

SBML Model Report

Model name: “Sonntag2012 - mTOR model - IRS dependent regulation of AMPK by insulin”



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 Chelliah¹ and Piero Dalle Pezze² at August twelveth 2015 at 10:12 p. m. and last time modified at August thirteenth 2015 at 11:54 a. m. Table 1 provides an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	39
events	0	constraints	0
reactions	26	function definitions	15
global parameters	37	unit definitions	3
rules	13	initial assignments	0

Model Notes

Sonntag2012 - mTOR model - IRS dependent regulation of AMPK by insulinTSC1-TSC2 complex has two states: 1)active (TSC1_TSC2_pS1387), regulated by AMPK_pT172; 2) inactive(TSC1_TSC2_pT1462)

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regulated by Akt_pT308. Particularly, mTORC1 is inhibited by TSC1_TSC2 in active state. AMPK is activated at T172 by the species IRS1_p activated by the insulin receptor upon insulin stimulation. Consequently, AMPK_pT172 is inhibited by mTORC1_pS2448 indirectly by the p70-S6K-negative feedback loop.

This model is described in the article: [A modelling-experimental approach reveals insulin receptor substrate \(IRS\)-dependent regulation of adenosine monophosphate-dependent kinase \(AMPK\) by insulin](#). Sonntag AG, Dalle Pezze P, Shanley DP, Thedieck K. FEBS J. 2012 Sep; 279(18): 3314-3328

Abstract:

Mammalian target of rapamycin (mTOR) kinase responds to growth factors, nutrients and cellular energy status and is a central controller of cellular growth. mTOR exists in two multiprotein complexes that are embedded into a complex signalling network. Adenosine monophosphate-dependent kinase (AMPK) is activated by energy deprivation and shuts off adenosine 5'-triphosphate (ATP)-consuming anabolic processes, in part via the inactivation of mTORC1. Surprisingly, we observed that AMPK not only responds to energy deprivation but can also be activated by insulin, and is further induced in mTORC1-deficient cells. We have recently modelled the mTOR network, covering both mTOR complexes and their insulin and nutrient inputs. In the present study we extended the network by an AMPK module to generate the to date most comprehensive data-driven dynamic AMPK-mTOR network model. In order to define the intersection via which AMPK is activated by the insulin network, we compared simulations for six different hypothetical model structures to our observed AMPK dynamics. Hypotheses ranking suggested that the most probable intersection between insulin and AMPK was the insulin receptor substrate (IRS) and that the effects of canonical IRS downstream cues on AMPK would be mediated via an mTORC1-driven negative-feedback loop. We tested these predictions experimentally in multiple set-ups, where we inhibited or induced players along the insulin-mTORC1 signalling axis and observed AMPK induction or inhibition. We confirmed the identified model and therefore report a novel connection within the insulin-mTOR-AMPK network: we conclude that AMPK is positively regulated by IRS and can be inhibited via the negative-feedback loop.

This model is hosted on [BioModels Database](#) and identified by: [BIOMD0000000580](#).

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

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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 60 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 m²

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	<input checked="" type="checkbox"/>	

3.1 Compartment Cell

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

Name Cell

4 Species

This model contains 39 species. The boundary condition of 13 of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 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
IR_beta	IR_beta	Cell	dimensionless dimensionless ⁻¹	· ☐	☐
IR_beta_pY1146	IR_beta_pY1146	Cell	dimensionless dimensionless ⁻¹	· ☐	☐
IR_beta-refractory	IR_beta-refractory	Cell	dimensionless dimensionless ⁻¹	· ☐	☐
IRS1	IRS1	Cell	dimensionless dimensionless ⁻¹	· ☐	☐
IRS1_p	IRS1_p	Cell	dimensionless dimensionless ⁻¹	· ☐	☐
IRS1_pS636	IRS1_pS636	Cell	dimensionless dimensionless ⁻¹	· ☐	☐
AMPK	AMPK	Cell	dimensionless dimensionless ⁻¹	· ☐	☐
AMPK_pT172	AMPK_pT172	Cell	dimensionless dimensionless ⁻¹	· ☐	☐
Akt_T308	Akt_T308	Cell	dimensionless dimensionless ⁻¹	· ☐	☐
Akt_pT308	Akt_pT308	Cell	dimensionless dimensionless ⁻¹	· ☐	☐

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
Akt_S473	Akt_S473	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
Akt_pS473	Akt_pS473	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
mTORC1	mTORC1	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
mTORC1_pS2448	mTORC1_pS2448	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
mTORC2	mTORC2	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
mTORC2_pS2481	mTORC2_pS2481	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
p70S6K	p70S6K	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
p70S6K_pT389	p70S6K_pT389	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
PRAS40_T246	PRAS40_T246	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
PRAS40_pT246	PRAS40_pT246	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
PRAS40_S183	PRAS40_S183	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
PRAS40_pS183	PRAS40_pS183	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖
TSC1_TSC2_pT1462	TSC1_TSC2_pT1462	Cell	dimensionless dimensionless ⁻¹	· ⊖	⊖

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
TSC1_TSC2_pS1387	TSC1_TSC2_pS1387	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input type="checkbox"/>
PI3K_variant	PI3K_variant	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input type="checkbox"/>
PI3K_variant_p	PI3K_variant_p	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input type="checkbox"/>
Insulin	Insulin	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>
AminoAcids	Amino_Acids	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>
IR_beta_pY1146_obs	IR_beta_pY1146_obs	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>
IRS1_pS636_obs	IRS1_pS636_obs	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>
AMPK_pT172_obs	AMPK_pT172_obs	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>
Akt_pT308_obs	Akt_pT308_obs	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>
Akt_pS473_obs	Akt_pS473_obs	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>
TSC1_TSC2_pS1387- _obs	TSC1_TSC2_pS1387_obs	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>
mTOR_pS2448_obs	mTOR_pS2448_obs	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>
mTOR_pS2481_obs	mTOR_pS2481_obs	Cell	dimensionless dimensionless ⁻¹	· <input type="checkbox"/>	<input checked="" type="checkbox"/>

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
p70S6K_pT389_obs	p70S6K_pT389_obs	Cell	dimensionless dimensionless ⁻¹	· ☐	☑
PRAS40_pT246_obs	PRAS40_pT246_obs	Cell	dimensionless dimensionless ⁻¹	· ☐	☑
PRAS40_pS183_obs	PRAS40_pS183_obs	Cell	dimensionless dimensionless ⁻¹	· ☐	☑

5 Parameters

This model contains 37 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
IR_beta- _phosphorylation- _by_Insulin	IR_beta- phosphorylation- _by_Insulin		0.124		✓
IR_beta- _pY1146- _dephosphorylation	IR_beta_pY1146- _dephosphorylation		0.396		✓
IR_beta- _ready	IR_beta_ready		0.053		✓
IRS1- _phosphorylation- _by_IR_beta- _pY1146	IRS1- phosphorylation- _by_IR_beta- _pY1146		0.005		✓
IRS1_p- _phosphorylation- _by_p70S6K- _pT389	IRS1_p- phosphorylation- _by_p70S6K- _pT389		1682.748		✓
IRS1_pS636- _dephosphorylation	IRS1_pS636- dephosphorylation		0.013		✓
AMPK_T172- _phosphorylation	AMPK_T172- phosphorylation		9.798		✓
AMPK_pT172- _dephosphorylation	AMPK_pT172- dephosphorylation		0.011		✓
Akt_pT308- _dephosphorylation	Akt_pT308- dephosphorylation		0.003		✓
Akt_pS473- _dephosphorylation	Akt_pS473- dephosphorylation		0.006		✓
Akt_S473- _phosphorylation- _by_mTORC2- _pS2481_n- _IRS1_p	Akt_S473- phosphorylation- _by_mTORC2- _pS2481_n- IRS1_p		13.144		✓
Akt_T308- _phosphorylation- _by_IRS1_p	Akt_T308- phosphorylation- _by_IRS1_p		6.918		✓

Id	Name	SBO	Value	Unit	Constant
mTORC1- _pS2448- _dephosphorylation- _by_TSC1- _TSC2_pS1387	mTORC1_pS2448- _dephosphorylation- by_TSC1_TSC2- _pS1387		0.011		✓
mTORC1- _S2448- _activation- _by_Amino- _Acids	mTORC1_S2448- _activation_by- _Amino_Acids		0.004		✓
mTORC2- _pS2481- _dephosphorylation	mTORC2_pS2481- _dephosphorylation		0.018		✓
mTORC2- _S2481- _phosphorylation- _phosphorylation- _by_PI3K- _variant_p	mTORC2_S2481- _phosphorylation- _phosphorylation- by_PI3K_variant_p		0.375		✓
p70S6K- _pT389- _dephosphorylation	p70S6K_pT389- _dephosphorylation		0.011		✓
p70S6K_T389- _phosphorylation- _by_mTORC1- _pS2448	p70S6K_T389- _phosphorylation- _by_mTORC1- _pS2448		0.002		✓
PRAS40- _pS183- _dephosphorylation	PRAS40_pS183- _dephosphorylation		2.330		✓
PRAS40- _pT246- _dephosphorylation	PRAS40_pT246- _dephosphorylation		1.605		✓
PRAS40_S183- _phosphorylation- _by_mTORC1- _pS2448	PRAS40_S183- _phosphorylation- _by_mTORC1- _pS2448		0.188		✓
PRAS40_T246- _phosphorylation- _by_Akt_pT308	PRAS40_T246- _phosphorylation- _by_Akt_pT308		0.138		✓

