SBML Model Report

Model name: “McAuley2012 - Whole-body Cholesterol Metabolism”

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah[1] and Mark Mc Auley[2] at November 27th 2012 at 4:32 p. m. and last time modified at October nineth 2014 at 3:44 p. m. Table 1 shows an overview of the quantities of all components of this model.

Table 1: Number of components in this model, which are described in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	6
species types	0	species	34
events	0	constraints	0
reactions	35	function definitions	23
global parameters	0	unit definitions	3
rules	0	initial assignments	0

Model Notes

McAuley2012 - Whole-body Cholesterol Metabolism

Lipid metabolism has a key role to play in human longevity and healthy aging. A whole-body mathematical model of cholesterol metabolism that explores the changes in both the rate of intestinal cholesterol absorption and the hepatic rate of clearance of LDL-C from the plasma,

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has been presented here. The model showed that of these two mechanisms, changes to the rate of LDL-C removal from the plasma with age had the most significant effect on cholesterol metabolism.

The original SBML model file was generated using MathSBML 2.5.1.

This model is described in the article:A whole-body mathematical model of cholesterol metabolism and its age-associated dysregulation.Mc Auley MM, Wilkinson DJ, Jones JJ, Kirkwood TT.BMC Syst Biol. 2012 Oct 10;6(1):130.

Abstract:

BACKGROUND: Global demographic changes have stimulated marked interest in the process of ageing. There has been, and will continue to be, an unrelenting rise in the number of the oldest old (>85 years of age). Together with an ageing population there comes an increase in the prevalence of age related disease. Of the diseases of ageing, cardiovascular disease (CVD) has by far the highest prevalence. It is regarded that a finely tuned lipid profile may help to prevent CVD as there is a long established relationship between alterations to lipid metabolism and CVD risk. In fact elevated plasma cholesterol, particularly Low Density Lipoprotein Cholesterol (LDL-C) has consistently stood out as a risk factor for having a cardiovascular event. Moreover it is widely acknowledged that LDL-C may rise with age in both sexes in a wide variety of groups. The aim of this work was to use a whole-body mathematical model to investigate why LDL-C rises with age, and to test the hypothesis that mechanistic changes to cholesterol absorption and LDL-C removal from the plasma are responsible for the rise. The whole-body mechanistic nature of the model differs from previous models of cholesterol metabolism which have either focused on intracellular cholesterol homeostasis or have concentrated on an isolated area of lipoprotein dynamics. The model integrates both current and previously published data relating to molecular biology, physiology, ageing and nutrition in an integrated fashion.

RESULTS: The model was used to test the hypothesis that alterations to the rate of cholesterol absorption and changes to the rate of removal of LDL-C from the plasma are integral to understanding why LDL-C rises with age. The model demonstrates that increasing the rate of intestinal cholesterol absorption from 50% to 80% by age 65 years can result in an increase of LDL-C by as much as 34mg/dL in a hypothetical male subject. The model also shows that decreasing the rate of hepatic clearance of LDL-C gradually to 50% by age 65 years can result in an increase of LDL-C by as much as 116mg/dL.

CONCLUSIONS: Our model clearly demonstrates that of the two putative mechanisms that have been implicated in the dysregulation of cholesterol metabolism with age, alterations to the removal rate of plasma LDL-C has the most significant impact on cholesterol metabolism and small changes to the number of hepatic LDL receptors can result in a significant rise in LDL-C. This first whole-body systems based model of cholesterol balance could potentially be used as a tool to further improve our understanding of whole-body cholesterol metabolism and its dysregulation with age. Furthermore, given further fine tuning the model may help to investigate potential dietary and lifestyle regimes that have the potential to mitigate the effects aging has on cholesterol metabolism.

This model is hosted on BioModels Database and identified by: MODEL1206010000 .

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

2 Unit Definitions

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

2.1 Unit `volume`

Name volume

Definition dimensionless

2.2 Unit `time`

Name time

Definition 86400 s

2.3 Unit `substance`

Name substance

Definition dimensionless

2.4 Unit `area`

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

Definition m^2

2.5 Unit `length`

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

Definition m

3 Compartments

This model contains six compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`Intake`	Intake		3	1	dimensionless	☑	
`Intestine`	Intestine		3	1	dimensionless	☑	
`HepaticTissue`	HepaticTissue		3	1	dimensionless	☑	
`PeripheralTissue`	PeripheralTissue		3	1	dimensionless	☑	
`Plasma`	Plasma		3	1	dimensionless	☑	
`Excreted`	Excreted		3	1	dimensionless	☑	

3.1 Compartment `Intake`

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

Name Intake

3.2 Compartment `Intestine`

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

Name Intestine

3.3 Compartment `HepaticTissue`

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

Name HepaticTissue

3.4 Compartment `PeripheralTissue`

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

Name PeripheralTissue

3.5 Compartment `Plasma`

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

Name Plasma

3.6 Compartment `Excreted`

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

Name Excreted

4 Species

This model contains 34 species. The boundary condition of eight of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 7 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
species_1	DC	Intake	dimensionless · dimensionless^{-1}	☑	☑
species_2	IC	Intestine	dimensionless · dimensionless^{-1}	☐	☐
species_3	ICS	Intestine	dimensionless · dimensionless^{-1}	☑	☑
species_4	HBS	HepaticTissue	dimensionless · dimensionless^{-1}	☐	☐
species_5	IBS	Intestine	dimensionless · dimensionless^{-1}	☐	☐
species_6	EBS	Excreted	dimensionless · dimensionless^{-1}	☐	☐
species_7	HFC	HepaticTissue	dimensionless · dimensionless^{-1}	☐	☐
species_8	EC	Excreted	dimensionless · dimensionless^{-1}	☐	☐
species_9	INHDLS	Plasma	dimensionless · dimensionless^{-1}	☑	☑
species_10	NHDL	Plasma	dimensionless · dimensionless^{-1}	☐	☐

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
species_11	PFC	PeripheralTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_12	HCS	HepaticTissue	dimensionless · dimensionless^{-1}	☑	☑
species_13	HCE	HepaticTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_14	ACAT	HepaticTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_15	CEH	HepaticTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_16	HNHDLS	HepaticTissue	dimensionless · dimensionless^{-1}	☑	☑
species_17	VLDLC	Plasma	dimensionless · dimensionless^{-1}	⊟	⊟
species_18	HLDLRs	HepaticTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_19	HLDLRsS	HepaticTissue	dimensionless · dimensionless^{-1}	☑	☑
species_20	HLDLRD	HepaticTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_21	IDLC	Plasma	dimensionless · dimensionless^{-1}	⊟	⊟
species_22	LPL	Plasma	dimensionless · dimensionless^{-1}	⊟	⊟
species_23	LDLC	Plasma	dimensionless · dimensionless^{-1}	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
species_24	HSL	Plasma	dimensionless · dimensionless^{-1}	⊟	⊟
species_25	PLDLRs	PeripheralTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_26	PLDLRsS	PeripheralTissue	dimensionless · dimensionless^{-1}	☑	☑
species_27	PLDLRD	PeripheralTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_28	PCE	PeripheralTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_29	PSS	PeripheralTissue	dimensionless · dimensionless^{-1}	⊟	⊟
species_30	HDLC	Plasma	dimensionless · dimensionless^{-1}	⊟	⊟
species_31	LCAT	Plasma	dimensionless · dimensionless^{-1}	⊟	⊟
species_32	PCS	PeripheralTissue	dimensionless · dimensionless^{-1}	☑	☑
species_33	CETP	Plasma	dimensionless · dimensionless^{-1}	⊟	⊟
species_34	SRB1	HepaticTissue	dimensionless · dimensionless^{-1}	⊟	⊟

5 Function definitions

This is an overview of 23 function definitions.

