SBML Model Report

Model name: "DallePezze2012 - TSC-independent mTORC2 regulation"

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: Piero Dalle Pezze[1] and Vijayalakshmi Chelliah[2] at August twelveth 2015 at 10:15 p. m. and last time modified at August thirteenth 2015 at 12:14 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	2
species types	0	species	28
events	0	constraints	0
reactions	32	function definitions	0
global parameters	0	unit definitions	3
rules	0	initial assignments	2

Model Notes

DallePezze2012 - TSC-independent mTORC2regulation

This model is described in the article:A dynamic network model of mTOR signaling reveals TSC-independent mTORC2 regulation.Dalle Pezze P, Sonntag AG, Thien A, Prentzell MT, Gdel

---

[1]Newcastle University, `piero.dallepezze@gmail.com`
[2]EMBL-EBI, `viji@ebi.ac.uk`

M, Fischer S, Neumann-Haefelin E, Huber TB, Baumeister R, Shanley DP, Thedieck K.Sci Signal 2012 Mar; 5(217): ra25

Abstract:

The kinase mammalian target of rapamycin (mTOR) exists in two multiprotein complexes (mTORC1 and mTORC2) and is a central regulator of growth and metabolism. Insulin activation of mTORC1, mediated by phosphoinositide 3-kinase (PI3K), Akt, and the inhibitory tuberous sclerosis complex 1/2 (TSC1-TSC2), initiates a negative feedback loop that ultimately inhibits PI3K. We present a data-driven dynamic insulin-mTOR network model that integrates the entire core network and used this model to investigate the less well understood mechanisms by which insulin regulates mTORC2. By analyzing the effects of perturbations targeting several levels within the network in silico and experimentally, we found that, in contrast to current hypotheses, the TSC1-TSC2 complex was not a direct or indirect (acting through the negative feedback loop) regulator of mTORC2. Although mTORC2 activation required active PI3K, this was not affected by the negative feedback loop. Therefore, we propose an mTORC2 activation pathway through a PI3K variant that is insensitive to the negative feedback loop that regulates mTORC1. This putative pathway predicts that mTORC2 would be refractory to Akt, which inhibits TSC1-TSC2, and, indeed, we found that mTORC2 was insensitive to constitutive Akt activation in several cell types. Our results suggest that a previously unknown network structure connects mTORC2 to its upstream cues and clarifies which molecular connectors contribute to mTORC2 activation.

This model is hosted on BioModels Database and identified by: BIOMD0000000581.

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

2 Unit Definitions

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

2.1 Unit `volume`

Name volume

Definition dimensionless

2.2 Unit `time`

Name time

Definition $60\,\mathrm{s}$

Produced by SBML2LATEX

2.3 Unit `substance`

Name substance

Definition dimensionless

2.4 Unit `area`

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

Definition m^2

2.5 Unit `length`

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

Definition m

3 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
compartment_1	Membrane		3	1	dimensionless	☑	
compartment_2	Cytoplasm		3	1	dimensionless	☑	

3.1 Compartment `compartment_1`

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

Name Membrane

3.2 Compartment `compartment_2`

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

Name Cytoplasm

4 Species

This model contains 28 species. The boundary condition of three of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 7 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit		Constant	Boundary Condition
species_20	IR_beta	compartment_1	dimensionless $\cdot$ dimensionless^{-1}		⊟	⊟
species_21	IR_beta_pY1146	compartment_1	dimensionless $\cdot$ dimensionless^{-1}		⊟	⊟
species_15	IR_beta_refractory	compartment_1	dimensionless $\cdot$ dimensionless^{-1}		⊟	⊟
species_41	Insulin	compartment_1	dimensionless $\cdot$ dimensionless^{-1}		☑	☑
species_28	Amino_Acids	compartment_2	dimensionless $\cdot$ dimensionless^{-1}		☑	☑
species_1	Sink	compartment_2	dimensionless $\cdot$ dimensionless^{-1}		⊟	⊟
species_5	mTORC2	compartment_2	dimensionless $\cdot$ dimensionless^{-1}		⊟	⊟
species_2	mTORC1_pS2448	compartment_2	dimensionless $\cdot$ dimensionless^{-1}		⊟	⊟
species_11	mTORC1	compartment_2	dimensionless $\cdot$ dimensionless^{-1}		⊟	⊟
species_19	IRS1_pS636_PI3K	compartment_2	dimensionless $\cdot$ dimensionless^{-1}		⊟	⊟

Id	Name	Compartment	Derived Unit		Constant	Boundary Condition
species_7	IRS1_p_PI3K	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_22	mTORC2_pS2481	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_17	p70S6K_pT389	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_42	IRS1_PI3K	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_3	Akt_pT308	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_6	TSC_clx	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_9	PRAS40	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_12	PRAS40_pS183	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_10	PRAS40_pT246	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_27	Akt	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_4	Akt_pT308_pS473	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_47	p70S6K	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟
species_8	TSC_p_clx	compartment_2	dimensionless dimensionless^{-1}	·	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
species_13	PDK2	compartment_2	dimensionless · dimensionless^{-1}	⊟	⊟
species_14	PDK2_p	compartment_2	dimensionless · dimensionless^{-1}	⊟	⊟
species_16	PI3K_variant_p	compartment_2	dimensionless · dimensionless^{-1}	⊟	⊟
species_18	PI3K_variant	compartment_2	dimensionless · dimensionless^{-1}	⊟	⊟
species_23	PI3K	compartment_2	dimensionless · dimensionless^{-1}	☑	☑

5 Initialassignments

This is an overview of two initialassignments.