Id	Name	SBO	Value	Unit	Constant
TSC1_TSC2- _S1387- _phosphorylation- _by_AMPK- _pT172	TSC1_TSC2- _S1387- _phosphorylation- _by_AMPK_pT172		0.037		✓
TSC1_TSC2- _T1462- _phosphorylation- _by_Akt_pT308	TSC1_TSC2- _T1462- _phosphorylation- _by_Akt_pT308		0.018		✓
PI3K- _variant_p- _dephosphorylation	PI3K_variant_p- _dephosphorylation		10.000		✓
PI3K- _variant- _phosphorylation- _by_IR_beta- _pY1146	PI3K_variant- _phosphorylation- _by_IR_beta- _pY1146		0.010		✓
scale_IR- _beta_pY1146- _obs	scale_IR_beta- _pY1146_obs		1.000		✓
scale_IRS1- _pS636_obs	scale_IRS1_pS636- _obs		1.000		✓
scale_AMPK- _pT172_obs	scale_AMPK- _pT172_obs		1.000		✓
scale_Akt- _pT308_obs	scale_Akt_pT308- _obs		1.000		✓
scale_Akt- _pS473_obs	scale_Akt_pS473- _obs		1.000		✓
scale_TSC1- _TSC2_pS1387- _obs	scale_TSC1_TSC2- _pS1387_obs		1.000		✓
scale_mTOR- _pS2448_obs	scale_mTOR- _pS2448_obs		1.000		✓
scale_mTOR- _pS2481_obs	scale_mTOR- _pS2481_obs		1.000		✓
scale- _p70S6K- _pT389_obs	scale_p70S6K- _pT389_obs		1.000		✓
scale- _PRAS40- _pT246_obs	scale_PRAS40- _pT246_obs		1.000		✓

Id	Name	SBO	Value	Unit	Constant
scale- _PRAS40- _pS183_obs	scale_PRAS40- _pS183_obs		1.000		<input checked="" type="checkbox"/>

6 Function definitions

This is an overview of 15 function definitions.

6.1 Function definition [function_4_IR_beta_phosphorylation_by_Insulin](#)

Name function_4_IR_beta_phosphorylation_by_Insulin

Arguments [IR_beta], IR_beta_phosphorylation_by_Insulin, [Insulin]

Mathematical Expression

$$\text{IR_beta_phosphorylation_by_Insulin} \cdot [\text{IR_beta}] \cdot [\text{Insulin}] \quad (1)$$

6.2 Function definition [function_4_IRS1_phosphorylation_by_IR_beta_pY1146](#)

Name function_4_IRS1_phosphorylation_by_IR_beta_pY1146

Arguments [IRS1], IRS1_phosphorylation_by_IR_beta_pY1146, [IR_beta_pY1146]

Mathematical Expression

$$\text{IRS1_phosphorylation_by_IR_beta_pY1146} \cdot [\text{IRS1}] \cdot [\text{IR_beta_pY1146}] \quad (2)$$

6.3 Function definition [function_4_IRS1_p_phosphorylation_by_p70S6K_pT389](#)

Name function_4_IRS1_p_phosphorylation_by_p70S6K_pT389

Arguments [IRS1_p], IRS1_p_phosphorylation_by_p70S6K_pT389, [p70S6K_pT389]

Mathematical Expression

$$\text{IRS1_p_phosphorylation_by_p70S6K_pT389} \cdot [\text{IRS1_p}] \cdot [\text{p70S6K_pT389}] \quad (3)$$

6.4 Function definition [function_4_AMPK_T172_phosphorylation](#)

Name function_4_AMPK_T172_phosphorylation

Arguments [AMPK], AMPK_T172_phosphorylation, [IRS1_p]

Mathematical Expression

$$\text{AMPK_T172_phosphorylation} \cdot [\text{AMPK}] \cdot [\text{IRS1_p}] \quad (4)$$

6.5 Function definition

[function_4_Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p](#)

Name function_4_Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p

Arguments [Akt_S473], Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p, [IRS1_p], [mTORC2_pS2481]

Mathematical Expression

$$\text{Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p} \quad (5)$$
$$\cdot [\text{Akt_S473}] \cdot [\text{mTORC2_pS2481}] \cdot [\text{IRS1_p}]$$

6.6 Function definition [function_4_Akt_T308_phosphorylation_by_IRS1_p](#)

Name function_4_Akt_T308_phosphorylation_by_IRS1_p

Arguments [Akt_T308], Akt_T308_phosphorylation_by_IRS1_p, [IRS1_p]

Mathematical Expression

$$\text{Akt_T308_phosphorylation_by_IRS1_p} \cdot [\text{Akt_T308}] \cdot [\text{IRS1_p}] \quad (6)$$

6.7 Function definition

[function_4_mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387](#)

Name function_4_mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387

Arguments [TSC1_TSC2_pS1387], [mTORC1_pS2448], mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387

Mathematical Expression

$$\text{mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387} \quad (7)$$
$$\cdot [\text{mTORC1_pS2448}] \cdot [\text{TSC1_TSC2_pS1387}]$$

6.8 Function definition [function_4_mTORC1_S2448_activation_by_Amino_Acids](#)

Name function_4_mTORC1_S2448_activation_by_Amino_Acids

Arguments [Amino_Acids], [mTORC1], mTORC1_S2448_activation_by_Amino_Acids

Mathematical Expression

$$\text{mTORC1_S2448_activation_by_Amino_Acids} \cdot [\text{mTORC1}] \cdot [\text{Amino_Acids}] \quad (8)$$

6.9 Function definition

[function_4_mTORC2_S2481_phosphorylation_by_PI3K_variant_p](#)

Name function_4_mTORC2_S2481_phosphorylation_by_PI3K_variant_p

Arguments [PI3K_variant_p], [mTORC2], mTORC2_S2481_phosphorylation_by_PI3K_variant_p

Mathematical Expression

$$\text{mTORC2_S2481_phosphorylation_by_PI3K_variant_p} \cdot [\text{mTORC2}] \cdot [\text{PI3K_variant_p}]$$

6.10 Function definition

[function_4_p70S6K_T389_phosphorylation_by_mTORC1_pS2448](#)

Name function_4_p70S6K_T389_phosphorylation_by_mTORC1_pS2448

Arguments [mTORC1_pS2448], [p70S6K], p70S6K_T389_phosphorylation_by_mTORC1_pS2448

Mathematical Expression

$$\text{p70S6K_T389_phosphorylation_by_mTORC1_pS2448} \cdot [\text{p70S6K}] \cdot [\text{mTORC1_pS2448}] \quad (10)$$

6.11 Function definition

[function_4_PRAS40_S183_phosphorylation_by_mTORC1_pS2448](#)

Name function_4_PRAS40_S183_phosphorylation_by_mTORC1_pS2448

Arguments [PRAS40_S183], PRAS40_S183_phosphorylation_by_mTORC1_pS2448, [mTORC1_pS2448]

Mathematical Expression

$$\text{PRAS40_S183_phosphorylation_by_mTORC1_pS2448} \cdot [\text{PRAS40_S183}] \cdot [\text{mTORC1_pS2448}] \quad (11)$$

6.12 Function definition

[function_4_PRAS40_T246_phosphorylation_by_Akt_pT308](#)

Name function_4_PRAS40_T246_phosphorylation_by_Akt_pT308

Arguments [Akt_pT308], [PRAS40_T246], PRAS40_T246_phosphorylation_by_Akt_pT308

Mathematical Expression

$$\text{PRAS40_T246_phosphorylation_by_Akt_pT308} \cdot [\text{PRAS40_T246}] \cdot [\text{Akt_pT308}] \quad (12)$$

6.13 Function definition

[function_4_TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172](#)

Name function_4_TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172

Arguments [AMPK_pT172], TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172, [TSC1_TSC2_pT1462]

Mathematical Expression

$$\begin{aligned} & \text{TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172} \\ & \cdot [\text{TSC1_TSC2_pT1462}] \cdot [\text{AMPK_pT172}] \end{aligned} \quad (13)$$

6.14 Function definition

[function_4_TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308](#)

Name function_4_TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308

Arguments [Akt_pT308], TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308, [TSC1_TSC2_pS1387]

Mathematical Expression

$$\begin{aligned} & \text{TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308} \\ & \cdot [\text{TSC1_TSC2_pS1387}] \cdot [\text{Akt_pT308}] \end{aligned} \quad (14)$$

6.15 Function definition

[function_4_PI3K_variant_phosphorylation_by_IR_beta_pY1146](#)

Name function_4_PI3K_variant_phosphorylation_by_IR_beta_pY1146

Arguments [IR_beta_pY1146], [PI3K_variant], PI3K_variant_phosphorylation_by_IR_beta_pY1146

Mathematical Expression

$$\begin{aligned} & \text{PI3K_variant_phosphorylation_by_IR_beta_pY1146} \cdot [\text{PI3K_variant}] \\ & \cdot [\text{IR_beta_pY1146}] \end{aligned} \quad (15)$$

7 Rules

This is an overview of 13 rules.

