SBML Model Report

Model name: "Cloutier2009 - Brain Energy Metabolism"

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following three authors: Catherine Lloyd[1], Vijayalakshmi Chelliah[2] and Audald Lloret i Villas[3] at June 25th 2010 at 12:46 a. m. and last time modified at April 17th 2015 at 11:01 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.

Element	Quantity	Element	Quantity
compartment types	0	compartments	4
species types	0	species	51
events	0	constraints	0
reactions	0	function definitions	0
global parameters	174	unit definitions	0
rules	100	initial assignments	0

Model Notes

Cloutier2009 - Brain Energy Metabolism

This model was taken from the CellMLrepositoryandautomatically converted to SBML.Following

[1]University of Auckland, c.lloyd@auckland.ac.nz
[2]EMBL-EBI, viji@ebi.ac.uk
[3]EMBL-EBI, lloret@ebi.ac.uk

thesubmission the parameters are manually encoded and annotated asspices and global quantities by BioModels curators.
Theoriginal model was:**Cloutier M, Bolger FB, Lowry JP, Wellstead P. (2009) -version=1.0**
Theoriginal CellML model was created by:
CatherineLloyd
c.lloyd@auckland.ac.nz
TheUniversity of Auckland

This model is described in the article:An integrative dynamic model of brain energy metabolism using in vivo neurochemical measurements.Cloutier M, Bolger FB, Lowry JP, Wellstead P.J Comput Neurosci 2009 Dec; 27(3): 391-414

Abstract:

An integrative, systems approach to the modelling of brain energy metabolism is presented. Mechanisms such as glutamate cycling between neurons and astrocytes and glycogen storage in astrocytes have been implemented. A unique feature of the model is its calibration using in vivo data of brain glucose and lactate from freely moving rats under various stimuli. The model has been used to perform simulated perturbation experiments that show that glycogen breakdown in astrocytes is significantly activated during sensory (tail pinch) stimulation. This mechanism provides an additional input of energy substrate during high consumption phases. By way of validation, data from the perfusion of 50 microM propranolol in the rat brain was compared with the model outputs. Propranolol affects the glucose dynamics during stimulation, and this was accurately reproduced in the model by a reduction in the glycogen breakdown in astrocytes. The model's predictive capacity was verified by using data from a sensory stimulation (restraint) that was not used for model calibration. Finally, a sensitivity analysis was conducted on the model parameters, this showed that the control of energy metabolism and transport processes are critical in the metabolic behaviour of cerebral tissue.

This model is hosted on BioModels Database and identified by: BIOMD0000000554.

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models.

2 Unit Definitions

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

2.1 Unit `substance`

Notes Mole is the predefined SBML unit for `substance`.

Definition mol

2.2 Unit `volume`

Notes Litre is the predefined SBML unit for `volume`.

Definition l

2.3 Unit `area`

Notes Square metre is the predefined SBML unit for `area` since SBML Level 2 Version 1.

Definition m^2

2.4 Unit `length`

Notes Metre is the predefined SBML unit for `length` since SBML Level 2 Version 1.

Definition m

2.5 Unit `time`

Notes Second is the predefined SBML unit for `time`.

Definition s

3 Compartments

This model contains four compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`Astrocytes`	Astrocytes		3	1	litre	☑	
`Capillaries`	Capillaries		3	1	litre	☑	
`Extracellular_space`	Extracellular space		3	1	litre	☑	
`Neurons`	Neurons		3	1	litre	☑	

3.1 Compartment `Astrocytes`

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

Name Astrocytes

Notes `Variables indexed {\textquotestraightdblbase}g{\textquotestraightdblbase}`

3.2 Compartment Capillaries

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

Name Capillaries

Notes `Variables indexed {\textquotestraightdblbase}c{\textquotestraightdblbase}`

3.3 Compartment Extracellular_space

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

Name Extracellular space

Notes `Variables indexed {\textquotestraightdblbase}e{\textquotestraightdblbase}`

3.4 Compartment Neurons

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

Name Neurons

Notes `Variables indexed {\textquotestraightdblbase}n{\textquotestraightdblbase}`

4 Species

This model contains 51 species. The boundary condition of 51 of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 7 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
NAg	NAg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
GLCg	GLCg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
G6Pg	G6Pg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
F6Pg	F6Pg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
GAPg	GAPg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
PEPg	PEPg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
PYRg	PYRg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
LACg	LACg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
NADHg	NADHg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
ATPg	ATPg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
PCrg	PCrg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
O2g	O2g	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
GLYg	GLYg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
GLUg	GLUg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
NADg	NADg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
ADPg	ADPg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
CRg	CRg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
NADH_g_tot	NADH_g_tot	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
PCrg_tot	PCrg_tot	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
AMPg	AMPg	Astrocytes	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
O2c	O2c	Capillaries	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
GLCc	GLCc	Capillaries	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
LACc	LACc	Capillaries	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
CO2c	CO2c	Capillaries	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
GLCe	GLCe	Extracellular_space	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
LACe	LACe	Extracellular_space	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
GLUe	GLUe	Extracellular_space	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
NAe	NAe	Extracellular_space	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
O2a	O2a	Extracellular_space	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
CO2a	CO2a	Extracellular_space	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
GLCa	GLCa	Extracellular_space	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
LACa	LACa	Extracellular_space	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
NAn	NAn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
GLCn	GLCn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
G6Pn	G6Pn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
F6Pn	F6Pn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
GAPn	GAPn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
PEPn	PEPn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
PYRn	PYRn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
LACn	LACn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
NADHn	NADHn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
ATPn	ATPn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
PCrn	PCrn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
O2n	O2n	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
GLUn	GLUn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
ADPn	ADPn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
CRn	CRn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
NADn	NADn	Neurons	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
`NADH_n_tot`	NADH_n_tot	`Neurons`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
`PCrn_tot`	PCrn_tot	`Neurons`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
`AMPn`	AMPn	`Neurons`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑

5 Parameters

This model contains 174 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
u_n	u_n		1.042		☐
u_g	u_g		1.075		☐
dAMP_dATPn	dAMP_dATPn		−0.101		☐
dAMP_dATPg	dAMP_dATPg		−0.116		☐
Vv	Vv		0.024		☐
dHb	dHb		0.022		☐
Vn_leak_Na	Vn_leak_Na		0.475		☐
gn_NA	gn_NA		0.004		☑
Vn_pump	Vn_pump		0.158		☐
Vn_stim	Vn_stim		0.000		☐
V_en_GLC	V_en_GLC		0.006		☐
Km_en_GLC	Km_en_GLC		5.320		☑
Vm_en_GLC	Vm_en_GLC		0.504		☑
Vn_hk	Vn_hk		0.006		☐
Vmax_n_hk	Vmax_n_hk		0.051		☑
Vn_pgi	Vn_pgi		0.006		☐
Vmaxf_n_pgi	Vmaxf_n_pgi		0.500		☑
Vmaxr_n_pgi	Vmaxr_n_pgi		0.450		☑
Vn_pfk	Vn_pfk		0.006		☐
kn_pfk	kn_pfk		0.558		☑
Vn_pgk	Vn_pgk		0.012		☐
kn_pgk	kn_pgk		0.429		☑
Vn_pk	Vn_pk		0.012		☐
kn_pk	kn_pk		28.600		☑
Vn_ldh	Vn_ldh		−0.001		☐
kfn_ldh	kfn_ldh		5.300		☑
krn_ldh	krn_ldh		0.105		☑
Vn_mito	Vn_mito		0.013		☐
Vmax_n_mito	Vmax_n_mito		0.056		☑
Vne_LAC	Vne_LAC		−0.001		☐
Vmax_ne_LAC	Vmax_ne_LAC		0.198		☑
Km_ne_LAC	Km_ne_LAC		0.093		☑
Vn_ATPase	Vn_ATPase		0.049		☐
Vmax_n-_ATPase	Vmax_n_ATPase		0.049		☑
Vn_ck	Vn_ck		$2.93701651940294 \cdot 10^{-5}$		☐
krn_ck	krn_ck		0.015		☑

