SBML Model Report

Model name: "DallePezze2014 - Cellular senescene-induced mitochondrial dysfunction"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah[1] and Piero Dalle Pezze[2] at August twelveth 2015 at 10:31 p. m. and last time modified at September tenth 2015 at 12:37 a. 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	1
species types	0	species	40
events	0	constraints	0
reactions	41	function definitions	32
global parameters	55	unit definitions	3
rules	17	initial assignments	0

Model Notes

DallePazze2014 - Cellular senescene-inducedmitochondrial dysfunction

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This model is described in the article:Dynamic modelling of pathways to cellular senescence reveals strategies for targeted interventions.Dalle Pezze P, Nelson G, Otten EG, Korolchuk VI, Kirkwood TB, von Zglinicki T, Shanley DP.PLoS Comput. Biol. 2014 Aug; 10(8): e1003728

Abstract:

Cellular senescence, a state of irreversible cell cycle arrest, is thought to help protect an organism from cancer, yet also contributes to ageing. The changes which occur in senescence are controlled by networks of multiple signalling and feedback pathways at the cellular level, and the interplay between these is difficult to predict and understand. To unravel the intrinsic challenges of understanding such a highly networked system, we have taken a systems biology approach to cellular senescence. We report a detailed analysis of senescence signalling via DNA damage, insulin-TOR, FoxO3a transcription factors, oxidative stress response, mitochondrial regulation and mitophagy. We show in silico and in vitro that inhibition of reactive oxygen species can prevent loss of mitochondrial membrane potential, whilst inhibition of mTOR shows a partial rescue of mitochondrial mass changes during establishment of senescence. Dual inhibition of ROS and mTOR in vitro confirmed computational model predictions that it was possible to further reduce senescence-induced mitochondrial dysfunction and DNA double-strand breaks. However, these interventions were unable to abrogate the senescence-induced mitochondrial dysfunction completely, and we identified decreased mitochondrial fission as the potential driving force for increased mitochondrial mass via prevention of mitophagy. Dynamic sensitivity analysis of the model showed the network stabilised at a new late state of cellular senescence. This was characterised by poor network sensitivity, high signalling noise, low cellular energy, high inflammation and permanent cell cycle arrest suggesting an unsatisfactory outcome for treatments aiming to delay or reverse cellular senescence at late time points. Combinatorial targeted interventions are therefore possible for intervening in the cellular pathway to senescence, but in the cases identified here, are only capable of delaying senescence onset.

This model is hosted on BioModels Database and identified by: BIOMD0000000582.

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 `time`

Name time

Definition 86400 s

2.2 Unit substance

Name substance

Definition dimensionless

2.3 Unit volume

Name volume

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 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
Cell	Cell		3	1	dimensionless	☑	

3.1 Compartment Cell

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

Name Cell

4 Species

This model contains 40 species. The boundary condition of 17 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 Condition
`Akt`	Akt	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟
`Akt_pS473`	Akt_pS473	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟
`AMPK`	AMPK	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟
`AMPK_pT172`	AMPK_pT172	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟
`mTORC1`	mTORC1	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟
`mTORC1_pS2448`	mTORC1_pS2448	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟
`Mitophagy`	Mitophagy	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟
`FoxO3a`	FoxO3a	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟
`FoxO3a_pS253`	FoxO3a_pS253	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟
`CDKN1A`	CDKN1A	`Cell`	dimensionless · dimensionless^{-1}	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
CDKN1B	CDKN1B	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
JNK	JNK	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
JNK_pT183	JNK_pT183	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
ROS	ROS	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
DNA_damage	DNA_damage	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
SA_beta_gal	SA_beta_gal	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
IKKbeta	IKKbeta	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
Mito_mass_new	Mito_mass_new	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
Mito_mass_old	Mito_mass_old	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
Mito_mass_turnover	Mito_mass_turnover	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
Mito_membr_pot_new	Mito_membr_pot_new	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
Mito_membr_pot_old	Mito_membr_pot_old	Cell	dimensionless · dimensionless^{-1}	⊟	⊟
Nil	Nil	Cell	dimensionless · dimensionless^{-1}	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
Insulin	Insulin	Cell	dimensionless · dimensionless^{-1}	⊟	☑
Amino_Acids	Amino_Acids	Cell	dimensionless · dimensionless^{-1}	⊟	☑
Irradiation	Irradiation	Cell	dimensionless · dimensionless^{-1}	⊟	☑
DNA_damage_gammaH2AX_obs	DNA_damage_gammaH2AX_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
Akt_pS473_obs	Akt_pS473_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
mTOR_pS2448_obs	mTOR_pS2448_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
AMPK_pT172_obs	AMPK_pT172_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
CDKN1A_obs	CDKN1A_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
CDKN1B_obs	CDKN1B_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
FoxO3a_pS253_obs	FoxO3a_pS253_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
FoxO3a_total_obs	FoxO3a_total_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
Mito_Mass_obs	Mito_Mass_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
Mito_Membr_Pot_obs	Mito_Membr_Pot_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
Mitophagy_obs	Mitophagy_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
ROS_obs	ROS_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
JNK_pT183_obs	JNK_pT183_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑
SA_beta_gal_obs	SA_beta_gal_obs	Cell	dimensionless · dimensionless^{-1}	⊟	☑

5 Parameters

This model contains 55 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Akt_S473-_phos_by-_insulin	Akt_S473_phos-_by_insulin		0.589		☑
Akt_pS473-_dephos-_by_mTORC1-_pS2448	Akt_pS473-_dephos_by-_mTORC1_pS2448		0.115		☑
AMPK_T172-_phos	AMPK_T172_phos		0.355		☑
AMPK_pT172-_dephos_by-_Mito_membr-_pot_new	AMPK_pT172-_dephos_by_Mito-_membr_pot_new		0.118		☑
AMPK_pT172-_dephos_by-_Mito_membr-_pot_old	AMPK_pT172-_dephos_by_Mito-_membr_pot_old		$1.00000000000003 \cdot 10^{-6}$		☑
mTORC1-_S2448_phos-_by_AA	mTORC1_S2448-_phos_by_AA		$1.00008999860285 \cdot 10^{-6}$		☑
mTORC1-_S2448_phos-_by_AA_n_Akt-_pS473	mTORC1_S2448-_phos_by_AA_n-_Akt_pS473		162.471		☑
mTORC1-_pS2448-_dephos_by-_AMPK_pT172	mTORC1_pS2448-_dephos_by-_AMPK_pT172		191.297		☑
mitophagy-_activ_by-_FoxO3a_n-_AMPK_pT172	mitophagy_activ-_by_FoxO3a_n-_AMPK_pT172		1319.842		☑
mitophagy-_inactiv-_by_mTORC1-_pS2448	mitophagy_inactiv-_by_mTORC1-_pS2448		645.999		☑

Id	Name	SBO	Value	Unit	Constant
FoxO3a_phos_by_Akt_pS473	FoxO3a_phos_by_Akt_pS473		6.835		☑
FoxO3a_phos_by_JNK_pT183	FoxO3a_phos_by_JNK_pT183		0.113		☑
FoxO3a_pS253_degrad	FoxO3a_pS253_degrad		39.407		☑
FoxO3a_synthesis	FoxO3a_synthesis		407.307		☑
CDKN1A_transcr_by_FoxO3a_n_DNA_damage	CDKN1A_transcr_by_FoxO3a_n_DNA_damage		0.085		☑
CDKN1A_inactiv_by_Akt_pS473	CDKN1A_inactiv_by_Akt_pS473		0.067		☑
CDKN1B_transcr_by_FoxO3a_n_DNA_damage	CDKN1B_transcr_by_FoxO3a_n_DNA_damage		0.092		☑
CDKN1B_inactiv_by_Akt_pS473	CDKN1B_inactiv_by_Akt_pS473		0.060		☑
DNA_damaged_by_irradiation	DNA_damaged_by_irradiation		9237.723		☑
DNA_repair	DNA_repair		0.326		☑
DNA_damaged_by_ROS	DNA_damaged_by_ROS		0.119		☑
ROS_prod_by_Mito_membr_pot_new	ROS_prod_by_Mito_membr_pot_new		4.555		☑
ROS_prod_by_Mito_membr_pot_old	ROS_prod_by_Mito_membr_pot_old		772.829		☑
ROS_turnover	ROS_turnover		3.231		☑
JNK_activ_by_ROS	JNK_activ_by_ROS		0.005		☑
JNK_pT183_inactiv	JNK_pT183_inactiv		0.072		☑
IKKbeta_activ_by_ROS	IKKbeta_activ_by_ROS		1.000		☑

Id	Name	SBO	Value	Unit	Constant
IKKbeta_inactiv	IKKbeta_inactiv		1.000		☑
mTORC1_S2448_phos_by_AA_n_IKKbeta	mTORC1_S2448_phos_by_AA_n_IKKbeta		$1.00008996727694 \cdot 10^{-5}$		☑
sen_ass_beta_gal_inc_by_ROS	sen_ass_beta_gal_inc_by_ROS		0.070		☑
sen_ass_beta_gal_inc_by_Mitophagy	sen_ass_beta_gal_inc_by_Mitophagy		$1.00000000000011 \cdot 10^{-6}$		☑
sen_ass_beta_gal_dec	sen_ass_beta_gal_dec		0.155		☑
mito_biogenesis_by_mTORC1_pS2448	mito_biogenesis_by_mTORC1_pS2448		0.013		☑
mito_biogenesis_by_AMPK_pT172	mito_biogenesis_by_AMPK_pT172		$5.8915457309741 \cdot 10^{-5}$		☑
mitophagy_new	mitophagy_new		0.225		☑
mitophagy_old	mitophagy_old		0.001		☑
mito_dysfunction	mito_dysfunction		0.027		☑
mito_membr_pot_new_inc	mito_membr_pot_new_inc		9882.027		☑
mito_membr_pot_old_inc	mito_membr_pot_old_inc		0.006		☑
mito_membr_pot_new_dec	mito_membr_pot_new_dec		1094.584		☑
mito_membr_pot_old_dec	mito_membr_pot_old_dec		0.955		☑
scale_Akt_pS473_obs	scale_Akt_pS473_obs		1.000		☑
scale_FoxO3a_pS253_obs	scale_FoxO3a_pS253_obs		1.000		☑

Id	Name	SBO	Value	Unit	Constant
scale_FoxO3a_total_obs	scale_FoxO3a_total_obs		1.000		☑
scale_AMPK_pT172_obs	scale_AMPK_pT172_obs		1.000		☑
scale_mTOR_pS2448_obs	scale_mTOR_pS2448_obs		1.000		☑
scale_Mitophagy_obs	scale_Mitophagy_obs		1.000		☑
scale_Mito_Mass_obs	scale_Mito_Mass_obs		1.000		☑
scale_Mito_Membr_Pot_obs	scale_Mito_Membr_Pot_obs		1.000		☑
scale_CDKN1A_obs	scale_CDKN1A_obs		1.000		☑
scale_CDKN1B_obs	scale_CDKN1B_obs		1.000		☑
scale_ROS_obs	scale_ROS_obs		1.000		☑
scale_DNA_damage_gammaH2AX_obs	scale_DNA_damage_gammaH2AX_obs		1.000		☑
scale_JNK_pT183_obs	scale_JNK_pT183_obs		1.000		☑
scale_SA_beta_gal_obs	scale_SA_beta_gal_obs		1.000		☑

6 Function definitions

This is an overview of 32 function definitions.

