SBML Model Report

Model name: "Pappalardo2016 - PI3K/AKT and MAPK Signaling Pathways in Melanoma Cancer"

May 17, 2018

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following three authors: Matthew Grant Roberts[1], Kun Yang[2] and Emma Louise Fairbanks[3] at September 25th 2015 at 9:34 a. m. and last time modified at September 25th 2015 at 9:34 a. m. Table 1 gives an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	48
events	0	constraints	0
reactions	48	function definitions	39
global parameters	0	unit definitions	2
rules	0	initial assignments	0

Model Notes

Pappalardo2016 - PI3K/AKT and MAPK SignalingPathways in Melanoma Cancer

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This model is described in the article:Computational Modeling of PI3K/AKT and MAPK Signaling Pathways in Melanoma Cancer.Pappalardo F, Russo G, Candido S, Pennisi M, Cavalieri S, Motta S, McCubrey JA, Nicoletti F, Libra M.PLoS ONE 2016; 11(3): e0152104

Abstract:

Malignant melanoma is an aggressive tumor of the skin and seems to be resistant to current therapeutic approaches. Melanocytic transformation is thought to occur by sequential accumulation of genetic and molecular alterations able to activate the Ras/Raf/MEK/ERK (MAPK) and/or the PI3K/AKT (AKT) signalling pathways. Specifically, mutations of B-RAF activate MAPK pathway resulting in cell cycle progression and apoptosis prevention. According to these findings, MAPK and AKT pathways may represent promising therapeutic targets for an otherwise devastating disease.Here we show a computational model able to simulate the main biochemical and metabolic interactions in the PI3K/AKT and MAPK pathways potentially involved in melanoma development. Overall, this computational approach may accelerate the drug discovery process and encourages the identification of novel pathway activators with consequent development of novel antioncogenic compounds to overcome tumor cell resistance to conventional therapeutic agents. The source code of the various versions of the model are available as S1 Archive.

This model is hosted on BioModels Database and identified by: MODEL1609190000.

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 three are predefined by SBML and not mentioned in the model.

2.1 Unit `volume`

Name volume

Definition ml

2.2 Unit `substance`

Name substance

Definition mmol

2.3 Unit `area`

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

Definition m^2

2.4 Unit `length`

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

Definition m

2.5 Unit `time`

Notes Second is the predefined SBML unit for `time`.

Definition s

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`compartment_0`	Melanoma cell		3	1	litre	☑	

3.1 Compartment `compartment_0`

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

Name Melanoma cell

4 Species

This model contains 48 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 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_0	boundRTK	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_1	freeRTK	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_2	SosActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_3	SosInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_4	RasActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_5	RasInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_6	Raf1Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_7	Raf1Inactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_8	MekActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_9	MekInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_10	ErkActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_11	ErkInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_12	P90RskActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_13	P90RskInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_14	PI3KActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_15	PI3KInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_16	AktActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_17	AktInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_19	C3GActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_20	C3GInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
species_21	Rap1Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_22	Rap1Inactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_25	GF	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
species_26	PP2AActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
species_27	Raf1PPtase	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
species_28	RasGapActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
species_29	Rap1Gap	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
species_30	proRTK	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
PIP3Active	PIP3Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
PIP3Inactive	PIP3Inactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
PTENActive	PTENActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
IRS1Active	IRS1Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
IRS1Inactive	IRS1Inactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
PDK1Inactive	PDK1Inactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
PDK1Active	PDK1Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
HSP90_Cdc37Active	HSP90-Cdc37Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
PHLPPActive	PHLPPActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
mTORC2Active	mTORC2Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
TCL1Active	TCL1Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
CTMPActive	CTMPActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
mTORC1Active	mTORC1Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
mTORC1Inactive	mTORC1Inactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
S6K1Active	S6K1Active	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
S6K1Inactive	S6K1Inactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
bRafMutated	bRafMutated	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
Dabrafenib	Dabrafenib	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
bRafMutatedInactive	bRafMutatedInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
probRafMutated	probRafMutated	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑

5 Function definitions

This is an overview of 39 function definitions.

5.1 Function definition Constant_flux__irreversible

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$\mathrm{v} \tag{1}$$

5.2 Function definition HMM_Modified_9

Name HMM_Modified_9

Arguments Kcat, km, [species_10], [species_26]

Mathematical Expression

$$\frac{\mathrm{Kcat} \cdot [\mathrm{species\_26}] \cdot [\mathrm{species\_10}]}{\mathrm{km} + [\mathrm{species\_10}]} \tag{2}$$

5.3 Function definition HMM_Modified_4

Name HMM_Modified_4

Arguments Kcat, km, [species_4], [species_7]

Mathematical Expression

$$\frac{\mathrm{Kcat} \cdot [\mathrm{species\_4}] \cdot [\mathrm{species\_7}]}{\mathrm{km} + [\mathrm{species\_7}]} \tag{3}$$

5.4 Function definition HMM_Modified_34

Name HMM_Modified_34

Arguments Kcat, km, [mTORC1Inactive], [species_16]

Mathematical Expression

$$\frac{\mathrm{Kcat} \cdot [\mathrm{species\_16}] \cdot [\mathrm{mTORC1Inactive}]}{\mathrm{km} + [\mathrm{mTORC1Inactive}]} \tag{4}$$

5.5 Function definition HMM_Modified_7

Name HMM_Modified_7

Arguments Kcat, km, [species_26], [species_8]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_26}] \cdot [\text{species\_8}]}{\text{km} + [\text{species\_8}]} \tag{5}$$

5.6 Function definition HMM_Modified_23

Name HMM_Modified_23

Arguments [IRS1Inactive], Kcat, km, [species_0]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{IRS1Inactive}]}{\text{km} + [\text{IRS1Inactive}]} \tag{6}$$

5.7 Function definition HMM_Modified_31

Name HMM_Modified_31

Arguments Kcat, km, [species_16], [species_26]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_26}] \cdot [\text{species\_16}]}{\text{km} + [\text{species\_16}]} \tag{7}$$

5.8 Function definition HMM_Modified_8

Name HMM_Modified_8

Arguments Kcat, km, [species_11], [species_8]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_8}] \cdot [\text{species\_11}]}{\text{km} + [\text{species\_11}]} \tag{8}$$

5.9 Function definition HMM_Modified_20

Name HMM_Modified_20

Arguments Kcat, [PIP3Active], [PTENActive], km

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{PTENActive}] \cdot [\text{PIP3Active}]}{\text{km} + [\text{PIP3Active}]} \tag{9}$$

5.10 Function definition HMM_Modified_2

Name HMM_Modified_2

Arguments Kcat, km, [species_2], [species_5]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_2}] \cdot [\text{species\_5}]}{\text{km} + [\text{species\_5}]} \tag{10}$$

5.11 Function definition HMM_Modified_5

Name HMM_Modified_5

Arguments Kcat, km, [species_27], [species_6]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_27}] \cdot [\text{species\_6}]}{\text{km} + [\text{species\_6}]} \tag{11}$$

5.12 Function definition HMM_Modified_6

Name HMM_Modified_6

Arguments Kcat, km, [species_6], [species_9]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_6}] \cdot [\text{species\_9}]}{\text{km} + [\text{species\_9}]} \tag{12}$$

5.13 Function definition HMM_Modified_10

Name HMM_Modified_10

Arguments Kcat, km, [species_10], [species_13]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_10}] \cdot [\text{species\_13}]}{\text{km} + [\text{species\_13}]} \tag{13}$$

5.14 Function definition HMM_Modified_11

Name HMM_Modified_11

Arguments Kcat, km, [species_12], [species_2]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_12}] \cdot [\text{species\_2}]}{\text{km} + [\text{species\_2}]} \tag{14}$$

5.15 Function definition HMM_Modified_12

Name HMM_Modified_12

Arguments Kcat, km, [species_0], [species_15]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{species\_15}]}{\text{km} + [\text{species\_15}]} \tag{15}$$

5.16 Function definition HMM_Modified_28

Name HMM_Modified_28

Arguments Kcat, km, [mTORC2Active], [species_17]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{mTORC2Active}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]} \tag{16}$$

5.17 Function definition HMM_Modified_13

Name HMM_Modified_13

Arguments Kcat, km, [species_15], [species_4]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_4}] \cdot [\text{species\_15}]}{\text{km} + [\text{species\_15}]} \tag{17}$$

5.18 Function definition HMM_Modified_26

Name HMM_Modified_26

Arguments [HSP90_Cdc37Active], Kcat, km, [species_17]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{HSP90\_Cdc37Active}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]} \tag{18}$$

5.19 Function definition HMM_Modified

Name HMM_Modified

Arguments Kcat, km, [species_14], [species_17]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_14}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]} \tag{19}$$

5.20 Function definition HMM_Modified_30

Name HMM_Modified_30

Arguments [CTMPActive], Kcat, km, [species_16]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{CTMPActive}] \cdot [\text{species\_16}]}{\text{km} + [\text{species\_16}]} \tag{20}$$

5.21 Function definition HMM_Modified_14

Name HMM_Modified_14

Arguments Kcat, km, [species_16], [species_6]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_16}] \cdot [\text{species\_6}]}{\text{km} + [\text{species\_6}]} \tag{21}$$

5.22 Function definition HMM_Modified_15

Name HMM_Modified_15

Arguments Kcat, km, [species_0], [species_20]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{species\_20}]}{\text{km} + [\text{species\_20}]} \tag{22}$$

5.23 Function definition HMM_Modified_32

Name HMM_Modified_32

Arguments Kcat, km, [species_10], [species_6]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_6}] \cdot [\text{species\_10}]}{\text{km} + [\text{species\_10}]} \tag{23}$$

5.24 Function definition HMM_Modified_21

Name HMM_Modified_21

Arguments Kcat, [PIP3Active], km, [species_17]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{PIP3Active}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]} \tag{24}$$

5.25 Function definition HMM_Modified_3

Name HMM_Modified_3

Arguments Kcat, km, [species_28], [species_4]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_28}] \cdot [\text{species\_4}]}{\text{km} + [\text{species\_4}]} \tag{25}$$

5.26 Function definition HMM_Modified_1

Name HMM_Modified_1

Arguments Kcat, km, [species_0], [species_3]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{species\_3}]}{\text{km} + [\text{species\_3}]} \tag{26}$$

5.27 Function definition HMM_Modified_16

Name HMM_Modified_16

Arguments Kcat, km, [species_19], [species_22]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_19}] \cdot [\text{species\_22}]}{\text{km} + [\text{species\_22}]} \tag{27}$$

5.28 Function definition HMM_Modified_18

Name HMM_Modified_18

Arguments Kcat, [bRafMutated], km, [species_9]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{bRafMutated}] \cdot [\text{species\_9}]}{\text{km} + [\text{species\_9}]} \tag{28}$$

5.29 Function definition HMM_Modified_22

Name HMM_Modified_22

Arguments [IRS1Active], Kcat, km, [species_15]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{IRS1Active}] \cdot [\text{species\_15}]}{\text{km} + [\text{species\_15}]} \tag{29}$$

5.30 Function definition HMM_Modified_19

Name HMM_Modified_19

Arguments Kcat, [PIP3Inactive], km, [species_14]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_14}] \cdot [\text{PIP3Inactive}]}{\text{km} + [\text{PIP3Inactive}]} \tag{30}$$