5.1 Function definition `function_1`

Name Rate Law for Intestinal Cholesterol Synthesis

Arguments ICSmax, IC, ICt, IS

Mathematical Expression

$$\frac{\mathrm{ICSmax}}{1 + \left(\frac{\mathrm{IC}}{\mathrm{ICt}}\right)^{\mathrm{IS}}} \tag{1}$$

5.2 Function definition `function_2`

Name Rate Law for Bile Salt Synthesis

Arguments k5, HFC, HBS

Mathematical Expression

$$\frac{\mathrm{k5} \cdot \mathrm{HFC}}{\mathrm{HBS}} \tag{2}$$

5.3 Function definition `function_3`

Name Rate Law for Cholesterol Absorption

Arguments k6, IC, IBS

Mathematical Expression

$$\mathrm{k6} \cdot \mathrm{IC} \cdot \mathrm{IBS} \tag{3}$$

5.4 Function definition `function_4`

Name Rate Law for Cholesterol Excretion

Arguments k7, IC, IBS

Mathematical Expression

$$\mathrm{k7} \cdot \mathrm{IC} \cdot \mathrm{IBS} \tag{4}$$

5.5 Function definition `function_5`

Name Rate Law for Intestinal Nascent HDL Synthesis

Arguments k8, PFC

Mathematical Expression

$$\mathrm{k8} \cdot \mathrm{PFC} \tag{5}$$

5.6 Function definition function_6

Name Rate Law for Billary Cholesterol Release

Arguments BCRmax, BCRt, HFC, BS

Mathematical Expression

$$\frac{\mathrm{BCRmax}}{1 + \left(\frac{\mathrm{BCRt}}{\mathrm{HFC}}\right)^{\mathrm{BS}}} \tag{6}$$

5.7 Function definition function_7

Name Rate Law for Hepatic Cholesterol Synthesis

Arguments HCSmax, HFC, HCSt, HS

Mathematical Expression

$$\frac{\mathrm{HCSmax}}{1 + \left(\frac{\mathrm{HFC}}{\mathrm{HCSt}}\right)^{\mathrm{HS}}} \tag{7}$$

5.8 Function definition function_8

Name Rate Law for Hepatic Cholesterol Storage_1

Arguments k9, ACAT, HFC

Mathematical Expression

$$\mathrm{k9} \cdot \mathrm{ACAT} \cdot \mathrm{HFC} \tag{8}$$

5.9 Function definition function_9

Name Rate Law for Release of Stored Cholesterol

Arguments k10, CEH, HCE

Mathematical Expression

$$\mathrm{k10} \cdot \mathrm{CEH} \cdot \mathrm{HCE} \tag{9}$$

5.10 Function definition function_10

Name Rate Law for Hepatic Nascent HDL Synthesis

Arguments k11, PFC

Mathematical Expression

$$\mathrm{k11} \cdot \mathrm{PFC} \tag{10}$$

5.11 Function definition function_11

Name Rate Law for Hepatic LDLR Synthesis

Arguments khrs, HLDLRsS, HFC

Mathematical Expression

$$\frac{\text{khrs} \cdot \text{HLDLRsS}}{\text{HFC}} \tag{11}$$

5.12 Function definition function_12

Name Rate Law for IDL Cholesterol Formation

Arguments k15, VLDLC, LPL

Mathematical Expression

$$\text{k15} \cdot \text{VLDLC} \cdot \text{LPL} \tag{12}$$

5.13 Function definition function_13

Name Rate Law for LDL Cholesterol Formation

Arguments k17, IDLC, HSL

Mathematical Expression

$$\text{k17} \cdot \text{IDLC} \cdot \text{HSL} \tag{13}$$

5.14 Function definition function_14

Name Rate Law for Receptor Dependent Hepatic Uptake

Arguments k18, LDLC, HLDLRs

Mathematical Expression

$$\text{k18} \cdot \text{LDLC} \cdot \text{HLDLRs} \tag{14}$$

5.15 Function definition function_15

Name Rate Law for Receptor Dependent Peripheral Uptake

Arguments k20, PLDLRs, LDLC

Mathematical Expression

$$\text{k20} \cdot \text{PLDLRs} \cdot \text{LDLC} \tag{15}$$

5.16 Function definition function_16

Name Rate Law for Peripheral LDLR Synthesis

Arguments kprs, PLDLRsS, PFC

Mathematical Expression

$$\frac{\text{kprs} \cdot \text{PLDLRsS}}{\text{PFC}} \tag{16}$$

5.17 Function definition function_17

Name Rate Law for Peripheral Cholesterol Storage

Arguments k23, ACAT, PFC

Mathematical Expression

$$\text{k23} \cdot \text{ACAT} \cdot \text{PFC} \tag{17}$$

5.18 Function definition function_18

Name Rate Law for Release of Stored Peripheral Cholesterol

Arguments k24, CEH, PCE

Mathematical Expression

$$\text{k24} \cdot \text{CEH} \cdot \text{PCE} \tag{18}$$

5.19 Function definition function_19

Name Rate Law for HDL Cholesterol Formation

Arguments k26, PFC, NHDL, LCAT

Mathematical Expression

$$\text{k26} \cdot \text{PFC} \cdot \text{NHDL} \cdot \text{LCAT} \tag{19}$$

5.20 Function definition function_20

Name Rate Law for Peripheral Cholesterol Synthesis

Arguments PCSmax, PFC, PPCt, PCSS

Mathematical Expression

$$\frac{\text{PCSmax}}{1 + \left(\frac{\text{PFC}}{\text{PPCt}}\right)^{\text{PCSS}}} \tag{20}$$