6.1 Function definition function_2

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$v \tag{1}$$

6.2 Function definition function_4_reaction_1_1

Name function_4_reaction_1_1

Arguments [Akt], Akt_S473_phos_by_insulin, [Insulin]

Mathematical Expression

$$\text{Akt\_S473\_phos\_by\_insulin} \cdot [\text{Akt}] \cdot [\text{Insulin}] \tag{2}$$

6.3 Function definition function_4_reaction_2_1

Name function_4_reaction_2_1

Arguments [Akt_pS473], Akt_pS473_dephos_by_mTORC1_pS2448, [mTORC1_pS2448]

Mathematical Expression

$$\text{Akt\_pS473\_dephos\_by\_mTORC1\_pS2448} \cdot [\text{Akt\_pS473}] \cdot [\text{mTORC1\_pS2448}] \tag{3}$$

6.4 Function definition function_4_reaction_4_1

Name function_4_reaction_4_1

Arguments [AMPK_pT172], AMPK_pT172_dephos_by_Mito_membr_pot_new, [Mito_membr_pot_new]

Mathematical Expression

$$\text{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_new} \cdot [\text{AMPK\_pT172}] \cdot [\text{Mito\_membr\_pot\_new}] \tag{4}$$

6.5 Function definition function_4_reaction_5_1

Name function_4_reaction_5_1

Arguments [AMPK_pT172], AMPK_pT172_dephos_by_Mito_membr_pot_old, [Mito_membr_pot_old]

Mathematical Expression

$$\text{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_old} \cdot [\text{AMPK\_pT172}] \cdot [\text{Mito\_membr\_pot\_old}] \tag{5}$$

6.6 Function definition function_4_reaction_6_1

Name function_4_reaction_6_1

Arguments [Amino_Acids], [mTORC1], mTORC1_S2448_phos_by_AA

Mathematical Expression

$$\text{mTORC1\_S2448\_phos\_by\_AA} \cdot [\text{mTORC1}] \cdot [\text{Amino\_Acids}] \tag{6}$$

6.7 Function definition function_4_reaction_7_1

Name function_4_reaction_7_1

Arguments [Akt_pS473], [Amino_Acids], [mTORC1], mTORC1_S2448_phos_by_AA_n_Akt_pS473

Mathematical Expression

$$\text{mTORC1\_S2448\_phos\_by\_AA\_n\_Akt\_pS473} \cdot [\text{mTORC1}] \cdot [\text{Amino\_Acids}] \cdot [\text{Akt\_pS473}] \tag{7}$$

6.8 Function definition function_4_reaction_8_1

Name function_4_reaction_8_1

Arguments [AMPK_pT172], [mTORC1_pS2448], mTORC1_pS2448_dephos_by_AMPK_pT172

Mathematical Expression

$$\text{mTORC1\_pS2448\_dephos\_by\_AMPK\_pT172} \cdot [\text{mTORC1\_pS2448}] \cdot [\text{AMPK\_pT172}] \tag{8}$$

6.9 Function definition function_4_reaction_9_1

Name function_4_reaction_9_1

Arguments [AMPK_pT172], [FoxO3a], mitophagy_activ_by_FoxO3a_n_AMPK_pT172

Mathematical Expression

$$\text{mitophagy\_activ\_by\_FoxO3a\_n\_AMPK\_pT172} \cdot [\text{FoxO3a}] \cdot [\text{AMPK\_pT172}] \tag{9}$$

6.10 Function definition function_4_reaction_10_1

Name function_4_reaction_10_1

Arguments [Mitophagy], [mTORC1_pS2448], mitophagy_inactiv_by_mTORC1_pS2448

Mathematical Expression

$$\text{mitophagy\_inactiv\_by\_mTORC1\_pS2448} \cdot [\text{Mitophagy}] \cdot [\text{mTORC1\_pS2448}] \tag{10}$$

6.11 Function definition function_4_reaction_11_1

Name function_4_reaction_11_1

Arguments [Akt_pS473], [FoxO3a], FoxO3a_phos_by_Akt_pS473

Mathematical Expression

$$\text{FoxO3a\_phos\_by\_Akt\_pS473} \cdot [\text{FoxO3a}] \cdot [\text{Akt\_pS473}] \tag{11}$$

6.12 Function definition function_4_reaction_12_1

Name function_4_reaction_12_1

Arguments [FoxO3a_pS253], FoxO3a_phos_by_JNK_pT183, [JNK_pT183]

Mathematical Expression

$$\text{FoxO3a\_phos\_by\_JNK\_pT183} \cdot [\text{FoxO3a\_pS253}] \cdot [\text{JNK\_pT183}] \tag{12}$$

6.13 Function definition function_4_reaction_15_1

Name function_4_reaction_15_1

Arguments CDKN1A_transcr_by_FoxO3a_n_DNA_damage, [DNA_damage], [FoxO3a]

Mathematical Expression

$$\text{CDKN1A\_transcr\_by\_FoxO3a\_n\_DNA\_damage} \cdot [\text{DNA\_damage}] \cdot [\text{FoxO3a}] \tag{13}$$

6.14 Function definition function_4_reaction_16_1

Name function_4_reaction_16_1

Arguments [Akt_pS473], [CDKN1A], CDKN1A_inactiv_by_Akt_pS473

Mathematical Expression

$$\text{CDKN1A\_inactiv\_by\_Akt\_pS473} \cdot [\text{CDKN1A}] \cdot [\text{Akt\_pS473}] \tag{14}$$

6.15 Function definition function_4_reaction_17_1

Name function_4_reaction_17_1

Arguments CDKN1B_transcr_by_FoxO3a_n_DNA_damage, [DNA_damage], [FoxO3a]

Mathematical Expression

$$\text{CDKN1B\_transcr\_by\_FoxO3a\_n\_DNA\_damage} \cdot [\text{DNA\_damage}] \cdot [\text{FoxO3a}] \tag{15}$$

6.16 Function definition function_4_reaction_18_1

Name function_4_reaction_18_1

Arguments [Akt_pS473], [CDKN1B], CDKN1B_inactiv_by_Akt_pS473

Mathematical Expression

$$\text{CDKN1B\_inactiv\_by\_Akt\_pS473} \cdot [\text{CDKN1B}] \cdot [\text{Akt\_pS473}] \tag{16}$$

6.17 Function definition function_4_reaction_19_1

Name function_4_reaction_19_1

Arguments DNA_damaged_by_irradiation, [Irradiation]

Mathematical Expression

$$\text{DNA\_damaged\_by\_irradiation} \cdot [\text{Irradiation}] \tag{17}$$

6.18 Function definition function_4_reaction_20_1

Name function_4_reaction_20_1

Arguments DNA_damaged_by_ROS, [ROS]

Mathematical Expression

$$\text{DNA\_damaged\_by\_ROS} \cdot [\text{ROS}] \tag{18}$$

6.19 Function definition function_4_reaction_22_1

Name function_4_reaction_22_1

Arguments [Mito_membr_pot_new], ROS_prod_by_Mito_membr_pot_new

Mathematical Expression

$$\text{ROS\_prod\_by\_Mito\_membr\_pot\_new} \cdot [\text{Mito\_membr\_pot\_new}] \tag{19}$$

6.20 Function definition function_4_reaction_23_1

Name function_4_reaction_23_1

Arguments [Mito_membr_pot_old], ROS_prod_by_Mito_membr_pot_old

Mathematical Expression

$$\text{ROS\_prod\_by\_Mito\_membr\_pot\_old} \cdot [\text{Mito\_membr\_pot\_old}] \tag{20}$$

6.21 Function definition function_4_reaction_25_1

Name function_4_reaction_25_1

Arguments [JNK], JNK_activ_by_ROS, [ROS]

Mathematical Expression

$$\text{JNK\_activ\_by\_ROS} \cdot [\text{JNK}] \cdot [\text{ROS}] \tag{21}$$

6.22 Function definition function_4_reaction_27_1

Name function_4_reaction_27_1

Arguments [ROS], sen_ass_beta_gal_inc_by_ROS

Mathematical Expression

$$\text{sen\_ass\_beta\_gal\_inc\_by\_ROS} \cdot [\text{ROS}] \tag{22}$$

6.23 Function definition function_4_reaction_28_1

Name function_4_reaction_28_1

Arguments [Mitophagy], sen_ass_beta_gal_inc_by_Mitophagy

Mathematical Expression

$$\text{sen\_ass\_beta\_gal\_inc\_by\_Mitophagy} \cdot [\text{Mitophagy}] \tag{23}$$

6.24 Function definition function_4_reaction_30_1

Name function_4_reaction_30_1

Arguments [Mito_mass_turnover], [mTORC1_pS2448], mito_biogenesis_by_mTORC1_pS2448

Mathematical Expression

$$\text{mito\_biogenesis\_by\_mTORC1\_pS2448} \cdot [\text{Mito\_mass\_turnover}] \cdot [\text{mTORC1\_pS2448}] \tag{24}$$

6.25 Function definition function_4_reaction_31_1

Name function_4_reaction_31_1

Arguments [Mito_mass_turnover], [mTORC1_pS2448], mito_biogenesis_by_AMPK_pT172

Mathematical Expression

$$\text{mito\_biogenesis\_by\_AMPK\_pT172} \cdot [\text{Mito\_mass\_turnover}] \cdot [\text{mTORC1\_pS2448}] \tag{25}$$

6.26 Function definition function_4_reaction_32_1

Name function_4_reaction_32_1

Arguments [Mito_mass_new], [Mitophagy], mitophagy_new

Mathematical Expression

$$\text{mitophagy\_new} \cdot [\text{Mito\_mass\_new}] \cdot [\text{Mitophagy}] \tag{26}$$

6.27 Function definition function_4_reaction_33_1

Name function_4_reaction_33_1

Arguments [Mito_mass_old], [Mitophagy], mitophagy_old

Mathematical Expression

$$\text{mitophagy\_old} \cdot [\text{Mito\_mass\_old}] \cdot [\text{Mitophagy}] \tag{27}$$

6.28 Function definition function_4_reaction_34_1

Name function_4_reaction_34_1

Arguments [CDKN1A], [Mito_mass_new], mito_dysfunction

Mathematical Expression

$$\text{mito\_dysfunction} \cdot [\text{Mito\_mass\_new}] \cdot [\text{CDKN1A}] \tag{28}$$

6.29 Function definition function_4_reaction_35_1

Name function_4_reaction_35_1

Arguments [Mito_mass_new], mito_membr_pot_new_inc

Mathematical Expression

$$\text{mito\_membr\_pot\_new\_inc} \cdot [\text{Mito\_mass\_new}] \tag{29}$$

6.30 Function definition function_4_reaction_36_1

Name function_4_reaction_36_1

Arguments [Mito_mass_old], mito_membr_pot_old_inc

Mathematical Expression

$$\text{mito\_membr\_pot\_old\_inc} \cdot [\text{Mito\_mass\_old}] \tag{30}$$

6.31 Function definition function_4_reaction_39_1

Name function_4_reaction_39_1

Arguments IKKbeta_activ_by_ROS, [ROS]

Mathematical Expression

$$\text{IKKbeta\_activ\_by\_ROS} \cdot [\text{ROS}] \tag{31}$$

6.32 Function definition function_4_reaction_41_1

Name function_4_reaction_41_1

Arguments [Amino_Acids], [IKKbeta], [mTORC1], mTORC1_S2448_phos_by_AA_n_IKKbeta

Mathematical Expression

$$\text{mTORC1\_S2448\_phos\_by\_AA\_n\_IKKbeta} \cdot [\text{mTORC1}] \cdot [\text{Amino\_Acids}] \cdot [\text{IKKbeta}] \tag{32}$$

7 Rules

This is an overview of 17 rules.

7.1 Rule DNA_damage_gammaH2AX_obs

Rule DNA_damage_gammaH2AX_obs is an assignment rule for species DNA_damage_gammaH2AX_obs:

$$\text{DNA\_damage\_gammaH2AX\_obs} = \text{scale\_DNA\_damage\_gammaH2AX\_obs} \cdot [\text{DNA\_damage}] \tag{33}$$

7.2 Rule Insulin

Rule Insulin is an assignment rule for species Insulin:

$$\text{Insulin} = \begin{cases} 1 & \text{if time} < 1 \\ \begin{cases} 1 & \text{if time} < 0 \\ 1 & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{34}$$

7.3 Rule Amino_Acids

Rule Amino_Acids is an assignment rule for species Amino_Acids:

$$\text{Amino\_Acids} = \begin{cases} 1 & \text{if time} < 1 \\ \begin{cases} 1 & \text{if time} < 0 \\ 1 & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{35}$$

7.4 Rule Irradiation

Rule Irradiation is an assignment rule for species Irradiation:

$$\text{Irradiation} = \begin{cases} 0 & \text{if time} < 1 \\ \begin{cases} 0 & \text{if time} < 0 \\ \begin{cases} 1 & \text{if time} < 0.003472 \\ 0 & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{36}$$

7.5 Rule Akt_pS473_obs

Rule Akt_pS473_obs is an assignment rule for species Akt_pS473_obs:

$$\text{Akt\_pS473\_obs} = \text{scale\_Akt\_pS473\_obs} \cdot [\text{Akt\_pS473}] \tag{37}$$

7.6 Rule SA_beta_gal_obs

Rule SA_beta_gal_obs is an assignment rule for species SA_beta_gal_obs:

$$\text{SA\_beta\_gal\_obs} = \text{scale\_SA\_beta\_gal\_obs} \cdot [\text{SA\_beta\_gal}] \tag{38}$$

7.7 Rule JNK_pT183_obs

Rule JNK_pT183_obs is an assignment rule for species JNK_pT183_obs:

$$\text{JNK\_pT183\_obs} = \text{scale\_JNK\_pT183\_obs} \cdot [\text{JNK\_pT183}] \tag{39}$$

7.8 Rule ROS_obs

Rule ROS_obs is an assignment rule for species ROS_obs:

$$\text{ROS\_obs} = \text{scale\_ROS\_obs} \cdot [\text{ROS}] \tag{40}$$

7.9 Rule FoxO3a_total_obs

Rule FoxO3a_total_obs is an assignment rule for species FoxO3a_total_obs:

$$\text{FoxO3a\_total\_obs} = \text{scale\_FoxO3a\_total\_obs} \cdot ([\text{FoxO3a}] + [\text{FoxO3a\_pS253}]) \tag{41}$$

7.10 Rule Mitophagy_obs

Rule Mitophagy_obs is an assignment rule for species Mitophagy_obs:

$$\text{Mitophagy\_obs} = \text{scale\_Mitophagy\_obs} \cdot [\text{Mitophagy}] \tag{42}$$