Id	Name	SBO	Value	Unit	Constant
kfn_ck	kfn_ck		0.052		☑
Vcn_O2	Vcn_O2		0.039		☐
nh_O2_Vcn_O2	nh_O2		2.700		☑
PScapn	PScapn		0.220		☑
Vg_leak_Na	Vg_leak_Na		0.190		☐
gg_NA	gg_NA		0.003		☑
Vg_pump	Vg_pump		0.063		☐
Veg_GLC	Veg_GLC		0.002		☐
Km_eg_GLC	Km_eg_GLC		3.530		☑
Vm_eg_GLC	Vm_eg_GLC		0.038		☑
Vcg_GLC	Vcg_GLC		0.003		☐
Km_cg_GLC	Km_cg_GLC		9.920		☑
Vm_cg_GLC	Vm_cg_GLC		0.010		☑
Vg_hk	Vg_hk		0.005		☐
Vmax_g_hk	Vmax_g_hk		0.050		☑
Vg_pgi	Vg_pgi		0.005		☐
Vmaxf_g_pgi	Vmaxf_g_pgi		0.500		☑
Vmaxr_g_pgi	Vmaxr_g_pgi		0.450		☑
Vg_pfk	Vg_pfk		0.005		☐
kg_pfk	kg_pfk		0.403		☑
Vg_pgk	Vg_pgk		0.009		☐
kg_pgk	kg_pgk		0.251		☑
Vg_pk	Vg_pk		0.009		☐
kg_pk	kg_pk		2.730		☑
Vg_ldh	Vg_ldh		0.003		☐
kfg_ldh	kfg_ldh		6.261		☑
krg_ldh	krg_ldh		0.547		☑
Vg_mito	Vg_mito		0.006		☐
Vmax_g_mito	Vmax_g_mito		0.008		☑
Vge_LAC	Vge_LAC		0.003		☐
Vmax_ge_LAC	Vmax_ge_LAC		0.086		☑
Km_ge_LAC	Km_ge_LAC		0.222		☑
Vgc_LAC	Vgc_LAC		$1.46095762940601 \cdot 10^{-5}$		☐
Vmax_gc_LAC	Vmax_gc_LAC		$2.1856 \cdot 10^{-4}$		☑
Km_gc_LAC	Km_gc_LAC		0.129		☑
Vg_ATPase	Vg_ATPase		0.036		☐
Vmax_g-_ATPase	Vmax_g_ATPase		0.036		☑
Vg_ck	Vg_ck		$8.98869880248884 \cdot 10^{-5}$		☐
krg_ck	krg_ck		0.021		☑
kfg_ck	kfg_ck		0.024		☑
Vcg_O2	Vcg_O2		0.018		☐

Id	Name	SBO	Value	Unit	Constant
PScapg	PScapg		0.246		☑
Vc_O2	Vc_O2		4.014		☐
Vc_GLC	Vc_GLC		0.698		☐
Vce_GLC	Vce_GLC		0.015		☐
Km_ce_GLC	Km_ce_GLC		8.457		☑
Vm_ce_GLC	Vm_ce_GLC		0.049		☑
Vc_LAC	Vc_LAC		-0.053		☐
Vec_LAC	Vec_LAC		0.001		☐
Km_ec_LAC	Km_ec_LAC		0.765		☑
Vm_ec_LAC	Vm_ec_LAC		0.033		☑
Vnc_CO2	Vnc_CO2		0.039		☐
Vgc_CO2	Vgc_CO2		0.018		☐
Vn_stim_GLU	Vn_stim_GLU		0.000		☐
Vg_gs	Vg_gs		0.000		☐
Vmax_g_gs	Vmax_g_gs		0.300		☑
Veg_GLU	Veg_GLU		0.000		☐
Vmax_eg_GLU	Vmax_eg_GLU		0.021		☑
Vc_CO2	Vc_CO2		4.015		☐
Vg_glys	Vg_glys		$9.08171994158688 \cdot 10^{-5}$		☐
Vmax_glys	Vmax_glys		$1.528 \cdot 10^{-4}$		☑
Km_G6P_glys	Km_G6P_glys		0.500		☑
Vg_glyp	Vg_glyp		$3.51571428571429 \cdot 10^{-5}$		☐
Vmax_glyp	Vmax_glyp		$4.922 \cdot 10^{-5}$		☑
Km_GLY	Km_GLY		1.000		☑
deltaVt_GLY	deltaVt_GLY		1.000		☐
Fin_t	Fin_t		0.012		☐
CBF0_Fin_t	CBF0		0.012		☑
Fout_t	Fout_t		0.012		☐
BOLD	BOLD		0.042		☐
v_stim	v_stim		0.000		☐
unitpulseSB	unitpulseSB		0.000		☐
unitstepSB	unitstepSB		0.000		☐
Km_PYR	Km_PYR		0.063		☑
Km_ATP	Km_ATP		0.015		☑
Ki_ATP	Ki_ATP		0.760		☑
Km_ADP	Km_ADP		0.001		☑
Km_O2	Km_O2		0.003		☑
Km_GLC	Km_GLC		0.105		☑
Km_GLU	Km_GLU		0.050		☑
Km_G6P	Km_G6P		0.500		☑
Km_F6P_pgi	Km_F6P_pgi		0.060		☑
Km_F6P_pfk	Km_F6P_pfk		0.180		☑

Id	Name	SBO	Value	Unit	Constant
Km_pump	Km_pump		0.424		☑
nh_O2_model-_parameters	nh_O2_2		2.700		☑
Ko2	Ko2		0.090		☑
kpump	kpump		$3.17 \cdot 10^{-7}$		☑
ATPtot	ATPtot		2.379		☑
nH	nH		4.000		☑
nOP	nOP		15.000		☑
NAero	NAero		3.000		☑
Rng	Rng		1.800		☑
Reg	Reg		0.800		☑
Ren	Ren		0.444		☑
Rcn	Rcn		0.012		☑
Rcg	Rcg		0.022		☑
Rce	Rce		0.028		☑
Sm_n	Sm_n		40500.000		☑
Vm	Vm		−70.000		☑
RT	RT		2577340.000		☑
F	F		96500.000		☑
Vn	Vn		0.450		☑
G6P_inh_hk	G6P_inh_hk		0.600		☑
aG6P_inh_hk	aG6P_inh_hk		20.000		☑
rATP_mito	rATP_mito		20.000		☑
aATP_mito	aATP_mito		5.000		☑
HbOP	HbOP		8.600		☑
Sm_g	Sm_g		10500.000		☑
Vg	Vg		0.250		☑
KO1	KO1		1.000		☑
Vc	Vc		0.006		☑
R_GLU_NA	R_GLU_NA		0.075		☑
KO2	KO2		1.000		☑
KO3	KO3		1.000		☑
GLY_inh	GLY_inh		4.200		☑
aGLY_inh	aGLY_inh		20.000		☑
CBF0_model-_parameters	CBF0_2		0.012		☑
Vv0	Vv0		0.024		☑
tv	tv		35.000		☑
qak	qak		0.920		☑
k1	k1		2.220		☑
k2	k2		0.460		☑
k3	k3		0.430		☑

Id	Name	SBO	Value	Unit	Constant
dHb0	dHb0		0.064		☑
stim	stim		1.000		☑
to	to		200.000		☑
tend	tend		300.000		☑
v1_n	v1_n		0.041		☑
v2_n	v2_n		2.550		☑
t_n_stim	t_n_stim		2.000		☑
sr	sr		4.592		☑
t1	t1		2.000		☑
delta_GLY	delta_GLY		62.000		☑
deltaf	deltaf		0.420		☑
tend_GLY	tend_GLY		440.000		☑
to_GLY	to_GLY		83.000		☑
sr_GLY	sr_GLY		4.000		☑
unitstepSB2	unitstepSB2		0.000		☐

6 Rules

This is an overview of 100 rules.

