SBML Model Report

Model name: "Wolf2001_Respiratory_Oscillations"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 1 format. This model was created by Rainer Machne[1] at January 23rd 2007 at 3:42 p. m. and last time modified at July fifth 2012 at 2:48 p. 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	3
species types	0	species	26
events	0	constraints	0
reactions	21	function definitions	0
global parameters	28	unit definitions	0
rules	4	initial assignments	0

Model Notes

This model by Jana Wolf et al. 2001 is the first mechanistic model of respiratory oscillations in Saccharomyces cerevisae. It is based on the assumption that feedback inhibition of cysteine on the sulfate transporters leads to oscillations in this pathway and causes oscillations in respiratory activity via inhibition of cytochrome c oxidase by hydrogen disulfide. The model is qualitative/semi-quantitative and reproduces the respiratory oscillation pattern quite well. It is

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based on very coarse-grained representations of the mitochondrial tricarboxylic acid cycle and the mitochondrial electron transport chain (oxidative phosphorylation). The sulfate assimilatory pathways also contains some significant simplifcations.

The model corresponds to Fig. 2B of the paper, with a slight phase shift of the oscillations. No initial conditions were given in the paper, and thus they were chosen arbitrarily in a range that lies within the basin of attraction of the limit cycle oscillations. Species IDs correspond to IDs used by the authors, while SBML names are more common abbreviations.

Caveats:
1) Equilibrated transport:
The model assumes fast equilibration between mitochondria and cytoplasm for the metabolites NADH, NAD+, H2S and Acetyl-CoA.
2) Cytosolic mass conservation ATP/ADP:
The model uses mass conservation for cytosolic adenosine nucleotides with is however not encoded in the stoichiometry, but is implied by the lumped reaction v4. This reaction combines the enzymatic reactions of phosphoadenylyl-sulfate reductase (thioredoxin) (yeast protein Met16p, EC 1.8.4.8) and sulfite reductase (NADPH) (subunits Met5p and Met10p, EC 1.8.1.2). EC 1.8.4.8 also has adenosine-3',5'-bismonophosphate (PAP, not to confuse with ID pap in this model, standing for PAPS) as a product. PAP is the substrate for enzyme 3'(2'),5'-bisphosphate nucleotidase (Met22p, EC:3.1.3.7) which would revover AMP (and Pi). Then AMP can be assumed to be equilibrated with ATP and ADP via adenylate kinase, as often used in metabolic models. This AMP production is implied in the mass conservation for cytosolic adenosine phosphates. Accounting for these reactions explicitly does not change the dynamics of the model significantly. An according version can be obtained from the SBML creator (Rainer Machne, mailto:raim@tbi.univie.ac.at).
3) Redox balance:
The enzyme sulfite reductase (NADPH) (subunits Met5p and Met10p, EC 1.8.1.2, part of reaction v4) actually uses NADPH, and the authors assume equilibration of NADH and NADPH. But actually S. cerevisiae specifically is missing the according enzyme transhydrogenase (EC 1.6.1.1 or EC 1.6.1.2). EC 1.8.4.8 also oxidizes thioredoxin and would actually require an additional NADPH for thioredoxin recovery (reduction). This would slightly affect the redox balance of the model.
4) Energy balance:
Reaction v7 lumps NAD-dependent alcohol dehydrogenase (EC 1.1.1.1), aldehyde dehydrogenase (NAD+) (EC 1.2.1.3) and acetyl-CoA synthase (EC 6.2.1.1). The latter reaction would actually consume ATP as a co-factor, producing AMP+PPi, and this is not included in the model. This would slightly bias the model's energy balance.

To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler L, Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novre N, Laibe C (2010) BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

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 three compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
c0	external		3	1	litre	☑	
c1	cytosol		3	1	litre	☑	c0
c2	mitochondria		3	1	litre	☑	c1

3.1 Compartment c0

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

Name external

3.2 Compartment c1

This is a three dimensional compartment with a constant size of one litre, which is surrounded by c0 (external).

Name cytosol

3.3 Compartment c2

This is a three dimensional compartment with a constant size of one litre, which is surrounded by c1 (cytosol).

