1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah and Hannes Hettling at January 26th 2012 at 1:59 p.m. and last time modified at February 25th 2015 at 12:27 a.m. Table 1 shows an overview of the quantities of all components of this model.

Table 1: Number of components in this model, which are described in the following sections.

<table>
<thead>
<tr>
<th>Element</th>
<th>Quantity</th>
<th>Element</th>
<th>Quantity</th>
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Model Notes

This model is from the article:

Analyzing the functional properties of the creatine kinase system with multiscale 'sloppy' modeling.


Abstract:

1EMBL-EBI, viji@ebi.ac.uk
2VU University Amsterdam, hettling@few.vu.nl
In this study the function of the two isoforms of creatine kinase (CK; EC 2.7.3.2) in myocardium is investigated. The ‘phosphocreatine shuttle’ hypothesis states that mitochondrial and cytosolic CK plays a pivotal role in the transport of high-energy phosphate (HEP) groups from mitochondria to myofibrils in contracting muscle. Temporal buffering of changes in ATP and ADP is another potential role of CK. With a mathematical model, we analyzed energy transport and damping of high peaks of ATP hydrolysis during the cardiac cycle. The analysis was based on multiscale data measured at the level of isolated enzymes, isolated mitochondria and on dynamic response times of oxidative phosphorylation measured at the whole heart level. Using ‘sloppy modeling’ ensemble simulations, we derived confidence intervals for predictions of the contributions by phosphocreatine (PCr) and ATP to the transfer of HEP from mitochondria to sites of ATP hydrolysis. Our calculations indicate that only 158% (meanSD) of transcytosolic energy transport is carried by PCr, contradicting the PCr shuttle hypothesis. We also predicted temporal buffering capabilities of the CK isoforms protecting against high peaks of ATP hydrolysis (3750 M*s(-1)) in myofibrils. CK inhibition by 98% in silico leads to an increase in amplitude of mitochondrial ATP synthesis pulsation from 21523 to 56631 M*s(-1), while amplitudes of oscillations in cytosolic ADP concentration double from 7711 to 1461 M. Our findings indicate that CK acts as a large bandwidth high-capacity temporal energy buffer maintaining cellular ATP homeostasis and reducing oscillations in mitochondrial metabolism. However, the contribution of CK to the transport of high-energy phosphate groups appears limited. Mitochondrial CK activity lowers cytosolic inorganic phosphate levels while cytosolic CK has the opposite effect.

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2 Unit Definitions

This is an overview of ten unit definitions of which five are predefined by SBML and not mentioned in the model.

2.1 Unit micromole
Definition µmol

2.2 Unit micromole_per_litre
Definition µmol·l⁻¹

2.3 Unit micromole_per_litre_per_second
Definition µmol·l⁻¹·s⁻¹
2.4 Unit Name per_minute
   Definition (60 s)$^{-1}$

2.5 Unit Name per_second
   Definition s$^{-1}$

2.6 Unit Notes Mole is the predefined SBML unit for substance.
   Name substance
   Definition mol

2.7 Unit Notes Litre is the predefined SBML unit for volume.
   Name volume
   Definition l

2.8 Unit Notes Square metre is the predefined SBML unit for area since SBML Level 2 Version 1.
   Name area
   Definition m$^2$

2.9 Unit Notes Metre is the predefined SBML unit for length since SBML Level 2 Version 1.
   Name length
   Definition m

2.10 Unit Notes Second is the predefined SBML unit for time.
    Name time
    Definition s

3 Compartments

This model contains three compartments.
Table 2: Properties of all compartments.

<table>
<thead>
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<th>Spatial Dimensions</th>
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<th>Unit</th>
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3.1 **Compartment** IMS

This is a three dimensional compartment with a constant size of 0.0625 litre.

**Name** IMS

3.2 **Compartment** CYT

This is a three dimensional compartment with a constant size of 0.75 litre.

**Name** CYT

3.3 **Compartment** cell

This is a three dimensional compartment with a constant size of one litre.

**Name** cell
4 Species

This model contains ten species. Section 9 provides further details and the derived rates of change of each species.

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5 Parameters

This model contains 57 global parameters.