7.11 Rule Mito_Membr_Pot_obs

Rule Mito_Membr_Pot_obs is an assignment rule for species Mito_Membr_Pot_obs:

$$\begin{aligned} \text{Mito\_Membr\_Pot\_obs} = {} & \text{scale\_Mito\_Membr\_Pot\_obs} \\ & \cdot ([\text{Mito\_membr\_pot\_new}] + [\text{Mito\_membr\_pot\_old}]) \end{aligned} \tag{43}$$

7.12 Rule CDKN1B_obs

Rule CDKN1B_obs is an assignment rule for species CDKN1B_obs:

$$\text{CDKN1B\_obs} = \text{scale\_CDKN1B\_obs} \cdot [\text{CDKN1B}] \tag{44}$$

7.13 Rule CDKN1A_obs

Rule CDKN1A_obs is an assignment rule for species CDKN1A_obs:

$$\text{CDKN1A\_obs} = \text{scale\_CDKN1A\_obs} \cdot [\text{CDKN1A}] \tag{45}$$

7.14 Rule Mito_Mass_obs

Rule Mito_Mass_obs is an assignment rule for species Mito_Mass_obs:

$$\text{Mito\_Mass\_obs} = \text{scale\_Mito\_Mass\_obs} \cdot ([\text{Mito\_mass\_new}] + [\text{Mito\_mass\_old}]) \tag{46}$$

7.15 Rule AMPK_pT172_obs

Rule AMPK_pT172_obs is an assignment rule for species AMPK_pT172_obs:

$$\text{AMPK\_pT172\_obs} = \text{scale\_AMPK\_pT172\_obs} \cdot [\text{AMPK\_pT172}] \tag{47}$$

7.16 Rule FoxO3a_pS253_obs

Rule FoxO3a_pS253_obs is an assignment rule for species FoxO3a_pS253_obs:

$$\text{FoxO3a\_pS253\_obs} = \text{scale\_FoxO3a\_pS253\_obs} \cdot [\text{FoxO3a\_pS253}] \tag{48}$$

7.17 Rule mTOR_pS2448_obs

Rule mTOR_pS2448_obs is an assignment rule for species mTOR_pS2448_obs:

$$\text{mTOR\_pS2448\_obs} = \text{scale\_mTOR\_pS2448\_obs} \cdot [\text{mTORC1\_pS2448}] \tag{49}$$

8 Reactions

This model contains 41 reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	reaction_1	reaction_1	$\text{Akt} \xrightarrow{\text{Insulin, Akt, Insulin}} \text{Akt\_pS473}$	
2	reaction_2	reaction_2	$\text{Akt\_pS473} \xrightarrow{\text{mTORC1\_pS2448, Akt\_pS473, mTORC1\_pS2448}} \text{Akt}$	
3	reaction_3	reaction_3	$\text{AMPK} \xrightarrow{\text{AMPK}} \text{AMPK\_pT172}$	
4	reaction_4	reaction_4	$\text{AMPK\_pT172} \xrightarrow{\text{Mito\_membr\_pot\_new, AMPK\_pT172, Mito\_membr\_pot\_new}} \text{AMPK}$	
5	reaction_5	reaction_5	$\text{AMPK\_pT172} \xrightarrow{\text{Mito\_membr\_pot\_old, AMPK\_pT172, Mito\_membr\_pot\_old}} \text{AMPK}$	
6	reaction_6	reaction_6	$\text{mTORC1} \xrightarrow{\text{Amino\_Acids, Amino\_Acids, mTORC1}} \text{mTORC1\_pS2448}$	
7	reaction_7	reaction_7	$\text{mTORC1} \xrightarrow{\text{Amino\_Acids, Akt\_pS473, Akt\_pS473, Amino\_Acids, mTORC1}} \text{mTORC1\_p}$	
8	reaction_8	reaction_8	$\text{mTORC1\_pS2448} \xrightarrow{\text{AMPK\_pT172, AMPK\_pT172, mTORC1\_pS2448}} \text{mTORC1}$	
9	reaction_9	reaction_9	$\emptyset \xrightarrow{\text{FoxO3a, AMPK\_pT172, AMPK\_pT172, FoxO3a}} \text{Mitophagy}$	
10	reaction_10	reaction_10	$\text{Mitophagy} \xrightarrow{\text{mTORC1\_pS2448, Mitophagy, mTORC1\_pS2448}} \text{Nil}$	
11	reaction_11	reaction_11	$\text{FoxO3a} \xrightarrow{\text{Akt\_pS473, Akt\_pS473, FoxO3a}} \text{FoxO3a\_pS253}$	
12	reaction_12	reaction_12	$\text{FoxO3a\_pS253} \xrightarrow{\text{JNK\_pT183, FoxO3a\_pS253, JNK\_pT183}} \text{FoxO3a}$	
13	reaction_13	reaction_13	$\text{FoxO3a\_pS253} \xrightarrow{\text{FoxO3a\_pS253}} \text{Nil}$	
14	reaction_14	reaction_14	$\emptyset \longrightarrow \text{FoxO3a}$	
15	reaction_15	reaction_15	$\emptyset \xrightarrow{\text{DNA\_damage, FoxO3a, DNA\_damage, FoxO3a}} \text{CDKN1A}$	
16	reaction_16	reaction_16	$\text{CDKN1A} \xrightarrow{\text{Akt\_pS473, Akt\_pS473, CDKN1A}} \text{Nil}$	

№	Id	Name	Reaction Equation	SBO
17	reaction_17	reaction_17	$\emptyset \xrightarrow{\text{DNA\_damage, FoxO3a, DNA\_damage, FoxO3a}} \text{CDKN1B}$	
18	reaction_18	reaction_18	$\text{CDKN1B} \xrightarrow{\text{Akt\_pS473, Akt\_pS473, CDKN1B}} \text{Nil}$	
19	reaction_19	reaction_19	$\emptyset \xrightarrow{\text{Irradiation, Irradiation}} \text{DNA\_damage}$	
20	reaction_20	reaction_20	$\emptyset \xrightarrow{\text{ROS, ROS}} \text{DNA\_damage}$	
21	reaction_21	reaction_21	$\text{DNA\_damage} \xrightarrow{\text{DNA\_damage}} \text{Nil}$	
22	reaction_22	reaction_22	$\emptyset \xrightarrow{\text{Mito\_membr\_pot\_new, Mito\_membr\_pot\_new}} \text{ROS}$	
23	reaction_23	reaction_23	$\emptyset \xrightarrow{\text{Mito\_membr\_pot\_old, Mito\_membr\_pot\_old}} \text{ROS}$	
24	reaction_24	reaction_24	$\text{ROS} \xrightarrow{\text{ROS}} \text{Nil}$	
25	reaction_25	reaction_25	$\text{JNK} \xrightarrow{\text{ROS, JNK, ROS}} \text{JNK\_pT183}$	
26	reaction_26	reaction_26	$\text{JNK\_pT183} \xrightarrow{\text{JNK\_pT183}} \text{JNK}$	
27	reaction_27	reaction_27	$\emptyset \xrightarrow{\text{ROS, ROS}} \text{SA\_beta\_gal}$	
28	reaction_28	reaction_28	$\emptyset \xrightarrow{\text{Mitophagy, Mitophagy}} \text{SA\_beta\_gal}$	
29	reaction_29	reaction_29	$\text{SA\_beta\_gal} \xrightarrow{\text{SA\_beta\_gal}} \emptyset$	
30	reaction_30	reaction_30	$\text{Mito\_mass\_turnover} \xrightarrow{\text{mTORC1\_pS2448, Mito\_mass\_turnover, mTORC1\_pS2448}} \text{Mito\_}$	
31	reaction_31	reaction_31	$\text{Mito\_mass\_turnover} \xrightarrow{\text{mTORC1\_pS2448, Mito\_mass\_turnover, mTORC1\_pS2448}} \text{Mito\_}$	
32	reaction_32	reaction_32	$\text{Mito\_mass\_new} \xrightarrow{\text{Mitophagy, Mito\_mass\_new, Mitophagy}} \text{Mito\_mass\_turnover}$	
33	reaction_33	reaction_33	$\text{Mito\_mass\_old} \xrightarrow{\text{Mitophagy, Mito\_mass\_old, Mitophagy}} \text{Mito\_mass\_turnover}$	
34	reaction_34	reaction_34	$\text{Mito\_mass\_new} \xrightarrow{\text{CDKN1A, CDKN1A, Mito\_mass\_new}} \text{Mito\_mass\_old}$	
35	reaction_35	reaction_35	$\emptyset \xrightarrow{\text{Mito\_mass\_new, Mito\_mass\_new}} \text{Mito\_membr\_pot\_new}$	
36	reaction_36	reaction_36	$\emptyset \xrightarrow{\text{Mito\_mass\_old, Mito\_mass\_old}} \text{Mito\_membr\_pot\_old}$	

№	Id	Name	Reaction Equation	SBO
37	reaction_37	reaction_37	Mito_membr_pot_new $\xrightarrow{\text{Mito\_membr\_pot\_new}}$ Nil	
38	reaction_38	reaction_38	Mito_membr_pot_old $\xrightarrow{\text{Mito\_membr\_pot\_old}}$ Nil	
39	reaction_39	reaction_39	$\emptyset \xrightarrow{\text{ROS, ROS}}$ IKKbeta	
40	reaction_40	reaction_40	IKKbeta $\xrightarrow{\text{IKKbeta}}$ Nil	
41	reaction_41	reaction_41	mTORC1 $\xrightarrow{\text{Amino\_Acids, IKKbeta, Amino\_Acids, IKKbeta, mTORC1}}$ mTORC1_pS24	

8.1 Reaction reaction_1

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

Name reaction_1

Reaction equation

$$\text{Akt} \xrightarrow{\text{Insulin, Akt, Insulin}} \text{Akt\_pS473} \tag{50}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
Akt	Akt	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
Insulin	Insulin	
Akt	Akt	
Insulin	Insulin	

Product

Table 8: Properties of each product.

Id	Name	SBO
Akt_pS473	Akt_pS473	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{Cell}) \cdot \text{function\_4\_reaction\_1\_1}([\text{Akt}], \text{Akt\_S473\_phos\_by\_insulin}, [\text{Insulin}]) \tag{51}$$

$$\begin{aligned} &\text{function\_4\_reaction\_1\_1}([\text{Akt}], \text{Akt\_S473\_phos\_by\_insulin}, [\text{Insulin}]) \\ &\quad = \text{Akt\_S473\_phos\_by\_insulin} \cdot [\text{Akt}] \cdot [\text{Insulin}] \end{aligned} \tag{52}$$

$$\begin{aligned}&\text{function\_4\_reaction\_1\_1}\left([\text{Akt}], \text{Akt\_S473\_phos\_by\_insulin}, [\text{Insulin}]\right)\\&\quad = \text{Akt\_S473\_phos\_by\_insulin} \cdot [\text{Akt}] \cdot [\text{Insulin}]\end{aligned} \tag{53}$$

8.2 Reaction `reaction_2`

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

Name reaction_2

Reaction equation

$$\text{Akt\_pS473} \xrightarrow{\text{mTORC1\_pS2448, Akt\_pS473, mTORC1\_pS2448}} \text{Akt} \tag{54}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
`Akt_pS473`	Akt_pS473	

Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
`mTORC1_pS2448`	mTORC1_pS2448	
`Akt_pS473`	Akt_pS473	
`mTORC1_pS2448`	mTORC1_pS2448	

Product

Table 11: Properties of each product.

Id	Name	SBO
`Akt`	Akt	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_2\_1}\,([\mathrm{Akt\_pS473}], \mathrm{Akt\_pS473\_dephos\_by\_mTORC1\_pS2448}, [\mathrm{mTORC1\_pS2448}]) \tag{55}$$

$$\mathrm{function\_4\_reaction\_2\_1}\,([\mathrm{Akt\_pS473}], \mathrm{Akt\_pS473\_dephos\_by\_mTORC1\_pS2448}, [\mathrm{mTORC1\_pS2448}]) = \mathrm{Akt\_pS473\_dephos\_by\_mTORC1\_pS2448} \cdot [\mathrm{Akt\_pS473}] \cdot [\mathrm{mTORC1\_pS2448}] \tag{56}$$

$$\mathrm{function\_4\_reaction\_2\_1}\,([\mathrm{Akt\_pS473}], \mathrm{Akt\_pS473\_dephos\_by\_mTORC1\_pS2448}, [\mathrm{mTORC1\_pS2448}]) = \mathrm{Akt\_pS473\_dephos\_by\_mTORC1\_pS2448} \cdot [\mathrm{Akt\_pS473}] \cdot [\mathrm{mTORC1\_pS2448}] \tag{57}$$

8.3 Reaction `reaction_3`

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

Name reaction_3

Reaction equation

$$\mathrm{AMPK} \xrightarrow{\mathrm{AMPK}} \mathrm{AMPK\_pT172} \tag{58}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
AMPK	AMPK	

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
AMPK	AMPK	

Product

Table 14: Properties of each product.

