SBML Model Report

Model name: "Mitchell2013 - Liver Iron Metabolism"



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1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah¹ and Simon Mitchell² at November 27th 2013 at 11:28 a.m. and last time modified at October tenth 2014 at 10:37 a.m. Table 1 gives 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	2
species types	0	species	21
events	0	constraints	0
reactions	44	function definitions	12
global parameters	1	unit definitions	0
rules	1	initial assignments	0

Model Notes

Mitchell2013 - Liver Iron Metabolism

The model includes the core regulatory components of human liver iron metabolism.

This model is described in the article: A computational model of liver iron metabolism. Mitchell S, Mendes P.PLoS Comput. Biol. 2013 Nov; 9(11): e1003299

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Abstract:

Iron is essential for all known life due to its redox properties; however, these same properties can also lead to its toxicity in overload through the production of reactive oxygen species. Robust systemic and cellular control are required to maintain safe levels of iron, and the liver seems to be where this regulation is mainly located. Iron misregulation is implicated in many diseases, and as our understanding of iron metabolism improves, the list of iron-related disorders grows. Recent developments have resulted in greater knowledge of the fate of iron in the body and have led to a detailed map of its metabolism; however, a quantitative understanding at the systems level of how its components interact to produce tight regulation remains elusive. A mechanistic computational model of human liver iron metabolism, which includes the core regulatory components, is presented here. It was constructed based on known mechanisms of regulation and on their kinetic properties, obtained from several publications. The model was then quantitatively validated by comparing its results with previously published physiological data, and it is able to reproduce multiple experimental findings. A time course simulation following an oral dose of iron was compared to a clinical time course study and the simulation was found to recreate the dynamics and time scale of the systems response to iron challenge. A disease state simulation of haemochromatosis was created by altering a single reaction parameter that mimics a human haemochromatosis gene (HFE) mutation. The simulation provides a quantitative understanding of the liver iron overload that arises in this disease. This model supports and supplements understanding of the role of the liver as an iron sensor and provides a framework for further modelling, including simulations to identify valuable drug targets and design of experiments to improve further our knowledge of this system.

This model is hosted on BioModels Database and identifiedby: BIOMD0000000498.

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

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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 1

2.3 Unit area

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

Definition m²

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 two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
compartment_1 compartment_3			3 3	1	litre litre	1	

3.1 Compartment compartment_1

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

Name LiverCell

SBO:0000290 physical compartment

3.2 Compartment compartment_3

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

Name intercell

SBO:0000290 physical compartment

4 Species

This model contains 21 species. The boundary condition of two of these species is set to true so that these species' amount cannot be changed by any reaction. Section 9 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 Condi- tion
species_7	Hamp	compartment_1	$\text{mol} \cdot l^{-1}$		
species_24	Fe-FT	${\tt compartment_1}$	$\text{mol} \cdot l^{-1}$		\Box
species_25	FT	${\tt compartment_1}$	$\text{mol} \cdot l^{-1}$		
species_26	FT1	${\tt compartment_1}$	$\text{mol} \cdot l^{-1}$		\Box
species_1	HO-1	${\tt compartment_1}$	$\text{mol} \cdot l^{-1}$		\Box
species_5	Heme	${\tt compartment_1}$	$\text{mol} \cdot l^{-1}$		
species_2	LIP	${\tt compartment_1}$	$\text{mol} \cdot l^{-1}$		
species_4	Fpn	${\tt compartment_1}$	$\text{mol} \cdot l^{-1}$		
species_6	IRP	${\tt compartment_1}$	$\text{mol} \cdot l^{-1}$		
species_43	Tf-Fe_intercell	${\tt compartment_3}$	$\text{mol} \cdot l^{-1}$		\square
species_3	TfR	compartment_3	$\text{mol} \cdot l^{-1}$		
species_12	Tf-Fe-TfR1	compartment_3	$\text{mol} \cdot l^{-1}$		
species_8	HFE	compartment_3	$\text{mol} \cdot l^{-1}$		
species_9	HFE-TfR	compartment_3	$\text{mol} \cdot l^{-1}$		
species_15	Tf-Fe-TfR2	compartment_3	$\text{mol} \cdot l^{-1}$		
species_16	2(Tf-Fe)-TfR1	${\tt compartment_3}$	$\text{mol} \cdot l^{-1}$		
species_17	2HFE-TfR	compartment_3	$\text{mol} \cdot l^{-1}$		\Box
species_18	2HFE-TfR2	compartment_3	$\text{mol} \cdot l^{-1}$		
species_19	2(Tf-Fe)-TfR2	compartment_3	$\text{mol} \cdot l^{-1}$		
species_10	TfR2	compartment_3	$\text{mol} \cdot l^{-1}$		\Box
species_11	Heme_intercell	${\tt compartment_3}$	$\text{mol} \cdot l^{-1}$		

Id	Name	Compartment	Derived Unit	Constant	Boundary
					Condi-
					tion

5 Parameter

This model contains one global parameter.

Table 4: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
parameter_1	Fe2GutQUant	10^{-7}	

6 Function definitions

This is an overview of twelve function definitions.

6.1 Function definition function_5

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$v$$
 (1)

6.2 Function definition function_10

Name Henri-Michaelis-Menten (irreversible)

Arguments substrate, Km, V

Mathematical Expression

$$\frac{V \cdot substrate}{Km + substrate}$$
 (2)

6.3 Function definition function_3

Name Hill Function ---

Arguments a, M, n, K

Mathematical Expression

$$a\cdot \left(1-\frac{M^n}{K^n+M^n}\right) \hspace{1.5cm} (3)$$

6.4 Function definition function_2

Name Hill Function ->

Arguments a, n, K, M

Mathematical Expression

$$\frac{a\cdot M^n}{K^n+M^n} \tag{4}$$

6.5 Function definition function_7

Name Biochemical Hill Function -> (workaround)

Arguments a, M, n, K, L

Mathematical Expression

$$a \cdot \frac{M^n}{K^n + M^n} \cdot L \tag{5}$$

6.6 Function definition function_4

Name Biochemical Hill Function -— (workaround)

Arguments a, M, n, K, L

Mathematical Expression

$$a \cdot \left(1 - \frac{M^n}{K^n + M^n}\right) \cdot L \tag{6}$$

6.7 Function definition function_9

Name Hill expression

Arguments a, M, K

Mathematical Expression

$$a \cdot \frac{M}{K + M} \tag{7}$$

6.8 Function definition function_8

Name Kloss Hill [1]

Arguments S, kloss, FT1, FT

Mathematical Expression

$$S \cdot kloss \cdot \left(1 + \frac{0.048 \cdot \frac{FT1}{FT}}{1 + \frac{FT1}{FT}}\right) \tag{8}$$

6.9 Function definition function_12

Name Mass Action Ferritin [2]

Arguments K, FT1, FT, S

Mathematical Expression

$$K \cdot \frac{FT1}{FT} \cdot S \tag{9}$$

6.10 Function definition function_1

Name Biochemical Hill Function General

Arguments a, M, n, K, S

Mathematical Expression

$$a \cdot \frac{M^n}{K^n + M^n} \cdot S \tag{10}$$

6.11 Function definition function_6

Name Henri-Michaelis-Menten kcat (irreversible) [1]

Arguments E, C, S, K

Mathematical Expression

$$\frac{E \cdot C \cdot S}{K + S} \tag{11}$$

6.12 Function definition function_11

Name Hepc Expression 7 [1]

Arguments basal, a, M, n, K, a1, M1, K1

Mathematical Expression

$$basal + \frac{a \cdot M^n}{K^n + M^n} + \frac{a1 \cdot M1}{K1 + M1}$$
 (12)

7 Rule

This is an overview of one rule.

