SBML Model Report

Model name: "Orton2009 - Modelling cancerous mutations in the EGFR/ERK pathway - EGF Model"

November 28, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Thawfeek Varusai[1] at November 28th 2016 at 9:09 a. m. and last time modified at November 28th 2016 at 9:09 a. m. Table 1 shows an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	31
events	0	constraints	0
reactions	31	function definitions	23
global parameters	0	unit definitions	3
rules	0	initial assignments	0

Model Notes

Orton2009 - Modelling cancerous mutations inthe EGFR/ERK pathway - EGF ModelThis model studies the aberrations inERK signalling for different cancer mutations. The authors alter apreviously existing EGF model (Brown et al 2004) to include newinteractionsthatbetterfit empirical data.Predictions show that the ERK signalling is a robust mechanismtaking different courses

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for different cancer mutations. Mostparameter values are used from the previous model and the newparameters areestimated using experimental data performed bythe authors on PC12 cells (adrenal gland, rat).The authorsprovide an SBML version of the model in the paper.

This model is described in the article:Computational modelling of cancerous mutations in the EGFR/ERK signalling pathway.Orton RJ, Adriaens ME, Gormand A, Sturm OE, Kolch W, Gilbert DR.BMC Syst Biol 2009 Oct; 3: 100

Abstract:

The Epidermal Growth Factor Receptor (EGFR) activated Extracellular-signal Regulated Kinase (ERK) pathway is a critical cell signalling pathway that relays the signal for a cell to proliferate from the plasma membrane to the nucleus. Deregulation of the EGFR/ERK pathway due to alterations affecting the expression or function of a number of pathway components has long been associated with numerous forms of cancer. Under normal conditions, Epidermal Growth Factor (EGF) stimulates a rapid but transient activation of ERK as the signal is rapidly shutdown. Whereas, under cancerous mutation conditions the ERK signal cannot be shutdown and is sustained resulting in the constitutive activation of ERK and continual cell proliferation. In this study, we have used computational modelling techniques to investigate what effects various cancerous alterations have on the signalling flow through the ERK pathway.We have generated a new model of the EGFR activated ERK pathway, which was verified by our own experimental data. We then altered our model to represent various cancerous situations such as Ras, B-Raf and EGFR mutations, as well as EGFR overexpression. Analysis of the models showed that different cancerous situations resulted in different signalling patterns through the ERK pathway, especially when compared to the normal EGF signal pattern. Our model predicts that cancerous EGFR mutation and overexpression signals almost exclusively via the Rap1 pathway, predicting that this pathway is the best target for drugs. Furthermore, our model also highlights the importance of receptor degradation in normal and cancerous EGFR signalling, and suggests that receptor degradation is a key difference between the signalling from the EGF and Nerve Growth Factor (NGF) receptors.Our results suggest that different routes to ERK activation are being utilised in different cancerous situations which therefore has interesting implications for drug selection strategies. We also conducted a comparison of the critical differences between signalling from different growth factor receptors (namely EGFR, mutated EGFR, NGF, and Insulin) with our results suggesting the difference between the systems are large scale and can be attributed to the presence/absence of entire pathways rather than subtle difference in individual rate constants between the systems.

This model is hosted on BioModels Database and identified by: BIOMD0000000623.

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

2 Unit Definitions

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

2.1 Unit `volume`

Name volume

Definition ml

2.2 Unit `time`

Name time

Definition 60 s

2.3 Unit `substance`

Name substance

Definition mmol

2.4 Unit `area`

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

Definition m^2

2.5 Unit `length`

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

Definition m

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

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

3.1 Compartment compartment_0

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

Name compartment

4 Species

This model contains 31 species. The boundary condition of six 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	boundEGFReceptor	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_1	freeEGFReceptor	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_18	degradedEGFReceptor	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_23	bRafActive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
species_24	bRafInactive	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
species_25	EGF	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	proEGFReceptor	compartment_0	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑

5 Function definitions

This is an overview of 23 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 Menten_Explicit_Enzyme_12

Name Menten_Explicit_Enzyme_12

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

Mathematical Expression

$$\frac{\mathrm{Kcat} \cdot [\mathrm{species\_0}] \cdot [\mathrm{species\_15}]}{\mathrm{km} + [\mathrm{species\_15}]} \tag{2}$$

5.3 Function definition MM_Explicit_Enzyme_5

Name MM Explicit Enzyme_5

Arguments kcat, km, [species_23], [species_27]

Mathematical Expression

$$\frac{\mathrm{kcat} \cdot [\mathrm{species\_27}] \cdot [\mathrm{species\_23}]}{\mathrm{km} + [\mathrm{species\_23}]} \tag{3}$$

5.4 Function definition Menten_Explicit_Enzyme_14

Name Menten_Explicit_Enzyme_14

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

Mathematical Expression

$$\frac{\mathrm{Kcat} \cdot [\mathrm{species\_14}] \cdot [\mathrm{species\_17}]}{\mathrm{km} + [\mathrm{species\_17}]} \tag{4}$$

5.5 Function definition Menten_Explicit_Enzyme_9

Name Menten_Explicit_Enzyme_9

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_26}] \cdot [\text{species\_10}]}{\text{km} + [\text{species\_10}]} \tag{5}$$

5.6 Function definition MM_Explicit_Enzyme_7

Name MM Explicit Enzyme_7

Arguments kcat, km, [species_24], [species_4]

Mathematical Expression

$$\frac{\text{kcat} \cdot [\text{species\_4}] \cdot [\text{species\_24}]}{\text{km} + [\text{species\_24}]} \tag{6}$$

5.7 Function definition Menten_Explicit_Enzyme_4

Name Menten_Explicit_Enzyme_4

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_4}] \cdot [\text{species\_7}]}{\text{km} + [\text{species\_7}]} \tag{7}$$

5.8 Function definition Menten_Explicit_Enzyme_6

Name Menten_Explicit_Enzyme_6

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_6}] \cdot [\text{species\_9}]}{\text{km} + [\text{species\_9}]} \tag{8}$$

5.9 Function definition MM_Explicit_Enzyme_4

Name MM Explicit Enzyme_4

Arguments kcat, km, [species_21], [species_24]

Mathematical Expression

$$\frac{\text{kcat} \cdot [\text{species\_21}] \cdot [\text{species\_24}]}{\text{km} + [\text{species\_24}]} \tag{9}$$

5.10 Function definition Menten_Explicit_Enzyme_2

Name Menten_Explicit_Enzyme_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 Menten_Explicit_Enzyme_7