Id	Name	SBO
AMPK_pT172	AMPK_pT172	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{AMPK\_T172\_phos} \cdot [\mathrm{AMPK}] \tag{59}$$

8.4 Reaction reaction_4

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

Name reaction_4

Reaction equation

$$\mathrm{AMPK\_pT172} \xrightarrow{\text{Mito\_membr\_pot\_new, AMPK\_pT172, Mito\_membr\_pot\_new}} \mathrm{AMPK} \tag{60}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
AMPK_pT172	AMPK_pT172	

Modifiers

Table 16: Properties of each modifier.

Id	Name	SBO
Mito_membr_pot_new	Mito_membr_pot_new	
AMPK_pT172	AMPK_pT172	
Mito_membr_pot_new	Mito_membr_pot_new	

Product

Table 17: Properties of each product.

Id	Name	SBO
AMPK	AMPK	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_4\_1}\,([\mathrm{AMPK\_pT172}], \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_new}, [\mathrm{Mito\_membr\_pot\_new}]) \tag{61}$$

$$\mathrm{function\_4\_reaction\_4\_1}\,([\mathrm{AMPK\_pT172}], \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_new}, [\mathrm{Mito\_membr\_pot\_new}]) = \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_new} \cdot [\mathrm{AMPK\_pT172}] \cdot [\mathrm{Mito\_membr\_pot\_new}] \tag{62}$$

$$\mathrm{function\_4\_reaction\_4\_1}\,([\mathrm{AMPK\_pT172}], \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_new}, [\mathrm{Mito\_membr\_pot\_new}]) = \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_new} \cdot [\mathrm{AMPK\_pT172}] \cdot [\mathrm{Mito\_membr\_pot\_new}] \tag{63}$$

8.5 Reaction reaction_5

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

Name reaction_5

Reaction equation

$$\mathrm{AMPK\_pT172} \xrightarrow{\mathrm{Mito\_membr\_pot\_old,\ AMPK\_pT172,\ Mito\_membr\_pot\_old}} \mathrm{AMPK} \tag{64}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
AMPK_pT172	AMPK_pT172	

Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
Mito_membr_pot_old	Mito_membr_pot_old	
AMPK_pT172	AMPK_pT172	
Mito_membr_pot_old	Mito_membr_pot_old	

Product

Table 20: Properties of each product.

Id	Name	SBO
AMPK	AMPK	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_5\_1}\,([\mathrm{AMPK\_pT172}], \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_old}, [\mathrm{Mito\_membr\_pot\_old}]) \tag{65}$$

$$\mathrm{function\_4\_reaction\_5\_1}\,([\mathrm{AMPK\_pT172}], \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_old}, [\mathrm{Mito\_membr\_pot\_old}]) = \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_old} \cdot [\mathrm{AMPK\_pT172}] \cdot [\mathrm{Mito\_membr\_pot\_old}] \tag{66}$$

$$\mathrm{function\_4\_reaction\_5\_1}\,([\mathrm{AMPK\_pT172}], \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_old}, [\mathrm{Mito\_membr\_pot\_old}]) = \mathrm{AMPK\_pT172\_dephos\_by\_Mito\_membr\_pot\_old} \cdot [\mathrm{AMPK\_pT172}] \cdot [\mathrm{Mito\_membr\_pot\_old}] \tag{67}$$

8.6 Reaction reaction_6

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

Name reaction_6

Reaction equation

$$\mathrm{mTORC1} \xrightarrow{\mathrm{Amino\_Acids,\ Amino\_Acids,\ mTORC1}} \mathrm{mTORC1\_pS2448} \tag{68}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
mTORC1	mTORC1	

Modifiers

Table 22: Properties of each modifier.

Id	Name	SBO
Amino_Acids	Amino_Acids	
Amino_Acids	Amino_Acids	
mTORC1	mTORC1	

Product

Table 23: Properties of each product.

Id	Name	SBO
mTORC1_pS2448	mTORC1_pS2448	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_6\_1}\,([\mathrm{Amino\_Acids}], [\mathrm{mTORC1}], \mathrm{mTORC1\_S2448\_phos\_by\_AA}) \tag{69}$$

$$\mathrm{function\_4\_reaction\_6\_1}\,([\mathrm{Amino\_Acids}], [\mathrm{mTORC1}], \mathrm{mTORC1\_S2448\_phos\_by\_AA}) = \mathrm{mTORC1\_S2448\_phos\_by\_AA} \cdot [\mathrm{mTORC1}] \cdot [\mathrm{Amino\_Acids}] \tag{70}$$

$$\mathrm{function\_4\_reaction\_6\_1}\,([\mathrm{Amino\_Acids}], [\mathrm{mTORC1}], \mathrm{mTORC1\_S2448\_phos\_by\_AA}) = \mathrm{mTORC1\_S2448\_phos\_by\_AA} \cdot [\mathrm{mTORC1}] \cdot [\mathrm{Amino\_Acids}] \tag{71}$$

8.7 Reaction reaction_7

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

Name reaction_7

Reaction equation

$$\text{mTORC1} \xrightarrow{\text{Amino\_Acids, Akt\_pS473, Akt\_pS473, Amino\_Acids, mTORC1}} \text{mTORC1\_pS2448} \tag{72}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
mTORC1	mTORC1	

Modifiers

Table 25: Properties of each modifier.

Id	Name	SBO
Amino_Acids	Amino_Acids	
Akt_pS473	Akt_pS473	
Akt_pS473	Akt_pS473	
Amino_Acids	Amino_Acids	
mTORC1	mTORC1	

Product

Table 26: Properties of each product.

Id	Name	SBO
mTORC1_pS2448	mTORC1_pS2448	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{vol}\,(\text{Cell}) \cdot \text{function\_4\_reaction\_7\_1}\,([\text{Akt\_pS473}], [\text{Amino\_Acids}], [\text{mTORC1}], \text{mTORC1\_S2448\_phos\_by\_AA\_n\_Akt\_pS473}) \tag{73}$$

$$\text{function\_4\_reaction\_7\_1}\,([\text{Akt\_pS473}], [\text{Amino\_Acids}], [\text{mTORC1}], \text{mTORC1\_S2448\_phos\_by\_AA\_n\_Akt\_pS473}) = \text{mTORC1\_S2448\_phos\_by\_AA\_n\_Akt\_pS473} \cdot [\text{mTORC1}] \cdot [\text{Amino\_Acids}] \cdot [\text{Akt\_pS473}] \tag{74}$$

$$\begin{aligned}&\text{function\_4\_reaction\_7\_1}\left([\text{Akt\_pS473}], [\text{Amino\_Acids}], [\text{mTORC1}],\right.\\&\left.\text{mTORC1\_S2448\_phos\_by\_AA\_n\_Akt\_pS473}\right) = \text{mTORC1\_S2448\_phos\_by\_AA\_n\_Akt\_pS473}\\&\quad\cdot [\text{mTORC1}] \cdot [\text{Amino\_Acids}] \cdot [\text{Akt\_pS473}]\end{aligned} \tag{75}$$

8.8 Reaction `reaction_8`

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

Name reaction_8

Reaction equation

$$\text{mTORC1\_pS2448} \xrightarrow{\text{AMPK\_pT172, AMPK\_pT172, mTORC1\_pS2448}} \text{mTORC1} \tag{76}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
`mTORC1_pS2448`	mTORC1_pS2448	

Modifiers

Table 28: Properties of each modifier.

Id	Name	SBO
`AMPK_pT172`	AMPK_pT172	
`AMPK_pT172`	AMPK_pT172	
`mTORC1_pS2448`	mTORC1_pS2448	

Product

Table 29: Properties of each product.

Id	Name	SBO
`mTORC1`	mTORC1	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_8\_1}\,([\mathrm{AMPK\_pT172}], [\mathrm{mTORC1\_pS2448}], \mathrm{mTORC1\_pS2448\_dephos\_by\_AMPK\_pT172}) \tag{77}$$

$$\mathrm{function\_4\_reaction\_8\_1}\,([\mathrm{AMPK\_pT172}], [\mathrm{mTORC1\_pS2448}], \mathrm{mTORC1\_pS2448\_dephos\_by\_AMPK\_pT172}) = \mathrm{mTORC1\_pS2448\_dephos\_by\_AMPK\_pT172} \cdot [\mathrm{mTORC1\_pS2448}] \cdot [\mathrm{AMPK\_pT172}] \tag{78}$$

$$\mathrm{function\_4\_reaction\_8\_1}\,([\mathrm{AMPK\_pT172}], [\mathrm{mTORC1\_pS2448}], \mathrm{mTORC1\_pS2448\_dephos\_by\_AMPK\_pT172}) = \mathrm{mTORC1\_pS2448\_dephos\_by\_AMPK\_pT172} \cdot [\mathrm{mTORC1\_pS2448}] \cdot [\mathrm{AMPK\_pT172}] \tag{79}$$

8.9 Reaction `reaction_9`

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

Name reaction_9

Reaction equation

$$\emptyset \xrightarrow{\text{FoxO3a, AMPK\_pT172, AMPK\_pT172, FoxO3a}} \text{Mitophagy} \tag{80}$$

Modifiers

Table 30: Properties of each modifier.

Id	Name	SBO
`FoxO3a`	FoxO3a	
`AMPK_pT172`	AMPK_pT172	
`AMPK_pT172`	AMPK_pT172	
`FoxO3a`	FoxO3a	

Product

Table 31: Properties of each product.

Id	Name	SBO
`Mitophagy`	Mitophagy	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_9\_1}\,([\mathrm{AMPK\_pT172}], [\mathrm{FoxO3a}], \mathrm{mitophagy\_activ\_by\_FoxO3a\_n\_AMPK\_pT172}) \tag{81}$$

$$\begin{aligned}&\mathrm{function\_4\_reaction\_9\_1}\,([\mathrm{AMPK\_pT172}], [\mathrm{FoxO3a}],\\ &\quad \mathrm{mitophagy\_activ\_by\_FoxO3a\_n\_AMPK\_pT172})\\ &\quad = \mathrm{mitophagy\_activ\_by\_FoxO3a\_n\_AMPK\_pT172} \cdot [\mathrm{FoxO3a}] \cdot [\mathrm{AMPK\_pT172}]\end{aligned} \tag{82}$$

$$\begin{aligned}&\mathrm{function\_4\_reaction\_9\_1}\,([\mathrm{AMPK\_pT172}], [\mathrm{FoxO3a}],\\ &\quad \mathrm{mitophagy\_activ\_by\_FoxO3a\_n\_AMPK\_pT172})\\ &\quad = \mathrm{mitophagy\_activ\_by\_FoxO3a\_n\_AMPK\_pT172} \cdot [\mathrm{FoxO3a}] \cdot [\mathrm{AMPK\_pT172}]\end{aligned} \tag{83}$$

8.10 Reaction `reaction_10`

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

Name reaction_10

Reaction equation

$$\mathrm{Mitophagy} \xrightarrow{\text{mTORC1\_pS2448, Mitophagy, mTORC1\_pS2448}} \mathrm{Nil} \tag{84}$$

Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
`Mitophagy`	Mitophagy	

Modifiers

Table 33: Properties of each modifier.

Id	Name	SBO
`mTORC1_pS2448`	mTORC1_pS2448	
`Mitophagy`	Mitophagy	
`mTORC1_pS2448`	mTORC1_pS2448	

Product

Table 34: Properties of each product.

Id	Name	SBO
`Nil`	Nil	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{vol}\,(\text{Cell}) \cdot \text{function\_4\_reaction\_10\_1}\,([\text{Mitophagy}], [\text{mTORC1\_pS2448}], \text{mitophagy\_inactiv\_by\_mTORC1\_pS2448}) \tag{85}$$

$$\text{function\_4\_reaction\_10\_1}\,([\text{Mitophagy}], [\text{mTORC1\_pS2448}], \text{mitophagy\_inactiv\_by\_mTORC1\_pS2448}) = \text{mitophagy\_inactiv\_by\_mTORC1\_pS2448} \cdot [\text{Mitophagy}] \cdot [\text{mTORC1\_pS2448}] \tag{86}$$

$$\text{function\_4\_reaction\_10\_1}\,([\text{Mitophagy}], [\text{mTORC1\_pS2448}], \text{mitophagy\_inactiv\_by\_mTORC1\_pS2448}) = \text{mitophagy\_inactiv\_by\_mTORC1\_pS2448} \cdot [\text{Mitophagy}] \cdot [\text{mTORC1\_pS2448}] \tag{87}$$

8.11 Reaction `reaction_11`

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

Name reaction_11

Reaction equation

$$\text{FoxO3a} \xrightarrow{\text{Akt\_pS473, Akt\_pS473, FoxO3a}} \text{FoxO3a\_pS253} \tag{88}$$

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
`FoxO3a`	FoxO3a	

Modifiers

Table 36: Properties of each modifier.

Id	Name	SBO
Akt_pS473	Akt_pS473	
Akt_pS473	Akt_pS473	
FoxO3a	FoxO3a	

Product

Table 37: Properties of each product.