7.1 Rule Amino_Acids

Rule Amino_Acids is an assignment rule for species Amino_Acids:

$$\text{Amino_Acids} = \begin{cases} 0 & \text{if time} < 1 \\ \begin{cases} 0 & \text{if time} < 0 \\ 10 & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \quad (16)$$

7.2 Rule Akt_pT308_obs

Rule Akt_pT308_obs is an assignment rule for species Akt_pT308_obs:

$$\text{Akt_pT308_obs} = \text{scale_Akt_pT308_obs} \cdot [\text{Akt_pT308}] \quad (17)$$

7.3 Rule TSC1_TSC2_pS1387_obs

Rule TSC1_TSC2_pS1387_obs is an assignment rule for species TSC1_TSC2_pS1387_obs:

$$\text{TSC1_TSC2_pS1387_obs} = \text{scale_TSC1_TSC2_pS1387_obs} \cdot [\text{TSC1_TSC2_pS1387}] \quad (18)$$

7.4 Rule PRAS40_pS183_obs

Rule PRAS40_pS183_obs is an assignment rule for species PRAS40_pS183_obs:

$$\text{PRAS40_pS183_obs} = \text{scale_PRAS40_pS183_obs} \cdot [\text{PRAS40_pS183}] \quad (19)$$

7.5 Rule IR_beta_pY1146_obs

Rule IR_beta_pY1146_obs is an assignment rule for species IR_beta_pY1146_obs:

$$\text{IR_beta_pY1146_obs} = \text{scale_IR_beta_pY1146_obs} \cdot [\text{IR_beta_pY1146}] \quad (20)$$

7.6 Rule Insulin

Rule Insulin is an assignment rule for species Insulin:

$$\text{Insulin} = \begin{cases} 0 & \text{if time} < 1 \\ \begin{cases} 0 & \text{if time} < 0 \\ 10 & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \quad (21)$$

7.7 Rule IRS1_pS636_obs

Rule IRS1_pS636_obs is an assignment rule for species IRS1_pS636_obs:

$$\text{IRS1_pS636_obs} = \text{scale_IRS1_pS636_obs} \cdot [\text{IRS1_pS636}] \quad (22)$$

7.8 Rule Akt_pS473_obs

Rule Akt_pS473_obs is an assignment rule for species Akt_pS473_obs:

$$\text{Akt_pS473_obs} = \text{scale_Akt_pS473_obs} \cdot [\text{Akt_pS473}] \quad (23)$$

7.9 Rule AMPK_pT172_obs

Rule AMPK_pT172_obs is an assignment rule for species AMPK_pT172_obs:

$$\text{AMPK_pT172_obs} = \text{scale_AMPK_pT172_obs} \cdot [\text{AMPK_pT172}] \quad (24)$$

7.10 Rule `mTOR_pS2448_obs`

Rule `mTOR_pS2448_obs` is an assignment rule for species `mTOR_pS2448_obs`:

$$\text{mTOR_pS2448_obs} = \text{scale_mTOR_pS2448_obs} \cdot [\text{mTORC1_pS2448}] \quad (25)$$

7.11 Rule `p70S6K_pT389_obs`

Rule `p70S6K_pT389_obs` is an assignment rule for species `p70S6K_pT389_obs`:

$$\text{p70S6K_pT389_obs} = \text{scale_p70S6K_pT389_obs} \cdot [\text{p70S6K_pT389}] \quad (26)$$

7.12 Rule `mTOR_pS2481_obs`

Rule `mTOR_pS2481_obs` is an assignment rule for species `mTOR_pS2481_obs`:

$$\text{mTOR_pS2481_obs} = \text{scale_mTOR_pS2481_obs} \cdot [\text{mTORC2_pS2481}] \quad (27)$$

7.13 Rule `PRAS40_pT246_obs`

Rule `PRAS40_pT246_obs` is an assignment rule for species `PRAS40_pT246_obs`:

$$\text{PRAS40_pT246_obs} = \text{scale_PRAS40_pT246_obs} \cdot [\text{PRAS40_pT246}] \quad (28)$$

8 Reactions

This model contains 26 reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

Nº	Id	Name	Reaction Equation	SBO
1	reaction_1	IR_beta_phosphorylation_by_Insulin	$\text{IR_beta} \xrightarrow{\text{Insulin, IR_beta, Insulin}} \text{IR_beta_pY1146}$	
2	reaction_2	IR_beta_pY1146_dephosphorylation	$\text{IR_beta_pY1146} \xrightarrow{\text{IR_beta_pY1146}} \text{IR_beta_refractory}$	
3	reaction_3	IR_beta_ready	$\text{IR_beta_refractory} \xrightarrow{\text{IR_beta_refractory}} \text{IR_beta}$	
4	reaction_4	IRS1_phosphorylation_by_IR_beta_pY1146	$\text{IRS1} \xrightarrow{\text{IR_beta_pY1146, IRS1, IR_beta_pY1146}} \text{IRS1_p}$	
5	reaction_5	IRS1_p_phosphorylation_by_p70S6K_pT389	$\text{IRS1_p} \xrightarrow{\text{p70S6K_pT389, IRS1_p, p70S6K_pT389}} \text{IRS1_pS636}$	
6	reaction_6	IRS1_pS636_dephosphorylation	$\text{IRS1_pS636} \xrightarrow{\text{IRS1_pS636}} \text{IRS1}$	
7	reaction_7	AMPK_T172_phosphorylation	$\text{AMPK} \xrightarrow{\text{IRS1_p, AMPK, IRS1_p}} \text{AMPK_pT172}$	
8	reaction_8	AMPK_pT172_dephosphorylation	$\text{AMPK_pT172} \xrightarrow{\text{AMPK_pT172}} \text{AMPK}$	
9	reaction_9	Akt_pT308_dephosphorylation	$\text{Akt_pT308} \xrightarrow{\text{Akt_pT308}} \text{Akt_T308}$	
10	reaction_10	Akt_pS473_dephosphorylation	$\text{Akt_pS473} \xrightarrow{\text{Akt_pS473}} \text{Akt_S473}$	
11	reaction_11	Akt_S473_phosphorylation_by_mTORC2-pS2481_n_IRS1_p	$\text{Akt_S473} \xrightarrow{\text{mTORC2_pS2481, IRS1_p, Akt_S473, IRS1_p, mTORC2_pS2481}} \text{Akt_pS473}$	
12	reaction_12	Akt_T308_phosphorylation_by_IRS1_p	$\text{Akt_T308} \xrightarrow{\text{IRS1_p, Akt_T308, IRS1_p}} \text{Akt_pT308}$	
13	reaction_13	mTORC1_pS2448_dephosphorylation_by-TSC1_TSC2_pS1387	$\text{mTORC1_pS2448} \xrightarrow{\text{TSC1_TSC2_pS1387, TSC1_TSC2_pS1387, mTORC1_pS2448}} \text{mTORC1_T308}$	

Nº	Id	Name	Reaction Equation	SBO
14	reaction_14	mTORC1_S2448_activation_by_Amino-Acids	$\text{mTORC1} \xrightarrow{\text{Amino_Acids, Amino_Acids, mTORC1}} \text{mTORC1_pS2448}$	
15	reaction_15	mTORC2_pS2481_dephosphorylation	$\text{mTORC2_pS2481} \xrightarrow{\text{mTORC2_pS2481}} \text{mTORC2}$	
16	reaction_16	mTORC2_S2481_phosphorylation_by_P13K-variant_p	$\text{mTORC2} \xrightarrow{\text{PI3K_variant_p, PI3K_variant_p, mTORC2}} \text{mTORC2_pS2481}$	
17	reaction_17	p70S6K_pT389_dephosphorylation	$\text{p70S6K_pT389} \xrightarrow{\text{p70S6K_pT389}} \text{p70S6K}$	
18	reaction_18	p70S6K_T389_phosphorylation_by-mTORC1_pS2448	$\text{p70S6K} \xrightarrow{\text{mTORC1_pS2448, mTORC1_pS2448, p70S6K}} \text{p70S6K_pT389}$	
19	reaction_19	PRAS40_pS183_dephosphorylation	$\text{PRAS40_pS183} \xrightarrow{\text{PRAS40_pS183}} \text{PRAS40_S183}$	
20	reaction_20	PRAS40_pT246_dephosphorylation	$\text{PRAS40_pT246} \xrightarrow{\text{PRAS40_pT246}} \text{PRAS40_T246}$	
21	reaction_21	PRAS40_S183_phosphorylation_by-mTORC1_pS2448	$\text{PRAS40_S183} \xrightarrow{\text{mTORC1_pS2448, PRAS40_S183, mTORC1_pS2448}} \text{PRAS40_pS183}$	
22	reaction_22	PRAS40_T246_phosphorylation_by_Akt-pT308	$\text{PRAS40_T246} \xrightarrow{\text{Akt_pT308, Akt_pT308, PRAS40_T246}} \text{PRAS40_pT246}$	
23	reaction_23	TSC1_TSC2_S1387_phosphorylation_by-AMPK_pT172	$\text{TSC1_TSC2_pT1462} \xrightarrow{\text{AMPK_pT172, AMPK_pT172, TSC1_TSC2_pT1462}} \text{TSC1_TSC2_pT1462}$	
24	reaction_24	TSC1_TSC2_T1462_phosphorylation_by-Akt_pT308	$\text{TSC1_TSC2_pS1387} \xrightarrow{\text{Akt_pT308, Akt_pT308, TSC1_TSC2_pS1387}} \text{TSC1_TSC2_pT1462}$	
25	reaction_25	PI3K_variant_p_dephosphorylation	$\text{PI3K_variant_p} \xrightarrow{\text{PI3K_variant_p}} \text{PI3K_variant}$	
26	reaction_26	PI3K_variant_phosphorylation_by_IR_beta-pY1146	$\text{PI3K_variant} \xrightarrow{\text{IR_beta_pY1146, IR_beta_pY1146, PI3K_variant}} \text{PI3K_variant_p}$	

8.1 Reaction `reaction_1`

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

Name `IR_beta_phosphorylation_by_Insulin`

Reaction equation



Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
<code>IR_beta</code>	<code>IR_beta</code>	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
<code>Insulin</code>	<code>Insulin</code>	
<code>IR_beta</code>	<code>IR_beta</code>	
<code>Insulin</code>	<code>Insulin</code>	

Product

Table 8: Properties of each product.

