BrainPiglet

Full model details

Contents

1 Settable Parameters

Name	Model Name	Value	Units	Description
CV_{inh}	`CVinh`	1	none	a control parameter representing the action of complex V inhibitors
C_{im}	`C_im`	0.00675	$\mathrm{mM\,mV^{-1}}$	Capacitance of mitochondrial inner membrane
C_v	`C_v`	0.047	$\mathrm{mmHg^{-1}}$	Compliance of the veins (normalised)
F	`Fdy`	96.48	$\mathrm{C\,mmol^{-1}}$	Faraday constant
$G_{\mathrm{VArat,n}}$	`G_VAratn`	4	none	Normal ratio of conductances between arteries and veins G_v/G_n (determines venous pressure) [16].

Name	Model Name	Value	Units	Description
I	`Inh_glucN`	50	none	the parameter which describes how strongly the AMP/ATP ratio inhibits the conversion of glucose to pyruvate
K_σ	`K_sigma`	10	none	parameter controlling sensitivity of σ_e to radius
$L_{CV,0}$	`L_CV0`	0.4	none	normal complex V flux as a fraction of maximum possible flux
$L_{lk,\mathrm{frac}}$	`L_lkfrac`	0.25	none	normal fraction of proton entry into mitochondria which is via leak channels
P_a	`P_a`	50	mmHg	arterial blood pressure
$P_a\mathrm{CO_2}$	`Pa_CO2`	40	mmHg	arterial partial pressure of CO2
$P_a\mathrm{CO}_{2,\mathrm{n}}$	`Pa_CO2n`	40	mmHg	normal arterial partial pressure of CO2
$P_{a,\mathrm{n}}$	`P_an`	50	mmHg	Normal value of ABP
$P_{ic,\mathrm{n}}$	`P_icn`	4.5	mmHg	normal intracranial blood pressure
P_{ic}	`P_ic`	4.5	mmHg	intracranial blood pressure
P_{vs}	`P_vs`	1.5	mmHg	Pressure in the venous sinuses [12].
R_C	`R_autc`	2.2	none	parameter controlling sensitivity of η to $P_a\mathrm{CO_2}$
R_O	`R_auto`	1.5	none	parameter controlling sensitivity of η to $[\mathrm{O}_{2,c}]$
R_P	`R_autp`	4	none	parameter controlling sensitivity of η to P_a
R_u	`R_autu`	0	none	parameter controlling sensitivity of η to u

Name	Model Name	Value	Units	Description
$V_{\mathrm{blood,n}}$	`blood_frac`	0.0325	none	normal blood volume as a fraction of brain tissue volume
V_{mit}	`Vol_mit`	0.067	none	fraction of brain water which is mitochondria
$V_{\mathrm{t,n}}$	`Vol_totn`	1	none	normal total blood volume
Z	`Z`	59.03	mV	2.303*RT/F
$\Delta\Psi_n$	`Dpsi_n`	145	mV	normal mitochondrial inner membrane potential
$\mathcal{E}_0(\mathrm{Cu_A})$	`E_c0`	247	mV	$\mathrm{Cu_A}$ standard redox potential
$\mathcal{E}_0(\mathrm{NADH})$	`E_N0`	-320	mV	NADH standard redox potential
$\mathcal{E}_0(\mathrm{cyt\,a_3})$	`E_a30`	350	mV	cyt a3 standard redox potential
$\mathrm{CBF_n}$	`CBFn`	0.008	$\mathrm{ml\,ml^{-1}\,s^{-1}}$	normal cerebral blood flow
CBFscale	`CBFscale`	5000	cm	Ratio between Vmca and CBF
$\mathrm{CMRO_{2,n}}$	`CMRO2_n`	0.02	$\mathrm{mM\,s^{-1}}$	The resting CMRO2.
$\mathrm{CMR_{gluc,n}}$	`CMRglucn`	0.0044	$\mathrm{mM\,s^{-1}}$	Normal rate of glucose metabolism for the brain [8].
$\mathrm{C_{buffi}}$	`C_buffi`	0.022	none	buffering capacity for protons in mitochondria
$\mathrm{Cu_{A,frac,n}}$	`a_frac_n`	0.67	none	normal oxidised fraction of $\mathrm{Cu_A}$
$\mathrm{K^*_{eq,PCr}}$	`k_PCrATP_eq_ef`	166	none	Effective equilibrium constant for the reaction in which phosphocreatine combines with ADP to give creatine and ATP [11]
$\mathrm{N_t}$	`NADpool`	3	mM	total mitochondrial NAD + NADH concentration

Name	Model Name	Value	Units	Description
$SaO2_n$	`SaO2_n`	0.96	none	normal saturation of the arterial haemoglobin
SaO2	`SaO2sup`	0.96	none	saturation of the arterial haemoglobin
$VArat_n$	`VArat_n`	3	none	The normal ratio of the volume of the veins to the volume of the arteries
$[ADP]_n$	`_ADPn`	0.012	mM	the normal concentration of ADP in the cytoplasm [14]
$[ATP]_n$	`_ATPn`	2.2	mM	the normal concentration of ATP in the cytoplasm [5]
$[CCO]_{tis}$	`cytox_tot_tis`	0.0022	mM	concentration of cytochrome c oxidase in tissue
$[Hbtot]_n$	`Xtot_n`	5.4	mM	Normal total haemoglobin concentration in the arteries and veins.
$[NAD]_n/[NADH]_n$	`NADNADHratn`	1.5	none	normal NAD/NADH ratio
$[O_2]_n$	`O2_n`	0.024	mM	normal oxygen concentration in mitochondria.
$[PCr]_n$	`_PCrn`	2.6	mM	normal concentration of phosphocreatine in cell cytoplasm [5]
$[PCr]_n/[P_i]_n$	`PCrPn`	2.73	none	Normal Pcr/Pi concentration in the cytoplasm. Set this way because this is often measured by MRS (although mitochondria/cytoplasm differences are ignored).
$[Py]_n$	`_PyOn`	0.1	mM	Normal concentration of pyruvate ions in the cytoplasm [7].
$[gluc]_n$	`_glucn`	1.2	mM	Normal cellular concentration of glucose [1].
$[gluc_c]$	`gluc_c`	5.3	mM	Concentration of glucose in the blood [15].
$[lac]_n$	`_LOn`	3	mM	Normal concentration of lactate in the cytoplasm [13].

Name	Model Name	Value	Units	Description
$[\mathrm{lac_c}]$	`lac_c`	2	mM	Capillary lactate concentration [15].
ΔG°	`Gp0`	-3.05e+04	$\mathrm{J\,mol^{-1}}$	Standard Gibbs free energy of ATP hydrolysis
$\Delta \mathrm{HHb_{offset}}$	`DHHb_offset`	0	µM	an arbitrary baseline offset to the HHb signal (NIRS)
$\Delta \mathrm{HbO_{2,offset}}$	`DHbO2_offset`	0	µM	an arbitrary baseline offset to the HbO_2 signal (NIRS)
$\Delta \mathrm{HbT_{offset}}$	`DHbT_offset`	0	µM	an arbitrary baseline offset to the HbT signal (NIRS)
$\Delta \mathrm{Hbdiff_{offset}}$	`DHbdiff_offset`	0	µM	an arbitrary baseline offset to the HHb signal (NIRS)
$\Delta \mathrm{oxCCO_{offset}}$	`CCO_offset`	0	µM	an arbitrary baseline offset to the CCO signal (NIRS)
$\Delta \mathrm{p_{3,corr}}$	`Dp3_corr`	-25	mV	$\Delta p_3 0$ minus normal PMF
dpH	`dpH`	0.001	none	a constant in the buffering relationship
$\mathrm{k_{H,O_2}}$	`henry_O2`	0.0014	$\mathrm{mM\,mmHg^{-1}}$	constant setting relationship between oxygen saturation and oxygen concentration in artery
$\mathrm{pH_o}$	`pH_o`	7	none	extra-mitochondrial pH
$\mathrm{pH_{m,n}}$	`pH_mn`	7.4	none	normal mitochondrial pH
$\mathrm{pH_{o,n}}$	`pH_on`	7	none	normal extra-mitochondrial pH
μ_{max}	`mu_max`	1	none	maximum value of mu
μ_{min}	`mu_min`	-1	none	minimum value of mu
μ_n	`mu_n`	0	none	normal value of mu