Id	Name	SBO
FoxO3a_pS253	FoxO3a_pS253	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_11\_1}\,([\mathrm{Akt\_pS473}], [\mathrm{FoxO3a}], \mathrm{FoxO3a\_phos\_by\_Akt\_pS473}) \tag{89}$$

$$\mathrm{function\_4\_reaction\_11\_1}\,([\mathrm{Akt\_pS473}], [\mathrm{FoxO3a}], \mathrm{FoxO3a\_phos\_by\_Akt\_pS473}) = \mathrm{FoxO3a\_phos\_by\_Akt\_pS473} \cdot [\mathrm{FoxO3a}] \cdot [\mathrm{Akt\_pS473}] \tag{90}$$

$$\mathrm{function\_4\_reaction\_11\_1}\,([\mathrm{Akt\_pS473}], [\mathrm{FoxO3a}], \mathrm{FoxO3a\_phos\_by\_Akt\_pS473}) = \mathrm{FoxO3a\_phos\_by\_Akt\_pS473} \cdot [\mathrm{FoxO3a}] \cdot [\mathrm{Akt\_pS473}] \tag{91}$$

8.12 Reaction reaction_12

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

Name reaction_12

Reaction equation

$$\mathrm{FoxO3a\_pS253} \xrightarrow{\mathrm{JNK\_pT183,\ FoxO3a\_pS253,\ JNK\_pT183}} \mathrm{FoxO3a} \tag{92}$$

Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
FoxO3a_pS253	FoxO3a_pS253	

Modifiers

Table 39: Properties of each modifier.

Id	Name	SBO
JNK_pT183	JNK_pT183	
FoxO3a_pS253	FoxO3a_pS253	
JNK_pT183	JNK_pT183	

Product

Table 40: Properties of each product.

Id	Name	SBO
FoxO3a	FoxO3a	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_12\_1}\,([\mathrm{FoxO3a\_pS253}], \mathrm{FoxO3a\_phos\_by\_JNK\_pT183}, [\mathrm{JNK\_pT183}]) \tag{93}$$

$$\mathrm{function\_4\_reaction\_12\_1}\,([\mathrm{FoxO3a\_pS253}], \mathrm{FoxO3a\_phos\_by\_JNK\_pT183}, [\mathrm{JNK\_pT183}]) = \mathrm{FoxO3a\_phos\_by\_JNK\_pT183} \cdot [\mathrm{FoxO3a\_pS253}] \cdot [\mathrm{JNK\_pT183}] \tag{94}$$

$$\mathrm{function\_4\_reaction\_12\_1}\,([\mathrm{FoxO3a\_pS253}], \mathrm{FoxO3a\_phos\_by\_JNK\_pT183}, [\mathrm{JNK\_pT183}]) = \mathrm{FoxO3a\_phos\_by\_JNK\_pT183} \cdot [\mathrm{FoxO3a\_pS253}] \cdot [\mathrm{JNK\_pT183}] \tag{95}$$

8.13 Reaction reaction_13

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

Name reaction_13

Reaction equation

$$\text{FoxO3a\_pS253} \xrightarrow{\text{FoxO3a\_pS253}} \text{Nil} \tag{96}$$

Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
`FoxO3a_pS253`	FoxO3a_pS253	

Modifier

Table 42: Properties of each modifier.

Id	Name	SBO
`FoxO3a_pS253`	FoxO3a_pS253	

Product

Table 43: Properties of each product.

Id	Name	SBO
`Nil`	Nil	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{vol}(\text{Cell}) \cdot \text{FoxO3a\_pS253\_degrad} \cdot [\text{FoxO3a\_pS253}] \tag{97}$$

8.14 Reaction `reaction_14`

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

Name reaction_14

Reaction equation

$$\emptyset \longrightarrow \text{FoxO3a} \tag{98}$$

Product

Table 44: Properties of each product.

Id	Name	SBO
FoxO3a	FoxO3a	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{function\_2}\left(\mathrm{FoxO3a\_synthesis}\right) \tag{99}$$

$$\mathrm{function\_2}\left(\mathrm{v}\right) = \mathrm{v} \tag{100}$$

$$\mathrm{function\_2}\left(\mathrm{v}\right) = \mathrm{v} \tag{101}$$

8.15 Reaction reaction_15

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

Name reaction_15

Reaction equation

$$\emptyset \xrightarrow{\text{DNA\_damage, FoxO3a, DNA\_damage, FoxO3a}} \text{CDKN1A} \tag{102}$$

Modifiers

Table 45: Properties of each modifier.

Id	Name	SBO
DNA_damage	DNA_damage	
FoxO3a	FoxO3a	
DNA_damage	DNA_damage	
FoxO3a	FoxO3a	

Product

Table 46: Properties of each product.

Id	Name	SBO
CDKN1A	CDKN1A	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_15\_1}\,(\mathrm{CDKN1A\_transcr\_by\_FoxO3a\_n\_DNA\_damage}, [\mathrm{DNA\_damage}], [\mathrm{FoxO3a}]) \tag{103}$$

$$\mathrm{function\_4\_reaction\_15\_1}\,(\mathrm{CDKN1A\_transcr\_by\_FoxO3a\_n\_DNA\_damage}, [\mathrm{DNA\_damage}], [\mathrm{FoxO3a}]) = \mathrm{CDKN1A\_transcr\_by\_FoxO3a\_n\_DNA\_damage} \cdot [\mathrm{DNA\_damage}] \cdot [\mathrm{FoxO3a}] \tag{104}$$

$$\mathrm{function\_4\_reaction\_15\_1}\,(\mathrm{CDKN1A\_transcr\_by\_FoxO3a\_n\_DNA\_damage}, [\mathrm{DNA\_damage}], [\mathrm{FoxO3a}]) = \mathrm{CDKN1A\_transcr\_by\_FoxO3a\_n\_DNA\_damage} \cdot [\mathrm{DNA\_damage}] \cdot [\mathrm{FoxO3a}] \tag{105}$$

8.16 Reaction `reaction_16`

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

Name reaction_16

Reaction equation

$$\mathrm{CDKN1A} \xrightarrow{\mathrm{Akt\_pS473,\ Akt\_pS473,\ CDKN1A}} \mathrm{Nil} \tag{106}$$

Reactant

Table 47: Properties of each reactant.

Id	Name	SBO
`CDKN1A`	CDKN1A	

Modifiers

Table 48: Properties of each modifier.

Id	Name	SBO
`Akt_pS473`	Akt_pS473	
`Akt_pS473`	Akt_pS473	
`CDKN1A`	CDKN1A	

Product

Table 49: Properties of each product.

Id	Name	SBO
Nil	Nil	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \text{vol}\,(\text{Cell}) \cdot \text{function\_4\_reaction\_16\_1}\,([\text{Akt\_pS473}], [\text{CDKN1A}], \text{CDKN1A\_inactiv\_by\_Akt\_pS473}) \tag{107}$$

$$\text{function\_4\_reaction\_16\_1}\,([\text{Akt\_pS473}], [\text{CDKN1A}], \text{CDKN1A\_inactiv\_by\_Akt\_pS473}) = \text{CDKN1A\_inactiv\_by\_Akt\_pS473} \cdot [\text{CDKN1A}] \cdot [\text{Akt\_pS473}] \tag{108}$$

$$\text{function\_4\_reaction\_16\_1}\,([\text{Akt\_pS473}], [\text{CDKN1A}], \text{CDKN1A\_inactiv\_by\_Akt\_pS473}) = \text{CDKN1A\_inactiv\_by\_Akt\_pS473} \cdot [\text{CDKN1A}] \cdot [\text{Akt\_pS473}] \tag{109}$$

8.17 Reaction `reaction_17`

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

Name reaction_17

Reaction equation

$$\emptyset \xrightarrow{\text{DNA\_damage, FoxO3a, DNA\_damage, FoxO3a}} \text{CDKN1B} \tag{110}$$

Modifiers

Table 50: Properties of each modifier.

Id	Name	SBO
DNA_damage	DNA_damage	
FoxO3a	FoxO3a	
DNA_damage	DNA_damage	
FoxO3a	FoxO3a	

Product

Table 51: Properties of each product.

Id	Name	SBO
CDKN1B	CDKN1B	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_17\_1}\,(\mathrm{CDKN1B\_transcr\_by\_FoxO3a\_n\_DNA\_damage}, [\mathrm{DNA\_damage}], [\mathrm{FoxO3a}]) \tag{111}$$

$$\mathrm{function\_4\_reaction\_17\_1}\,(\mathrm{CDKN1B\_transcr\_by\_FoxO3a\_n\_DNA\_damage}, [\mathrm{DNA\_damage}], [\mathrm{FoxO3a}]) = \mathrm{CDKN1B\_transcr\_by\_FoxO3a\_n\_DNA\_damage} \cdot [\mathrm{DNA\_damage}] \cdot [\mathrm{FoxO3a}] \tag{112}$$

$$\mathrm{function\_4\_reaction\_17\_1}\,(\mathrm{CDKN1B\_transcr\_by\_FoxO3a\_n\_DNA\_damage}, [\mathrm{DNA\_damage}], [\mathrm{FoxO3a}]) = \mathrm{CDKN1B\_transcr\_by\_FoxO3a\_n\_DNA\_damage} \cdot [\mathrm{DNA\_damage}] \cdot [\mathrm{FoxO3a}] \tag{113}$$

8.18 Reaction reaction_18

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

Name reaction_18

Reaction equation

$$\mathrm{CDKN1B} \xrightarrow{\mathrm{Akt\_pS473},\ \mathrm{Akt\_pS473},\ \mathrm{CDKN1B}} \mathrm{Nil} \tag{114}$$

Reactant

Table 52: Properties of each reactant.

Id	Name	SBO
CDKN1B	CDKN1B	

Modifiers

Table 53: Properties of each modifier.

Id	Name	SBO
Akt_pS473	Akt_pS473	
Akt_pS473	Akt_pS473	
CDKN1B	CDKN1B	

Product

Table 54: Properties of each product.

Id	Name	SBO
Nil	Nil	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_18\_1}\,([\mathrm{Akt\_pS473}], [\mathrm{CDKN1B}], \mathrm{CDKN1B\_inactiv\_by\_Akt\_pS473}) \tag{115}$$

$$\mathrm{function\_4\_reaction\_18\_1}\,([\mathrm{Akt\_pS473}], [\mathrm{CDKN1B}], \mathrm{CDKN1B\_inactiv\_by\_Akt\_pS473}) = \mathrm{CDKN1B\_inactiv\_by\_Akt\_pS473} \cdot [\mathrm{CDKN1B}] \cdot [\mathrm{Akt\_pS473}] \tag{116}$$

$$\mathrm{function\_4\_reaction\_18\_1}\,([\mathrm{Akt\_pS473}], [\mathrm{CDKN1B}], \mathrm{CDKN1B\_inactiv\_by\_Akt\_pS473}) = \mathrm{CDKN1B\_inactiv\_by\_Akt\_pS473} \cdot [\mathrm{CDKN1B}] \cdot [\mathrm{Akt\_pS473}] \tag{117}$$

8.19 Reaction reaction_19

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

Name reaction_19

Reaction equation

$$\emptyset \xrightarrow{\text{Irradiation, Irradiation}} \mathrm{DNA\_damage} \tag{118}$$

Modifiers

Table 55: Properties of each modifier.

Id	Name	SBO
Irradiation	Irradiation	
Irradiation	Irradiation	

Product

Table 56: Properties of each product.

Id	Name	SBO
DNA_damage	DNA_damage	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{function\_4\_reaction\_19\_1}\left(\mathrm{DNA\_damaged\_by\_irradiation}, [\mathrm{Irradiation}]\right) \quad (119)$$

$$\begin{aligned} &\mathrm{function\_4\_reaction\_19\_1}\left(\mathrm{DNA\_damaged\_by\_irradiation}, [\mathrm{Irradiation}]\right) \\ &\quad = \mathrm{DNA\_damaged\_by\_irradiation} \cdot [\mathrm{Irradiation}] \end{aligned} \quad (120)$$

$$\begin{aligned} &\mathrm{function\_4\_reaction\_19\_1}\left(\mathrm{DNA\_damaged\_by\_irradiation}, [\mathrm{Irradiation}]\right) \\ &\quad = \mathrm{DNA\_damaged\_by\_irradiation} \cdot [\mathrm{Irradiation}] \end{aligned} \quad (121)$$

8.20 Reaction reaction_20

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

Name reaction_20

Reaction equation

$$\emptyset \xrightarrow{\mathrm{ROS},\ \mathrm{ROS}} \mathrm{DNA\_damage} \quad (122)$$

Modifiers

Table 57: Properties of each modifier.

Id	Name	SBO
ROS	ROS	
ROS	ROS	

Product

Table 58: Properties of each product.

Id	Name	SBO
DNA_damage	DNA_damage	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{function\_4\_reaction\_20\_1}\left(\mathrm{DNA\_damaged\_by\_ROS}, [\mathrm{ROS}]\right) \tag{123}$$

$$\mathrm{function\_4\_reaction\_20\_1}\left(\mathrm{DNA\_damaged\_by\_ROS}, [\mathrm{ROS}]\right) = \mathrm{DNA\_damaged\_by\_ROS} \cdot [\mathrm{ROS}] \tag{124}$$

$$\mathrm{function\_4\_reaction\_20\_1}\left(\mathrm{DNA\_damaged\_by\_ROS}, [\mathrm{ROS}]\right) = \mathrm{DNA\_damaged\_by\_ROS} \cdot [\mathrm{ROS}] \tag{125}$$

8.21 Reaction reaction_21

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

Name reaction_21

Reaction equation

$$\mathrm{DNA\_damage} \xrightarrow{\mathrm{DNA\_damage}} \mathrm{Nil} \tag{126}$$

Reactant

Table 59: Properties of each reactant.