Id	Name	SBO
<code>IR_beta_pY1146</code>	<code>IR_beta_pY1146</code>	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{Cell}) \cdot \text{function_4_IR_beta_phosphorylation_by_Insulin}([\text{IR_beta}], \quad (30) \\ \text{IR_beta_phosphorylation_by_Insulin}, [\text{Insulin}])$$

$$\begin{aligned} &\text{function_4_IR_beta_phosphorylation_by_Insulin}([\text{IR_beta}], \\ &\quad \text{IR_beta_phosphorylation_by_Insulin}, [\text{Insulin}]) = \text{IR_beta_phosphorylation_by_Insulin} \quad (31) \\ &\quad \cdot [\text{IR_beta}] \cdot [\text{Insulin}] \end{aligned}$$

$$\begin{aligned} &\text{function_4_IR_beta_phosphorylation_by_Insulin}([\text{IR_beta}], \\ &\quad \text{IR_beta_phosphorylation_by_Insulin}, [\text{Insulin}]) = \text{IR_beta_phosphorylation_by_Insulin} \quad (32) \\ &\quad \cdot [\text{IR_beta}] \cdot [\text{Insulin}] \end{aligned}$$

8.2 Reaction *reaction_2*

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

Name IR_beta_pY1146.dephosphorylation

Reaction equation



Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
IR_beta_pY1146	IR_beta_pY1146	

Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
IR_beta_pY1146	IR_beta_pY1146	

Product

Table 11: Properties of each product.

Id	Name	SBO
IR_beta_refractory	IR_beta_refractory	

Kinetic Law

Derived unit contains undeclared units

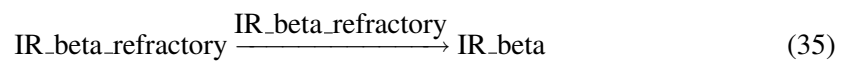
$$v_2 = \text{vol}(\text{Cell}) \cdot \text{IR_beta_pY1146_dephosphorylation} \cdot [\text{IR_beta_pY1146}] \quad (34)$$

8.3 Reaction `reaction_3`

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

Name IR_beta_ready

Reaction equation



Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
IR_beta_refractory	IR_beta_refractory	

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
IR_beta_refractory	IR_beta_refractory	

Product

Table 14: Properties of each product.

Id	Name	SBO
IR_beta	IR_beta	

Kinetic Law

Derived unit contains undeclared units

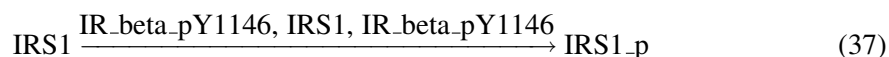
$$v_3 = \text{vol}(\text{Cell}) \cdot \text{IR_beta_ready} \cdot [\text{IR_beta_refractory}] \quad (36)$$

8.4 Reaction `reaction_4`

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

Name `IRS1_phosphorylation_by_IR_beta_pY1146`

Reaction equation



Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
IRS1	IRS1	

Modifiers

Table 16: Properties of each modifier.

Id	Name	SBO
IR_beta_pY1146	IR_beta_pY1146	
IRS1	IRS1	
IR_beta_pY1146	IR_beta_pY1146	

Product

Table 17: Properties of each product.

Id	Name	SBO
IRS1_p	IRS1_p	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}(\text{Cell}) \cdot \text{function_4_IRS1_phosphorylation_by_IR_beta_pY1146}([\text{IRS1}], \quad (38) \\ \text{IRS1_phosphorylation_by_IR_beta_pY1146}, [\text{IR_beta_pY1146}])$$

$$\begin{aligned} &\text{function_4_IRS1_phosphorylation_by_IR_beta_pY1146} ([\text{IRS1}], \\ &\quad \text{IRS1_phosphorylation_by_IR_beta_pY1146}, \\ &\quad [\text{IR_beta_pY1146}]) = \text{IRS1_phosphorylation_by_IR_beta_pY1146} \cdot [\text{IRS1}] \cdot [\text{IR_beta_pY1146}] \end{aligned} \quad (39)$$

$$\begin{aligned} &\text{function_4_IRS1_phosphorylation_by_IR_beta_pY1146} ([\text{IRS1}], \\ &\quad \text{IRS1_phosphorylation_by_IR_beta_pY1146}, \\ &\quad [\text{IR_beta_pY1146}]) = \text{IRS1_phosphorylation_by_IR_beta_pY1146} \cdot [\text{IRS1}] \cdot [\text{IR_beta_pY1146}] \end{aligned} \quad (40)$$

8.5 Reaction `reaction_5`

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

Name `IRS1_p_phosphorylation_by_p70S6K_pT389`

Reaction equation



Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
IRS1_p	IRS1_p	

Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
p70S6K_pT389	p70S6K_pT389	
IRS1_p	IRS1_p	
p70S6K_pT389	p70S6K_pT389	

Product

Table 20: Properties of each product.

Id	Name	SBO
IRS1_pS636	IRS1_pS636	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}(\text{Cell}) \cdot \text{function_4_IRS1_p_phosphorylation_by_p70S6K_pT389}([\text{IRS1_p}], \text{IRS1_p_phosphorylation_by_p70S6K_pT389}, [\text{p70S6K_pT389}]) \quad (42)$$

$$\begin{aligned} &\text{function_4_IRS1_p_phosphorylation_by_p70S6K_pT389}([\text{IRS1_p}], \\ &\text{IRS1_p_phosphorylation_by_p70S6K_pT389}, \\ &[\text{p70S6K_pT389}]) = \text{IRS1_p_phosphorylation_by_p70S6K_pT389} \\ &\quad \cdot [\text{IRS1_p}] \cdot [\text{p70S6K_pT389}] \end{aligned} \quad (43)$$

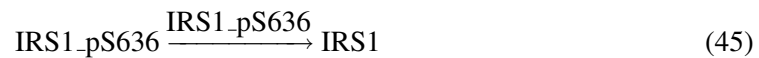
$$\begin{aligned} &\text{function_4_IRS1_p_phosphorylation_by_p70S6K_pT389}([\text{IRS1_p}], \\ &\text{IRS1_p_phosphorylation_by_p70S6K_pT389}, \\ &[\text{p70S6K_pT389}]) = \text{IRS1_p_phosphorylation_by_p70S6K_pT389} \\ &\quad \cdot [\text{IRS1_p}] \cdot [\text{p70S6K_pT389}] \end{aligned} \quad (44)$$

8.6 Reaction `reaction_6`

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

Name IRS1_pS636_dephosphorylation

Reaction equation



Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
IRS1_pS636	IRS1_pS636	

Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
IRS1_pS636	IRS1_pS636	

Product

Table 23: Properties of each product.

Id	Name	SBO
IRS1	IRS1	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{vol}(\text{Cell}) \cdot \text{IRS1_pS636_dephosphorylation} \cdot [\text{IRS1_pS636}] \quad (46)$$

8.7 Reaction `reaction_7`

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

Name AMPK_T172_phosphorylation

Reaction equation



Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
AMPK	AMPK	

Modifiers

Table 25: Properties of each modifier.

Id	Name	SBO
IRS1_p	IRS1_p	
AMPK	AMPK	
IRS1_p	IRS1_p	

Product

Table 26: Properties of each product.

Id	Name	SBO
AMPK_pT172	AMPK_pT172	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{vol}(\text{Cell}) \cdot \text{function_4_AMPK_T172_phosphorylation}([AMPK], \text{AMPK_T172_phosphorylation}, [IRS1_p]) \quad (48)$$

$$\text{function_4_AMPK_T172_phosphorylation}([AMPK], \text{AMPK_T172_phosphorylation}, [IRS1_p]) = \text{AMPK_T172_phosphorylation} \cdot [AMPK] \cdot [IRS1_p] \quad (49)$$

$$\text{function_4_AMPK_T172_phosphorylation}([AMPK], \text{AMPK_T172_phosphorylation}, [IRS1_p]) = \text{AMPK_T172_phosphorylation} \cdot [AMPK] \cdot [IRS1_p] \quad (50)$$

8.8 Reaction [reaction_8](#)

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

Name AMPK_pT172_dephosphorylation

Reaction equation



Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
AMPK_pT172	AMPK_pT172	

Modifier

Table 28: Properties of each modifier.

Id	Name	SBO
AMPK_pT172	AMPK_pT172	

Product

Table 29: Properties of each product.

Id	Name	SBO
AMPK	AMPK	

Kinetic Law

Derived unit contains undeclared units

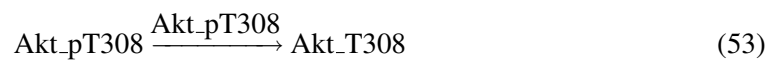
$$v_8 = \text{vol}(\text{Cell}) \cdot \text{AMPK_pT172_dephosphorylation} \cdot [\text{AMPK_pT172}] \quad (52)$$

8.9 Reaction `reaction_9`

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

Name Akt_pT308_dephosphorylation

Reaction equation



Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
Akt_pT308	Akt_pT308	

Modifier

Table 31: Properties of each modifier.

Id	Name	SBO
Akt_pT308	Akt_pT308	

Product

Table 32: Properties of each product.

Id	Name	SBO
Akt_T308	Akt_T308	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{vol}(\text{Cell}) \cdot \text{Akt_pT308_dephosphorylation} \cdot [\text{Akt_pT308}] \quad (54)$$

8.10 Reaction `reaction_10`

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

Name Akt_pS473_dephosphorylation

Reaction equation



Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
Akt_pS473	Akt_pS473	

Modifier

Table 34: Properties of each modifier.

Id	Name	SBO
Akt_pS473	Akt_pS473	

Product

Table 35: Properties of each product.

Id	Name	SBO
Akt_S473	Akt_S473	

Kinetic Law

Derived unit contains undeclared units

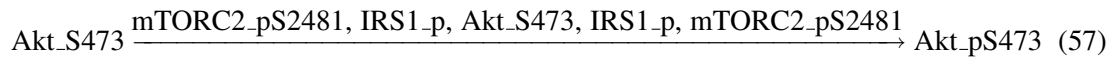
$$v_{10} = \text{vol}(\text{Cell}) \cdot \text{Akt_pS473_dephosphorylation} \cdot [\text{Akt_pS473}] \quad (56)$$

8.11 Reaction [reaction_11](#)

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

Name Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p

Reaction equation



Reactant

Table 36: Properties of each reactant.

Id	Name	SBO
Akt_S473	Akt_S473	

Modifiers

Table 37: Properties of each modifier.

Id	Name	SBO
mTORC2_pS2481	mTORC2_pS2481	

Id	Name	SBO
IRS1_p	IRS1_p	
Akt_S473	Akt_S473	
IRS1_p	IRS1_p	
mTORC2_pS2481	mTORC2_pS2481	

Product

Table 38: Properties of each product.

Id	Name	SBO
Akt_pS473	Akt_pS473	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{vol}(\text{Cell}) \cdot \text{function_4_Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p}([Akt_S473], \text{Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p}, [IRS1_p], [mTORC2_pS2481]) \quad (58)$$

$$\text{function_4_Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p}([Akt_S473], \text{Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p}, [IRS1_p], [mTORC2_pS2481]) = \text{Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p} \cdot [Akt_S473] \cdot [mTORC2_pS2481] \cdot [IRS1_p] \quad (59)$$

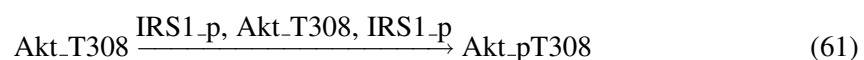
$$\text{function_4_Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p}([Akt_S473], \text{Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p}, [IRS1_p], [mTORC2_pS2481]) = \text{Akt_S473_phosphorylation_by_mTORC2_pS2481_n_IRS1_p} \cdot [Akt_S473] \cdot [mTORC2_pS2481] \cdot [IRS1_p] \quad (60)$$

8.12 Reaction [reaction_12](#)

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

Name Akt_T308_phosphorylation_by_IRS1_p

Reaction equation



Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
Akt_T308	Akt_T308	

Modifiers

Table 40: Properties of each modifier.

Id	Name	SBO
IRS1_p	IRS1_p	
Akt_T308	Akt_T308	
IRS1_p	IRS1_p	

Product

Table 41: Properties of each product.

Id	Name	SBO
Akt_pT308	Akt_pT308	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{vol}(\text{Cell}) \cdot \text{function_4_Akt_T308_phosphorylation_by_IRS1_p}([\text{Akt_T308}], \text{Akt_T308_phosphorylation_by_IRS1_p}, [\text{IRS1_p}]) \quad (62)$$

$$\begin{aligned} &\text{function_4_Akt_T308_phosphorylation_by_IRS1_p}([\text{Akt_T308}], \\ &\text{Akt_T308_phosphorylation_by_IRS1_p}, \\ &[\text{IRS1_p}]) = \text{Akt_T308_phosphorylation_by_IRS1_p} \cdot [\text{Akt_T308}] \cdot [\text{IRS1_p}] \end{aligned} \quad (63)$$

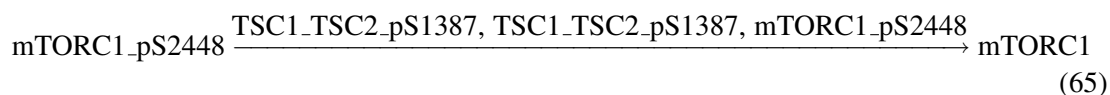
$$\begin{aligned} &\text{function_4_Akt_T308_phosphorylation_by_IRS1_p}([\text{Akt_T308}], \\ &\text{Akt_T308_phosphorylation_by_IRS1_p}, \\ &[\text{IRS1_p}]) = \text{Akt_T308_phosphorylation_by_IRS1_p} \cdot [\text{Akt_T308}] \cdot [\text{IRS1_p}] \end{aligned} \quad (64)$$

8.13 Reaction `reaction_13`

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

Name `mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387`

Reaction equation



Reactant

Table 42: Properties of each reactant.

Id	Name	SBO
<code>mTORC1_pS2448</code>	<code>mTORC1_pS2448</code>	

Modifiers

Table 43: Properties of each modifier.

Id	Name	SBO
<code>TSC1_TSC2_pS1387</code>	<code>TSC1_TSC2_pS1387</code>	
<code>TSC1_TSC2_pS1387</code>	<code>TSC1_TSC2_pS1387</code>	
<code>mTORC1_pS2448</code>	<code>mTORC1_pS2448</code>	

Product

Table 44: Properties of each product.

Id	Name	SBO
<code>mTORC1</code>	<code>mTORC1</code>	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{vol}(\text{Cell}) \quad (66)$$
$$\cdot \text{function_4_mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387}([\text{TSC1_TSC2_pS1387}],$$
$$[\text{mTORC1_pS2448}], \text{mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387})$$

function_4_mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387 ([TSC1_TSC2_pS1387],
 [mTORC1_pS2448], mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387)
 = mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387
 · [mTORC1_pS2448] · [TSC1_TSC2_pS1387]

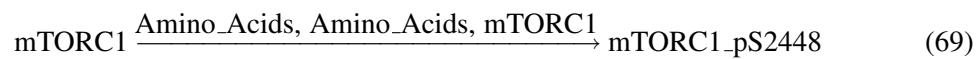
function_4_mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387 ([TSC1_TSC2_pS1387],
 [mTORC1_pS2448], mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387)
 = mTORC1_pS2448_dephosphorylation_by_TSC1_TSC2_pS1387
 · [mTORC1_pS2448] · [TSC1_TSC2_pS1387]

8.14 Reaction [reaction_14](#)

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

Name mTORC1_S2448_activation_by_Amino_Acids

Reaction equation



Reactant

Table 45: Properties of each reactant.

Id	Name	SBO
mTORC1	mTORC1	

Modifiers

Table 46: Properties of each modifier.

Id	Name	SBO
Amino_Acids	Amino_Acids	
Amino_Acids	Amino_Acids	
mTORC1	mTORC1	

Product

Table 47: Properties of each product.

Id	Name	SBO
mTORC1_pS2448	mTORC1_pS2448	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \text{vol}(\text{Cell}) \cdot \text{function_4_mTORC1_S2448_activation_by_Amino_Acids}([\text{Amino_Acids}], [\text{mTORC1}], \text{mTORC1_S2448_activation_by_Amino_Acids}) \quad (70)$$

$$\begin{aligned} &\text{function_4_mTORC1_S2448_activation_by_Amino_Acids}([\text{Amino_Acids}], \\ &[\text{mTORC1}], \text{mTORC1_S2448_activation_by_Amino_Acids}) \quad (71) \\ &= \text{mTORC1_S2448_activation_by_Amino_Acids} \cdot [\text{mTORC1}] \cdot [\text{Amino_Acids}] \end{aligned}$$

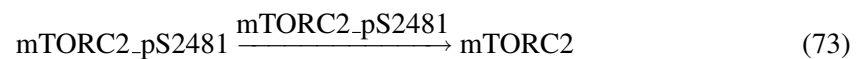
$$\begin{aligned} &\text{function_4_mTORC1_S2448_activation_by_Amino_Acids}([\text{Amino_Acids}], \\ &[\text{mTORC1}], \text{mTORC1_S2448_activation_by_Amino_Acids}) \quad (72) \\ &= \text{mTORC1_S2448_activation_by_Amino_Acids} \cdot [\text{mTORC1}] \cdot [\text{Amino_Acids}] \end{aligned}$$

8.15 Reaction reaction_15

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

Name mTORC2_pS2481_dephosphorylation

Reaction equation



Reactant

Table 48: Properties of each reactant.

Id	Name	SBO
mTORC2_pS2481	mTORC2_pS2481	

Modifier

Table 49: Properties of each modifier.

Id	Name	SBO
mTORC2_pS2481	mTORC2_pS2481	

Product

Table 50: Properties of each product.

Id	Name	SBO
mTORC2	mTORC2	

Kinetic Law

Derived unit contains undeclared units

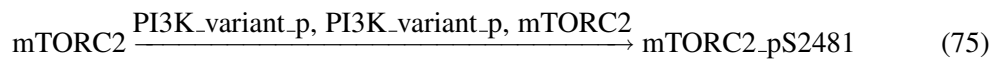
$$v_{15} = \text{vol}(\text{Cell}) \cdot \text{mTORC2_pS2481_dephosphorylation} \cdot [\text{mTORC2_pS2481}] \quad (74)$$

8.16 Reaction [reaction_16](#)

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

Name mTORC2.S2481_phosphorylation_by_PI3K_variant_p

Reaction equation



Reactant

Table 51: Properties of each reactant.

Id	Name	SBO
mTORC2	mTORC2	

Modifiers

Table 52: Properties of each modifier.

Id	Name	SBO
PI3K_variant_p	PI3K_variant_p	

Id	Name	SBO
PI3K_variant_p mTORC2	PI3K_variant_p mTORC2	

Product

Table 53: Properties of each product.

Id	Name	SBO
mTORC2_pS2481	mTORC2_pS2481	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \text{vol}(\text{Cell}) \cdot \text{function_4_mTORC2_S2481_phosphorylation_by_PI3K_variant_p}([\text{PI3K_variant_p}], [\text{mTORC2}], \text{mTORC2_S2481_phosphorylation_by_PI3K_variant_p}) \quad (76)$$

$$\begin{aligned} & \text{function_4_mTORC2_S2481_phosphorylation_by_PI3K_variant_p}([\text{PI3K_variant_p}], \\ & [\text{mTORC2}], \text{mTORC2_S2481_phosphorylation_by_PI3K_variant_p}) \\ & = \text{mTORC2_S2481_phosphorylation_by_PI3K_variant_p} \cdot [\text{mTORC2}] \cdot [\text{PI3K_variant_p}] \end{aligned} \quad (77)$$

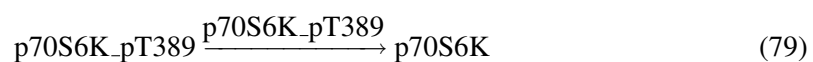
$$\begin{aligned} & \text{function_4_mTORC2_S2481_phosphorylation_by_PI3K_variant_p}([\text{PI3K_variant_p}], \\ & [\text{mTORC2}], \text{mTORC2_S2481_phosphorylation_by_PI3K_variant_p}) \\ & = \text{mTORC2_S2481_phosphorylation_by_PI3K_variant_p} \cdot [\text{mTORC2}] \cdot [\text{PI3K_variant_p}] \end{aligned} \quad (78)$$

8.17 Reaction [reaction_17](#)

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

Name p70S6K_pT389_dephosphorylation

Reaction equation



Reactant

Table 54: Properties of each reactant.

Id	Name	SBO
p70S6K_pT389	p70S6K_pT389	

Modifier

Table 55: Properties of each modifier.

Id	Name	SBO
p70S6K_pT389	p70S6K_pT389	

Product

Table 56: Properties of each product.

Id	Name	SBO
p70S6K	p70S6K	

Kinetic Law

Derived unit contains undeclared units

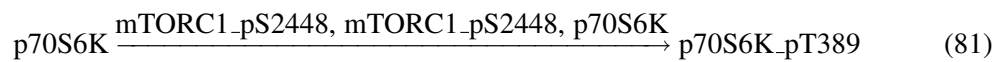
$$v_{17} = \text{vol}(\text{Cell}) \cdot \text{p70S6K_pT389_dephosphorylation} \cdot [\text{p70S6K_pT389}] \quad (80)$$

8.18 Reaction [reaction_18](#)

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

Name p70S6K_T389_phosphorylation_by_mTORC1_pS2448

Reaction equation



Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
p70S6K	p70S6K	

Modifiers

Table 58: Properties of each modifier.

Id	Name	SBO
mTORC1_pS2448	mTORC1_pS2448	
mTORC1_pS2448	mTORC1_pS2448	
p70S6K	p70S6K	

Product

Table 59: Properties of each product.

Id	Name	SBO
p70S6K_T389	p70S6K_T389	

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{18} = & \text{vol}(\text{Cell}) \\ & \cdot \text{function_4_p70S6K_T389_phosphorylation_by_mTORC1_pS2448}([mTORC1_pS2448], \\ & [p70S6K], p70S6K_T389_phosphorylation_by_mTORC1_pS2448) \end{aligned} \quad (82)$$

$$\begin{aligned} & \text{function_4_p70S6K_T389_phosphorylation_by_mTORC1_pS2448}([mTORC1_pS2448], \\ & [p70S6K], p70S6K_T389_phosphorylation_by_mTORC1_pS2448) \\ & = p70S6K_T389_phosphorylation_by_mTORC1_pS2448 \cdot [p70S6K] \cdot [mTORC1_pS2448] \end{aligned} \quad (83)$$

$$\begin{aligned} & \text{function_4_p70S6K_T389_phosphorylation_by_mTORC1_pS2448}([mTORC1_pS2448], \\ & [p70S6K], p70S6K_T389_phosphorylation_by_mTORC1_pS2448) \\ & = p70S6K_T389_phosphorylation_by_mTORC1_pS2448 \cdot [p70S6K] \cdot [mTORC1_pS2448] \end{aligned} \quad (84)$$

8.19 Reaction `reaction_19`

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

Name PRAS40_pS183_dephosphorylation

Reaction equation



Reactant

Table 60: Properties of each reactant.

Id	Name	SBO
PRAS40_pS183	PRAS40_pS183	

Modifier

Table 61: Properties of each modifier.

Id	Name	SBO
PRAS40_pS183	PRAS40_pS183	

Product

Table 62: Properties of each product.

Id	Name	SBO
PRAS40_S183	PRAS40_S183	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{vol}(\text{Cell}) \cdot \text{PRAS40_pS183_dephosphorylation} \cdot [\text{PRAS40_pS183}] \quad (86)$$

8.20 Reaction [reaction_20](#)

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

Name PRAS40_pT246_dephosphorylation

Reaction equation



Reactant

Table 63: Properties of each reactant.

Id	Name	SBO
PRAS40_pT246	PRAS40_pT246	

Modifier

Table 64: Properties of each modifier.

Id	Name	SBO
PRAS40_pT246	PRAS40_pT246	

Product

Table 65: Properties of each product.

Id	Name	SBO
PRAS40_T246	PRAS40_T246	

Kinetic Law

Derived unit contains undeclared units

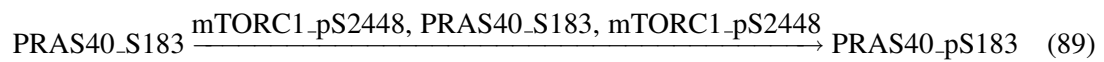
$$v_{20} = \text{vol}(\text{Cell}) \cdot \text{PRAS40_pT246_dephosphorylation} \cdot [\text{PRAS40_pT246}] \quad (88)$$

8.21 Reaction [reaction_21](#)

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

Name PRAS40_S183_phosphorylation_by_mTORC1_pS2448

Reaction equation



Reactant

Table 66: Properties of each reactant.

Id	Name	SBO
PRAS40_S183	PRAS40_S183	

Modifiers

Table 67: Properties of each modifier.

Id	Name	SBO
mTORC1_pS2448	mTORC1_pS2448	
PRAS40_S183	PRAS40_S183	
mTORC1_pS2448	mTORC1_pS2448	

Product

Table 68: Properties of each product.

Id	Name	SBO
PRAS40_pS183	PRAS40_pS183	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \text{vol}(\text{Cell}) \cdot \text{function_4_PRAS40_S183_phosphorylation_by_mTORC1_pS2448}([PRAS40_S183], PRAS40_S183_phosphorylation_by_mTORC1_pS2448, [mTORC1_pS2448]) \quad (90)$$

$$\begin{aligned} &\text{function_4_PRAS40_S183_phosphorylation_by_mTORC1_pS2448}([PRAS40_S183], \\ &PRAS40_S183_phosphorylation_by_mTORC1_pS2448, \\ &[mTORC1_pS2448]) = PRAS40_S183_phosphorylation_by_mTORC1_pS2448 \\ &\cdot [PRAS40_S183] \cdot [mTORC1_pS2448] \end{aligned} \quad (91)$$

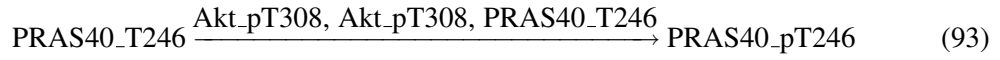
$$\begin{aligned} &\text{function_4_PRAS40_S183_phosphorylation_by_mTORC1_pS2448}([PRAS40_S183], \\ &PRAS40_S183_phosphorylation_by_mTORC1_pS2448, \\ &[mTORC1_pS2448]) = PRAS40_S183_phosphorylation_by_mTORC1_pS2448 \\ &\cdot [PRAS40_S183] \cdot [mTORC1_pS2448] \end{aligned} \quad (92)$$

8.22 Reaction [reaction_22](#)

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

Name PRAS40_T246_phosphorylation_by_Akt_pT308

Reaction equation



Reactant

Table 69: Properties of each reactant.

Id	Name	SBO
PRAS40_T246	PRAS40_T246	

Modifiers

Table 70: Properties of each modifier.

Id	Name	SBO
Akt_pT308	Akt_pT308	
Akt_pT308	Akt_pT308	
PRAS40_T246	PRAS40_T246	

Product

Table 71: Properties of each product.