Name Menten_Explicit_Enzyme_7

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_26}] \cdot [\text{species\_8}]}{\text{km} + [\text{species\_8}]} \tag{11}$$

5.12 Function definition Menten_Explicit_Enzyme_11

Name Menten_Explicit_Enzyme_11

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_12}] \cdot [\text{species\_2}]}{\text{km} + [\text{species\_2}]} \tag{12}$$

5.13 Function definition Menten_Explicit_Enzyme_15

Name Menten_Explicit_Enzyme_15

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_16}] \cdot [\text{species\_6}]}{\text{km} + [\text{species\_6}]} \tag{13}$$

5.14 Function definition MM_Explicit_Enzyme_1

Name MM Explicit Enzyme_1

Arguments kcat, km, [species_0], [species_20]

Mathematical Expression

$$\frac{\text{kcat} \cdot [\text{species\_0}] \cdot [\text{species\_20}]}{\text{km} + [\text{species\_20}]} \tag{14}$$

5.15 Function definition Menten_Explicit_Enzyme_10

Name Menten_Explicit_Enzyme_10

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_10}] \cdot [\text{species\_13}]}{\text{km} + [\text{species\_13}]} \tag{15}$$

5.16 Function definition Menten_Explicit_Enzyme_5

Name Menten_Explicit_Enzyme_5

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_27}] \cdot [\text{species\_6}]}{\text{km} + [\text{species\_6}]} \tag{16}$$

5.17 Function definition Menten_Explicit_Enzyme_8

Name Menten_Explicit_Enzyme_8

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_8}] \cdot [\text{species\_11}]}{\text{km} + [\text{species\_11}]} \tag{17}$$

5.18 Function definition Menten_Explicit_Enzyme_13

Name Menten_Explicit_Enzyme_13

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_4}] \cdot [\text{species\_15}]}{\text{km} + [\text{species\_15}]} \tag{18}$$

5.19 Function definition Menten_Explicit_Enzyme_3

Name Menten_Explicit_Enzyme_3

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_28}] \cdot [\text{species\_4}]}{\text{km} + [\text{species\_4}]} \tag{19}$$

5.20 Function definition MM_Explicit_Enzyme_2

Name MM Explicit Enzyme_2

Arguments kcat, km, [species_19], [species_22]

Mathematical Expression

$$\frac{\text{kcat} \cdot [\text{species\_19}] \cdot [\text{species\_22}]}{\text{km} + [\text{species\_22}]} \tag{20}$$

5.21 Function definition Menten_Explicit_Enzyme_1

Name Menten_Explicit_Enzyme_1

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

Mathematical Expression

$$\frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{species\_3}]}{\text{km} + [\text{species\_3}]} \tag{21}$$

5.22 Function definition MM_Explicit_Enzyme_3

Name MM Explicit Enzyme_3

Arguments kcat, km, [species_21], [species_29]

Mathematical Expression

$$\frac{\text{kcat} \cdot [\text{species\_29}] \cdot [\text{species\_21}]}{\text{km} + [\text{species\_21}]} \tag{22}$$

5.23 Function definition MM_Explicit_Enzyme_6

Name MM Explicit Enzyme_6

Arguments kcat, km, [species_23], [species_9]

Mathematical Expression

$$\frac{\text{kcat} \cdot [\text{species\_23}] \cdot [\text{species\_9}]}{\text{km} + [\text{species\_9}]} \tag{23}$$

6 Reactions

This model contains 31 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	EGF_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_2	Sos_Deactivation	$\text{species\_2} \longrightarrow \text{species\_3}$	
4	reaction_3	Ras_Activation	$\text{species\_5} \xrightarrow{\text{species\_2}} \text{species\_4}$	
5	reaction_4	Ras_Deactivation	$\text{species\_4} \xrightarrow{\text{species\_28}} \text{species\_5}$	
6	reaction_5	Raf1_Activation	$\text{species\_7} \xrightarrow{\text{species\_4}} \text{species\_6}$	
7	reaction_6	Raf1_Deactivation	$\text{species\_6} \xrightarrow{\text{species\_27}} \text{species\_7}$	
8	reaction_7	Mek_Activation	$\text{species\_9} \xrightarrow{\text{species\_6}} \text{species\_8}$	
9	reaction_8	Mek_Deactivation	$\text{species\_8} \xrightarrow{\text{species\_26}} \text{species\_9}$	
10	reaction_9	Erk_Activation	$\text{species\_11} \xrightarrow{\text{species\_8}} \text{species\_10}$	
11	reaction_10	Erk_Deactivation	$\text{species\_10} \xrightarrow{\text{species\_26}} \text{species\_11}$	
12	reaction_11	P90Rsk_Activation	$\text{species\_13} \xrightarrow{\text{species\_10}} \text{species\_12}$	
13	reaction_12	P90Rsk_Deactivation	$\text{species\_12} \longrightarrow \text{species\_13}$	
14	reaction_13	Sos_Feedback_Deactivation	$\text{species\_2} \xrightarrow{\text{species\_12}} \text{species\_3}$	
15	reaction_14	PI3K_Activation_EGFR	$\text{species\_15} \xrightarrow{\text{species\_0}} \text{species\_14}$	
16	reaction_15	PI3K_Activation_Ras	$\text{species\_15} \xrightarrow{\text{species\_4}} \text{species\_14}$	

№	Id	Name	Reaction Equation	SBO
17	reaction_16	PI3K_Deactivation	species_14 $\longrightarrow$ species_15	
18	reaction_17	Akt_Activation	species_17 $\xrightarrow{\text{species\_14}}$ species_16	
19	reaction_18	Akt_Deactivation	species_16 $\longrightarrow$ species_17	
20	reaction_19	Raf1_Deactivation_Akt	species_6 $\xrightarrow{\text{species\_16}}$ species_7	
21	reaction_20	EGFReceptor_Degradation	species_0 $\longrightarrow$ species_18	
22	reaction_21	C3G_Activation	species_20 $\xrightarrow{\text{species\_0}}$ species_19	
23	reaction_22	C3G_Deactivation	species_19 $\longrightarrow$ species_20	
24	reaction_23	Rap1_Activation	species_22 $\xrightarrow{\text{species\_19}}$ species_21	
25	reaction_24	Rap1_Deactivation	species_21 $\xrightarrow{\text{species\_29}}$ species_22	
26	reaction_25	bRaf_Activation	species_24 $\xrightarrow{\text{species\_21}}$ species_23	
27	reaction_26	bRaf_Deactivation	species_23 $\xrightarrow{\text{species\_27}}$ species_24	
28	reaction_27	Mek_Activation_bRaf	species_9 $\xrightarrow{\text{species\_23}}$ species_8	
29	reaction_28	EGFReceptor_Production	species_30 $\longrightarrow$ species_1	
30	reaction_29	EGFReceptor_Degradtion_Free	species_1 $\longrightarrow$ species_18	
31	reaction_30	bRaf_Activation_Ras	species_24 $\xrightarrow{\text{species\_4}}$ species_23	

6.1 Reaction reaction_0

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

Name EGF_Binding_Unbinding

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_25} + \text{species\_1} \rightleftharpoons \text{species\_0} \tag{24}$$

Reactants

Table 5: Properties of each reactant.