Name	Model Name	Value	Units	Description
ϕ	`phi`	0.036	mM	value of O2 at half maximal saturation
σ_{coll}	`sigma_coll`	62.79	mmHg	value of pressure at which vessels collapse
σ_{e0}	`sigma_e0`	0.1425	mmHg	parameter in relationship determining σ_e
τ_{P_a}	`t_p`	5	s	the time constant associated with v_{P_a}
$\tau_{\mathrm{CO_2}}$	`t_c`	5	s	the time constant associated with $v_{\mathrm{CO_2}}$
$\tau_{\mathrm{O_2}}$	`t_o`	20	s	the time constant associated with $v_{\mathrm{O_2}}$
τ_u	`t_u`	0.5	s	the time constant associated with v_u
$c3$	`c3`	0.11	$\mathrm{mV^{-1}}$	parameter controlling the sensitivity of reaction 3 to PMF
c_{k1}	`ck1`	0.01	$\mathrm{mV^{-1}}$	parameter constrolling sensitivity of k1 to PMF
c_{k2}	`ck2`	0.02	$\mathrm{mV^{-1}}$	parameter constrolling sensitivity of k2 to PMF
h_0	`h_0`	0.003	cm	vascular wall thickness when radius is r_0
k^{-}_{AK}	`k_nADPATP`	379	$\mathrm{mM^{-1}\,s^{-1}}$	the backward rate constant for the conversion of two molecules of ADP to one of ATP and one of AMP [10, 3].
k_{MCT}	`k_lac_trans`	2	mM	k_m for the transport of lactate in and out of the cell. This is an average of the different types of MCT and the different cell types [1].
k_{glut}	`k_gluc_trans`	6.2	mM	k_m for the transport of glucose in and out of the cell [9].
$k_{3,0}$	`k30`	2.5e+05	$\mathrm{mM^{-1}\,s^{-1}}$	an apparent second-order rate constant for reaction 3 at zero PMF

Name	Model Name	Value	Units	Description
k_{AK}	`k_ADPATP`	1055	$\mathrm{mM}^{-1}\,\mathrm{s}^{-1}$	the forward rate constant for the conversion of two molecules of ADP to one of ATP and one of AMP [10, 3].
k_{aut}	`k_aut`	0.5	none	control parameter allowing destruction of autoregulation
k_{lk2}	`k_lk2`	0.038	mV^{-1}	Second constant controlling rate of L_{lk} of Δp.
$k_{m,\mathrm{ATP}}$	`km`	0.025	none	Km for ATP use as a fraction of normal ATP concentration [10].
$k_{m,\mathrm{glycA,f}}$	`Km_glucNAf`	0.2	none	Km for ADP in glycolysis as a fration of normal ADP concentration [3].
$k_{m,\mathrm{glycG}}$	`Km_glucNgl`	0.05	mM	Km for glucose in the caricature of glycolysis [6].
$k_{m,\mathrm{glycP,f}}$	`Km_glucNPf`	0.2	none	Km for inorganic phosphate in glycolysis as a fraction of normal phosphate concentration [3].
$k_{m,\mathrm{tcaN,f}}$	`Km_NADf`	0.6	none	k_m for NAD in the TCA cycle as a fraction of normal NAD concentration
$k_{m,\mathrm{tcaP,f}}$	`Km_Pyf`	0.005	none	k_m for pyruvate in the TCA cycle as a fraction of normal pyruvate concentration
k_{unc}	`k_unc`	1	none	a parameter representing the action of uncouplers
n_a	`na`	4.33	none	number of protons passing through Complex V for each ATP synthesised [4]
n_h	`n_h`	2.5	none	Hill coefficient for haemoglobin saturation
n_m	`n_m`	1.83	none	exponent in the muscular tension relationship
p_2	`p2`	4	none	total protons pumped by reaction 2

Name	Model Name	Value	Units	Description
p_{23}	p23	8	none	total protons pumped by reactions 2 and 3
p_{tot}	p_tot	18.4	none	total protons pumped by reactions 1, 2 and 3
r_0	r_0	0.0126	cm	a special radius in the elastic tension relationship
r_m	r_m	0.027	cm	value of vessel radius giving maximum muscular tension
r_n	r_n	0.0187	cm	normal radius of blood vessels
r_t	r_t	0.018	cm	parameter in the muscular tension relationship
r_{CV}	r_CV	5	none	a parameter controlling the ratio of maximal to minimal rates of oxidative phosphorylation
$t_{1/2,\mathrm{pl}}$	k_PytoLac_ht	10	s^{-1}	Time constant for pyruvate to lactate interconvertion
$t_{1/2,\mathrm{PCr}}$	k_PCrATP_ht	2e-05	s	halftime for the reaction in which phosphocreatine combines with ADP to give creatine and ATP
u	u	1	none	The representation of ”demand” in the model.
u_n	u_n	1	none	Resting ”demand”

2 Derived Parameters

Name	Model Name	Expression	Value	Units
$C_{\mathrm{NADH},n}$	C_NADH_n	$\frac{Z}{2}\log\left(\frac{1}{[\mathrm{NAD}]_\mathrm{n}/[\mathrm{NADH}]_\mathrm{n}}\right)$	-5.197	mV

Name	Model Name	Expression	Value	Units
D_{O2}	`D_O2`	$\frac{J_{\mathrm{O2},n}}{[\mathrm{O_{2,c}}]_\mathrm{n}-[\mathrm{O_2}]_\mathrm{n}}$	0.6796	s^{-1}
E_2	`E_2`	$\mathcal{E}_0(\mathrm{cyt\,a_3}) - \mathcal{E}_0(\mathrm{Cu_A})$	103	mV
$E_{1,NADH,n}$	`E1NADH_n`	$\mathcal{E}_0(\mathrm{Cu_A}) - \mathcal{E}_0(\mathrm{NADH}) + C_{\mathrm{NADH},n}$	561.8	mV
$E_{1,n}$	`E_1n`	$E_{1,NADH,n}$	561.8	mV
G_n	`Gn`	$\frac{\mathrm{CBF_n}(1+G_{\mathrm{VArat,n}})}{G_{\mathrm{VArat,n}}(P_{a,\mathrm{n}}-P_{vs})}$	0.0002062	$\mathrm{mmHg}^{-1}\,\mathrm{s}^{-1}$
G_v	`G_v`	$G_{\mathrm{VArat,n}} G_n$	0.0008247	$\mathrm{mmHg}^{-1}\,\mathrm{s}^{-1}$
$J_{\mathrm{O2},n}$	`J_O2n`	$\mathrm{CMRO_{2,n}}$	0.02	$\mathrm{mM\,s^{-1}}$
K_G	`K_G`	$\frac{G_n}{r_n^4}$	1686	$\mathrm{mmHg}^{-1}\,\mathrm{s}^{-1}\,\mathrm{cm}^{-4}$
L_n	`L_n`	$p_{tot} f_n$	5.492	$\mathrm{mM\,s^{-1}}$
$L_{CV,\mathrm{frac}}$	`L_CVfrac`	$1 - L_{lk,\mathrm{frac}}$	0.75	none
$L_{CV,\mathrm{max}}$	`L_CVmax`	$\frac{L_{CV,\mathrm{n}}}{L_{CV,0}}$	10.3	$\mathrm{mM\,s^{-1}}$
$L_{CV,\mathrm{n}}$	`L_CVn`	$L_n L_{CV,\mathrm{frac}}$	4.119	$\mathrm{mM\,s^{-1}}$
$L_{lk,\mathrm{n}}$	`L_lkn`	$L_n L_{lk,\mathrm{frac}}$	1.373	$\mathrm{mM\,s^{-1}}$
L_{lk0}	`L_lk0`	$\frac{L_{lk,\mathrm{n}}}{\exp(\Delta \mathrm{p_n} k_{lk2})-1}$	0.002269	$\mathrm{mM\,s^{-1}}$
$P_{1,n}$	`P_1n`	$\frac{P_{a,\mathrm{n}}+P_{v,\mathrm{n}}}{2}$	30.6	mmHg
$P_{v,\mathrm{n}}$	`P_vn`	$\frac{G_v P_{vs}+G_n P_{a,\mathrm{n}}}{G_n+G_v}$	11.2	mmHg