Id	Name	SBO
DNA_damage	DNA_damage	

Modifier

Table 60: Properties of each modifier.

Id	Name	SBO
DNA_damage	DNA_damage	

Product

Table 61: Properties of each product.

Id	Name	SBO
Nil	Nil	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{DNA\_repair} \cdot [\mathrm{DNA\_damage}] \tag{127}$$

8.22 Reaction reaction_22

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

Name reaction_22

Reaction equation

$$\emptyset \xrightarrow{\text{Mito\_membr\_pot\_new, Mito\_membr\_pot\_new}} \mathrm{ROS} \tag{128}$$

Modifiers

Table 62: Properties of each modifier.

Id	Name	SBO
Mito_membr_pot_new	Mito_membr_pot_new	
Mito_membr_pot_new	Mito_membr_pot_new	

Product

Table 63: Properties of each product.

Id	Name	SBO
ROS	ROS	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_22\_1}\,([\mathrm{Mito\_membr\_pot\_new}], \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_new}) \tag{129}$$

$$\mathrm{function\_4\_reaction\_22\_1}\,([\mathrm{Mito\_membr\_pot\_new}], \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_new}) = \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_new} \cdot [\mathrm{Mito\_membr\_pot\_new}] \tag{130}$$

$$\mathrm{function\_4\_reaction\_22\_1}\,([\mathrm{Mito\_membr\_pot\_new}], \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_new}) = \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_new} \cdot [\mathrm{Mito\_membr\_pot\_new}] \tag{131}$$

8.23 Reaction reaction_23

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

Name reaction_23

Reaction equation

$$\emptyset \xrightarrow{\mathrm{Mito\_membr\_pot\_old},\ \mathrm{Mito\_membr\_pot\_old}} \mathrm{ROS} \tag{132}$$

Modifiers

Table 64: Properties of each modifier.

Id	Name	SBO
Mito_membr_pot_old	Mito_membr_pot_old	
Mito_membr_pot_old	Mito_membr_pot_old	

Product

Table 65: Properties of each product.

Id	Name	SBO
ROS	ROS	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_23\_1}\,([\mathrm{Mito\_membr\_pot\_old}], \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_old}) \tag{133}$$

$$\mathrm{function\_4\_reaction\_23\_1}\,([\mathrm{Mito\_membr\_pot\_old}], \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_old}) = \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_old} \cdot [\mathrm{Mito\_membr\_pot\_old}] \tag{134}$$

$$\mathrm{function\_4\_reaction\_23\_1}\,([\mathrm{Mito\_membr\_pot\_old}], \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_old}) = \mathrm{ROS\_prod\_by\_Mito\_membr\_pot\_old} \cdot [\mathrm{Mito\_membr\_pot\_old}] \tag{135}$$

8.24 Reaction reaction_24

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

Name reaction_24

Reaction equation

$$\mathrm{ROS} \xrightarrow{\mathrm{ROS}} \mathrm{Nil} \tag{136}$$

Reactant

Table 66: Properties of each reactant.

Id	Name	SBO
ROS	ROS	

Modifier

Table 67: Properties of each modifier.

Id	Name	SBO
ROS	ROS	

Product

Table 68: Properties of each product.

Id	Name	SBO
Nil	Nil	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \text{vol}\,(\text{Cell}) \cdot \text{ROS\_turnover} \cdot [\text{ROS}] \tag{137}$$

8.25 Reaction reaction_25

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

Name reaction_25

Reaction equation

$$\text{JNK} \xrightarrow{\text{ROS, JNK, ROS}} \text{JNK\_pT183} \tag{138}$$

Reactant

Table 69: Properties of each reactant.

Id	Name	SBO
JNK	JNK	

Modifiers

Table 70: Properties of each modifier.

Id	Name	SBO
ROS	ROS	

Id	Name	SBO
JNK	JNK	
ROS	ROS	

Product

Table 71: Properties of each product.

Id	Name	SBO
JNK_pT183	JNK_pT183	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_25\_1}\,([\mathrm{JNK}], \mathrm{JNK\_activ\_by\_ROS}, [\mathrm{ROS}]) \tag{139}$$

$$\begin{aligned} &\mathrm{function\_4\_reaction\_25\_1}\,([\mathrm{JNK}], \mathrm{JNK\_activ\_by\_ROS}, [\mathrm{ROS}]) \\ &\quad = \mathrm{JNK\_activ\_by\_ROS} \cdot [\mathrm{JNK}] \cdot [\mathrm{ROS}] \end{aligned} \tag{140}$$

$$\begin{aligned} &\mathrm{function\_4\_reaction\_25\_1}\,([\mathrm{JNK}], \mathrm{JNK\_activ\_by\_ROS}, [\mathrm{ROS}]) \\ &\quad = \mathrm{JNK\_activ\_by\_ROS} \cdot [\mathrm{JNK}] \cdot [\mathrm{ROS}] \end{aligned} \tag{141}$$

8.26 Reaction reaction_26

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

Name reaction_26

Reaction equation

$$\mathrm{JNK\_pT183} \xrightarrow{\mathrm{JNK\_pT183}} \mathrm{JNK} \tag{142}$$

Reactant

Table 72: Properties of each reactant.

Id	Name	SBO
JNK_pT183	JNK_pT183	

Modifier

Table 73: Properties of each modifier.

Id	Name	SBO
JNK_pT183	JNK_pT183	

Product

Table 74: Properties of each product.

Id	Name	SBO
JNK	JNK	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{JNK\_pT183\_inactiv} \cdot [\mathrm{JNK\_pT183}] \tag{143}$$

8.27 Reaction reaction_27

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

Name reaction_27

Reaction equation

$$\emptyset \xrightarrow{\mathrm{ROS},\ \mathrm{ROS}} \mathrm{SA\_beta\_gal} \tag{144}$$

Modifiers

Table 75: Properties of each modifier.

Id	Name	SBO
ROS	ROS	
ROS	ROS	

Product

Table 76: Properties of each product.

Id	Name	SBO
SA_beta_gal	SA_beta_gal	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \text{vol}(\text{Cell}) \cdot \text{function\_4\_reaction\_27\_1}([\text{ROS}], \text{sen\_ass\_beta\_gal\_inc\_by\_ROS}) \quad (145)$$

$$\begin{aligned} &\text{function\_4\_reaction\_27\_1}([\text{ROS}], \text{sen\_ass\_beta\_gal\_inc\_by\_ROS}) \\ &\quad = \text{sen\_ass\_beta\_gal\_inc\_by\_ROS} \cdot [\text{ROS}] \end{aligned} \quad (146)$$

$$\begin{aligned} &\text{function\_4\_reaction\_27\_1}([\text{ROS}], \text{sen\_ass\_beta\_gal\_inc\_by\_ROS}) \\ &\quad = \text{sen\_ass\_beta\_gal\_inc\_by\_ROS} \cdot [\text{ROS}] \end{aligned} \quad (147)$$

8.28 Reaction reaction_28

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

Name reaction_28

Reaction equation

$$\emptyset \xrightarrow{\text{Mitophagy, Mitophagy}} \text{SA\_beta\_gal} \quad (148)$$

Modifiers

Table 77: Properties of each modifier.

Id	Name	SBO
Mitophagy	Mitophagy	
Mitophagy	Mitophagy	

Product

Table 78: Properties of each product.

Id	Name	SBO
SA_beta_gal	SA_beta_gal	

Id	Name	SBO

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{function\_4\_reaction\_28\_1}\left(\left[\mathrm{Mitophagy}\right], \mathrm{sen\_ass\_beta\_gal\_inc\_by\_Mitophagy}\right) \tag{149}$$

$$\begin{aligned}&\mathrm{function\_4\_reaction\_28\_1}\left(\left[\mathrm{Mitophagy}\right], \mathrm{sen\_ass\_beta\_gal\_inc\_by\_Mitophagy}\right)\\ &\quad = \mathrm{sen\_ass\_beta\_gal\_inc\_by\_Mitophagy} \cdot \left[\mathrm{Mitophagy}\right]\end{aligned} \tag{150}$$

$$\begin{aligned}&\mathrm{function\_4\_reaction\_28\_1}\left(\left[\mathrm{Mitophagy}\right], \mathrm{sen\_ass\_beta\_gal\_inc\_by\_Mitophagy}\right)\\ &\quad = \mathrm{sen\_ass\_beta\_gal\_inc\_by\_Mitophagy} \cdot \left[\mathrm{Mitophagy}\right]\end{aligned} \tag{151}$$

8.29 Reaction `reaction_29`

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

Name reaction_29

Reaction equation

$$\mathrm{SA\_beta\_gal} \xrightarrow{\mathrm{SA\_beta\_gal}} \emptyset \tag{152}$$

Reactant

Table 79: Properties of each reactant.

Id	Name	SBO
`SA_beta_gal`	SA_beta_gal	

Modifier

Table 80: Properties of each modifier.

Id	Name	SBO
`SA_beta_gal`	SA_beta_gal	

Kinetic Law

Derived unit contains undeclared units

$$v_{29} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{sen\_ass\_beta\_gal\_dec} \cdot [\mathrm{SA\_beta\_gal}] \tag{153}$$

8.30 Reaction `reaction_30`

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

Name reaction_30

Reaction equation

$$\mathrm{Mito\_mass\_turnover} \xrightarrow{\mathrm{mTORC1\_pS2448,\ Mito\_mass\_turnover,\ mTORC1\_pS2448}} \mathrm{Mito\_mass\_new} \tag{154}$$

Reactant

Table 81: Properties of each reactant.

Id	Name	SBO
`Mito_mass_turnover`	Mito_mass_turnover	

Modifiers

Table 82: Properties of each modifier.

Id	Name	SBO
`mTORC1_pS2448`	mTORC1_pS2448	
`Mito_mass_turnover`	Mito_mass_turnover	
`mTORC1_pS2448`	mTORC1_pS2448	

Product

Table 83: Properties of each product.

Id	Name	SBO
`Mito_mass_new`	Mito_mass_new	

Kinetic Law

Derived unit contains undeclared units

$$v_{30} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_30\_1}\,([\mathrm{Mito\_mass\_turnover}], [\mathrm{mTORC1\_pS2448}], \mathrm{mito\_biogenesis\_by\_mTORC1\_pS2448}) \tag{155}$$

$$\mathrm{function\_4\_reaction\_30\_1}\,([\mathrm{Mito\_mass\_turnover}], [\mathrm{mTORC1\_pS2448}], \mathrm{mito\_biogenesis\_by\_mTORC1\_pS2448}) = \mathrm{mito\_biogenesis\_by\_mTORC1\_pS2448} \cdot [\mathrm{Mito\_mass\_turnover}] \cdot [\mathrm{mTORC1\_pS2448}] \tag{156}$$

$$\mathrm{function\_4\_reaction\_30\_1}\,([\mathrm{Mito\_mass\_turnover}], [\mathrm{mTORC1\_pS2448}], \mathrm{mito\_biogenesis\_by\_mTORC1\_pS2448}) = \mathrm{mito\_biogenesis\_by\_mTORC1\_pS2448} \cdot [\mathrm{Mito\_mass\_turnover}] \cdot [\mathrm{mTORC1\_pS2448}] \tag{157}$$

8.31 Reaction `reaction_31`

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

Name reaction_31

Reaction equation

$$\mathrm{Mito\_mass\_turnover} \xrightarrow{\mathrm{mTORC1\_pS2448,\ Mito\_mass\_turnover,\ mTORC1\_pS2448}} \mathrm{Mito\_mass\_new} \tag{158}$$

Reactant

Table 84: Properties of each reactant.

Id	Name	SBO
`Mito_mass_turnover`	Mito_mass_turnover	

Modifiers

Table 85: Properties of each modifier.

Id	Name	SBO
`mTORC1_pS2448`	mTORC1_pS2448	
`Mito_mass_turnover`	Mito_mass_turnover	

Id	Name	SBO
mTORC1_pS2448	mTORC1_pS2448	

Product

Table 86: Properties of each product.