6.1 Rule V_en_GLC

Rule V_en_GLC is an assignment rule for parameter V_en_GLC:

$$\mathrm{V\_en\_GLC} = \mathrm{Vm\_en\_GLC} \cdot \left(\frac{[\mathrm{GLCe}]}{[\mathrm{GLCe}] + \mathrm{Km\_en\_GLC}} - \frac{[\mathrm{GLCn}]}{[\mathrm{GLCn}] + \mathrm{Km\_en\_GLC}} \right) \tag{1}$$

6.2 Rule Vn_hk

Rule Vn_hk is an assignment rule for parameter Vn_hk:

$$\begin{aligned} \mathrm{Vn\_hk} = {} & \mathrm{Vmax\_n\_hk} \cdot [\mathrm{ATPn}] \cdot \frac{[\mathrm{GLCn}]}{[\mathrm{GLCn}] + \mathrm{Km\_GLC}} \\ & \cdot \left(1 - \frac{1}{1 + \exp\left(\mathrm{aG6P\_inh\_hk} \cdot 1 \cdot \left([\mathrm{G6Pn}] - \mathrm{G6P\_inh\_hk}\right)\right)} \right) \end{aligned} \tag{2}$$

6.3 Rule Vn_pgi

Rule Vn_pgi is an assignment rule for parameter Vn_pgi:

$$\mathrm{Vn\_pgi} = \mathrm{Vmaxf\_n\_pgi} \cdot \frac{[\mathrm{G6Pn}]}{[\mathrm{G6Pn}] + \mathrm{Km\_G6P}} - \mathrm{Vmaxr\_n\_pgi} \cdot \frac{[\mathrm{F6Pn}]}{[\mathrm{F6Pn}] + \mathrm{Km\_F6P\_pgi}} \tag{3}$$

6.4 Rule NADg

Rule NADg is an assignment rule for species NADg:

$$\mathrm{NADg} = [\mathrm{NADH\_g\_tot}] - [\mathrm{NADHg}] \tag{4}$$

Derived unit $\mathrm{mol} \cdot \mathrm{l}^{-1}$

6.5 Rule ADPg

Rule ADPg is an assignment rule for species ADPg:

$$\mathrm{ADPg} = \frac{[\mathrm{ATPg}]}{2} \cdot \left(\mathrm{qak} + \left(\mathrm{qak}^2 + 4 \cdot \mathrm{qak} \cdot \left(\frac{\mathrm{ATPtot}}{[\mathrm{ATPg}]} - 1\right)\right)^{\frac{1}{2}}\right) \tag{5}$$

6.6 Rule CRg

Rule CRg is an assignment rule for species CRg:

$$\mathrm{CRg} = [\mathrm{PCrg\_tot}] - [\mathrm{PCrg}] \tag{6}$$

Derived unit $\mathrm{mol} \cdot \mathrm{l}^{-1}$

6.7 Rule AMPg

Rule AMPg is an assignment rule for species AMPg:

$$\mathrm{AMPg} = \mathrm{ATPtot} - ([\mathrm{ATPg}] + [\mathrm{ADPg}]) \tag{7}$$

6.8 Rule Vg_ck

Rule Vg_ck is an assignment rule for parameter Vg_ck:

$$\mathrm{Vg\_ck} = \mathrm{kfg\_ck} \cdot [\mathrm{PCrg}] \cdot [\mathrm{ADPg}] - \mathrm{krg\_ck} \cdot [\mathrm{CRg}] \cdot [\mathrm{ATPg}] \tag{8}$$

6.9 Rule ADPn

Rule ADPn is an assignment rule for species ADPn:

$$\mathrm{ADPn} = \frac{[\mathrm{ATPn}]}{2} \cdot \left(\mathrm{qak} + \left(\mathrm{qak}^2 + 4 \cdot \mathrm{qak} \cdot \left(\frac{\mathrm{ATPtot}}{[\mathrm{ATPn}]} - 1\right)\right)^{\frac{1}{2}}\right) \tag{9}$$

6.10 Rule CRn

Rule CRn is an assignment rule for species CRn:

$$\mathrm{CRn} = [\mathrm{PCrn\_tot}] - [\mathrm{PCrn}] \tag{10}$$

Derived unit $\mathrm{mol} \cdot \mathrm{l}^{-1}$

6.11 Rule NADn

Rule NADn is an assignment rule for species NADn:

$$\mathrm{NADn} = [\mathrm{NADH\_n\_tot}] - [\mathrm{NADHn}] \tag{11}$$

Derived unit $\mathrm{mol} \cdot \mathrm{l}^{-1}$

6.12 Rule AMPn

Rule AMPn is an assignment rule for species AMPn:

$$\mathrm{AMPn} = \mathrm{ATPtot} - ([\mathrm{ATPn}] + [\mathrm{ADPn}]) \tag{12}$$

6.13 Rule u_n

Rule u_n is an assignment rule for parameter u_n:

$$\mathrm{u\_n} = \mathrm{qak}^2 + 4 \cdot \mathrm{qak} \cdot \left(\frac{\mathrm{ATPtot}}{[\mathrm{ATPn}]} - 1\right) \tag{13}$$

6.14 Rule u_g

Rule u_g is an assignment rule for parameter u_g:

$$\mathrm{u\_g} = \mathrm{qak}^2 + 4 \cdot \mathrm{qak} \cdot \left(\frac{\mathrm{ATPtot}}{[\mathrm{ATPg}]} - 1\right) \tag{14}$$

6.15 Rule dAMP_dATPn

Rule dAMP_dATPn is an assignment rule for parameter dAMP_dATPn:

$$\mathrm{dAMP\_dATPn} = \frac{\mathrm{qak}}{2} + \mathrm{qak} \cdot \frac{\mathrm{ATPtot}}{[\mathrm{ATPn}] \cdot \mathrm{u\_n}^{\frac{1}{2}}} - \left(1 + 0.5 \cdot \mathrm{u\_n}^{\frac{1}{2}}\right) \tag{15}$$

6.16 Rule dAMP_dATPg

Rule dAMP_dATPg is an assignment rule for parameter dAMP_dATPg:

$$\mathrm{dAMP\_dATPg} = \frac{\mathrm{qak}}{2} + \mathrm{qak} \cdot \frac{\mathrm{ATPtot}}{[\mathrm{ATPg}] \cdot \mathrm{u\_g}^{\frac{1}{2}}} - \left(1 + 0.5 \cdot \mathrm{u\_g}^{\frac{1}{2}}\right) \tag{16}$$

6.17 Rule Vn_leak_Na

Rule Vn_leak_Na is an assignment rule for parameter Vn_leak_Na:

$$\mathrm{Vn\_leak\_Na} = \frac{\mathrm{Sm\_n}}{\mathrm{Vn}} \cdot \frac{\mathrm{gn\_NA}}{\mathrm{F}} \cdot \left(\frac{\mathrm{RT}}{\mathrm{F}} \cdot \left(\frac{[\mathrm{NAe}]}{[\mathrm{NAn}]}\right) - \mathrm{Vm}\right) \tag{17}$$

6.18 Rule Vn_pump

Rule Vn_pump is an assignment rule for parameter Vn_pump:

$$\text{Vn\_pump} = \frac{\text{Sm\_n}}{\text{Vn}} \cdot \text{kpump} \cdot [\text{ATPn}] \cdot [\text{NAn}] \cdot \left(1 + \frac{[\text{ATPn}]}{\text{Km\_pump}}\right)^{1} \tag{18}$$

6.19 Rule Vn_pfk

Rule Vn_pfk is an assignment rule for parameter Vn_pfk:

$$\text{Vn\_pfk} = \text{kn\_pfk} \cdot [\text{ATPn}] \cdot \frac{[\text{F6Pn}]}{[\text{F6Pn}] + \text{Km\_F6P\_pfk}} \cdot \left(1 + \left(\frac{[\text{ATPn}]}{\text{Ki\_ATP}}\right)^{\text{nH}}\right)^{1} \tag{19}$$