5.21 Function definition function_21

Name Rate Law for CETP Mediated Transfer To VLDL

Arguments k27, HDLC, CETP

Mathematical Expression

$$k27 \cdot HDLC \cdot CETP \tag{21}$$

5.22 Function definition function_22

Name Rate Law for CETP Mediated TransferTo LDL

Arguments k28, HDLC, CETP

Mathematical Expression

$$k28 \cdot HDLC \cdot CETP \tag{22}$$

5.23 Function definition function_23

Name Rate Law for Reverse Cholesterol Transport

Arguments k29, HDLC, SRB1

Mathematical Expression

$$k29 \cdot HDLC \cdot SRB1 \tag{23}$$

6 Reactions

This model contains 35 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 4: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	reaction_1	Ingestion	$\text{species\_1} \xrightarrow{\text{species\_1}} \text{species\_2}$	
2	reaction_2	Intestinal Cholesterol Synthesis	$\text{species\_3} \xrightarrow{\text{species\_2, species\_2}} \text{species\_2}$	
3	reaction_3	Bile Salt Release	$\text{species\_4} \xrightarrow{\text{species\_4}} \text{species\_5}$	
4	reaction_4	Bile Salt Return	$\text{species\_5} \xrightarrow{\text{species\_5}} \text{species\_4}$	
5	reaction_5	Bile Salt Excretion	$\text{species\_5} \xrightarrow{\text{species\_5}} \text{species\_6}$	
6	reaction_6	Bile Salt Synthesis	$\text{species\_7} \xrightarrow{\text{species\_4, species\_7, species\_4}} \text{species\_4}$	
7	reaction_7	Cholesterol Absorption	$\text{species\_2} \xrightarrow{\text{species\_5, species\_2, species\_5}} \text{species\_7}$	
8	reaction_8	Cholesterol Excretion	$\text{species\_2} \xrightarrow{\text{species\_5, species\_2, species\_5}} \text{species\_8}$	
9	reaction_9	Intestinal Nascent HDL Synthesis	$\text{species\_9} \xrightarrow{\text{species\_11, species\_11}} \text{species\_10}$	
10	reaction_10	Billary Cholesterol Release	$\text{species\_7} \xrightarrow{\text{species\_7, species\_7}} \text{species\_2}$	
11	reaction_11	Hepatic Cholesterol Synthesis	$\text{species\_12} \xrightarrow{\text{species\_7, species\_7}} \text{species\_7}$	
12	reaction_12	Hepatic Cholesterol Storage	$\text{species\_7} \xrightarrow{\text{species\_14, species\_7, species\_14, species\_7}} \text{species\_13}$	
13	reaction_13	Release of Stored Cholesterol	$\text{species\_13} \xrightarrow{\text{species\_15, species\_13, species\_15, species\_13}} \text{species\_7}$	
14	reaction_14	Hepatic Nascent HDL Synthesis	$\text{species\_16} \xrightarrow{\text{species\_11, species\_11}} \text{species\_10}$	
15	reaction_15	VLDL Cholesterol Formation	$\text{species\_7} \xrightarrow{\text{species\_7}} \text{species\_17}$	

№	Id	Name	Reaction Equation	SBO
16	reaction_16	Hepatic LDLR Synthesis	species_19 $\xrightarrow{\text{species\_19, species\_7, species\_19, species\_7}}$ species_18	
17	reaction_17	Hepatic LDL Receptor Degradation	species_18 $\xrightarrow{\text{species\_18}}$ species_20	
18	reaction_18	VLDL Cholesterol ReUptake	species_17 $\xrightarrow{\text{species\_17}}$ species_7	
19	reaction_19	IDL Cholesterol Formation	species_17 $\xrightarrow{\text{species\_17, species\_22, species\_17, species\_22}}$ species_21	
20	reaction_20	IDL Cholesterol ReUptake	species_21 $\xrightarrow{\text{species\_21}}$ species_7	
21	reaction_21	LDL Cholesterol Formation	species_21 $\xrightarrow{\text{species\_24, species\_21, species\_24}}$ species_23	
22	reaction_22	Receptor Dependent Hepatic Uptake	species_23 $\xrightarrow{\text{species\_18, species\_23, species\_18}}$ species_7	
23	reaction_23	Receptor Independent Hepatic Uptake	species_23 $\xrightarrow{\text{species\_23}}$ species_7	
24	reaction_24	Receptor Dependent Peripheral Uptake	species_23 $\xrightarrow{\text{species\_25, species\_25, species\_23}}$ species_11	
25	reaction_25	Receptor Independent Peripheral Uptake	species_23 $\xrightarrow{\text{species\_23}}$ species_11	
26	reaction_26	Peripheral LDLR Synthesis	species_26 $\xrightarrow{\text{species\_11, species\_26, species\_11}}$ species_25	
27	reaction_27	Peripheral LDL Receptor Degradation	species_25 $\xrightarrow{\text{species\_25}}$ species_27	
28	reaction_28	Peripheral Cholesterol Storage	species_11 $\xrightarrow{\text{species\_14, species\_14, species\_11}}$ species_28	
29	reaction_29	Release of Stored Peripheral Cholesterol	species_28 $\xrightarrow{\text{species\_15, species\_15, species\_28}}$ species_11	
30	reaction_30	Peripheral Steroid Production	species_11 $\xrightarrow{\text{species\_11}}$ species_29	
31	reaction_31	HDL Cholesterol Formation	species_11 + species_10 $\xrightarrow{\text{species\_31, species\_11, species\_10, species\_31}}$ species_30	
32	reaction_32	Peripheral Cholesterol Synthesis	species_32 $\xrightarrow{\text{species\_11}}$ species_11	
33	reaction_33	CETP Mediated Transfer To VLDL	species_30 $\xrightarrow{\text{species\_33, species\_30, species\_33}}$ species_17	
34	reaction_34	CETP Mediated TransferTo LDL	species_30 $\xrightarrow{\text{species\_33, species\_30, species\_33}}$ species_23	

№	Id	Name	Reaction Equation	SBO
35	`reaction_35`	Reverse Cholesterol Transport	species_30 $\xrightarrow{\text{species\_34, species\_30, species\_34}}$ species_7	

6.1 Reaction reaction_1

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

Name Ingestion

Reaction equation

$$\text{species\_1} \xrightarrow{\text{species\_1}} \text{species\_2} \tag{24}$$

Reactant

Table 5: Properties of each reactant.

Id	Name	SBO
species_1	DC	

Modifier

Table 6: Properties of each modifier.

Id	Name	SBO
species_1	DC	

Product

Table 7: Properties of each product.

Id	Name	SBO
species_2	IC	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{k1} \cdot [\text{species\_1}] \tag{25}$$

Table 8: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.0		☑

6.2 Reaction reaction_2

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

Name Intestinal Cholesterol Synthesis

Reaction equation

$$\text{species\_3} \xrightarrow{\text{species\_2, species\_2}} \text{species\_2} \tag{26}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
species_3	ICS	

Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
species_2	IC	
species_2	IC	

Product

Table 11: Properties of each product.

Id	Name	SBO
species_2	IC	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{function\_1}\left(\text{ICSmax}, [\text{species\_2}], \text{ICt}, \text{IS}\right) \tag{27}$$

$$\text{function\_1}\left(\text{ICSmax}, \text{IC}, \text{ICt}, \text{IS}\right) = \frac{\text{ICSmax}}{1 + \left(\frac{\text{IC}}{\text{ICt}}\right)^{\text{IS}}} \tag{28}$$

Table 12: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
ICSmax	ICSmax		100.0		☑
ICt	ICt		3120.0		☑
IS	IS		5.0		☑

6.3 Reaction reaction_3

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

Name Bile Salt Release

Reaction equation

$$\text{species\_4} \xrightarrow{\text{species\_4}} \text{species\_5} \tag{29}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
species_4	HBS	

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
species_4	HBS	

Product

Table 15: Properties of each product.

Id	Name	SBO
species_5	IBS	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{k1} \cdot [\mathrm{species\_4}] \tag{30}$$

Table 16: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		6.0		☑

6.4 Reaction reaction_4

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

Name Bile Salt Return

Reaction equation

$$\mathrm{species\_5} \xrightarrow{\mathrm{species\_5}} \mathrm{species\_4} \tag{31}$$

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
species_5	IBS	

Modifier

Table 18: Properties of each modifier.