Name mitochondria

4 Species

This model contains 26 species. The boundary condition of 13 of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 8 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
sul_ex	SO4_ex	c0	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
eth_ex	EtOH_ex	c0	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
oxy_ex	O2_ex	c0	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
oxy	O2	c2	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
H2O	H2O	c2	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
A3c	ATP	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
aps	APS	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
PPi	PPi	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
pap	PAPS	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
sul	SO4	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
eth	EtOH	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
A2c	ADP	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
hyd	H2S	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
cys	CYS	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
N2	NADH	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
N1	NAD	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
aco	AcCoA	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
oah	OAH	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
S1	S1	c2	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
S2	S2	c2	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
C1	C1	c2	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
C2	C2	c2	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
A2m	ADP_mit	c2	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
A3m	ATP_mit	c2	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
Ho	Ho	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑
Hm	Hm	c2	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑	☑

5 Parameters

This model contains 28 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_v0			1.60		☑
k2			0.20		☑
k3			0.20		☑
k4			0.20		☑
k5			0.10		☑
k6			0.12		☑
k7			10.00		☑
k8			10.00		☑
k9			10.00		☑
k_v10			80.00		☑
k11			10.00		☑
k12			5.00		☑
k_v13			4.00		☑
k14			10.00		☑
k15			5.00		☑
k16			10.00		☑
k17			0.02		☑
k18			1.00		☑
n			4.00		☑
m			4.00		☑
Ka			1.00		☑
Kc			0.10		☑
a			0.10		☑
Ac			2.00		☑
Am			2.00		☑
S			2.00		☑
N			2.00		☑
Kh			0.50		☑

6 Rules

This is an overview of four rules.

6.1 Rule A2c

Rule A2c is an assignment rule for species A2c:

$$\mathrm{A2c} = \mathrm{Ac} - [\mathrm{A3c}] \tag{1}$$

Notes mass conservation for cytosolicadenosine nucleotides. This mass conservation is not reflected in themodel's stoichiometry directly, but implied by other simplifcations. See model notes for details.

6.2 Rule A2m

Rule A2m is an assignment rule for species A2m:

$$\mathrm{A2m} = \mathrm{Am} - [\mathrm{A3m}] \tag{2}$$

Notes mass conservation for mitochondrial adenosine nucleotides

6.3 Rule N1

Rule N1 is an assignment rule for species N1:

$$\mathrm{N1} = \mathrm{N} - [\mathrm{N2}] \tag{3}$$

Notes mass conservation for all cellular nicotine amid dinucleotides

6.4 Rule S2

Rule S2 is an assignment rule for species S2:

$$\mathrm{S2} = \mathrm{S} - [\mathrm{S1}] \tag{4}$$

Notes mass conservation for mitochondrial TCA enzymes

7 Reactions

This model contains 21 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	v1	v1	$\mathrm{sul\_ex} \xrightarrow{\mathrm{cys}} \mathrm{sul}$	
2	v13	v13	$\mathrm{eth\_ex} \longrightarrow \mathrm{eth}$	
3	v2	v2	$\mathrm{sul} + \mathrm{A3c} \longrightarrow \mathrm{aps} + \mathrm{PPi}$	
4	v10	v10	$\mathrm{oxy\_ex} \longrightarrow \mathrm{oxy}$	
5	v14	v14	$\mathrm{oxy} \longrightarrow \mathrm{oxy\_ex}$	
6	v3	v3	$\mathrm{aps} + \mathrm{A3c} \longrightarrow \mathrm{pap} + \mathrm{A2c}$	
7	v4	v4	$\mathrm{pap} + 3\,\mathrm{N2} \longrightarrow \mathrm{hyd} + 3\,\mathrm{N1}$	
8	v5	v5	$\mathrm{hyd} + \mathrm{oah} \longrightarrow \mathrm{cys}$	
9	v6	v6	$\mathrm{cys} \longrightarrow \emptyset$	
10	v7	v7	$\mathrm{eth} + 2\,\mathrm{N1} \longrightarrow \mathrm{aco} + 2\,\mathrm{N2}$	
11	v15	v15	$\mathrm{aco} \longrightarrow \mathrm{oah}$	
12	v17	v17	$\mathrm{hyd} \longrightarrow \emptyset$	
13	v18	v18	$\mathrm{oah} \longrightarrow \emptyset$	
14	v8	v8	$\mathrm{S2} + \mathrm{aco} \longrightarrow \mathrm{S1}$	
15	v9	v9	$\mathrm{S1} + 4\,\mathrm{N1} \longrightarrow \mathrm{S2} + 4\,\mathrm{N2}$	
16	v11a	vET1	$\mathrm{C1} + \mathrm{Hm} + \mathrm{N2} \xrightarrow{\mathrm{hyd,\ oxy}} \mathrm{C2} + \mathrm{Ho} + \mathrm{N1}$	
17	v11a2	vET2	$\mathrm{C2} + \mathrm{oxy} \xrightarrow{\mathrm{hyd,\ N2}} \mathrm{C1} + \mathrm{H2O}$	
18	v16	v16	$\mathrm{A2c} + \mathrm{A3m} \longrightarrow \mathrm{A2m} + \mathrm{A3c}$	
19	v11b	vSYNT	$\mathrm{Ho} + \mathrm{A2m} \xrightarrow{\mathrm{hyd,\ N2,\ oxy}} \mathrm{Hm} + \mathrm{A3m}$	
20	vLEAK	vLEAK	$\mathrm{Ho} \longrightarrow \mathrm{Hm}$	
21	v12	v12	$\mathrm{A3c} \longrightarrow \mathrm{A2c}$	