Name	Model Name	Expression	Value	Units
$T_{\mathrm{max,n}}$	`T_maxn`	$\frac{T_{m,\mathrm{n}}}{\exp\left(-\left(\left\lvert\frac{r_n - r_m}{r_t - r_m}\right\rvert\right)^{n_m}\right)}$	1.383	mmHg cm
T_{max0}	`T_max0`	$\frac{T_{\mathrm{max,n}}}{1+k_{aut}\mu_n}$	1.383	mmHg cm
$T_{e,\mathrm{n}}$	`T_en`	$\sigma_{e,n}h_n$	-0.09604	mmHg cm
$T_{m,\mathrm{n}}$	`T_mn`	$\left(P_{1,n} - P_{ic,\mathrm{n}}\right) r_n - T_{e,\mathrm{n}}$	0.5841	mmHg cm
$V_{\mathrm{a,n}}$	`Vol_artn`	$\frac{V_{\mathrm{t,n}}}{1+\mathrm{VArat_n}}$	0.25	none
$V_{\mathrm{v,n}}$	`Vol_venn`	$V_{\mathrm{t,n}} \frac{\mathrm{VArat_n}}{1+\mathrm{VArat_n}}$	0.75	none
$[\mathrm{HHb_a}]$	`Xa`	$[\mathrm{Hbtot}]\left(1 - \mathrm{SaO2}\right)$	0.216	mM
$[\mathrm{O_{2,a}}]$	`O2a`	$\phi\left(\frac{\mathrm{SaO2}}{1-\mathrm{SaO2}}\right)^{\frac{1}{n_h}}$	0.1283	mM
$\Delta G_{1,n}$	`DG1_n`	$-4\left(E_{1,n} + Z\log\left(\frac{\mathrm{Cu_{A,o,n}}}{\mathrm{Cu_{A,o,n}}}\right)\right) + p_1\Delta\mathrm{p_n}$	-566.3	mV
$\Delta G_{2,n}$	`DG2_n`	$-4\left(E_2 + Z\left(\log\left(\frac{\mathrm{Cu_{A,o,n}}}{\mathrm{Cu_{A,o,n}}}\right) - \log\left(\frac{[\mathrm{a3r}]_\mathrm{n}}{\mathrm{a3_{o,n}}}\right)\right)\right) + p_2\Delta\mathrm{p_n}$	-39.7	mV
$\Delta\Psi_{init}$	`Dpsi_init`	$\Delta\Psi_n$	145	mV
$\mathrm{Cu_{A,o,n}}$	`ared_n`	$[\mathrm{CCO}]_\mathrm{mit} - \mathrm{Cu_{A,o,n}}$	0.01084	mM
$\mathrm{Cu_{A,o,init}}$	`a_init`	$\mathrm{Cu_{A,o,n}}$	0.022	mM
$\mathrm{Cu_{A,o,n}}$	`a_n`	$[\mathrm{CCO}]_\mathrm{mit}\mathrm{Cu_{A,frac,n}}$	0.022	mM
$\mathrm{HHb_n}$	`HHbn`	$1000\frac{V_{\mathrm{a,n}}[\mathrm{HHb_a}]_\mathrm{n} + V_{\mathrm{v,n}}[\mathrm{HHb_v}]_\mathrm{n}}{4}V_{\mathrm{blood,n}}$	16.99	µM
$\mathrm{H^+_{m,init}}$	`H_init`	$\mathrm{H^+_{m,n}}$	3.981e-05	mM

Name	Model Name	Expression	Value	Units
$H^+_{m,n}$	`H_n`	$10^{3-\mathrm{pH}_{m,n}}$	3.981e-05	mM
$HbO2_n$	`HbO2n`	$1000\frac{V_{a,n}[HbO_{2,a}]_n+V_{v,n}[HbO_{2,v}]_n}{4}V_{blood,n}$	26.89	µM
Hbt_n	`HbTn`	$1000\frac{(V_{a,n}+V_{v,n})[Hbtot]_n}{4}V_{blood,n}$	43.88	µM
$K_{eq,PCr}$	`k_PCrATP_eq`	$\frac{K^*_{eq,PCr}}{[H^+]_n}$	1.66e+06	mM^{-1}
$Keq_{1,n}$	`Keq1_n`	$10^{\frac{-1}{Z}\left(\frac{p_1\Delta p_n}{4}-E_{1,n}\right)}$	123.2	none
$Keq_{2,n}$	`Keq2_n`	$10^{\frac{-1}{Z}\left(\frac{p_2\Delta p_n}{4}-E_2\right)}$	0.07735	none
Keq_{ADPATP}	`k_ADPATP_eq`	$\frac{k_{AK}}{k^-_{AK}}$	2.784	none
$NADH_n$	`NADHn`	$N_t - [NAD]_n$	1.2	mM
PaO_2	`PaO2`	$\frac{[O_{2,a}]}{k_{H,O_2}}$	91.68	mmHg
$ScO2_n$	`ScO2_n`	$\frac{SaO2_n+SvO2_n}{2}$	0.7285	none
$SvO2_n$	`SvO2_n`	$\frac{[HbO_{2,v}]_n}{[Hbtot]_n}$	0.497	none
$V_{glucosein}$	`v_gluc_in`	$\frac{[gluc_c]}{k_{glut}+[gluc_c]}$	0.4609	none
V_{lacin}	`v_lac_in`	$\frac{[lac_c]}{k_{MCT}+[lac_c]}$	0.5	none
$[AMP]_n$	`_AMPn`	$\frac{Keq_{ADPATP}[ADP]_n{}^2}{[ATP]_n}$	0.0001822	mM
$[CCO]_{mit}$	`cytox_tot`	$\frac{[CCO]_{tis}}{V_{mit}}$	0.03284	mM