5.31 Function definition HMM_Modified_17

Name HMM_Modified_17

Arguments Kcat, km, [species_21], [species_29]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_29}] \cdot [\text{species\_21}]}{\text{km} + [\text{species\_21}]} \tag{31}$$

5.32 Function definition HMM_Modified_24

Name HMM_Modified_24

Arguments Kcat, [PDK1Inactive], [PIP3Active], km

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{PIP3Active}] \cdot [\text{PDK1Inactive}]}{\text{km} + [\text{PDK1Inactive}]} \tag{32}$$

5.33 Function definition HMM_Modified_25

Name HMM_Modified_25

Arguments Kcat, [PDK1Active], km, [species_17]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{PDK1Active}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]} \tag{33}$$

5.34 Function definition HMM_Modified_27

Name HMM_Modified_27

Arguments Kcat, [PHLPPActive], km, [species_16]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{PHLPPActive}] \cdot [\text{species\_16}]}{\text{km} + [\text{species\_16}]} \tag{34}$$

5.35 Function definition HMM_Modified_33

Name HMM_Modified_33

Arguments Kcat, km, [species_10], [species_2]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_10}] \cdot [\text{species\_2}]}{\text{km} + [\text{species\_2}]} \tag{35}$$

5.36 Function definition HMM_Modified_29

Name HMM_Modified_29

Arguments Kcat, [TCL1Active], km, [species_17]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{TCL1Active}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]} \tag{36}$$

5.37 Function definition HMM_Modified_35

Name HMM_Modified_35

Arguments Kcat, [S6K1Inactive], km, [mTORC1Active]

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{mTORC1Active}] \cdot [\text{S6K1Inactive}]}{\text{km} + [\text{S6K1Inactive}]} \tag{37}$$

5.38 Function definition HMM_Modified_36

Name HMM_Modified_36

Arguments [IRS1Active], Kcat, [S6K1Active], km

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{S6K1Active}] \cdot [\text{IRS1Active}]}{\text{km} + [\text{IRS1Active}]} \tag{38}$$

5.39 Function definition HMM_Modified_37

Name HMM_Modified_37

Arguments [Dabrafenib], Kcat, [bRafMutated], km

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{Dabrafenib}] \cdot [\text{bRafMutated}]}{\text{km} + [\text{bRafMutated}]} \tag{39}$$

6 Reactions

This model contains 48 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_0	GF_Binding_Unbinding	$\text{species\_25} + \text{species\_1} \rightleftharpoons \text{species\_0}$	
2	reaction_1	Sos_Activation	$\text{species\_3} \xrightarrow{\text{species\_0}} \text{species\_2}$	
3	reaction_3	Ras_Activation	$\text{species\_5} \xrightarrow{\text{species\_2}} \text{species\_4}$	
4	reaction_4	Ras_Feedback_Deactivation_RasGap	$\text{species\_4} \xrightarrow{\text{species\_28}} \text{species\_5}$	
5	reaction_5	Raf1_Activation	$\text{species\_7} \xrightarrow{\text{species\_4}} \text{species\_6}$	
6	reaction_6	Raf1_Feedback_Deactivation_Raf1PPtase	$\text{species\_6} \xrightarrow{\text{species\_27}} \text{species\_7}$	
7	reaction_7	Mek_Activation_Raf1	$\text{species\_9} \xrightarrow{\text{species\_6}} \text{species\_8}$	
8	reaction_8	Mek_Feedback_Deactivation_PP2A	$\text{species\_8} \xrightarrow{\text{species\_26}} \text{species\_9}$	
9	reaction_9	Erk_Activation	$\text{species\_11} \xrightarrow{\text{species\_8}} \text{species\_10}$	
10	reaction_10	Erk_Feedback_Deactivation_PP2A	$\text{species\_10} \xrightarrow{\text{species\_26}} \text{species\_11}$	
11	reaction_11	P90Rsk_Activation	$\text{species\_13} \xrightarrow{\text{species\_10}} \text{species\_12}$	
12	reaction_12	P90Rsk_Deactivation	$\text{species\_12} \longrightarrow \text{species\_13}$	
13	reaction_13	Sos_Feedback_Deactivation_P90Rsk	$\text{species\_2} \xrightarrow{\text{species\_12}} \text{species\_3}$	
14	reaction_14	PI3K_Activation_RTK	$\text{species\_15} \xrightarrow{\text{species\_0}} \text{species\_14}$	
15	reaction_15	PI3K_Activation_Ras	$\text{species\_15} \xrightarrow{\text{species\_4}} \text{species\_14}$	
16	reaction_16	PI3K_Deactivation	$\text{species\_14} \longrightarrow \text{species\_15}$	

№	Id	Name	Reaction Equation	SBO
17	reaction_17	Akt_Activation_PI3K	species_17 $\xrightarrow{\text{species\_14}}$ species_16	
18	reaction_19	Raf1_Deactivation_Akt	species_6 $\xrightarrow{\text{species\_16}}$ species_7	
19	reaction_20	RTK_Degradation	species_0 $\longrightarrow \emptyset$	
20	reaction_21	C3G_Activation	species_20 $\xrightarrow{\text{species\_0}}$ species_19	
21	reaction_22	C3G_Deactivation	species_19 $\longrightarrow$ species_20	
22	reaction_23	Rap1_Activation	species_22 $\xrightarrow{\text{species\_19}}$ species_21	
23	reaction_24	Rap1_Feedback_Deactivation_Rap1Gap	species_21 $\xrightarrow{\text{species\_29}}$ species_22	
24	reaction_27	Mek_Activation_bRaf	species_9 $\xrightarrow{\text{bRafMutated}}$ species_8	
25	reaction_28	RTK_Production	species_30 $\longrightarrow$ species_1	
26	reaction_29	RTK_Degradation_Free	species_1 $\longrightarrow \emptyset$	
27	PIP3_Activation	PIP3_Activation	PIP3Inactive $\xrightarrow{\text{species\_14}}$ PIP3Active	
28	PIP3_Feedback_Deactivation_PTEN	PIP3_Feedback_Deactivation_PTEN	PIP3Active $\xrightarrow{\text{PTENActive}}$ PIP3Inactive	
29	Akt_Activation_PIP3	Akt_Activation_PIP3	species_17 $\xrightarrow{\text{PIP3Active}}$ species_16	
30	PI3K_Activation_IRS1	PI3K_Activation_IRS1	species_15 $\xrightarrow{\text{IRS1Active}}$ species_14	
31	IRS1_Activation	IRS1_Activation	IRS1Inactive $\xrightarrow{\text{species\_0}}$ IRS1Active	
32	PDK1_Activation	PDK1_Activation	PDK1Inactive $\xrightarrow{\text{PIP3Active}}$ PDK1Active	
33	PDK1_Deactivation	PDK1_Deactivation	PDK1Active $\longrightarrow$ PDK1Inactive	

№	Id	Name	Reaction Equation	SBO
34	Akt_Activation_PDK1	Akt_Activation_PDK1	species_17 $\xrightarrow{\text{PDK1Active}}$ species_16	
35	Akt_Feedback_Activation_HSP90_Cdc37	Akt_Feedback_Activation_HSP90-Cdc37	species_17 $\xrightarrow{\text{HSP90_Cdc37Active}}$ species_16	
36	Akt_Feedback_Deactivation_PHLPP	Akt_Feedback_Deactivation_PHLPP	species_16 $\xrightarrow{\text{PHLPPActive}}$ species_17	
37	Akt_Feedback_Activation_mTORC2	Akt_Feedback_Activation_mTORC2	species_17 $\xrightarrow{\text{mTORC2Active}}$ species_16	
38	Akt_Feedback_Activation_TCL1	Akt_Feedback_Activation_TCL1	species_17 $\xrightarrow{\text{TCL1Active}}$ species_16	
39	Akt_Feedback_Deactivation_CTMP	Akt_Feedback_Deactivation_CTMP	species_16 $\xrightarrow{\text{CTMPActive}}$ species_17	
40	Akt_Feedback_Deactivation_PP2A	Akt_Feedback_Deactivation_PP2A	species_16 $\xrightarrow{\text{species_26}}$ species_17	
41	Erk_Feedback_Deactivation_Raf1	Erk_Feedback_Deactivation_Raf1	species_10 $\xrightarrow{\text{species_6}}$ species_11	

№	Id	Name	Reaction Equation	SBO
42	Sos_Feedback_Deactivation_Erk	Sos_Feedback_Deactivation_Erk	species_2 $\xrightarrow{\text{species\_10}}$ species_3	
43	mTORC1_Activation_Akt	mTORC1_Activation_Akt	mTORC1Inactive $\xrightarrow{\text{species\_16}}$ mTORC1Active	
44	S6K1_Activation_mTORC1	S6K1_Activation_mTORC1	S6K1Inactive $\xrightarrow{\text{mTORC1Active}}$ S6K1Active	
45	IRS1_Feedback_Deactivation_S6K1	IRS1_Feedback_Deactivation_S6K1	IRS1Active $\xrightarrow{\text{S6K1Active}}$ IRS1Inactive	
46	Dabrafenib_degradation	Dabrafenib_degradation	Dabrafenib $\longrightarrow \emptyset$	
47	bRaf_Deactivation_Dabrafenib	bRaf_Deactivation_Dabrafenib	bRafMutated $\xrightarrow{\text{Dabrafenib}}$ bRafMutatedInactive	
48	bRafMutated_Production	bRafMutated_Production	probRafMutated $\longrightarrow$ bRafMutated	

6.1 Reaction reaction_0

This is a reversible reaction of two reactants forming one product.

Name GF_Binding_Unbinding

Reaction equation

$$\text{species\_25} + \text{species\_1} \rightleftharpoons \text{species\_0} \tag{40}$$

Reactants

Table 5: Properties of each reactant.

Id	Name	SBO
species_25	GF	
species_1	freeRTK	

Product

Table 6: Properties of each product.

Id	Name	SBO
species_0	boundRTK	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{compartment\_0}) \cdot (\text{k1} \cdot [\text{species\_25}] \cdot [\text{species\_1}] - \text{k2} \cdot [\text{species\_0}]) \tag{41}$$

Table 7: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$2.18503 \cdot 10^{-5}$		☑
k2	k2		0.121		☑

6.2 Reaction `reaction_1`

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

Name Sos_Activation

Reaction equation

$$\text{species\_3} \xrightarrow{\text{species\_0}} \text{species\_2} \tag{42}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
`species_3`	SosInactive	

Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
`species_0`	boundRTK	

Product

Table 10: Properties of each product.

Id	Name	SBO
`species_2`	SosActive	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{HMM\_Modified\_1}\left(\text{Kcat}, \text{km}, [\text{species\_0}], [\text{species\_3}]\right) \tag{43}$$

$$\text{HMM\_Modified\_1}\left(\text{Kcat}, \text{km}, [\text{species\_0}], [\text{species\_3}]\right) = \frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{species\_3}]}{\text{km} + [\text{species\_3}]} \tag{44}$$

$$\text{HMM\_Modified\_1}\left(\text{Kcat}, \text{km}, [\text{species\_0}], [\text{species\_3}]\right) = \frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{species\_3}]}{\text{km} + [\text{species\_3}]} \quad (45)$$

Table 11: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		694.731		☑
`km`	km		6086070.000		☑

6.3 Reaction `reaction_3`

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

Name Ras_Activation

Reaction equation

$$\text{species\_5} \xrightarrow{\text{species\_2}} \text{species\_4} \quad (46)$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
`species_5`	RasInactive	

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
`species_2`	SosActive	

Product

Table 14: Properties of each product.

