="forward" delta_variable="delta_active_ERK_i_rxn10" />
    </variable_ref>
    <variable_ref variable="active_ERK_n">
      <role role="product" direction="forward" delta_variable="delta_active_ERK_n_rxn10" />
    </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>k10</ci>
                <ci>active_ERK_i</ci>
              </apply>
              <apply>
                <minus />
                <apply>
                  <times />
                  <ci>k10_</ci>
                  <ci>active_ERK_n</ci>
                </apply>
              </apply>
            </apply>
          </math>
        </role>
      </variable_ref>
    </reaction>
  </component>

<component name="reaction11">

```

```

<variable name="DNA" public_interface="in" units="micromolar" />
<variable name="mRNA" public_interface="in" units="micromolar" />
<variable name="active_Elk_1" public_interface="in" units="micromolar" />
<variable name="delta_DNA_rxn11" public_interface="out" units="flux" />
<variable name="delta_mRNA_rxn11" public_interface="out" units="flux" />
<variable name="k11" initial_value="1.0" units="first_order_rate_constant" />
<variable name="km11" initial_value="1.0" units="micromolar" />
<variable name="vmax11" initial_value="1.0" units="flux" />
<variable name="rate" units="flux" />
<reaction reversible="no">
  <variable_ref variable="DNA">
    <role role="reactant" delta_variable="delta_DNA_rxn11" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="mRNA">
    <role role="product" delta_variable="delta_mRNA_rxn11" stoichiometry="1" />
  </variable_ref>
  <variable_ref variable="active_Elk_1">
    <role role="activator" />
  </variable_ref>
  <variable_ref variable="rate">
    <role role="rate">
      <math xmlns="http://www.w3.org/1998/Math/MathML">
        <apply>
          <eq />
          <ci>rate</ci>
          <apply>
            <times />
            <ci>k11</ci>
            <ci>DNA</ci>
            <apply>
              <plus />
              <cn cellml:units="dimensionless">1.0</cn>
            <apply>
              <times />
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                <ci>vmax11</ci>
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                  <divide />
                  <ci>active_Elk_1</ci>
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        </math>
      </role>
    </variable_ref>
  </reaction>

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        </role>
      </variable_ref>
    </reaction>
  </component>

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  <connection>
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  <connection>
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  <connection>
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<connection>
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<connection>
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  </connection>

</model>
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