7.1 Rule parameter_1

Rule parameter_1 is an assignment rule for parameter parameter_1:

$$= \begin{cases} 1.0E - 7 & \text{if } 5.0E - 13 \cdot (\text{time} - 40000)^2 + 10^{-4} < 1.0E - 7 \\ 5.0E - 13 \cdot (\text{time} - 40000)^2 + 10^{-4} & \text{otherwise} \end{cases}$$
(13)

8 Reactions

This model contains 44 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

No	Id	Name	Reaction Equation SBO	_
1	reaction_1	Fpn Export	2 species_2 species_4, species_4, species_2, species_4, species_2	species_43
2	reaction_2	TfR1 expression	$\emptyset \xrightarrow{\text{species_6, species_6, species_6}} \text{species_3}$	
3	reaction_3	TfR1 degradation	species_3 $\xrightarrow{\text{species}_3} \emptyset$	
4	${\tt reaction_4}$	Ferroportin Expression	$\emptyset \xrightarrow{\text{species}_6, \text{species}_6, \text{species}_6} \text{species}_4$	
5	reaction_8	IRP expresion	$\emptyset \xrightarrow{\text{species}_2, \text{species}_2, \text{species}_2} \text{species}_6$	
6	reaction_9	IRP degradation	species_6 $\xrightarrow{\text{species}_6}$, $\xrightarrow{\text{species}_6}$ \emptyset	
7	reaction_11	Fpn degradation	species_4 species_7, species_4, species_4, species_4 \emptyset	
8	reaction_12	HFE degradation	species_8 $\xrightarrow{\text{species}_8, \text{ species}_8} \emptyset$	
9	$reaction_{-}13$	HFE expression	$\emptyset \longrightarrow \text{species}_8$	
10	${\tt reaction_14}$	TfR2 expression	$\emptyset \longrightarrow \text{species}_10$	
11	reaction_15	TfR2 degradation	species_10 species_43, species_43, species_10, species_43, species_43	$\xrightarrow{s_10} \emptyset$
12	reaction_17	Hepcidin expression	g species_18, species_19, species_18, species_19, species_18, species_18	$\xrightarrow{\text{cies}_19} \text{spe}$
13	reaction_18	Hepcidin degradation	species_7 $\xrightarrow{\text{species}_7} \emptyset$	
14	reaction_21	HFE TfR1 binding	species_8 + species_3 species_8, species_3, species_8, species_3 s	pecies_9
15	reaction_22	HFE TfR1 release	species_9 species_9, species_9 species_8 + species_3	
16	reaction_23	TfR1 binding	species_43 + species_3 species_43, species_3, species_43, species_	_3 → species_

N⁰	Id	Name	Reaction Equation	SBO
17	reaction_24	TfR1 release	species_12 species_12, species_12 species_43 species_3	+
18	reaction_25	HFE TfR2 binding	2 species_8 + species_10 species_8, species_10, s	species_8, species_10 species_18
19	reaction_26	HFE TfR2 release	species_18 $\xrightarrow{\text{species}_18, \text{ species}_18}$ 2 species_8 $\xrightarrow{\text{species}_10}$	+
20	reaction_27	TfR2 binding	species_43 + species_10 species_43, species_10,	
21	reaction_28	TfR2 release	species_15 species_15, species_15 species_43 species_10	+
22	reaction_29	TfR1 binding 2	species_12+species_43 species_12, species_43,	
23	reaction_30	TfR1 release 2	species_16 species_16, species_16 species_12 species_43	+
24	reaction_31	HFE TfR1 binding 2	species_9+species_8 species_9, species_8, species_8	
25	reaction_32	HFE TfR1 release 2	species_17 species_17, species_17 species_9 species_8	+
26	reaction_35	TfR2 binding 2	species_15 + species_43 species_15, species_43,	species_15, species_43 species_19
27	reaction_36	TfR2 release 2	species_19 species_19, species_19 species_15	+
28	reaction_6	TfR1 iron internalisation	species_16 species_16, species_16 species_2 species_3 4 species_2	+
29	reaction_7	TfR2 iron internalisation	species_19 $\xrightarrow{\text{species}_19, \text{species}_19} 4 \text{ species}_2$ species_10	+
30	reaction_44	outFlow	species_2 $\xrightarrow{\text{species}_2}$, $\xrightarrow{\text{species}_2}$ \emptyset	

12	N₀	Id	Name	Reaction Equation SBO
	31	reaction_45	Ferritin Iron binding	species_2+species_25 species_2, species_25, species_2, species_25 species_24
	32	${\tt reaction_46}$	Ferritin Iron release	species_24 $\xrightarrow{\text{species}_24, \text{species}_24}$ species_2 +
	33	reaction_47	Ferritin Iron internalisation	species_25 species_24 species_24, species_24 species_25 + species_25
	34	reaction_48	Ferritin internalised iron release	species_26, species_25, species_26, species_25, species_25, species_25 species_26
	35	reaction_49	ferritin expression	$\emptyset \xrightarrow{\text{species_6, species_6, species_6}} \text{species_25}$
Pro	36	reaction_67	Ferritin Degredation Full	species_25 $\xrightarrow{\text{species}_25} \emptyset$
duce	37	reaction_73	Ferritin Degredation Full Iron Release	species_26 species_26, species_25, species_26, species_25, species_25, species_25 species_26
Produced by SBML2l ^{ET} EX	38	reaction_5	HFETfR degradation	species_17 $\xrightarrow{\text{species}_17, \text{ species}_17} \emptyset$
88 M	39	${\tt reaction_10}$	HFETfR2 degradation	species_18 $\xrightarrow{\text{species}_18, \text{species}_18} \emptyset$
	40	reaction_16	Heme uptake	species_11 $\xrightarrow{\text{species}_11, \text{ species}_11}$ species_5
7	41	reaction_19	Heme export	species_5 $\xrightarrow{\text{species}_5}$, species_11
	42	reaction_20	HO1 exp	$\emptyset \xrightarrow{\text{species_5, species_5}} \text{species_1}$
	43	reaction_33	HO1 Deg	species_1 $\xrightarrow{\text{species}_1, \text{species}_1} \emptyset$
	44	reaction_34	Heme oxygenation	species_5 species_1, species_5, species_1, species_5 species_2

8.1 Reaction reaction_1

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

Name Fpn Export

Reaction equation

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
species_2	LIP	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
species_4 species_4 species_2	Fpn Fpn LIP	
species_4 species_2	Fpn LIP	

Product

Table 8: Properties of each product.

Id	Name	SBO
species_43	Tf-Fe_intercell	

Kinetic Law

$$v_1 = \text{function}_1(a, [\text{species}_4], n, K, [\text{species}_2])$$
 (15)

$$function_1\left(a,M,n,K,S\right) = a \cdot \frac{M^n}{K^n + M^n} \cdot S \tag{16} \label{eq:16}$$

Table 9: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a	a	2.000	$ \mathbf{Z} $
n	n	$ \begin{array}{c} 1.000 \\ 3 \cdot 10^{-6} \end{array} $	\checkmark
K	K	$3 \cdot 10^{-6}$	\square

8.2 Reaction reaction_2

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

Name TfR1 expression

Reaction equation

$$\emptyset \xrightarrow{\text{species_6, species_6, species_6}} \text{species_3}$$
 (17)

Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
species_6	IRP	
species_6	IRP	
species_6	IRP	

Product

Table 11: Properties of each product.