Name	Model Name	Expression	Value	Units
$[\mathrm{Cr}]_\mathrm{n}$	`_Crn`	$\frac{\mathrm{K}^*_{\mathrm{eq,PCr}}[\mathrm{ADP}]_\mathrm{n}[\mathrm{PCr}]_\mathrm{n}}{[\mathrm{ATP}]_\mathrm{n}}$	2.354	mM
$[\mathrm{HHb_a}]_\mathrm{n}$	`Xa_n`	$[\mathrm{Hbtot}]_\mathrm{n}\,(1-\mathrm{SaO2_n})$	0.216	mM
$[\mathrm{HHb_v}]_\mathrm{n}$	`Xv_n`	$[\mathrm{Hbtot}]_\mathrm{n}-[\mathrm{HbO_{2,v}}]_\mathrm{n}$	2.716	mM
$[\mathrm{H^+}]_\mathrm{n}$	`_Hyn`	$1000\times10^{-\mathrm{pH_{o,n}}}$	0.0001	mM
$[\mathrm{H^+}]$	`_Hy`	$1000\times10^{-\mathrm{pH_o}}$	0.0001	mM
$[\mathrm{HbO_{2,a}}]_\mathrm{n}$	`XOa_n`	$[\mathrm{Hbtot}]_\mathrm{n}\mathrm{SaO2_n}$	5.184	mM
$[\mathrm{HbO_{2,a}}]$	`XOa`	$[\mathrm{Hbtot}]\mathrm{SaO2}$	5.184	mM
$[\mathrm{HbO_{2,v}}]_\mathrm{n}$	`XOv_n`	$\frac{\mathrm{CBF_n}[\mathrm{HbO_{2,a}}]_\mathrm{n}-J_{\mathrm{O2},n}}{\mathrm{CBF_n}}$	2.684	mM
$[\mathrm{HbO_{2,v}}]_\mathrm{init}$	`XOv_init`	$[\mathrm{HbO_{2,v}}]_\mathrm{n}$	2.684	mM
$[\mathrm{Hbtot}]$	`Xtot`	$[\mathrm{Hbtot}]_\mathrm{n}$	5.4	mM
$[\mathrm{NAD}]_\mathrm{n}$	`NADn`	$\frac{\mathrm{N_t}}{1+\frac{1}{[\mathrm{NAD}]_\mathrm{n}/[\mathrm{NADH}]_\mathrm{n}}}$	1.8	mM
$[\mathrm{O_2}]_\mathrm{init}$	`O2_init`	$[\mathrm{O_2}]_\mathrm{n}$	0.024	mM
$[\mathrm{O_{2,c}}]_\mathrm{n}$	`O2c_n`	$\phi\left(\frac{\mathrm{ScO2_n}}{1-\mathrm{ScO2_n}}\right)^{\frac{1}{n_h}}$	0.05343	mM
$[\mathrm{O_{2,c}}]_\mathrm{init}$	`O2c_init`	$[\mathrm{O_{2,c}}]_\mathrm{n}$	0.05343	mM
$[\mathrm{P}]_\mathrm{n}$	`_Pn`	$\frac{[\mathrm{PCr}]_\mathrm{n}}{[\mathrm{PCr}]_\mathrm{n}/[\mathrm{P_i}]_\mathrm{n}}$	0.9524	mM
$[\mathrm{a3r}]_\mathrm{n}$	`bred_n`	$\frac{f_n(1+\exp(-c3(\Delta\mathrm{p_n}-\Delta\mathrm{p_{30}})))}{k_3[\mathrm{O_2}]_\mathrm{n}\exp(-c3(\Delta\mathrm{p_n}-\Delta\mathrm{p_{30}}))}$	0.000828	mM

Name	Model Name	Expression	Value	Units
$[\mathrm{a3r}]_{\mathrm{init}}$	`bred_init`	$[\mathrm{a3r}]_{\mathrm{n}}$	0.000828	mM
$\Delta\mathrm{G}_{\mathrm{n}}$	`DGpn`	$\Delta\mathrm{G}^{\circ} + ZF\log\left(g_{p,\mathrm{n}}\right)$	-6.06e+04	$\mathrm{J\,mol^{-1}}$
$\Delta\mathrm{pH}_{n}$	`DpH_n`	$\mathrm{pH}_{\mathrm{m,n}} - \mathrm{pH}_{\mathrm{o,n}}$	0.4	none
$\Delta\mathrm{p}_{\mathrm{n}}$	`Dp_n`	$\Delta\Psi_{n} + Z\Delta\mathrm{pH}_{n}$	168.6	mV
$\Delta\mathrm{p}_{\mathrm{CV0}}$	`Dp_CV0`	$\frac{-\Delta\mathrm{G}_{\mathrm{n}}}{n_a F}$	145	mV
$\Delta\mathrm{p}_{30}$	`Dp_30`	$\Delta\mathrm{p}_{\mathrm{n}} + \Delta\mathrm{p}_{3,\mathrm{corr}}$	143.6	mV
$\mathrm{a3}_{\mathrm{frac,n}}$	`b_frac_n`	$1 - \frac{[\mathrm{a3r}]_{\mathrm{n}}}{[\mathrm{CCO}]_{\mathrm{mit}}}$	0.9748	none
$\mathrm{a3}_{\mathrm{o,n}}$	`b_n`	$[\mathrm{CCO}]_{\mathrm{mit}} - [\mathrm{a3r}]_{\mathrm{n}}$	0.03201	mM
$\mathrm{glyc}_{\mathrm{a,n}}$	`glyc_an`	$\frac{{[\mathrm{ADP}]_{\mathrm{n}}}^2}{k_{m,\mathrm{glycA}}^2 + {[\mathrm{ADP}]_{\mathrm{n}}}^2}$	0.9615	none
$\mathrm{glyc}_{\mathrm{g,n}}$	`glyc_gn`	$\frac{[\mathrm{gluc}]_{\mathrm{n}}}{k_{m,\mathrm{glycG}} + [\mathrm{gluc}]_{\mathrm{n}}}$	0.96	none
$\mathrm{glyc}_{\mathrm{p,n}}$	`glyc_pn`	$\frac{{[\mathrm{P}]_{\mathrm{n}}}^2}{k_{m,\mathrm{glycP}}^2 + {[\mathrm{P}]_{\mathrm{n}}}^2}$	0.9615	none
$\mathrm{k}_{1,\mathrm{n}}$	`k1_n`	$\frac{f_n}{\mathrm{Cu}_{\mathrm{A,o,n}} - \frac{1}{\mathrm{Keq}_{1,\mathrm{n}}}\mathrm{Cu}_{\mathrm{A,o,n}}}$	13.62	$\mathrm{s^{-1}}$
$\mathrm{k}_{2,\mathrm{n}}$	`k2_n`	$\frac{f_n}{\mathrm{Cu}_{\mathrm{A,o,n}}\mathrm{a3}_{\mathrm{o,n}} - \frac{1}{\mathrm{Keq}_{2,\mathrm{n}}}\mathrm{Cu}_{\mathrm{A,o,n}}[\mathrm{a3r}]_{\mathrm{n}}}$	2681	$\mathrm{mM^{-1}\,s^{-1}}$
$\nu_{P_a,n}$	`v_pn`	$P_{a,\mathrm{n}}$	50	mmHg
$\nu_{\mathrm{CO_2},n}$	`v_cn`	$P_a\mathrm{CO}_{2,\mathrm{n}}$	40	mmHg
$\nu_{\mathrm{O_2},n}$	`v_on`	$[\mathrm{O}_{2,\mathrm{c}}]_{\mathrm{n}}$	0.05343	mM