Id	Name	SBO
Mito_mass_new	Mito_mass_new	

Kinetic Law

Derived unit contains undeclared units

$$v_{31} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_31\_1}\,([\mathrm{Mito\_mass\_turnover}], [\mathrm{mTORC1\_pS2448}], \mathrm{mito\_biogenesis\_by\_AMPK\_pT172}) \tag{159}$$

$$\mathrm{function\_4\_reaction\_31\_1}\,([\mathrm{Mito\_mass\_turnover}], [\mathrm{mTORC1\_pS2448}], \mathrm{mito\_biogenesis\_by\_AMPK\_pT172}) = \mathrm{mito\_biogenesis\_by\_AMPK\_pT172} \cdot [\mathrm{Mito\_mass\_turnover}] \cdot [\mathrm{mTORC1\_pS2448}] \tag{160}$$

$$\mathrm{function\_4\_reaction\_31\_1}\,([\mathrm{Mito\_mass\_turnover}], [\mathrm{mTORC1\_pS2448}], \mathrm{mito\_biogenesis\_by\_AMPK\_pT172}) = \mathrm{mito\_biogenesis\_by\_AMPK\_pT172} \cdot [\mathrm{Mito\_mass\_turnover}] \cdot [\mathrm{mTORC1\_pS2448}] \tag{161}$$

8.32 Reaction reaction_32

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

Name reaction_32

Reaction equation

$$\mathrm{Mito\_mass\_new} \xrightarrow{\mathrm{Mitophagy,\ Mito\_mass\_new,\ Mitophagy}} \mathrm{Mito\_mass\_turnover} \tag{162}$$

Reactant

Table 87: Properties of each reactant.

Id	Name	SBO
Mito_mass_new	Mito_mass_new	

Modifiers

Table 88: Properties of each modifier.

Id	Name	SBO
Mitophagy	Mitophagy	
Mito_mass_new	Mito_mass_new	
Mitophagy	Mitophagy	

Product

Table 89: Properties of each product.

Id	Name	SBO
Mito_mass_turnover	Mito_mass_turnover	

Kinetic Law

Derived unit contains undeclared units

$$v_{32} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_32\_1}\,([\mathrm{Mito\_mass\_new}], [\mathrm{Mitophagy}], \mathrm{mitophagy\_new}) \tag{163}$$

$$\begin{aligned} &\mathrm{function\_4\_reaction\_32\_1}\,([\mathrm{Mito\_mass\_new}], [\mathrm{Mitophagy}], \mathrm{mitophagy\_new}) \\ &\quad = \mathrm{mitophagy\_new} \cdot [\mathrm{Mito\_mass\_new}] \cdot [\mathrm{Mitophagy}] \end{aligned} \tag{164}$$

$$\begin{aligned} &\mathrm{function\_4\_reaction\_32\_1}\,([\mathrm{Mito\_mass\_new}], [\mathrm{Mitophagy}], \mathrm{mitophagy\_new}) \\ &\quad = \mathrm{mitophagy\_new} \cdot [\mathrm{Mito\_mass\_new}] \cdot [\mathrm{Mitophagy}] \end{aligned} \tag{165}$$

8.33 Reaction reaction_33

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

Name reaction_33

Reaction equation

$$\text{Mito\_mass\_old} \xrightarrow{\text{Mitophagy, Mito\_mass\_old, Mitophagy}} \text{Mito\_mass\_turnover} \tag{166}$$

Reactant

Table 90: Properties of each reactant.

Id	Name	SBO
`Mito_mass_old`	Mito_mass_old	

Modifiers

Table 91: Properties of each modifier.

Id	Name	SBO
`Mitophagy`	Mitophagy	
`Mito_mass_old`	Mito_mass_old	
`Mitophagy`	Mitophagy	

Product

Table 92: Properties of each product.

Id	Name	SBO
`Mito_mass_turnover`	Mito_mass_turnover	

Kinetic Law

Derived unit contains undeclared units

$$v_{33} = \text{vol}\,(\text{Cell}) \cdot \text{function\_4\_reaction\_33\_1}\,([\text{Mito\_mass\_old}], [\text{Mitophagy}], \text{mitophagy\_old}) \tag{167}$$

$$\begin{aligned}&\text{function\_4\_reaction\_33\_1}\,([\text{Mito\_mass\_old}], [\text{Mitophagy}], \text{mitophagy\_old})\\ &\quad = \text{mitophagy\_old} \cdot [\text{Mito\_mass\_old}] \cdot [\text{Mitophagy}]\end{aligned} \tag{168}$$

$$\begin{aligned}&\text{function\_4\_reaction\_33\_1}\,([\text{Mito\_mass\_old}], [\text{Mitophagy}], \text{mitophagy\_old})\\ &\quad = \text{mitophagy\_old} \cdot [\text{Mito\_mass\_old}] \cdot [\text{Mitophagy}]\end{aligned} \tag{169}$$

8.34 Reaction reaction_34

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

Name reaction_34

Reaction equation

$$\text{Mito\_mass\_new} \xrightarrow{\text{CDKN1A, CDKN1A, Mito\_mass\_new}} \text{Mito\_mass\_old} \tag{170}$$

Reactant

Table 93: Properties of each reactant.

Id	Name	SBO
Mito_mass_new	Mito_mass_new	

Modifiers

Table 94: Properties of each modifier.

Id	Name	SBO
CDKN1A	CDKN1A	
CDKN1A	CDKN1A	
Mito_mass_new	Mito_mass_new	

Product

Table 95: Properties of each product.

Id	Name	SBO
Mito_mass_old	Mito_mass_old	

Kinetic Law

Derived unit contains undeclared units

$$v_{34} = \text{vol}\left(\text{Cell}\right) \cdot \text{function\_4\_reaction\_34\_1}\left(\left[\text{CDKN1A}\right], \left[\text{Mito\_mass\_new}\right], \text{mito\_dysfunction}\right) \tag{171}$$

$$\begin{aligned} &\text{function\_4\_reaction\_34\_1}\left(\left[\text{CDKN1A}\right], \left[\text{Mito\_mass\_new}\right], \text{mito\_dysfunction}\right) \\ &\quad = \text{mito\_dysfunction} \cdot \left[\text{Mito\_mass\_new}\right] \cdot \left[\text{CDKN1A}\right] \end{aligned} \tag{172}$$

$$\begin{aligned}&\text{function\_4\_reaction\_34\_1}\left([\text{CDKN1A}], [\text{Mito\_mass\_new}], \text{mito\_dysfunction}\right)\\&\quad = \text{mito\_dysfunction} \cdot [\text{Mito\_mass\_new}] \cdot [\text{CDKN1A}]\end{aligned} \tag{173}$$

8.35 Reaction `reaction_35`

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

Name reaction_35

Reaction equation

$$\emptyset \xrightarrow{\text{Mito\_mass\_new, Mito\_mass\_new}} \text{Mito\_membr\_pot\_new} \tag{174}$$

Modifiers

Table 96: Properties of each modifier.

Id	Name	SBO
`Mito_mass_new`	Mito_mass_new	
`Mito_mass_new`	Mito_mass_new	

Product

Table 97: Properties of each product.

Id	Name	SBO
`Mito_membr_pot_new`	Mito_membr_pot_new	

Kinetic Law

Derived unit contains undeclared units

$$v_{35} = \text{vol}\left(\text{Cell}\right) \cdot \text{function\_4\_reaction\_35\_1}\left([\text{Mito\_mass\_new}], \text{mito\_membr\_pot\_new\_inc}\right) \tag{175}$$

$$\begin{aligned}&\text{function\_4\_reaction\_35\_1}\left([\text{Mito\_mass\_new}], \text{mito\_membr\_pot\_new\_inc}\right)\\&\quad = \text{mito\_membr\_pot\_new\_inc} \cdot [\text{Mito\_mass\_new}]\end{aligned} \tag{176}$$

$$\begin{aligned}&\text{function\_4\_reaction\_35\_1}\left([\text{Mito\_mass\_new}], \text{mito\_membr\_pot\_new\_inc}\right)\\&\quad = \text{mito\_membr\_pot\_new\_inc} \cdot [\text{Mito\_mass\_new}]\end{aligned} \tag{177}$$

8.36 Reaction reaction_36

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

Name reaction_36

Reaction equation

$$\emptyset \xrightarrow{\text{Mito\_mass\_old, Mito\_mass\_old}} \text{Mito\_membr\_pot\_old} \tag{178}$$

Modifiers

Table 98: Properties of each modifier.

Id	Name	SBO
Mito_mass_old	Mito_mass_old	
Mito_mass_old	Mito_mass_old	

Product

Table 99: Properties of each product.

Id	Name	SBO
Mito_membr_pot_old	Mito_membr_pot_old	

Kinetic Law

Derived unit contains undeclared units

$$v_{36} = \text{vol}(\text{Cell}) \cdot \text{function\_4\_reaction\_36\_1}([\text{Mito\_mass\_old}], \text{mito\_membr\_pot\_old\_inc}) \tag{179}$$

$$\begin{aligned} &\text{function\_4\_reaction\_36\_1}([\text{Mito\_mass\_old}], \text{mito\_membr\_pot\_old\_inc}) \\ &\quad = \text{mito\_membr\_pot\_old\_inc} \cdot [\text{Mito\_mass\_old}] \end{aligned} \tag{180}$$

$$\begin{aligned} &\text{function\_4\_reaction\_36\_1}([\text{Mito\_mass\_old}], \text{mito\_membr\_pot\_old\_inc}) \\ &\quad = \text{mito\_membr\_pot\_old\_inc} \cdot [\text{Mito\_mass\_old}] \end{aligned} \tag{181}$$

8.37 Reaction reaction_37

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

Name reaction_37

Reaction equation

$$\text{Mito\_membr\_pot\_new} \xrightarrow{\text{Mito\_membr\_pot\_new}} \text{Nil} \tag{182}$$

Reactant

Table 100: Properties of each reactant.

Id	Name	SBO
`Mito_membr_pot_new`	Mito_membr_pot_new	

Modifier

Table 101: Properties of each modifier.

Id	Name	SBO
`Mito_membr_pot_new`	Mito_membr_pot_new	

Product

Table 102: Properties of each product.

Id	Name	SBO
`Nil`	Nil	

Kinetic Law

Derived unit contains undeclared units

$$v_{37} = \text{vol}\,(\text{Cell}) \cdot \text{mito\_membr\_pot\_new\_dec} \cdot [\text{Mito\_membr\_pot\_new}] \tag{183}$$

8.38 Reaction `reaction_38`

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

Name reaction_38

Reaction equation

$$\text{Mito\_membr\_pot\_old} \xrightarrow{\text{Mito\_membr\_pot\_old}} \text{Nil} \tag{184}$$

Reactant

Table 103: Properties of each reactant.

Id	Name	SBO
Mito_membr_pot_old	Mito_membr_pot_old	

Modifier

Table 104: Properties of each modifier.

Id	Name	SBO
Mito_membr_pot_old	Mito_membr_pot_old	

Product

Table 105: Properties of each product.

Id	Name	SBO
Nil	Nil	

Kinetic Law

Derived unit contains undeclared units

$$v_{38} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{mito\_membr\_pot\_old\_dec} \cdot [\mathrm{Mito\_membr\_pot\_old}] \tag{185}$$

8.39 Reaction reaction_39

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

Name reaction_39

Reaction equation

$$\emptyset \xrightarrow{\text{ROS, ROS}} \text{IKKbeta} \tag{186}$$

Modifiers

Table 106: Properties of each modifier.

Id	Name	SBO
ROS	ROS	
ROS	ROS	

Product

Table 107: Properties of each product.

Id	Name	SBO
IKKbeta	IKKbeta	

Kinetic Law

Derived unit contains undeclared units

$$v_{39} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{function\_4\_reaction\_39\_1}\left(\mathrm{IKKbeta\_activ\_by\_ROS}, [\mathrm{ROS}]\right) \tag{187}$$

$$\mathrm{function\_4\_reaction\_39\_1}\left(\mathrm{IKKbeta\_activ\_by\_ROS}, [\mathrm{ROS}]\right) = \mathrm{IKKbeta\_activ\_by\_ROS} \cdot [\mathrm{ROS}] \tag{188}$$

$$\mathrm{function\_4\_reaction\_39\_1}\left(\mathrm{IKKbeta\_activ\_by\_ROS}, [\mathrm{ROS}]\right) = \mathrm{IKKbeta\_activ\_by\_ROS} \cdot [\mathrm{ROS}] \tag{189}$$

8.40 Reaction reaction_40

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

Name reaction_40

Reaction equation

$$\mathrm{IKKbeta} \xrightarrow{\mathrm{IKKbeta}} \mathrm{Nil} \tag{190}$$

Reactant

Table 108: Properties of each reactant.

Id	Name	SBO
IKKbeta	IKKbeta	

Modifier

Table 109: Properties of each modifier.

Id	Name	SBO
IKKbeta	IKKbeta	

Product

Table 110: Properties of each product.

Id	Name	SBO
Nil	Nil	

Kinetic Law

Derived unit contains undeclared units

$$v_{40} = \text{vol}\,(\text{Cell}) \cdot \text{IKKbeta\_inactiv} \cdot [\text{IKKbeta}] \tag{191}$$

8.41 Reaction reaction_41

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

Name reaction_41

Reaction equation

$$\text{mTORC1} \xrightarrow{\text{Amino\_Acids, IKKbeta, Amino\_Acids, IKKbeta, mTORC1}} \text{mTORC1\_pS2448} \tag{192}$$

Reactant

Table 111: Properties of each reactant.

Id	Name	SBO
mTORC1	mTORC1	

Modifiers

Table 112: Properties of each modifier.

Id	Name	SBO
Amino_Acids	Amino_Acids	
IKKbeta	IKKbeta	
Amino_Acids	Amino_Acids	
IKKbeta	IKKbeta	
mTORC1	mTORC1	

Product

Table 113: Properties of each product.