Id	Name	SBO
species_5	IBS	

Product

Table 19: Properties of each product.

Id	Name	SBO
species_4	HBS	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{k1} \cdot [\mathrm{species\_5}] \tag{32}$$

Table 20: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		4.29		☑

6.5 Reaction reaction_5

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

Name Bile Salt Excretion

Reaction equation

$$\mathrm{species\_5} \xrightarrow{\mathrm{species\_5}} \mathrm{species\_6} \tag{33}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
species_5	IBS	

Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
species_5	IBS	

Product

Table 23: Properties of each product.

Id	Name	SBO
species_6	EBS	

Id	Name	SBO

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{k1} \cdot [\mathrm{species\_5}] \tag{34}$$

Table 24: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.856		☑

6.6 Reaction reaction_6

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

Name Bile Salt Synthesis

Reaction equation

$$\mathrm{species\_7} \xrightarrow{\mathrm{species\_4,\ species\_7,\ species\_4}} \mathrm{species\_4} \tag{35}$$

Reactant

Table 25: Properties of each reactant.

Id	Name	SBO
species_7	HFC	

Modifiers

Table 26: Properties of each modifier.

Id	Name	SBO
species_4	HBS	
species_7	HFC	
species_4	HBS	

Product

Table 27: Properties of each product.

Id	Name	SBO
species_4	HBS	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{function\_2}\,(\text{k5}, [\text{species\_7}], [\text{species\_4}]) \tag{36}$$

$$\text{function\_2}\,(\text{k5}, \text{HFC}, \text{HBS}) = \frac{\text{k5} \cdot \text{HFC}}{\text{HBS}} \tag{37}$$

Table 28: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k5	k5		2.66		☑

6.7 Reaction reaction_7

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

Name Cholesterol Absorption

Reaction equation

$$\text{species\_2} \xrightarrow{\text{species\_5, species\_2, species\_5}} \text{species\_7} \tag{38}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
species_2	IC	

Modifiers

Table 30: Properties of each modifier.

Id	Name	SBO
species_5	IBS	
species_2	IC	
species_5	IBS	

Product

Table 31: Properties of each product.

Id	Name	SBO
species_7	HFC	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{function\_3}\,(\text{k6}, [\text{species\_2}], [\text{species\_5}]) \tag{39}$$

$$\text{function\_3}\,(\text{k6}, \text{IC}, \text{IBS}) = \text{k6} \cdot \text{IC} \cdot \text{IBS} \tag{40}$$

Table 32: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k6	k6		$5.286 \cdot 10^{-4}$		☑

6.8 Reaction reaction_8

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

Name Cholesterol Excretion

Reaction equation

$$\text{species\_2} \xrightarrow{\text{species\_5, species\_2, species\_5}} \text{species\_8} \tag{41}$$

Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
species_2	IC	

Modifiers

Table 34: Properties of each modifier.

Id	Name	SBO
species_5	IBS	
species_2	IC	
species_5	IBS	

Product

Table 35: Properties of each product.

Id	Name	SBO
species_8	EC	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{function\_4}\,(\text{k7}, [\text{species\_2}], [\text{species\_5}]) \tag{42}$$

$$\text{function\_4}\,(\text{k7}, \text{IC}, \text{IBS}) = \text{k7} \cdot \text{IC} \cdot \text{IBS} \tag{43}$$

Table 36: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k7	k7		$5.286 \cdot 10^{-4}$		☑

6.9 Reaction reaction_9

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

Name Intestinal Nascent HDL Synthesis

Reaction equation

$$\text{species\_9} \xrightarrow{\text{species\_11, species\_11}} \text{species\_10} \tag{44}$$

Reactant

Table 37: Properties of each reactant.

Id	Name	SBO
species_9	INHDLS	

Modifiers

Table 38: Properties of each modifier.

Id	Name	SBO
species_11	PFC	
species_11	PFC	

Product

Table 39: Properties of each product.

Id	Name	SBO
species_10	NHDL	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{function\_5}\,(\text{k8}, [\text{species\_11}]) \tag{45}$$

$$\text{function\_5}\,(\text{k8}, \text{PFC}) = \text{k8} \cdot \text{PFC} \tag{46}$$

Table 40: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k8	k8		$5 \cdot 10^{-4}$		☑

6.10 Reaction reaction_10

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

Name Billary Cholesterol Release

Reaction equation

$$\text{species\_7} \xrightarrow{\text{species\_7, species\_7}} \text{species\_2} \tag{47}$$

Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
species_7	HFC	

Modifiers

Table 42: Properties of each modifier.

Id	Name	SBO
species_7	HFC	
species_7	HFC	

Product

Table 43: Properties of each product.

Id	Name	SBO
species_2	IC	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{function\_6}(\text{BCRmax}, \text{BCRt}, [\text{species\_7}], \text{BS}) \tag{48}$$

$$\text{function\_6}(\text{BCRmax}, \text{BCRt}, \text{HFC}, \text{BS}) = \frac{\text{BCRmax}}{1 + \left(\frac{\text{BCRt}}{\text{HFC}}\right)^{\text{BS}}} \tag{49}$$

Table 44: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
BCRmax	BCRmax		2000.0		☑
BCRt	BCRt		55326.0		☑
BS	BS		5.0		☑

6.11 Reaction reaction_11

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

Name Hepatic Cholesterol Synthesis

Reaction equation

$$\text{species\_12} \xrightarrow{\text{species\_7, species\_7}} \text{species\_7} \tag{50}$$

Reactant

Table 45: Properties of each reactant.

Id	Name	SBO
species_12	HCS	

Modifiers

Table 46: Properties of each modifier.

Id	Name	SBO
species_7	HFC	
species_7	HFC	

Product

Table 47: Properties of each product.

Id	Name	SBO
species_7	HFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{function\_7}\,(\text{HCSmax}, [\text{species\_7}], \text{HCSt}, \text{HS}) \tag{51}$$

$$\text{function\_7}\,(\text{HCSmax}, \text{HFC}, \text{HCSt}, \text{HS}) = \frac{\text{HCSmax}}{1 + \left(\frac{\text{HFC}}{\text{HCSt}}\right)^{\text{HS}}} \tag{52}$$

Table 48: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
HCSmax	HCSmax		500.0		☑
HCSt	HCSt		93925.0		☑
HS	HS		5.0		☑

6.12 Reaction reaction_12

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

Name Hepatic Cholesterol Storage

Reaction equation

$$\text{species\_7} \xrightarrow{\text{species\_14, species\_7, species\_14, species\_7}} \text{species\_13} \tag{53}$$

Reactant

Table 49: Properties of each reactant.

Id	Name	SBO
species_7	HFC	

Modifiers

Table 50: Properties of each modifier.

Id	Name	SBO
species_14	ACAT	
species_7	HFC	

Id	Name	SBO
species_14	ACAT	
species_7	HFC	

Product

Table 51: Properties of each product.

Id	Name	SBO
species_13	HCE	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{function\_8}\,(\text{k9}, [\text{species\_14}], [\text{species\_7}]) \tag{54}$$

$$\text{function\_8}\,(\text{k9}, \text{ACAT}, \text{HFC}) = \text{k9} \cdot \text{ACAT} \cdot \text{HFC} \tag{55}$$

Table 52: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k9	k9		1.0		☑

6.13 Reaction reaction_13

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

Name Release of Stored Cholesterol

Reaction equation

$$\text{species\_13} \xrightarrow{\text{species\_15, species\_13, species\_15, species\_13}} \text{species\_7} \tag{56}$$

Reactant

Table 53: Properties of each reactant.