Name	Model Name	Expression	Value	Units
$\nu_{u,n}$	`v_un`	u_n	1	none
$\sigma_{e,n}$	`sigma_en`	$\sigma_{e0}\left(\exp\left(\frac{K_\sigma(r_n-r_0)}{r_0}\right)-1\right)-\sigma_{coll}$	-44.89	mmHg
f_n	`f_n`	$\frac{\mathrm{CMRO_{2,n}}}{V_{\mathrm{mit}}}$	0.2985	$\mathrm{mM\,s^{-1}}$
$g_{p,\mathrm{n}}$	`gp_n`	$\frac{[\mathrm{ADP}]_\mathrm{n}[\mathrm{P}]_\mathrm{n}}{1000[\mathrm{ATP}]_\mathrm{n}}$	5.195e-06	none
h_n	`h_n`	$-r_n+\sqrt{r_n^2+2r_0h_0+h_0h_0}$	0.00214	cm
k^-_{PCr}	`k_nPCrATP`	$\frac{\ln(2)}{(\mathrm{K_{eq,PCr}}[\mathrm{PCr}]_\mathrm{n}[\mathrm{ADP}]_\mathrm{n}+[\mathrm{Cr}]_\mathrm{n}+[\mathrm{ATP}]_\mathrm{n})t_{1/2,\mathrm{PCr}}}$	0.6691	$\mathrm{mM^{-1}\,s^{-1}}$
k^-_{pl}	`k_nPytoLac`	$t_{1/2,\mathrm{pl}}$	10	$\mathrm{s^{-1}}$
k_3	`k3`	$\frac{k_{3,0}(1+\exp(-c3(0-\Delta\mathrm{p}_{30})))}{\exp(-c3(0-\Delta\mathrm{p}_{30}))}$	2.5e+05	$\mathrm{mM^{-1}\,s^{-1}}$
k_{PCr}	`k_PCrATP`	$\frac{\ln(2)}{\left([\mathrm{PCr}]_\mathrm{n}[\mathrm{ADP}]_\mathrm{n}+\frac{[\mathrm{Cr}]_\mathrm{n}+[\mathrm{ATP}]_\mathrm{n}}{\mathrm{K_{eq,PCr}}}\right)t_{1/2,\mathrm{PCr}}}[\mathrm{H^+}]$	111.1	$\mathrm{mM^{-1}\,s^{-1}}$
k_m	`kmATP`	$[\mathrm{ATP}]_\mathrm{n}k_{m,\mathrm{ATP}}$	0.055	mM
k_{CV}	`kCV`	$\frac{-1}{\Delta\mathrm{p_n}-\Delta\mathrm{p_{CV0}}}\ln\left(\frac{1-L_{CV,0}}{1+r_{CV}L_{CV,0}}\right)$	0.06829	$\mathrm{mV^{-1}}$
$k_{\mathrm{TCA_n}}$	`k_TCAn`	$\frac{1}{3}\frac{\mathrm{CMRO_{2,n}}}{V_{\mathrm{mit}}}$	0.0995	$\mathrm{mM\,s^{-1}}$
k_{pl}	`k_PytoLac`	$\frac{\left(2\mathrm{CMR_{gluc,n}}-\frac{\mathrm{CMRO_{2,n}}}{3}+k^-_{\mathrm{pl}}[\mathrm{lac}]_\mathrm{n}\right)[\mathrm{H^+}]}{[\mathrm{Py}]_\mathrm{n}[\mathrm{H^+}]_\mathrm{n}}$	300	$\mathrm{s^{-1}}$
$k_{m,\mathrm{glycA}}$	`Km_glucNA`	$k_{m,\mathrm{glycA,f}}[\mathrm{ADP}]_\mathrm{n}$	0.0024	mM
$k_{m,\mathrm{glycP}}$	`Km_glucNP`	$k_{m,\mathrm{glycP,f}}[\mathrm{P}]_\mathrm{n}$	0.1905	mM

Name	Model Name	Expression	Value	Units
$k_{m,\mathrm{tcaN}}$	Km_NAD	$k_{m,\mathrm{tcaN,f}}[\mathrm{NAD}]_\mathrm{n}$	1.08	mM
$k_{m,\mathrm{tcaP}}$	Km_Py	$k_{m,\mathrm{tcaP,f}}[\mathrm{Py}]_\mathrm{n}$	0.0005	mM
p_1	p1	$p_{tot} - p_{23}$	10.4	none
p_3	p3	$p_{23} - p_2$	4	none
r_{init}	r_init	r_n	0.0187	cm
v_MCT	v_lac_trans	$\frac{2\mathrm{CMR}_{\mathrm{gluc,n}} - \frac{\mathrm{CMRO}_{2,\mathrm{n}}}{3}}{\frac{[\mathrm{lac}]_\mathrm{n}}{[\mathrm{lac}]_\mathrm{n} + k_\mathrm{MCT}} - \mathrm{V}_\mathrm{lacin}}$	0.02133	$\mathrm{mM\,s^{-1}}$
v_glut	v_gluc_trans	$\frac{\mathrm{CMR}_{\mathrm{gluc,n}}}{\mathrm{V}_\mathrm{glucosein} - \frac{[\mathrm{gluc}]_\mathrm{n}}{[\mathrm{gluc}]_\mathrm{n} + k_\mathrm{glut}}}$	0.01473	$\mathrm{mM\,s^{-1}}$
v_TCA	v_TCA	$\frac{k_{\mathrm{TCA_n}}}{[\mathrm{Py}]_\mathrm{n}[\mathrm{NAD}]_\mathrm{n}}\left(k_{m,\mathrm{tcaN}} + [\mathrm{NAD}]_\mathrm{n}\right)\left(k_{m,\mathrm{tcaP}} + [\mathrm{Py}]_\mathrm{n}\right)$	0.16	$\mathrm{mM\,s^{-1}}$
$v_\mathrm{glyc,n}$	Vmax_glucNn	$\frac{\mathrm{CMR}_{\mathrm{gluc,n}}}{\mathrm{glyc}_{\mathrm{g,n}}\mathrm{glyc}_{\mathrm{p,n}}\mathrm{glyc}_{\mathrm{a,n}}}$	0.004957	$\mathrm{mM\,s^{-1}}$

3 Model Variables

Name	Model Name	Expression	Initial Value	Units	Description
$[\mathrm{HbO}_{2,\mathrm{v}}]$	XOv	$\mathrm{CBF}\left([\mathrm{HbO}_{2,\mathrm{a}}] - [\mathrm{HbO}_{2,\mathrm{v}}]\right) - J_{\mathrm{O2}}$	2.684	mM	The concentration of bound oxygen in the veins.
$\Delta\Psi$	Dpsi	$\frac{\mathrm{d}\Delta\Psi}{\mathrm{d}t} = \frac{p_2 f_2 + p_1 f_1 + p_3 f_3 - L}{C_{im}}$	145	mV	mitochondrial inner membrane potential

Name	Model Name	Expression	Initial Value	Units	Description
$Cu_{A,o}$	`a`	$\frac{dCu_{A,o}}{dt} = 4T_{a\_ox} - 4T_{a\_red}$	0.022	mM	The concentration of oxidised cytochrome-c-oxidase
H_m^+	`H`	$\frac{dH_m^+}{dt} = \frac{-p_2 T_{a\_ox}}{R_{Hi}} - \frac{p_1 T_{a\_red}}{R_{Hi}} - \frac{p_3 T_{b\_ox}}{R_{Hi}} + \frac{T_{psi\_out}}{R_{Hi}}$	3.981e-05	mM	concentration of hydrogen ions in mitochondria
[ADP]	`_ADP`	$\frac{d[ADP]}{dt} = -T_{PCrtoATP} - T_{ADPtoATP} + T_{ATPtoADP} - 2T_{aden1} - 2T_{glycol}$	0.012	mM	ADP concentration in cytoplasm and mitochondria [2]
[AMP]	`_AMP`	$\frac{d[AMP]}{dt} = T_{aden1}$	0.0001822	mM	AMP concentration in cytoplasm
[ATP]	`_ATP`	$\frac{d[ATP]}{dt} = T_{PCrtoATP} + T_{ADPtoATP} - T_{ATPtoADP} + T_{aden1} + 2T_{glycol}$	2.2	mM	ATP concentration in cytoplasm and mitochondira
[Cr]	`_Cr`	$\frac{d[Cr]}{dt} = T_{PCrtoATP}$	2.354	mM	creatine concentration in cytoplasm
[NAD]	`NAD`	$\frac{d[NAD]}{dt} = 2T_{a\_red} - 6T_{TCA}$	1.8	mM	Concentration of NAD in the mitochondria
$[O_{2,c}]$	`O2c`	$\phi\left(\frac{ScO2}{1-ScO2}\right)^{\frac{1}{n_h}} - [O_{2,c}]$	0.05343	mM	The concentration of oxygen in the capillary.
$[O_2]$	`O2`	$\frac{d[O_2]}{dt} = -T_{b\_ox} + \frac{T_{O2\_in}}{V_{mit}}$	0.024	mM	The concentration of oxygen in the mitochondria
[PCr]	`_PCr`	$\frac{d[PCr]}{dt} = -T_{PCrtoATP}$	2.6	mM	phosphocreatine concentration in cytoplasm