Id	Name	SBO
species_3	TfR	

Kinetic Law

$$v_2 = \text{vol} \left(\text{compartment_3} \right) \cdot \text{function_2} \left(a, n, K, [\text{species_6}] \right)$$
 (18)

$$function_2\left(a,n,K,M\right) = \frac{a\cdot M^n}{K^n + M^n} \tag{19}$$

$$function_2\left(a,n,K,M\right) = \frac{a\cdot M^n}{K^n + M^n} \eqno(20)$$

Table 12: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a	a	$6 \cdot 10^{-12}$	$ \mathbf{Z} $
n	n	1.000	
K	K	10^{-6}	

8.3 Reaction reaction_3

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

Name TfR1 degradation

Reaction equation

species_3
$$\xrightarrow{\text{species}_3}$$
, $\xrightarrow{\text{species}_3} \emptyset$ (21)

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
species_3	TfR	

Modifiers

Table 14: Properties of each modifier.

Id	Name	SBO
species_3	TfR TfR	

Kinetic Law

$$v_3 = \text{vol} (\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_3}]$$
 (22)

Table 15: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$8.37 \cdot 10^{-6}$		

8.4 Reaction reaction_4

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

Name Ferroportin Expression

Reaction equation

$$\emptyset \xrightarrow{\text{species_6, species_6, species_6}} \text{species_4}$$
 (23)

Modifiers

Table 16: Properties of each modifier.

Id	Name	SBO
species_6	IRP	
species_6	IRP	
${ t species_6}$	IRP	

Product

Table 17: Properties of each product.

Id	Name	SBO
species_4	Fpn	

Kinetic Law

$$v_4 = \text{vol} (\text{compartment}_1) \cdot \text{function}_3 (a, [\text{species}_6], n, K)$$
 (24)

$$function_3\left(a,M,n,K\right) = a \cdot \left(1 - \frac{M^n}{K^n + M^n}\right) \eqno(25)$$

$$function_3\left(a,M,n,K\right) = a \cdot \left(1 - \frac{M^n}{K^n + M^n}\right) \eqno(26)$$

Table 18: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a	a	10^{-9}	
n	n	1.000 $5 \cdot 10^{-6}$	\mathbf{Z}
K	K	$5 \cdot 10^{-6}$	\checkmark

8.5 Reaction reaction_8

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

Name IRP expresion

Reaction equation

$$\emptyset \xrightarrow{\text{species}_2, \text{ species}_2, \text{ species}_2} \text{ species}_6$$
 (27)

Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
species_2	LIP	
species_2	LIP	
species_2	LIP	

Product

Table 20: Properties of each product.

Id	Name	SBO
species_6	IRP	

Kinetic Law

$$v_5 = \text{vol} (\text{compartment_1}) \cdot \text{function_3} (a, [\text{species_2}], n, K)$$
 (28)

$$function_3\left(a,M,n,K\right) = a \cdot \left(1 - \frac{M^n}{K^n + M^n}\right) \tag{29}$$

$$function_3\left(a,M,n,K\right) = a \cdot \left(1 - \frac{M^n}{K^n + M^n}\right) \eqno(30)$$

Table 21: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a	a	$4 \cdot 10^{-11}$	
n	n	1.000	\mathbf{Z}
K	K	10^{-6}	

8.6 Reaction reaction_9

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

Name IRP degradation

Reaction equation

species_6
$$\xrightarrow{\text{species}_6}$$
, $\xrightarrow{\text{species}_6} \emptyset$ (31)

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
species_6	IRP	

Modifiers

Table 23: Properties of each modifier.

Id	Name	SBO
species_6		
species_6	IRP	

Kinetic Law

$$v_6 = \text{vol}(\text{compartment_1}) \cdot \text{k1} \cdot [\text{species_6}]$$
 (32)

Table 24: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1	1	$1.597 \cdot 10^{-5}$	i	

8.7 Reaction reaction_11

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

Name Fpn degradation

Reaction equation

species_4
$$\xrightarrow{\text{species}_7, \text{ species}_4, \text{ species}_7, \text{ species}_4} \emptyset$$
 (33)

Reactant

Table 25: Properties of each reactant.

Id	Name	SBO
species_4	Fpn	

Modifiers

Table 26: Properties of each modifier.

Id	Name	SBO
species_7	Hamp	
${\tt species_7}$	Hamp	
${ t species_4}$	Fpn	
species_7	Hamp	
species_4	Fpn	

Kinetic Law

$$v_7 = \text{vol} \left(\text{compartment_1} \right) \cdot \text{function_7} \left(a, [\text{species_7}], n, K, [\text{species_4}] \right)$$
 (34)

$$function_7\left(a,M,n,K,L\right) = a \cdot \frac{M^n}{K^n + M^n} \cdot L \tag{35} \label{eq:35}$$

$$\label{eq:function_7} \text{function_7}\left(a,M,n,K,L\right) = a \cdot \frac{M^n}{K^n + M^n} \cdot L \tag{36}$$

Table 27: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a	a	$2.315 \cdot 10^{-4}$	
n	n	5.000	
K	K	$5 \cdot 10^{-9}$	

8.8 Reaction reaction_12

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

Name HFE degradation

Reaction equation

species_8
$$\xrightarrow{\text{species}_8, \text{ species}_8} \emptyset$$
 (37)

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
species_8	HFE	

Modifiers

Table 29: Properties of each modifier.

Id	Name	SBO
species_8 species_8	HFE HFE	

Kinetic Law

$$v_8 = \text{vol}(\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_8}]$$
 (38)

Table 30: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$6.418 \cdot 10^{-5}$	5	

8.9 Reaction reaction_13

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

Name HFE expression

Reaction equation

$$\emptyset \longrightarrow \text{species_8}$$
 (39)

Product

Table 31: Properties of each product.

Id	Name	SBO
species_8	HFE	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{vol} (\text{compartment}_3) \cdot \text{function}_5(v)$$
 (40)

$$function_5(v) = v (41)$$

$$function_5(v) = v (42)$$

Table 32: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
v	V	2	$2.3469 \cdot 10^{-1}$	1	Ø

8.10 Reaction reaction_14

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

Name TfR2 expression

Reaction equation

$$\emptyset \longrightarrow \text{species}_10$$
 (43)

Product

Table 33: Properties of each product.

Id	Name	SBO
species_10	TfR2	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{vol} (\text{compartment}_3) \cdot \text{function}_5(v)$$
 (44)

function_5 (v) = v
$$(45)$$

function_5
$$(v) = v$$
 (46)

Table 34: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
V	V	$3 \cdot 10^{-11}$	

8.11 Reaction reaction_15

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

Name TfR2 degradation

Reaction equation

species_10
$$\xrightarrow{\text{species}_43, \text{ species}_43, \text{ species}_10} \emptyset$$
 (47)

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
species_10	TfR2	

Modifiers

Table 36: Properties of each modifier.

Id	Name	SBO
species_43 species_43 species_10 species_43 species_10	Tf-Fe_intercell Tf-Fe_intercell TfR2 Tf-Fe_intercell TfR2	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{vol}(\text{compartment_3}) \cdot \text{function_4}(\text{a}, [\text{species_43}], \text{n}, \text{K}, [\text{species_10}])$$
 (48)

$$function_4\left(a,M,n,K,L\right) = a \cdot \left(1 - \frac{M^n}{K^n + M^n}\right) \cdot L \tag{49}$$

$$function_4\left(a,M,n,K,L\right) = a \cdot \left(1 - \frac{M^n}{K^n + M^n}\right) \cdot L \tag{50}$$

Table 37: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
a	a		$3.2\cdot 10^{-5}$		\overline{Z}
n	n		1.000		
K	K		$2.5\cdot 10^{-6}$		

8.12 Reaction reaction_17

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

Name Hepcidin expression

Reaction equation

$$\emptyset$$
 species_18, species_19, species_18, species_19, species_18, species_19 \longrightarrow species_7 (51)

Modifiers

Table 38: Properties of each modifier

14010 30. 110	rable 50. I roperties of each infoamer.		
Id	Name	SBO	
species_18	2HFE-TfR2		
species_19	2(Tf-Fe)-TfR2		
species_18	2HFE-TfR2		
species_19	2(Tf-Fe)-TfR2		
species_18	2HFE-TfR2		
${\tt species_19}$	2(Tf-Fe)-TfR2		

Product

Table 39: Properties of each product.