Table 4: Properties of each parameter.

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### 6 Rules

This is an overview of 20 rules.

**Produced by SML2TEX**
6.1 Rule \textit{tmito}

Rule \textit{tmito} is a rate rule for parameter \textit{tmito}:

\[
\frac{d}{dt} tmito = vatpnorm \tag{1}
\]

6.2 Rule \textit{densyn}

Rule \textit{densyn} is an assignment rule for parameter \textit{densyn}:

\[
densyn = 1 + \frac{[ADPi]}{Kadp} + \frac{[P_{ii}]}{Kpi} + \frac{[ADPi] \cdot [P_{ii}]}{Kadp \cdot Kpi} \tag{2}
\]

6.3 Rule \textit{jsyn}

Rule \textit{jsyn} is an assignment rule for parameter \textit{jsyn}:

\[
jsyn = V_{maxsyn} \cdot \frac{[ADPi] \cdot [P_{ii}]}{Kpi \cdot Kadp \cdot densyn} \tag{3}
\]

6.4 Rule \textit{vatpnorm}

Rule \textit{vatpnorm} is an assignment rule for parameter \textit{vatpnorm}:

\[
vatpnorm = tmito\_factor \cdot \frac{J_{hyd\_test} - jsyn}{J_{hyd\_test} - J_{hyd\_basis}} \tag{4}
\]

6.5 Rule \textit{VmaxMif}

Rule \textit{VmaxMif} is an assignment rule for parameter \textit{VmaxMif}:

\[
V_{maxMif} = V_{maxMif\_full\_activity} \cdot ck\_factor\_iaa \tag{5}
\]

6.6 Rule \textit{VmaxMMf}

Rule \textit{VmaxMMf} is an assignment rule for parameter \textit{VmaxMMf}:

\[
V_{maxMMf} = V_{maxMMf\_full\_activity} \cdot ck\_factor\_iaa \tag{6}
\]

6.7 Rule \textit{VmaxMib}

Rule \textit{VmaxMib} is an assignment rule for parameter \textit{VmaxMib}:

\[
V_{maxMib} = \frac{K_{CK\_eq} \cdot KicMi \cdot KdMi \cdot V_{maxMif}}{KiaMi \cdot KbMi} \tag{7}
\]
6.8 Rule $V_{\text{maxMMb}}$

Rule $V_{\text{maxMMb}}$ is an assignment rule for parameter $V_{\text{maxMMb}}$:

$$V_{\text{maxMMb}} = \frac{K_{\text{CK, eq}} \cdot K_{\text{icMM}} \cdot K_{\text{dMM}} \cdot V_{\text{maxMMf}}}{K_{\text{iaMM}} \cdot K_{\text{bMM}}}$$  \hspace{1cm} (8)

6.9 Rule $j_{\text{diff_pcr}}$

Rule $j_{\text{diff_pcr}}$ is an assignment rule for parameter $j_{\text{diff_pcr}}$:

$$j_{\text{diff_pcr}} = PS_{\text{momPCr}} \cdot ([PCri] - [PCr])$$  \hspace{1cm} (9)

Derived unit $s^{-1} \cdot \mu\text{mol} \cdot l^{-1}$

6.10 Rule $j_{\text{diff_atp}}$

Rule $j_{\text{diff_atp}}$ is an assignment rule for parameter $j_{\text{diff_atp}}$:

$$j_{\text{diff_atp}} = PS_{\text{momATP}} \cdot ([ATPi] - [ATP])$$  \hspace{1cm} (10)

Derived unit $s^{-1} \cdot \mu\text{mol} \cdot l^{-1}$

6.11 Rule $r_{\text{diff_pcr}}$

Rule $r_{\text{diff_pcr}}$ is an assignment rule for parameter $r_{\text{diff_pcr}}$:

$$r_{\text{diff_pcr}} = \frac{j_{\text{diff_pcr}}}{j_{\text{diff_pcr}} + j_{\text{diff_atp}}}$$  \hspace{1cm} (11)

Derived unit dimensionless

6.12 Rule $\text{phase}$

Rule $\text{phase}$ is an assignment rule for parameter $\text{phase}$:

$$\text{phase} = \frac{|t - \text{time}_{\text{Jhyd_step}}| - \frac{|\text{time}_{\text{Jhyd_step}}|}{60 \text{ heartrate BPM}}}{60 \text{ heartrate BPM}}$$  \hspace{1cm} (12)

6.13 Rule $\text{fracDia}$

Rule $\text{fracDia}$ is an assignment rule for parameter $\text{fracDia}$:

$$\text{fracDia} = 1 - \text{fracSysUp} - \text{fracSysDown}$$  \hspace{1cm} (13)
6.14 Rule VhydAmp\_basis

Rule VhydAmp\_basis is an assignment rule for parameter VhydAmp\_basis:

\[
VhydAmp\_basis = \frac{2 \cdot Jhyd\_basis}{\text{fracSysUp} + \text{fracSysDown}} \tag{14}
\]

6.15 Rule VhydAmp\_test

Rule VhydAmp\_test is an assignment rule for parameter VhydAmp\_test:

\[
VhydAmp\_test = \frac{2 \cdot Jhyd\_test}{\text{fracSysUp} + \text{fracSysDown}} \tag{15}
\]

6.16 Rule j\_ck\_mi

Rule j\_ck\_mi is an assignment rule for parameter j\_ck\_mi:

\[
j\_ck\_mi = \frac{V_{\text{maxMif}} / [\text{ATP}] \cdot [\text{Cr}]}{K_{\text{iaMM}} \cdot K_{\text{BM}}} - \frac{V_{\text{maxMib}} / [\text{ADP}] \cdot [\text{PCr}]}{K_{\text{icMM}} \cdot K_{\text{DM}}} = \frac{1}{1 + \frac{[\text{Cr}]}{K_{\text{iaMM}}} + \frac{[\text{PCr}]}{K_{\text{icMM}}} + [\text{ATP}] \cdot \left( \frac{1}{K_{\text{iaMM}}} + \frac{[\text{Cr}]}{K_{\text{iaMM}} \cdot K_{\text{BM}}} \right)} + [\text{ADP}] \cdot \left( \frac{1}{K_{\text{icMM}}} + \frac{[\text{Cr}]}{K_{\text{icMM}} \cdot K_{\text{BM}}} + \frac{[\text{PCr}]}{K_{\text{icMM}} \cdot K_{\text{BM}}} \right) \tag{16}
\]

6.17 Rule j\_ck\_mm

Rule j\_ck\_mm is an assignment rule for parameter j\_ck\_mm:

\[
j\_ck\_mm = \frac{V_{\text{maxMMf}} / [\text{ATP}] \cdot [\text{Cr}]}{K_{\text{iaMM}} \cdot K_{\text{BM}}} - \frac{V_{\text{maxMMb}} / [\text{ADP}] \cdot [\text{PCr}]}{K_{\text{icMM}} \cdot K_{\text{DM}}} = \frac{1}{1 + \frac{[\text{Cr}]}{K_{\text{iaMM}}} + \frac{[\text{PCr}]}{K_{\text{icMM}}} + [\text{ATP}] \cdot \left( \frac{1}{K_{\text{iaMM}}} + \frac{[\text{Cr}]}{K_{\text{iaMM}} \cdot K_{\text{BM}}} \right)} + [\text{ADP}] \cdot \left( \frac{1}{K_{\text{icMM}}} + \frac{[\text{Cr}]}{K_{\text{icMM}} \cdot K_{\text{BM}}} + \frac{[\text{PCr}]}{K_{\text{icMM}} \cdot K_{\text{BM}}} \right) \tag{17}
\]

6.18 Rule j\_diff\_adp

Rule j\_diff\_adp is an assignment rule for parameter j\_diff\_adp:

\[
j\_diff\_adp = \text{PSmomATP} \cdot ([\text{ADPi}] - [\text{ADP}]) \tag{18}
\]

**Derived unit** $s^{-1} \cdot \mu\text{mol} \cdot \text{l}^{-1}$

6.19 Rule j\_diff\_pi

Rule j\_diff\_pi is an assignment rule for parameter j\_diff\_pi:

\[
j\_diff\_pi = \text{PSmomPi} \cdot ([\text{P}\_ii] - [\text{P}\_i]) \tag{19}
\]