Id	Name	SBO
PRAS40_pT246	PRAS40_pT246	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \text{vol}(\text{Cell}) \cdot \text{function_4_PRAS40_T246_phosphorylation_by_Akt_pT308}([\text{Akt_pT308}], [\text{PRAS40_T246}], \text{PRAS40_T246_phosphorylation_by_Akt_pT308}) \quad (94)$$

$$\begin{aligned} & \text{function_4_PRAS40_T246_phosphorylation_by_Akt_pT308}([\text{Akt_pT308}], \\ & [\text{PRAS40_T246}], \text{PRAS40_T246_phosphorylation_by_Akt_pT308}) \\ & = \text{PRAS40_T246_phosphorylation_by_Akt_pT308} \cdot [\text{PRAS40_T246}] \cdot [\text{Akt_pT308}] \end{aligned} \quad (95)$$

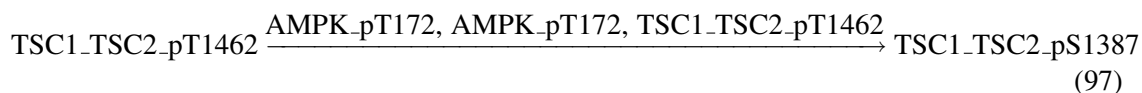
$$\begin{aligned} & \text{function_4_PRAS40_T246_phosphorylation_by_Akt_pT308}([\text{Akt_pT308}], \\ & [\text{PRAS40_T246}], \text{PRAS40_T246_phosphorylation_by_Akt_pT308}) \\ & = \text{PRAS40_T246_phosphorylation_by_Akt_pT308} \cdot [\text{PRAS40_T246}] \cdot [\text{Akt_pT308}] \end{aligned} \quad (96)$$

8.23 Reaction [reaction_23](#)

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

Name TSC1_TSC2_S1387_phosphorylation.by_AMPK_pT172

Reaction equation



Reactant

Table 72: Properties of each reactant.

Id	Name	SBO
TSC1_TSC2_pT1462	TSC1_TSC2_pT1462	

Modifiers

Table 73: Properties of each modifier.

Id	Name	SBO
AMPK_pT172	AMPK_pT172	
AMPK_pT172	AMPK_pT172	
TSC1_TSC2_pT1462	TSC1_TSC2_pT1462	

Product

Table 74: Properties of each product.

Id	Name	SBO
TSC1_TSC2_pS1387	TSC1_TSC2_pS1387	

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{23} = & \text{vol}(\text{Cell}) \\ & \cdot \text{function_4_TSC1_TSC2_S1387_phosphorylation.by_AMPK_pT172}([\text{AMPK_pT172}], \\ & \text{TSC1_TSC2_S1387_phosphorylation.by_AMPK_pT172}, [\text{TSC1_TSC2_pT1462}]) \end{aligned} \quad (98)$$

$$\begin{aligned} &\text{function_4_TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172} ([\text{AMPK_pT172}], \\ &\text{TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172}, \\ &[\text{TSC1_TSC2_pT1462}]) = \text{TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172} \\ &\cdot [\text{TSC1_TSC2_pT1462}] \cdot [\text{AMPK_pT172}] \end{aligned} \quad (99)$$

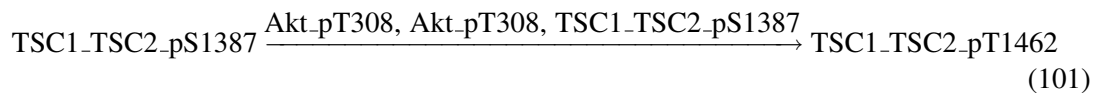
$$\begin{aligned} &\text{function_4_TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172} ([\text{AMPK_pT172}], \\ &\text{TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172}, \\ &[\text{TSC1_TSC2_pT1462}]) = \text{TSC1_TSC2_S1387_phosphorylation_by_AMPK_pT172} \\ &\cdot [\text{TSC1_TSC2_pT1462}] \cdot [\text{AMPK_pT172}] \end{aligned} \quad (100)$$

8.24 Reaction [reaction_24](#)

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

Name TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308

Reaction equation



Reactant

Table 75: Properties of each reactant.

Id	Name	SBO
TSC1_TSC2_pS1387	TSC1_TSC2_pS1387	

Modifiers

Table 76: Properties of each modifier.

Id	Name	SBO
Akt_pT308	Akt_pT308	
Akt_pT308	Akt_pT308	
TSC1_TSC2_pS1387	TSC1_TSC2_pS1387	

Product

Table 77: Properties of each product.

Id	Name	SBO
TSC1_TSC2_pT1462	TSC1_TSC2_pT1462	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \text{vol}(\text{Cell}) \cdot \text{function_4_TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308}([\text{Akt_pT308}], \text{TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308}, [\text{TSC1_TSC2_pS1387}]) \quad (102)$$

$$\begin{aligned} &\text{function_4_TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308}([\text{Akt_pT308}], \\ &\text{TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308}, \\ &[\text{TSC1_TSC2_pS1387}]) = \text{TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308} \\ &\cdot [\text{TSC1_TSC2_pS1387}] \cdot [\text{Akt_pT308}] \end{aligned} \quad (103)$$

$$\begin{aligned} &\text{function_4_TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308}([\text{Akt_pT308}], \\ &\text{TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308}, \\ &[\text{TSC1_TSC2_pS1387}]) = \text{TSC1_TSC2_T1462_phosphorylation_by_Akt_pT308} \\ &\cdot [\text{TSC1_TSC2_pS1387}] \cdot [\text{Akt_pT308}] \end{aligned} \quad (104)$$

8.25 Reaction [reaction_25](#)

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

Name PI3K_variant_p_dephosphorylation

Reaction equation



Reactant

Table 78: Properties of each reactant.

Id	Name	SBO
PI3K_variant_p	PI3K_variant_p	

Modifier

Table 79: Properties of each modifier.

Id	Name	SBO
PI3K_variant_p	PI3K_variant_p	

Product

Table 80: Properties of each product.

Id	Name	SBO
PI3K_variant	PI3K_variant	

Kinetic Law

Derived unit contains undeclared units

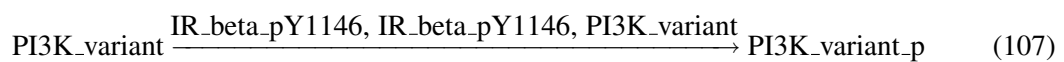
$$v_{25} = \text{vol}(\text{Cell}) \cdot \text{PI3K_variant_p_dephosphorylation} \cdot [\text{PI3K_variant_p}] \quad (106)$$

8.26 Reaction [reaction_26](#)

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

Name PI3K_variant_phosphorylation_by_IR_beta_pY1146

Reaction equation



Reactant

Table 81: Properties of each reactant.

Id	Name	SBO
PI3K_variant	PI3K_variant	

Modifiers

Table 82: Properties of each modifier.

Id	Name	SBO
IR_beta_pY1146	IR_beta_pY1146	
IR_beta_pY1146	IR_beta_pY1146	
PI3K_variant	PI3K_variant	

Product

Table 83: Properties of each product.

Id	Name	SBO
PI3K_variant_p	PI3K_variant_p	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \text{vol}(\text{Cell}) \cdot \text{function_4_PI3K_variant_phosphorylation_by_IR_beta_pY1146}([IR_beta_pY1146], [PI3K_variant], PI3K_variant_phosphorylation_by_IR_beta_pY1146) \quad (108)$$

$$\begin{aligned} &\text{function_4_PI3K_variant_phosphorylation_by_IR_beta_pY1146}([IR_beta_pY1146], \\ &[PI3K_variant], PI3K_variant_phosphorylation_by_IR_beta_pY1146) \\ &= PI3K_variant_phosphorylation_by_IR_beta_pY1146 \cdot [PI3K_variant] \cdot [IR_beta_pY1146] \end{aligned} \quad (109)$$

$$\begin{aligned} &\text{function_4_PI3K_variant_phosphorylation_by_IR_beta_pY1146}([IR_beta_pY1146], \\ &[PI3K_variant], PI3K_variant_phosphorylation_by_IR_beta_pY1146) \\ &= PI3K_variant_phosphorylation_by_IR_beta_pY1146 \cdot [PI3K_variant] \cdot [IR_beta_pY1146] \end{aligned} \quad (110)$$

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 IR_beta

Name IR_beta

Initial concentration 16.5607 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_1](#) and as a product in [reaction_3](#) and as a modifier in [reaction_1](#)).

$$\frac{d}{dt} \text{IR_beta} = v_3 - v_1 \quad (111)$$

9.2 Species IR_beta_pY1146

Name IR_beta_pY1146

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in seven reactions (as a reactant in [reaction_2](#) and as a product in [reaction_1](#) and as a modifier in [reaction_2](#), [reaction_4](#), [reaction_4](#), [reaction_26](#), [reaction_26](#)).

$$\frac{d}{dt} \text{IR_beta_pY1146} = v_1 - v_2 \quad (112)$$

9.3 Species IR_beta_refractory

Name IR_beta_refractory

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_3](#) and as a product in [reaction_2](#) and as a modifier in [reaction_3](#)).

$$\frac{d}{dt} \text{IR_beta_refractory} = v_2 - v_3 \quad (113)$$

9.4 Species IRS1

Name IRS1

Initial concentration 18.9345 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_4](#) and as a product in [reaction_6](#) and as a modifier in [reaction_4](#)).