Id	Name	SBO
species_7	Hamp	

Kinetic Law

Derived unit contains undeclared units

 $v_{12} = \text{vol}(\text{compartment_1}) \cdot \text{function_11}(\text{basal}, \text{a}, [\text{species_18}], \text{n}, \text{K}, \text{a1}, [\text{species_19}], \text{K1})$ (52)

$$function_11 \left(basal, a, M, n, K, a1, M1, K1\right) = basal + \frac{a \cdot M^n}{K^n + M^n} + \frac{a1 \cdot M1}{K1 + M1} \tag{53}$$

$$function_11\left(basal,a,M,n,K,a1,M1,K1\right) = basal + \frac{a\cdot M^n}{K^n + M^n} + \frac{a1\cdot M1}{K1 + M1} \tag{54}$$

Table 40: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
basal	basal	0.000	Ø
a	a	$5 \cdot 10^{-12}$	\checkmark

Id	Name	SBO Value Unit	Constant
n	n	5.000	$ \overline{\checkmark} $
K	K	$1.35 \cdot 10^{-7}$	
a1	a1	$5 \cdot 10^{-12} \\ 6 \cdot 10^{-7}$	
K1	K1	$6 \cdot 10^{-7}$	

8.13 Reaction reaction_18

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

Name Hepcidin degradation

Reaction equation

species_7
$$\xrightarrow{\text{species}_7, \text{ species}_7} \emptyset$$
 (55)

Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
species_7	Hamp	

Modifiers

Table 42: Properties of each modifier.

Id	Name	SBO
species_7		

Kinetic Law

$$v_{13} = \text{vol} (\text{compartment}_1) \cdot \text{k1} \cdot [\text{species}_7]$$
 (56)

Table 43: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	$5.6 \cdot 10^{-4}$	

8.14 Reaction reaction_21

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

Name HFE TfR1 binding

Reaction equation

species_8 + species_3
$$\xrightarrow{\text{species}_8, \text{ species}_8, \text{ species}_8, \text{ species}_9}$$
 species_9 (57)

Reactants

Table 44: Properties of each reactant.

Id	Name	SBO
species_8 species_3		

Modifiers

Table 45: Properties of each modifier.

Id	Name	SBO
species_8	HFE	
species_3	TfR	
species_8	HFE	
species_3	TfR	

Product

Table 46: Properties of each product.

Id	Name	SBO
species_9	HFE-TfR	

Kinetic Law

$$v_{14} = \text{vol} (\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_8}] \cdot [\text{species_3}]$$
 (58)

Table 47: Properties of each parameter.

Id	Name	SBO V	alue Unit	Constant
k1	k 1	1102	2000.0	

8.15 Reaction reaction_22

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

Name HFE TfR1 release

Reaction equation

$$species_9 \xrightarrow{species_9, species_9} species_8 + species_3$$
 (59)

Reactant

Table 48: Properties of each reactant.

Id	Name	SBO
species_9	HFE-TfR	

Modifiers

Table 49: Properties of each modifier.

Id	Name	SBO
species_9	HFE-TfR	
species_9	HFE-TfR	

Products

Table 50: Properties of each product.

Name	SBO
HFE TfR	

Kinetic Law

$$v_{15} = \text{vol} (\text{compartment}_3) \cdot \text{k1} \cdot [\text{species}_9]$$
 (60)

Table 51: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	0.08	

8.16 Reaction reaction_23

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

Name TfR1 binding

Reaction equation

Reactants

Table 52: Properties of each reactant.

Id	Name	SBO
species_43 species_3	Tf-Fe_intercell TfR	

Modifiers

Table 53: Properties of each modifier.

Id	Name	SBO
species_43	Tf-Fe_intercell	
species_3	TfR	
species_43	Tf-Fe_intercell	
species_3	TfR	

Product

Table 54: Properties of each product.

Tueste e Trep	erence or cuting	
Id	Name	SBO
species_12	Tf-Fe-TfR1	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \text{vol} (\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_43}] \cdot [\text{species_3}]$$
 (62)

Table 55: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	837400.0	

8.17 Reaction reaction_24

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

Name TfR1 release

Reaction equation

$$species_{12} \xrightarrow{species_{12}, species_{12}} species_{43} + species_{3}$$
 (63)

Reactant

Table 56: Properties of each reactant.

Id	Name	SBO
species_12	Tf-Fe-TfR1	

Modifiers

Table 57: Properties of each modifier.

Id	Name	SBO
species_12 species_12		

Products

Table 58: Properties of each product.

ruete e et rieperines er euen prouden		
Id	Name	SBO
species_43 species_3	Tf-Fe_intercell TfR	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \text{vol} \left(\text{compartment_3} \right) \cdot \text{k1} \cdot \left[\text{species_12} \right]$$
 (64)

Table 59: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	$9.142 \cdot 10^{-4}$	Ø

8.18 Reaction reaction_25

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

Name HFE TfR2 binding

Reaction equation

Reactants

Table 60: Properties of each reactant.

Id	Name	SBO
species_8	HFE	
${\tt species_10}$	TfR2	

Modifiers

Table 61: Properties of each modifier.

Id	Name	SBO
species_8	HFE	
species_10	TfR2	
species_8	HFE	
${\tt species_10}$	TfR2	

Product

Table 62: Properties of each product.

Id	Name	SBO
species_18	2HFE-TfR2	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \text{vol} (\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_8}]^2 \cdot [\text{species_10}]$$
 (66)

Table 63: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$3.9438 \cdot 10^{11}$	[\overline{Z}

8.19 Reaction reaction_26

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

Name HFE TfR2 release

Reaction equation

species_18
$$\xrightarrow{\text{species}_18, \text{ species}_18}$$
 2 species_8 + species_10 (67)

Reactant

Table 64: Properties of each reactant.

Id	Name	SBO
species_18	2HFE-TfR2	

Modifiers

Table 65: Properties of each modifier.

fR2 fR2

Products

Table 66: Properties of each product.

Id	Name	SBO
species_8	HFE	
species_10	TfR2	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{vol}(\text{compartment}_3) \cdot \text{k1} \cdot [\text{species}_18]$$
 (68)

Table 67: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	0.002	$\overline{\hspace{1cm}}$

8.20 Reaction reaction_27

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

Name TfR2 binding

Reaction equation

species_43 + species_10
$$\xrightarrow{\text{species}_43, \text{ species}_10, \text{ species}_43, \text{ species}_10}$$
 species_15 (69)

Reactants

Table 68: Properties of each reactant.

Id	Name	SBO
species_43 species_10	Tf-Fe_intercell TfR2	

Modifiers

Table 69: Properties of each modifier.

Tuest extraperates of tuest incommen.			
Id	Name	SBO	
species_43	Tf-Fe_intercell		
species_10	TfR2		
species_43	Tf-Fe_intercell		
${\tt species_10}$	TfR2		

Product

Table 70: Properties of each product.

		1
Id	Name	SBO
species_15	Tf-Fe-TfR2	

Kinetic Law

$$v_{20} = \text{vol}(\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_43}] \cdot [\text{species_10}]$$
 (70)

Table 71: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	222390.0	

8.21 Reaction reaction_28

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

Name TfR2 release

Reaction equation

$$species_15 \xrightarrow{species_15, species_15} species_43 + species_10$$
 (71)

Reactant

Table 72: Properties of each reactant.

Id Name		SBO
species_15	Tf-Fe-TfR2	

Modifiers

Table 73: Properties of each modifier.