7.1 Reaction v1

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

Name v1

Reaction equation

$$\text{sul\_ex} \xrightarrow{\text{cys}} \text{sul} \tag{5}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
sul_ex	SO4_ex	

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
cys	CYS	

Product

Table 8: Properties of each product.

Id	Name	SBO
sul	SO4	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{\text{vol}(\text{c0}) \cdot \text{k\_v0}}{1 + \left(\frac{[\text{cys}]}{\text{Kc}}\right)^{\text{n}}} \tag{6}$$

7.2 Reaction v13

This is an irreversible reaction of one reactant forming one product.

Name v13

Reaction equation

$$\text{eth\_ex} \longrightarrow \text{eth} \tag{7}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
eth_ex	EtOH_ex	

Product

Table 10: Properties of each product.

Id	Name	SBO
eth	EtOH	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}(\text{c0}) \cdot \text{k\_v13} \tag{8}$$

7.3 Reaction v2

This is an irreversible reaction of two reactants forming two products.

Name v2

Reaction equation

$$\text{sul} + \text{A3c} \longrightarrow \text{aps} + \text{PPi} \tag{9}$$

Reactants

Table 11: Properties of each reactant.

Id	Name	SBO
sul	SO4	
A3c	ATP	

Products

Table 12: Properties of each product.

Id	Name	SBO
aps	APS	
PPi	PPi	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}(\mathrm{c1}) \cdot \mathrm{k2} \cdot [\mathrm{sul}] \cdot [\mathrm{A3c}] \tag{10}$$

7.4 Reaction v10

This is an irreversible reaction of one reactant forming one product.

Name v10

Notes oxygen diffusion

Reaction equation

$$\mathrm{oxy\_ex} \longrightarrow \mathrm{oxy} \tag{11}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
oxy_ex	O2_ex	

Product

Table 14: Properties of each product.

Id	Name	SBO
oxy	O2	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\,(\mathrm{c0}) \cdot \mathrm{k\_v10} \tag{12}$$

7.5 Reaction v14

This is an irreversible reaction of one reactant forming one product.

Name v14

Notes oxygen diffusion

Reaction equation

$$\mathrm{oxy} \longrightarrow \mathrm{oxy\_ex} \tag{13}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
oxy	O2	

Product

Table 16: Properties of each product.

Id	Name	SBO
oxy_ex	O2_ex	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\,(\mathrm{c2}) \cdot \mathrm{k14} \cdot [\mathrm{oxy}] \tag{14}$$

7.6 Reaction v3

This is an irreversible reaction of two reactants forming two products.

Name v3

Reaction equation

$$\mathrm{aps} + \mathrm{A3c} \longrightarrow \mathrm{pap} + \mathrm{A2c} \tag{15}$$

Reactants

Table 17: Properties of each reactant.

Id	Name	SBO
aps	APS	
A3c	ATP	

Products

Table 18: Properties of each product.

Id	Name	SBO
pap	PAPS	
A2c	ADP	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}(\mathrm{c1}) \cdot \mathrm{k3} \cdot [\mathrm{aps}] \cdot [\mathrm{A3c}] \tag{16}$$

7.7 Reaction v4

This is an irreversible reaction of two reactants forming two products.