5.1 Initialassignment `species_42`

Derived unit dimensionless^{-1}

Math [species_23]

5.2 Initialassignment `species_18`

Derived unit dimensionless^{-1}

Math [species_23]

6 Reactions

This model contains 32 reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 4: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	reaction_9	TSC_p_clx_dephosphorylation	$species\_8 \xrightarrow{species\_8} species\_6$	
2	reaction_16	p70S6K_T389_phosphorylation_by-_mTORC1_pS2448	$species\_47 + species\_2 \xrightarrow{species\_47,\ species\_2} species\_17 + species\_2$	
3	reaction_17	p70S6K_pT389_dephosphorylation	$species\_17 \xrightarrow{species\_17} species\_47$	
4	reaction_22	IRS1_S636_phosphorylation_by_p70S6K-_pT389	$species\_42 + species\_17 \xrightarrow{species\_42,\ species\_17} species\_19 + species\_17$	
5	reaction_23	IRS1_PI3K_phosphorylation_by_IR_beta-_pY1146	$species\_42 + species\_21 \xrightarrow{species\_42,\ species\_21} species\_7 + species\_21$	
6	reaction_31	Akt_T308_phosphorylation_by_IRS1_phos-_PI3K	$species\_27 + species\_7 \xrightarrow{species\_27,\ species\_7} species\_3 + species\_7$	
7	reaction_32	Akt_pT308_S473_phosphorylation_by-_mTORC2_pS2481	$species\_3 + species\_22 \xrightarrow{species\_3,\ species\_22} species\_4 + species\_22$	
8	reaction_33	TSC_clx_phosphorylation_by_Akt_pT308	$species\_6 + species\_3 \xrightarrow{species\_6,\ species\_3} species\_8 + species\_3$	
9	reaction_40	mTORC1_S2448_activation_by_Amino-_Acids	$species\_11 + species\_28 \xrightarrow{species\_11,\ species\_28} species\_2$	
10	reaction_41	IR_beta_Y1146_phosphorylation	$species\_20 + species\_41 \xrightarrow{species\_20,\ species\_41} species\_21$	

№	Id	Name	Reaction Equation	SBO
11	reaction_46	IRS1_p_pi3K_phosphorylation_by_p70S6K-_pT389	species_7+species_17 $\xrightarrow{\text{species\_7, species\_17}}$ species_19+species_17	
12	reaction_53	IRS1_pS636_degradation	species_19 $\xrightarrow{\text{species\_19}}$ species_1	
13	reaction_55	IRS1_p_PI3K_dephosphorylation	species_7 $\xrightarrow{\text{species\_7}}$ species_42	
14	reaction_44	Akt_pT308_pS473_dephosphorylation	species_4 $\xrightarrow{\text{species\_4}}$ species_3	
15	reaction_61	Akt_pT308_dephosphorylation	species_3 $\xrightarrow{\text{species\_3}}$ species_27	
16	reaction_1	mTORC2_pS2481_dephosphorylation	species_22 $\xrightarrow{\text{species\_22}}$ species_5	
17	reaction_2	IR_beta_pY1146_dephosphorylation	species_21 $\xrightarrow{\text{species\_21}}$ species_15	
18	reaction_3	TSC_clx_phosphorylation_by_Akt_pT308-_pS473	species_6+species_4 $\xrightarrow{\text{species\_6, species\_4}}$ species_8+species_4	
19	reaction_4	IRS1_synthesis	species_1 $\xrightarrow{\text{species\_1}}$ species_42	
20	reaction_5	IR_beta_ready	species_15 $\xrightarrow{\text{species\_15}}$ species_20	
21	reaction_6	PRAS40_T246_phosphorylation_by_Akt-_pT308_pS473	species_9+species_4 $\xrightarrow{\text{species\_9, species\_4}}$ species_10+species_4	
22	reaction_7	mTORC1_pS2448_dephosphorylation_by-_TSC_clx	species_2+species_6 $\xrightarrow{\text{species\_2, species\_6}}$ species_11+species_6	
23	reaction_8	PRAS40_T246_phosphorylation_by_Akt-_pT308	species_9+species_3 $\xrightarrow{\text{species\_9, species\_3}}$ species_10+species_3	
24	reaction_10	PRAS40_pT246_dephosphorylation	species_10 $\xrightarrow{\text{species\_10}}$ species_9	
25	reaction_11	PRAS40_pS183_dephosphorylation	species_12 $\xrightarrow{\text{species\_12}}$ species_9	

№	Id	Name	Reaction Equation	SBO
26	reaction_12	PRAS40_S183_phosphorylation_by-_mTORC1_pS2448	species_9+species_2 $\xrightarrow{\text{species\_9, species\_2}}$ species_12+species_2	
27	reaction_18	mTORC2_S2481_phosphorylation_by_PI3K-_variant_p	species_5+species_16 $\xrightarrow{\text{species\_5, species\_16}}$ species_22+species_16	
28	reaction_13	Akt_pT308_S473_phosphorylation_by_PDK2	species_3+species_14 $\xrightarrow{\text{species\_3, species\_14}}$ species_4+species_14	
29	reaction_14	PDK2_p_dephosphorylation	species_14 $\xrightarrow{\text{species\_14}}$ species_13	
30	reaction_15	PDK2_phosphorylation	species_13+species_21 $\xrightarrow{\text{species\_13, species\_21}}$ species_14+species_21	
31	reaction_19	PI3K_variant_phosphorylation_by_IR_beta-_pY1146	species_18+species_21 $\xrightarrow{\text{species\_18, species\_21}}$ species_16+species_21	
32	reaction_20	PI3K_variant_p_dephosphorylation	species_16 $\xrightarrow{\text{species\_16}}$ species_18	

6.1 Reaction `reaction_9`

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

Name TSC_p_clx_dephosphorylation

Reaction equation

$$\text{species\_8} \xrightarrow{\text{species\_8}} \text{species\_6} \tag{1}$$

Reactant

Table 5: Properties of each reactant.

Id	Name	SBO
species_8	TSC_p_clx	

Modifier

Table 6: Properties of each modifier.

Id	Name	SBO
species_8	TSC_p_clx	

Product

Table 7: Properties of each product.

Id	Name	SBO
species_6	TSC_clx	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_8}] \tag{2}$$

Table 8: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.008		☑

6.2 Reaction `reaction_16`

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

Name p70S6K_T389_phosphorylation_by_mTORC1_pS2448

Reaction equation

$$\text{species\_47} + \text{species\_2} \xrightarrow{\text{species\_47, species\_2}} \text{species\_17} + \text{species\_2} \tag{3}$$

Reactants

Table 9: Properties of each reactant.

Id	Name	SBO
species_47	p70S6K	
species_2	mTORC1_pS2448	

Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
species_47	p70S6K	
species_2	mTORC1_pS2448	

Products

Table 11: Properties of each product.

Id	Name	SBO
species_17	p70S6K_pT389	
species_2	mTORC1_pS2448	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}\left(\text{compartment\_2}\right) \cdot \text{k1} \cdot [\text{species\_47}] \cdot [\text{species\_2}] \tag{4}$$

Table 12: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.006		☑

6.3 Reaction `reaction_17`

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

Name p70S6K_pT389_dephosphorylation

Reaction equation

$$\text{species\_17} \xrightarrow{\text{species\_17}} \text{species\_47} \tag{5}$$
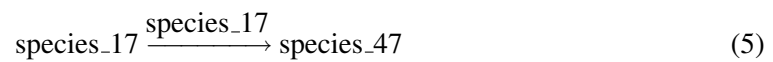
Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
species_17	p70S6K_pT389	

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
species_17	p70S6K_pT389	

Product

Table 15: Properties of each product.