Id	Name	SBO
species_4	RasActive	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_2}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_2}], [\mathrm{species\_5}]\right) \quad (47)$$

$$\mathrm{HMM\_Modified\_2}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_2}], [\mathrm{species\_5}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_2}] \cdot [\mathrm{species\_5}]}{\mathrm{km} + [\mathrm{species\_5}]} \quad (48)$$

$$\mathrm{HMM\_Modified\_2}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_2}], [\mathrm{species\_5}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_2}] \cdot [\mathrm{species\_5}]}{\mathrm{km} + [\mathrm{species\_5}]} \quad (49)$$

Table 15: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		32.344		☑
km	km		35954.300		☑

6.4 Reaction reaction_4

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

Name Ras_Feedback_Deactivation_RasGap

Reaction equation

$$\mathrm{species\_4} \xrightarrow{\mathrm{species\_28}} \mathrm{species\_5} \quad (50)$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
species_4	RasActive	

Modifier

Table 17: Properties of each modifier.

Id	Name	SBO
species_28	RasGapActive	

Product

Table 18: Properties of each product.

Id	Name	SBO
species_5	RasInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_3}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_28}], [\mathrm{species\_4}]\right) \quad (51)$$

$$\mathrm{HMM\_Modified\_3}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_28}], [\mathrm{species\_4}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_28}] \cdot [\mathrm{species\_4}]}{\mathrm{km} + [\mathrm{species\_4}]} \quad (52)$$

$$\mathrm{HMM\_Modified\_3}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_28}], [\mathrm{species\_4}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_28}] \cdot [\mathrm{species\_4}]}{\mathrm{km} + [\mathrm{species\_4}]} \quad (53)$$

Table 19: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		1509.36		☑
km	km		1432410.00		☑

6.5 Reaction reaction_5

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

Name Raf1_Activation

Reaction equation

$$\text{species\_7} \xrightarrow{\text{species\_4}} \text{species\_6} \tag{54}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
species_7	Raf1Inactive	

Modifier

Table 21: Properties of each modifier.

Id	Name	SBO
species_4	RasActive	

Product

Table 22: Properties of each product.

Id	Name	SBO
species_6	Raf1Active	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{HMM\_Modified\_4}\left(\text{Kcat}, \text{km}, [\text{species\_4}], [\text{species\_7}]\right) \tag{55}$$

$$\text{HMM\_Modified\_4}\left(\text{Kcat}, \text{km}, [\text{species\_4}], [\text{species\_7}]\right) = \frac{\text{Kcat} \cdot [\text{species\_4}] \cdot [\text{species\_7}]}{\text{km} + [\text{species\_7}]} \tag{56}$$

$$\text{HMM\_Modified\_4}\left(\text{Kcat}, \text{km}, [\text{species\_4}], [\text{species\_7}]\right) = \frac{\text{Kcat} \cdot [\text{species\_4}] \cdot [\text{species\_7}]}{\text{km} + [\text{species\_7}]} \quad (57)$$

Table 23: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		0.884		☑
`km`	km		62464.600		☑

6.6 Reaction `reaction_6`

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

Name Raf1_Feedback_Deactivation_Raf1PPtase

Reaction equation

$$\text{species\_6} \xrightarrow{\text{species\_27}} \text{species\_7} \quad (58)$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
`species_6`	Raf1Active	

Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
`species_27`	Raf1PPtase	

Product

Table 26: Properties of each product.

Id	Name	SBO
species_7	Raf1Inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_5}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_27}], [\mathrm{species\_6}]\right) \quad (59)$$

$$\mathrm{HMM\_Modified\_5}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_27}], [\mathrm{species\_6}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_27}] \cdot [\mathrm{species\_6}]}{\mathrm{km} + [\mathrm{species\_6}]} \quad (60)$$

$$\mathrm{HMM\_Modified\_5}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_27}], [\mathrm{species\_6}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_27}] \cdot [\mathrm{species\_6}]}{\mathrm{km} + [\mathrm{species\_6}]} \quad (61)$$

Table 27: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.126		☑
km	km		1061.710		☑

6.7 Reaction reaction_7

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

Name Mek_Activation_Raf1

Reaction equation

$$\mathrm{species\_9} \xrightarrow{\mathrm{species\_6}} \mathrm{species\_8} \quad (62)$$

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
species_9	MekInactive	

Modifier

Table 29: Properties of each modifier.

Id	Name	SBO
species_6	Raf1Active	

Product

Table 30: Properties of each product.

Id	Name	SBO
species_8	MekActive	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_6}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_6}], [\mathrm{species\_9}]\right) \quad (63)$$

$$\mathrm{HMM\_Modified\_6}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_6}], [\mathrm{species\_9}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_6}] \cdot [\mathrm{species\_9}]}{\mathrm{km} + [\mathrm{species\_9}]} \quad (64)$$

$$\mathrm{HMM\_Modified\_6}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_6}], [\mathrm{species\_9}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_6}] \cdot [\mathrm{species\_9}]}{\mathrm{km} + [\mathrm{species\_9}]} \quad (65)$$

Table 31: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		185.759		☑
km	km		4768350.000		☑

6.8 Reaction reaction_8

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

Name Mek_Feedback_Deactivation_PP2A

Reaction equation

$$\text{species\_8} \xrightarrow{\text{species\_26}} \text{species\_9} \tag{66}$$

Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
species_8	MekActive	

Modifier

Table 33: Properties of each modifier.

Id	Name	SBO
species_26	PP2AActive	

Product

Table 34: Properties of each product.

Id	Name	SBO
species_9	MekInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{HMM\_Modified\_7}\left(\text{Kcat}, \text{km}, [\text{species\_26}], [\text{species\_8}]\right) \tag{67}$$

$$\text{HMM\_Modified\_7}\left(\text{Kcat}, \text{km}, [\text{species\_26}], [\text{species\_8}]\right) = \frac{\text{Kcat} \cdot [\text{species\_26}] \cdot [\text{species\_8}]}{\text{km} + [\text{species\_8}]} \tag{68}$$

$$\text{HMM\_Modified\_7}\left(\text{Kcat}, \text{km}, [\text{species\_26}], [\text{species\_8}]\right) = \frac{\text{Kcat} \cdot [\text{species\_26}] \cdot [\text{species\_8}]}{\text{km} + [\text{species\_8}]} \quad (69)$$

Table 35: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		2.832		☑
`km`	km		518753.000		☑

6.9 Reaction `reaction_9`

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

Name Erk_Activation

Reaction equation

$$\text{species\_11} \xrightarrow{\text{species\_8}} \text{species\_10} \quad (70)$$

Reactant

Table 36: Properties of each reactant.

Id	Name	SBO
`species_11`	ErkInactive	

Modifier

Table 37: Properties of each modifier.

Id	Name	SBO
`species_8`	MekActive	

Product

Table 38: Properties of each product.

Id	Name	SBO
species_10	ErkActive	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{vol}(\text{compartment\_0}) \cdot \text{HMM\_Modified\_8}(\text{Kcat}, \text{km}, [\text{species\_11}], [\text{species\_8}]) \quad (71)$$

$$\text{HMM\_Modified\_8}(\text{Kcat}, \text{km}, [\text{species\_11}], [\text{species\_8}]) = \frac{\text{Kcat} \cdot [\text{species\_8}] \cdot [\text{species\_11}]}{\text{km} + [\text{species\_11}]} \quad (72)$$

$$\text{HMM\_Modified\_8}(\text{Kcat}, \text{km}, [\text{species\_11}], [\text{species\_8}]) = \frac{\text{Kcat} \cdot [\text{species\_8}] \cdot [\text{species\_11}]}{\text{km} + [\text{species\_11}]} \quad (73)$$

Table 39: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		9.854		☑
km	km		1007340.000		☑

6.10 Reaction reaction_10

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

Name Erk_Feedback_Deactivation_PP2A

Notes http://link.springer.com/article/10.1007%2Fs10555-008-9119-x

Reaction equation

$$\text{species\_10} \xrightarrow{\text{species\_26}} \text{species\_11} \quad (74)$$

Reactant

Table 40: Properties of each reactant.

Id	Name	SBO
species_10	ErkActive	

Modifier

Table 41: Properties of each modifier.

Id	Name	SBO
species_26	PP2AActive	

Product

Table 42: Properties of each product.

Id	Name	SBO
species_11	ErkInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_9}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_26}]\right) \quad (75)$$

$$\mathrm{HMM\_Modified\_9}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_26}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_26}] \cdot [\mathrm{species\_10}]}{\mathrm{km} + [\mathrm{species\_10}]} \quad (76)$$

$$\mathrm{HMM\_Modified\_9}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_26}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_26}] \cdot [\mathrm{species\_10}]}{\mathrm{km} + [\mathrm{species\_10}]} \quad (77)$$

Table 43: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		8.891		☑
km	km		3496490.000		☑

6.11 Reaction reaction_11

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

Name P90Rsk_Activation

Reaction equation

$$\text{species\_13} \xrightarrow{\text{species\_10}} \text{species\_12} \tag{78}$$

Reactant

Table 44: Properties of each reactant.

Id	Name	SBO
species_13	P90RskInactive	

Modifier

Table 45: Properties of each modifier.

Id	Name	SBO
species_10	ErkActive	

Product

Table 46: Properties of each product.

Id	Name	SBO
species_12	P90RskActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{vol}(\text{compartment\_0}) \cdot \text{HMM\_Modified\_10}(\text{Kcat}, \text{km}, [\text{species\_10}], [\text{species\_13}]) \tag{79}$$

$$\text{HMM\_Modified\_10}(\text{Kcat}, \text{km}, [\text{species\_10}], [\text{species\_13}]) = \frac{\text{Kcat} \cdot [\text{species\_10}] \cdot [\text{species\_13}]}{\text{km} + [\text{species\_13}]} \tag{80}$$

$$\text{HMM\_Modified\_10}\left(\text{Kcat}, \text{km}, [\text{species\_10}], [\text{species\_13}]\right) = \frac{\text{Kcat} \cdot [\text{species\_10}] \cdot [\text{species\_13}]}{\text{km} + [\text{species\_13}]} \tag{81}$$

Table 47: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		0.021		☑
`km`	km		763523.000		☑

6.12 Reaction `reaction_12`

This is an irreversible reaction of one reactant forming one product.

Name P90Rsk_Deactivation

Reaction equation

$$\text{species\_12} \longrightarrow \text{species\_13} \tag{82}$$

Reactant

Table 48: Properties of each reactant.

Id	Name	SBO
`species_12`	P90RskActive	

Product

Table 49: Properties of each product.

Id	Name	SBO
`species_13`	P90RskInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{k1} \cdot [\text{species\_12}] \tag{83}$$

Table 50: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.005		☑

6.13 Reaction reaction_13

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

Name Sos_Feedback_Deactivation_P90Rsk

Notes https://en.wikipedia.org/wiki/Ribosomal_s6_kinase#/media/File:P90Rsk.svg

Reaction equation

$$\text{species\_2} \xrightarrow{\text{species\_12}} \text{species\_3} \tag{84}$$

Reactant

Table 51: Properties of each reactant.