Id	Name	SBO
species_15 species_15		

Products

Table 74: Properties of each product.

	r · · · · · · · · · · · · · · · · · · ·	
Id	Name	SBO
-	Tf-Fe_intercell TfR2	

Kinetic Law

$$v_{21} = \text{vol}(\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_15}]$$
 (72)

Table 75: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	0.006	

8.22 Reaction reaction_29

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

Name TfR1 binding 2

Reaction equation

Reactants

Table 76: Properties of each reactant.

Id	Name	SBO
species_12	Tf-Fe-TfR1	
$species_43$	Tf-Fe_intercell	

Modifiers

Table 77: Properties of each modifier.

Id	Name	SBO
species_12	Tf-Fe-TfR1	
species_43	Tf-Fe_intercell	
species_12	Tf-Fe-TfR1	
species_43	Tf-Fe_intercell	

Product

Table 78: Properties of each product.

Id	Name	SBO
species_16	2(Tf-Fe)-TfR1	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \text{vol} (\text{compartment}_3) \cdot \text{k1} \cdot [\text{species}_12] \cdot [\text{species}_43]$$
 (74)

Table 79: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		121400.0		$ \mathbf{Z} $

8.23 Reaction reaction_30

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

Name TfR1 release 2

Reaction equation

species_16
$$\xrightarrow{\text{species}_16, \text{ species}_16}$$
 species_12 + species_43 (75)

Reactant

Table 80: Properties of each reactant.

Id Name		SBO
species_16	2(Tf-Fe)-TfR1	

Modifiers

Table 81: Properties of each modifier.

Id	Name	SBO
species_16		

Products

Table 82: Properties of each product.

THE COLUMN PROBLEM		
Id	Name	SBO
species_12 species_43	Tf-Fe-TfR1 Tf-Fe_intercell	

Derived unit contains undeclared units

$$v_{23} = \text{vol} (\text{compartment}_{-3}) \cdot \text{k1} \cdot [\text{species}_{-16}]$$
 (76)

Table 83: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	0.004	

8.24 Reaction reaction_31

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

Name HFE TfR1 binding 2

Reaction equation

species_9 + species_8
$$\xrightarrow{\text{species}_9, \text{ species}_9, \text{ species}_9}$$
 species_17 (77)

Reactants

Table 84: Properties of each reactant.

Id	Name	SBO
species_9	HFE-TfR	
species_8	HFE	

Modifiers

Table 85: Properties of each modifier.

Id	Name	SBO
species_9	HFE-TfR	
species_8	HFE	
species_9	HFE-TfR	
species_8	HFE	

Product

Table 86: Properties of each product.

Id	Name	SBO
species_17	2HFE-TfR	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \text{vol} (\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_9}] \cdot [\text{species_8}]$$
 (78)

Table 87: Properties of each parameter.

Id	Name	SBO Value	Unit	Constant
k1	k1	1102000.0		

8.25 Reaction reaction_32

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

Name HFE TfR1 release 2

Reaction equation

species_17
$$\xrightarrow{\text{species}_17, \text{ species}_17}$$
 species_9 + species_8 (79)

Reactant

Table 88: Properties of each reactant.

Id	Name	SBO
species_17	2HFE-TfR	

Modifiers

Table 89: Properties of each modifier.

Id	Name	SBO
species_17 species_17		

Products

Table 90: Properties of each product.

Id	Name	SBO
species_9	HFE-TfR	
species_8	HFE	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \text{vol}(\text{compartment}_3) \cdot \text{k1} \cdot [\text{species}_17]$$
 (80)

Table 91: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	0.08	\overline{Z}

8.26 Reaction reaction_35

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

Name TfR2 binding 2

Reaction equation

Reactants

Table 92: Properties of each reactant.

Id	Name	SBO
species_15 species_43	Tf-Fe-TfR2 Tf-Fe_intercell	

Modifiers

Table 93: Properties of each modifier.

Name	SBO
Tf-Fe-TfR2	
Tf-Fe_intercell	
Tf-Fe-TfR2	
Tf-Fe_intercell	
	Tf-Fe-TfR2 Tf-Fe_intercell Tf-Fe-TfR2

Product

Table 94: Properties of each product.

Id	Name	SBO
species_19	2(Tf-Fe)-TfR2	

Kinetic Law

$$v_{26} = \text{vol}(\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_15}] \cdot [\text{species_43}]$$
 (82)

Table 95: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	69600.0	

8.27 Reaction reaction_36

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

Name TfR2 release 2

Reaction equation

species_19
$$\xrightarrow{\text{species}_19, \text{ species}_19}$$
 species_15 + species_43 (83)

Reactant

Table 96: Properties of each reactant.

Id	Name	SBO
species_19	2(Tf-Fe)-TfR2	

Modifiers

Table 97: Properties of each modifier.

Id	Name	SBO
species_19 species_19	2(Tf-Fe)-TfR2 2(Tf-Fe)-TfR2	

Products

Table 98: Properties of each product.

	r · · · · · · · r	
Id	Name	SBO
species_15 species_43	Tf-Fe-TfR2 Tf-Fe_intercell	

Kinetic Law

$$v_{27} = \text{vol} (\text{compartment}_3) \cdot \text{k1} \cdot [\text{species}_19]$$
 (84)

Table 99: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	0.024	

8.28 Reaction reaction_6

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

Name TfR1 iron internalisation

Reaction equation

species_16
$$\xrightarrow{\text{species}_16, \text{ species}_16}$$
 4 species_2 + species_3 (85)

Reactant

Table 100: Properties of each reactant.

Id	Name	SBO
species_16	2(Tf-Fe)-TfR1	

Modifiers

Table 101: Properties of each modifier.

Id	Name	SBO
species_16	2(Tf-Fe)-TfR1	_
species_16	2(Tf-Fe)-TfR1	

Products

Table 102: Properties of each product.

Id	Name	SBO
species_2	LIP	
species_3	TfR	

Kinetic Law

$$v_{28} = k1 \cdot [\text{species}_16] \tag{86}$$

Table 103: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	0.833	

8.29 Reaction reaction_7

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

Name TfR2 iron internalisation

Reaction equation

$$species_{1}9 \xrightarrow{species_{1}9, species_{1}9} 4 species_{2} + species_{1}0$$
(87)

Reactant

Table 104: Properties of each reactant.

Id	Name	SBO
species_19	2(Tf-Fe)-TfR2	

Modifiers

Table 105: Properties of each modifier.

Id	Name	SBO
species_19 species_19	2(Tf-Fe)-TfR2 2(Tf-Fe)-TfR2	

Products

Table 106: Properties of each product.

Id	Name	SBO
species_2	LIP	
species_10	TfR2	

Derived unit contains undeclared units

$$v_{29} = k1 \cdot [\text{species}_19] \tag{88}$$

Table 107: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	0.833	

8.30 Reaction reaction_44

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

Name outFlow

Reaction equation

species_2
$$\xrightarrow{\text{species}_2, \text{ species}_2} \emptyset$$
 (89)

Reactant

Table 108: Properties of each reactant.

Id	Name	SBO
species_2	LIP	

Modifiers

Table 109: Properties of each modifier.

Id	Name	SBO
species_2 species_2		
species_2	LIP	

Kinetic Law

$$v_{30} = \text{vol}(\text{compartment_1}) \cdot \text{k1} \cdot [\text{species_2}]$$
 (90)

Table 110: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	$4\cdot 10^{-4}$	

8.31 Reaction reaction_45

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

Name Ferritin Iron binding

Reaction equation

Reactants

Table 111: Properties of each reactant.

Id	Name	SBO
species_2	LIP	
species_25	FT	

Modifiers

Table 112: Properties of each modifier.

Id	Name	SBO
species_2	LIP	
species_25	FT	
species_2	LIP	
species_25	FT	

Product

Table 113: Properties of each product.