Name	Model Name	Expression	Initial Value	Units	Description
$[\mathrm{P_i}]$	`_P`	$\frac{\mathrm{d}[\mathrm{P_i}]}{\mathrm{d}t} = -T_{\mathrm{ADPtoATP}} + T_{\mathrm{ATPtoADP}} - 2T_{\mathrm{glycol}}$	0.9524	mM	Inorganic phosphate concentration in cytoplasm and mitochondria
$[\mathrm{Py}]$	`_Py0`	$\frac{\mathrm{d}[\mathrm{Py}]}{\mathrm{d}t} = 2T_{\mathrm{glycol}} - T_{\mathrm{PytoLac}} - \frac{T_{\mathrm{TCA}} V_{\mathrm{mit}}}{1}$	0.1	mM	Concentration of pyruvate in the cytoplasm
$[\mathrm{a3r}]$	`bred`	$\frac{\mathrm{d}[\mathrm{a3r}]}{\mathrm{d}t} = 4T_{\mathrm{a\_ox}} - 4T_{\mathrm{b\_ox}}$	0.000828	mM	concentration of reduced cyt a3 in mitochondria
$[\mathrm{gluc}]$	`_gluc`	$\frac{\mathrm{d}[\mathrm{gluc}]}{\mathrm{d}t} = -T_{\mathrm{glycol}} + T_{\mathrm{glucose\_in}} - T_{\mathrm{glucose\_out}}$	1.2	mM	Concentration of glucose in the cytoplasm
$[\mathrm{lac}]$	`_L0`	$\frac{\mathrm{d}[\mathrm{lac}]}{\mathrm{d}t} = T_{\mathrm{PytoLac}} + T_{\mathrm{lactate\_in}} - T_{\mathrm{lactate\_out}}$	3	mM	Concentration of lactate in the cytoplasm
ν_u	`v_u`	$\frac{\mathrm{d}\nu_u}{\mathrm{d}t} = \frac{1}{\tau_u}\left(u - \nu_u\right)$	1	none	The demand parameter u passed through a first order filter.
ν_{P_a}	`v_p`	$\frac{\mathrm{d}\nu_{P_a}}{\mathrm{d}t} = \frac{1}{\tau_{P_a}}\left(P_a - \nu_{P_a}\right)$	50	mmHg	ABP passed through a first order filter.
$\nu_{\mathrm{CO_2}}$	`v_c`	$\frac{\mathrm{d}\nu_{\mathrm{CO_2}}}{\mathrm{d}t} = \frac{1}{\tau_{\mathrm{CO_2}}}\left(P_a\mathrm{CO_2} - \nu_{\mathrm{CO_2}}\right)$	40	mmHg	CO2 passed through a first order filter.
$\nu_{\mathrm{O_2}}$	`v_o`	$\frac{\mathrm{d}\nu_{\mathrm{O_2}}}{\mathrm{d}t} = \frac{1}{\tau_{\mathrm{O_2}}}\left([\mathrm{O_{2,c}}] - \nu_{\mathrm{O_2}}\right)$	0.05343	mM	capillary O2 passed through a first order filter.
r	`r`	$T_e + T_m - \left(P_1 - P_{ic}\right) r$	0.0187	cm	typical radius of cerebral vessels

4 Temporary Variables

Name	Model Name	Expression	Initial Value	Units
C_{0i}	`C_0i`	$\frac{10^{-\mathrm{pH_m}} - 10^{-\mathrm{pH_m} - \mathrm{dpH}}}{\mathrm{dpH}}$	9.156e-08	none
C_{NADH}	`C_NADH`	$\frac{Z}{2} \log\left(\frac{1}{[\mathrm{NAD}]/[\mathrm{NADH}]}\right)$	-5.197	mV
E_1	`E_1`	$E_{1,NADH}$	561.8	mV
$E_{1,NADH}$	`E1NADH`	$\mathcal{E}_0(\mathrm{Cu_A}) - \mathcal{E}_0(\mathrm{NADH}) + C_{\mathrm{NADH}}$	561.8	mV
G	`G`	$K_G r^4$	0.0002062	$\mathrm{mmHg^{-1}\,s^{-1}}$
$J_{\mathrm{O2,min}}$	`JO2`	$\min\left(D_{\mathrm{O2}}\left([\mathrm{O_{2,c}}] - [\mathrm{O_2}]\right), \mathrm{CBF}[\mathrm{HbO_{2,a}}]\right)$	0.02	$\mathrm{mM\,s^{-1}}$
J_{O2}	`J_O2`	$J_{\mathrm{O2,min}}$	0.02	$\mathrm{mM\,s^{-1}}$
L	`L`	$L_{CV} + L_{lk}$	5.494	$\mathrm{mM\,s^{-1}}$
L_{CV}	`L_CV`	$\frac{CV_{inh} L_{CV,\max}\left(1 - \mathrm{e}^{-\theta}\right)}{1 + r_{CV}\mathrm{e}^{-\theta}}$	4.12	$\mathrm{mM\,s^{-1}}$
L_{lk}	`L_lk`	$k_{unc} L_{lk0}\left(\exp\left(\Delta \mathrm{p} k_{lk2}\right) - 1\right)$	1.373	$\mathrm{mM\,s^{-1}}$
P_1	`P_1`	$\frac{P_a + P_v}{2}$	30.6	mmHg
P_v	`P_v`	$\frac{G_v P_{vs} + G P_a}{G + G_v}$	11.2	mmHg
R_{ATPtoADP}	`R_ATPtoADP`	$\frac{[\mathrm{ATP}]}{k_m + [\mathrm{ATP}]}$	0.9756	none
$R_{\mathrm{glucose\_in}}$	`R_glucose_in`	$\mathrm{V_{glucosein}}$	0.4609	none
$R_{\mathrm{glucose\_out}}$	`R_glucose_out`	$\frac{[\mathrm{gluc}]}{k_{\mathrm{glut}} + [\mathrm{gluc}]}$	0.1622	none

Name	Model Name	Expression	Initial Value	Units
R_{glycol}	`R_glycol`	$\frac{[\mathrm{ADP}]^2[\mathrm{P_i}]^2[\mathrm{gluc}]}{\left(k_{m,\mathrm{glycA}}^2+[\mathrm{ADP}]^2\right)\left(k_{m,\mathrm{glycP}}^2+[\mathrm{P_i}]^2\right)\left(k_{m,\mathrm{glycG}}+[\mathrm{gluc}]\right)}$	0.8876	none
$R_{\mathrm{lactate\_in}}$	`R_lactate_in`	$\mathrm{V_{lacin}}$	0.5	none
$R_{\mathrm{lactate\_out}}$	`R_lactate_out`	$\frac{[\mathrm{lac}]}{k_{\mathrm{MCT}}+[\mathrm{lac}]}$	0.6	none
T_e	`T_e`	$\sigma_e h$	-0.09604	mmHg cm
T_m	`T_m`	$T_{\max}\exp\left(-\left(\left\lvert\frac{r-r_m}{r_t-r_m}\right\rvert\right)^{n_m}\right)$	0.5841	mmHg cm
T_{ADPtoATP}	`T_ADPtoATP`	$\mathrm{k_{ATP,C_V}}$	0.06376	$\mathrm{mM\,s^{-1}}$
T_{ATPtoADP}	`T_ATPtoADP`	$\frac{\mathrm{V_{max,ATP}}[\mathrm{ATP}]}{k_m+[\mathrm{ATP}]}$	0.07254	$\mathrm{mM\,s^{-1}}$
$T_{\mathrm{O2\_in}}$	`T_O2_in`	J_{O2}	0.02	$\mathrm{mM\,s^{-1}}$
T_{PCrtoATP}	`T_PCrtoATP`	$k_{\mathrm{PCr}}[\mathrm{PCr}][\mathrm{ADP}]-k_{\mathrm{PCr}}^{-}[\mathrm{ATP}][\mathrm{Cr}]$	-9.728e-05	$\mathrm{mM\,s^{-1}}$
T_{PytoLac}	`T_PytoLac`	$k_{\mathrm{pl}}[\mathrm{Py}]-k_{\mathrm{pl}}^{-}[\mathrm{lac}]$	0.002	$\mathrm{mM\,s^{-1}}$
T_{TCA}	`T_TCA`	k_{TCA}	0.0995	$\mathrm{mM\,s^{-1}}$
$T_{\mathrm{a\_ox}}$	`T_a_ox`	f_2	0.2985	$\mathrm{mM\,s^{-1}}$
$T_{\mathrm{a\_red}}$	`T_a_red`	f_1	0.2985	$\mathrm{mM\,s^{-1}}$
T_{aden1}	`T_aden1`	$k_{\mathrm{AK}}[\mathrm{ADP}]^2-k_{\mathrm{AK}}^{-}[\mathrm{ATP}][\mathrm{AMP}]$	1.64e-06	$\mathrm{mM\,s^{-1}}$
$T_{\mathrm{b\_ox}}$	`T_b_ox`	f_3	0.2985	$\mathrm{mM\,s^{-1}}$
$T_{\mathrm{glucose\_in}}$	`T_glucose_in`	$v_{\mathrm{glut}}\mathrm{V_{glucosein}}$	0.006789	$\mathrm{mM\,s^{-1}}$

Name	Model Name	Expression	Initial Value	Units
$T_{\mathrm{glucose\_out}}$	`T_glucose_out`	$\frac{v_{\mathrm{glut}}[\mathrm{gluc}]}{k_{\mathrm{glut}}+[\mathrm{gluc}]}$	0.002389	$\mathrm{mM\,s^{-1}}$
T_{glycol}	`T_glycol`	$\frac{v_{\mathrm{glyc}}[\mathrm{ADP}]^2[\mathrm{P_i}]^2[\mathrm{gluc}]}{\left(k_{m,\mathrm{glycA}}^2+[\mathrm{ADP}]^2\right)\left(k_{m,\mathrm{glycP}}^2+[\mathrm{P_i}]^2\right)\left(k_{m,\mathrm{glycG}}+[\mathrm{gluc}]\right)}$	0.0044	$\mathrm{mM\,s^{-1}}$
$T_{\mathrm{lactate\_in}}$	`T_lactate_in`	$v_{\mathrm{MCT}}\mathrm{V_{lacin}}$	0.01067	$\mathrm{mM\,s^{-1}}$
$T_{\mathrm{lactate\_out}}$	`T_lactate_out`	$\frac{v_{\mathrm{MCT}}[\mathrm{lac}]}{k_{\mathrm{MCT}}+[\mathrm{lac}]}$	0.0128	$\mathrm{mM\,s^{-1}}$
T_{max}	`T_max`	$T_{\mathrm{max0}}\left(1+k_{aut}\mu\right)$	1.383	$\mathrm{mmHg\,cm}$
$T_{\mathrm{psi\_out}}$	`T_psi_out`	L	5.494	$\mathrm{mM\,s^{-1}}$
V_{a}	`Vol_art`	$V_{\mathrm{a,n}}\left(\frac{r}{r_n}\right)^2$	0.25	none
V_{t}	`Vol_tot`	$V_{\mathrm{a}}+V_{\mathrm{v}}$	1	none
V_{v}	`Vol_ven`	$V_{\mathrm{v,n}}+C_v\left(P_v-P_{v,\mathrm{n}}\right)$	0.75	none
$Vmca$	`Vmca`	CBFCBFscale	40	$\mathrm{cm\,s^{-1}}$
$[\mathrm{HHb_v}]$	`Xv`	$[\mathrm{Hbtot}]-[\mathrm{HbO_{2,v}}]$	2.716	mM
ΔG_1	`DG1`	$-4\left(E_1+Z\log\left(\frac{\mathrm{Cu_{A,o}}}{\mathrm{Cu_{A,o}}}\right)\right)+p_1\Delta\mathrm{p}$	-566.3	mV
ΔG_2	`DG2`	$-4\left(E_2+Z\left(\log\left(\frac{\mathrm{Cu_{A,o}}}{\mathrm{Cu_{A,o}}}\right)-\log\left(\frac{[\mathrm{a3r}]}{\mathrm{a3_o}}\right)\right)\right)+p_2\Delta\mathrm{p}$	-39.7	mV
$\Delta\mathrm{Hbt}$	`DHbT`	$\Delta\mathrm{HbT_{offset}}+\mathrm{Hbt}-\mathrm{Hbt_n}$	-0.0002694	µM

Name	Model Name	Expression	Initial Value	Units
η	`eta`	$R_P\left(\frac{\nu_{P_a}}{\nu_{P_a,n}}-1\right) + R_O\left(\frac{\nu_{O_2}}{\nu_{O_2,n}}-1\right) + R_u\left(1-\frac{\nu_u}{\nu_{u,n}}\right) + R_C\left(1-\frac{\nu_{CO_2}}{\nu_{CO_2,n}}\right)$	0	none
AVR	`AVR`	$\frac{V_a}{V_v}$	0.3333	none
CBF	`CBF`	$G\left(P_a - P_v\right)$	0.008	$ml\, ml^{-1}\, s^{-1}$
$CMRO_2$	`CMRO2`	$f_3 V_{mit}$	0.02	$mM\, s^{-1}$
CMR_{gluc}	`CMRgluc`	$T_{glucose\_in} - T_{glucose\_out}$	0.0044	$mM\, s^{-1}$
CMR_{lac}	`CMRlac`	$T_{lactate\_in} - T_{lactate\_out}$	-0.002133	$mM\, s^{-1}$
$Cu_{A,o}$	`ared`	$[CCO]_{mit} - Cu_{A,o}$	0.01084	mM
HHb	`HHb`	$1000\frac{V_a[HHb_a]+V_v[HHb_v]}{4}V_{blood,n}$	16.99	µM
HbO_2	`HbO2`	$1000\frac{V_a[HbO_{2,a}]+V_v[HbO_{2,v}]}{4}V_{blood,n}$	26.89	µM
Hbt	`HbT`	$1000\frac{(V_a+V_v)[Hbtot]}{4}V_{blood,n}$	43.87	µM
Keq_1	`Keq1`	$10^{\frac{-1}{Z}\left(\frac{p_1\Delta p}{4}-E_1\right)}$	123.2	none
Keq_2	`Keq2`	$10^{\frac{-1}{Z}\left(\frac{p_2\Delta p}{4}-E_2\right)}$	0.07735	none
R_{Hi}	`R_Hi`	r_{buffi}	2.403e+05	none
ScO2	`ScO2`	$\frac{SaO2+SvO2}{2}$	0.7285	none
SvO2	`SvO2`	$\frac{[HbO_{2,v}]}{[Hbtot]}$	0.497	none

Name	Model Name	Expression	Initial Value	Units
TOS	`TOI`	$\frac{100\left(\frac{\left(\frac{r}{r_n}\right)^2}{\left(\frac{r}{r_n}\right)^2+\frac{V_\mathrm{v}}{V_\mathrm{a,n}}}[\mathrm{HbO_{2,a}}]+\frac{V_\mathrm{v}}{V_\mathrm{a,n}\left(\left(\frac{r}{r_n}\right)^2+\frac{V_\mathrm{v}}{V_\mathrm{a,n}}\right)}[\mathrm{HbO_{2,v}}]\right)}{[\mathrm{Hbtot}]}$	61.28	none
$\mathrm{V_{max,ATP}}$	`v_ATP`	$\left(\frac{L_{CV,\mathrm{n}}V_\mathrm{mit}}{n_a}+2\mathrm{CMR_{gluc,n}}\right)(1+k_{m,\mathrm{ATP}})\,u$	0.07435	$\mathrm{mM\,s^{-1}}$
[NADH]	`NADH`	$\mathrm{N_t}-[\mathrm{NAD}]$	1.2	mM
[NAD]/[NADH]	`NADNADHrat`	$\frac{[\mathrm{NAD}]}{[\mathrm{NADH}]}$	1.5	none
ΔG	`DGp`	$\Delta\mathrm{G}^\circ+ZF\log(g_p)$	-6.06e+04	$\mathrm{J\,mol^{-1}}$
ΔHHb	`DHHb`	$\Delta\mathrm{HHb_{offset}}+\mathrm{HHb}-\mathrm{HHb_n}$	0.0002395	µM
ΔHbO2	`DHbO2`	$\Delta\mathrm{HbO_{2,offset}}+\mathrm{HbO_2}-\mathrm{HbO2_n}$	-0.0005089	µM
ΔHbdiff	`DHbdiff`	$\Delta\mathrm{Hbdiff_{offset}}+\Delta\mathrm{HbO2}-\Delta\mathrm{HHb}$	-0.0007484	µM
ΔoxCCO	`CCO`	$\Delta\mathrm{oxCCO_{offset}}+1000V_\mathrm{mit}(\mathrm{Cu_{A,o}}-\mathrm{Cu_{A,o,n}})$	0	µM
Δp	`Dp`	$\Delta\Psi+Z(\mathrm{pH_m}-\mathrm{pH_o})$	168.6	mV
$\mathrm{a3_o}$	`b`	$[\mathrm{CCO}]_\mathrm{mit}-[\mathrm{a3r}]$	0.03201	mM
$\mathrm{k_1}$	`k1`	$\mathrm{k_{1,0}}\exp(-c_{k1}(\Delta\mathrm{p}-\Delta\mathrm{p_n}))$	13.62	$\mathrm{s^{-1}}$
$\mathrm{k_2}$	`k2`	$\mathrm{k_{2,n}}\exp(-c_{k2}(\Delta\mathrm{p}-\Delta\mathrm{p_n}))$	2681	$\mathrm{mM^{-1}\,s^{-1}}$
$\mathrm{k_{-1}}$	`kn1`	$\frac{\mathrm{k_1}}{\mathrm{Keq_1}}$	0.1105	$\mathrm{s^{-1}}$
$\mathrm{k_{-2}}$	`kn2`	$\frac{\mathrm{k_2}}{\mathrm{Keq_2}}$	3.466e+04	$\mathrm{mM^{-1}\,s^{-1}}$
$\mathrm{k_{1,0}}$	`k10`	$\frac{\mathrm{k_{1,n}}\frac{\mathrm{N_t}}{1+[\mathrm{NAD}]/[\mathrm{NADH}]}}{\mathrm{NADH_n}}$	13.62	$\mathrm{s^{-1}}$

Name	Model Name	Expression	Initial Value	Units
$\mathrm{k_{ATP,C_V}}$	kATP	$\frac{L_{CV} V_{\mathrm{mit}}}{n_a}$	0.06376	$\mathrm{mM\,s^{-1}}$
$\mathrm{pH_m}$	pH_m	$-\log\left(\frac{\mathrm{H_m^+}}{1000}\right)$	7.4	none
$\mathrm{r_{buffi}}$	r_buffi	$\frac{\mathrm{C_{buffi}}}{C_{0i}}$	2.403e+05	none
μ	mu	$\frac{\mu_{min}+\mu_{max}\mathrm{e}^{\eta}}{1+\mathrm{e}^{\eta}}$	0	none
σ_e	sigma_e	$\sigma_{e0}\left(\exp\left(\frac{K_\sigma(r-r_0)}{r_0}\right)-1\right)-\sigma_{coll}$	-44.89	mmHg
θ	theta	$k_{CV}\left(\Delta\mathrm{p}+\frac{Z}{n_a}\log\left(\frac{g_p}{g_{p,\mathrm{n}}}\right)-\Delta\mathrm{p_{CV0}}\right)$	1.61	none
f_1	f1	$\mathrm{k_1Cu_{A,o}-k_{-1}Cu_{A,o}}$	0.2985	$\mathrm{mM\,s^{-1}}$
f_2	f2	$\mathrm{k_2Cu_{A,o}a3_o-k_{-2}Cu_{A,o}[a3r]}$	0.2985	$\mathrm{mM\,s^{-1}}$
f_3	f3	$\frac{k_3[\mathrm{O_2}][\mathrm{a3r}]\exp\left(-c3(\Delta\mathrm{p}-\Delta\mathrm{p_{30}})\right)}{1+\exp\left(-c3(\Delta\mathrm{p}-\Delta\mathrm{p_{30}})\right)}$	0.2985	$\mathrm{mM\,s^{-1}}$
g_p	gp	$\frac{[\mathrm{ADP}][\mathrm{P_i}]}{1000[\mathrm{ATP}]}$	5.195e-06	none
h	h	$-r+\sqrt{r^2+2r_0h_0+h_0h_0}$	0.00214	cm
k_{TCA}	k_TCA	$\frac{v_{\mathrm{TCA}}[\mathrm{Py}][\mathrm{NAD}]}{(k_{m,\mathrm{tcaN}}+[\mathrm{NAD}])(k_{m,\mathrm{tcaP}}+[\mathrm{Py}])}$	0.0995	$\mathrm{mM\,s^{-1}}$
v_{glyc}	Vmax_glucN	$\frac{v_{\mathrm{glyc,n}}(I+1)}{1+I\frac{[\mathrm{ATP}]}{[\mathrm{ATP}]_\mathrm{n}}\frac{[\mathrm{AMP}]_\mathrm{n}}{[\mathrm{AMP}]}}$	0.004957	$\mathrm{mM\,s^{-1}}$

5 Reactions

Model Name	Description	Reaction
ADPtoATP	Phosphorylation of ADP by Complex V	$ADP + P_i \rightarrow ATP$
ATPtoADP	Hydrolysis of ATP	$ATP \rightarrow ADP + P_i$
O2_in	The reaction in which O_2 is supplied to the mitochondria	$\rightarrow O_2$
PCrtoATP	A two way mass action reaction representing the interconversion of PCr + ADP to Cr + ATP.	$PCr + ADP \leftrightarrow ATP + Cr$
PytoLac	interconversion between pyruvate and lactate	$Py \leftrightarrow lac$
TCA	One step simple representation of pyruvate dehyrogenase and the TCA cycle	$Py + 6NAD \rightarrow$
a_ox	The reaction in which a3 oxidises Cu_A and p_2 protons are pumped out of the matrix	$p2H^+_m \rightarrow 4Cu_{A,o} + 4a3r$
a_red	The reaction in which a is reduced and p_1 protons are pumped out of the matrix	$4Cu_{A,o} + p1H^+_m \rightarrow 2NAD$
aden1	a two way reaction in which two molecules of ADP are converted into one of ATP and one of AMP.	$2ADP \leftrightarrow ATP + AMP$
b_ox	The reaction in which O_2 oxidises a3 and p_2 protons are pumped out of the matrix	$O_2 + 4a3r + p3H^+_m \rightarrow$
glucose_in	Transport of glucose from the blood to the cytoplasm (fixed rate)	$\rightarrow gluc$
glucose_out	Transport of glucose from the cytoplasm to the blood	$gluc \rightarrow$
glycol	a one way Michaelis Menten reaction which is assumed to capture the process of glycolysis	$2ADP + 2P_i + gluc \rightarrow 2ATP + 2Py$
lactate_in	Transport of lactate from the blood to the cytoplasm (fixed rate)	$\rightarrow lac$
lactate_out	Transport of lactate from the cytoplasm to the blood	$lac \rightarrow$
psi_out	The reaction in which protons re-enter the matrix (via leak and complex V)	$\rightarrow H^+_m$

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