Id	Name	SBO
species_47	p70S6K	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_17}] \tag{6}$$

Table 16: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.005		☑

6.4 Reaction `reaction_22`

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

Name IRS1_S636_phosphorylation_by_p70S6K_pT389

Reaction equation

$$\text{species\_42} + \text{species\_17} \xrightarrow{\text{species\_42, species\_17}} \text{species\_19} + \text{species\_17} \tag{7}$$

Reactants

Table 17: Properties of each reactant.

Id	Name	SBO
species_42	IRS1_PI3K	
species_17	p70S6K_pT389	

Modifiers

Table 18: Properties of each modifier.

Id	Name	SBO
species_42	IRS1_PI3K	
species_17	p70S6K_pT389	

Products

Table 19: Properties of each product.

Id	Name	SBO
species_19	IRS1_pS636_PI3K	
species_17	p70S6K_pT389	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_42}] \cdot [\text{species\_17}] \tag{8}$$
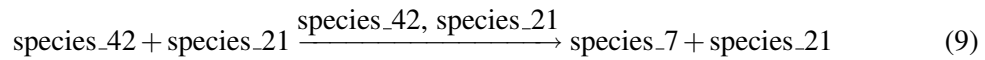
Table 20: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.0		☑

6.5 Reaction `reaction_23`

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

Name IRS1_PI3K_phosphorylation_by_IR_beta_pY1146

Reaction equation

$$\text{species\_42} + \text{species\_21} \xrightarrow{\text{species\_42, species\_21}} \text{species\_7} + \text{species\_21} \tag{9}$$

Reactants

Table 21: Properties of each reactant.

Id	Name	SBO
species_42	IRS1_PI3K	
species_21	IR_beta_pY1146	

Modifiers

Table 22: Properties of each modifier.

Id	Name	SBO
species_42	IRS1_PI3K	
species_21	IR_beta_pY1146	

Products

Table 23: Properties of each product.

Id	Name	SBO
species_7	IRS1_p_PI3K	
species_21	IR_beta_pY1146	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{k1} \cdot [\text{species\_42}] \cdot [\text{species\_21}] \tag{10}$$
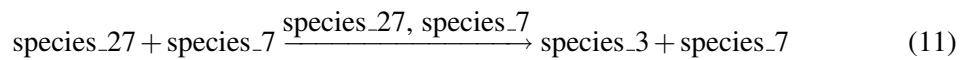
Table 24: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.135		☑

6.6 Reaction reaction_31

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

Name Akt_T308_phosphorylation_by_IRS1_phos_PI3K

Reaction equation

$$\text{species\_27} + \text{species\_7} \xrightarrow{\text{species\_27, species\_7}} \text{species\_3} + \text{species\_7} \tag{11}$$

Reactants

Table 25: Properties of each reactant.

Id	Name	SBO
species_27	Akt	
species_7	IRS1_p_PI3K	

Modifiers

Table 26: Properties of each modifier.

Id	Name	SBO
species_27	Akt	
species_7	IRS1_p_PI3K	

Products

Table 27: Properties of each product.

Id	Name	SBO
species_3	Akt_pT308	
species_7	IRS1_p_PI3K	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_27}] \cdot [\text{species\_7}] \qquad (12)$$
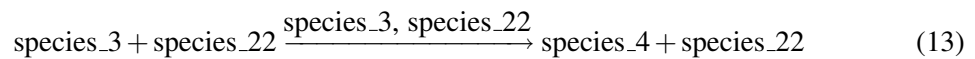
Table 28: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.700		☑

6.7 Reaction `reaction_32`

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

Name Akt_pT308_S473_phosphorylation_by_mTORC2_pS2481

Reaction equation

$$\text{species\_3} + \text{species\_22} \xrightarrow{\text{species\_3, species\_22}} \text{species\_4} + \text{species\_22} \qquad (13)$$

Reactants

Table 29: Properties of each reactant.

Id	Name	SBO
species_3	Akt_pT308	
species_22	mTORC2_pS2481	

Modifiers

Table 30: Properties of each modifier.

Id	Name	SBO
species_3	Akt_pT308	
species_22	mTORC2_pS2481	

Products

Table 31: Properties of each product.

Id	Name	SBO
species_4	Akt_pT308_pS473	
species_22	mTORC2_pS2481	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_3}] \cdot [\text{species\_22}] \tag{14}$$

Table 32: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		4.508		☑

6.8 Reaction reaction_33

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

Name TSC_clx_phosphorylation_by_Akt_pT308

Reaction equation

$$\text{species\_6} + \text{species\_3} \xrightarrow{\text{species\_6, species\_3}} \text{species\_8} + \text{species\_3} \tag{15}$$
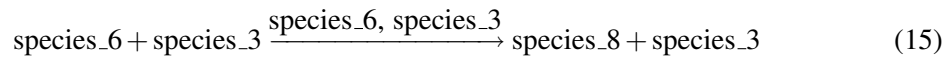
Reactants

Table 33: Properties of each reactant.

Id	Name	SBO
species_6	TSC_clx	
species_3	Akt_pT308	

Modifiers

Table 34: Properties of each modifier.

Id	Name	SBO
species_6	TSC_clx	
species_3	Akt_pT308	

Products

Table 35: Properties of each product.

Id	Name	SBO
species_8	TSC_p_clx	
species_3	Akt_pT308	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{vol}\left(\text{compartment\_2}\right) \cdot \text{k1} \cdot [\text{species\_6}] \cdot [\text{species\_3}] \tag{16}$$

Table 36: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.006		☑

6.9 Reaction `reaction_40`

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

Name mTORC1_S2448_activation_by_Amino_Acids

Reaction equation

$$\text{species\_11} + \text{species\_28} \xrightarrow{\text{species\_11, species\_28}} \text{species\_2} \tag{17}$$
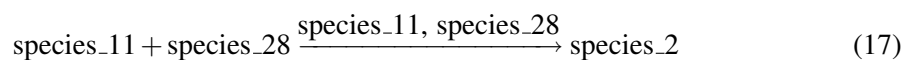
Reactants

Table 37: Properties of each reactant.

Id	Name	SBO
species_11	mTORC1	
species_28	Amino_Acids	

Modifiers

Table 38: Properties of each modifier.