Name v4

Notes This combined reaction contains phosphoadenylyl-sulfate reductase (thioredoxin) (yeast protein Met16p, EC:1.8.4.8) which also reduces thioredoxin and would actually require an additional NADPH for thioredoxin recovery (reduction), thus a correct stoichiometry would have to include an additional NADPH. This reaction also has adenosine 3',5'-bismonophosphate (PAP) as a product from which the enzyme 3'(2'),5'-bisphosphate nucleotidase (Met22p, EC:3.1.3.7) would revover AMP (and Pi). This latter AMP production is implied in the mass conservation for cytosolic adenosine phosphates (see model notes).

Reaction equation

$$\mathrm{pap} + 3\,\mathrm{N2} \longrightarrow \mathrm{hyd} + 3\,\mathrm{N1} \tag{17}$$

Reactants

Table 19: Properties of each reactant.

Id	Name	SBO
pap	PAPS	
N2	NADH	

Products

Table 20: Properties of each product.

Id	Name	SBO
hyd	H2S	
N1	NAD	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\,(\mathrm{c1}) \cdot \mathrm{k4} \cdot [\mathrm{pap}] \cdot [\mathrm{N2}] \tag{18}$$

7.8 Reaction v5

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

Name v5

Notes This combined reaction contains cystathionine -synthase (yeast protein Cys4p, EC:4.2.1.22) which would require an additional serine as reactant, and cystathionine -lyase (yeast protein Cys3p, EC:4.4.1.1) which has oxo-butanoate as an additional product

Reaction equation

$$\mathrm{hyd} + \mathrm{oah} \longrightarrow \mathrm{cys} \tag{19}$$

Reactants

Table 21: Properties of each reactant.

Id	Name	SBO
hyd	H2S	
oah	OAH	

Product

Table 22: Properties of each product.

Id	Name	SBO
cys	CYS	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}(\mathrm{c1}) \cdot \mathrm{k5} \cdot [\mathrm{hyd}] \cdot [\mathrm{oah}] \tag{20}$$

7.9 Reaction v6

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

Name v6

Notes cysteine usage for glutathione and protein synthesis, other pathways and degradation, no GO term applicable

Reaction equation

$$\mathrm{cys} \longrightarrow \emptyset \tag{21}$$

Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
cys	CYS	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}(\mathrm{c1}) \cdot \mathrm{k6} \cdot [\mathrm{cys}] \tag{22}$$

7.10 Reaction v7

This is an irreversible reaction of two reactants forming two products.

Name v7

Notes This combined reaction contains the acetyl-CoA synthase (yeast proteins Acs1p and Acs2p, EC 6.2.1.1) which would actually require ATP as a co-substrate (hydrolysed to AMP+PPi)

Reaction equation

$$\mathrm{eth} + 2\,\mathrm{N1} \longrightarrow \mathrm{aco} + 2\,\mathrm{N2} \tag{23}$$

Reactants

Table 24: Properties of each reactant.

Id	Name	SBO
`eth`	EtOH	
`N1`	NAD	

Products

Table 25: Properties of each product.

Id	Name	SBO
`aco`	AcCoA	
`N2`	NADH	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}(\mathrm{c1}) \cdot \mathrm{k7} \cdot [\mathrm{eth}] \cdot [\mathrm{N1}] \tag{24}$$

7.11 Reaction `v15`

This is an irreversible reaction of one reactant forming one product.

Name v15

Notes This reaction (L-homoserine-O-acetyltransferase, Met2p, EC:2.3.1.31) has homoserine as an additional reactant and Coenzyme A as an additional product.

Reaction equation

$$\mathrm{aco} \longrightarrow \mathrm{oah} \tag{25}$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
aco	AcCoA	

Product

Table 27: Properties of each product.