Id	Name	SBO
species_13	HCE	

Modifiers

Table 54: Properties of each modifier.

Id	Name	SBO
species_15	CEH	
species_13	HCE	
species_15	CEH	
species_13	HCE	

Product

Table 55: Properties of each product.

Id	Name	SBO
species_7	HFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{function\_9}\,(\text{k10}, [\text{species\_15}], [\text{species\_13}]) \tag{57}$$

$$\text{function\_9}\,(\text{k10}, \text{CEH}, \text{HCE}) = \text{k10} \cdot \text{CEH} \cdot \text{HCE} \tag{58}$$

Table 56: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k10	k10		5.998		☑

6.14 Reaction reaction_14

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

Name Hepatic Nascent HDL Synthesis

Reaction equation

$$\text{species\_16} \xrightarrow{\text{species\_11, species\_11}} \text{species\_10} \tag{59}$$

Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
species_16	HNHDLS	

Modifiers

Table 58: Properties of each modifier.

Id	Name	SBO
species_11	PFC	
species_11	PFC	

Product

Table 59: Properties of each product.

Id	Name	SBO
species_10	NHDL	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \text{function\_10}\,(\text{k11}, [\text{species\_11}]) \tag{60}$$

$$\text{function\_10}\,(\text{k11}, \text{PFC}) = \text{k11} \cdot \text{PFC} \tag{61}$$

Table 60: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k11	k11		0.005		☑

6.15 Reaction reaction_15

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

Name VLDL Cholesterol Formation

Reaction equation

$$\text{species\_7} \xrightarrow{\text{species\_7}} \text{species\_17} \tag{62}$$

Reactant

Table 61: Properties of each reactant.

Id	Name	SBO
species_7	HFC	

Modifier

Table 62: Properties of each modifier.

Id	Name	SBO
species_7	HFC	

Product

Table 63: Properties of each product.

Id	Name	SBO
species_17	VLDLC	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \text{k1} \cdot [\text{species\_7}] \tag{63}$$

Table 64: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.016		☑

6.16 Reaction reaction_16

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

Name Hepatic LDLR Synthesis

Reaction equation

$$\text{species\_19} \xrightarrow{\text{species\_19, species\_7, species\_19, species\_7}} \text{species\_18} \tag{64}$$

Reactant

Table 65: Properties of each reactant.

Id	Name	SBO
species_19	HLDLRsS	

Modifiers

Table 66: Properties of each modifier.

Id	Name	SBO
species_19	HLDLRsS	
species_7	HFC	
species_19	HLDLRsS	
species_7	HFC	

Product

Table 67: Properties of each product.

Id	Name	SBO
species_18	HLDLRs	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \text{function\_11}\left(\text{khrs}, [\text{species\_19}], [\text{species\_7}]\right) \tag{65}$$

$$\text{function\_11}\left(\text{khrs}, \text{HLDLRsS}, \text{HFC}\right) = \frac{\text{khrs} \cdot \text{HLDLRsS}}{\text{HFC}} \tag{66}$$

Table 68: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
khrs	khrs		100.0		☑

6.17 Reaction reaction_17

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

Name Hepatic LDL Receptor Degradation

Reaction equation

$$\text{species\_18} \xrightarrow{\text{species\_18}} \text{species\_20} \tag{67}$$

Reactant

Table 69: Properties of each reactant.

Id	Name	SBO
species_18	HLDLRs	

Modifier

Table 70: Properties of each modifier.

Id	Name	SBO
species_18	HLDLRs	

Product

Table 71: Properties of each product.

Id	Name	SBO
species_20	HLDLRD	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \text{k1} \cdot [\text{species\_18}] \tag{68}$$

Table 72: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.01		☑

6.18 Reaction reaction_18

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

Name VLDL Cholesterol ReUptake

Reaction equation

$$\text{species\_17} \xrightarrow{\text{species\_17}} \text{species\_7} \tag{69}$$

Reactant

Table 73: Properties of each reactant.

Id	Name	SBO
species_17	VLDLC	

Modifier

Table 74: Properties of each modifier.

Id	Name	SBO
species_17	VLDLC	

Product

Table 75: Properties of each product.

Id	Name	SBO
species_7	HFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \text{k1} \cdot [\text{species\_17}] \tag{70}$$

Table 76: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.050		☑

6.19 Reaction reaction_19

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

Name IDL Cholesterol Formation

Reaction equation

$$\text{species\_17} \xrightarrow{\text{species\_17, species\_22, species\_17, species\_22}} \text{species\_21} \tag{71}$$

Reactant

Table 77: Properties of each reactant.

Id	Name	SBO
species_17	VLDLC	

Modifiers

Table 78: Properties of each modifier.

Id	Name	SBO
species_17	VLDLC	
species_22	LPL	
species_17	VLDLC	
species_22	LPL	

Product

Table 79: Properties of each product.

Id	Name	SBO
species_21	IDLC	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{function\_12}\,(\text{k15}, [\text{species\_17}], [\text{species\_22}]) \tag{72}$$

$$\text{function\_12}\,(\text{k15}, \text{VLDLC}, \text{LPL}) = \text{k15} \cdot \text{VLDLC} \cdot \text{LPL} \tag{73}$$

Table 80: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k15	k15		0.43		☑

6.20 Reaction reaction_20

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

Name IDL Cholesterol ReUptake

Reaction equation

$$\text{species\_21} \xrightarrow{\text{species\_21}} \text{species\_7} \tag{74}$$

Reactant

Table 81: Properties of each reactant.

Id	Name	SBO
species_21	IDLC	

Modifier

Table 82: Properties of each modifier.

Id	Name	SBO
species_21	IDLC	

Product

Table 83: Properties of each product.

Id	Name	SBO
species_7	HFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \mathrm{k1} \cdot [\mathrm{species\_21}] \tag{75}$$

Table 84: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.054		☑

6.21 Reaction reaction_21

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

Name LDL Cholesterol Formation

Reaction equation

$$\mathrm{species\_21} \xrightarrow{\mathrm{species\_24,\ species\_21,\ species\_24}} \mathrm{species\_23} \tag{76}$$

Reactant

Table 85: Properties of each reactant.

Id	Name	SBO
species_21	IDLC	

Modifiers

Table 86: Properties of each modifier.

Id	Name	SBO
species_24	HSL	
species_21	IDLC	
species_24	HSL	

Id	Name	SBO

Product

Table 87: Properties of each product.

Id	Name	SBO
species_23	LDLC	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \text{function\_13}\,(\text{k17}, [\text{species\_21}], [\text{species\_24}]) \tag{77}$$

$$\text{function\_13}\,(\text{k17}, \text{IDLC}, \text{HSL}) = \text{k17} \cdot \text{IDLC} \cdot \text{HSL} \tag{78}$$

Table 88: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k17	k17		0.38		☑

6.22 Reaction reaction_22

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

Name Receptor Dependent Hepatic Uptake

Reaction equation

$$\text{species\_23} \xrightarrow{\text{species\_18, species\_23, species\_18}} \text{species\_7} \tag{79}$$

Reactant

Table 89: Properties of each reactant.