Id	Name	SBO
species_11	mTORC1	
species_28	Amino_Acids	

Product

Table 39: Properties of each product.

Id	Name	SBO
species_2	mTORC1_pS2448	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_11}] \cdot [\text{species\_28}] \tag{18}$$

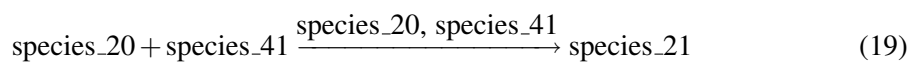Table 40: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.051		☑

6.10 Reaction `reaction_41`

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

Name IR_beta_Y1146_phosphorylation

Reaction equation

$$\text{species\_20} + \text{species\_41} \xrightarrow{\text{species\_20, species\_41}} \text{species\_21} \tag{19}$$

Reactants

Table 41: Properties of each reactant.

Id	Name	SBO
species_20	IR_beta	
species_41	Insulin	

Modifiers

Table 42: Properties of each modifier.

Id	Name	SBO
species_20	IR_beta	
species_41	Insulin	

Product

Table 43: Properties of each product.

Id	Name	SBO
species_21	IR_beta_pY1146	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{vol}(\text{compartment\_1}) \cdot \text{k1} \cdot [\text{species\_20}] \cdot [\text{species\_41}] \tag{20}$$
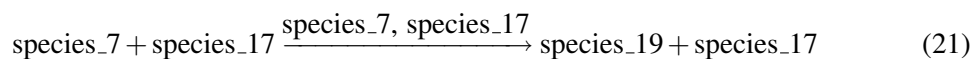
Table 44: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.025		☑

6.11 Reaction `reaction_46`

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

Name IRS1_p_pi3K_phosphorylation_by_p70S6K_pT389

Reaction equation

$$\text{species\_7} + \text{species\_17} \xrightarrow{\text{species\_7, species\_17}} \text{species\_19} + \text{species\_17} \tag{21}$$

Reactants

Table 45: Properties of each reactant.

Id	Name	SBO
species_7	IRS1_p_PI3K	
species_17	p70S6K_pT389	

Modifiers

Table 46: Properties of each modifier.

Id	Name	SBO
species_7	IRS1_p_PI3K	
species_17	p70S6K_pT389	

Products

Table 47: Properties of each product.

Id	Name	SBO
species_19	IRS1_pS636_PI3K	

Id	Name	SBO
species_17	p70S6K_pT389	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_7}] \cdot [\text{species\_17}] \qquad (22)$$
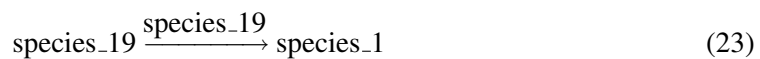
Table 48: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		10^{-4}		☑

6.12 Reaction reaction_53

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

Name IRS1_pS636_degradation

Reaction equation

$$\text{species\_19} \xrightarrow{\text{species\_19}} \text{species\_1} \qquad (23)$$

Reactant

Table 49: Properties of each reactant.

Id	Name	SBO
species_19	IRS1_pS636_PI3K	

Modifier

Table 50: Properties of each modifier.

Id	Name	SBO
species_19	IRS1_pS636_PI3K	

Product

Table 51: Properties of each product.

Id	Name	SBO
species_1	Sink	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_19}] \qquad (24)$$
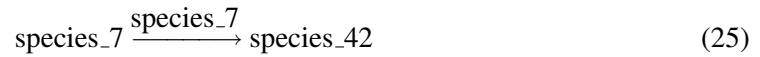
Table 52: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$1.00001 \cdot 10^{-4}$		☑

6.13 Reaction reaction_55

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

Name IRS1_p_PI3K_dephosphorylation

Reaction equation

$$\text{species\_7} \xrightarrow{\text{species\_7}} \text{species\_42} \qquad (25)$$

Reactant

Table 53: Properties of each reactant.

Id	Name	SBO
species_7	IRS1_p_PI3K	

Modifier

Table 54: Properties of each modifier.

Id	Name	SBO
species_7	IRS1_p_PI3K	

Product

Table 55: Properties of each product.

Id	Name	SBO
species_42	IRS1_PI3K	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_7}] \tag{26}$$
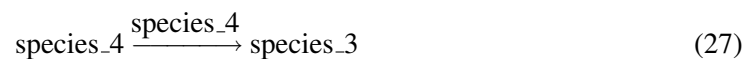
Table 56: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.003		☑

6.14 Reaction `reaction_44`

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

Name Akt_pT308_pS473_dephosphorylation

Reaction equation

$$\text{species\_4} \xrightarrow{\text{species\_4}} \text{species\_3} \tag{27}$$

Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
species_4	Akt_pT308_pS473	

Modifier

Table 58: Properties of each modifier.

Id	Name	SBO
species_4	Akt_pT308_pS473	

Id	Name	SBO

Product

Table 59: Properties of each product.

Id	Name	SBO
species_3	Akt_pT308	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_4}] \tag{28}$$

Table 60: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		7.528		☑

6.15 Reaction `reaction_61`

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

Name Akt_pT308_dephosphorylation

Reaction equation

$$\text{species\_3} \xrightarrow{\text{species\_3}} \text{species\_27} \tag{29}$$

Reactant

Table 61: Properties of each reactant.

Id	Name	SBO
species_3	Akt_pT308	

Modifier

Table 62: Properties of each modifier.

Id	Name	SBO
species_3	Akt_pT308	

Product

Table 63: Properties of each product.

Id	Name	SBO
species_27	Akt	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_3}] \tag{30}$$
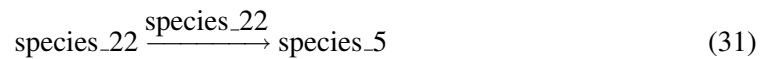
Table 64: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		4.074		☑

6.16 Reaction `reaction_1`

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

Name mTORC2_pS2481_dephosphorylation

Reaction equation

$$\text{species\_22} \xrightarrow{\text{species\_22}} \text{species\_5} \tag{31}$$

Reactant

Table 65: Properties of each reactant.

Id	Name	SBO
species_22	mTORC2_pS2481	

Modifier

Table 66: Properties of each modifier.

Id	Name	SBO
species_22	mTORC2_pS2481	

Product

Table 67: Properties of each product.