Id	Name	SBO
oah	OAH	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}(\mathrm{c1}) \cdot \mathrm{k15} \cdot [\mathrm{aco}] \tag{26}$$

7.12 Reaction v17

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

Name v17

Reaction equation

$$\mathrm{hyd} \longrightarrow \emptyset \tag{27}$$

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
hyd	H2S	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}(\mathrm{c1}) \cdot \mathrm{k17} \cdot [\mathrm{hyd}] \tag{28}$$

7.13 Reaction v18

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

Name v18

Notes O-acetyl-homoserine usage for other metabolic reactions, no GO term applicable

Reaction equation

$$\text{oah} \longrightarrow \emptyset \tag{29}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
oah	OAH	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{vol}(\text{c1}) \cdot \text{k18} \cdot [\text{oah}] \tag{30}$$

7.14 Reaction v8

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

Name v8

Notes A simplification of the (acetyl-CoA) assimilatory part of the tricarboxylic acid cycle, with implied equilibration of Acetyl-CoA between mitochondria and cytosol

Reaction equation

$$\text{S2} + \text{aco} \longrightarrow \text{S1} \tag{31}$$

Reactants

Table 30: Properties of each reactant.

Id	Name	SBO
S2	S2	
aco	AcCoA	

Product

Table 31: Properties of each product.

Id	Name	SBO
S1	S1	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\,(\mathrm{c2}) \cdot \mathrm{k8} \cdot [\mathrm{aco}] \cdot [\mathrm{S2}] \tag{32}$$

7.15 Reaction v9

This is an irreversible reaction of two reactants forming two products.

Name v9

Notes A simplification of the oxidative (NADH producing) part of the tricarboxylic acid cycle, with implied equilibration between mitochondrial and cytosolic NADH/NAD+

Reaction equation

$$\mathrm{S1} + 4\,\mathrm{N1} \longrightarrow \mathrm{S2} + 4\,\mathrm{N2} \tag{33}$$

Reactants

Table 32: Properties of each reactant.

Id	Name	SBO
S1	S1	
N1	NAD	

Products

Table 33: Properties of each product.

Id	Name	SBO
S2	S2	
N2	NADH	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\,(\mathrm{c2}) \cdot \mathrm{k9} \cdot [\mathrm{S1}] \cdot [\mathrm{N1}] \tag{34}$$

7.16 Reaction v11a

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

Name vET1

Notes Reactions v11a, v11a2 and v11b form a minimal description for the oxidative phosphorylation, v11a represents the electron transfer from NAD(P)H to the protein complexes of mitochondrial electron transport chain

Reaction equation

$$\mathrm{C1} + \mathrm{Hm} + \mathrm{N2} \xrightarrow{\text{hyd, oxy}} \mathrm{C2} + \mathrm{Ho} + \mathrm{N1} \tag{35}$$

Reactants

Table 34: Properties of each reactant.

Id	Name	SBO
C1	C1	
Hm	Hm	
N2	NADH	

Modifiers

Table 35: Properties of each modifier.

Id	Name	SBO
hyd	H2S	
oxy	O2	

Products

Table 36: Properties of each product.

Id	Name	SBO
C2	C2	
Ho	Ho	
N1	NAD	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \frac{\mathrm{vol}(\mathrm{c2}) \cdot \mathrm{k11} \cdot [\mathrm{N2}] \cdot [\mathrm{oxy}]}{(\mathrm{a} \cdot [\mathrm{N2}] + [\mathrm{oxy}]) \cdot \left(1 + \left(\frac{[\mathrm{hyd}]}{\mathrm{Kh}}\right)^{\mathrm{m}}\right)} \tag{36}$$

7.17 Reaction v11a2

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

Name vET2

Notes Reactions v11a, v11a2 and v11b form a minimal description for the oxidative phosphorylation, v11b represents the electron transfer from the protein complexes of mitochondrial electron transport chain to oxgyen

Reaction equation

$$\mathrm{C2} + \mathrm{oxy} \xrightarrow{\mathrm{hyd,\ N2}} \mathrm{C1} + \mathrm{H2O} \tag{37}$$

Reactants

Table 37: Properties of each reactant.

Id	Name	SBO
C2	C2	
oxy	O2	

Modifiers

Table 38: Properties of each modifier.

Id	Name	SBO
hyd	H2S	
N2	NADH	

Products

Table 39: Properties of each product.

Id	Name	SBO
C1	C1	
H2O	H2O	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \frac{\mathrm{vol}(\mathrm{c2}) \cdot \mathrm{k11} \cdot [\mathrm{N2}] \cdot [\mathrm{oxy}]}{(\mathrm{a} \cdot [\mathrm{N2}] + [\mathrm{oxy}]) \cdot \left(1 + \left(\frac{[\mathrm{hyd}]}{\mathrm{Kh}}\right)^{\mathrm{m}}\right)} \tag{38}$$

7.18 Reaction v16

This is an irreversible reaction of two reactants forming two products.