Id	Name	SBO
species_25	EGF	
species_1	freeEGFReceptor	

Product

Table 6: Properties of each product.

Id	Name	SBO
species_0	boundEGFReceptor	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{compartment\_0}) \cdot (\text{k1} \cdot [\text{species\_25}] \cdot [\text{species\_1}] - \text{k2} \cdot [\text{species\_0}]) \tag{25}$$

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

Notes `Parameters taken from Brown et al 2004`

Reaction equation

$$\text{species\_3} \xrightarrow{\text{species\_0}} \text{species\_2} \tag{26}$$

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`	boundEGFReceptor	

Product

Table 10: Properties of each product.

Id	Name	SBO
`species_2`	SosActive	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{Menten\_Explicit\_Enzyme\_1}\left(\text{Kcat}, \text{km}, [\text{species\_0}], [\text{species\_3}]\right) \tag{27}$$

$$\text{Menten\_Explicit\_Enzyme\_1}\left(\text{Kcat}, \text{km}, [\text{species\_0}], [\text{species\_3}]\right) = \frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{species\_3}]}{\text{km} + [\text{species\_3}]} \tag{28}$$

$$\text{Menten\_Explicit\_Enzyme\_1}\left(\text{Kcat}, \text{km}, [\text{species\_0}], [\text{species\_3}]\right) = \frac{\text{Kcat} \cdot [\text{species\_0}] \cdot [\text{species\_3}]}{\text{km} + [\text{species\_3}]} \tag{29}$$

Table 11: Properties of each parameter.

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

6.3 Reaction reaction_2

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

Name Sos_Deactivation

Notes Parameters were estimated from experiments

Reaction equation

$$\text{species\_2} \longrightarrow \text{species\_3} \tag{30}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
species_2	SosActive	

Product

Table 13: Properties of each product.

Id	Name	SBO
species_3	SosInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{vol}(\text{compartment\_0}) \cdot \text{k1} \cdot [\text{species\_2}] \tag{31}$$

Table 14: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		2.5		☑

6.4 Reaction reaction_3

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

Name Ras_Activation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_5} \xrightarrow{\text{species\_2}} \text{species\_4} \tag{32}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
species_5	RasInactive	

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
species_2	SosActive	

Product

Table 17: Properties of each product.

Id	Name	SBO
species_4	RasActive	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{Menten\_Explicit\_Enzyme\_2}\left(\text{Kcat}, \text{km}, [\text{species\_2}], [\text{species\_5}]\right) \tag{33}$$

$$\text{Menten\_Explicit\_Enzyme\_2}\left(\text{Kcat}, \text{km}, [\text{species\_2}], [\text{species\_5}]\right) = \frac{\text{Kcat} \cdot [\text{species\_2}] \cdot [\text{species\_5}]}{\text{km} + [\text{species\_5}]} \tag{34}$$

$$\text{Menten\_Explicit\_Enzyme\_2}\left(\text{Kcat}, \text{km}, [\text{species\_2}], [\text{species\_5}]\right) = \frac{\text{Kcat} \cdot [\text{species\_2}] \cdot [\text{species\_5}]}{\text{km} + [\text{species\_5}]} \tag{35}$$

Table 18: Properties of each parameter.

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

6.5 Reaction `reaction_4`

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

Name Ras_Deactivation

Notes `Parameters taken from Brown et al 2004`

Reaction equation

$$\text{species\_4} \xrightarrow{\text{species\_28}} \text{species\_5} \tag{36}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
`species_4`	RasActive	

Modifier

Table 20: Properties of each modifier.

Id	Name	SBO
`species_28`	RasGapActive	

Product

Table 21: Properties of each product.

Id	Name	SBO
species_5	RasInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{Menten\_Explicit\_Enzyme\_3}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_28}], [\mathrm{species\_4}]\right) \tag{37}$$

$$\mathrm{Menten\_Explicit\_Enzyme\_3}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_28}], [\mathrm{species\_4}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_28}] \cdot [\mathrm{species\_4}]}{\mathrm{km} + [\mathrm{species\_4}]} \tag{38}$$

$$\mathrm{Menten\_Explicit\_Enzyme\_3}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_28}], [\mathrm{species\_4}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_28}] \cdot [\mathrm{species\_4}]}{\mathrm{km} + [\mathrm{species\_4}]} \tag{39}$$

Table 22: Properties of each parameter.

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

6.6 Reaction reaction_5

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

Name Raf1_Activation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\mathrm{species\_7} \xrightarrow{\mathrm{species\_4}} \mathrm{species\_6} \tag{40}$$

Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
species_7	Raf1Inactive	

Modifier

Table 24: Properties of each modifier.

Id	Name	SBO
species_4	RasActive	

Product

Table 25: Properties of each product.

Id	Name	SBO
species_6	Raf1Active	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{Menten\_Explicit\_Enzyme\_4}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_4}], [\mathrm{species\_7}]\right) \quad (41)$$

$$\mathrm{Menten\_Explicit\_Enzyme\_4}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_4}], [\mathrm{species\_7}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_4}] \cdot [\mathrm{species\_7}]}{\mathrm{km} + [\mathrm{species\_7}]} \quad (42)$$

$$\mathrm{Menten\_Explicit\_Enzyme\_4}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_4}], [\mathrm{species\_7}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_4}] \cdot [\mathrm{species\_7}]}{\mathrm{km} + [\mathrm{species\_7}]} \quad (43)$$

Table 26: Properties of each parameter.

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

6.7 Reaction reaction_6

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

Name Raf1_Deactivation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_6} \xrightarrow{\text{species\_27}} \text{species\_7} \tag{44}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
species_6	Raf1Active	

Modifier

Table 28: Properties of each modifier.

Id	Name	SBO
species_27	Raf1PPtase	

Product

Table 29: Properties of each product.