Id	Name	SBO
species_5	mTORC2	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{vol}\,(\mathrm{compartment\_2}) \cdot \mathrm{k1} \cdot [\mathrm{species\_22}] \tag{32}$$

Table 68: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.026		☑

6.17 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

$$\mathrm{species\_21} \xrightarrow{\mathrm{species\_21}} \mathrm{species\_15} \tag{33}$$
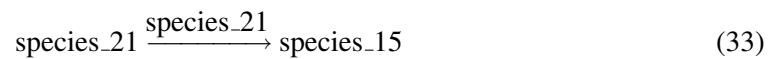
Reactant

Table 69: Properties of each reactant.

Id	Name	SBO
species_21	IR_beta_pY1146	

Id	Name	SBO

Modifier

Table 70: Properties of each modifier.

Id	Name	SBO
species_21	IR_beta_pY1146	

Product

Table 71: Properties of each product.

Id	Name	SBO
species_15	IR_beta_refractory	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_21}] \tag{34}$$

Table 72: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.149		☑

6.18 Reaction reaction_3

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

Name TSC_clx_phosphorylation_by_Akt_pT308_pS473

Reaction equation

$$\mathrm{species\_6} + \mathrm{species\_4} \xrightarrow{\mathrm{species\_6,\ species\_4}} \mathrm{species\_8} + \mathrm{species\_4} \tag{35}$$
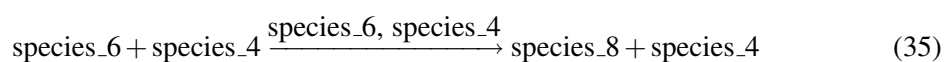
Reactants

Table 73: Properties of each reactant.

Id	Name	SBO
species_6	TSC_clx	
species_4	Akt_pT308_pS473	

Modifiers

Table 74: Properties of each modifier.

Id	Name	SBO
species_6	TSC_clx	
species_4	Akt_pT308_pS473	

Products

Table 75: Properties of each product.

Id	Name	SBO
species_8	TSC_p_clx	
species_4	Akt_pT308_pS473	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{vol}\,(\mathrm{compartment\_2}) \cdot \mathrm{k1} \cdot [\mathrm{species\_6}] \cdot [\mathrm{species\_4}] \tag{36}$$

Table 76: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$1.00039 \cdot 10^{-4}$		✓

6.19 Reaction `reaction_4`

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

Name IRS1_synthesis

Reaction equation

$$\text{species\_1} \xrightarrow{\text{species\_1}} \text{species\_42} \tag{37}$$

Reactant

Table 77: Properties of each reactant.

Id	Name	SBO
species_1	Sink	

Modifier

Table 78: Properties of each modifier.

Id	Name	SBO
species_1	Sink	

Product

Table 79: Properties of each product.

Id	Name	SBO
species_42	IRS1_PI3K	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_1}] \tag{38}$$
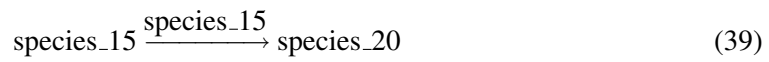
Table 80: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.100		☑

6.20 Reaction reaction_5

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

Name IR_beta_ready

Reaction equation

$$\text{species\_15} \xrightarrow{\text{species\_15}} \text{species\_20} \qquad (39)$$

Reactant

Table 81: Properties of each reactant.

Id	Name	SBO
species_15	IR_beta_refractory	

Modifier

Table 82: Properties of each modifier.

Id	Name	SBO
species_15	IR_beta_refractory	

Product

Table 83: Properties of each product.

Id	Name	SBO
species_20	IR_beta	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \text{vol}\,(\text{compartment\_1}) \cdot \text{k1} \cdot [\text{species\_15}] \qquad (40)$$
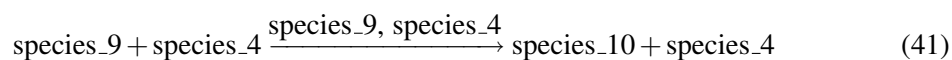
Table 84: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.031		☑

6.21 Reaction `reaction_6`

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

Name PRAS40_T246_phosphorylation_by_Akt_pT308_pS473

Reaction equation

$$\text{species\_9} + \text{species\_4} \xrightarrow{\text{species\_9, species\_4}} \text{species\_10} + \text{species\_4} \tag{41}$$

Reactants

Table 85: Properties of each reactant.

Id	Name	SBO
species_9	PRAS40	
species_4	Akt_pT308_pS473	

Modifiers

Table 86: Properties of each modifier.

Id	Name	SBO
species_9	PRAS40	
species_4	Akt_pT308_pS473	

Products

Table 87: Properties of each product.

Id	Name	SBO
species_10	PRAS40_pT246	
species_4	Akt_pT308_pS473	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_9}] \cdot [\text{species\_4}] \tag{42}$$
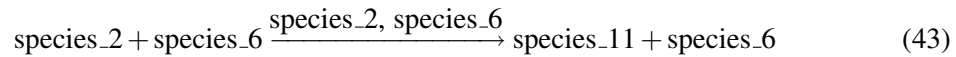
Table 88: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$1.00001 \cdot 10^{-4}$		☑

6.22 Reaction `reaction_7`

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

Name mTORC1_pS2448_dephosphorylation_by_TSC_clx

Reaction equation

$$\text{species\_2} + \text{species\_6} \xrightarrow{\text{species\_2, species\_6}} \text{species\_11} + \text{species\_6} \qquad (43)$$

Reactants

Table 89: Properties of each reactant.

Id	Name	SBO
species_2	mTORC1_pS2448	
species_6	TSC_clx	

Modifiers

Table 90: Properties of each modifier.

Id	Name	SBO
species_2	mTORC1_pS2448	
species_6	TSC_clx	

Products

Table 91: Properties of each product.

Id	Name	SBO
species_11	mTORC1	
species_6	TSC_clx	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_2}] \cdot [\text{species\_6}] \tag{44}$$
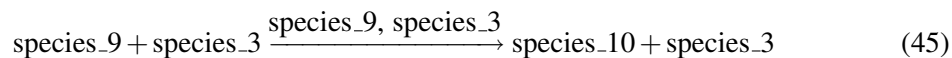
Table 92: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.000		☑

6.23 Reaction `reaction_8`

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

Name PRAS40_T246_phosphorylation_by_Akt_pT308

Reaction equation

$$\text{species\_9} + \text{species\_3} \xrightarrow{\text{species\_9, species\_3}} \text{species\_10} + \text{species\_3} \tag{45}$$

Reactants

Table 93: Properties of each reactant.

Id	Name	SBO
species_9	PRAS40	
species_3	Akt_pT308	

Modifiers

Table 94: Properties of each modifier.