6.20 Rule Vn_pgk

Rule Vn_pgk is an assignment rule for parameter Vn_pgk:

$$\text{Vn\_pgk} = \text{kn\_pgk} \cdot [\text{GAPn}] \cdot [\text{ADPn}] \cdot \frac{[\text{NADn}]}{[\text{NADHn}]} \tag{20}$$

6.21 Rule Vn_pk

Rule Vn_pk is an assignment rule for parameter Vn_pk:

$$\text{Vn\_pk} = \text{kn\_pk} \cdot [\text{PEPn}] \cdot [\text{ADPn}] \tag{21}$$

6.22 Rule Vn_ldh

Rule Vn_ldh is an assignment rule for parameter Vn_ldh:

$$\text{Vn\_ldh} = \text{kfn\_ldh} \cdot [\text{PYRn}] \cdot [\text{NADHn}] - \text{krn\_ldh} \cdot [\text{LACn}] \cdot [\text{NADn}] \tag{22}$$

6.23 Rule Vn_mito

Rule Vn_mito is an assignment rule for parameter Vn_mito:

$$\begin{aligned}\text{Vn\_mito} = \text{Vmax\_n\_mito} \cdot \frac{[\text{O2n}]}{[\text{O2n}] + \text{Km\_O2}} \cdot \frac{[\text{ADPn}]}{[\text{ADPn}] + \text{Km\_ADP}} \cdot \frac{[\text{PYRn}]}{[\text{PYRn}] + \text{Km\_PYR}} \\ \cdot \left(1 - \frac{1}{1 + \exp\left(\text{aATP\_mito} \cdot 1 \cdot \left(\frac{[\text{ATPn}]}{[\text{ADPn}]} - 1 \cdot \text{rATP\_mito}\right)\right)}\right)\end{aligned} \tag{23}$$

6.24 Rule Vne_LAC

Rule Vne_LAC is an assignment rule for parameter Vne_LAC:

$$\text{Vne\_LAC} = \text{Vmax\_ne\_LAC} \cdot \left(\frac{[\text{LACn}]}{[\text{LACn}] + \text{Km\_ne\_LAC}} - \frac{[\text{LACe}]}{[\text{LACe}] + \text{Km\_ne\_LAC}}\right) \tag{24}$$

6.25 Rule Vn_ATPase

Rule Vn_ATPase is an assignment rule for parameter Vn_ATPase:

$$\mathrm{Vn\_ATPase} = \mathrm{Vmax\_n\_ATPase} \cdot \frac{[\mathrm{ATPn}]}{[\mathrm{ATPn}] + 0.0010} \tag{25}$$

6.26 Rule Vge_LAC

Rule Vge_LAC is an assignment rule for parameter Vge_LAC:

$$\mathrm{Vge\_LAC} = \mathrm{Vmax\_ge\_LAC} \cdot \left(\frac{[\mathrm{LACg}]}{[\mathrm{LACg}] + \mathrm{Km\_ge\_LAC}} - \frac{[\mathrm{LACe}]}{[\mathrm{LACe}] + \mathrm{Km\_ge\_LAC}}\right) \tag{26}$$

6.27 Rule Vn_ck

Rule Vn_ck is an assignment rule for parameter Vn_ck:

$$\mathrm{Vn\_ck} = \mathrm{kfn\_ck} \cdot [\mathrm{PCrn}] \cdot [\mathrm{ADPn}] - \mathrm{krn\_ck} \cdot [\mathrm{CRn}] \cdot [\mathrm{ATPn}] \tag{27}$$

6.28 Rule Vcn_O2

Rule Vcn_O2 is an assignment rule for parameter Vcn_O2:

$$\mathrm{Vcn\_O2} = \frac{\mathrm{PScapn}}{\mathrm{Vn}} \cdot \left(\mathrm{Ko2} \cdot \left(\frac{\mathrm{HbOP}}{[\mathrm{O2c}]} - 1\right)^{\frac{1}{\mathrm{nh\_O2\_Vcn\_O2}}} - [\mathrm{O2n}]\right) \tag{28}$$

6.29 Rule Vg_leak_Na

Rule Vg_leak_Na is an assignment rule for parameter Vg_leak_Na:

$$\mathrm{Vg\_leak\_Na} = \frac{\mathrm{Sm\_g}}{\mathrm{Vg}} \cdot \frac{\mathrm{gg\_NA}}{\mathrm{F}} \cdot \left(\frac{\mathrm{RT}}{\mathrm{F}} \cdot \left(\frac{[\mathrm{NAe}]}{[\mathrm{NAg}]}\right) - \mathrm{Vm}\right) \tag{29}$$

6.30 Rule Vg_pump

Rule Vg_pump is an assignment rule for parameter Vg_pump:

$$\mathrm{Vg\_pump} = \frac{\mathrm{Sm\_g}}{\mathrm{Vg}} \cdot \mathrm{kpump} \cdot [\mathrm{ATPg}] \cdot [\mathrm{NAg}] \cdot \left(1 + \frac{[\mathrm{ATPg}]}{\mathrm{Km\_pump}}\right)^{1} \tag{30}$$

6.31 Rule Veg_GLC

Rule Veg_GLC is an assignment rule for parameter Veg_GLC:

$$\mathrm{Veg\_GLC} = \mathrm{KO1} \cdot \mathrm{Vm\_eg\_GLC} \cdot \left(\frac{[\mathrm{GLCe}]}{[\mathrm{GLCe}] + \mathrm{Km\_eg\_GLC}} - \frac{[\mathrm{GLCg}]}{[\mathrm{GLCg}] + \mathrm{Km\_eg\_GLC}}\right) \tag{31}$$

6.32 Rule Vcg_GLC

Rule Vcg_GLC is an assignment rule for parameter Vcg_GLC:

$$\mathrm{Vcg\_GLC} = \mathrm{Vm\_cg\_GLC} \cdot \left(\frac{[\mathrm{GLCc}]}{[\mathrm{GLCc}] + \mathrm{Km\_cg\_GLC}} - \frac{[\mathrm{GLCg}]}{[\mathrm{GLCg}] + \mathrm{Km\_cg\_GLC}}\right) \tag{32}$$

6.33 Rule Vg_hk

Rule Vg_hk is an assignment rule for parameter Vg_hk:

$$\begin{aligned}\mathrm{Vg\_hk} = {} & \mathrm{Vmax\_g\_hk} \cdot [\mathrm{ATPg}] \cdot \frac{[\mathrm{GLCg}]}{[\mathrm{GLCg}] + \mathrm{Km\_GLC}} \\ & \cdot \left(1 - \frac{1}{1 + \exp\left(\mathrm{aG6P\_inh\_hk} \cdot 1 \cdot \left([\mathrm{G6Pg}] - \mathrm{G6P\_inh\_hk}\right)\right)}\right)\end{aligned} \tag{33}$$

6.34 Rule Vg_pgi

Rule Vg_pgi is an assignment rule for parameter Vg_pgi:

$$\mathrm{Vg\_pgi} = \mathrm{Vmaxf\_g\_pgi} \cdot \frac{[\mathrm{G6Pg}]}{[\mathrm{G6Pg}] + \mathrm{Km\_G6P}} - \mathrm{Vmaxr\_g\_pgi} \cdot \frac{[\mathrm{F6Pg}]}{[\mathrm{F6Pg}] + \mathrm{Km\_F6P\_pgi}} \tag{34}$$

6.35 Rule Vg_pfk

Rule Vg_pfk is an assignment rule for parameter Vg_pfk:

$$\mathrm{Vg\_pfk} = \mathrm{kg\_pfk} \cdot [\mathrm{ATPg}] \cdot \frac{[\mathrm{F6Pg}]}{[\mathrm{F6Pg}] + \mathrm{Km\_F6P\_pfk}} \cdot \left(1 + \left(\frac{[\mathrm{ATPg}]}{\mathrm{Ki\_ATP}}\right)^{\mathrm{nH}}\right)^{1} \tag{35}$$