Id	Name	SBO
species_7	Raf1Inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{Menten\_Explicit\_Enzyme\_5}\left(\text{Kcat}, \text{km}, [\text{species\_27}], [\text{species\_6}]\right) \tag{45}$$

$$\begin{aligned} &\text{Menten\_Explicit\_Enzyme\_5}\left(\text{Kcat}, \text{km}, [\text{species\_27}], [\text{species\_6}]\right) \\ &= \frac{\text{Kcat} \cdot [\text{species\_27}] \cdot [\text{species\_6}]}{\text{km} + [\text{species\_6}]} \end{aligned} \tag{46}$$

$$\begin{aligned}&\text{Menten\_Explicit\_Enzyme\_5}\left(\text{Kcat}, \text{km}, [\text{species\_27}], [\text{species\_6}]\right)\\ &= \frac{\text{Kcat} \cdot [\text{species\_27}] \cdot [\text{species\_6}]}{\text{km} + [\text{species\_6}]}\end{aligned} \tag{47}$$

Table 30: Properties of each parameter.

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

6.8 Reaction `reaction_7`

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

Name Mek_Activation

Notes `Parameters taken from Brown et al 2004`

Reaction equation

$$\text{species\_9} \xrightarrow{\text{species\_6}} \text{species\_8} \tag{48}$$

Reactant

Table 31: Properties of each reactant.

Id	Name	SBO
`species_9`	MekInactive	

Modifier

Table 32: Properties of each modifier.

Id	Name	SBO
`species_6`	Raf1Active	

Product

Table 33: Properties of each product.

Id	Name	SBO
species_8	MekActive	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{Menten\_Explicit\_Enzyme\_6}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_6}], [\mathrm{species\_9}]\right) \quad (49)$$

$$\mathrm{Menten\_Explicit\_Enzyme\_6}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_6}], [\mathrm{species\_9}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_6}] \cdot [\mathrm{species\_9}]}{\mathrm{km} + [\mathrm{species\_9}]} \quad (50)$$

$$\mathrm{Menten\_Explicit\_Enzyme\_6}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_6}], [\mathrm{species\_9}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_6}] \cdot [\mathrm{species\_9}]}{\mathrm{km} + [\mathrm{species\_9}]} \quad (51)$$

Table 34: Properties of each parameter.

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

6.9 Reaction reaction_8

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

Name Mek_Deactivation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\mathrm{species\_8} \xrightarrow{\mathrm{species\_26}} \mathrm{species\_9} \quad (52)$$

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
species_8	MekActive	

Modifier

Table 36: Properties of each modifier.

Id	Name	SBO
species_26	PP2AActive	

Product

Table 37: Properties of each product.

Id	Name	SBO
species_9	MekInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{Menten\_Explicit\_Enzyme\_7}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_26}], [\mathrm{species\_8}]\right) \tag{53}$$

$$\begin{aligned} &\mathrm{Menten\_Explicit\_Enzyme\_7}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_26}], [\mathrm{species\_8}]\right) \\ &= \frac{\mathrm{Kcat} \cdot [\mathrm{species\_26}] \cdot [\mathrm{species\_8}]}{\mathrm{km} + [\mathrm{species\_8}]} \end{aligned} \tag{54}$$

$$\begin{aligned} &\mathrm{Menten\_Explicit\_Enzyme\_7}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_26}], [\mathrm{species\_8}]\right) \\ &= \frac{\mathrm{Kcat} \cdot [\mathrm{species\_26}] \cdot [\mathrm{species\_8}]}{\mathrm{km} + [\mathrm{species\_8}]} \end{aligned} \tag{55}$$

Table 38: Properties of each parameter.

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

6.10 Reaction reaction_9

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

Name Erk_Activation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_11} \xrightarrow{\text{species\_8}} \text{species\_10} \tag{56}$$

Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
species_11	ErkInactive	

Modifier

Table 40: Properties of each modifier.

Id	Name	SBO
species_8	MekActive	

Product

Table 41: Properties of each product.

Id	Name	SBO
species_10	ErkActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{Menten\_Explicit\_Enzyme\_8}\left(\text{Kcat}, \text{km}, [\text{species\_11}], [\text{species\_8}]\right) \tag{57}$$

$$\begin{aligned} &\text{Menten\_Explicit\_Enzyme\_8}\left(\text{Kcat}, \text{km}, [\text{species\_11}], [\text{species\_8}]\right) \\ &= \frac{\text{Kcat} \cdot [\text{species\_8}] \cdot [\text{species\_11}]}{\text{km} + [\text{species\_11}]} \end{aligned} \tag{58}$$

$$\begin{aligned}&\text{Menten\_Explicit\_Enzyme\_8}\left(\text{Kcat}, \text{km}, [\text{species\_11}], [\text{species\_8}]\right)\\ &= \frac{\text{Kcat} \cdot [\text{species\_8}] \cdot [\text{species\_11}]}{\text{km} + [\text{species\_11}]}\end{aligned} \tag{59}$$

Table 42: Properties of each parameter.

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

6.11 Reaction `reaction_10`

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

Name Erk_Deactivation

Notes `Parameters taken from Brown et al 2004`

Reaction equation

$$\text{species\_10} \xrightarrow{\text{species\_26}} \text{species\_11} \tag{60}$$

Reactant

Table 43: Properties of each reactant.

Id	Name	SBO
`species_10`	ErkActive	

Modifier

Table 44: Properties of each modifier.

Id	Name	SBO
`species_26`	PP2AActive	

Product

Table 45: Properties of each product.

Id	Name	SBO
species_11	ErkInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot \mathrm{Menten\_Explicit\_Enzyme\_9}\,(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_26}]) \tag{61}$$

$$\begin{aligned} &\mathrm{Menten\_Explicit\_Enzyme\_9}\,(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_26}]) \\ &= \frac{\mathrm{Kcat} \cdot [\mathrm{species\_26}] \cdot [\mathrm{species\_10}]}{\mathrm{km} + [\mathrm{species\_10}]} \end{aligned} \tag{62}$$

$$\begin{aligned} &\mathrm{Menten\_Explicit\_Enzyme\_9}\,(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_26}]) \\ &= \frac{\mathrm{Kcat} \cdot [\mathrm{species\_26}] \cdot [\mathrm{species\_10}]}{\mathrm{km} + [\mathrm{species\_10}]} \end{aligned} \tag{63}$$

Table 46: Properties of each parameter.

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

6.12 Reaction reaction_11

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

Name P90Rsk_Activation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\mathrm{species\_13} \xrightarrow{\mathrm{species\_10}} \mathrm{species\_12} \tag{64}$$

Reactant

Table 47: Properties of each reactant.