Id	Name	SBO
species_24	Fe-FT	

Derived unit contains undeclared units

$$v_{31} = \text{vol} (\text{compartment_1}) \cdot \text{k1} \cdot [\text{species_2}] \cdot [\text{species_25}]$$
 (92)

Table 114: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$4.71 \cdot 10^{10}$		$ \mathbf{Z} $

8.32 Reaction reaction_46

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

Name Ferritin Iron release

Reaction equation

$$species_24 \xrightarrow{species_24, species_24} species_2 + species_25$$
 (93)

Reactant

Table 115: Properties of each reactant.

Id	Name	SBO
species_24	Fe-FT	

Modifiers

Table 116: Properties of each modifier.

Id	Name	SBO
species_24	Fe-FT	
species_24	Fe-FT	

Products

Table 117: Properties of each product.

Id	Name	SBO
species_2 species_25	LIP FT	

Derived unit contains undeclared units

$$v_{32} = \text{vol}(\text{compartment}_1) \cdot \text{k1} \cdot [\text{species}_24]$$
 (94)

Table 118: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	22922.0	

8.33 Reaction reaction_47

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

Name Ferritin Iron internalisation

Reaction equation

species_24
$$\xrightarrow{\text{species}_24, \text{ species}_24}$$
 species_26 + species_25 (95)

Reactant

Table 119: Properties of each reactant.

Id	Name	SBO
species_24	Fe-FT	

Modifiers

Table 120: Properties of each modifier.

Id	Name	SBO
species_24	Fe-FT	
species_24	Fe-FT	

Id	Name	SBO

Products

Table 121: Properties of each product.

Id	Name	SBO
species_26	FT1	
species_25	FT	

Kinetic Law

Derived unit contains undeclared units

$$v_{33} = \text{vol}(\text{compartment}_{-1}) \cdot \text{k1} \cdot [\text{species}_{-24}]$$
 (96)

Table 122: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		108000.0		

8.34 Reaction reaction_48

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

Name Ferritin internalised iron release

Reaction equation

Reactant

Table 123: Properties of each reactant.

Id	Name	SBO
species_26	FT1	

Modifiers

Table 124: Properties of each modifier.

Id	Name	SBO
species_26	FT1	
species_25	FT	
species_26	FT1	
species_25	FT	
species_26	FT1	
species_25	FT	

Product

Table 125: Properties of each product.

Id	Name	SBO
species_2	LIP	

Kinetic Law

Derived unit contains undeclared units

 $v_{34} = \text{vol}(\text{compartment_1}) \cdot \text{function_8}([\text{species_26}], \text{kloss}, [\text{species_26}], [\text{species_25}])$ (98)

$$function_8\left(S, kloss, FT1, FT\right) = S \cdot kloss \cdot \left(1 + \frac{0.048 \cdot \frac{FT1}{FT}}{1 + \frac{FT1}{FT}}\right) \tag{99}$$

$$\text{function_8}\left(S, \text{kloss}, \text{FT1}, \text{FT}\right) = S \cdot \text{kloss} \cdot \left(1 + \frac{0.048 \cdot \frac{\text{FT1}}{\text{FT}}}{1 + \frac{\text{FT1}}{\text{FT}}}\right) \tag{100}$$

Table 126: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
kloss	kloss	13.112	

8.35 Reaction reaction_49

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

Name ferritin expression

Reaction equation

$$\emptyset \xrightarrow{\text{species_6, species_6, species_6}} \text{species_25}$$

Modifiers

Table 127: Properties of each modifier.

Id	Name	SBO
species_6	IRP	
${ t species_6}$	IRP	
${\tt species_6}$	IRP	

Product

Table 128: Properties of each product.

Id	Name	SBO
species_25	FT	

Kinetic Law

$$v_{35} = \text{vol}(\text{compartment_1}) \cdot \text{function_3}(\text{a}, [\text{species_6}], \text{n}, \text{K})$$
 (102)

$$function_3\left(a,M,n,K\right) = a \cdot \left(1 - \frac{M^n}{K^n + M^n}\right) \eqno(103)$$

$$function_3\left(a,M,n,K\right) = a \cdot \left(1 - \frac{M^n}{K^n + M^n}\right) \eqno(104)$$

Table 129: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
a	a	2.31	$2\cdot 10^{-13}$		
n	n	-	1.000		\square
K	K		10^{-6}		

8.36 Reaction reaction_67

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

Name Ferritin Degredation Full

Reaction equation

species_25
$$\xrightarrow{\text{species}_25, \text{ species}_25} \emptyset$$
 (105)

Reactant

Table 130: Properties of each reactant.

Id	Name	SBO
species_25	FT	

Modifiers

Table 131: Properties of each modifier.

Id	Name	SBO
species_25	FT FT	
species_25	ГІ	

Kinetic Law

$$v_{36} = \text{vol}(\text{compartment}_1) \cdot \text{k1} \cdot [\text{species}_25]$$
 (106)

Table 132: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1	1.3	$203 \cdot 10^{-5}$		

8.37 Reaction reaction_73

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

Name Ferritin Degredation Full Iron Release

Reaction equation

Reactant

Table 133: Properties of each reactant.

Id	Name	SBO
species_26	FT1	_

Modifiers

Table 134: Properties of each modifier.

Id	Name	SBO
species_26	FT1	
species_25	FT	
species_26	FT1	
species_25	FT	
species_26	FT1	
species_25	FT	

Product

Table 135: Properties of each product.

Id	Name	SBO
species_2	LIP	

Derived unit contains undeclared units

$$v_{37} = \text{vol}(\text{compartment_1}) \cdot \text{function_12}(K, [\text{species_26}], [\text{species_25}], [\text{species_25}])$$
 (108)

$$function_{-}12\left(K,FT1,FT,S\right) = K \cdot \frac{FT1}{FT} \cdot S \tag{109} \label{eq:109}$$

$$function_{-}12\left(K,FT1,FT,S\right) = K \cdot \frac{FT1}{FT} \cdot S \tag{110} \label{eq:110}$$

Table 136: Properties of each parameter.

Id	Name	SBO Value	Unit	Constant
K	K	$1.203 \cdot 10^{-5}$		

8.38 Reaction reaction_5

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

Name HFETfR degradation

Reaction equation

species_17
$$\xrightarrow{\text{species}_17, \text{ species}_17} \emptyset$$
 (111)

Reactant

Table 137: Properties of each reactant.

Id	Name	SBO
species_17	2HFE-TfR	

Modifiers

Table 138: Properties of each modifier.

Id	Name	SBO
species_17	2HFE-TfR	
species_17	2HFE-TfR	

Id	Name	SBO

Derived unit contains undeclared units

$$v_{38} = \text{vol}(\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_17}]$$
 (112)

Table 139: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	$8.37 \cdot 10^{-7}$	

8.39 Reaction reaction_10

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

Name HFETfR2 degradation

Reaction equation

species_18
$$\xrightarrow{\text{species}_18, \text{ species}_18} \emptyset$$
 (113)

Reactant

Table 140: Properties of each reactant.

Id	Name	SBO
species_18	2HFE-TfR2	

Modifiers

Table 141: Properties of each modifier.

Id	Name	SBO
species_18	2HFE-TfR2	
species_18	2HFE-TfR2	

Derived unit contains undeclared units

$$v_{39} = \text{vol}(\text{compartment_3}) \cdot \text{k1} \cdot [\text{species_18}]$$
 (114)

Table 142: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	$8.37 \cdot 10^{-5}$	\square

8.40 Reaction reaction_16

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

Name Heme uptake

Reaction equation

species_11
$$\xrightarrow{\text{species}_11, \text{ species}_11}$$
 species_5 (115)

Reactant

Table 143: Properties of each reactant.

Id	Name	SBO
species_11	Heme_intercell	

Modifiers

Table 144: Properties of each modifier.