6.36 Rule Vg_pgk

Rule Vg_pgk is an assignment rule for parameter Vg_pgk:

$$\mathrm{Vg\_pgk} = \mathrm{kg\_pgk} \cdot [\mathrm{GAPg}] \cdot [\mathrm{ADPg}] \cdot \frac{[\mathrm{NADg}]}{[\mathrm{NADHg}]} \tag{36}$$

6.37 Rule Vg_pk

Rule Vg_pk is an assignment rule for parameter Vg_pk:

$$\mathrm{Vg\_pk} = \mathrm{kg\_pk} \cdot [\mathrm{PEPg}] \cdot [\mathrm{ADPg}] \tag{37}$$

6.38 Rule Vg_ldh

Rule Vg_ldh is an assignment rule for parameter Vg_ldh:

$$\mathrm{Vg\_ldh} = \mathrm{kfg\_ldh} \cdot [\mathrm{PYRg}] \cdot [\mathrm{NADHg}] - \mathrm{krg\_ldh} \cdot [\mathrm{LACg}] \cdot [\mathrm{NADg}] \tag{38}$$

6.39 Rule Vg_mito

Rule Vg_mito is an assignment rule for parameter Vg_mito:

$$\mathrm{Vg\_mito} = \mathrm{Vmax\_g\_mito} \cdot \frac{[\mathrm{O2g}]}{[\mathrm{O2g}] + \mathrm{Km\_O2}} \cdot \frac{[\mathrm{ADPg}]}{[\mathrm{ADPg}] + \mathrm{Km\_ADP}} \cdot \frac{[\mathrm{PYRg}]}{[\mathrm{PYRg}] + \mathrm{Km\_PYR}} \cdot \left(1 - \frac{1}{1 + \exp\left(1 \cdot (\mathrm{aATP\_mito}) \cdot \left(\frac{[\mathrm{ATPg}]}{[\mathrm{ADPg}]} - 1 \cdot \mathrm{rATP\_mito}\right)\right)}\right) \tag{39}$$

6.40 Rule Vgc_LAC

Rule Vgc_LAC is an assignment rule for parameter Vgc_LAC:

$$\mathrm{Vgc\_LAC} = \mathrm{Vmax\_gc\_LAC} \cdot \left(\frac{[\mathrm{LACg}]}{[\mathrm{LACg}] + \mathrm{Km\_gc\_LAC}} - \frac{[\mathrm{LACc}]}{[\mathrm{LACc}] + \mathrm{Km\_gc\_LAC}}\right) \tag{40}$$

6.41 Rule Vg_ATPase

Rule Vg_ATPase is an assignment rule for parameter Vg_ATPase:

$$\mathrm{Vg\_ATPase} = \mathrm{Vmax\_g\_ATPase} \cdot \frac{[\mathrm{ATPg}]}{[\mathrm{ATPg}] + 0.0010} \tag{41}$$

6.42 Rule Vcg_O2

Rule Vcg_O2 is an assignment rule for parameter Vcg_O2:

$$\mathrm{Vcg\_O2} = \frac{\mathrm{PScapg}}{\mathrm{Vg}} \cdot \left(\mathrm{Ko2} \cdot \left(\frac{\mathrm{HbOP}}{[\mathrm{O2c}]} - 1\right)^{\frac{1}{\mathrm{nh\_O2\_model\_parameters}}} - [\mathrm{O2g}]\right) \tag{42}$$

6.43 Rule Vce_GLC

Rule Vce_GLC is an assignment rule for parameter Vce_GLC:

$$\mathrm{Vce\_GLC} = \mathrm{Vm\_ce\_GLC} \cdot \left(\frac{[\mathrm{GLCc}]}{[\mathrm{GLCc}] + \mathrm{Km\_ce\_GLC}} - \frac{[\mathrm{GLCe}]}{[\mathrm{GLCe}] + \mathrm{Km\_ce\_GLC}}\right) \tag{43}$$

6.44 Rule Vec_LAC

Rule Vec_LAC is an assignment rule for parameter Vec_LAC:

$$\mathrm{Vec\_LAC} = \mathrm{Vm\_ec\_LAC} \cdot \left(\frac{[\mathrm{LACe}]}{[\mathrm{LACe}] + \mathrm{Km\_ec\_LAC}} - \frac{[\mathrm{LACc}]}{[\mathrm{LACc}] + \mathrm{Km\_ec\_LAC}}\right) \tag{44}$$

6.45 Rule Vnc_CO2

Rule Vnc_CO2 is an assignment rule for parameter Vnc_CO2:

$$\text{Vnc\_CO2} = 3 \cdot \text{Vn\_mito} \tag{45}$$

6.46 Rule Vgc_CO2

Rule Vgc_CO2 is an assignment rule for parameter Vgc_CO2:

$$\text{Vgc\_CO2} = 3 \cdot \text{Vg\_mito} \tag{46}$$

6.47 Rule Vg_gs

Rule Vg_gs is an assignment rule for parameter Vg_gs:

$$\text{Vg\_gs} = \text{Vmax\_g\_gs} \cdot \frac{[\text{GLUg}]}{[\text{GLUg}] + \text{Km\_GLU}} \cdot \frac{[\text{ATPg}]}{[\text{ATPg}] + \text{Km\_ATP}} \tag{47}$$

6.48 Rule Veg_GLU

Rule Veg_GLU is an assignment rule for parameter Veg_GLU:

$$\text{Veg\_GLU} = \text{Vmax\_eg\_GLU} \cdot \frac{[\text{GLUe}]}{[\text{GLUe}] + \text{Km\_GLU}} \tag{48}$$

6.49 Rule Vg_glys

Rule Vg_glys is an assignment rule for parameter Vg_glys:

$$\begin{aligned}\text{Vg\_glys} = \text{Vmax\_glys} \cdot \frac{[\text{G6Pg}]}{[\text{G6Pg}] + \text{Km\_G6P\_glys}} \\ \cdot \left(1 - \frac{1}{1 + \exp\left(\text{aGLY\_inh} \cdot 1 \cdot \left([\text{GLYg}] - \text{GLY\_inh}\right)\right)}\right)\end{aligned} \tag{49}$$

6.50 Rule Fin_t

Rule Fin_t is an assignment rule for parameter Fin_t:

$$\begin{aligned}\text{Fin\_t} = \text{CBF0\_Fin\_t} + \Bigg(\text{stim} \cdot \text{CBF0\_Fin\_t} \cdot \text{deltaf} \cdot \frac{1}{1 + \exp\left(1 \cdot (\text{sr}) \cdot (\text{time} - \text{to} + \text{t1} - 3)\right)} \\ - \text{stim} \cdot \text{CBF0\_Fin\_t} \cdot \text{deltaf} \cdot \frac{1}{1 + \exp\left(1 \cdot (\text{sr}) \cdot (\text{time} - (\text{to} + \text{tend} + \text{t1} + 3))\right)}\Bigg)\end{aligned} \tag{50}$$

6.51 Rule Vc_O2

Rule Vc_O2 is an assignment rule for parameter Vc_O2:

$$\text{Vc\_O2} = 2 \cdot \frac{\text{Fin\_t}}{\text{Vc}} \cdot \left([\text{O2a}] - [\text{O2c}]\right) \tag{51}$$

6.52 Rule Vc_GLC

Rule Vc_GLC is an assignment rule for parameter Vc_GLC:

$$\mathrm{Vc\_GLC} = 2 \cdot \frac{\mathrm{Fin\_t}}{\mathrm{Vc}} \cdot ([\mathrm{GLCa}] - [\mathrm{GLCc}]) \tag{52}$$