**Derived unit** $s^{-1} \cdot \mu\text{mol} \cdot \text{l}^{-1}$
6.20 Rule \textit{j\_diff\_cr}

Rule \textit{j\_diff\_cr} is an assignment rule for parameter \textit{j\_diff\_cr}:

\[ j_{\text{diff\_cr}} = P_{\text{SmomCr}} \cdot ([\text{Cri}] - [\text{Cr}]) \]  \hspace{1cm} (20)

\textbf{Derived unit} \: s^{-1} \cdot \mu\text{mol} \cdot l^{-1}

7 Events

This is an overview of three events. Each event is initiated whenever its trigger condition switches from \textit{false} to \textit{true}. A delay function postpones the effects of an event to a later time point. At the time of execution, an event can assign values to species, parameters or compartments if these are not set to constant.

7.1 Event \textit{event\_0}

\textbf{Name} pulsatile\_test

\textbf{Trigger condition}

\[ ((t \geq \text{time\_Jhyd\_step}) \land (t - \text{last\_time\_fired} > \text{stepsize})) \land (\text{pulsatility} = 1) \]  \hspace{1cm} (21)

\textbf{Delay}

\[ 0 \]  \hspace{1cm} (22)

\textbf{Assignments}

\[
\begin{align*}
J_{\text{hyd}} &= \begin{cases} 
(1 - \frac{\text{phase} - \text{fracSysUp}}{\text{fracSysDown}}) \cdot V_{\text{hyd\_Amp\_test}} & \text{if } \text{phase} > \text{fracSysUp} \land \text{phase} \leq 1 - \text{fracDia} \\
\frac{\text{phase}}{\text{fracSysUp}} \cdot V_{\text{hyd\_Amp\_test}} & \text{if } \text{phase} \leq \text{fracSysUp} \\
0 & \text{if } \text{phase} \geq 1 - \text{fracDia} \\
J_{\text{hyd}} & \text{otherwise}
\end{cases} 
\end{align*}
\]  \hspace{1cm} (23)

\text{last\_time\_fired} = t  \hspace{1cm} (24)

7.2 Event \textit{event\_1}

\textbf{Name} pulsatile\_basis

\textbf{Trigger condition}

\[ ((t < \text{time\_Jhyd\_step}) \land (t - \text{last\_time\_fired} \geq \text{stepsize})) \land (\text{pulsatility} = 1) \]  \hspace{1cm} (25)

\textbf{Delay}

\[ 0 \]  \hspace{1cm} (26)
Assignments

\[
J_{hyd} = \begin{cases} 
0 & \text{if phase} \leq \text{fracDia} \\
\frac{\text{phase} - \text{fracDia}}{\text{fracSysDown}} \cdot \text{V}_{hydAmp\_basis} & \text{if } (\text{phase} > \text{fracDia}) \land (\text{phase} \leq 1 - \text{fracSysUp}) \\
\frac{(1 - \text{phase}) \cdot \text{V}_{hydAmp\_basis}}{\text{fracSysUp}} & \text{if } \text{phase} > 1 - \text{fracSysUp} \\
J_{hyd} & \text{otherwise} 
\end{cases}
\]  

(27)

\[\text{last\_time\_fired} = t\]  

(28)

7.3 Event event_2

Name  nonpulsatile\_step

Trigger condition  

\[t \geq \text{time\_Jhyd\_step}\]  

(29)

Delay  

\[0\]  

(30)

Assignments

\[J_{hyd} = \begin{cases} 
J_{hyd\_test} & \text{if pulsatility} = 0 \\
J_{hyd} & \text{otherwise} 
\end{cases}\]  

(31)

\[\text{heartrate\_bpm} = \text{heartrate\_test}\]  

(32)

\[\text{tmito\_factor} = 1\]  