$$\frac{d}{dt} \text{IRS1} = v_6 - v_4 \quad (114)$$

9.5 Species IRS1_p

Name IRS1_p

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in nine reactions (as a reactant in [reaction_5](#) and as a product in [reaction_4](#) and as a modifier in [reaction_5](#), [reaction_7](#), [reaction_7](#), [reaction_11](#), [reaction_11](#), [reaction_12](#), [reaction_12](#)).

$$\frac{d}{dt}\text{IRS1_p} = v_4 - v_5 \quad (115)$$

9.6 Species IRS1_pS636

Name IRS1_pS636

Initial concentration 0 dimensionless · dimensionless⁻¹

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

$$\frac{d}{dt}\text{IRS1_pS636} = v_5 - v_6 \quad (116)$$

9.7 Species AMPK

Name AMPK

Initial concentration 20.5064 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_7](#) and as a product in [reaction_8](#) and as a modifier in [reaction_7](#)).

$$\frac{d}{dt}\text{AMPK} = v_8 - v_7 \quad (117)$$

9.8 Species AMPK_pT172

Name AMPK_pT172

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in five reactions (as a reactant in [reaction_8](#) and as a product in [reaction_7](#) and as a modifier in [reaction_8](#), [reaction_23](#), [reaction_23](#)).

$$\frac{d}{dt}\text{AMPK_pT172} = v_7 - v_8 \quad (118)$$

9.9 Species Akt_T308

Name Akt_T308

Initial concentration 21.4109 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_12](#) and as a product in [reaction_9](#) and as a modifier in [reaction_12](#)).

$$\frac{d}{dt}\text{Akt_T308} = v_9 - v_{12} \quad (119)$$

9.10 Species Akt_pT308

Name Akt_pT308

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in seven reactions (as a reactant in [reaction_9](#) and as a product in [reaction_12](#) and as a modifier in [reaction_9](#), [reaction_22](#), [reaction_22](#), [reaction_24](#), [reaction_24](#)).

$$\frac{d}{dt}\text{Akt_pT308} = v_{12} - v_9 \quad (120)$$

9.11 Species Akt_S473

Name Akt_S473

Initial concentration 12.2517 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_11](#) and as a product in [reaction_10](#) and as a modifier in [reaction_11](#)).

$$\frac{d}{dt}\text{Akt_S473} = v_{10} - v_{11} \quad (121)$$

9.12 Species Akt_pS473

Name Akt_pS473

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_10](#) and as a product in [reaction_11](#) and as a modifier in [reaction_10](#)).

$$\frac{d}{dt}\text{Akt_pS473} = v_{11} - v_{10} \quad (122)$$

9.13 Species `mTORC1`

Name `mTORC1`

Initial concentration 25.14 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_14](#) and as a product in [reaction_13](#) and as a modifier in [reaction_14](#)).

$$\frac{d}{dt}mTORC1 = v_{13} - v_{14} \quad (123)$$

9.14 Species `mTORC1_pS2448`

Name `mTORC1_pS2448`

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in seven reactions (as a reactant in [reaction_13](#) and as a product in [reaction_14](#) and as a modifier in [reaction_13](#), [reaction_18](#), [reaction_18](#), [reaction_21](#), [reaction_21](#)).

$$\frac{d}{dt}mTORC1_pS2448 = v_{14} - v_{13} \quad (124)$$

9.15 Species `mTORC2`

Name `mTORC2`

Initial concentration 18.7959 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_16](#) and as a product in [reaction_15](#) and as a modifier in [reaction_16](#)).

$$\frac{d}{dt}mTORC2 = v_{15} - v_{16} \quad (125)$$

9.16 Species `mTORC2_pS2481`

Name `mTORC2_pS2481`

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in five reactions (as a reactant in [reaction_15](#) and as a product in [reaction_16](#) and as a modifier in [reaction_11](#), [reaction_11](#), [reaction_15](#)).

$$\frac{d}{dt}mTORC2_pS2481 = v_{16} - v_{15} \quad (126)$$

9.17 Species p70S6K

Name p70S6K

Initial concentration 14.301 dimensionless · 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](#)).

$$\frac{d}{dt}p70S6K = v_{17} - v_{18} \quad (127)$$

9.18 Species p70S6K_pT389

Name p70S6K_pT389

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in five reactions (as a reactant in [reaction_17](#) and as a product in [reaction_18](#) and as a modifier in [reaction_5](#), [reaction_5](#), [reaction_17](#)).

$$\frac{d}{dt}p70S6K_pT389 = v_{18} - v_{17} \quad (128)$$

9.19 Species PRAS40_T246

Name PRAS40_T246

Initial concentration 13.5613 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_22](#) and as a product in [reaction_20](#) and as a modifier in [reaction_22](#)).

$$\frac{d}{dt}PRAS40_T246 = v_{20} - v_{22} \quad (129)$$

9.20 Species PRAS40_pT246

Name PRAS40_pT246

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_20](#) and as a product in [reaction_22](#) and as a modifier in [reaction_20](#)).

$$\frac{d}{dt}PRAS40_pT246 = v_{22} - v_{20} \quad (130)$$

9.21 Species PRAS40_S183

Name PRAS40_S183

Initial concentration 17.55 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_21](#) and as a product in [reaction_19](#) and as a modifier in [reaction_21](#)).

$$\frac{d}{dt}\text{PRAS40_S183} = v_{19} - v_{21} \quad (131)$$

9.22 Species PRAS40_pS183

Name PRAS40_pS183

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_19](#) and as a product in [reaction_21](#) and as a modifier in [reaction_19](#)).

$$\frac{d}{dt}\text{PRAS40_pS183} = v_{21} - v_{19} \quad (132)$$

9.23 Species TSC1_TSC2_pT1462

Name TSC1_TSC2_pT1462

Initial concentration 14.9175 dimensionless · dimensionless⁻¹

This species takes part in three reactions (as a reactant in [reaction_23](#) and as a product in [reaction_24](#) and as a modifier in [reaction_23](#)).

$$\frac{d}{dt}\text{TSC1_TSC2_pT1462} = v_{24} - v_{23} \quad (133)$$

9.24 Species TSC1_TSC2_pS1387

Name TSC1_TSC2_pS1387

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in five reactions (as a reactant in [reaction_24](#) and as a product in [reaction_23](#) and as a modifier in [reaction_13](#), [reaction_13](#), [reaction_24](#)).

$$\frac{d}{dt}\text{TSC1_TSC2_pS1387} = v_{23} - v_{24} \quad (134)$$

9.25 Species [PI3K_variant](#)

Name PI3K_variant

Initial concentration 18.9345 dimensionless · dimensionless⁻¹

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

$$\frac{d}{dt}\text{PI3K_variant} = v_{25} - v_{26} \quad (135)$$

9.26 Species [PI3K_variant_p](#)

Name PI3K_variant_p

Initial concentration 0 dimensionless · dimensionless⁻¹

This species takes part in five reactions (as a reactant in [reaction_25](#) and as a product in [reaction_26](#) and as a modifier in [reaction_16](#), [reaction_16](#), [reaction_25](#)).

$$\frac{d}{dt}\text{PI3K_variant_p} = v_{26} - v_{25} \quad (136)$$

9.27 Species [Insulin](#)

Name Insulin

Initial concentration 10 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.

9.28 Species [Amino_Acids](#)

Name Amino_Acids

Initial concentration 10 dimensionless · dimensionless⁻¹

Involved in rule [Amino_Acids](#)

This species takes part in two reactions (as a modifier in [reaction_14](#), [reaction_14](#)). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

9.29 Species [IR_beta_pY1146_obs](#)

Name IR_beta_pY1146_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [IR_beta_pY1146_obs](#)

One rule determines the species' quantity.

9.30 Species [IRS1_pS636_obs](#)

Name IRS1_pS636_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [IRS1_pS636_obs](#)

One rule determines the species' quantity.

9.31 Species [AMPK_pT172_obs](#)

Name AMPK_pT172_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [AMPK_pT172_obs](#)

One rule determines the species' quantity.

9.32 Species [Akt_pT308_obs](#)

Name Akt_pT308_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [Akt_pT308_obs](#)

One rule determines the species' quantity.

9.33 Species [Akt_pS473_obs](#)

Name Akt_pS473_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [Akt_pS473_obs](#)

One rule determines the species' quantity.

9.34 Species [TSC1_TSC2_pS1387_obs](#)

Name TSC1_TSC2_pS1387_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [TSC1_TSC2_pS1387_obs](#)

One rule determines the species' quantity.

9.35 Species [mTOR_pS2448_obs](#)

Name mTOR_pS2448_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [mTOR_pS2448_obs](#)

One rule determines the species' quantity.

9.36 Species [mTOR_pS2481_obs](#)

Name mTOR_pS2481_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [mTOR_pS2481_obs](#)

One rule determines the species' quantity.

9.37 Species [p70S6K_pT389_obs](#)

Name p70S6K_pT389_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [p70S6K_pT389_obs](#)

One rule determines the species' quantity.

9.38 Species [PRAS40_pT246_obs](#)

Name PRAS40_pT246_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule [PRAS40_pT246_obs](#)

One rule determines the species' quantity.

9.39 Species PRAS40_pS183_obs

Name PRAS40_pS183_obs

Initial concentration 0 dimensionless · dimensionless⁻¹

Involved in rule PRAS40_pS183_obs

One rule determines the species' quantity.

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