Id	Name	SBO
species_23	LDLC	

Modifiers

Table 90: Properties of each modifier.

Id	Name	SBO
species_18	HLDLRs	
species_23	LDLC	
species_18	HLDLRs	

Product

Table 91: Properties of each product.

Id	Name	SBO
species_7	HFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \text{function\_14}\,(\text{k18}, [\text{species\_23}], [\text{species\_18}]) \tag{80}$$

$$\text{function\_14}\,(\text{k18}, \text{LDLC}, \text{HLDLRs}) = \text{k18} \cdot \text{LDLC} \cdot \text{HLDLRs} \tag{81}$$

Table 92: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k18	k18		0.068		☑

6.23 Reaction reaction_23

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

Name Receptor Independent Hepatic Uptake

Reaction equation

$$\text{species\_23} \xrightarrow{\text{species\_23}} \text{species\_7} \tag{82}$$

Reactant

Table 93: Properties of each reactant.

Id	Name	SBO
species_23	LDLC	

Modifier

Table 94: Properties of each modifier.

Id	Name	SBO
species_23	LDLC	

Product

Table 95: Properties of each product.

Id	Name	SBO
species_7	HFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = \mathrm{k1} \cdot [\mathrm{species\_23}] \tag{83}$$

Table 96: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.005		☑

6.24 Reaction reaction_24

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

Name Receptor Dependent Peripheral Uptake

Reaction equation

$$\mathrm{species\_23} \xrightarrow{\mathrm{species\_25,\ species\_25,\ species\_23}} \mathrm{species\_11} \tag{84}$$

Reactant

Table 97: Properties of each reactant.

Id	Name	SBO
species_23	LDLC	

Modifiers

Table 98: Properties of each modifier.

Id	Name	SBO
species_25	PLDLRs	
species_25	PLDLRs	
species_23	LDLC	

Product

Table 99: Properties of each product.

Id	Name	SBO
species_11	PFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \text{function\_15}\,(\text{k20}, [\text{species\_25}], [\text{species\_23}]) \tag{85}$$

$$\text{function\_15}\,(\text{k20}, \text{PLDLRs}, \text{LDLC}) = \text{k20} \cdot \text{PLDLRs} \cdot \text{LDLC} \tag{86}$$

Table 100: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k20	k20		0.007		☑

6.25 Reaction reaction_25

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

Name Receptor Independent Peripheral Uptake

Reaction equation

$$\text{species\_23} \xrightarrow{\text{species\_23}} \text{species\_11} \tag{87}$$

Reactant

Table 101: Properties of each reactant.

Id	Name	SBO
species_23	LDLC	

Modifier

Table 102: Properties of each modifier.

Id	Name	SBO
species_23	LDLC	

Product

Table 103: Properties of each product.

Id	Name	SBO
species_11	PFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \text{k1} \cdot [\text{species\_23}] \tag{88}$$

Table 104: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$5 \cdot 10^{-6}$		☑

6.26 Reaction reaction_26

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

Name Peripheral LDLR Synthesis

Reaction equation

$$\text{species\_26} \xrightarrow{\text{species\_11, species\_26, species\_11}} \text{species\_25} \tag{89}$$

Reactant

Table 105: Properties of each reactant.

Id	Name	SBO
species_26	PLDLRsS	

Modifiers

Table 106: Properties of each modifier.

Id	Name	SBO
species_11	PFC	
species_26	PLDLRsS	
species_11	PFC	

Product

Table 107: Properties of each product.

Id	Name	SBO
species_25	PLDLRs	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \text{function\_16}\left(\text{kprs}, [\text{species\_26}], [\text{species\_11}]\right) \tag{90}$$

$$\text{function\_16}\left(\text{kprs}, \text{PLDLRsS}, \text{PFC}\right) = \frac{\text{kprs} \cdot \text{PLDLRsS}}{\text{PFC}} \tag{91}$$

Table 108: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kprs	kprs		100.0		☑

6.27 Reaction reaction_27

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

Name Peripheral LDL Receptor Degradation

Reaction equation

$$\text{species\_25} \xrightarrow{\text{species\_25}} \text{species\_27} \tag{92}$$

Reactant

Table 109: Properties of each reactant.

Id	Name	SBO
species_25	PLDLRs	

Modifier

Table 110: Properties of each modifier.

Id	Name	SBO
species_25	PLDLRs	

Product

Table 111: Properties of each product.

Id	Name	SBO
species_27	PLDLRD	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \text{k1} \cdot [\text{species\_25}] \tag{93}$$

Table 112: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.01		☑

6.28 Reaction reaction_28

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

Name Peripheral Cholesterol Storage

Reaction equation

$$\text{species\_11} \xrightarrow{\text{species\_14, species\_14, species\_11}} \text{species\_28} \tag{94}$$

Reactant

Table 113: Properties of each reactant.

Id	Name	SBO
species_11	PFC	

Modifiers

Table 114: Properties of each modifier.

Id	Name	SBO
species_14	ACAT	
species_14	ACAT	
species_11	PFC	

Product

Table 115: Properties of each product.

Id	Name	SBO
species_28	PCE	

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \text{function\_17}\,(\text{k23}, [\text{species\_14}], [\text{species\_11}]) \tag{95}$$

$$\text{function\_17}\,(\text{k23}, \text{ACAT}, \text{PFC}) = \text{k23} \cdot \text{ACAT} \cdot \text{PFC} \tag{96}$$

Table 116: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k23	k23		0.017		☑

6.29 Reaction reaction_29

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

Name Release of Stored Peripheral Cholesterol

Reaction equation

$$\text{species\_28} \xrightarrow{\text{species\_15, species\_15, species\_28}} \text{species\_11} \tag{97}$$

Reactant

Table 117: Properties of each reactant.

Id	Name	SBO
species_28	PCE	

Modifiers

Table 118: Properties of each modifier.

Id	Name	SBO
species_15	CEH	
species_15	CEH	
species_28	PCE	

Product

Table 119: Properties of each product.

Id	Name	SBO
species_11	PFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{29} = \text{function\_18}\,(\text{k24}, [\text{species\_15}], [\text{species\_28}]) \tag{98}$$

$$\text{function\_18}\,(\text{k24}, \text{CEH}, \text{PCE}) = \text{k24} \cdot \text{CEH} \cdot \text{PCE} \tag{99}$$

Table 120: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k24	k24		0.107		☑

6.30 Reaction reaction_30

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

Name Peripheral Steroid Production

Reaction equation

$$\text{species\_11} \xrightarrow{\text{species\_11}} \text{species\_29} \tag{100}$$

Reactant

Table 121: Properties of each reactant.

Id	Name	SBO
species_11	PFC	

Modifier

Table 122: Properties of each modifier.

Id	Name	SBO
species_11	PFC	

Product

Table 123: Properties of each product.