Id	Name	SBO
species_13	P90RskInactive	

Modifier

Table 48: Properties of each modifier.

Id	Name	SBO
species_10	ErkActive	

Product

Table 49: Properties of each product.

Id	Name	SBO
species_12	P90RskActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{Menten\_Explicit\_Enzyme\_10}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_13}]\right) \tag{65}$$

$$\begin{aligned} &\mathrm{Menten\_Explicit\_Enzyme\_10}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_13}]\right) \\ &= \frac{\mathrm{Kcat} \cdot [\mathrm{species\_10}] \cdot [\mathrm{species\_13}]}{\mathrm{km} + [\mathrm{species\_13}]} \end{aligned} \tag{66}$$

$$\begin{aligned} &\mathrm{Menten\_Explicit\_Enzyme\_10}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_10}], [\mathrm{species\_13}]\right) \\ &= \frac{\mathrm{Kcat} \cdot [\mathrm{species\_10}] \cdot [\mathrm{species\_13}]}{\mathrm{km} + [\mathrm{species\_13}]} \end{aligned} \tag{67}$$

Table 50: Properties of each parameter.

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

6.13 Reaction reaction_12

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

Name P90Rsk_Deactivation

Notes Parameters were estimated from experiments

Reaction equation

$$\text{species\_12} \longrightarrow \text{species\_13} \tag{68}$$

Reactant

Table 51: Properties of each reactant.

Id	Name	SBO
species_12	P90RskActive	

Product

Table 52: Properties of each product.

Id	Name	SBO
species_13	P90RskInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{k1} \cdot [\text{species\_12}] \tag{69}$$

Table 53: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.005		☑

6.14 Reaction reaction_13

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

Name Sos_Feedback_Deactivation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_2} \xrightarrow{\text{species\_12}} \text{species\_3} \tag{70}$$

Reactant

Table 54: Properties of each reactant.

Id	Name	SBO
species_2	SosActive	

Modifier

Table 55: Properties of each modifier.

Id	Name	SBO
species_12	P90RskActive	

Product

Table 56: Properties of each product.

Id	Name	SBO
species_3	SosInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{Menten\_Explicit\_Enzyme\_11}\left(\text{Kcat}, \text{km}, [\text{species\_12}], [\text{species\_2}]\right) \tag{71}$$

$$\begin{aligned} &\text{Menten\_Explicit\_Enzyme\_11}\left(\text{Kcat}, \text{km}, [\text{species\_12}], [\text{species\_2}]\right) \\ &= \frac{\text{Kcat} \cdot [\text{species\_12}] \cdot [\text{species\_2}]}{\text{km} + [\text{species\_2}]} \end{aligned} \tag{72}$$

$$\begin{aligned} &\text{Menten\_Explicit\_Enzyme\_11}\left(\text{Kcat}, \text{km}, [\text{species\_12}], [\text{species\_2}]\right) \\ &= \frac{\text{Kcat} \cdot [\text{species\_12}] \cdot [\text{species\_2}]}{\text{km} + [\text{species\_2}]} \end{aligned} \tag{73}$$

Table 57: Properties of each parameter.

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

6.15 Reaction reaction_14

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

Name PI3K_Activation_EGFR

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_15} \xrightarrow{\text{species\_0}} \text{species\_14} \tag{74}$$

Reactant

Table 58: Properties of each reactant.

Id	Name	SBO
species_15	PI3KInactive	

Modifier

Table 59: Properties of each modifier.

Id	Name	SBO
species_0	boundEGFReceptor	

Product

Table 60: Properties of each product.

Id	Name	SBO
species_14	PI3KActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{Menten\_Explicit\_Enzyme\_12}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_15}]\right) \tag{75}$$

$$\mathrm{Menten\_Explicit\_Enzyme\_12}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_15}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_0}] \cdot [\mathrm{species\_15}]}{\mathrm{km} + [\mathrm{species\_15}]} \tag{76}$$

$$\mathrm{Menten\_Explicit\_Enzyme\_12}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_15}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_0}] \cdot [\mathrm{species\_15}]}{\mathrm{km} + [\mathrm{species\_15}]} \tag{77}$$

Table 61: Properties of each parameter.

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

6.16 Reaction `reaction_15`

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

Name PI3K_Activation_Ras

Notes `Parameters taken from Brown et al 2004`

Reaction equation

$$\mathrm{species\_15} \xrightarrow{\mathrm{species\_4}} \mathrm{species\_14} \tag{78}$$

Reactant

Table 62: Properties of each reactant.

Id	Name	SBO
`species_15`	PI3KInactive	

Modifier

Table 63: Properties of each modifier.

Id	Name	SBO
species_4	RasActive	

Product

Table 64: Properties of each product.

Id	Name	SBO
species_14	PI3KActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{Menten\_Explicit\_Enzyme\_13}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_15}], [\mathrm{species\_4}]\right) \tag{79}$$

$$\mathrm{Menten\_Explicit\_Enzyme\_13}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_15}], [\mathrm{species\_4}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_4}] \cdot [\mathrm{species\_15}]}{\mathrm{km} + [\mathrm{species\_15}]} \tag{80}$$

$$\mathrm{Menten\_Explicit\_Enzyme\_13}\left(\mathrm{Kcat}, \mathrm{km}, [\mathrm{species\_15}], [\mathrm{species\_4}]\right) = \frac{\mathrm{Kcat} \cdot [\mathrm{species\_4}] \cdot [\mathrm{species\_15}]}{\mathrm{km} + [\mathrm{species\_15}]} \tag{81}$$

Table 65: Properties of each parameter.

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

6.17 Reaction reaction_16

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

Name PI3K_Deactivation

Notes `Parameters taken from Brown et al 2004`

Reaction equation

$$\text{species\_14} \longrightarrow \text{species\_15} \tag{82}$$

Reactant

Table 66: Properties of each reactant.

Id	Name	SBO
`species_14`	PI3KActive	

Product

Table 67: Properties of each product.

Id	Name	SBO
`species_15`	PI3KInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{k1} \cdot \left[\text{species\_14}\right] \tag{83}$$

Table 68: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`k1`	k1		0.005		☑

6.18 Reaction `reaction_17`

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

Name Akt_Activation

Notes `Parameters taken from Brown et al 2004`

Reaction equation

$$\text{species\_17} \xrightarrow{\text{species\_14}} \text{species\_16} \tag{84}$$

Reactant

Table 69: Properties of each reactant.