6.53 Rule Vc_LAC

Rule Vc_LAC is an assignment rule for parameter Vc_LAC:

$$\mathrm{Vc\_LAC} = 2 \cdot \frac{\mathrm{Fin\_t}}{\mathrm{Vc}} \cdot ([\mathrm{LACa}] - [\mathrm{LACc}]) \tag{53}$$

6.54 Rule Vc_CO2

Rule Vc_CO2 is an assignment rule for parameter Vc_CO2:

$$\mathrm{Vc\_CO2} = 2 \cdot \frac{\mathrm{Fin\_t}}{\mathrm{Vc}} \cdot ([\mathrm{CO2c}] - [\mathrm{CO2a}]) \tag{54}$$

6.55 Rule Fout_t

Rule Fout_t is an assignment rule for parameter Fout_t:

$$\mathrm{Fout\_t} = \mathrm{CBF0\_model\_parameters} \cdot \frac{\left(\frac{\mathrm{Vv}}{\mathrm{Vv0}}\right)^2 + \mathrm{tv} \cdot \left(\frac{\mathrm{Vv}}{\mathrm{Vv0}}\right)^{0.5} \cdot \frac{\mathrm{Fin\_t}}{\mathrm{Vv0}}}{1 + \mathrm{CBF0\_model\_parameters} \cdot \mathrm{tv} \cdot \left(\frac{\mathrm{Vv}}{\mathrm{Vv0}}\right)^{0.5} \cdot \frac{1}{\mathrm{Vv0}}} \tag{55}$$

6.56 Rule BOLD

Rule BOLD is an assignment rule for parameter BOLD:

$$\mathrm{BOLD} = \mathrm{Vv0} \cdot \left((\mathrm{k1} + \mathrm{k2}) \cdot \left(1 - \frac{\mathrm{dHb}}{\mathrm{dHb0}}\right) - (\mathrm{k2} + \mathrm{k3}) \cdot \left(1 - \frac{\mathrm{Vv}}{\mathrm{Vv0}}\right)\right) \tag{56}$$

6.57 Rule unitpulseSB

Rule unitpulseSB is an assignment rule for parameter unitpulseSB:

$$\mathrm{unitpulseSB} = \begin{cases} 1 & \text{if } (\mathrm{time} \geq \mathrm{to}) \wedge (\mathrm{time} \leq \mathrm{to} + \mathrm{tend}) \\ 0 & \text{otherwise} \end{cases} \tag{57}$$

6.58 Rule v_stim

Rule v_stim is an assignment rule for parameter v_stim:

$$\mathrm{v\_stim} = \mathrm{stim} \cdot \left(\mathrm{v1\_n} + \mathrm{v2\_n} \cdot \frac{\mathrm{time} - \mathrm{to}}{\mathrm{t\_n\_stim}} \cdot \exp\left(\left((\mathrm{time} - \mathrm{to}) \cdot \frac{\mathrm{unitpulseSB}}{\mathrm{t\_n\_stim}}\right)\right)\right) \cdot \mathrm{unitpulseSB} \tag{58}$$

6.59 Rule Vn_stim

Rule Vn_stim is an assignment rule for parameter Vn_stim:

$$\mathrm{Vn\_stim} = \mathrm{v\_stim} \tag{59}$$

6.60 Rule Vn_stim_GLU

Rule Vn_stim_GLU is an assignment rule for parameter Vn_stim_GLU:

$$\mathrm{Vn\_stim\_GLU} = \mathrm{Vn\_stim} \cdot \mathrm{R\_GLU\_NA} \cdot \mathrm{KO2} \cdot \frac{[\mathrm{GLUn}]}{[\mathrm{GLUn}] + \mathrm{Km\_GLU}} \tag{60}$$

6.61 Rule unitstepSB

Rule unitstepSB is an assignment rule for parameter unitstepSB:

$$\mathrm{unitstepSB} = \begin{cases} 1 & \text{if } \mathrm{time} - (\mathrm{tend} + \mathrm{to}) \geq 0 \\ 0 & \text{otherwise} \end{cases} \tag{61}$$

6.62 Rule unitstepSB2

Rule unitstepSB2 is an assignment rule for parameter unitstepSB2:

$$\mathrm{unitstepSB2} = \begin{cases} 1 & \text{if } \mathrm{time} - (\mathrm{tend\_GLY} + \mathrm{to} + \mathrm{to\_GLY}) \geq 0 \\ 0 & \text{otherwise} \end{cases} \tag{62}$$

6.63 Rule deltaVt_GLY

Rule deltaVt_GLY is an assignment rule for parameter deltaVt_GLY:

$$\begin{aligned} \mathrm{deltaVt\_GLY} = {} & 1 + \mathrm{stim} \cdot \mathrm{delta\_GLY} \cdot \mathrm{KO3} \\ & \cdot \frac{1}{1 + \exp\left(1 \cdot (\mathrm{sr\_GLY}) \cdot (\mathrm{time} - (\mathrm{to} + \mathrm{to\_GLY}))\right)} \cdot (1 - \mathrm{unitstepSB2}) \end{aligned} \tag{63}$$

6.64 Rule Vg_glyp

Rule Vg_glyp is an assignment rule for parameter Vg_glyp:

$$\mathrm{Vg\_glyp} = \mathrm{Vmax\_glyp} \cdot \frac{[\mathrm{GLYg}]}{[\mathrm{GLYg}] + \mathrm{Km\_GLY}} \cdot \mathrm{deltaVt\_GLY} \tag{64}$$

6.65 Rule NAg

Rule NAg is a rate rule for species NAg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NAg} = \mathrm{Vg\_leak\_Na} + 3 \cdot \mathrm{Veg\_GLU} - 3 \cdot \mathrm{Vg\_pump} \tag{65}$$

6.66 Rule GLCg

Rule GLCg is a rate rule for species GLCg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GLCg} = \mathrm{Vcg\_GLC} + \mathrm{Veg\_GLC} - \mathrm{Vg\_hk} \tag{66}$$

6.67 Rule G6Pg

Rule G6Pg is a rate rule for species G6Pg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G6Pg} = \mathrm{Vg\_hk} + \mathrm{Vg\_glyp} - (\mathrm{Vg\_pgi} + \mathrm{Vg\_glys}) \tag{67}$$

6.68 Rule F6Pg

Rule F6Pg is a rate rule for species F6Pg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{F6Pg} = \mathrm{Vg\_pgi} - \mathrm{Vg\_pfk} \tag{68}$$

6.69 Rule GAPg

Rule GAPg is a rate rule for species GAPg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GAPg} = 2 \cdot \mathrm{Vg\_pfk} - \mathrm{Vg\_pgk} \tag{69}$$

6.70 Rule PEPg

Rule PEPg is a rate rule for species PEPg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PEPg} = \mathrm{Vg\_pgk} - \mathrm{Vg\_pk} \tag{70}$$

6.71 Rule PYRg

Rule PYRg is a rate rule for species PYRg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PYRg} = \mathrm{Vg\_pk} - (\mathrm{Vg\_ldh} + \mathrm{Vg\_mito}) \tag{71}$$

6.72 Rule LACg

Rule LACg is a rate rule for species LACg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{LACg} = \mathrm{Vg\_ldh} - (\mathrm{Vge\_LAC} + \mathrm{Vgc\_LAC}) \tag{72}$$

6.73 Rule NADHg

Rule NADHg is a rate rule for species NADHg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NADHg} = \mathrm{Vg\_pgk} - (\mathrm{Vg\_ldh} + \mathrm{Vg\_mito}) \tag{73}$$

6.74 Rule ATPg

Rule ATPg is a rate rule for species ATPg:

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ATPg} = (&\mathrm{Vg\_pgk} + \mathrm{Vg\_pk} + \mathrm{nOP} \cdot \mathrm{Vg\_mito} + \mathrm{Vg\_ck} \\ &- (\mathrm{Vg\_hk} + \mathrm{Vg\_pfk} + \mathrm{Vg\_ATPase} + \mathrm{Vg\_pump} + \mathrm{Vg\_gs})) \cdot (1 - \mathrm{dAMP\_dATPg})^{1}\end{aligned} \tag{74}$$