	1	
Id	Name	SBO
-	Heme_intercell Heme_intercell	

Product

Table 145: Properties of each product.

Id	Name	SBO
species_5	Heme	

Derived unit contains undeclared units

$$v_{40} = \text{function}_{10}([\text{species}_{11}], \text{Km}, \text{V})$$
(116)

$$function_10 (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate}$$
 (117)

Table 146: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
Km	Km	$1.25 \cdot 10^{-4}$	
V	V	$1.034 \cdot 10^{-5}$	\mathbf{Z}

8.41 Reaction reaction_19

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

Name Heme export

Reaction equation

species_5
$$\xrightarrow{\text{species}_5, \text{ species}_5}$$
 species_11 (118)

Reactant

Table 147: Properties of each reactant.

Id	Name	SBO
species_5	Heme	

Modifiers

Table 148: Properties of each modifier.

Id	Name	SBO
species_5	Heme	
species_5	Heme	

Product

Table 149: Properties of each product.

Id	Name	SBO
species_11	Heme_intercell	

Kinetic Law

Derived unit contains undeclared units

$$v_{41} = \text{function}_{10}([\text{species}_{5}], \text{Km}, \text{V})$$
 (119)

$$function_10 (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate}$$
 (120)

Table 150: Properties of each parameter.

Id	Name	SBO Value	Unit	Constant
Km V	Km V	$1.78 \cdot 10^{-5} \\ 2.18 \cdot 10^{-5}$		

8.42 Reaction reaction_20

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

Name HO1 exp

Reaction equation

$$\emptyset \xrightarrow{\text{species_5, species_5, species_5}} \text{species_1}$$
 (121)

Modifiers

Table 151: Properties of each modifier.

Id	Name	SBO
species_5	Heme	
species_5	Heme	
species_5	Heme	

Product

Table 152: Properties of each product.

Id	Name	SBO
species_1	HO-1	

Kinetic Law

Derived unit contains undeclared units

$$v_{42} = \text{vol}(\text{compartment_1}) \cdot \text{function_9}(\text{a}, [\text{species_5}], \text{K})$$
 (122)

$$function_9 (a, M, K) = a \cdot \frac{M}{K + M}$$
 (123)

function_9
$$(a, M, K) = a \cdot \frac{M}{K + M}$$
 (124)

Table 153: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
a K	a K	2	$2.1432 \cdot 10^{-1}$ 10^{-1}		

8.43 Reaction reaction_33

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

Name HO1 Deg

Reaction equation

species_1
$$\xrightarrow{\text{species}_1, \text{species}_1} \emptyset$$
 (125)

Reactant

Table 154: Properties of each reactant.

Id	Name	SBO
species_1	HO-1	

Modifiers

Table 155: Properties of each modifier.

Id	Name	SBO
species_1 species_1		

Kinetic Law

Derived unit contains undeclared units

$$v_{43} = \text{vol}(\text{compartment}_{-1}) \cdot \text{k1} \cdot [\text{species}_{-1}]$$
 (126)

Table 156: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1	3.	$209 \cdot 10^{-5}$		

8.44 Reaction reaction_34

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

Name Heme oxygenation

Reaction equation

species_5
$$\xrightarrow{\text{species}_1, \text{ species}_5, \text{ species}_5, \text{ species}_5}$$
 species_2 (127)

Reactant

Table 157: Properties of each reactant.

Id	Name	SBO
species_5	Heme	

Modifiers

Table 158: Properties of each modifier.

Id	Name	SBO
species_1	HO-1	
${ t species_1}$	HO-1	
species_5	Heme	
species_1	HO-1	
species_5	Heme	

Product

Table 159: Properties of each product.

Id	Name	SBO
species_2	LIP	

Kinetic Law

$$v_{44} = \text{vol}(\text{compartment_1}) \cdot \text{function_6}([\text{species_1}], C, [\text{species_5}], K)$$
 (128)

function_6(E,C,S,K) =
$$\frac{E \cdot C \cdot S}{K+S}$$
 (129)

function_6(E,C,S,K) =
$$\frac{E \cdot C \cdot S}{K+S}$$
 (130)

Table 160: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
С	C	17777.700	
K	K	$2 \cdot 10^{-6}$	

9 Derived Rate Equations

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

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

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

9.1 Species species_7

Name Hamp

SBO:0000252 polypeptide chain

Initial concentration $5 \cdot 10^{-9} \text{ mol} \cdot l^{-1}$

This species takes part in seven reactions (as a reactant in reaction_18 and as a product in reaction_17 and as a modifier in reaction_11, reaction_11, reaction_11, reaction_18, reaction_18).

$$\frac{d}{dt} \text{species}_{-7} = |v_{12}| - |v_{13}| \tag{131}$$

9.2 Species species_24

Name Fe-FT

SBO:0000296 macromolecular complex

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

This species takes part in seven reactions (as a reactant in reaction_46, reaction_47 and as a product in reaction_45 and as a modifier in reaction_46, reaction_46, reaction_47, reaction_47).

$$\frac{d}{dt} \text{species} 24 = |v_{31}| - |v_{32}| - |v_{33}|$$
 (132)

9.3 Species species_25

Name FT

SBO:0000252 polypeptide chain

Initial concentration $1.66 \cdot 10^{-10} \text{ mol} \cdot l^{-1}$

This species takes part in 15 reactions (as a reactant in reaction_45, reaction_67 and as a product in reaction_46, reaction_47, reaction_49 and as a modifier in reaction_45, reaction_45, reaction_48, reaction_48, reaction_48, reaction_67, reaction_67, reaction_73, reaction_73, reaction_73).

$$\frac{d}{dt} \text{species}_2 = |v_{32}| + |v_{33}| + |v_{35}| - |v_{31}| - |v_{36}|$$
(133)

9.4 Species species_26

Name FT1

SBO:0000247 simple chemical

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

This species takes part in nine reactions (as a reactant in reaction_48, reaction_73 and as a product in reaction_47 and as a modifier in reaction_48, reaction_48, reaction_73, reaction_73, reaction_73).

$$\frac{d}{dt} \text{species} \cdot 26 = |v_{33}| - |v_{34}| - |v_{37}| \tag{134}$$

9.5 Species species_1

Name HO-1

SBO:0000252 polypeptide chain

Initial concentration $3.56 \cdot 10^{-11} \text{ mol} \cdot l^{-1}$

This species takes part in seven reactions (as a reactant in reaction_33 and as a product in reaction_20 and as a modifier in reaction_33, reaction_33, reaction_34, reaction_34, reaction_34).

$$\frac{d}{dt} \text{species}_{1} = v_{42} - v_{43} \tag{135}$$

9.6 Species species_5

Name Heme

SBO:0000252 polypeptide chain

Initial concentration $10^{-9} \text{ mol} \cdot l^{-1}$

This species takes part in ten reactions (as a reactant in reaction_19, reaction_34 and as a product in reaction_16 and as a modifier in reaction_19, reaction_19, reaction_20, reaction_20, reaction_34, reaction_34).

$$\frac{d}{dt} \text{species} _{5} = |v_{40}| - |v_{41}| - |v_{44}| \tag{136}$$

9.7 Species species_2

Name LIP

SBO:0000327 non-macromolecular ion

Initial concentration $1.3 \cdot 10^{-6} \text{ mol} \cdot 1^{-1}$

This species takes part in 18 reactions (as a reactant in reaction_1, reaction_44, reaction_45 and as a product in reaction_6, reaction_7, reaction_46, reaction_48, reaction_73, reaction_34 and as a modifier in reaction_1, reaction_1, reaction_8, reaction_8, reaction_44, reaction_44, reaction_45, reaction_45).