(33)
8 Reactions

This model contains nine reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

<table>
<thead>
<tr>
<th>№</th>
<th>Id</th>
<th>Name</th>
<th>Reaction Equation</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Jsyn</td>
<td>P_ii + ADPi ⇐⇒ ATPi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>J_CK_Mi</td>
<td>ATPi + Cri ⇐⇒ PCri + ADPi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>J_CK_MM</td>
<td>Cr + ATP ⇐⇒ PCr + ADP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Jhyd_reaction</td>
<td>ATP ⇐⇒ ADP + P_i</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>J_diff_Pi</td>
<td>Pi ⇐⇒ Pi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>J_diff_Cr</td>
<td>Cri ⇐⇒ Cr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>J_diff_ADP</td>
<td>ADPi ⇐⇒ ADP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>J_diff_PCr</td>
<td>PCri ⇐⇒ PCr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>J_diff_ATP</td>
<td>ATPi ⇐⇒ ATP</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
8.1 Reaction $J_{syn}$

This is a reversible reaction of two reactants forming one product.

**Reaction equation**

$$P_{ii} + ADPi \rightleftharpoons ATPi \quad (34)$$

**Reactants**

Table 6: Properties of each reactant.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{ii}$</td>
<td>$P_{ii}$</td>
<td></td>
</tr>
<tr>
<td>ADPi</td>
<td>ADPi</td>
<td></td>
</tr>
</tbody>
</table>

**Product**

Table 7: Properties of each product.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATPi</td>
<td>ATPi</td>
<td></td>
</tr>
</tbody>
</table>

**Kinetic Law**

**Derived unit** contains undeclared units

$$v_1 = \frac{V_{maxsyn} \cdot [ADPi] \cdot [P_{ii}]}{K_{adp} \cdot K_{pi} \cdot \left(1 + \frac{[ADPi]}{K_{adp}} + \frac{[P_{ii}]}{K_{pi}} + \frac{[ADPi] \cdot [P_{ii}]}{K_{adp} K_{pi}}\right)} \quad (35)$$

8.2 Reaction $J_{CK, Mi}$

This is a reversible reaction of two reactants forming two products.

**Reaction equation**

$$ATPi + Cri \rightleftharpoons PCri + ADPi \quad (36)$$

**Reactants**
Table 8: Properties of each reactant.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP</td>
<td>ATP</td>
<td></td>
</tr>
<tr>
<td>Cri</td>
<td>Cri</td>
<td></td>
</tr>
</tbody>
</table>

Products

Table 9: Properties of each product.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCri</td>
<td>PCri</td>
<td></td>
</tr>
<tr>
<td>ADPi</td>
<td>ADPi</td>
<td></td>
</tr>
</tbody>
</table>

Kinetic Law

Derived unit $\mu$mol $\cdot$1$^{-1}$ $\cdot$s$^{-1}$

$$v_2 = j_{ck} \_mi$$ (37)

8.3 Reaction $J\_CK\_MM$

This is a reversible reaction of two reactants forming two products.

Reaction equation

$$Cr + ATP \rightleftharpoons PCr + ADP$$ (38)

Reactants

Table 10: Properties of each reactant.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr</td>
<td>Cr</td>
<td></td>
</tr>
<tr>
<td>ATP</td>
<td>ATP</td>
<td></td>
</tr>
</tbody>
</table>

Products
### Table 11: Properties of each product.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCr</td>
<td>PCr</td>
<td></td>
</tr>
<tr>
<td>ADP</td>
<td>ADP</td>
<td></td>
</tr>
</tbody>
</table>

**Kinetic Law**

**Derived unit** $\mu\text{mol} \cdot \text{l}^{-1} \cdot \text{s}^{-1}$

\[
v_3 = j_{\text{ck_mm}}
\]  

(39)

### 8.4 Reaction Jhyd_reaction

This is a reversible reaction of one reactant forming two products.

**Reaction equation**

\[
\text{ATP} \rightleftharpoons \text{ADP} + \text{P}_i
\]

(40)

### Reactant

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP</td>
<td>ATP</td>
<td></td>
</tr>
</tbody>
</table>

### Products

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADP</td>
<td>ADP</td>
<td></td>
</tr>
<tr>
<td>P_i</td>
<td>P_i</td>
<td></td>
</tr>
</tbody>
</table>

**Kinetic Law**

**Derived unit** $\mu\text{mol} \cdot \text{l}^{-1} \cdot \text{s}^{-1}$

\[
v_4 = \text{Jhyd}
\]

(41)
8.5 Reaction $J_{\text{diff.Pi}}$

This is a reversible reaction of one reactant forming one product.