6.75 Rule PCrg

Rule PCrg is a rate rule for species PCrg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PCrg} = \mathrm{Vg\_ck} \tag{75}$$

6.76 Rule O2g

Rule O2g is a rate rule for species O2g:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{O2g} = \mathrm{Vcg\_O2} - \mathrm{NAero} \cdot \mathrm{Vg\_mito} \tag{76}$$

6.77 Rule GLYg

Rule GLYg is a rate rule for species GLYg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GLYg} = \mathrm{Vg\_glys} - \mathrm{Vg\_glyp} \tag{77}$$

6.78 Rule GLUg

Rule GLUg is a rate rule for species GLUg:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GLUg} = \mathrm{Veg\_GLU} - \mathrm{Vg\_gs} \tag{78}$$

6.79 Rule O2c

Rule O2c is a rate rule for species O2c:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{O2c} = \mathrm{Vc\_O2} - \left(\mathrm{Vcn\_O2} \cdot \frac{1}{\mathrm{Rcn}} + \mathrm{Vcg\_O2} \cdot \frac{1}{\mathrm{Rcg}}\right) \tag{79}$$

6.80 Rule GLCc

Rule GLCc is a rate rule for species GLCc:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GLCc} = \mathrm{Vc\_GLC} - \left(\mathrm{Vce\_GLC} \cdot \frac{1}{\mathrm{Rce}} + \mathrm{Vcg\_GLC} \cdot \frac{1}{\mathrm{Rcg}}\right) \tag{80}$$

6.81 Rule LACc

Rule LACc is a rate rule for species LACc:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{LACc} = \mathrm{Vc\_LAC} + \mathrm{Vec\_LAC} \cdot \frac{1}{\mathrm{Rce}} + \mathrm{Vgc\_LAC} \cdot \frac{1}{\mathrm{Rcg}} \tag{81}$$

6.82 Rule CO2c

Rule CO2c is a rate rule for species CO2c:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CO2c} = \mathrm{Vnc\_CO2} \cdot \frac{1}{\mathrm{Rcn}} + \mathrm{Vgc\_CO2} \cdot \frac{1}{\mathrm{Rcg}} - \mathrm{Vc\_CO2} \tag{82}$$

6.83 Rule GLCe

Rule GLCe is a rate rule for species GLCe:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GLCe} = \mathrm{Vce\_GLC} - \left(\mathrm{Veg\_GLC} \cdot \frac{1}{\mathrm{Reg}} + \mathrm{V\_en\_GLC} \cdot \frac{1}{\mathrm{Ren}}\right) \tag{83}$$

6.84 Rule LACe

Rule LACe is a rate rule for species LACe:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{LACe} = \mathrm{Vne\_LAC} \cdot \frac{1}{\mathrm{Ren}} + \mathrm{Vge\_LAC} \cdot \frac{1}{\mathrm{Reg}} - \mathrm{Vec\_LAC} \tag{84}$$

6.85 Rule GLUe

Rule GLUe is a rate rule for species GLUe:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GLUe} = \mathrm{Vn\_stim\_GLU} \cdot \frac{1}{\mathrm{Ren}} - \mathrm{Veg\_GLU} \cdot \frac{1}{\mathrm{Reg}} \tag{85}$$

6.86 Rule NAn

Rule NAn is a rate rule for species NAn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NAn} = \mathrm{Vn\_leak\_Na} + \mathrm{Vn\_stim} - 3 \cdot \mathrm{Vn\_pump} \tag{86}$$

6.87 Rule GLCn

Rule GLCn is a rate rule for species GLCn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GLCn} = \mathrm{V\_en\_GLC} - \mathrm{Vn\_hk} \tag{87}$$

6.88 Rule G6Pn

Rule G6Pn is a rate rule for species G6Pn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G6Pn} = \mathrm{Vn\_hk} - \mathrm{Vn\_pgi} \tag{88}$$

6.89 Rule F6Pn

Rule F6Pn is a rate rule for species F6Pn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{F6Pn} = \mathrm{Vn\_pgi} - \mathrm{Vn\_pfk} \tag{89}$$

6.90 Rule GAPn

Rule GAPn is a rate rule for species GAPn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GAPn} = 2 \cdot \mathrm{Vn\_pfk} - \mathrm{Vn\_pgk} \tag{90}$$

6.91 Rule PEPn

Rule PEPn is a rate rule for species PEPn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PEPn} = \mathrm{Vn\_pgk} - \mathrm{Vn\_pk} \tag{91}$$

6.92 Rule PYRn

Rule PYRn is a rate rule for species PYRn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PYRn} = \mathrm{Vn\_pk} - (\mathrm{Vn\_ldh} + \mathrm{Vn\_mito}) \tag{92}$$

6.93 Rule LACn

Rule LACn is a rate rule for species LACn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{LACn} = \mathrm{Vn\_ldh} - \mathrm{Vne\_LAC} \tag{93}$$

6.94 Rule NADHn

Rule NADHn is a rate rule for species NADHn:

$$\frac{d}{dt}\text{NADHn} = \text{Vn\_pgk} - (\text{Vn\_ldh} + \text{Vn\_mito}) \tag{94}$$

6.95 Rule ATPn

Rule ATPn is a rate rule for species ATPn:

$$\begin{aligned}\frac{d}{dt}\text{ATPn} = &(\text{Vn\_pgk} + \text{Vn\_pk} + \text{nOP} \cdot \text{Vn\_mito} + \text{Vn\_ck} \\ &- (\text{Vn\_hk} + \text{Vn\_pfk} + \text{Vn\_ATPase} + \text{Vn\_pump})) \cdot (1 - \text{dAMP\_dATPn})^{1}\end{aligned} \tag{95}$$

6.96 Rule PCrn

Rule PCrn is a rate rule for species PCrn:

$$\frac{d}{dt}\text{PCrn} = \text{Vn\_ck} \tag{96}$$

6.97 Rule O2n

Rule O2n is a rate rule for species O2n:

$$\frac{d}{dt}\text{O2n} = \text{Vcn\_O2} - \text{NAero} \cdot \text{Vn\_mito} \tag{97}$$

6.98 Rule GLUn

Rule GLUn is a rate rule for species GLUn:

$$\frac{d}{dt}\text{GLUn} = \text{Vg\_gs} \cdot \frac{1}{\text{Rng}} - \text{Vn\_stim\_GLU} \tag{98}$$

6.99 Rule Vv

Rule Vv is a rate rule for parameter Vv:

$$\frac{d}{dt}\text{Vv} = \text{Fin\_t} - \text{Fout\_t} \tag{99}$$

6.100 Rule dHb

Rule dHb is a rate rule for parameter dHb:

$$\frac{d}{dt}\text{dHb} = \text{Fin\_t} \cdot ([\text{O2a}] - [\text{O2c}]) - \text{Fout\_t} \cdot \frac{\text{dHb}}{\text{Vv}} \tag{100}$$

7 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.

7.1 Species NAg

Name NAg

Notes `Sodium`

Initial concentration $13.36 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule NAg

One rule determines the species' quantity.

7.2 Species GLCg

Name GLCg

Notes `Glucose`

Initial concentration $0.1656 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule GLCg

One rule determines the species' quantity.

7.3 Species G6Pg

Name G6Pg

Notes `Glucose-6-P`

Initial concentration $0.7326 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule G6Pg

One rule determines the species' quantity.

7.4 Species F6Pg

Name F6Pg

Notes `Fructose-6-P`

Initial concentration $0.1116 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule F6Pg

One rule determines the species' quantity.

7.5 Species GAPg

Name GAPg

Notes Glyceraldehyde-3-P

Initial concentration $0.0698\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule GAPg

One rule determines the species' quantity.

7.6 Species PEPg

Name PEPg

Notes Phosphoenolpyruvate

Initial concentration $0.0254\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule PEPg

One rule determines the species' quantity.