Id	Name	SBO
species_2	SosActive	

Modifier

Table 52: Properties of each modifier.

Id	Name	SBO
species_12	P90RskActive	

Product

Table 53: Properties of each product.

Id	Name	SBO
species_3	SosInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_11}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_12}], [\mathrm{species\_2}]\right) \quad (85)$$

$$\mathrm{HMM\_Modified\_11}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_12}], [\mathrm{species\_2}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_12}] \cdot [\mathrm{species\_2}]}{\mathrm{km} + [\mathrm{species\_2}]} \quad (86)$$

$$\mathrm{HMM\_Modified\_11}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_12}], [\mathrm{species\_2}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_12}] \cdot [\mathrm{species\_2}]}{\mathrm{km} + [\mathrm{species\_2}]} \quad (87)$$

Table 54: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		1611.97		☑
`km`	km		896896.00		☑

6.14 Reaction `reaction_14`

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

Name PI3K_Activation_RTK

Reaction equation

$$\mathrm{species\_15} \xrightarrow{\mathrm{species\_0}} \mathrm{species\_14} \quad (88)$$

Reactant

Table 55: Properties of each reactant.

Id	Name	SBO
`species_15`	PI3KInactive	

Modifier

Table 56: Properties of each modifier.

Id	Name	SBO
species_0	boundRTK	

Product

Table 57: Properties of each product.

Id	Name	SBO
species_14	PI3KActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_12}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_15}]\right) \quad (89)$$

$$\mathrm{HMM\_Modified\_12}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_15}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_0}] \cdot [\mathrm{species\_15}]}{\mathrm{km} + [\mathrm{species\_15}]} \quad (90)$$

$$\mathrm{HMM\_Modified\_12}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_15}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_0}] \cdot [\mathrm{species\_15}]}{\mathrm{km} + [\mathrm{species\_15}]} \quad (91)$$

Table 58: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		10.674		☑
km	km		184912.000		☑

6.15 Reaction reaction_15

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

Name PI3K_Activation_Ras

Reaction equation

$$\text{species\_15} \xrightarrow{\text{species\_4}} \text{species\_14} \tag{92}$$

Reactant

Table 59: Properties of each reactant.

Id	Name	SBO
species_15	PI3KInactive	

Modifier

Table 60: Properties of each modifier.

Id	Name	SBO
species_4	RasActive	

Product

Table 61: Properties of each product.

Id	Name	SBO
species_14	PI3KActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{HMM\_Modified\_13}\left(\text{Kcat}, \text{km}, [\text{species\_15}], [\text{species\_4}]\right) \tag{93}$$

$$\text{HMM\_Modified\_13}\left(\text{Kcat}, \text{km}, [\text{species\_15}], [\text{species\_4}]\right) = \frac{\text{Kcat} \cdot [\text{species\_4}] \cdot [\text{species\_15}]}{\text{km} + [\text{species\_15}]} \tag{94}$$

$$\text{HMM\_Modified\_13}\left(\text{Kcat}, \text{km}, [\text{species\_15}], [\text{species\_4}]\right) = \frac{\text{Kcat} \cdot [\text{species\_4}] \cdot [\text{species\_15}]}{\text{km} + [\text{species\_15}]} \tag{95}$$

Table 62: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.077		☑
km	km		272056.000		☑

6.16 Reaction reaction_16

This is an irreversible reaction of one reactant forming one product.

Name PI3K_Deactivation

Reaction equation

$$\text{species\_14} \longrightarrow \text{species\_15} \tag{96}$$

Reactant

Table 63: Properties of each reactant.

Id	Name	SBO
species_14	PI3KActive	

Product

Table 64: Properties of each product.

Id	Name	SBO
species_15	PI3KInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \text{vol}\,(\text{compartment\_0}) \cdot \text{k1} \cdot [\text{species\_14}] \tag{97}$$

Table 65: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.005		☑

6.17 Reaction reaction_17

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

Name Akt_Activation_PI3K

Reaction equation

$$\text{species\_17} \xrightarrow{\text{species\_14}} \text{species\_16} \tag{98}$$

Reactant

Table 66: Properties of each reactant.

Id	Name	SBO
species_17	AktInactive	

Modifier

Table 67: Properties of each modifier.

Id	Name	SBO
species_14	PI3KActive	

Product

Table 68: Properties of each product.

Id	Name	SBO
species_16	AktActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_14}], [\mathrm{species\_17}]\right) \quad (99)$$

$$\mathrm{HMM\_Modified}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_14}], [\mathrm{species\_17}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_14}] \cdot [\mathrm{species\_17}]}{\mathrm{km} + [\mathrm{species\_17}]} \quad (100)$$

$$\mathrm{HMM\_Modified}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_14}], [\mathrm{species\_17}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_14}] \cdot [\mathrm{species\_17}]}{\mathrm{km} + [\mathrm{species\_17}]} \quad (101)$$

Table 69: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.057		☑
km	km		653951.000		☑

6.18 Reaction reaction_19

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

Name Raf1_Deactivation_Akt

Reaction equation

$$\mathrm{species\_6} \xrightarrow{\mathrm{species\_16}} \mathrm{species\_7} \quad (102)$$

Reactant

Table 70: Properties of each reactant.

Id	Name	SBO
species_6	Raf1Active	

Modifier

Table 71: Properties of each modifier.

Id	Name	SBO
species_16	AktActive	

Product

Table 72: Properties of each product.

Id	Name	SBO
species_7	Raf1Inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_14}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_16}], [\mathrm{species\_6}]\right) \quad (103)$$

$$\mathrm{HMM\_Modified\_14}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_16}], [\mathrm{species\_6}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_16}] \cdot [\mathrm{species\_6}]}{\mathrm{km} + [\mathrm{species\_6}]} \quad (104)$$

$$\mathrm{HMM\_Modified\_14}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_16}], [\mathrm{species\_6}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_16}] \cdot [\mathrm{species\_6}]}{\mathrm{km} + [\mathrm{species\_6}]} \quad (105)$$

Table 73: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		15.121		☑
km	km		119355.000		☑

6.19 Reaction reaction_20

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

Name RTK_Degradation

Reaction equation

$$\text{species\_0} \longrightarrow \emptyset \tag{106}$$

Reactant

Table 74: Properties of each reactant.

Id	Name	SBO
species_0	boundRTK	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{vol}\,(\text{compartment\_0}) \cdot \text{k1} \cdot [\text{species\_0}] \tag{107}$$

Table 75: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.2		☑

6.20 Reaction reaction_21

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

Name C3G_Activation

Reaction equation

$$\text{species\_20} \xrightarrow{\text{species\_0}} \text{species\_19} \tag{108}$$

Reactant

Table 76: Properties of each reactant.

Id	Name	SBO
species_20	C3GInactive	

Modifier

Table 77: Properties of each modifier.

Id	Name	SBO
species_0	boundRTK	

Product

Table 78: Properties of each product.

Id	Name	SBO
species_19	C3GActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_15}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_20}]\right) \quad (109)$$

$$\mathrm{HMM\_Modified\_15}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_20}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_0}] \cdot [\mathrm{species\_20}]}{\mathrm{km} + [\mathrm{species\_20}]} \quad (110)$$

$$\mathrm{HMM\_Modified\_15}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_20}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_0}] \cdot [\mathrm{species\_20}]}{\mathrm{km} + [\mathrm{species\_20}]} \quad (111)$$

Table 79: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		694.731		☑
km	km		6086070.000		☑

6.21 Reaction reaction_22

This is an irreversible reaction of one reactant forming one product.

Name C3G_Deactivation

Reaction equation

$$\text{species\_19} \longrightarrow \text{species\_20} \tag{112}$$

Reactant

Table 80: Properties of each reactant.

Id	Name	SBO
species_19	C3GActive	

Product

Table 81: Properties of each product.

Id	Name	SBO
species_20	C3GInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \text{vol}(\text{compartment\_0}) \cdot \text{k1} \cdot [\text{species\_19}] \tag{113}$$

Table 82: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		2.5		☑

6.22 Reaction reaction_23

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

Name Rap1_Activation

Reaction equation

$$\text{species\_22} \xrightarrow{\text{species\_19}} \text{species\_21} \tag{114}$$

Reactant

Table 83: Properties of each reactant.

Id	Name	SBO
species_22	Rap1Inactive	

Modifier

Table 84: Properties of each modifier.

Id	Name	SBO
species_19	C3GActive	

Product

Table 85: Properties of each product.

Id	Name	SBO
species_21	Rap1Active	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{HMM\_Modified\_16}\left(\text{Kcat}, \text{km}, [\text{species\_19}], [\text{species\_22}]\right) \tag{115}$$

$$\text{HMM\_Modified\_16}\left(\text{Kcat}, \text{km}, [\text{species\_19}], [\text{species\_22}]\right) = \frac{\text{Kcat} \cdot [\text{species\_19}] \cdot [\text{species\_22}]}{\text{km} + [\text{species\_22}]} \tag{116}$$

$$\text{HMM\_Modified\_16}\left(\text{Kcat}, \text{km}, [\text{species\_19}], [\text{species\_22}]\right) = \frac{\text{Kcat} \cdot [\text{species\_19}] \cdot [\text{species\_22}]}{\text{km} + [\text{species\_22}]} \tag{117}$$

Table 86: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		32.344		☑
km	km		35954.300		☑

6.23 Reaction reaction_24

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

Name Rap1_Feedback_Deactivation_Rap1Gap

Reaction equation

$$\text{species\_21} \xrightarrow{\text{species\_29}} \text{species\_22} \tag{118}$$

Reactant

Table 87: Properties of each reactant.

Id	Name	SBO
species_21	Rap1Active	

Modifier

Table 88: Properties of each modifier.

Id	Name	SBO
species_29	Rap1Gap	

Product

Table 89: Properties of each product.

Id	Name	SBO
species_22	Rap1Inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_17}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_21}], [\mathrm{species\_29}]\right) \quad (119)$$

$$\mathrm{HMM\_Modified\_17}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_21}], [\mathrm{species\_29}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_29}] \cdot [\mathrm{species\_21}]}{\mathrm{km} + [\mathrm{species\_21}]} \quad (120)$$

$$\mathrm{HMM\_Modified\_17}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_21}], [\mathrm{species\_29}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_29}] \cdot [\mathrm{species\_21}]}{\mathrm{km} + [\mathrm{species\_21}]} \quad (121)$$

Table 90: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		1509.36		☑
`km`	km		1432410.00		☑

6.24 Reaction `reaction_27`

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

Name Mek_Activation_bRaf

Reaction equation

$$\mathrm{species\_9} \xrightarrow{\mathrm{bRafMutated}} \mathrm{species\_8} \quad (122)$$

Reactant

Table 91: Properties of each reactant.

Id	Name	SBO
`species_9`	MekInactive	

Modifier

Table 92: Properties of each modifier.

Id	Name	SBO
bRafMutated	bRafMutated	

Product

Table 93: Properties of each product.