Id	Name	SBO
species_9	PRAS40	
species_3	Akt_pT308	

Products

Table 95: Properties of each product.

Id	Name	SBO
species_10	PRAS40_pT246	
species_3	Akt_pT308	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_9}] \cdot [\text{species\_3}] \tag{46}$$
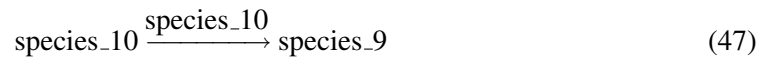
Table 96: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.024		☑

6.24 Reaction `reaction_10`

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

Name PRAS40_pT246_dephosphorylation

Reaction equation

$$\text{species\_10} \xrightarrow{\text{species\_10}} \text{species\_9} \tag{47}$$

Reactant

Table 97: Properties of each reactant.

Id	Name	SBO
species_10	PRAS40_pT246	

Modifier

Table 98: Properties of each modifier.

Id	Name	SBO
species_10	PRAS40_pT246	

Product

Table 99: Properties of each product.

Id	Name	SBO
species_9	PRAS40	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_10}] \tag{48}$$
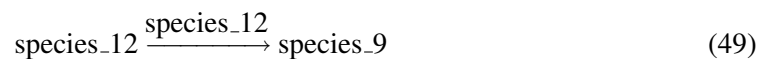
Table 100: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.000		☑

6.25 Reaction `reaction_11`

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

Name PRAS40_pS183_dephosphorylation

Reaction equation

$$\text{species\_12} \xrightarrow{\text{species\_12}} \text{species\_9} \tag{49}$$

Reactant

Table 101: Properties of each reactant.

Id	Name	SBO
species_12	PRAS40_pS183	

Modifier

Table 102: Properties of each modifier.

Id	Name	SBO
species_12	PRAS40_pS183	

Id	Name	SBO

Product

Table 103: Properties of each product.

Id	Name	SBO
species_9	PRAS40	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_12}] \tag{50}$$
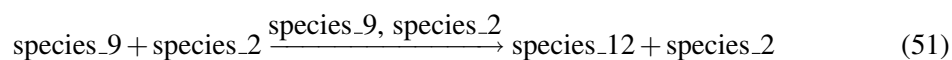
Table 104: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.404		☑

6.26 Reaction `reaction_12`

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

Name PRAS40_S183_phosphorylation_by_mTORC1_pS2448

Reaction equation

$$\text{species\_9} + \text{species\_2} \xrightarrow{\text{species\_9, species\_2}} \text{species\_12} + \text{species\_2} \tag{51}$$

Reactants

Table 105: Properties of each reactant.

Id	Name	SBO
species_9	PRAS40	
species_2	mTORC1_pS2448	

Modifiers

Table 106: Properties of each modifier.

Id	Name	SBO
species_9	PRAS40	
species_2	mTORC1_pS2448	

Products

Table 107: Properties of each product.

Id	Name	SBO
species_12	PRAS40_pS183	
species_2	mTORC1_pS2448	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_9}] \cdot [\text{species\_2}] \tag{52}$$
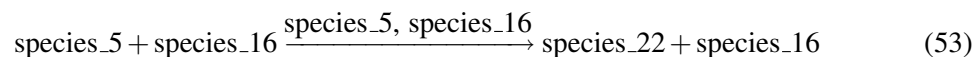
Table 108: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.073		☑

6.27 Reaction `reaction_18`

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

Name mTORC2_S2481_phosphorylation_by_PI3K_variant_p

Reaction equation

$$\text{species\_5} + \text{species\_16} \xrightarrow{\text{species\_5, species\_16}} \text{species\_22} + \text{species\_16} \tag{53}$$

Reactants

Table 109: Properties of each reactant.

Id	Name	SBO
species_5	mTORC2	
species_16	PI3K_variant_p	

Modifiers

Table 110: Properties of each modifier.

Id	Name	SBO
species_5	mTORC2	
species_16	PI3K_variant_p	

Products

Table 111: Properties of each product.

Id	Name	SBO
species_22	mTORC2_pS2481	
species_16	PI3K_variant_p	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \mathrm{vol}\,(\mathrm{compartment\_2}) \cdot \mathrm{k1} \cdot [\mathrm{species\_5}] \cdot [\mathrm{species\_16}] \tag{54}$$

Table 112: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.032		☑

6.28 Reaction `reaction_13`

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

Name Akt_pT308_S473_phosphorylation_by_PDK2

Reaction equation

$$\text{species\_3} + \text{species\_14} \xrightarrow{\text{species\_3, species\_14}} \text{species\_4} + \text{species\_14} \qquad (55)$$
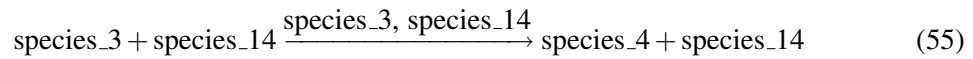
Reactants

Table 113: Properties of each reactant.

Id	Name	SBO
species_3	Akt_pT308	
species_14	PDK2_p	

Modifiers

Table 114: Properties of each modifier.

Id	Name	SBO
species_3	Akt_pT308	
species_14	PDK2_p	

Products

Table 115: Properties of each product.

Id	Name	SBO
species_4	Akt_pT308_pS473	
species_14	PDK2_p	

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_3}] \cdot [\text{species\_14}] \qquad (56)$$
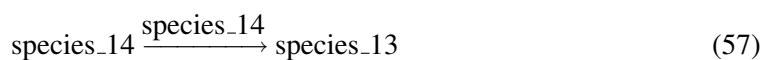
Table 116: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		5.904		☑

6.29 Reaction `reaction_14`

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

Name PDK2_p_dephosphorylation

Reaction equation

$$\text{species\_14} \xrightarrow{\text{species\_14}} \text{species\_13} \tag{57}$$

Reactant

Table 117: Properties of each reactant.

Id	Name	SBO
species_14	PDK2_p	

Modifier

Table 118: Properties of each modifier.

Id	Name	SBO
species_14	PDK2_p	

Product

Table 119: Properties of each product.