7.7 Species PYRg

Name PYRg

Notes Pyruvate

Initial concentration $0.1711\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule PYRg

One rule determines the species' quantity.

7.8 Species LACg

Name LACg

Notes Lactate

Initial concentration $0.4651\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule LACg

One rule determines the species' quantity.

7.9 Species NADHg

Name NADHg

Notes Nicotinamide adenine dinucleotide reduced

Initial concentration $0.0445 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule NADHg

One rule determines the species' quantity.

7.10 Species ATPg

Name ATPg

Notes Adenosine triphosphate

Initial concentration $2.24 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule ATPg

One rule determines the species' quantity.

7.11 Species PCrg

Name PCrg

Notes Phosphocreatine

Initial concentration $4.6817 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule PCrg

One rule determines the species' quantity.

7.12 Species O2g

Name O2g

Notes Oxygen

Initial concentration $0.1589 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule O2g

One rule determines the species' quantity.

7.13 Species GLYg

Name GLYg

Notes Glycogen

Initial concentration $2.5 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule GLYg

One rule determines the species' quantity.

7.14 Species GLUg

Name GLUg

Notes Glutamate

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule GLUg

One rule determines the species' quantity.

7.15 Species NADg

Name NADg

Notes Nicotinamide adenine dinucleotide oxidized

Initial concentration $0.1755 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule NADg

One rule determines the species' quantity.

7.16 Species ADPg

Name ADPg

Notes Adenosine diphosphate

Initial concentration $0.13070953832961 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule ADPg

One rule determines the species' quantity.

7.17 Species CRg

Name CRg

Notes Creatine

Initial concentration $0.318300000000001 \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule CRg

One rule determines the species' quantity.

7.18 Species NADH_g_tot

Name NADH_g_tot

Notes Nicotinamide adenine dinucleotide reduced

Initial concentration $0.22 \mathrm{mol} \cdot \mathrm{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NADH\_g\_tot} = 0 \tag{101}$$

7.19 Species PCrg_tot

Name PCrg_tot

Notes Phosphocreatine

Initial concentration $5 \mathrm{mol} \cdot \mathrm{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PCrg\_tot} = 0 \tag{102}$$

7.20 Species AMPg

Name AMPg

Notes Adenosine monophosphate

Initial concentration $0.00829046167039005 \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule AMPg

One rule determines the species' quantity.

7.21 Species O2c

Name O2c

Notes Oxygen

Initial concentration $7.4201 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule O2c

One rule determines the species' quantity.

7.22 Species GLCc

Name GLCc

Notes Glucose

Initial concentration $4.6401 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule GLCc

One rule determines the species' quantity.

7.23 Species LACc

Name LACc

Notes Lactate

Initial concentration $0.3251 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule LACc

One rule determines the species' quantity.

7.24 Species CO2c

Name CO2c

Notes Carbon dioxide

Initial concentration $2.12 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule CO2c

One rule determines the species' quantity.

7.25 Species GLCe

Name GLCe

Notes Glucose

Initial concentration $0.3339\,\text{mol}\cdot\text{l}^{-1}$

Involved in rule GLCe

One rule determines the species' quantity.

7.26 Species LACe

Name LACe

Notes Lactate

Initial concentration $0.3986\,\text{mol}\cdot\text{l}^{-1}$

Involved in rule LACe

One rule determines the species' quantity.

7.27 Species GLUe

Name GLUe

Notes Glutamate

Initial concentration $0\,\text{mol}\cdot\text{l}^{-1}$

Involved in rule GLUe

One rule determines the species' quantity.

7.28 Species NAe

Name NAe

Notes Sodium

Initial concentration $150\,\text{mol}\cdot\text{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NAe} = 0 \tag{103}$$

7.29 Species O2a

Name O2a

Notes Oxygen

Initial concentration $8.34 \text{ mol} \cdot \text{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{O2a} = 0 \tag{104}$$

7.30 Species CO2a

Name CO2a

Notes Carbon dioxide

Initial concentration $1.2 \text{ mol} \cdot \text{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CO2a} = 0 \tag{105}$$

7.31 Species GLCa

Name GLCa

Notes Glucose

Initial concentration $4.8 \text{ mol} \cdot \text{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GLCa} = 0 \tag{106}$$

7.32 Species LACa

Name LACa

Notes Lactate

Initial concentration $0.313 \text{ mol} \cdot \text{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{LACa} = 0 \tag{107}$$

7.33 Species NAn

Name NAn

Notes Sodium

Initial concentration $15.533 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule NAn

One rule determines the species' quantity.

7.34 Species GLCn

Name GLCn

Notes Glucose

Initial concentration $0.2633 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule GLCn

One rule determines the species' quantity.

7.35 Species G6Pn

Name G6Pn

Notes Glucose-6-P

Initial concentration $0.7275 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule G6Pn

One rule determines the species' quantity.

7.36 Species F6Pn

Name F6Pn

Notes Fructose-6-P

Initial concentration $0.1091 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule F6Pn

One rule determines the species' quantity.

7.37 Species GAPn

Name GAPn

Notes Glyceraldehyde-3-P

Initial concentration $0.0418 \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule GAPn

One rule determines the species' quantity.

7.38 Species PEPn

Name PEPn

Notes Phosphoenolpyruvate

Initial concentration $0.0037 \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule PEPn

One rule determines the species' quantity.

7.39 Species PYRn

Name PYRn

Notes Pyruvate

Initial concentration $0.0388 \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule PYRn

One rule determines the species' quantity.

7.40 Species LACn

Name LACn

Notes Lactate

Initial concentration $0.3856 \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule LACn

One rule determines the species' quantity.

7.41 Species NADHn

Name NADHn

Notes `Nicotinamide adenine dinucleotide reduced`

Initial concentration $0.0319\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule NADHn

One rule determines the species' quantity.

7.42 Species ATPn

Name ATPn

Notes `Adenosine triphosphate`

Initial concentration $2.2592\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule ATPn

One rule determines the species' quantity.

7.43 Species PCrn

Name PCrn

Notes `Posphocreatine`

Initial concentration $4.2529\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule PCrn

One rule determines the species' quantity.

7.44 Species O2n

Name O2n

Notes `Oxygen`

Initial concentration $0.0975\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule O2n

One rule determines the species' quantity.

7.45 Species GLUn

Name GLUn

Notes Glutamate

Initial concentration $3 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule GLUn

One rule determines the species' quantity.

7.46 Species ADPn

Name ADPn

Notes Adenosine diphosphate

Initial concentration $0.113591983539553 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule ADPn

One rule determines the species' quantity.

7.47 Species CRn

Name CRn

Notes Creatine

Initial concentration $0.7471 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule CRn

One rule determines the species' quantity.

7.48 Species NADn

Name NADn

Notes Nicotinamide adenine dinucleotide oxidized

Initial concentration $0.1881 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule NADn

One rule determines the species' quantity.

7.49 Species NADH_n_tot

Name NADH_n_tot

Notes Nicotinamide adenine dinucleotide reduced

Initial concentration $0.22 \text{ mol} \cdot \text{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{NADH\_n\_tot} = 0 \tag{108}$$

7.50 Species PCrn_tot

Name PCrn_tot

Notes Phosphocreatine

Initial concentration $5 \text{ mol} \cdot \text{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PCrn\_tot} = 0 \tag{109}$$

7.51 Species AMPn

Name AMPn

Notes Adenosine monophosphate

Initial concentration $0.006208016460449 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule AMPn

One rule determines the species' quantity.

SBML2LaTeX was developed by Andreas Dräger[a], Hannes Planatscher[a], Dieudonné M Wouamba[a], Adrian Schröder[a], Michael Hucka[b], Lukas Endler[c], Martin Golebiewski[d] and Andreas Zell[a]. Please see http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX for more information.

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany