SBML Model Report

Model name: "Aubert2002 - Coupling between Brain electrical activity, Metabolism and Hemodynamics"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Felix Winter[1] and Audald Lloret i Villas[2] at April nineth 2014 at 4:25 p. m. and last time modified at May twelveth 2015 at 11:18 a. m. Table 1 provides 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	20
events	3	constraints	0
reactions	18	function definitions	13
global parameters	69	unit definitions	2
rules	21	initial assignments	7

Model Notes

Aubert2002 - Coupling between Brainelectrical activity, Metabolism and HemodynamicsFelix Winter encoded this model in SBMLas part of his work at ASD GmbH

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This model is described in the article:A model of the coupling between brain electrical activity, metabolism, and hemodynamics: application to the interpretation of functional neuroimaging.Aubert A, Costalat R.Neuroimage 2002 Nov; 17(3): 1162-1181

Abstract:

In order to improve the interpretation of functional neuroimaging data, we implemented a mathematical model of the coupling between membrane ionic currents, energy metabolism (i.e., ATP regeneration via phosphocreatine buffer effect, glycolysis, and mitochondrial respiration), blood-brain barrier exchanges, and hemodynamics. Various hypotheses were tested for the variation of the cerebral metabolic rate of oxygen (CMRO(2)): (H1) the CMRO(2) remains at its baseline level; (H2) the CMRO(2) is enhanced as soon as the cerebral blood flow (CBF) increases; (H3) the CMRO(2) increase depends on intracellular oxygen and pyruvate concentrations, and intracellular ATP/ADP ratio; (H4) in addition to hypothesis H3, the CMRO(2) progressively increases, due to the action of a second messenger. A good agreement with experimental data from magnetic resonance imaging and spectroscopy (MRI and MRS) was obtained when we simulated sustained and repetitive activation protocols using hypotheses (H3) or (H4), rather than hypotheses (H1) or (H2). Furthermore, by studying the effect of the variation of some physiologically important parameters on the time course of the modeled blood-oxygenation-level-dependent (BOLD) signal, we were able to formulate hypotheses about the physiological or biochemical significance of functional magnetic resonance data, especially the poststimulus undershoot and the baseline drift.

This model is hosted on BioModels Database and identified by: BIOMD0000000570.

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 of which three are predefined by SBML and not mentioned in the model.

2.1 Unit volume

Name volume

Definition ml

2.2 Unit substance

Name substance

Definition mmol

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
compartment_1	Tissue		3	1	litre	☑	
compartment_2	Arteries		3	1	litre	☑	
compartment_3	Capillaries		3	1	litre	☑	
compartment_4	Venous balloon		3	0.0237	ml	☐	

3.1 Compartment compartment_1

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

Name Tissue

3.2 Compartment compartment_2

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

Name Arteries

3.3 Compartment compartment_3

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

Name Capillaries

3.4 Compartment compartment_4

This is a three dimensional compartment with a not constant size of 0.0237 ml.

Name Venous balloon

4 Species

This model contains 20 species. The boundary condition of seven of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 11 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
species_1	Na+	compartment_1	mmol	☐	☐
species_2	ATP	compartment_1	mmol	☐	☑
species_3	ADP	compartment_1	mmol	☐	☑
species_4	GLC	compartment_1	mmol	☐	☐
species_5	GAP	compartment_1	mmol	☐	☐
species_6	NAD+	compartment_1	mmol	☐	☑
species_7	NADH	compartment_1	mmol	☐	☐
species_8	PYR	compartment_1	mmol	☐	☐
species_9	PEP	compartment_1	mmol	☐	☐
species_10	LAC	compartment_1	mmol	☐	☐
species_11	PCr	compartment_1	mmol	☐	☐
species_12	Cr	compartment_1	mmol	☐	☑
species_13	O2	compartment_1	mmol	☐	☐
species_14	O2	compartment_2	mmol	☑	☑
species_15	GLC	compartment_2	mmol	☑	☑
species_16	LAC	compartment_2	mmol	☑	☑
species_17	GLC	compartment_3	mmol	☐	☐
species_18	LAC	compartment_3	mmol	☐	☐
species_19	O2	compartment_3	mmol	☐	☐
dHb	dHb	compartment_3	mmol	☐	☐

5 Parameters

This model contains 69 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
parameter_1	S/V		90000.000		☑
parameter_2	gNa		0.004		☑
parameter_3	F		96500.000		☑
parameter_4	RT/F		26.730		☑
parameter_5	Vm		-70.000		☑
parameter_6	Na_extracellular		150.000		☑
parameter_7	ATP		2.200		☐
parameter_8	k_pump		$2.9 \cdot 10^{-7}$		☑
parameter_9	Km_pump		0.500		☑
parameter_10	ADP		0.012		☐
parameter_11	qAK		0.920		☑
parameter_12	A		2.212		☑
parameter_13	AMP		$7.03149141540894 \cdot 10^{-5}$		☐
parameter_14	Tmax,GLC		0.048		☑
parameter_15	Kt,GLC		9.000		☑
parameter_16	kHK-PFK		0.120		☑
parameter_17	KI,ATP		1.000		☑
parameter_18	nH		4.000		☑
parameter_19	Kg		0.050		☑
parameter_20	kPGK		42.600		☑
parameter_21	N		0.212		☑
parameter_22	NAD+		0.186		☐
parameter_23	kPK		86.700		☑
parameter_24	k+LDH		2000.000		☑
parameter_25	k-LDH		44.800		☑
parameter_26	Tmax,LAC		0.006		☑
parameter_27	Kt,LAC		0.500		☑
parameter_28	vATPase		0.149		☑
parameter_29	k+CK		3666.000		☑
parameter_30	k-CK		20.000		☑
parameter_31	C		10.000		☑
parameter_32	PS/V		1.600		☑
parameter_33	KO2		0.036		☑
parameter_34	Hb*OP		8.600		☑
parameter_35	nh		2.730		☑
parameter_36	F0		0.012		☑
parameter_37	F_in		0.012		☐

Id	Name	SBO	Value	Unit	Constant
parameter_38	V_cap		0.006		☑
parameter_47	v_Mito		0.019		☑
dAMP_dATP	dAMP/dATP		−0.012		⊟
v_Mito_H3	v_Mito_H3		0.019		⊟
V_max_Mito	V_max_Mito		0.052		☑
Km_Mito	Km,Mito		0.050		☑
KI_Mito	KI,Mito		183.300		☑
n_Mito	n_Mito		0.100		☑
K_O2_Mito	K_O2_Mito		0.001		☑
is_maximum	is_maximum		0.000		⊟
is_rising	is_rising		1.000		⊟
is_falling	is_falling		0.000		⊟
slope_up	slope_up		0.000		⊟
alpha_F_in	alpha_F_in		0.500		☑
maximum	maximum		0.006		⊟
t_on	t_on		5.000		☑
t_end	t_end		360.000		☑
slope_down	slope_down		0.438		⊟
F_out	F_out		0.012		⊟
v_stim_constant	v_stim_constant		0.230		⊟
rCBF	rCBF		1.000		⊟
rCMRO2	rCMRO2		0.000		⊟
rVv	rVv		1.000		⊟
O2c_bar	O2c_bar		5.680		⊟
ratioO2c_bar	ratioO2c_bar		1.000		⊟
Compartment_7	Initial for Venous balloon		0.024		☑
ModelValue_35	Initial for F0		0.012		☑
ModelValue_60	Initial for O2c_bar		5.680		☑
ModelValue_50	Initial for alpha_F_in		0.500		☑
ModelValue_51	Initial for maximum		0.006		☑
ModelValue_53	Initial for t_end		360.000		☑
ModelValue_52	Initial for t_on		5.000		☑

6 Initialassignments

This is an overview of seven initialassignments.

6.1 Initialassignment `Compartment_7`

Derived unit ml

Math vol (compartment_4)

6.2 Initialassignment `ModelValue_35`

Derived unit contains undeclared units

Math parameter_36

6.3 Initialassignment `ModelValue_60`

Derived unit contains undeclared units

Math O2c_bar

6.4 Initialassignment `ModelValue_50`

Derived unit contains undeclared units

Math alpha_F_in

6.5 Initialassignment `ModelValue_51`

Derived unit contains undeclared units

Math maximum

6.6 Initialassignment `ModelValue_53`

Derived unit contains undeclared units

Math t_end

6.7 Initialassignment `ModelValue_52`

Derived unit contains undeclared units

Math t_on

7 Function definitions

This is an overview of 13 function definitions.

7.1 Function definition Constant_flux__irreversible

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$v \tag{1}$$

7.2 Function definition v_pump

Name v_pump

Arguments S_V, k_pump, ATP, NA, Km_pump

Mathematical Expression

$$\frac{\mathrm{S\_V} \cdot \mathrm{k\_pump} \cdot \mathrm{ATP} \cdot \mathrm{NA}}{1 + \frac{\mathrm{ATP}}{\mathrm{Km\_pump}}} \tag{2}$$

7.3 Function definition function_1

Name v_Leak-Na

Arguments S_V, gNA, F, RT_F, Na_e, Na, Vm

Mathematical Expression

$$\mathrm{S\_V} \cdot \frac{\mathrm{gNA}}{\mathrm{F}} \cdot \left(\mathrm{RT\_F} \cdot \left(\frac{\mathrm{Na\_e}}{\mathrm{Na}}\right) - \mathrm{Vm}\right) \tag{3}$$

7.4 Function definition v_GLC_m

Name v_GLC_m

Arguments Tmax, GLC_c, Kt_GLC, GLC_i

Mathematical Expression

$$\mathrm{Tmax} \cdot \left(\frac{\mathrm{GLC\_c}}{\mathrm{GLC\_c} + \mathrm{Kt\_GLC}} - \frac{\mathrm{GLC\_i}}{\mathrm{GLC\_i} + \mathrm{Kt\_GLC}}\right) \tag{4}$$

7.5 Function definition function_2

Name v_HK-PFK

Arguments ATP, GLC_i, Kg, KI_ATP, nH, kHK_PFK

Mathematical Expression

$$\frac{\mathrm{kHK\_PFK} \cdot \mathrm{ATP} \cdot \frac{\mathrm{GLC\_i}}{\mathrm{GLC\_i}+\mathrm{Kg}}}{1+\left(\frac{\mathrm{ATP}}{\mathrm{KI\_ATP}}\right)^{\mathrm{nH}}} \tag{5}$$

7.6 Function definition v_PGK

Name v_PGK

Arguments kPGK, GAP, ADP, NAD, NADH

Mathematical Expression

$$\mathrm{kPGK} \cdot \mathrm{GAP} \cdot \mathrm{ADP} \cdot \frac{\mathrm{NAD}}{\mathrm{NADH}} \tag{6}$$

7.7 Function definition v_LAC_m

Name v_LAC_m

Arguments Tmax, LAC_i, Kt_LAC, LAC_c

Mathematical Expression

$$\mathrm{Tmax} \cdot \left(\frac{\mathrm{LAC\_i}}{\mathrm{LAC\_i}+\mathrm{Kt\_LAC}} - \frac{\mathrm{LAC\_c}}{\mathrm{LAC\_c}+\mathrm{Kt\_LAC}}\right) \tag{7}$$

7.8 Function definition v_O2_m

Name v_O2_m

Arguments PS_V, KO2, HbOP, O2_c, nh, O2_i

Mathematical Expression

$$\mathrm{PS\_V} \cdot \left(\mathrm{KO2} \cdot \left(\frac{\mathrm{HbOP}}{\mathrm{O2\_c}} - 1\right)^{\frac{1}{\mathrm{nh}}} - \mathrm{O2\_i}\right) \tag{8}$$

7.9 Function definition v_O2_c

Name v_O2_c

Arguments F_in, V_cap, O2_a, O2_c

Mathematical Expression

$$\frac{2 \cdot \mathrm{F\_in}}{\mathrm{V\_cap}} \cdot (\mathrm{O2\_a} - \mathrm{O2\_c}) \tag{9}$$

7.10 Function definition v_GLC_c

Name v_GLC_c

Arguments F_in, V_cap, GLC_a, GLC_c

Mathematical Expression

$$\frac{2 \cdot \mathrm{F\_in}}{\mathrm{V\_cap}} \cdot (\mathrm{GLC\_a} - \mathrm{GLC\_c}) \tag{10}$$

7.11 Function definition v_LAC_c

Name v_LAC_c

Arguments F_in, V_cap, LAC_a, LAC_c

Mathematical Expression

$$\frac{2 \cdot \mathrm{F\_in}}{\mathrm{V\_cap}} \cdot (\mathrm{LAC\_a} - \mathrm{LAC\_c}) \tag{11}$$

7.12 Function definition v_dHb_in

Name v_dHb_in

Arguments F_in, O2_a, O2_c

Mathematical Expression

$$\mathrm{F\_in} \cdot 2 \cdot (\mathrm{O2\_a} - \mathrm{O2\_c}) \tag{12}$$

7.13 Function definition v_dHb_out

Name v_dHb_out

Arguments F_out, dHb, V_v

Mathematical Expression

$$\frac{\mathrm{F\_out} \cdot \mathrm{dHb}}{\mathrm{V\_v}} \tag{13}$$

8 Rules

This is an overview of 21 rules.

8.1 Rule species_2

Rule species_2 is an assignment rule for species species_2:

$$[\text{species\_2}] = \text{parameter\_7} \cdot \text{vol}\left(\text{compartment\_1}\right) \tag{14}$$

8.2 Rule species_12

Rule species_12 is an assignment rule for species species_12:

$$[\text{species\_12}] = \left(\text{parameter\_31} - \frac{\text{species\_11}}{\text{vol}\left(\text{compartment\_1}\right)}\right) \cdot \text{vol}\left(\text{compartment\_1}\right) \tag{15}$$

8.3 Rule parameter_10

Rule parameter_10 is an assignment rule for parameter parameter_10:

$$\begin{aligned} \text{parameter\_10} = \frac{\text{parameter\_7}}{2} \cdot \Bigg(&\text{parameter\_11} \\ &+ \left(\text{parameter\_11}^2 + 4 \cdot \text{parameter\_11} \cdot \left(\frac{\text{parameter\_12}}{\text{parameter\_7}} - 1\right)\right)^{0.5}\Bigg) \end{aligned} \tag{16}$$

8.4 Rule species_3

Rule species_3 is an assignment rule for species species_3:

$$[\text{species\_3}] = \text{parameter\_10} \cdot \text{vol}\left(\text{compartment\_1}\right) \tag{17}$$

8.5 Rule parameter_13

Rule parameter_13 is an assignment rule for parameter parameter_13:

$$\text{parameter\_13} = \text{parameter\_12} - \text{parameter\_7} - \text{parameter\_10} \tag{18}$$

8.6 Rule parameter_22

Rule parameter_22 is an assignment rule for parameter parameter_22:

$$\text{parameter\_22} = \text{parameter\_21} - \frac{\text{species\_7}}{\text{vol}\left(\text{compartment\_1}\right)} \tag{19}$$

8.7 Rule species_6

Rule species_6 is an assignment rule for species species_6:

$$[\text{species\_6}] = \text{parameter\_22} \cdot \text{vol}\left(\text{compartment\_1}\right) \tag{20}$$

8.8 Rule dAMP_dATP

Rule dAMP_dATP is an assignment rule for parameter dAMP_dATP:

$$\begin{aligned} \text{dAMP\_dATP} = 1 + \frac{\text{parameter\_11}}{2} - \frac{1}{2} \\ \cdot \left(\text{parameter\_11}^2 + 4 \cdot \text{parameter\_11} \cdot \left(\frac{\text{parameter\_12}}{\text{parameter\_7}} - 1\right)\right)^{\frac{1}{2}} \\ + \frac{\text{parameter\_11} \cdot \text{parameter\_12}}{\text{parameter\_7} \cdot \left(\text{parameter\_11}^2 + 4 \cdot \text{parameter\_11} \cdot \left(\frac{\text{parameter\_12}}{\text{parameter\_7}} - 1\right)\right)^{\frac{1}{2}}} \end{aligned} \tag{21}$$

8.9 Rule v_Mito_H3

Rule v_Mito_H3 is an assignment rule for parameter v_Mito_H3:

$$\begin{aligned} \text{v\_Mito\_H3} = \text{V\_max\_Mito} \cdot \frac{\frac{\text{species\_8}}{\text{vol}(\text{compartment\_1})}}{\text{Km\_Mito} + \frac{\text{species\_8}}{\text{vol}(\text{compartment\_1})}} \\ \cdot \frac{1}{1 + \left(\frac{\text{parameter\_7}}{\text{parameter\_10} \cdot \text{KI\_Mito}}\right)^{\text{n\_Mito}}} \cdot \frac{\frac{\text{species\_13}}{\text{vol}(\text{compartment\_1})}}{\text{K\_O2\_Mito} + \frac{\text{species\_13}}{\text{vol}(\text{compartment\_1})}} \end{aligned} \tag{22}$$

8.10 Rule maximum

Rule maximum is an assignment rule for parameter maximum:

$$\text{maximum} = \text{ModelValue\_35} \cdot \text{ModelValue\_50} \tag{23}$$

8.11 Rule slope_up

Rule slope_up is an assignment rule for parameter slope_up:

$$\text{slope\_up} = \frac{\text{ModelValue\_51}}{\text{ModelValue\_52}} \cdot \text{time} \tag{24}$$

8.12 Rule slope_down

Rule slope_down is an assignment rule for parameter slope_down:

$$\text{slope\_down} = \frac{\text{maximum} \cdot (\text{t\_on} + \text{t\_end} - \text{time})}{\text{t\_on}} \tag{25}$$

8.13 Rule parameter_37

Rule parameter_37 is an assignment rule for parameter parameter_37:

$$\begin{aligned} \text{parameter\_37} = {} & \text{parameter\_36} + \text{is\_rising} \cdot \text{slope\_up} + \text{is\_maximum} \\ & \cdot \text{maximum} + \text{is\_falling} \cdot \text{slope\_down} \end{aligned} \tag{26}$$

8.14 Rule F_out

Rule F_out is an assignment rule for parameter F_out:

$$\text{F\_out} = \frac{\text{parameter\_36} \cdot \left(\left(\frac{\text{vol}(\text{compartment\_4})}{\text{Compartment\_7}} \right)^2 + \left(\frac{\text{vol}(\text{compartment\_4})}{\text{Compartment\_7}} \right)^{0.5} \cdot 35 \cdot \frac{1}{\text{Compartment\_7}} \cdot \text{parameter\_37} \right)}{1 + \text{parameter\_36} \cdot \left(\frac{\text{vol}(\text{compartment\_4})}{\text{Compartment\_7}} \right)^{0.5} \cdot 35 \cdot \frac{1}{\text{Compartment\_7}}} \tag{27}$$

8.15 Rule rCBF

Rule rCBF is an assignment rule for parameter rCBF:

$$\text{rCBF} = \frac{\text{parameter\_37}}{\text{ModelValue\_35}} \tag{28}$$

8.16 Rule rCMRO2

Rule rCMRO2 is an assignment rule for parameter rCMRO2:

$$\text{rCMRO2} = \frac{\text{mitochondrial\_respiration}}{0.0192} \tag{29}$$

8.17 Rule rVv

Rule rVv is an assignment rule for parameter rVv:

$$\text{rVv} = \frac{\text{vol}(\text{compartment\_4})}{\text{Compartment\_7}} \tag{30}$$

8.18 Rule O2c_bar

Rule O2c_bar is an assignment rule for parameter O2c_bar:

$$\text{O2c\_bar} = 2 \cdot \frac{\text{species\_19}}{\text{vol}(\text{compartment\_3})} - \frac{\text{species\_14}}{\text{vol}(\text{compartment\_2})} \tag{31}$$

8.19 Rule ratioO2c_bar

Rule ratioO2c_bar is an assignment rule for parameter ratioO2c_bar:

$$\text{ratioO2c\_bar} = \frac{\text{O2c\_bar}}{\text{ModelValue\_60}} \tag{32}$$

8.20 Rule compartment_4

Rule compartment_4 is a rate rule for compartment compartment_4:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{vol}\left(\mathrm{compartment\_4}\right) = \mathrm{parameter\_37} - \mathrm{F\_out} \tag{33}$$

8.21 Rule parameter_7

Rule parameter_7 is a rate rule for parameter parameter_7:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{parameter\_7} = (2 \cdot \mathrm{reaction\_4} + \mathrm{reaction\_5} + \mathrm{reaction\_6} - \mathrm{reaction\_2} + 15 \cdot \mathrm{mitochondrial\_respiration} + \mathrm{reaction\_9} - \mathrm{ATPases}) \cdot (1 - \mathrm{dAMP\_dATP})^1 \tag{34}$$

9 Events

This is an overview of three events. Each event is initiated whenever its trigger condition switches from false to 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.

9.1 Event from_increase_to_stable

Name from increase to stable

Trigger condition

$$\mathrm{time} = \mathrm{ModelValue\_52} \tag{35}$$

Assignments

$$\mathrm{is\_maximum} = 1 \tag{36}$$

$$\mathrm{is\_rising} = 0 \tag{37}$$

9.2 Event from_stable_to_decrease__end_of_stimulation

Name from stable to decrease (end of stimulation)

Trigger condition

$$\mathrm{time} = \mathrm{ModelValue\_53} \tag{38}$$

Assignments

$$\mathrm{is\_maximum} = 0 \tag{39}$$

$$\mathrm{is\_falling} = 1 \tag{40}$$

$$\mathrm{v\_stim\_constant} = 0 \tag{41}$$

9.3 Event from_decrease_to_at_rest

Name from decrease to at_rest

Trigger condition

$$\text{time} = \text{ModelValue\_53} + \text{ModelValue\_52} \tag{42}$$

Assignment

$$\text{is\_falling} = 0 \tag{43}$$

10 Reactions

This model contains 18 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

№	Id	Name	Reaction Equation	SBO
1	`reaction_1`	Sodium leak	$\emptyset \xrightarrow{\text{species\_1}} \text{species\_1}$	
2	`reaction_2`	Na/K - pump	$3\,\text{species\_1} + \text{species\_2} \xrightarrow{\text{species\_2, species\_1}} \text{species\_3}$	
3	`reaction_3`	Blood-brain transport of glucose	$100\,\text{species\_17} \xrightarrow{\text{species\_17, species\_4}} \text{species\_4}$	
4	`reaction_4`	Hexokinase-phosphofructokinase system	$\text{species\_4} + \text{species\_2} \xrightarrow{\text{species\_2, species\_4}} 2\,\text{species\_5} + \text{species\_3}$	
5	`reaction_5`	Phosphoglycerate kinase	$\text{species\_5} + \text{species\_6} \xrightarrow{\text{species\_3, species\_5, species\_3, species\_6, species\_7}} \text{species\_7} + \text{species\_9}$	
6	`reaction_6`	Pyruvate kinase	$\text{species\_3} + \text{species\_9} \xrightarrow{\text{species\_3, species\_9}} \text{species\_2} + \text{species\_8}$	
7	`reaction_7`	Lactate dehydrogenase	$\text{species\_8} + \text{species\_7} \xrightleftharpoons{\text{species\_8, species\_7, species\_10, species\_6}} \text{species\_10} + \text{species\_6}$	
8	`reaction_8`	Blood-brain transport of lactate	$\text{species\_10} \xrightarrow{\text{species\_10, species\_18}} 100\,\text{species\_18}$	
9	`reaction_9`	Creatine Kinase	$\text{species\_11} + \text{species\_3} \xrightleftharpoons{\text{species\_11, species\_3, species\_12, species\_2}} \text{species\_12} + \text{species\_2}$	
10	`reaction_10`	Blood-brain transport of oxygen	$100\,\text{species\_19} \xrightarrow{\text{species\_19, species\_13}} \text{species\_13}$	
11	`reaction_11`	Blood flow contribution to O2 variation	$\text{species\_14} \xrightarrow{\text{species\_14, species\_19}} \text{species\_19}$	
12	`reaction_12`	Blood flow contribution to GLC_c variation	$\text{species\_15} \xrightarrow{\text{species\_15, species\_17}} \text{species\_17}$	

№	Id	Name	Reaction Equation	SBO
13	reaction_13	Blood flow contribution to LAC_c variation	$\text{species\_16} \xrightarrow{\text{species\_16, species\_18}} \text{species\_18}$	
14	mitochondrial-_respiration	mitochondrial respiration	$\text{species\_8} + \text{species\_7} + 3\ \text{species\_13} \longrightarrow \text{species\_2}$	
15	ATPases	ATPases	$\text{species\_2} \longrightarrow \emptyset$	
16	Na__inflow-_after-_stimulation	Na+ inflow after stimulation	$\emptyset \longrightarrow \text{species\_1}$	
17	inflow_of_dHb	inflow of dHb	$\emptyset \xrightarrow{\text{species\_14, species\_19, species\_14, species\_19}} \text{dHb}$	
18	outflow_of_dHb	outflow of dHb	$\text{dHb} \xrightarrow{\text{dHb}} \emptyset$	

10.1 Reaction `reaction_1`

This is an irreversible reaction of no reactant forming one product influenced by one modifier.

Name Sodium leak

Reaction equation

$$\emptyset \xrightarrow{\text{species\_1}} \text{species\_1} \tag{44}$$

Modifier

Table 6: Properties of each modifier.

Id	Name	SBO
`species_1`	Na+	

Product

Table 7: Properties of each product.

Id	Name	SBO
`species_1`	Na+	

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_1 = {} & \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{function\_1}\left(\mathrm{parameter\_1}, \mathrm{parameter\_2}, \mathrm{parameter\_3}, \right.\\ & \left. \mathrm{parameter\_4}, \mathrm{parameter\_6}, \frac{\mathrm{species\_1}}{\mathrm{vol}\left(\mathrm{compartment\_1}\right)}, \mathrm{parameter\_5}\right) \end{aligned} \tag{45}$$

$$\mathrm{function\_1}\left(\mathrm{S\_V}, \mathrm{gNA}, \mathrm{F}, \mathrm{RT\_F}, \mathrm{Na\_e}, \mathrm{Na}, \mathrm{Vm}\right) = \mathrm{S\_V} \cdot \frac{\mathrm{gNA}}{\mathrm{F}} \cdot \left(\mathrm{RT\_F} \cdot \left(\frac{\mathrm{Na\_e}}{\mathrm{Na}}\right) - \mathrm{Vm}\right) \tag{46}$$

$$\mathrm{function\_1}\left(\mathrm{S\_V}, \mathrm{gNA}, \mathrm{F}, \mathrm{RT\_F}, \mathrm{Na\_e}, \mathrm{Na}, \mathrm{Vm}\right) = \mathrm{S\_V} \cdot \frac{\mathrm{gNA}}{\mathrm{F}} \cdot \left(\mathrm{RT\_F} \cdot \left(\frac{\mathrm{Na\_e}}{\mathrm{Na}}\right) - \mathrm{Vm}\right) \tag{47}$$

10.2 Reaction `reaction_2`

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name Na/K - pump

Reaction equation

$$3\,\text{species\_1} + \text{species\_2} \xrightarrow{\text{species\_2, species\_1}} \text{species\_3} \tag{48}$$

Reactants

Table 8: Properties of each reactant.

Id	Name	SBO
species_1	Na+	
species_2	ATP	

Modifiers

Table 9: Properties of each modifier.

Id	Name	SBO
species_2	ATP	
species_1	Na+	

Product

Table 10: Properties of each product.

Id	Name	SBO
species_3	ADP	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}(\text{compartment\_1}) \cdot \text{v\_pump}\left(\text{parameter\_1}, \text{parameter\_8}, \frac{\text{species\_2}}{\text{vol}(\text{compartment\_1})}, \frac{\text{species\_1}}{\text{vol}(\text{compartment\_1})}, \text{parameter\_9}\right) \tag{49}$$

$$\text{v\_pump}(\text{S\_V}, \text{k\_pump}, \text{ATP}, \text{NA}, \text{Km\_pump}) = \frac{\text{S\_V} \cdot \text{k\_pump} \cdot \text{ATP} \cdot \text{NA}}{1 + \frac{\text{ATP}}{\text{Km\_pump}}} \tag{50}$$

$$\text{v\_pump}(\text{S\_V}, \text{k\_pump}, \text{ATP}, \text{NA}, \text{Km\_pump}) = \frac{\text{S\_V} \cdot \text{k\_pump} \cdot \text{ATP} \cdot \text{NA}}{1 + \frac{\text{ATP}}{\text{Km\_pump}}} \tag{51}$$

10.3 Reaction `reaction_3`

This is an irreversible reaction of one reactant forming one product influenced by two modifiers.

Name Blood-brain transport of glucose

Reaction equation

$$100\,\text{species\_17} \xrightarrow{\text{species\_17, species\_4}} \text{species\_4} \tag{52}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
`species_17`	GLC	

Modifiers

Table 12: Properties of each modifier.

Id	Name	SBO
`species_17`	GLC	
`species_4`	GLC	

Product

Table 13: Properties of each product.

Id	Name	SBO
`species_4`	GLC	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{v\_GLC\_m}\left(\text{parameter\_14}, \frac{\text{species\_17}}{\text{vol}\left(\text{compartment\_3}\right)}, \text{parameter\_15}, \frac{\text{species\_4}}{\text{vol}\left(\text{compartment\_1}\right)}\right) \tag{53}$$

$$\begin{aligned} & \mathrm{v\_GLC\_m}\left(\mathrm{Tmax}, \mathrm{GLC\_c}, \mathrm{Kt\_GLC}, \mathrm{GLC\_i}\right) \\ & = \mathrm{Tmax} \cdot \left(\frac{\mathrm{GLC\_c}}{\mathrm{GLC\_c} + \mathrm{Kt\_GLC}} - \frac{\mathrm{GLC\_i}}{\mathrm{GLC\_i} + \mathrm{Kt\_GLC}}\right) \end{aligned} \tag{54}$$

10.4 Reaction `reaction_4`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name Hexokinase-phosphofructokinase system

Reaction equation

$$\mathrm{species\_4} + \mathrm{species\_2} \xrightarrow{\mathrm{species\_2},\ \mathrm{species\_4}} 2\,\mathrm{species\_5} + \mathrm{species\_3} \tag{55}$$

Reactants

Table 14: Properties of each reactant.

Id	Name	SBO
`species_4`	GLC	
`species_2`	ATP	

Modifiers

Table 15: Properties of each modifier.

Id	Name	SBO
`species_2`	ATP	
`species_4`	GLC	

Products

Table 16: Properties of each product.

Id	Name	SBO
`species_5`	GAP	
`species_3`	ADP	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{function\_2}\left(\frac{\mathrm{species\_2}}{\mathrm{vol}\left(\mathrm{compartment\_1}\right)}, \frac{\mathrm{species\_4}}{\mathrm{vol}\left(\mathrm{compartment\_1}\right)}, \mathrm{parameter\_19}, \mathrm{parameter\_17}, \mathrm{parameter\_18}, \mathrm{parameter\_16}\right) \quad (56)$$

$$\mathrm{function\_2}\left(\mathrm{ATP}, \mathrm{GLC\_i}, \mathrm{Kg}, \mathrm{KI\_ATP}, \mathrm{nH}, \mathrm{kHK\_PFK}\right) = \frac{\mathrm{kHK\_PFK} \cdot \mathrm{ATP} \cdot \frac{\mathrm{GLC\_i}}{\mathrm{GLC\_i}+\mathrm{Kg}}}{1 + \left(\frac{\mathrm{ATP}}{\mathrm{KI\_ATP}}\right)^{\mathrm{nH}}} \quad (57)$$

$$\mathrm{function\_2}\left(\mathrm{ATP}, \mathrm{GLC\_i}, \mathrm{Kg}, \mathrm{KI\_ATP}, \mathrm{nH}, \mathrm{kHK\_PFK}\right) = \frac{\mathrm{kHK\_PFK} \cdot \mathrm{ATP} \cdot \frac{\mathrm{GLC\_i}}{\mathrm{GLC\_i}+\mathrm{Kg}}}{1 + \left(\frac{\mathrm{ATP}}{\mathrm{KI\_ATP}}\right)^{\mathrm{nH}}} \quad (58)$$

10.5 Reaction `reaction_5`

This is an irreversible reaction of two reactants forming two products influenced by five modifiers.

Name Phosphoglycerate kinase

Reaction equation

$$\mathrm{species\_5} + \mathrm{species\_6} \xrightarrow{\mathrm{species\_3},\ \mathrm{species\_5},\ \mathrm{species\_3},\ \mathrm{species\_6},\ \mathrm{species\_7}} \mathrm{species\_7} + \mathrm{species\_9} \quad (59)$$

Reactants

Table 17: Properties of each reactant.

Id	Name	SBO
`species_5`	GAP	
`species_6`	NAD+	

Modifiers

Table 18: Properties of each modifier.

Id	Name	SBO
species_3	ADP	
species_5	GAP	
species_3	ADP	
species_6	NAD+	
species_7	NADH	

Products

Table 19: Properties of each product.

Id	Name	SBO
species_7	NADH	
species_9	PEP	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}(\mathrm{compartment\_1}) \cdot \mathrm{v\_PGK}\left(\mathrm{parameter\_20}, \frac{\mathrm{species\_5}}{\mathrm{vol}(\mathrm{compartment\_1})}, \frac{\mathrm{species\_3}}{\mathrm{vol}(\mathrm{compartment\_1})}, \frac{\mathrm{species\_6}}{\mathrm{vol}(\mathrm{compartment\_1})}, \frac{\mathrm{species\_7}}{\mathrm{vol}(\mathrm{compartment\_1})}\right) \quad (60)$$

$$\mathrm{v\_PGK}(\mathrm{kPGK}, \mathrm{GAP}, \mathrm{ADP}, \mathrm{NAD}, \mathrm{NADH}) = \mathrm{kPGK} \cdot \mathrm{GAP} \cdot \mathrm{ADP} \cdot \frac{\mathrm{NAD}}{\mathrm{NADH}} \quad (61)$$

$$\mathrm{v\_PGK}(\mathrm{kPGK}, \mathrm{GAP}, \mathrm{ADP}, \mathrm{NAD}, \mathrm{NADH}) = \mathrm{kPGK} \cdot \mathrm{GAP} \cdot \mathrm{ADP} \cdot \frac{\mathrm{NAD}}{\mathrm{NADH}} \quad (62)$$

10.6 Reaction `reaction_6`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name Pyruvate kinase

Reaction equation

$$\mathrm{species\_3} + \mathrm{species\_9} \xrightarrow{\mathrm{species\_3},\ \mathrm{species\_9}} \mathrm{species\_2} + \mathrm{species\_8} \quad (63)$$

Reactants

Table 20: Properties of each reactant.

Id	Name	SBO
species_3	ADP	
species_9	PEP	

Modifiers

Table 21: Properties of each modifier.

Id	Name	SBO
species_3	ADP	
species_9	PEP	

Products

Table 22: Properties of each product.

Id	Name	SBO
species_2	ATP	
species_8	PYR	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{parameter\_23} \cdot \text{species\_3} \cdot \frac{\text{species\_9}}{\text{vol}\left(\text{compartment\_1}\right)} \tag{64}$$

10.7 Reaction `reaction_7`

This is a reversible reaction of two reactants forming two products influenced by four modifiers.

Name Lactate dehydrogenase

Reaction equation

$$\text{species\_8} + \text{species\_7} \xrightleftharpoons{\text{species\_8, species\_7, species\_10, species\_6}} \text{species\_10} + \text{species\_6} \tag{65}$$

Reactants

Table 23: Properties of each reactant.

Id	Name	SBO
species_8	PYR	
species_7	NADH	

Modifiers

Table 24: Properties of each modifier.

Id	Name	SBO
species_8	PYR	
species_7	NADH	
species_10	LAC	
species_6	NAD+	

Products

Table 25: Properties of each product.

Id	Name	SBO
species_10	LAC	
species_6	NAD+	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \left(\mathrm{parameter\_24} \cdot \frac{\mathrm{species\_8}}{\mathrm{vol}\left(\mathrm{compartment\_1}\right)} \cdot \frac{\mathrm{species\_7}}{\mathrm{vol}\left(\mathrm{compartment\_1}\right)} - \mathrm{parameter\_25} \cdot \frac{\mathrm{species\_10}}{\mathrm{vol}\left(\mathrm{compartment\_1}\right)} \cdot \frac{\mathrm{species\_6}}{\mathrm{vol}\left(\mathrm{compartment\_1}\right)}\right) \tag{66}$$

10.8 Reaction `reaction_8`

This is an irreversible reaction of one reactant forming one product influenced by two modifiers.

Name Blood-brain transport of lactate

Reaction equation

$$\mathrm{species\_10} \xrightarrow{\mathrm{species\_10},\ \mathrm{species\_18}} 100\,\mathrm{species\_18} \tag{67}$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
species_10	LAC	

Modifiers

Table 27: Properties of each modifier.

Id	Name	SBO
species_10	LAC	
species_18	LAC	

Product

Table 28: Properties of each product.

Id	Name	SBO
species_18	LAC	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{v\_LAC\_m}\left(\mathrm{parameter\_26}, \frac{\mathrm{species\_10}}{\mathrm{vol}\left(\mathrm{compartment\_1}\right)}, \mathrm{parameter\_27}, \frac{\mathrm{species\_18}}{\mathrm{vol}\left(\mathrm{compartment\_3}\right)}\right) \tag{68}$$

$$\mathrm{v\_LAC\_m}\left(\mathrm{Tmax}, \mathrm{LAC\_i}, \mathrm{Kt\_LAC}, \mathrm{LAC\_c}\right) = \mathrm{Tmax} \cdot \left(\frac{\mathrm{LAC\_i}}{\mathrm{LAC\_i} + \mathrm{Kt\_LAC}} - \frac{\mathrm{LAC\_c}}{\mathrm{LAC\_c} + \mathrm{Kt\_LAC}}\right) \tag{69}$$

10.9 Reaction `reaction_9`

This is a reversible reaction of two reactants forming two products influenced by four modifiers.

Name Creatine Kinase

Reaction equation

$$\text{species\_11} + \text{species\_3} \xrightleftharpoons{\text{species\_11, species\_3, species\_12, species\_2}} \text{species\_12} + \text{species\_2} \tag{70}$$

Reactants

Table 29: Properties of each reactant.

Id	Name	SBO
species_11	PCr	
species_3	ADP	

Modifiers

Table 30: Properties of each modifier.

Id	Name	SBO
species_11	PCr	
species_3	ADP	
species_12	Cr	
species_2	ATP	

Products

Table 31: Properties of each product.

Id	Name	SBO
species_12	Cr	
species_2	ATP	

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_9 = \mathrm{vol}\left(\text{compartment\_1}\right) \cdot \Bigg(&\text{parameter\_29} \cdot \frac{\text{species\_11}}{\mathrm{vol}\left(\text{compartment\_1}\right)} \cdot \frac{\text{species\_3}}{\mathrm{vol}\left(\text{compartment\_1}\right)} \\ &- \text{parameter\_30} \cdot \frac{\text{species\_12}}{\mathrm{vol}\left(\text{compartment\_1}\right)} \cdot \frac{\text{species\_2}}{\mathrm{vol}\left(\text{compartment\_1}\right)}\Bigg) \end{aligned} \tag{71}$$

10.10 Reaction `reaction_10`

This is an irreversible reaction of one reactant forming one product influenced by two modifiers.

Name Blood-brain transport of oxygen

Reaction equation

$$100\,\text{species\_19} \xrightarrow{\text{species\_19},\ \text{species\_13}} \text{species\_13} \tag{72}$$

Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
`species_19`	O2	

Modifiers

Table 33: Properties of each modifier.

Id	Name	SBO
`species_19`	O2	
`species_13`	O2	

Product

Table 34: Properties of each product.

Id	Name	SBO
`species_13`	O2	

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{10} = \text{v\_O2\_m}\Bigg(&\text{parameter\_32}, \text{parameter\_33}, \text{parameter\_34}, \frac{\text{species\_19}}{\text{vol}\left(\text{compartment\_3}\right)}, \\ &\text{parameter\_35}, \frac{\text{species\_13}}{\text{vol}\left(\text{compartment\_1}\right)}\Bigg) \end{aligned} \tag{73}$$

$$\mathrm{v\_O2\_m}\left(\mathrm{PS\_V}, \mathrm{KO2}, \mathrm{HbOP}, \mathrm{O2\_c}, \mathrm{nh}, \mathrm{O2\_i}\right) = \mathrm{PS\_V} \cdot \left(\mathrm{KO2} \cdot \left(\frac{\mathrm{HbOP}}{\mathrm{O2\_c}} - 1\right)^{\frac{1}{\mathrm{nh}}} - \mathrm{O2\_i}\right) \tag{74}$$

10.11 Reaction `reaction_11`

This is an irreversible reaction of one reactant forming one product influenced by two modifiers.

Name Blood flow contribution to O2 variation

Reaction equation

$$\mathrm{species\_14} \xrightarrow{\mathrm{species\_14},\ \mathrm{species\_19}} \mathrm{species\_19} \tag{75}$$

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
`species_14`	O2	

Modifiers

Table 36: Properties of each modifier.

Id	Name	SBO
`species_14`	O2	
`species_19`	O2	

Product

Table 37: Properties of each product.

Id	Name	SBO
`species_19`	O2	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{v\_O2\_c}\left(\mathrm{parameter\_37}, \mathrm{parameter\_38}, \frac{\mathrm{species\_14}}{\mathrm{vol}\left(\mathrm{compartment\_2}\right)}, \frac{\mathrm{species\_19}}{\mathrm{vol}\left(\mathrm{compartment\_3}\right)}\right) \tag{76}$$

$$v\_O2\_c\left(F\_in, V\_cap, O2\_a, O2\_c\right) = \frac{2 \cdot F\_in}{V\_cap} \cdot \left(O2\_a - O2\_c\right) \tag{77}$$

10.12 Reaction `reaction_12`

This is an irreversible reaction of one reactant forming one product influenced by two modifiers.

Name Blood flow contribution to GLC_c variation

Reaction equation

$$\text{species\_15} \xrightarrow{\text{species\_15, species\_17}} \text{species\_17} \tag{78}$$

Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
`species_15`	GLC	

Modifiers

Table 39: Properties of each modifier.

Id	Name	SBO
`species_15`	GLC	
`species_17`	GLC	

Product

Table 40: Properties of each product.

Id	Name	SBO
`species_17`	GLC	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = v\_GLC\_c\left(parameter\_37, parameter\_38, \frac{species\_15}{vol\left(compartment\_2\right)}, \frac{species\_17}{vol\left(compartment\_3\right)}\right) \tag{79}$$

$$\mathrm{v\_GLC\_c}\left(\mathrm{F\_in}, \mathrm{V\_cap}, \mathrm{GLC\_a}, \mathrm{GLC\_c}\right) = \frac{2 \cdot \mathrm{F\_in}}{\mathrm{V\_cap}} \cdot \left(\mathrm{GLC\_a} - \mathrm{GLC\_c}\right) \tag{80}$$

10.13 Reaction reaction_13

This is an irreversible reaction of one reactant forming one product influenced by two modifiers.

Name Blood flow contribution to LAC_c variation

Reaction equation

$$\mathrm{species\_16} \xrightarrow{\mathrm{species\_16},\ \mathrm{species\_18}} \mathrm{species\_18} \tag{81}$$

Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
species_16	LAC	

Modifiers

Table 42: Properties of each modifier.

Id	Name	SBO
species_16	LAC	
species_18	LAC	

Product

Table 43: Properties of each product.

Id	Name	SBO
species_18	LAC	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{v\_LAC\_c}\left(\mathrm{parameter\_37}, \mathrm{parameter\_38}, \frac{\mathrm{species\_16}}{\mathrm{vol}\left(\mathrm{compartment\_2}\right)}, \frac{\mathrm{species\_18}}{\mathrm{vol}\left(\mathrm{compartment\_3}\right)}\right) \tag{82}$$

$$v\_LAC\_c\left(F\_in, V\_cap, LAC\_a, LAC\_c\right) = \frac{2 \cdot F\_in}{V\_cap} \cdot \left(LAC\_a - LAC\_c\right) \tag{83}$$

10.14 Reaction `mitochondrial_respiration`

This is an irreversible reaction of three reactants forming one product.

Name mitochondrial respiration

Reaction equation

$$species\_8 + species\_7 + 3\,species\_13 \longrightarrow species\_2 \tag{84}$$

Reactants

Table 44: Properties of each reactant.

Id	Name	SBO
`species_8`	PYR	
`species_7`	NADH	
`species_13`	O2	

Product

Table 45: Properties of each product.

Id	Name	SBO
`species_2`	ATP	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = vol\left(compartment\_1\right) \cdot Constant\_flux\_\_irreversible\left(v\_Mito\_H3\right) \tag{85}$$

$$Constant\_flux\_\_irreversible\left(v\right) = v \tag{86}$$

$$Constant\_flux\_\_irreversible\left(v\right) = v \tag{87}$$

10.15 Reaction `ATPases`

This is an irreversible reaction of one reactant forming no product.

Name ATPases

Reaction equation

$$\text{species\_2} \longrightarrow \emptyset \tag{88}$$

Reactant

Table 46: Properties of each reactant.

Id	Name	SBO
species_2	ATP	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) \tag{89}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{90}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{91}$$

Table 47: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
v	v		0.149		☑

10.16 Reaction Na__inflow_after_stimulation

This is an irreversible reaction of no reactant forming one product.

Name Na+ inflow after stimulation

Reaction equation

$$\emptyset \longrightarrow \text{species\_1} \tag{92}$$

Product

Table 48: Properties of each product.

Id	Name	SBO
species_1	Na+	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v\_stim\_constant}\right) \tag{93}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{94}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{95}$$

10.17 Reaction inflow_of_dHb

This is an irreversible reaction of no reactant forming one product influenced by four modifiers.

Name inflow of dHb

Reaction equation

$$\emptyset \xrightarrow{\mathrm{species\_14},\ \mathrm{species\_19},\ \mathrm{species\_14},\ \mathrm{species\_19}} \mathrm{dHb} \tag{96}$$

Modifiers

Table 49: Properties of each modifier.

Id	Name	SBO
species_14	O2	
species_19	O2	
species_14	O2	
species_19	O2	

Product

Table 50: Properties of each product.

Id	Name	SBO
dHb	dHb	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}\left(\mathrm{compartment\_3}\right) \cdot \mathrm{v\_dHb\_in}\left(\mathrm{parameter\_37}, \frac{\mathrm{species\_14}}{\mathrm{vol}\left(\mathrm{compartment\_2}\right)}, \frac{\mathrm{species\_19}}{\mathrm{vol}\left(\mathrm{compartment\_3}\right)}\right) \tag{97}$$

$$\mathrm{v\_dHb\_in}\left(\mathrm{F\_in}, \mathrm{O2\_a}, \mathrm{O2\_c}\right) = \mathrm{F\_in} \cdot 2 \cdot \left(\mathrm{O2\_a} - \mathrm{O2\_c}\right) \tag{98}$$

$$\mathrm{v\_dHb\_in}\left(\mathrm{F\_in}, \mathrm{O2\_a}, \mathrm{O2\_c}\right) = \mathrm{F\_in} \cdot 2 \cdot \left(\mathrm{O2\_a} - \mathrm{O2\_c}\right) \tag{99}$$

10.18 Reaction `outflow_of_dHb`

This is an irreversible reaction of one reactant forming no product influenced by one modifier.

Name outflow of dHb

Reaction equation

$$\mathrm{dHb} \xrightarrow{\mathrm{dHb}} \emptyset \tag{100}$$

Reactant

Table 51: Properties of each reactant.

Id	Name	SBO
`dHb`	dHb	

Modifier

Table 52: Properties of each modifier.

Id	Name	SBO
`dHb`	dHb	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{vol}\left(\mathrm{compartment\_3}\right) \cdot \mathrm{v\_dHb\_out}\left(\mathrm{F\_out}, \frac{\mathrm{dHb}}{\mathrm{vol}\left(\mathrm{compartment\_3}\right)}, \mathrm{vol}\left(\mathrm{compartment\_4}\right)\right) \tag{101}$$

$$v\_dHb\_out\left(F\_out, dHb, V\_v\right) = \frac{F\_out \cdot dHb}{V\_v} \tag{102}$$

$$v\_dHb\_out\left(F\_out, dHb, V\_v\right) = \frac{F\_out \cdot dHb}{V\_v} \tag{103}$$

11 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.

11.1 Species species_1

Name Na+

Initial amount 15 mmol

This species takes part in five reactions (as a reactant in reaction_2 and as a product in reaction_1, Na__inflow_after_stimulation and as a modifier in reaction_1, reaction_2).

$$\frac{d}{dt}species\_1 = v_1 + v_{16} - 3\, v_2 \tag{104}$$

11.2 Species species_2

Name ATP

Initial amount 2.2 mmol

Involved in rule species_2

This species takes part in nine reactions (as a reactant in reaction_2, reaction_4, ATPases and as a product in reaction_6, reaction_9, mitochondrial_respiration and as a modifier in reaction_2, reaction_4, reaction_9). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

11.3 Species species_3

Name ADP

Initial amount 0.0119296850858459 mmol

Involved in rule species_3

This species takes part in eight reactions (as a reactant in reaction_6, reaction_9 and as a product in reaction_2, reaction_4 and as a modifier in reaction_5, reaction_5, reaction_6, reaction_9). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

11.4 Species species_4

Name GLC

Initial amount 1.2 mmol

This species takes part in four reactions (as a reactant in reaction_4 and as a product in reaction_3 and as a modifier in reaction_3, reaction_4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_4} = v_3 - v_4 \tag{105}$$

11.5 Species species_5

Name GAP

Initial amount 0.0057 mmol

This species takes part in three reactions (as a reactant in reaction_5 and as a product in reaction_4 and as a modifier in reaction_5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_5} = 2\,v_4 - v_5 \tag{106}$$

11.6 Species species_6

Name NAD+

Initial amount 0.186 mmol

Involved in rule species_6

This species takes part in four reactions (as a reactant in reaction_5 and as a product in reaction_7 and as a modifier in reaction_5, reaction_7). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

11.7 Species species_7

Name NADH

Initial amount 0.026 mmol

This species takes part in five reactions (as a reactant in reaction_7, mitochondrial_respiration and as a product in reaction_5 and as a modifier in reaction_5, reaction_7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_7} = v_5 - v_7 - v_{14} \tag{107}$$

11.8 Species species_8

Name PYR

Initial amount 0.16 mmol

This species takes part in four reactions (as a reactant in reaction_7, mitochondrial_respiration and as a product in reaction_6 and as a modifier in reaction_7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_8} = v_6 - v_7 - v_{14} \tag{108}$$

11.9 Species species_9

Name PEP

Initial amount 0.02 mmol

This species takes part in three reactions (as a reactant in reaction_6 and as a product in reaction_5 and as a modifier in reaction_6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_9} = v_5 - v_6 \tag{109}$$

11.10 Species species_10

Name LAC

Initial amount 1 mmol

This species takes part in four reactions (as a reactant in reaction_8 and as a product in reaction_7 and as a modifier in reaction_7, reaction_8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_10} = v_7 - v_8 \tag{110}$$

11.11 Species species_11

Name PCr

Initial amount 5 mmol

This species takes part in two reactions (as a reactant in reaction_9 and as a modifier in reaction_9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_11} = -v_9 \tag{111}$$

11.12 Species species_12

Name Cr

Initial amount 5 mmol

Involved in rule species_12

This species takes part in two reactions (as a product in reaction_9 and as a modifier in reaction_9). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

11.13 Species species_13

Name O2

Initial amount 0.0262 mmol

This species takes part in three reactions (as a reactant in mitochondrial_respiration and as a product in reaction_10 and as a modifier in reaction_10).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_13} = v_{10} - 3\,v_{14} \tag{112}$$

11.14 Species species_14

Name O2

Initial amount 8.34 mmol

This species takes part in four reactions (as a reactant in reaction_11 and as a modifier in reaction_11, inflow_of_dHb, inflow_of_dHb), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_14} = 0 \tag{113}$$

11.15 Species species_15

Name GLC

Initial amount 4.8 mmol

This species takes part in two reactions (as a reactant in reaction_12 and as a modifier in reaction_12), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_15} = 0 \tag{114}$$

11.16 Species species_16

Name LAC

Initial amount 0.313 mmol

This species takes part in two reactions (as a reactant in reaction_13 and as a modifier in reaction_13), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_16} = 0 \tag{115}$$

11.17 Species species_17

Name GLC

Initial amount 4.56 mmol

This species takes part in four reactions (as a reactant in reaction_3 and as a product in reaction_12 and as a modifier in reaction_3, reaction_12).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_17} = v_{12} - 100\, v_3 \tag{116}$$

11.18 Species species_18

Name LAC

Initial amount 0.35 mmol

This species takes part in four reactions (as a product in reaction_8, reaction_13 and as a modifier in reaction_8, reaction_13).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_18} = 100\, v_8 + v_{13} \tag{117}$$

11.19 Species species_19

Name O2

Initial amount 7.01 mmol

This species takes part in six reactions (as a reactant in reaction_10 and as a product in reaction_11 and as a modifier in reaction_10, reaction_11, inflow_of_dHb, inflow_of_dHb).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_19} = v_{11} - 100\, v_{10} \tag{118}$$

11.20 Species dHb

Name dHb

Initial amount 0.0630000000000001 mmol

This species takes part in three reactions (as a reactant in outflow_of_dHb and as a product in inflow_of_dHb and as a modifier in outflow_of_dHb).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{dHb} = v_{17} - v_{18} \tag{119}$$

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