Id	Name	SBO
species_17	AktInactive	

Modifier

Table 70: Properties of each modifier.

Id	Name	SBO
species_14	PI3KActive	

Product

Table 71: Properties of each product.

Id	Name	SBO
species_16	AktActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{Menten\_Explicit\_Enzyme\_14}\left(\text{Kcat}, \text{km}, [\text{species\_14}], [\text{species\_17}]\right) \tag{85}$$

$$\begin{aligned} &\text{Menten\_Explicit\_Enzyme\_14}\left(\text{Kcat}, \text{km}, [\text{species\_14}], [\text{species\_17}]\right) \\ &= \frac{\text{Kcat} \cdot [\text{species\_14}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]} \end{aligned} \tag{86}$$

$$\begin{aligned} &\text{Menten\_Explicit\_Enzyme\_14}\left(\text{Kcat}, \text{km}, [\text{species\_14}], [\text{species\_17}]\right) \\ &= \frac{\text{Kcat} \cdot [\text{species\_14}] \cdot [\text{species\_17}]}{\text{km} + [\text{species\_17}]} \end{aligned} \tag{87}$$

Table 72: Properties of each parameter.

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

6.19 Reaction reaction_18

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

Name Akt_Deactivation

Notes Parameters were estimated from experiments

Reaction equation

$$\text{species\_16} \longrightarrow \text{species\_17} \tag{88}$$

Reactant

Table 73: Properties of each reactant.

Id	Name	SBO
species_16	AktActive	

Product

Table 74: Properties of each product.

Id	Name	SBO
species_17	AktInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{k1} \cdot \left[\text{species\_16}\right] \tag{89}$$

Table 75: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.005		☑

6.20 Reaction reaction_19

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

Name Raf1_Deactivation_Akt

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_6} \xrightarrow{\text{species\_16}} \text{species\_7} \tag{90}$$

Reactant

Table 76: Properties of each reactant.

Id	Name	SBO
species_6	Raf1Active	

Modifier

Table 77: Properties of each modifier.

Id	Name	SBO
species_16	AktActive	

Product

Table 78: Properties of each product.

Id	Name	SBO
species_7	Raf1Inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{Menten\_Explicit\_Enzyme\_15}\left(\text{Kcat}, \text{km}, [\text{species\_16}], [\text{species\_6}]\right) \tag{91}$$

$$\begin{aligned} &\text{Menten\_Explicit\_Enzyme\_15}\left(\text{Kcat}, \text{km}, [\text{species\_16}], [\text{species\_6}]\right) \\ &= \frac{\text{Kcat} \cdot [\text{species\_16}] \cdot [\text{species\_6}]}{\text{km} + [\text{species\_6}]} \end{aligned} \tag{92}$$

$$\begin{aligned}&\text{Menten\_Explicit\_Enzyme\_15}\left(\text{Kcat}, \text{km}, [\text{species\_16}], [\text{species\_6}]\right)\\&= \frac{\text{Kcat} \cdot [\text{species\_16}] \cdot [\text{species\_6}]}{\text{km} + [\text{species\_6}]}\end{aligned} \tag{93}$$

Table 79: Properties of each parameter.

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

6.21 Reaction `reaction_20`

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

Name EGFReceptor_Degradation

Notes `Parameters were estimated from experiments`

Reaction equation

$$\text{species\_0} \longrightarrow \text{species\_18} \tag{94}$$

Reactant

Table 80: Properties of each reactant.

Id	Name	SBO
`species_0`	boundEGFReceptor	

Product

Table 81: Properties of each product.

Id	Name	SBO
`species_18`	degradedEGFReceptor	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{k1} \cdot [\text{species\_0}] \tag{95}$$

Table 82: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.2		☑

6.22 Reaction reaction_21

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

Name C3G_Activation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_20} \xrightarrow{\text{species\_0}} \text{species\_19} \tag{96}$$

Reactant

Table 83: Properties of each reactant.

Id	Name	SBO
species_20	C3GInactive	

Modifier

Table 84: Properties of each modifier.

Id	Name	SBO
species_0	boundEGFReceptor	

Product

Table 85: Properties of each product.

Id	Name	SBO
species_19	C3GActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{MM\_Explicit\_Enzyme\_1}\left(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_20}]\right) \quad (97)$$

$$\mathrm{MM\_Explicit\_Enzyme\_1}\left(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_20}]\right) = \frac{\mathrm{kcat} \cdot [\mathrm{species\_0}] \cdot [\mathrm{species\_20}]}{\mathrm{km} + [\mathrm{species\_20}]} \quad (98)$$

$$\mathrm{MM\_Explicit\_Enzyme\_1}\left(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_0}], [\mathrm{species\_20}]\right) = \frac{\mathrm{kcat} \cdot [\mathrm{species\_0}] \cdot [\mathrm{species\_20}]}{\mathrm{km} + [\mathrm{species\_20}]} \quad (99)$$

Table 86: Properties of each parameter.

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

6.23 Reaction reaction_22

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

Name C3G_Deactivation

Notes Parameters were estimated from experiments

Reaction equation

$$\mathrm{species\_19} \longrightarrow \mathrm{species\_20} \quad (100)$$

Reactant

Table 87: Properties of each reactant.

Id	Name	SBO
species_19	C3GActive	

Product

Table 88: Properties of each product.

Id	Name	SBO
species_20	C3GInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot \mathrm{k1} \cdot [\mathrm{species\_19}] \tag{101}$$

Table 89: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		2.5		☑

6.24 Reaction reaction_23

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

Name Rap1_Activation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\mathrm{species\_22} \xrightarrow{\mathrm{species\_19}} \mathrm{species\_21} \tag{102}$$

Reactant

Table 90: Properties of each reactant.

Id	Name	SBO
species_22	Rap1Inactive	

Modifier

Table 91: Properties of each modifier.

Id	Name	SBO
species_19	C3GActive	

Product

Table 92: Properties of each product.

Id	Name	SBO
species_21	Rap1Active	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot \mathrm{MM\_Explicit\_Enzyme\_2}\,(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_19}], [\mathrm{species\_22}]) \tag{103}$$

$$\begin{aligned} &\mathrm{MM\_Explicit\_Enzyme\_2}\,(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_19}], [\mathrm{species\_22}]) \\ &= \frac{\mathrm{kcat} \cdot [\mathrm{species\_19}] \cdot [\mathrm{species\_22}]}{\mathrm{km} + [\mathrm{species\_22}]} \end{aligned} \tag{104}$$

$$\begin{aligned} &\mathrm{MM\_Explicit\_Enzyme\_2}\,(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_19}], [\mathrm{species\_22}]) \\ &= \frac{\mathrm{kcat} \cdot [\mathrm{species\_19}] \cdot [\mathrm{species\_22}]}{\mathrm{km} + [\mathrm{species\_22}]} \end{aligned} \tag{105}$$

Table 93: Properties of each parameter.

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

6.25 Reaction reaction_24

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

Name Rap1_Deactivation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\mathrm{species\_21} \xrightarrow{\mathrm{species\_29}} \mathrm{species\_22} \tag{106}$$

Reactant

Table 94: Properties of each reactant.

Id	Name	SBO
species_21	Rap1Active	

Modifier

Table 95: Properties of each modifier.

Id	Name	SBO
species_29	Rap1Gap	

Product

Table 96: Properties of each product.

Id	Name	SBO
species_22	Rap1Inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot \mathrm{MM\_Explicit\_Enzyme\_3}\,(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_21}], [\mathrm{species\_29}]) \tag{107}$$

$$\begin{aligned} &\mathrm{MM\_Explicit\_Enzyme\_3}\,(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_21}], [\mathrm{species\_29}]) \\ &= \frac{\mathrm{kcat} \cdot [\mathrm{species\_29}] \cdot [\mathrm{species\_21}]}{\mathrm{km} + [\mathrm{species\_21}]} \end{aligned} \tag{108}$$

$$\begin{aligned} &\mathrm{MM\_Explicit\_Enzyme\_3}\,(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_21}], [\mathrm{species\_29}]) \\ &= \frac{\mathrm{kcat} \cdot [\mathrm{species\_29}] \cdot [\mathrm{species\_21}]}{\mathrm{km} + [\mathrm{species\_21}]} \end{aligned} \tag{109}$$

Table 97: Properties of each parameter.

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

6.26 Reaction reaction_25

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

Name bRaf_Activation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_24} \xrightarrow{\text{species\_21}} \text{species\_23} \tag{110}$$

Reactant

Table 98: Properties of each reactant.

Id	Name	SBO
species_24	bRafInactive	

Modifier

Table 99: Properties of each modifier.

Id	Name	SBO
species_21	Rap1Active	

Product

Table 100: Properties of each product.

Id	Name	SBO
species_23	bRafActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{MM\_Explicit\_Enzyme\_4}\left(\text{kcat}, \text{km}, [\text{species\_21}], [\text{species\_24}]\right) \tag{111}$$

$$\begin{aligned} &\text{MM\_Explicit\_Enzyme\_4}\left(\text{kcat}, \text{km}, [\text{species\_21}], [\text{species\_24}]\right) \\ &= \frac{\text{kcat} \cdot [\text{species\_21}] \cdot [\text{species\_24}]}{\text{km} + [\text{species\_24}]} \end{aligned} \tag{112}$$

$$\begin{aligned} &\text{MM\_Explicit\_Enzyme\_4}\left(\text{kcat}, \text{km}, [\text{species\_21}], [\text{species\_24}]\right) \\ &= \frac{\text{kcat} \cdot [\text{species\_21}] \cdot [\text{species\_24}]}{\text{km} + [\text{species\_24}]} \end{aligned} \tag{113}$$

Table 101: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcat	kcat		0.884		☑
km	km		62464.600		☑

6.27 Reaction reaction_26

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

Name bRaf_Deactivation

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\text{species\_23} \xrightarrow{\text{species\_27}} \text{species\_24} \tag{114}$$

Reactant

Table 102: Properties of each reactant.

Id	Name	SBO
species_23	bRafActive	

Modifier

Table 103: Properties of each modifier.

Id	Name	SBO
species_27	Raf1PPtase	

Product

Table 104: Properties of each product.

Id	Name	SBO
species_24	bRafInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot \mathrm{MM\_Explicit\_Enzyme\_5}\,(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_23}], [\mathrm{species\_27}]) \tag{115}$$

$$\begin{aligned} &\mathrm{MM\_Explicit\_Enzyme\_5}\,(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_23}], [\mathrm{species\_27}]) \\ &= \frac{\mathrm{kcat} \cdot [\mathrm{species\_27}] \cdot [\mathrm{species\_23}]}{\mathrm{km} + [\mathrm{species\_23}]} \end{aligned} \tag{116}$$

$$\begin{aligned} &\mathrm{MM\_Explicit\_Enzyme\_5}\,(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_23}], [\mathrm{species\_27}]) \\ &= \frac{\mathrm{kcat} \cdot [\mathrm{species\_27}] \cdot [\mathrm{species\_23}]}{\mathrm{km} + [\mathrm{species\_23}]} \end{aligned} \tag{117}$$

Table 105: Properties of each parameter.

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

6.28 Reaction reaction_27

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

Name Mek_Activation_bRaf

Notes Parameters taken from Brown et al 2004

Reaction equation

$$\mathrm{species\_9} \xrightarrow{\mathrm{species\_23}} \mathrm{species\_8} \tag{118}$$

Reactant

Table 106: Properties of each reactant.

Id	Name	SBO
species_9	MekInactive	

Modifier

Table 107: Properties of each modifier.

Id	Name	SBO
species_23	bRafActive	

Product

Table 108: Properties of each product.

Id	Name	SBO
species_8	MekActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{MM\_Explicit\_Enzyme\_6}\left(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_23}], [\mathrm{species\_9}]\right) \quad (119)$$

$$\mathrm{MM\_Explicit\_Enzyme\_6}\left(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_23}], [\mathrm{species\_9}]\right) = \frac{\mathrm{kcat} \cdot [\mathrm{species\_23}] \cdot [\mathrm{species\_9}]}{\mathrm{km} + [\mathrm{species\_9}]} \quad (120)$$

$$\mathrm{MM\_Explicit\_Enzyme\_6}\left(\mathrm{kcat}, \mathrm{km}, [\mathrm{species\_23}], [\mathrm{species\_9}]\right) = \frac{\mathrm{kcat} \cdot [\mathrm{species\_23}] \cdot [\mathrm{species\_9}]}{\mathrm{km} + [\mathrm{species\_9}]} \quad (121)$$

Table 109: Properties of each parameter.

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

6.29 Reaction reaction_28

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

Name EGFReceptor_Production

Notes Parameters were estimated from experiments

Reaction equation

$$\text{species\_30} \longrightarrow \text{species\_1} \tag{122}$$

Reactant

Table 110: Properties of each reactant.

Id	Name	SBO
species_30	proEGFReceptor	

Product

Table 111: Properties of each product.