Name v16

Notes TODO: NOT CLEAR ABOUT CORRECT VOLUME CORRECTION FOR THIS KINETIC LAW OF A TRANSPORT REACTION

Reaction equation

$$\mathrm{A2c} + \mathrm{A3m} \longrightarrow \mathrm{A2m} + \mathrm{A3c} \tag{39}$$

Reactants

Table 40: Properties of each reactant.

Id	Name	SBO
A2c	ADP	
A3m	ATP_mit	

Products

Table 41: Properties of each product.

Id	Name	SBO
A2m	ADP_mit	
A3c	ATP	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{vol}(\mathrm{c2}) \cdot \mathrm{k16} \cdot [\mathrm{A3m}] \cdot [\mathrm{A2c}] \tag{40}$$

7.19 Reaction v11b

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

Name vSYNT

Notes Reactions v11a, v11a2 and v11b form a minimal description for the oxidative phosphorylation, v11b represents the production of ATP, coupled to the flux of protons from the cytosol to the mitochondria

Reaction equation

$$\mathrm{Ho} + \mathrm{A2m} \xrightarrow{\text{hyd, N2, oxy}} \mathrm{Hm} + \mathrm{A3m} \tag{41}$$

Reactants

Table 42: Properties of each reactant.

Id	Name	SBO
Ho	Ho	
A2m	ADP_mit	

Modifiers

Table 43: Properties of each modifier.

Id	Name	SBO
hyd	H2S	
N2	NADH	
oxy	O2	

Products

Table 44: Properties of each product.

Id	Name	SBO
Hm	Hm	
A3m	ATP_mit	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \frac{\frac{\mathrm{vol(c2)} \cdot 3 \cdot \mathrm{k11} \cdot [\mathrm{N2}] \cdot [\mathrm{oxy}]}{(\mathrm{a} \cdot [\mathrm{N2}] + [\mathrm{oxy}]) \cdot \left(1 + \left(\frac{[\mathrm{hyd}]}{\mathrm{Kh}}\right)^{\mathrm{m}}\right)} \cdot [\mathrm{A2m}]}{\mathrm{Ka} + [\mathrm{A2m}]} \tag{42}$$

7.20 Reaction vLEAK

This is an irreversible reaction of one reactant forming one product.

Name vLEAK

Notes proton leakage of the inner mitochondrial membrane, no GO term applicable. The kinetic law is set to 0 as the leakage is handled in reactions v11a, v11a2 and v11b and the proton gradient is assumed to be in equlibrium.

Reaction equation

$$\mathrm{Ho} \longrightarrow \mathrm{Hm} \tag{43}$$

Reactant

Table 45: Properties of each reactant.

Id	Name	SBO
Ho	Ho	

Product

Table 46: Properties of each product.

Id	Name	SBO
Hm	Hm	

Kinetic Law

Derived unit not available

$$v_{20} = 0 \tag{44}$$

7.21 Reaction v12

This is an irreversible reaction of one reactant forming one product.

Name v12

Reaction equation

$$\text{A3c} \longrightarrow \text{A2c} \tag{45}$$

Reactant

Table 47: Properties of each reactant.

Id	Name	SBO
A3c	ATP	

Product

Table 48: Properties of each product.

Id	Name	SBO
A2c	ADP	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \text{vol}(\text{c1}) \cdot \text{k12} \cdot [\text{A3c}] \tag{46}$$

8 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.

8.1 Species `sul_ex`

Name SO4_ex

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

Charge 0

This species takes part in one reaction (as a reactant in `v1`), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{sul\_ex} = 0 \tag{47}$$

8.2 Species `eth_ex`

Name EtOH_ex

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

Charge 0

This species takes part in one reaction (as a reactant in `v13`), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{eth\_ex} = 0 \tag{48}$$

8.3 Species `oxy_ex`

Name O2_ex

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

Charge 0

This species takes part in two reactions (as a reactant in v10 and as a product in v14), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{oxy\_ex} = 0 \tag{49}$$

8.4 Species oxy

Name O2

Initial concentration $7\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in five reactions (as a reactant in v14, v11a2 and as a product in v10 and as a modifier in v11a, v11b).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{oxy} = v_4 - v_5 - v_{17} \tag{50}$$