Id	Name	SBO
species_13	PDK2	

Kinetic Law

Derived unit contains undeclared units

$$v_{29} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_14}] \tag{58}$$
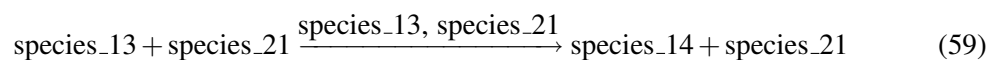
Table 120: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.0		✓

6.30 Reaction `reaction_15`

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

Name PDK2_phosphorylation

Reaction equation

$$\text{species\_13} + \text{species\_21} \xrightarrow{\text{species\_13, species\_21}} \text{species\_14} + \text{species\_21} \qquad (59)$$

Reactants

Table 121: Properties of each reactant.

Id	Name	SBO
species_13	PDK2	
species_21	IR_beta_pY1146	

Modifiers

Table 122: Properties of each modifier.

Id	Name	SBO
species_13	PDK2	
species_21	IR_beta_pY1146	

Products

Table 123: Properties of each product.

Id	Name	SBO
species_14	PDK2_p	
species_21	IR_beta_pY1146	

Kinetic Law

Derived unit contains undeclared units

$$v_{30} = \text{k1} \cdot [\text{species\_13}] \cdot [\text{species\_21}] \qquad (60)$$
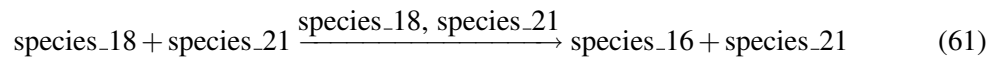
Table 124: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.1		✔

6.31 Reaction `reaction_19`

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

Name PI3K_variant_phosphorylation_by_IR_beta_pY1146

Reaction equation

$$\text{species\_18} + \text{species\_21} \xrightarrow{\text{species\_18, species\_21}} \text{species\_16} + \text{species\_21} \tag{61}$$

Reactants

Table 125: Properties of each reactant.

Id	Name	SBO
species_18	PI3K_variant	
species_21	IR_beta_pY1146	

Modifiers

Table 126: Properties of each modifier.

Id	Name	SBO
species_18	PI3K_variant	
species_21	IR_beta_pY1146	

Products

Table 127: Properties of each product.

Id	Name	SBO
species_16	PI3K_variant_p	
species_21	IR_beta_pY1146	

Kinetic Law

Derived unit contains undeclared units

$$v_{31} = k1 \cdot [\text{species\_18}] \cdot [\text{species\_21}] \tag{62}$$
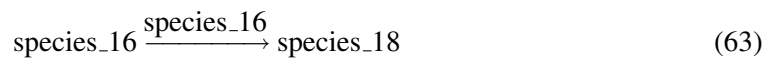
Table 128: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.000		☑

6.32 Reaction `reaction_20`

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

Name PI3K_variant_p_dephosphorylation

Reaction equation

$$\text{species\_16} \xrightarrow{\text{species\_16}} \text{species\_18} \tag{63}$$

Reactant

Table 129: Properties of each reactant.

Id	Name	SBO
species_16	PI3K_variant_p	

Modifier

Table 130: Properties of each modifier.

Id	Name	SBO
species_16	PI3K_variant_p	

Product

Table 131: Properties of each product.

Id	Name	SBO
species_18	PI3K_variant	

Id	Name	SBO

Kinetic Law

Derived unit contains undeclared units

$$v_{32} = \text{vol}\,(\text{compartment\_2}) \cdot \text{k1} \cdot [\text{species\_16}] \tag{64}$$

Table 132: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$2.32165 \cdot 10^{-4}$		☑

7 Derived Rate Equations

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

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

- parameters without an unit definition are involved or

- volume correction is necessary because the `hasOnlySubstanceUnits` flag may be set to `false` and `spacialDimensions` > 0 for certain species.

7.1 Species `species_20`

Name IR_beta

Initial concentration 12.1175 dimensionless $\cdot$ dimensionless^{-1}

This species takes part in three reactions (as a reactant in `reaction_41` and as a product in `reaction_5` and as a modifier in `reaction_41`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_20} = v_{20} - v_{10} \tag{65}$$

7.2 Species `species_21`

Name IR_beta_pY1146

Initial concentration 0 dimensionless $\cdot$ dimensionless^{-1}

This species takes part in twelve reactions (as a reactant in `reaction_23`, `reaction_2`, `reaction-_15`, `reaction_19` and as a product in `reaction_23`, `reaction_41`, `reaction_15`, `reaction-_19` and as a modifier in `reaction_23`, `reaction_2`, `reaction_15`, `reaction_19`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_21} = v_5 + v_{10} + v_{30} + v_{31} - v_5 - v_{17} - v_{30} - v_{31} \tag{66}$$

7.3 Species `species_15`

Name IR_beta_refractory

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

This species takes part in three reactions (as a reactant in `reaction_5` and as a product in `reaction_2` and as a modifier in `reaction_5`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_15} = v_{17} - v_{20} \tag{67}$$

7.4 Species `species_41`

Name Insulin

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

This species takes part in two reactions (as a reactant in `reaction_41` and as a modifier in `reaction_41`), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_41} = 0 \tag{68}$$

7.5 Species `species_28`

Name Amino_Acids

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

This species takes part in two reactions (as a reactant in `reaction_40` and as a modifier in `reaction_40`), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_28} = 0 \tag{69}$$

7.6 Species `species_1`

Name Sink

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

This species takes part in three reactions (as a reactant in `reaction_4` and as a product in `reaction_53` and as a modifier in `reaction_4`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_1} = v_{12} - v_{19} \tag{70}$$

7.7 Species `species_5`

Name mTORC2

Initial concentration $6.2175 \, \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in three reactions (as a reactant in `reaction_18` and as a product in `reaction_1` and as a modifier in `reaction_18`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_5} = v_{16} - v_{27} \tag{71}$$

7.8 Species `species_2`

Name mTORC1_pS2448

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

This species takes part in nine reactions (as a reactant in `reaction_16`, `reaction_7`, `reaction_12` and as a product in `reaction_16`, `reaction_40`, `reaction_12` and as a modifier in `reaction_16`, `reaction_7`, `reaction_12`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_2} = v_2 + v_9 + v_{26} - v_2 - v_{22} - v_{26} \tag{72}$$

7.9 Species `species_11`

Name mTORC1

Initial concentration $4.3225 \, \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in three reactions (as a reactant in `reaction_40` and as a product in `reaction_7` and as a modifier in `reaction_40`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_11} = v_{22} - v_9 \tag{73}$$

7.10 Species `species_19`

Name IRS1_pS636_PI3K

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

This species takes part in four reactions (as a reactant in `reaction_53` and as a product in `reaction_22`, `reaction_46` and as a modifier in `reaction_53`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_19} = v_4 + v_{11} - v_{12} \tag{74}$$