Id	Name	SBO
species_29	PSS	

Kinetic Law

Derived unit contains undeclared units

$$v_{30} = \mathrm{k1} \cdot [\mathrm{species\_11}] \tag{101}$$

Table 124: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$5 \cdot 10^{-4}$		☑

6.31 Reaction reaction_31

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

Name HDL Cholesterol Formation

Reaction equation

$$\mathrm{species\_11} + \mathrm{species\_10} \xrightarrow{\mathrm{species\_31,\ species\_11,\ species\_10,\ species\_31}} \mathrm{species\_30} \tag{102}$$

Reactants

Table 125: Properties of each reactant.

Id	Name	SBO
species_11	PFC	
species_10	NHDL	

Modifiers

Table 126: Properties of each modifier.

Id	Name	SBO
species_31	LCAT	
species_11	PFC	
species_10	NHDL	
species_31	LCAT	

Product

Table 127: Properties of each product.

Id	Name	SBO
species_30	HDLC	

Kinetic Law

Derived unit contains undeclared units

$$v_{31} = \text{function\_19}\,(\text{k26}, [\text{species\_11}], [\text{species\_10}], [\text{species\_31}]) \tag{103}$$

$$\text{function\_19}\,(\text{k26}, \text{PFC}, \text{NHDL}, \text{LCAT}) = \text{k26} \cdot \text{PFC} \cdot \text{NHDL} \cdot \text{LCAT} \tag{104}$$

Table 128: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k26	k26		$1.5 \cdot 10^{-5}$		☑

6.32 Reaction reaction_32

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

Name Peripheral Cholesterol Synthesis

Reaction equation

$$\text{species\_32} \xrightarrow{\text{species\_11}} \text{species\_11} \tag{105}$$

Reactant

Table 129: Properties of each reactant.

Id	Name	SBO
species_32	PCS	

Modifier

Table 130: Properties of each modifier.

Id	Name	SBO
species_11	PFC	

Product

Table 131: Properties of each product.

Id	Name	SBO
species_11	PFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{32} = \text{function\_20}\left(\text{PCSmax}, [\text{species\_11}], \text{PPCt}, \text{PCSS}\right) \tag{106}$$

$$\text{function\_20}\left(\text{PCSmax}, \text{PFC}, \text{PPCt}, \text{PCSS}\right) = \frac{\text{PCSmax}}{1 + \left(\frac{\text{PFC}}{\text{PPCt}}\right)^{\text{PCSS}}} \tag{107}$$

Table 132: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
PCSmax	PCSmax		500.0		☑
PPCt	PPCt		80342.0		☑
PCSS	PCSS		5.0		☑

6.33 Reaction reaction_33

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

Name CETP Mediated Transfer To VLDL

Reaction equation

$$\text{species\_30} \xrightarrow{\text{species\_33, species\_30, species\_33}} \text{species\_17} \tag{108}$$

Reactant

Table 133: Properties of each reactant.

Id	Name	SBO
species_30	HDLC	

Modifiers

Table 134: Properties of each modifier.

Id	Name	SBO
species_33	CETP	
species_30	HDLC	
species_33	CETP	

Product

Table 135: Properties of each product.

Id	Name	SBO
species_17	VLDLC	

Kinetic Law

Derived unit contains undeclared units

$$v_{33} = \text{function\_21}\,(\text{k27}, [\text{species\_30}], [\text{species\_33}]) \tag{109}$$

$$\text{function\_21}\,(\text{k27}, \text{HDLC}, \text{CETP}) = \text{k27} \cdot \text{HDLC} \cdot \text{CETP} \tag{110}$$

Table 136: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k27	k27		0.01		☑

6.34 Reaction reaction_34

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

Name CETP Mediated TransferTo LDL

Reaction equation

$$\text{species\_30} \xrightarrow{\text{species\_33, species\_30, species\_33}} \text{species\_23} \tag{111}$$

Reactant

Table 137: Properties of each reactant.

Id	Name	SBO
species_30	HDLC	

Modifiers

Table 138: Properties of each modifier.

Id	Name	SBO
species_33	CETP	
species_30	HDLC	
species_33	CETP	

Product

Table 139: Properties of each product.

Id	Name	SBO
species_23	LDLC	

Kinetic Law

Derived unit contains undeclared units

$$v_{34} = \text{function\_22}\,(\text{k28}, [\text{species\_30}], [\text{species\_33}]) \tag{112}$$

$$\text{function\_22}\,(\text{k28}, \text{HDLC}, \text{CETP}) = \text{k28} \cdot \text{HDLC} \cdot \text{CETP} \tag{113}$$

Table 140: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k28	k28		0.001		☑

6.35 Reaction reaction_35

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

Name Reverse Cholesterol Transport

Reaction equation

$$\text{species\_30} \xrightarrow{\text{species\_34, species\_30, species\_34}} \text{species\_7} \tag{114}$$

Reactant

Table 141: Properties of each reactant.

Id	Name	SBO
species_30	HDLC	

Modifiers

Table 142: Properties of each modifier.

Id	Name	SBO
species_34	SRB1	
species_30	HDLC	
species_34	SRB1	

Product

Table 143: Properties of each product.

Id	Name	SBO
species_7	HFC	

Kinetic Law

Derived unit contains undeclared units

$$v_{35} = \text{function\_23}\,(\text{k29}, [\text{species\_30}], [\text{species\_34}]) \tag{115}$$

$$\text{function\_23}\,(\text{k29}, \text{HDLC}, \text{SRB1}) = \text{k29} \cdot \text{HDLC} \cdot \text{SRB1} \tag{116}$$

Table 144: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k29	k29		0.05		☑

7 Derived Rate Equations

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

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.

7.1 Species species_1

Name DC

Initial concentration 304 dimensionless $\cdot$ dimensionless^{-1}

This species takes part in two reactions (as a reactant in reaction_1 and as a modifier in reaction_1), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_1} = 0 \tag{117}$$

7.2 Species species_2

Name IC

Initial concentration 3150 dimensionless · dimensionless^{-1}

This species takes part in nine reactions (as a reactant in reaction_7, reaction_8 and as a product in reaction_1, reaction_2, reaction_10 and as a modifier in reaction_2, reaction_2, reaction_7, reaction_8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_2} = v_1 + v_2 + v_{10} - v_7 - v_8 \tag{118}$$

7.3 Species species_3

Name ICS

SBO:0000291 empty set

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a reactant in reaction_2), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_3} = 0 \tag{119}$$

7.4 Species species_4

Name HBS

Initial concentration 400 dimensionless · dimensionless^{-1}

This species takes part in six reactions (as a reactant in reaction_3 and as a product in reaction_4, reaction_6 and as a modifier in reaction_3, reaction_6, reaction_6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_4} = v_4 + v_6 - v_3 \tag{120}$$

7.5 Species species_5

Name IBS

Initial concentration 467 dimensionless · dimensionless^{-1}

This species takes part in nine reactions (as a reactant in reaction_4, reaction_5 and as a product in reaction_3 and as a modifier in reaction_4, reaction_5, reaction_7, reaction_7, reaction_8, reaction_8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_5} = v_3 - v_4 - v_5 \tag{121}$$

7.6 Species species_6

Name EBS

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a product in reaction_5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_6} = v_5 \tag{122}$$