Id	Name	SBO
species_8	MekActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_18}\left(\mathrm{Kcat}, [\mathrm{bRafMutated}], \mathrm{km}, [\mathrm{species\_9}]\right) \quad (123)$$

$$\mathrm{HMM\_Modified\_18}\left(\mathrm{Kcat}, [\mathrm{bRafMutated}], \mathrm{km}, [\mathrm{species\_9}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{bRafMutated}] \cdot [\mathrm{species\_9}]}{\mathrm{km} + [\mathrm{species\_9}]} \quad (124)$$

$$\mathrm{HMM\_Modified\_18}\left(\mathrm{Kcat}, [\mathrm{bRafMutated}], \mathrm{km}, [\mathrm{species\_9}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{bRafMutated}] \cdot [\mathrm{species\_9}]}{\mathrm{km} + [\mathrm{species\_9}]} \quad (125)$$

Table 94: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		185.759		☑
km	km		4768350.000		☑

6.25 Reaction reaction_28

This is an irreversible reaction of one reactant forming one product.

Name RTK_Production

Reaction equation

$$\text{species\_30} \longrightarrow \text{species\_1} \tag{126}$$

Reactant

Table 95: Properties of each reactant.

Id	Name	SBO
species_30	proRTK	

Product

Table 96: Properties of each product.

Id	Name	SBO
species_1	freeRTK	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{Constant\_flux\_\_irreversible}\left(\text{v}\right) \tag{127}$$

$$\text{Constant\_flux\_\_irreversible}\left(\text{v}\right) = \text{v} \tag{128}$$

$$\text{Constant\_flux\_\_irreversible}\left(\text{v}\right) = \text{v} \tag{129}$$

Table 97: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
v	v		100.0		☑

6.26 Reaction reaction_29

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

Name RTK_Degradation_Free

Reaction equation

$$\text{species\_1} \longrightarrow \emptyset \tag{130}$$

Reactant

Table 98: Properties of each reactant.

Id	Name	SBO
species_1	freeRTK	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \text{vol}\,(\text{compartment\_0}) \cdot \text{k1} \cdot [\text{species\_1}] \tag{131}$$

Table 99: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.001		☑

6.27 Reaction PIP3_Activation

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

Name PIP3_Activation

Reaction equation

$$\text{PIP3Inactive} \xrightarrow{\text{species\_14}} \text{PIP3Active} \tag{132}$$

Reactant

Table 100: Properties of each reactant.

Id	Name	SBO
PIP3Inactive	PIP3Inactive	

Modifier

Table 101: Properties of each modifier.

Id	Name	SBO
species_14	PI3KActive	

Product

Table 102: Properties of each product.

Id	Name	SBO
PIP3Active	PIP3Active	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_19}\left(\mathrm{Kcat}, [\mathrm{PIP3Inactive}], \mathrm{km}, [\mathrm{species\_14}]\right) \quad (133)$$

$$\mathrm{HMM\_Modified\_19}\left(\mathrm{Kcat}, [\mathrm{PIP3Inactive}], \mathrm{km}, [\mathrm{species\_14}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_14}] \cdot [\mathrm{PIP3Inactive}]}{\mathrm{km} + [\mathrm{PIP3Inactive}]} \quad (134)$$

$$\mathrm{HMM\_Modified\_19}\left(\mathrm{Kcat}, [\mathrm{PIP3Inactive}], \mathrm{km}, [\mathrm{species\_14}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_14}] \cdot [\mathrm{PIP3Inactive}]}{\mathrm{km} + [\mathrm{PIP3Inactive}]} \quad (135)$$

Table 103: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.057		☑
km	km		653951.000		☑

6.28 Reaction PIP3_Feedback_Deactivation_PTEN

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

Name PIP3_Feedback_Deactivation_PTEN

Reaction equation

$$\text{PIP3Active} \xrightarrow{\text{PTENActive}} \text{PIP3Inactive} \tag{136}$$

Reactant

Table 104: Properties of each reactant.

Id	Name	SBO
PIP3Active	PIP3Active	

Modifier

Table 105: Properties of each modifier.

Id	Name	SBO
PTENActive	PTENActive	

Product

Table 106: Properties of each product.

Id	Name	SBO
PIP3Inactive	PIP3Inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{HMM\_Modified\_20}\left(\text{Kcat}, [\text{PIP3Active}], [\text{PTENActive}], \text{km}\right) \tag{137}$$

$$\begin{aligned} &\text{HMM\_Modified\_20}\left(\text{Kcat}, [\text{PIP3Active}], [\text{PTENActive}], \text{km}\right) \\ &= \frac{\text{Kcat} \cdot [\text{PTENActive}] \cdot [\text{PIP3Active}]}{\text{km} + [\text{PIP3Active}]} \end{aligned} \tag{138}$$

$$\begin{aligned}&\text{HMM\_Modified\_20}\left(\text{Kcat}, [\text{PIP3Active}], [\text{PTENActive}], \text{km}\right)\\ &= \frac{\text{Kcat} \cdot [\text{PTENActive}] \cdot [\text{PIP3Active}]}{\text{km} + [\text{PIP3Active}]}\end{aligned} \tag{139}$$

Table 107: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		2.832		☑
`km`	km		518753.000		☑

6.29 Reaction `Akt_Activation_PIP3`

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

Name Akt_Activation_PIP3

Reaction equation

$$\text{species\_17} \xrightarrow{\text{PIP3Active}} \text{species\_16} \tag{140}$$

Reactant

Table 108: Properties of each reactant.

Id	Name	SBO
`species_17`	AktInactive	

Modifier

Table 109: Properties of each modifier.

Id	Name	SBO
`PIP3Active`	PIP3Active	

Product

Table 110: Properties of each product.

Id	Name	SBO
species_16	AktActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{29} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_21}\left(\mathrm{Kcat}, [\mathrm{PIP3Active}], \mathrm{km}, [\mathrm{species\_17}]\right) \quad (141)$$

$$\mathrm{HMM\_Modified\_21}\left(\mathrm{Kcat}, [\mathrm{PIP3Active}], \mathrm{km}, [\mathrm{species\_17}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{PIP3Active}] \cdot [\mathrm{species\_17}]}{\mathrm{km} + [\mathrm{species\_17}]} \quad (142)$$

$$\mathrm{HMM\_Modified\_21}\left(\mathrm{Kcat}, [\mathrm{PIP3Active}], \mathrm{km}, [\mathrm{species\_17}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{PIP3Active}] \cdot [\mathrm{species\_17}]}{\mathrm{km} + [\mathrm{species\_17}]} \quad (143)$$

Table 111: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.057		☑
km	km		653951.000		☑

6.30 Reaction PI3K_Activation_IRS1

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

Name PI3K_Activation_IRS1

Reaction equation

$$\mathrm{species\_15} \xrightarrow{\mathrm{IRS1Active}} \mathrm{species\_14} \quad (144)$$

Reactant

Table 112: Properties of each reactant.

Id	Name	SBO
species_15	PI3KInactive	

Modifier

Table 113: Properties of each modifier.

Id	Name	SBO
IRS1Active	IRS1Active	

Product

Table 114: Properties of each product.

Id	Name	SBO
species_14	PI3KActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{30} = \mathrm{vol}(\mathrm{compartment\_0}) \cdot \mathrm{HMM\_Modified\_22}([\mathrm{IRS1Active}], \mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_15}]) \quad (145)$$

$$\mathrm{HMM\_Modified\_22}([\mathrm{IRS1Active}], \mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_15}]) = \frac{\mathrm{Kcat} \cdot [\mathrm{IRS1Active}] \cdot [\mathrm{species\_15}]}{\mathrm{km} + [\mathrm{species\_15}]} \quad (146)$$

$$\mathrm{HMM\_Modified\_22}([\mathrm{IRS1Active}], \mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_15}]) = \frac{\mathrm{Kcat} \cdot [\mathrm{IRS1Active}] \cdot [\mathrm{species\_15}]}{\mathrm{km} + [\mathrm{species\_15}]} \quad (147)$$

Table 115: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.077		☑
km	km		272056.000		☑

6.31 Reaction IRS1_Activation

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

Name IRS1_Activation

Reaction equation

$$\text{IRS1Inactive} \xrightarrow{\text{species\_0}} \text{IRS1Active} \tag{148}$$

Reactant

Table 116: Properties of each reactant.

Id	Name	SBO
IRS1Inactive	IRS1Inactive	

Modifier

Table 117: Properties of each modifier.

Id	Name	SBO
species_0	boundRTK	

Product

Table 118: Properties of each product.

Id	Name	SBO
IRS1Active	IRS1Active	

Kinetic Law

Derived unit contains undeclared units

$$v_{31} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{HMM\_Modified\_23}\left(\left[\text{IRS1Inactive}\right], \text{Kcat}, \text{km}, \left[\text{species\_0}\right]\right) \tag{149}$$

$$\text{HMM\_Modified\_23}\left(\left[\text{IRS1Inactive}\right], \text{Kcat}, \text{km}, \left[\text{species\_0}\right]\right) = \frac{\text{Kcat} \cdot \left[\text{species\_0}\right] \cdot \left[\text{IRS1Inactive}\right]}{\text{km} + \left[\text{IRS1Inactive}\right]} \tag{150}$$

$$\text{HMM\_Modified\_23}\left([\text{IRS1Inactive}], \text{Kcat}, \text{km}, [\text{species\_0}]\right) = \frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{IRS1Inactive}]}{\text{km} + [\text{IRS1Inactive}]} \tag{151}$$

Table 119: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		10.674		☑
`km`	km		184912.000		☑

6.32 Reaction `PDK1_Activation`

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

Name PDK1_Activation

Reaction equation

$$\text{PDK1Inactive} \xrightarrow{\text{PIP3Active}} \text{PDK1Active} \tag{152}$$

Reactant

Table 120: Properties of each reactant.

Id	Name	SBO
`PDK1Inactive`	PDK1Inactive	

Modifier

Table 121: Properties of each modifier.

Id	Name	SBO
`PIP3Active`	PIP3Active	

Product

Table 122: Properties of each product.

Id	Name	SBO
PDK1Active	PDK1Active	

Kinetic Law

Derived unit contains undeclared units

$$v_{32} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_24}\left(\mathrm{Kcat}, [\mathrm{PDK1Inactive}], [\mathrm{PIP3Active}], \mathrm{km}\right) \tag{153}$$

$$\mathrm{HMM\_Modified\_24}\left(\mathrm{Kcat}, [\mathrm{PDK1Inactive}], [\mathrm{PIP3Active}], \mathrm{km}\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{PIP3Active}] \cdot [\mathrm{PDK1Inactive}]}{\mathrm{km} + [\mathrm{PDK1Inactive}]} \tag{154}$$

$$\mathrm{HMM\_Modified\_24}\left(\mathrm{Kcat}, [\mathrm{PDK1Inactive}], [\mathrm{PIP3Active}], \mathrm{km}\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{PIP3Active}] \cdot [\mathrm{PDK1Inactive}]}{\mathrm{km} + [\mathrm{PDK1Inactive}]} \tag{155}$$

Table 123: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		9.854		☑
km	km		1007340.000		☑

6.33 Reaction PDK1_Deactivation

This is an irreversible reaction of one reactant forming one product.

Name PDK1_Deactivation

Reaction equation

$$\mathrm{PDK1Active} \longrightarrow \mathrm{PDK1Inactive} \tag{156}$$

Reactant

Table 124: Properties of each reactant.