Id	Name	SBO
mTORC1_pS2448	mTORC1_pS2448	

Kinetic Law

Derived unit contains undeclared units

$$v_{41} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{function\_4\_reaction\_41\_1}\,([\mathrm{Amino\_Acids}], [\mathrm{IKKbeta}], [\mathrm{mTORC1}], \mathrm{mTORC1\_S2448\_phos\_by\_AA\_n\_IKKbeta}) \tag{193}$$

$$\mathrm{function\_4\_reaction\_41\_1}\,([\mathrm{Amino\_Acids}], [\mathrm{IKKbeta}], [\mathrm{mTORC1}], \mathrm{mTORC1\_S2448\_phos\_by\_AA\_n\_IKKbeta}) = \mathrm{mTORC1\_S2448\_phos\_by\_AA\_n\_IKKbeta} \cdot [\mathrm{mTORC1}] \cdot [\mathrm{Amino\_Acids}] \cdot [\mathrm{IKKbeta}] \tag{194}$$

$$\mathrm{function\_4\_reaction\_41\_1}\,([\mathrm{Amino\_Acids}], [\mathrm{IKKbeta}], [\mathrm{mTORC1}], \mathrm{mTORC1\_S2448\_phos\_by\_AA\_n\_IKKbeta}) = \mathrm{mTORC1\_S2448\_phos\_by\_AA\_n\_IKKbeta} \cdot [\mathrm{mTORC1}] \cdot [\mathrm{Amino\_Acids}] \cdot [\mathrm{IKKbeta}] \tag{195}$$

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 `Akt`

Name Akt

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in three reactions (as a reactant in `reaction_1` and as a product in `reaction_2` and as a modifier in `reaction_1`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Akt} = v_2 - v_1 \tag{196}$$

9.2 Species `Akt_pS473`

Name Akt_pS473

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in eleven reactions (as a reactant in `reaction_2` and as a product in `reaction_1` and as a modifier in `reaction_2`, `reaction_7`, `reaction_7`, `reaction_11`, `reaction_11`, `reaction_16`, `reaction_16`, `reaction_18`, `reaction_18`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Akt\_pS473} = v_1 - v_2 \tag{197}$$

9.3 Species `AMPK`

Name AMPK

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in four reactions (as a reactant in `reaction_3` and as a product in `reaction_4`, `reaction_5` and as a modifier in `reaction_3`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AMPK} = v_4 + v_5 - v_3 \tag{198}$$

9.4 Species `AMPK_pT172`

Name AMPK_pT172

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

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_8, reaction_8, reaction_9, reaction_9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AMPK\_pT172} = v_3 - v_4 - v_5 \tag{199}$$

9.5 Species mTORC1

Name mTORC1

Initial concentration $10\ \mathrm{dimensionless} \cdot \mathrm{dimensionless}^{-1}$

This species takes part in seven reactions (as a reactant in reaction_6, reaction_7, reaction_41 and as a product in reaction_8 and as a modifier in reaction_6, reaction_7, reaction_41).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mTORC1} = v_8 - v_6 - v_7 - v_{41} \tag{200}$$

9.6 Species mTORC1_pS2448

Name mTORC1_pS2448

Initial concentration $10\ \mathrm{dimensionless} \cdot \mathrm{dimensionless}^{-1}$

This species takes part in 13 reactions (as a reactant in reaction_8 and as a product in reaction_6, reaction_7, reaction_41 and as a modifier in reaction_2, reaction_2, reaction_8, reaction_10, reaction_10, reaction_30, reaction_30, reaction_31, reaction_31).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mTORC1\_pS2448} = v_6 + v_7 + v_{41} - v_8 \tag{201}$$

9.7 Species Mitophagy

Name Mitophagy

Initial concentration $10\ \mathrm{dimensionless} \cdot \mathrm{dimensionless}^{-1}$

This species takes part in nine reactions (as a reactant in reaction_10 and as a product in reaction_9 and as a modifier in reaction_10, reaction_28, reaction_28, reaction_32, reaction_32, reaction_33, reaction_33).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mitophagy} = v_9 - v_{10} \tag{202}$$

9.8 Species FoxO3a

Name FoxO3a

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in ten reactions (as a reactant in reaction_11 and as a product in reaction_12, reaction_14 and as a modifier in reaction_9, reaction_9, reaction_11, reaction_15, reaction_15, reaction_17, reaction_17).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{FoxO3a} = v_{12} + v_{14} - v_{11} \tag{203}$$

9.9 Species FoxO3a_pS253

Name FoxO3a_pS253

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in five reactions (as a reactant in reaction_12, reaction_13 and as a product in reaction_11 and as a modifier in reaction_12, reaction_13).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{FoxO3a\_pS253} = v_{11} - v_{12} - v_{13} \tag{204}$$

9.10 Species CDKN1A

Name CDKN1A

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in five reactions (as a reactant in reaction_16 and as a product in reaction_15 and as a modifier in reaction_16, reaction_34, reaction_34).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CDKN1A} = v_{15} - v_{16} \tag{205}$$

9.11 Species CDKN1B

Name CDKN1B

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CDKN1B} = v_{17} - v_{18} \tag{206}$$

9.12 Species JNK

Name JNK

Initial concentration 25 dimensionless · dimensionless^{-1}

This species takes part in three reactions (as a reactant in reaction_25 and as a product in reaction_26 and as a modifier in reaction_25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{JNK} = v_{26} - v_{25} \tag{207}$$

9.13 Species JNK_pT183

Name JNK_pT183

Initial concentration 10 dimensionless · dimensionless^{-1}

This species takes part in five reactions (as a reactant in reaction_26 and as a product in reaction_25 and as a modifier in reaction_12, reaction_12, reaction_26).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{JNK\_pT183} = v_{25} - v_{26} \tag{208}$$

9.14 Species ROS

Name ROS

Initial concentration 10 dimensionless · dimensionless^{-1}

This species takes part in twelve reactions (as a reactant in reaction_24 and as a product in reaction_22, reaction_23 and as a modifier in reaction_20, reaction_20, reaction_24, reaction_25, reaction_25, reaction_27, reaction_27, reaction_39, reaction_39).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ROS} = v_{22} + v_{23} - v_{24} \tag{209}$$

9.15 Species DNA_damage

Name DNA_damage

Initial concentration 1 dimensionless · dimensionless^{-1}

This species takes part in eight reactions (as a reactant in reaction_21 and as a product in reaction_19, reaction_20 and as a modifier in reaction_15, reaction_15, reaction_17, reaction_17, reaction_21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{DNA\_damage} = v_{19} + v_{20} - v_{21} \tag{210}$$

9.16 Species SA_beta_gal

Name SA_beta_gal

Initial concentration 0.81 dimensionless · dimensionless^{-1}

This species takes part in four reactions (as a reactant in reaction_29 and as a product in reaction_27, reaction_28 and as a modifier in reaction_29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{SA\_beta\_gal} = v_{27} + v_{28} - v_{29} \tag{211}$$

9.17 Species IKKbeta

Name IKKbeta

Initial concentration 10 dimensionless · dimensionless^{-1}

This species takes part in five reactions (as a reactant in reaction_40 and as a product in reaction_39 and as a modifier in reaction_40, reaction_41, reaction_41).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IKKbeta} = v_{39} - v_{40} \tag{212}$$

9.18 Species Mito_mass_new

Name Mito_mass_new

Initial concentration 1 dimensionless · dimensionless^{-1}

This species takes part in eight reactions (as a reactant in reaction_32, reaction_34 and as a product in reaction_30, reaction_31 and as a modifier in reaction_32, reaction_34, reaction_35, reaction_35).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mito\_mass\_new} = v_{30} + v_{31} - v_{32} - v_{34} \tag{213}$$

9.19 Species Mito_mass_old

Name Mito_mass_old

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in five reactions (as a reactant in reaction_33 and as a product in reaction_34 and as a modifier in reaction_33, reaction_36, reaction_36).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mito\_mass\_old} = v_{34} - v_{33} \tag{214}$$

9.20 Species Mito_mass_turnover

Name Mito_mass_turnover

Initial concentration 25 dimensionless · dimensionless^{-1}

This species takes part in six reactions (as a reactant in reaction_30, reaction_31 and as a product in reaction_32, reaction_33 and as a modifier in reaction_30, reaction_31).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Mito\_mass\_turnover} = v_{32} + v_{33} - v_{30} - v_{31} \tag{215}$$

9.21 Species Mito_membr_pot_new

Name Mito_membr_pot_new

Initial concentration 12.12 dimensionless · dimensionless^{-1}

This species takes part in seven reactions (as a reactant in reaction_37 and as a product in reaction_35 and as a modifier in reaction_4, reaction_4, reaction_22, reaction_22, reaction_37).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Mito\_membr\_pot\_new} = v_{35} - v_{37} \tag{216}$$

9.22 Species Mito_membr_pot_old

Name Mito_membr_pot_old

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in seven reactions (as a reactant in reaction_38 and as a product in reaction_36 and as a modifier in reaction_5, reaction_5, reaction_23, reaction_23, reaction_38).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Mito\_membr\_pot\_old} = v_{36} - v_{38} \tag{217}$$

9.23 Species Nil

Name Nil

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in nine reactions (as a product in reaction_10, reaction_13, reaction_16, reaction_18, reaction_21, reaction_24, reaction_37, reaction_38, reaction_40).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Nil} = v_{10} + v_{13} + v_{16} + v_{18} + v_{21} + v_{24} + v_{37} + v_{38} + v_{40} \tag{218}$$

9.24 Species Insulin

Name Insulin

Initial concentration 1 dimensionless · dimensionless^{-1}

Involved in rule Insulin

This species takes part in two reactions (as a modifier in reaction_1, reaction_1). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

9.25 Species Amino_Acids

Name Amino_Acids

Initial concentration 1 dimensionless · dimensionless^{-1}

Involved in rule Amino_Acids

This species takes part in six reactions (as a modifier in reaction_6, reaction_6, reaction_7, reaction_7, reaction_41, reaction_41). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

9.26 Species Irradiation

Name Irradiation

Initial concentration 1 dimensionless · dimensionless^{-1}

Involved in rule Irradiation

This species takes part in two reactions (as a modifier in reaction_19, reaction_19). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

9.27 Species DNA_damage_gammaH2AX_obs

Name DNA_damage_gammaH2AX_obs

Initial concentration 1 dimensionless · dimensionless^{-1}

Involved in rule DNA_damage_gammaH2AX_obs

One rule determines the species' quantity.

9.28 Species Akt_pS473_obs

Name Akt_pS473_obs

Initial concentration 10 dimensionless · dimensionless^{-1}

Involved in rule Akt_pS473_obs

One rule determines the species' quantity.

9.29 Species mTOR_pS2448_obs

Name mTOR_pS2448_obs

Initial concentration 10 dimensionless · dimensionless^{-1}

Involved in rule mTOR_pS2448_obs

One rule determines the species' quantity.

9.30 Species AMPK_pT172_obs

Name AMPK_pT172_obs

Initial concentration 10 dimensionless · dimensionless^{-1}

Involved in rule AMPK_pT172_obs

One rule determines the species' quantity.

9.31 Species CDKN1A_obs

Name CDKN1A_obs

Initial concentration 10 dimensionless · dimensionless^{-1}

Involved in rule CDKN1A_obs

One rule determines the species' quantity.

9.32 Species CDKN1B_obs

Name CDKN1B_obs

Initial concentration 10 dimensionless · dimensionless^{-1}

Involved in rule CDKN1B_obs

One rule determines the species' quantity.

9.33 Species FoxO3a_pS253_obs

Name FoxO3a_pS253_obs

Initial concentration 10 dimensionless · dimensionless^{-1}

Involved in rule FoxO3a_pS253_obs

One rule determines the species' quantity.

9.34 Species FoxO3a_total_obs

Name FoxO3a_total_obs

Initial concentration 20 dimensionless · dimensionless^{-1}

Involved in rule FoxO3a_total_obs

One rule determines the species' quantity.

9.35 Species Mito_Mass_obs

Name Mito_Mass_obs

Initial concentration 1 dimensionless · dimensionless^{-1}

Involved in rule Mito_Mass_obs

One rule determines the species' quantity.

9.36 Species Mito_Membr_Pot_obs

Name Mito_Membr_Pot_obs

Initial concentration 12.12 dimensionless · dimensionless^{-1}

Involved in rule Mito_Membr_Pot_obs

One rule determines the species' quantity.

9.37 Species Mitophagy_obs

Name Mitophagy_obs

Initial concentration 10 dimensionless · dimensionless^{-1}

Involved in rule Mitophagy_obs

One rule determines the species' quantity.

9.38 Species ROS_obs

Name ROS_obs

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

Involved in rule ROS_obs

One rule determines the species' quantity.

9.39 Species JNK_pT183_obs

Name JNK_pT183_obs

Initial concentration $10\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

Involved in rule JNK_pT183_obs

One rule determines the species' quantity.

9.40 Species SA_beta_gal_obs

Name SA_beta_gal_obs

Initial concentration $0.81\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

Involved in rule SA_beta_gal_obs

One rule determines the species' quantity.

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