**Reaction equation**

\[ P_{\text{ii}} \rightleftharpoons P_{\text{i}} \]  \hspace{1cm} (42)

**Reactant**

Table 14: Properties of each reactant.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{\text{ii}}$</td>
<td>$P_{\text{ii}}$</td>
<td></td>
</tr>
</tbody>
</table>

**Product**

Table 15: Properties of each product.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{\text{i}}$</td>
<td>$P_{\text{i}}$</td>
<td></td>
</tr>
</tbody>
</table>

**Kinetic Law**

Derived unit $\mu\text{mol} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$

\[ v_S = j_{\text{diff.p}} \]  \hspace{1cm} (43)

8.6 Reaction $J_{\text{diff.Cr}}$

This is a reversible reaction of one reactant forming one product.

**Reaction equation**

\[ C_{\text{ri}} \rightleftharpoons C_{\text{r}} \]  \hspace{1cm} (44)

**Reactant**

Table 16: Properties of each reactant.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{ri}}$</td>
<td>$C_{\text{ri}}$</td>
<td></td>
</tr>
</tbody>
</table>
Product

Table 17: Properties of each product.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr</td>
<td>Cr</td>
<td></td>
</tr>
</tbody>
</table>

Kinetic Law

Derived unit $\mu$mol·l$^{-1}$·s$^{-1}$

$$v_6 = j_{\text{diff} \_cr} \quad (45)$$

8.7 Reaction $j_{\text{diff} \_ADP}$

This is a reversible reaction of one reactant forming one product.

Reaction equation

$$ADPi \rightleftharpoons ADP \quad (46)$$

Reactant

Table 18: Properties of each reactant.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADPi</td>
<td>ADPi</td>
<td></td>
</tr>
</tbody>
</table>

Product

Table 19: Properties of each product.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADP</td>
<td>ADP</td>
<td></td>
</tr>
</tbody>
</table>

Kinetic Law

Derived unit $\mu$mol·l$^{-1}$·s$^{-1}$

$$v_7 = j_{\text{diff} \_adp} \quad (47)$$
8.8 Reaction $J_{\text{diff} \_\text{PCr}}$

This is a reversible reaction of one reactant forming one product.

**Reaction equation**

\[
\text{PCr} \rightleftharpoons \text{PCr} \quad (48)
\]

**Reactant**

Table 20: Properties of each reactant.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCr</td>
<td>PCr</td>
<td></td>
</tr>
</tbody>
</table>

**Product**

Table 21: Properties of each product.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCr</td>
<td>PCr</td>
<td></td>
</tr>
</tbody>
</table>

**Kinetic Law**

**Derived unit** $\mu \text{mol} \cdot \text{L}^{-1} \cdot \text{s}^{-1}$

\[
v_8 = j_{\text{diff} \_\text{pcr}} \quad (49)
\]

8.9 Reaction $J_{\text{diff} \_\text{ATP}}$

This is a reversible reaction of one reactant forming one product.

**Reaction equation**

\[
\text{ATP}^i \rightleftharpoons \text{ATP} \quad (50)
\]

**Reactant**

Table 22: Properties of each reactant.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATPi</td>
<td>ATPi</td>
<td></td>
</tr>
</tbody>
</table>
Product

Table 23: Properties of each product.

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>SBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP</td>
<td>ATP</td>
<td></td>
</tr>
</tbody>
</table>

Kinetic Law

**Derived unit** $\mu\text{mol} \cdot \text{l}^{-1} \cdot \text{s}^{-1}$

$$v_9 = j_{\text{diff,atp}}$$  \hspace{1cm} (51)

9 Derived Rate Equations

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rates of change of each species.

Identifiers for kinetic laws highlighted in gray cannot be verified to evaluate to units of SBML substance per time. As a result, some SBML interpreters may not be able to verify the consistency of the units on quantities in the model. Please check if

- parameters without an unit definition are involved or
- volume correction is necessary because the hasOnlySubstanceUnits flag may be set to false and spacialDimensions > 0 for certain species.