Id	Name	SBO
PDK1Active	PDK1Active	

Product

Table 125: Properties of each product.

Id	Name	SBO
PDK1Inactive	PDK1Inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{33} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{k1} \cdot [\mathrm{PDK1Active}] \tag{157}$$

Table 126: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		2.5		☑

6.34 Reaction Akt_Activation_PDK1

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

Name Akt_Activation_PDK1

Reaction equation

$$\mathrm{species\_17} \xrightarrow{\mathrm{PDK1Active}} \mathrm{species\_16} \tag{158}$$

Reactant

Table 127: Properties of each reactant.

Id	Name	SBO
species_17	AktInactive	

Modifier

Table 128: Properties of each modifier.

Id	Name	SBO
PDK1Active	PDK1Active	

Product

Table 129: Properties of each product.

Id	Name	SBO
species_16	AktActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{34} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_25}\left(\mathrm{Kcat}, [\mathrm{PDK1Active}], \mathrm{km}, [\mathrm{species\_17}]\right) \quad (159)$$

$$\mathrm{HMM\_Modified\_25}\left(\mathrm{Kcat}, [\mathrm{PDK1Active}], \mathrm{km}, [\mathrm{species\_17}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{PDK1Active}] \cdot [\mathrm{species\_17}]}{\mathrm{km} + [\mathrm{species\_17}]} \quad (160)$$

$$\mathrm{HMM\_Modified\_25}\left(\mathrm{Kcat}, [\mathrm{PDK1Active}], \mathrm{km}, [\mathrm{species\_17}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{PDK1Active}] \cdot [\mathrm{species\_17}]}{\mathrm{km} + [\mathrm{species\_17}]} \quad (161)$$

Table 130: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.057		☑
km	km		653951.000		☑

6.35 Reaction Akt_Feedback_Activation_HSP90_Cdc37

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

Name Akt_Feedback_Activation_HSP90-Cdc37

Reaction equation

$$\text{species\_17} \xrightarrow{\text{HSP90\_Cdc37Active}} \text{species\_16} \tag{162}$$

Reactant

Table 131: Properties of each reactant.

Id	Name	SBO
species_17	AktInactive	

Modifier

Table 132: Properties of each modifier.

Id	Name	SBO
HSP90_Cdc37Active	HSP90-Cdc37Active	

Product

Table 133: Properties of each product.

Id	Name	SBO
species_16	AktActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{35} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_26}\left(\left[\mathrm{HSP90\_Cdc37Active}\right], \mathrm{Kcat}, \mathrm{km}, \left[\mathrm{species\_17}\right]\right) \tag{163}$$

$$\begin{aligned} &\mathrm{HMM\_Modified\_26}\left(\left[\mathrm{HSP90\_Cdc37Active}\right], \mathrm{Kcat}, \mathrm{km}, \left[\mathrm{species\_17}\right]\right) \\ &= \frac{\mathrm{Kcat} \cdot \left[\mathrm{HSP90\_Cdc37Active}\right] \cdot \left[\mathrm{species\_17}\right]}{\mathrm{km} + \left[\mathrm{species\_17}\right]} \end{aligned} \tag{164}$$

$$\begin{aligned} &\mathrm{HMM\_Modified\_26}\left(\left[\mathrm{HSP90\_Cdc37Active}\right], \mathrm{Kcat}, \mathrm{km}, \left[\mathrm{species\_17}\right]\right) \\ &= \frac{\mathrm{Kcat} \cdot \left[\mathrm{HSP90\_Cdc37Active}\right] \cdot \left[\mathrm{species\_17}\right]}{\mathrm{km} + \left[\mathrm{species\_17}\right]} \end{aligned} \tag{165}$$

Table 134: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		0.057		☑
`km`	km		653951.000		☑

6.36 Reaction `Akt_Feedback_Deactivation_PHLPP`

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

Name Akt_Feedback_Deactivation_PHLPP

Reaction equation

$$\mathrm{species\_16} \xrightarrow{\mathrm{PHLPPActive}} \mathrm{species\_17} \tag{166}$$

Reactant

Table 135: Properties of each reactant.

Id	Name	SBO
`species_16`	AktActive	

Modifier

Table 136: Properties of each modifier.

Id	Name	SBO
PHLPPActive	PHLPPActive	

Product

Table 137: Properties of each product.

Id	Name	SBO
species_17	AktInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{36} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_27}\left(\mathrm{Kcat}, [\mathrm{PHLPPActive}], \mathrm{km}, [\mathrm{species\_16}]\right) \quad (167)$$

$$\mathrm{HMM\_Modified\_27}\left(\mathrm{Kcat}, [\mathrm{PHLPPActive}], \mathrm{km}, [\mathrm{species\_16}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{PHLPPActive}] \cdot [\mathrm{species\_16}]}{\mathrm{km} + [\mathrm{species\_16}]} \quad (168)$$

$$\mathrm{HMM\_Modified\_27}\left(\mathrm{Kcat}, [\mathrm{PHLPPActive}], \mathrm{km}, [\mathrm{species\_16}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{PHLPPActive}] \cdot [\mathrm{species\_16}]}{\mathrm{km} + [\mathrm{species\_16}]} \quad (169)$$

Table 138: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.126		☑
km	km		1061.710		☑

6.37 Reaction Akt_Feedback_Activation_mTORC2

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

Name Akt_Feedback_Activation_mTORC2

Reaction equation

$$\text{species\_17} \xrightarrow{\text{mTORC2Active}} \text{species\_16} \tag{170}$$

Reactant

Table 139: Properties of each reactant.

Id	Name	SBO
species_17	AktInactive	

Modifier

Table 140: Properties of each modifier.

Id	Name	SBO
mTORC2Active	mTORC2Active	

Product

Table 141: Properties of each product.

Id	Name	SBO
species_16	AktActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{37} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{HMM\_Modified\_28}\left(\text{Kcat}, \text{km}, [\text{mTORC2Active}], [\text{species\_17}]\right) \tag{171}$$

$$\begin{aligned}&\text{HMM\_Modified\_28}\left(\text{Kcat}, \text{km}, [\text{mTORC2Active}], [\text{species\_17}]\right)\\&= \frac{\text{Kcat} \cdot [\text{mTORC2Active}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]}\end{aligned} \tag{172}$$

$$\begin{aligned}&\text{HMM\_Modified\_28}\left(\text{Kcat}, \text{km}, [\text{mTORC2Active}], [\text{species\_17}]\right)\\&= \frac{\text{Kcat} \cdot [\text{mTORC2Active}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]}\end{aligned} \tag{173}$$

Table 142: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		0.057		☑
`km`	km		653951.000		☑

6.38 Reaction `Akt_Feedback_Activation_TCL1`

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

Name Akt_Feedback_Activation_TCL1

Reaction equation

$$\text{species\_17} \xrightarrow{\text{TCL1Active}} \text{species\_16} \tag{174}$$

Reactant

Table 143: Properties of each reactant.

Id	Name	SBO
`species_17`	AktInactive	

Modifier

Table 144: Properties of each modifier.

Id	Name	SBO
`TCL1Active`	TCL1Active	

Product

Table 145: Properties of each product.

Id	Name	SBO
species_16	AktActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{38} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_29}\left(\mathrm{Kcat}, [\mathrm{TCL1Active}], \mathrm{km}, [\mathrm{species\_17}]\right) \quad (175)$$

$$\mathrm{HMM\_Modified\_29}\left(\mathrm{Kcat}, [\mathrm{TCL1Active}], \mathrm{km}, [\mathrm{species\_17}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{TCL1Active}] \cdot [\mathrm{species\_17}]}{\mathrm{km} + [\mathrm{species\_17}]} \quad (176)$$

$$\mathrm{HMM\_Modified\_29}\left(\mathrm{Kcat}, [\mathrm{TCL1Active}], \mathrm{km}, [\mathrm{species\_17}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{TCL1Active}] \cdot [\mathrm{species\_17}]}{\mathrm{km} + [\mathrm{species\_17}]} \quad (177)$$

Table 146: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.057		☑
km	km		653951.000		☑

6.39 Reaction Akt_Feedback_Deactivation_CTMP

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

Name Akt_Feedback_Deactivation_CTMP

Reaction equation

$$\mathrm{species\_16} \xrightarrow{\mathrm{CTMPActive}} \mathrm{species\_17} \quad (178)$$

Reactant

Table 147: Properties of each reactant.

Id	Name	SBO
species_16	AktActive	

Modifier

Table 148: Properties of each modifier.

Id	Name	SBO
CTMPActive	CTMPActive	

Product

Table 149: Properties of each product.

Id	Name	SBO
species_17	AktInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{39} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_30}\left(\left[\mathrm{CTMPActive}\right], \mathrm{Kcat}, \mathrm{km}, \left[\mathrm{species\_16}\right]\right) \quad (179)$$

$$\mathrm{HMM\_Modified\_30}\left(\left[\mathrm{CTMPActive}\right], \mathrm{Kcat}, \mathrm{km}, \left[\mathrm{species\_16}\right]\right) = \frac{\mathrm{Kcat} \cdot \left[\mathrm{CTMPActive}\right] \cdot \left[\mathrm{species\_16}\right]}{\mathrm{km} + \left[\mathrm{species\_16}\right]} \quad (180)$$

$$\mathrm{HMM\_Modified\_30}\left(\left[\mathrm{CTMPActive}\right], \mathrm{Kcat}, \mathrm{km}, \left[\mathrm{species\_16}\right]\right) = \frac{\mathrm{Kcat} \cdot \left[\mathrm{CTMPActive}\right] \cdot \left[\mathrm{species\_16}\right]}{\mathrm{km} + \left[\mathrm{species\_16}\right]} \quad (181)$$

Table 150: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.057		☑
km	km		653951.000		☑

6.40 Reaction Akt_Feedback_Deactivation_PP2A

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

Name Akt_Feedback_Deactivation_PP2A

Reaction equation

$$\text{species\_16} \xrightarrow{\text{species\_26}} \text{species\_17} \tag{182}$$

Reactant

Table 151: Properties of each reactant.

Id	Name	SBO
species_16	AktActive	

Modifier

Table 152: Properties of each modifier.

Id	Name	SBO
species_26	PP2AActive	

Product

Table 153: Properties of each product.

Id	Name	SBO
species_17	AktInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{40} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_31}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_16}], [\mathrm{species\_26}]\right) \quad (183)$$

$$\mathrm{HMM\_Modified\_31}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_16}], [\mathrm{species\_26}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_26}] \cdot [\mathrm{species\_16}]}{\mathrm{km} + [\mathrm{species\_16}]} \quad (184)$$

$$\mathrm{HMM\_Modified\_31}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_16}], [\mathrm{species\_26}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_26}] \cdot [\mathrm{species\_16}]}{\mathrm{km} + [\mathrm{species\_16}]} \quad (185)$$

Table 154: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		0.126		☑
`km`	km		1061.710		☑

6.41 Reaction `Erk_Feedback_Deactivation_Raf1`

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

Name Erk_Feedback_Deactivation_Raf1

Notes `http://link.springer.com/article/10.1007%2Fs10555-008-9119-x`

Reaction equation

$$\mathrm{species\_10} \xrightarrow{\mathrm{species\_6}} \mathrm{species\_11} \quad (186)$$

Reactant

Table 155: Properties of each reactant.