7.7 Species species_7

Name HFC

Initial concentration 60000 dimensionless · dimensionless^{-1}

This species takes part in 22 reactions (as a reactant in reaction_6, reaction_10, reaction_12, reaction_15 and as a product in reaction_7, reaction_11, reaction_13, reaction_18, reaction_20, reaction_22, reaction_23, reaction_35 and as a modifier in reaction_6, reaction_10, reaction_10, reaction_11, reaction_11, reaction_12, reaction_12, reaction_15, reaction_16, reaction_16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_7} = v_7 + v_{11} + v_{13} + v_{18} + v_{20} + v_{22} + v_{23} + v_{35} - v_6 - v_{10} - v_{12} - v_{15} \tag{123}$$

7.8 Species species_8

Name EC

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a product in reaction_8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_8} = v_8 \tag{124}$$

7.9 Species species_9

Name INHDLS

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a reactant in reaction_9), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_9} = 0 \tag{125}$$

7.10 Species species_10

Name NHDL

Initial concentration 100 dimensionless · dimensionless^{-1}

This species takes part in four reactions (as a reactant in reaction_31 and as a product in reaction_9, reaction_14 and as a modifier in reaction_31).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_10} = v_9 + v_{14} - v_{31} \tag{126}$$

7.11 Species species_11

Name PFC

Initial concentration 57516 dimensionless · dimensionless^{-1}

This species takes part in 17 reactions (as a reactant in reaction_28, reaction_30, reaction_31 and as a product in reaction_24, reaction_25, reaction_29, reaction_32 and as a modifier in reaction_9, reaction_9, reaction_14, reaction_14, reaction_26, reaction_26, reaction_28, reaction_30, reaction_31, reaction_32).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_11} = v_{24} + v_{25} + v_{29} + v_{32} - v_{28} - v_{30} - v_{31} \tag{127}$$

7.12 Species species_12

Name HCS

SBO:0000291 empty set

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a reactant in reaction_11), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_12} = 0 \tag{128}$$

7.13 Species species_13

Name HCE

Initial concentration 10000 dimensionless · dimensionless^{-1}

This species takes part in four reactions (as a reactant in reaction_13 and as a product in reaction_12 and as a modifier in reaction_13, reaction_13).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_13} = v_{12} - v_{13} \tag{129}$$

7.14 Species species_14

Name ACAT

Initial concentration 100 dimensionless · dimensionless^{-1}

This species takes part in four reactions (as a modifier in reaction_12, reaction_12, reaction_28, reaction_28).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_14} = 0 \tag{130}$$

7.15 Species species_15

Name CEH

Initial concentration 100 dimensionless · dimensionless^{-1}

This species takes part in four reactions (as a modifier in reaction_13, reaction_13, reaction_29, reaction_29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_15} = 0 \tag{131}$$

7.16 Species species_16

Name HNHDLS

SBO:0000291 empty set

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a reactant in reaction_14), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_16} = 0 \tag{132}$$

7.17 Species species_17

Name VLDLC

Initial concentration 20 dimensionless · dimensionless^{-1}

This species takes part in seven reactions (as a reactant in reaction_18, reaction_19 and as a product in reaction_15, reaction_33 and as a modifier in reaction_18, reaction_19, reaction_19).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_17} = v_{15} + v_{33} - v_{18} - v_{19} \tag{133}$$

7.18 Species species_18

Name HLDLRs

Initial concentration 100 dimensionless · dimensionless^{-1}

This species takes part in five reactions (as a reactant in reaction_17 and as a product in reaction_16 and as a modifier in reaction_17, reaction_22, reaction_22).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_18} = v_{16} - v_{17} \tag{134}$$

7.19 Species species_19

Name HLDLRsS

SBO:0000291 empty set

Initial concentration 600 dimensionless · dimensionless^{-1}

This species takes part in three reactions (as a reactant in reaction_16 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:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_19} = 0 \tag{135}$$

7.20 Species species_20

Name HLDLRD

SBO:0000291 empty set

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a product in reaction_17).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_20} = v_{17} \tag{136}$$

7.21 Species species_21

Name IDLC

Initial concentration 20 dimensionless · dimensionless^{-1}

This species takes part in five reactions (as a reactant in reaction_20, reaction_21 and as a product in reaction_19 and as a modifier in reaction_20, reaction_21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_21} = v_{19} - v_{20} - v_{21} \tag{137}$$

7.22 Species species_22

Name LPL

Initial concentration $100\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in two reactions (as a modifier in reaction_19, reaction_19).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_22} = 0 \tag{138}$$

7.23 Species species_23

Name LDLC

Initial concentration $100\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in ten reactions (as a reactant in reaction_22, reaction_23, reaction_24, reaction_25 and as a product in reaction_21, reaction_34 and as a modifier in reaction_22, reaction_23, reaction_24, reaction_25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_23} = v_{21} + v_{34} - v_{22} - v_{23} - v_{24} - v_{25} \tag{139}$$

7.24 Species species_24

Name HSL

Initial concentration $100\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in two reactions (as a modifier in reaction_21, reaction_21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_24} = 0 \tag{140}$$

7.25 Species species_25

Name PLDLRs

Initial concentration $100\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in five reactions (as a reactant in reaction_27 and as a product in reaction_26 and as a modifier in reaction_24, reaction_24, reaction_27).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_25} = v_{26} - v_{27} \tag{141}$$

7.26 Species species_26

Name PLDLRsS

SBO:0000291 empty set

Initial concentration 575.16 dimensionless · dimensionless^{-1}

This species takes part in two reactions (as a reactant in reaction_26 and as a modifier in reaction_26), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_26} = 0 \tag{142}$$

7.27 Species species_27

Name PLDLRD

SBO:0000291 empty set

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a product in reaction_27).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_27} = v_{27} \tag{143}$$

7.28 Species species_28

Name PCE

Initial concentration 9363 dimensionless · dimensionless^{-1}

This species takes part in three reactions (as a reactant in reaction_29 and as a product in reaction_28 and as a modifier in reaction_29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_28} = v_{28} - v_{29} \tag{144}$$

7.29 Species species_29

Name PSS

SBO:0000291 empty set

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a product in reaction_30).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_29} = v_{30} \tag{145}$$

7.30 Species species_30

Name HDLC

Initial concentration 45 dimensionless · dimensionless^{-1}

This species takes part in seven reactions (as a reactant in reaction_33, reaction_34, reaction_35 and as a product in reaction_31 and as a modifier in reaction_33, reaction_34, reaction_35).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_30} = v_{31} - v_{33} - v_{34} - v_{35} \tag{146}$$

7.31 Species species_31

Name LCAT

Initial concentration 100 dimensionless · dimensionless^{-1}

This species takes part in two reactions (as a modifier in reaction_31, reaction_31).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_31} = 0 \tag{147}$$

7.32 Species species_32

Name PCS

SBO:0000291 empty set

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in one reaction (as a reactant in reaction_32), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_32} = 0 \tag{148}$$

7.33 Species species_33

Name CETP

Initial concentration 100 dimensionless · dimensionless^{-1}

This species takes part in four reactions (as a modifier in reaction_33, reaction_33, reaction_34, reaction_34).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_33} = 0 \tag{149}$$

7.34 Species species_34

Name SRB1

Initial concentration $100\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in two reactions (as a modifier in reaction_35, reaction_35).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_34} = 0 \tag{150}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000291 empty set: Entity defined by the absence of any actual object. An empty set is often used to represent the source of a creation process or the result of a degradation process.

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