9.1 Species ADPi

**Name** ADPi

**Initial concentration** 39 $\mu\text{mol} \cdot \text{l}^{-1}$

This species takes part in three reactions (as a reactant in $J_{\text{syn}}, J_{\text{diff,ADP}}$ and as a product in $J_{\text{CK,MI}}$).

$$\frac{d}{dr} \text{ADPi} = v_2 - v_1 - v_7$$  \hspace{1cm} (52)

9.2 Species ATPi

**Name** ATPi

**Initial concentration** 5626 $\mu\text{mol} \cdot \text{l}^{-1}$

This species takes part in three reactions (as a reactant in $J_{\text{CK,MI}}, J_{\text{diff,ATP}}$ and as a product in $J_{\text{syn}}$).

$$\frac{d}{dr} \text{ATPi} = v_1 - v_2 - v_9$$  \hspace{1cm} (53)
9.3 Species Cri

Name  Cri

Initial concentration  9789 \, \mu \text{mol} \cdot l^{-1}

This species takes part in two reactions (as a reactant in $J_{CK\_Mi}, J_{diff\_Cr}$).

\[
\frac{d}{dt} \text{Cri} = -v_2 - v_6
\]  (54)

9.4 Species PCri

Name  PCri

Initial concentration  5711 \, \mu \text{mol} \cdot l^{-1}

This species takes part in two reactions (as a reactant in $J_{diff\_PCr}$ and as a product in $J_{CK\_Mi}$).

\[
\frac{d}{dt} \text{PCri} = v_2 - v_8
\]  (55)

9.5 Species PCr

Name  PCr

Initial concentration  5710 \, \mu \text{mol} \cdot l^{-1}

This species takes part in two reactions (as a product in $J_{CK\_MM}, J_{diff\_PCr}$).

\[
\frac{d}{dt} \text{PCr} = v_3 + v_8
\]  (56)

9.6 Species ADP

Name  ADP

Initial concentration  64 \, \mu \text{mol} \cdot l^{-1}

This species takes part in three reactions (as a product in $J_{CK\_MM}, J_{hyd\_reaction}, J_{diff\_ADP}$).

\[
\frac{d}{dt} \text{ADP} = v_3 + v_4 + v_7
\]  (57)
9.7 Species ATP

**Name** ATP

**Initial concentration** 5601 µmol·l$^{-1}$

This species takes part in three reactions (as a reactant in $J_{CK.MM}$, $J_{hyd.reaction}$ and as a product in $J_{diff.ATP}$).

$$\frac{d}{dt}ATP = v_9 - v_3 - v_4$$ (58)

9.8 Species Cr

**Name** Cr

**Initial concentration** 9789 µmol·l$^{-1}$

This species takes part in two reactions (as a reactant in $J_{CK.MM}$ and as a product in $J_{diff.Cr}$).

$$\frac{d}{dt}Cr = v_6 - v_3$$ (59)

9.9 Species P$_{ii}$

**Name** P$_{ii}$

**Initial concentration** 910 µmol·l$^{-1}$

This species takes part in two reactions (as a reactant in $J_{syn}$, $J_{diff.Pi}$).

$$\frac{d}{dt}P_{ii} = -v_1 - v_5$$ (60)

9.10 Species P$_i$

**Name** P$_i$

**Initial concentration** 912 µmol·l$^{-1}$

This species takes part in two reactions (as a product in $J_{hyd.reaction}$, $J_{diff.Pi}$).

$$\frac{d}{dt}P_i = v_4 + v_5$$ (61)
SBML2LaTeX was developed by Andreas Dräger\textsuperscript{a}, Hannes Planatscher\textsuperscript{a}, Dieudonné M Wouamba\textsuperscript{a}, Adrian Schröder\textsuperscript{a}, Michael Hucka\textsuperscript{b}, Lukas Endler\textsuperscript{c}, Martin Golebiewski\textsuperscript{d} and Andreas Zell\textsuperscript{a}. Please see \url{http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX} for more information.

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\textsuperscript{d}EML Research gGmbH, Heidelberg, Germany