Id	Name	SBO
`species_10`	ErkActive	

Modifier

Table 156: Properties of each modifier.

Id	Name	SBO
species_6	Raf1Active	

Product

Table 157: Properties of each product.

Id	Name	SBO
species_11	ErkInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{41} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_32}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_6}]\right) \quad (187)$$

$$\mathrm{HMM\_Modified\_32}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_6}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_6}] \cdot [\mathrm{species\_10}]}{\mathrm{km} + [\mathrm{species\_10}]} \quad (188)$$

$$\mathrm{HMM\_Modified\_32}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_6}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_6}] \cdot [\mathrm{species\_10}]}{\mathrm{km} + [\mathrm{species\_10}]} \quad (189)$$

Table 158: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		8.891		☑
km	km		3496490.000		☑

6.42 Reaction Sos_Feedback_Deactivation_Erk

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

Name Sos_Feedback_Deactivation_Erk

Notes `http://link.springer.com/article/10.1007%2Fs10555-008-9119-x`

Reaction equation

$$\text{species\_2} \xrightarrow{\text{species\_10}} \text{species\_3} \tag{190}$$

Reactant

Table 159: Properties of each reactant.

Id	Name	SBO
`species_2`	SosActive	

Modifier

Table 160: Properties of each modifier.

Id	Name	SBO
`species_10`	ErkActive	

Product

Table 161: Properties of each product.

Id	Name	SBO
`species_3`	SosInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{42} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{HMM\_Modified\_33}\left(\text{Kcat}, \text{km}, [\text{species\_10}], [\text{species\_2}]\right) \tag{191}$$

$$\text{HMM\_Modified\_33}\left(\text{Kcat}, \text{km}, [\text{species\_10}], [\text{species\_2}]\right) = \frac{\text{Kcat} \cdot [\text{species\_10}] \cdot [\text{species\_2}]}{\text{km} + [\text{species\_2}]} \tag{192}$$

$$\text{HMM\_Modified\_33}\left(\text{Kcat}, \text{km}, [\text{species\_10}], [\text{species\_2}]\right) = \frac{\text{Kcat} \cdot [\text{species\_10}] \cdot [\text{species\_2}]}{\text{km} + [\text{species\_2}]} \tag{193}$$

Table 162: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		0.021		☑
`km`	km		763523.000		☑

6.43 Reaction `mTORC1_Activation_Akt`

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

Name mTORC1_Activation_Akt

Reaction equation

$$\text{mTORC1Inactive} \xrightarrow{\text{species\_16}} \text{mTORC1Active} \tag{194}$$

Reactant

Table 163: Properties of each reactant.

Id	Name	SBO
`mTORC1Inactive`	mTORC1Inactive	

Modifier

Table 164: Properties of each modifier.

Id	Name	SBO
`species_16`	AktActive	

Product

Table 165: Properties of each product.

Id	Name	SBO
mTORC1Active	mTORC1Active	

Kinetic Law

Derived unit contains undeclared units

$$v_{43} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_34}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{mTORC1Inactive}], [\mathrm{species\_16}]\right) \tag{195}$$

$$\mathrm{HMM\_Modified\_34}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{mTORC1Inactive}], [\mathrm{species\_16}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_16}] \cdot [\mathrm{mTORC1Inactive}]}{\mathrm{km} + [\mathrm{mTORC1Inactive}]} \tag{196}$$

$$\mathrm{HMM\_Modified\_34}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{mTORC1Inactive}], [\mathrm{species\_16}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_16}] \cdot [\mathrm{mTORC1Inactive}]}{\mathrm{km} + [\mathrm{mTORC1Inactive}]} \tag{197}$$

Table 166: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		15.121		☑
km	km		119355.000		☑

6.44 Reaction S6K1_Activation_mTORC1

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

Name S6K1_Activation_mTORC1

Reaction equation

$$\mathrm{S6K1Inactive} \xrightarrow{\mathrm{mTORC1Active}} \mathrm{S6K1Active} \tag{198}$$

Reactant

Table 167: Properties of each reactant.

Id	Name	SBO
S6K1Inactive	S6K1Inactive	

Modifier

Table 168: Properties of each modifier.

Id	Name	SBO
mTORC1Active	mTORC1Active	

Product

Table 169: Properties of each product.

Id	Name	SBO
S6K1Active	S6K1Active	

Kinetic Law

Derived unit contains undeclared units

$$v_{44} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_35}\left(\mathrm{Kcat}, [\mathrm{S6K1Inactive}], \mathrm{km}, [\mathrm{mTORC1Active}]\right) \tag{199}$$

$$\mathrm{HMM\_Modified\_35}\left(\mathrm{Kcat}, [\mathrm{S6K1Inactive}], \mathrm{km}, [\mathrm{mTORC1Active}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{mTORC1Active}] \cdot [\mathrm{S6K1Inactive}]}{\mathrm{km} + [\mathrm{S6K1Inactive}]} \tag{200}$$

$$\mathrm{HMM\_Modified\_35}\left(\mathrm{Kcat}, [\mathrm{S6K1Inactive}], \mathrm{km}, [\mathrm{mTORC1Active}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{mTORC1Active}] \cdot [\mathrm{S6K1Inactive}]}{\mathrm{km} + [\mathrm{S6K1Inactive}]} \tag{201}$$

Table 170: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.021		☑
km	km		763523.000		☑

6.45 Reaction IRS1_Feedback_Deactivation_S6K1

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

Name IRS1_Feedback_Deactivation_S6K1

Reaction equation

$$\text{IRS1Active} \xrightarrow{\text{S6K1Active}} \text{IRS1Inactive} \tag{202}$$

Reactant

Table 171: Properties of each reactant.

Id	Name	SBO
IRS1Active	IRS1Active	

Modifier

Table 172: Properties of each modifier.

Id	Name	SBO
S6K1Active	S6K1Active	

Product

Table 173: Properties of each product.

Id	Name	SBO
IRS1Inactive	IRS1Inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{45} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_36}\left(\left[\mathrm{IRS1Active}\right], \mathrm{Kcat}, \left[\mathrm{S6K1Active}\right], \mathrm{km}\right) \quad (203)$$

$$\mathrm{HMM\_Modified\_36}\left(\left[\mathrm{IRS1Active}\right], \mathrm{Kcat}, \left[\mathrm{S6K1Active}\right], \mathrm{km}\right) = \frac{\mathrm{Kcat} \cdot \left[\mathrm{S6K1Active}\right] \cdot \left[\mathrm{IRS1Active}\right]}{\mathrm{km} + \left[\mathrm{IRS1Active}\right]} \quad (204)$$

$$\mathrm{HMM\_Modified\_36}\left(\left[\mathrm{IRS1Active}\right], \mathrm{Kcat}, \left[\mathrm{S6K1Active}\right], \mathrm{km}\right) = \frac{\mathrm{Kcat} \cdot \left[\mathrm{S6K1Active}\right] \cdot \left[\mathrm{IRS1Active}\right]}{\mathrm{km} + \left[\mathrm{IRS1Active}\right]} \quad (205)$$

Table 174: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kcat`	Kcat		1611.97		☑
`km`	km		896896.00		☑

6.46 Reaction `Dabrafenib_degradation`

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

Name Dabrafenib_degradation

Notes `The k1 parameter was set in a way that it reflects the half life of Dabrafenib drug`

`C(t)=C0*e^(-ket) where ke is the half life constant.`

Reaction equation

$$\mathrm{Dabrafenib} \longrightarrow \emptyset \quad (206)$$

Reactant

Table 175: Properties of each reactant.

Id	Name	SBO
`Dabrafenib`	Dabrafenib	

Kinetic Law

Derived unit contains undeclared units

$$v_{46} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot \mathrm{k1} \cdot [\mathrm{Dabrafenib}] \tag{207}$$

Table 176: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$1.92527 \cdot 10^{-5}$		☑

6.47 Reaction bRaf_Deactivation_Dabrafenib

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

Name bRaf_Deactivation_Dabrafenib

Reaction equation

$$\mathrm{bRafMutated} \xrightarrow{\mathrm{Dabrafenib}} \mathrm{bRafMutatedInactive} \tag{208}$$

Reactant

Table 177: Properties of each reactant.

Id	Name	SBO
bRafMutated	bRafMutated	

Modifier

Table 178: Properties of each modifier.

Id	Name	SBO
Dabrafenib	Dabrafenib	

Product

Table 179: Properties of each product.

Id	Name	SBO
bRafMutatedInactive	bRafMutatedInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{47} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{HMM\_Modified\_37}\left(\left[\mathrm{Dabrafenib}\right], \mathrm{Kcat}, \left[\mathrm{bRafMutated}\right], \mathrm{km}\right) \quad (209)$$

$$\mathrm{HMM\_Modified\_37}\left(\left[\mathrm{Dabrafenib}\right], \mathrm{Kcat}, \left[\mathrm{bRafMutated}\right], \mathrm{km}\right) = \frac{\mathrm{Kcat} \cdot \left[\mathrm{Dabrafenib}\right] \cdot \left[\mathrm{bRafMutated}\right]}{\mathrm{km} + \left[\mathrm{bRafMutated}\right]} \quad (210)$$

$$\mathrm{HMM\_Modified\_37}\left(\left[\mathrm{Dabrafenib}\right], \mathrm{Kcat}, \left[\mathrm{bRafMutated}\right], \mathrm{km}\right) = \frac{\mathrm{Kcat} \cdot \left[\mathrm{Dabrafenib}\right] \cdot \left[\mathrm{bRafMutated}\right]}{\mathrm{km} + \left[\mathrm{bRafMutated}\right]} \quad (211)$$

Table 180: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		$3.19 \cdot 10^{13}$		☑
km	km		3200.000		☑

6.48 Reaction bRafMutated_Production

This is an irreversible reaction of one reactant forming one product.

Name bRafMutated_Production

Reaction equation

$$\mathrm{probRafMutated} \longrightarrow \mathrm{bRafMutated} \quad (212)$$

Reactant

Table 181: Properties of each reactant.

Id	Name	SBO
probRafMutated	probRafMutated	

Product

Table 182: Properties of each product.