$$\frac{d}{dt} \text{species}_2 = 4 v_{28} + 4 v_{29} + v_{32} + v_{34} + v_{37} + v_{44} - 2 v_1 - v_{30} - v_{31}$$
 (137)

9.8 Species species_4

Name Fpn

SBO:0000252 polypeptide chain

Initial concentration $10^{-9} \text{ mol} \cdot l^{-1}$

This species takes part in seven reactions (as a reactant in reaction_11 and as a product in reaction_4 and as a modifier in reaction_1, reaction_1, reaction_1, reaction_11, reaction_11).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species}_{4} = |v_{4}| - |v_{7}| \tag{138}$$

9.9 Species species_6

Name IRP

SBO:0000252 polypeptide chain

Initial concentration $1.16 \cdot 10^{-6} \text{ mol} \cdot l^{-1}$

This species takes part in 13 reactions (as a reactant in reaction_9 and as a product in reaction_8 and as a modifier in reaction_2, reaction_2, reaction_2, reaction_4, reaction_4, reaction_9, reaction_9, reaction_49, reaction_49, reaction_49).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species}_{6} = |v_{5}| - |v_{6}| \tag{139}$$

9.10 Species species_43

Name Tf-Fe_intercell

SBO:0000297 protein complex

Initial concentration $5 \cdot 10^{-6} \text{ mol} \cdot l^{-1}$

This species takes part in 20 reactions (as a reactant in reaction_23, reaction_27, reaction_29, reaction_35 and as a product in reaction_1, reaction_24, reaction_28, reaction_30, reaction_36 and as a modifier in reaction_15, reaction_15, reaction_15, reaction_23, reaction_23, reaction_27, reaction_27, reaction_29, reaction_29, reaction_35, reaction_35), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species}_{43} = 0 \tag{140}$$

9.11 Species species_3

Name TfR

SBO:0000252 polypeptide chain

Initial concentration $4 \cdot 10^{-7} \text{ mol} \cdot l^{-1}$

This species takes part in 13 reactions (as a reactant in reaction_3, reaction_21, reaction_23 and as a product in reaction_2, reaction_22, reaction_24, reaction_6 and as a modifier in reaction_3, reaction_3, reaction_21, reaction_21, reaction_23, reaction_23).

$$\frac{d}{dt} \text{species}_{3} = |v_{2}| + |v_{15}| + |v_{17}| + |v_{28}| - |v_{3}| - |v_{14}| - |v_{16}|$$
(141)

9.12 Species species_12

Name Tf-Fe-TfR1

SBO:0000297 protein complex

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

This species takes part in eight reactions (as a reactant in reaction_24, reaction_29 and as a product in reaction_23, reaction_30 and as a modifier in reaction_24, reaction_24, reaction_29, reaction_29).

$$\frac{d}{dt} \text{species}_{12} = |v_{16}| + |v_{23}| - |v_{17}| - |v_{22}|$$
 (142)

9.13 Species species_8

Name HFE

SBO:0000252 polypeptide chain

Initial concentration $2 \cdot 10^{-7} \text{ mol} \cdot 1^{-1}$

This species takes part in 16 reactions (as a reactant in reaction_12, reaction_21, reaction_25, reaction_31 and as a product in reaction_13, reaction_22, reaction_26, reaction_32 and as a modifier in reaction_12, reaction_12, reaction_21, reaction_21, reaction_25, reaction_31, reaction_31).

$$\frac{d}{dt} \text{species_8} = |v_9| + |v_{15}| + 2|v_{19}| + |v_{25}| - |v_8| - |v_{14}| - 2|v_{18}| - |v_{24}|$$
(143)

9.14 Species species_9

Name HFE-TfR

SBO:0000297 protein complex

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

This species takes part in eight reactions (as a reactant in reaction_22, reaction_31 and as a product in reaction_21, reaction_32 and as a modifier in reaction_22, reaction_32, reaction_31).

$$\frac{d}{dt} \text{species}_{9} = |v_{14}| + |v_{25}| - |v_{15}| - |v_{24}| \tag{144}$$

9.15 Species species_15

Name Tf-Fe-TfR2

SBO:0000297 protein complex

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

This species takes part in eight reactions (as a reactant in reaction_28, reaction_35 and as a product in reaction_27, reaction_36 and as a modifier in reaction_28, reaction_28, reaction_35, reaction_35).

$$\frac{d}{dt} \text{species}_{15} = |v_{20}| + |v_{27}| - |v_{21}| - |v_{26}|$$
(145)

9.16 Species species_16

Name 2(Tf-Fe)-TfR1

SBO:0000297 protein complex

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

This species takes part in seven reactions (as a reactant in reaction_30, reaction_6 and as a product in reaction_29 and as a modifier in reaction_30, reaction_30, reaction_6, reaction_6).

$$\frac{d}{dt} \text{species}_{16} = |v_{22}| - |v_{23}| - |v_{28}| \tag{146}$$

9.17 Species species_17

Name 2HFE-TfR

SBO:0000297 protein complex

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

This species takes part in seven reactions (as a reactant in reaction_32, reaction_5 and as a product in reaction_31 and as a modifier in reaction_32, reaction_32, reaction_5, reaction_5).

$$\frac{d}{dt} \text{species}_{17} = |v_{24}| - |v_{25}| - |v_{38}| \tag{147}$$

9.18 Species species_18

Name 2HFE-TfR2

SBO:0000297 protein complex

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

This species takes part in ten reactions (as a reactant in reaction_26, reaction_10 and as a product in reaction_25 and as a modifier in reaction_17, reaction_17, reaction_17, reaction_10, reaction_10, reaction_10).

$$\frac{d}{dt} \text{species}_{-18} = |v_{18}| - |v_{19}| - |v_{39}| \tag{148}$$

9.19 Species species_19

Name 2(Tf-Fe)-TfR2

SBO:0000297 protein complex

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

This species takes part in ten reactions (as a reactant in reaction_36, reaction_7 and as a product in reaction_35 and as a modifier in reaction_17, reaction_17, reaction_17, reaction_36, reaction_36, reaction_7, reaction_7).

$$\frac{d}{dt} \text{species}_{19} = |v_{26}| - |v_{27}| - |v_{29}| \tag{149}$$

9.20 Species species_10

Name TfR2

SBO:0000252 polypeptide chain

Initial concentration $3 \cdot 10^{-6} \text{ mol} \cdot l^{-1}$

This species takes part in 13 reactions (as a reactant in reaction_15, reaction_25, reaction_27 and as a product in reaction_14, reaction_26, reaction_28, reaction_7 and as a modifier in reaction_15, reaction_15, reaction_25, reaction_25, reaction_27, reaction_27).

$$\frac{d}{dt} \text{species}_{10} = |v_{10}| + |v_{19}| + |v_{21}| + |v_{29}| - |v_{11}| - |v_{18}| - |v_{20}|$$
(150)

9.21 Species species_11

Name Heme_intercell

SBO:0000247 simple chemical

Initial concentration $10^{-7} \text{ mol} \cdot l^{-1}$

This species takes part in four reactions (as a reactant in reaction_16 and as a product in reaction_19 and as a modifier in reaction_16, reaction_16), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species}_{-}11 = 0 \tag{151}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000247 simple chemical: Simple, non-repetitive chemical entity

SBO:0000252 polypeptide chain: Naturally occurring macromolecule formed by the repetition of amino-acid residues linked by peptidic bonds. A polypeptide chain is synthesized by the ribosome. CHEBI:1654

SBO:0000290 physical compartment: Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions

SBO:0000296 macromolecular complex: Non-covalent complex of one or more macromolecules and zero or more simple chemicals

SBO:0000297 protein complex: Macromolecular complex containing one or more polypeptide chains possibly associated with simple chemicals. CHEBI:3608

SBO:0000327 non-macromolecular ion: Chemical entity having a net electric charge

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