8.5 Species H2O

Name H2O

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

Charge 0

This species takes part in one reaction (as a product in v11a2), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{H2O} = 0 \tag{51}$$

8.6 Species A3c

Name ATP

Initial concentration $1.5\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in four reactions (as a reactant in v2, v3, v12 and as a product in v16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{A3c} = v_{18} - v_3 - v_6 - v_{21} \tag{52}$$

8.7 Species aps

Name APS

Initial concentration $0.5\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in two reactions (as a reactant in v3 and as a product in v2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{aps} = v_3 - v_6 \tag{53}$$

8.8 Species PPi

Name PPi

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

Charge 0

This species takes part in one reaction (as a product in v2), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PPi} = 0 \tag{54}$$

8.9 Species pap

Name PAPS

Initial concentration $0.4\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in two reactions (as a reactant in v4 and as a product in v3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pap} = v_6 - v_7 \tag{55}$$

8.10 Species sul

Name SO4

Initial concentration $0.4\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in two reactions (as a reactant in v2 and as a product in v1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{sul} = v_1 - v_3 \tag{56}$$

8.11 Species eth

Name EtOH

Initial concentration $4\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in two reactions (as a reactant in v7 and as a product in v13).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{eth} = v_2 - v_{10} \tag{57}$$

8.12 Species A2c

Name ADP

Initial concentration $0.5\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

Involved in rule A2c

This species takes part in three reactions (as a reactant in v16 and as a product in v3, v12). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

8.13 Species hyd

Name H2S

Initial concentration $0.5\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in six reactions (as a reactant in v5, v17 and as a product in v4 and as a modifier in v11a, v11a2, v11b).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{hyd} = v_7 - v_8 - v_{12} \tag{58}$$

8.14 Species cys

Name CYS

Initial concentration $0.3\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in three reactions (as a reactant in v6 and as a product in v5 and as a modifier in v1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{cys} = v_8 - v_9 \tag{59}$$

8.15 Species N2

Name NADH

Initial concentration $2\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in six reactions (as a reactant in v4, v11a and as a product in v7, v9 and as a modifier in v11a2, v11b).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{N2} = 2\,v_{10} + 4\,v_{15} - 3\,v_{7} - v_{16} \tag{60}$$

8.16 Species N1

Name NAD

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

Charge 0

Involved in rule N1

This species takes part in four reactions (as a reactant in v7, v9 and as a product in v4, v11a). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

8.17 Species aco

Name AcCoA

Initial concentration $0.3\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in three reactions (as a reactant in v15, v8 and as a product in v7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{aco} = v_{10} - v_{11} - v_{14} \tag{61}$$

8.18 Species oah

Name OAH

Initial concentration $1.5\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in three reactions (as a reactant in v5, v18 and as a product in v15).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{oah} = v_{11} - v_{8} - v_{13} \tag{62}$$

8.19 Species S1

Name S1

Initial concentration $1.5\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in two reactions (as a reactant in v9 and as a product in v8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S1} = v_{14} - v_{15} \tag{63}$$

8.20 Species S2

Name S2

Initial concentration $0.5\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

Involved in rule S2

This species takes part in two reactions (as a reactant in v8 and as a product in v9). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

8.21 Species C1

Name C1

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

Charge 0

This species takes part in two reactions (as a reactant in v11a and as a product in v11a2), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C1} = 0 \tag{64}$$

8.22 Species C2

Name C2

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

Charge 0

This species takes part in two reactions (as a reactant in v11a2 and as a product in v11a), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C2} = 0 \tag{65}$$

8.23 Species A2m

Name ADP_mit

Initial concentration $0.5\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

Involved in rule A2m

This species takes part in two reactions (as a reactant in v11b and as a product in v16). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

8.24 Species A3m

Name ATP_mit

Initial concentration $1.5\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Charge 0

This species takes part in two reactions (as a reactant in v16 and as a product in v11b).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{A3m} = v_{19} - v_{18} \tag{66}$$

8.25 Species Ho

Name Ho

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

Charge 0

This species takes part in three reactions (as a reactant in v11b, vLEAK and as a product in v11a), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ho} = 0 \tag{67}$$

8.26 Species Hm

Name Hm

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

Charge 0

This species takes part in three reactions (as a reactant in v11a and as a product in v11b, vLEAK), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Hm} = 0 \tag{68}$$

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