Id	Name	SBO
bRafMutated	bRafMutated	

Kinetic Law

Derived unit contains undeclared units

$$v_{48} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) \tag{213}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{214}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{215}$$

Table 183: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
v	v		100.0		☑

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_0

Name boundRTK

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in six reactions (as a reactant in reaction_20 and as a product in reaction_0 and as a modifier in reaction_1, reaction_14, reaction_21, IRS1_Activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_0} = v_{1} - v_{19} \tag{216}$$

7.2 Species species_1

Name freeRTK

Initial concentration $80000.0000000001\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in reaction_0, reaction_29 and as a product in reaction_28).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_1} = v_{25} - v_{1} - v_{26} \tag{217}$$

7.3 Species species_2

Name SosActive

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in reaction_13, Sos_Feedback_Deactivation_Erk and as a product in reaction_1 and as a modifier in reaction_3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_2} = v_{2} - v_{13} - v_{42} \tag{218}$$

7.4 Species species_3

Name SosInactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in reaction_1 and as a product in reaction_13, Sos_Feedback_Deactivation_Erk).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_3} = v_{13} + v_{42} - v_{2} \tag{219}$$

7.5 Species species_4

Name RasActive

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in reaction_4 and as a product in reaction_3 and as a modifier in reaction_5, reaction_15).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_4} = v_3 - v_4 \tag{220}$$

7.6 Species species_5

Name RasInactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a reactant in reaction_3 and as a product in reaction_4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_5} = v_4 - v_3 \tag{221}$$

7.7 Species species_6

Name Raf1Active

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in five reactions (as a reactant in reaction_6, reaction_19 and as a product in reaction_5 and as a modifier in reaction_7, Erk_Feedback_Deactivation_Raf1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_6} = v_5 - v_6 - v_{18} \tag{222}$$

7.8 Species species_7

Name Raf1Inactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in reaction_5 and as a product in reaction_6, reaction_19).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_7} = v_6 + v_{18} - v_5 \tag{223}$$

7.9 Species species_8

Name MekActive

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in reaction_8 and as a product in reaction_7, reaction_27 and as a modifier in reaction_9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_8} = v_7 + v_{24} - v_8 \tag{224}$$

7.10 Species species_9

Name MekInactive

Initial concentration $600000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in reaction_7, reaction_27 and as a product in reaction_8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_9} = v_8 - v_7 - v_{24} \tag{225}$$

7.11 Species species_10

Name ErkActive

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in five reactions (as a reactant in reaction_10, Erk_Feedback_Deactivation_Raf1 and as a product in reaction_9 and as a modifier in reaction_11, Sos_Feedback_Deactivation_Erk).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_10} = v_9 - v_{10} - v_{41} \tag{226}$$

7.12 Species species_11

Name ErkInactive

Initial concentration $600000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in reaction_9 and as a product in reaction_10, Erk_Feedback_Deactivation_Raf1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_11} = v_{10} + v_{41} - v_9 \tag{227}$$

7.13 Species species_12

Name P90RskActive

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_12} = v_{11} - v_{12} \tag{228}$$

7.14 Species species_13

Name P90RskInactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_13} = v_{12} - v_{11} \tag{229}$$

7.15 Species species_14

Name PI3KActive

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in six reactions (as a reactant in reaction_16 and as a product in reaction_14, reaction_15, PI3K_Activation_IRS1 and as a modifier in reaction_17, PIP3_Activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_14} = v_{14} + v_{15} + v_{30} - v_{16} \tag{230}$$

7.16 Species species_15

Name PI3KInactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in reaction_14, reaction_15, PI3K-_Activation_IRS1 and as a product in reaction_16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_15} = v_{16} - v_{14} - v_{15} - v_{30} \tag{231}$$

7.17 Species species_16

Name AktActive

Initial concentration $0\ \mathrm{mmol}\cdot\mathrm{ml}^{-1}$

This species takes part in eleven reactions (as a reactant in Akt_Feedback_Deactivation_PHLPP, Akt_Feedback_Deactivation_CTMP, Akt_Feedback_Deactivation_PP2A and as a product in reaction_17, Akt_Activation_PIP3, Akt_Activation_PDK1, Akt_Feedback_Activation_HSP90_Cdc37, Akt_Feedback_Activation_mTORC2, Akt_Feedback_Activation_TCL1 and as a modifier in reaction_19, mTORC1_Activation_Akt).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_16} = v_{17} + v_{29} + v_{34} + v_{35} + v_{37} + v_{38} - v_{36} - v_{39} - v_{40} \tag{232}$$

7.18 Species species_17

Name AktInactive

Initial concentration $120000\ \mathrm{mmol}\cdot\mathrm{ml}^{-1}$

This species takes part in nine reactions (as a reactant in reaction_17, Akt_Activation_PIP3, Akt_Activation_PDK1, Akt_Feedback_Activation_HSP90_Cdc37, Akt_Feedback_Activation_mTORC2, Akt_Feedback_Activation_TCL1 and as a product in Akt_Feedback_Deactivation_PHLPP, Akt_Feedback_Deactivation_CTMP, Akt_Feedback_Deactivation_PP2A).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_17} = v_{36} + v_{39} + v_{40} - v_{17} - v_{29} - v_{34} - v_{35} - v_{37} - v_{38} \tag{233}$$

7.19 Species species_19

Name C3GActive

Initial concentration $0\ \mathrm{mmol}\cdot\mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in reaction_22 and as a product in reaction_21 and as a modifier in reaction_23).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_19} = v_{20} - v_{21} \tag{234}$$

7.20 Species species_20

Name C3GInactive

Initial concentration $120000\ \mathrm{mmol}\cdot\mathrm{ml}^{-1}$

This species takes part in two reactions (as a reactant in reaction_21 and as a product in reaction_22).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_20} = v_{21} - v_{20} \tag{235}$$

7.21 Species species_21

Name Rap1Active

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a reactant in reaction_24 and as a product in reaction_23).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_21} = v_{22} - v_{23} \tag{236}$$

7.22 Species species_22

Name Rap1Inactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a reactant in reaction_23 and as a product in reaction_24).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_22} = v_{23} - v_{22} \tag{237}$$

7.23 Species species_25

Name GF

Initial concentration $1.0002 \cdot 10^{7}\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in one reaction (as a reactant in reaction_0), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_25} = 0 \tag{238}$$

7.24 Species species_26

Name PP2AActive

Notes http://link.springer.com/article/10.1007%2Fs10555-008-9119-x

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a modifier in reaction_8, reaction_10, Akt_Feedback_Deactivation_PP2A), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_26} = 0 \tag{239}$$

7.25 Species species_27

Name Raf1PPtase

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in one reaction (as a modifier in reaction_6), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_27} = 0 \tag{240}$$

7.26 Species species_28

Name RasGapActive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in one reaction (as a modifier in reaction_4), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_28} = 0 \tag{241}$$

7.27 Species species_29

Name Rap1Gap

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in one reaction (as a modifier in reaction_24), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_29} = 0 \tag{242}$$

7.28 Species species_30

Name proRTK

Initial concentration $1\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in one reaction (as a reactant in reaction_28), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_30} = 0 \tag{243}$$

7.29 Species PIP3Active

Name PIP3Active

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in PIP3_Feedback_Deactivation_PTEN and as a product in PIP3_Activation and as a modifier in Akt_Activation_PIP3, PDK1-_Activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PIP3Active} = v_{27} - v_{28} \tag{244}$$

7.30 Species PIP3Inactive

Name PIP3Inactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a reactant in PIP3_Activation and as a product in PIP3_Feedback_Deactivation_PTEN).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PIP3Inactive} = v_{28} - v_{27} \tag{245}$$

7.31 Species PTENActive

Name PTENActive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in one reaction (as a modifier in PIP3_Feedback_Deactivation_PTEN), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PTENActive} = 0 \tag{246}$$

7.32 Species IRS1Active

Name IRS1Active

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in IRS1_Feedback_Deactivation_S6K1 and as a product in IRS1_Activation and as a modifier in PI3K_Activation_IRS1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRS1Active} = v_{31} - v_{45} \tag{247}$$

7.33 Species IRS1Inactive

Name IRS1Inactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a reactant in IRS1_Activation and as a product in IRS1_Feedback_Deactivation_S6K1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRS1Inactive} = v_{45} - v_{31} \tag{248}$$

7.34 Species PDK1Inactive

Name PDK1Inactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a reactant in PDK1_Activation and as a product in PDK1_Deactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PDK1Inactive} = v_{33} - v_{32} \tag{249}$$

7.35 Species PDK1Active

Name PDK1Active

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in PDK1_Deactivation and as a product in PDK1_Activation and as a modifier in Akt_Activation_PDK1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PDK1Active} = v_{32} - v_{33} \tag{250}$$

7.36 Species HSP90_Cdc37Active

Name HSP90-Cdc37Active

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in one reaction (as a modifier in Akt_Feedback_Activation_HSP90-_Cdc37), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{HSP90\_Cdc37Active} = 0 \tag{251}$$

7.37 Species PHLPPActive

Name PHLPPActive

Initial concentration $120000\ \mathrm{mmol \cdot ml^{-1}}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PHLPPActive} = 0 \tag{252}$$

7.38 Species mTORC2Active

Name mTORC2Active

Initial concentration $120000\ \mathrm{mmol \cdot ml^{-1}}$

This species takes part in one reaction (as a modifier in Akt_Feedback_Activation_mTORC2), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mTORC2Active} = 0 \tag{253}$$

7.39 Species TCL1Active

Name TCL1Active

Initial concentration $120000\ \mathrm{mmol \cdot ml^{-1}}$

This species takes part in one reaction (as a modifier in Akt_Feedback_Activation_TCL1), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{TCL1Active} = 0 \tag{254}$$

7.40 Species CTMPActive

Name CTMPActive

Initial concentration $120000\ \mathrm{mmol \cdot ml^{-1}}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CTMPActive} = 0 \tag{255}$$

7.41 Species mTORC1Active

Name mTORC1Active

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a product in mTORC1_Activation_Akt and as a modifier in S6K1_Activation_mTORC1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mTORC1Active} = v_{43} \tag{256}$$

7.42 Species mTORC1Inactive

Name mTORC1Inactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in one reaction (as a reactant in mTORC1_Activation_Akt).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mTORC1Inactive} = -v_{43} \tag{257}$$

7.43 Species S6K1Active

Name S6K1Active

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a product in S6K1_Activation_mTORC1 and as a modifier in IRS1_Feedback_Deactivation_S6K1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S6K1Active} = v_{44} \tag{258}$$

7.44 Species S6K1Inactive

Name S6K1Inactive

Initial concentration $120000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in one reaction (as a reactant in S6K1_Activation_mTORC1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S6K1Inactive} = -v_{44} \tag{259}$$

7.45 Species bRafMutated

Name bRafMutated

Notes We simulated the A375 cell lines having the bRaf mutation in this way:

1) We introduced the new species bRafMutated; with the same initaila concentration c
2) We deleted the bRaf activation by Rap1 as the new species bRafMutated is not affe
3) We inhibited the deactivation of Braf by Raf1PPtase (as Raf1PPtase does not anymo
4) bRafMutated accomplish the Mek activation subsituting the not mutated species bRa

Initial concentration $120000\ \mathrm{mmol \cdot ml^{-1}}$

This species takes part in three reactions (as a reactant in bRaf_Deactivation_Dabrafenib and as a product in bRafMutated_Production and as a modifier in reaction_27).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{bRafMutated} = v_{48} - v_{47} \tag{260}$$

7.46 Species Dabrafenib

Name Dabrafenib

Initial concentration $1.25 \cdot 10^{-10}\ \mathrm{mmol \cdot ml^{-1}}$

This species takes part in two reactions (as a reactant in Dabrafenib_degradation and as a modifier in bRaf_Deactivation_Dabrafenib).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Dabrafenib} = -v_{46} \tag{261}$$

7.47 Species bRafMutatedInactive

Name bRafMutatedInactive

Initial concentration $1\ \mathrm{mmol \cdot ml^{-1}}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{bRafMutatedInactive} = v_{47} \tag{262}$$

7.48 Species probRafMutated

Name probRafMutated

Initial concentration $1\ \mathrm{mmol \cdot ml^{-1}}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{probRafMutated} = 0 \tag{263}$$

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