7.11 Species `species_7`

Name IRS1_p_PI3K

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

This species takes part in eight reactions (as a reactant in `reaction_31`, `reaction_46`, `reaction_55` and as a product in `reaction_23`, `reaction_31` and as a modifier in `reaction_31`, `reaction_46`, `reaction_55`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_7} = v_5 + v_6 - v_6 - v_{11} - v_{13} \tag{75}$$

7.12 Species `species_22`

Name mTORC2_pS2481

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

This species takes part in six reactions (as a reactant in `reaction_32`, `reaction_1` and as a product in `reaction_32`, `reaction_18` and as a modifier in `reaction_32`, `reaction_1`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_22} = v_7 + v_{27} - v_7 - v_{16} \tag{76}$$

7.13 Species `species_17`

Name p70S6K_pT389

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

This species takes part in nine reactions (as a reactant in `reaction_17`, `reaction_22`, `reaction_46` and as a product in `reaction_16`, `reaction_22`, `reaction_46` and as a modifier in `reaction_17`, `reaction_22`, `reaction_46`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_17} = v_2 + v_4 + v_{11} - v_3 - v_4 - v_{11} \tag{77}$$

7.14 Species `species_42`

Name IRS1_PI3K

Initial concentration $2.965 \text{ dimensionless} \cdot \text{dimensionless}^{-1}$

Initial assignment `species_42`

This species takes part in six reactions (as a reactant in `reaction_22`, `reaction_23` and as a product in `reaction_55`, `reaction_4` and as a modifier in `reaction_22`, `reaction_23`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_42} = v_{13} + v_{19} - v_4 - v_5 \tag{78}$$

7.15 Species `species_3`

Name Akt_pT308

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

This species takes part in 14 reactions (as a reactant in `reaction_32`, `reaction_33`, `reaction-_61`, `reaction_8`, `reaction_13` and as a product in `reaction_31`, `reaction_33`, `reaction-_44`, `reaction_8` and as a modifier in `reaction_32`, `reaction_33`, `reaction_61`, `reaction-_8`, `reaction_13`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_3} = v_6 + v_8 + v_{14} + v_{23} - v_7 - v_8 - v_{15} - v_{23} - v_{28} \tag{79}$$

7.16 Species `species_6`

Name TSC_clx

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

This species takes part in eight reactions (as a reactant in `reaction_33`, `reaction_3`, `reaction-_7` and as a product in `reaction_9`, `reaction_7` and as a modifier in `reaction_33`, `reaction-_3`, `reaction_7`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_6} = v_1 + v_{22} - v_8 - v_{18} - v_{22} \tag{80}$$

7.17 Species `species_9`

Name PRAS40

Initial concentration $73.2175 \text{ dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in eight reactions (as a reactant in `reaction_6`, `reaction_8`, `reaction-_12` and as a product in `reaction_10`, `reaction_11` and as a modifier in `reaction_6`, `reaction-_8`, `reaction_12`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_9} = v_{24} + v_{25} - v_{21} - v_{23} - v_{26} \tag{81}$$

7.18 Species `species_12`

Name PRAS40_pS183

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in three reactions (as a reactant in `reaction_11` and as a product in `reaction_12` and as a modifier in `reaction_11`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_12} = v_{26} - v_{25} \tag{82}$$

7.19 Species `species_10`

Name PRAS40_pT246

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in four reactions (as a reactant in `reaction_10` and as a product in `reaction_6`, `reaction_8` and as a modifier in `reaction_10`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_10} = v_{21} + v_{23} - v_{24} \tag{83}$$

7.20 Species `species_27`

Name Akt

Initial concentration 144.13 dimensionless · dimensionless^{-1}

This species takes part in three reactions (as a reactant in `reaction_31` and as a product in `reaction_61` and as a modifier in `reaction_31`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_27} = v_{15} - v_{6} \tag{84}$$

7.21 Species `species_4`

Name Akt_pT308_pS473

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in ten reactions (as a reactant in `reaction_44`, `reaction_3`, `reaction_6` and as a product in `reaction_32`, `reaction_3`, `reaction_6`, `reaction_13` and as a modifier in `reaction_44`, `reaction_3`, `reaction_6`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_4} = v_{7} + v_{18} + v_{21} + v_{28} - v_{14} - v_{18} - v_{21} \tag{85}$$

7.22 Species `species_47`

Name p70S6K

Initial concentration 127.0725 dimensionless · dimensionless^{-1}

This species takes part in three reactions (as a reactant in `reaction_16` and as a product in `reaction_17` and as a modifier in `reaction_16`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_47} = v_3 - v_2 \qquad (86)$$

7.23 Species `species_8`

Name TSC_p_clx

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in four reactions (as a reactant in `reaction_9` and as a product in `reaction_33`, `reaction_3` and as a modifier in `reaction_9`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_8} = v_8 + v_{18} - v_1 \qquad (87)$$

7.24 Species `species_13`

Name PDK2

Initial concentration 12.1175 dimensionless · dimensionless^{-1}

This species takes part in three reactions (as a reactant in `reaction_15` and as a product in `reaction_14` and as a modifier in `reaction_15`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_13} = v_{29} - v_{30} \qquad (88)$$

7.25 Species `species_14`

Name PDK2_p

Initial concentration 0 dimensionless · dimensionless^{-1}

This species takes part in six reactions (as a reactant in `reaction_13`, `reaction_14` and as a product in `reaction_13`, `reaction_15` and as a modifier in `reaction_13`, `reaction_14`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_14} = v_{28} + v_{30} - v_{28} - v_{29} \qquad (89)$$

7.26 Species `species_16`

Name PI3K_variant_p

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

This species takes part in six reactions (as a reactant in `reaction_18`, `reaction_20` and as a product in `reaction_18`, `reaction_19` and as a modifier in `reaction_18`, `reaction_20`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_16} = v_{27} + v_{31} - v_{27} - v_{32} \tag{90}$$

7.27 Species `species_18`

Name PI3K_variant

Initial concentration $2.965 \, \text{dimensionless} \cdot \text{dimensionless}^{-1}$

Initial assignment `species_18`

This species takes part in three reactions (as a reactant in `reaction_19` and as a product in `reaction_20` and as a modifier in `reaction_19`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_18} = v_{32} - v_{31} \tag{91}$$

7.28 Species `species_23`

Name PI3K

Initial concentration $2.965 \, \text{dimensionless} \cdot \text{dimensionless}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_23} = 0 \tag{92}$$