Id	Name	SBO
species_1	freeEGFReceptor	

Kinetic Law

Derived unit contains undeclared units

$$v_{29} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{Constant\_flux\_\_irreversible}\left(\text{v}\right) \tag{123}$$

$$\text{Constant\_flux\_\_irreversible}\left(\text{v}\right) = \text{v} \tag{124}$$

$$\text{Constant\_flux\_\_irreversible}\left(\text{v}\right) = \text{v} \tag{125}$$

Table 112: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
v	v		100.0		☑

6.30 Reaction reaction_29

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

Name EGFReceptor_Degradtion_Free

Notes `Parameters were estimated from experiments`

Reaction equation

$$\text{species\_1} \longrightarrow \text{species\_18} \tag{126}$$

Reactant

Table 113: Properties of each reactant.

Id	Name	SBO
species_1	freeEGFReceptor	

Product

Table 114: Properties of each product.

Id	Name	SBO
species_18	degradedEGFReceptor	

Kinetic Law

Derived unit contains undeclared units

$$v_{30} = \text{vol}\,(\text{compartment\_0}) \cdot \text{k1} \cdot [\text{species\_1}] \tag{127}$$

Table 115: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.001		☑

6.31 Reaction reaction_30

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

Name bRaf_Activation_Ras

Notes `Parameters taken from Brown et al 2004`

Reaction equation

$$\text{species\_24} \xrightarrow{\text{species\_4}} \text{species\_23} \tag{128}$$

Reactant

Table 116: Properties of each reactant.

Id	Name	SBO
`species_24`	bRafInactive	

Modifier

Table 117: Properties of each modifier.

Id	Name	SBO
`species_4`	RasActive	

Product

Table 118: Properties of each product.

Id	Name	SBO
`species_23`	bRafActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{31} = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{MM\_Explicit\_Enzyme\_7}\left(\text{kcat}, \text{km}, [\text{species\_24}], [\text{species\_4}]\right) \tag{129}$$

$$\text{MM\_Explicit\_Enzyme\_7}\left(\text{kcat}, \text{km}, [\text{species\_24}], [\text{species\_4}]\right) = \frac{\text{kcat} \cdot [\text{species\_4}] \cdot [\text{species\_24}]}{\text{km} + [\text{species\_24}]} \tag{130}$$

$$\text{MM\_Explicit\_Enzyme\_7}\left(\text{kcat}, \text{km}, [\text{species\_24}], [\text{species\_4}]\right) = \frac{\text{kcat} \cdot [\text{species\_4}] \cdot [\text{species\_24}]}{\text{km} + [\text{species\_24}]} \tag{131}$$

Table 119: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcat	kcat		0.884		☑
km	km		62464.600		☑

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 boundEGFReceptor

Notes EGFR Receptor bound to EGF; Initial value was estimated from experiments

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

This species takes part in five 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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_0} = v_1 - v_{21} \tag{132}$$

7.2 Species species_1

Name freeEGFReceptor

Notes Free EGF receptor; Initial value taken from Brown et al 2004

Initial concentration $80000\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_1} = v_{29} - v_1 - v_{30} \tag{133}$$

7.3 Species species_2

Name SosActive

Notes `Active species of SOS; Initial value taken from Brown et al 2004`

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

This species takes part in four reactions (as a reactant in reaction_2, reaction_13 and as a product in reaction_1 and as a modifier in reaction_3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_2} = v_2 - v_3 - v_{14} \tag{134}$$

7.4 Species species_3

Name SosInactive

Notes `Active species of SOS; Initial value taken from Brown et al 2004`

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_2, reaction_13).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_3} = v_3 + v_{14} - v_2 \tag{135}$$

7.5 Species species_4

Name RasActive

Notes `Active species of Ras; Initial value taken from Brown et al 2004`

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

This species takes part in five reactions (as a reactant in reaction_4 and as a product in reaction_3 and as a modifier in reaction_5, reaction_15, reaction_30).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_4} = v_4 - v_5 \tag{136}$$

7.6 Species species_5

Name RasInactive

Notes `Inactive species of Ras; Initial value taken from Brown et al 2004`

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_5} = v_5 - v_4 \tag{137}$$

7.7 Species species_6

Name Raf1Active

Notes `Active species of Raf1; Initial value taken from Brown et al 2004`

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_6} = v_6 - v_7 - v_{20} \tag{138}$$

7.8 Species species_7

Name Raf1Inactive

Notes `Inactive species of Raf1; Initial value taken from Brown et al 2004`

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_7} = v_7 + v_{20} - v_6 \tag{139}$$

7.9 Species species_8

Name MekActive

Notes `Active species of MEK; Initial value taken from Brown et al 2004`

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_8} = v_8 + v_{28} - v_9 \tag{140}$$

7.10 Species species_9

Name MekInactive

Notes `Inactive species of MEK; Initial value taken from Brown et al 2004`

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_9} = v_9 - v_8 - v_{28} \tag{141}$$

7.11 Species species_10

Name ErkActive

Notes `Active species of ERK; Initial value taken from Brown et al 2004`

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

This species takes part in three reactions (as a reactant in reaction_10 and as a product in reaction_9 and as a modifier in reaction_11).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_10} = v_{10} - v_{11} \tag{142}$$

7.12 Species species_11

Name ErkInactive

Notes `Inactive species of ERK; Initial value taken from Brown et al 2004`

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_11} = v_{11} - v_{10} \tag{143}$$

7.13 Species species_12

Name P90RskActive

Notes `Active species of P90RSK; Initial value taken from Brown et al 2004`

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_12} = v_{12} - v_{13} \tag{144}$$

7.14 Species species_13

Name P90RskInactive

Notes `Inactive species of P90RSK; Initial value taken from Brown et al 2004`

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_13} = v_{13} - v_{12} \tag{145}$$

7.15 Species species_14

Name PI3KActive

Notes `Active species of PI3K; Initial value taken from Brown et al 2004`

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_14} = v_{15} + v_{16} - v_{17} \tag{146}$$

7.16 Species species_15

Name PI3KInactive

Notes `Inactive species of PI3K; Initial value taken from Brown et al 2004`

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

This species takes part in three reactions (as a reactant in reaction_14, reaction_15 and as a product in reaction_16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_15} = v_{17} - v_{15} - v_{16} \tag{147}$$

7.17 Species species_16

Name AktActive

Notes `Active species of Akt; Initial value taken from Brown et al 2004`

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

This species takes part in three reactions (as a reactant in reaction_18 and as a product in reaction_17 and as a modifier in reaction_19).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_16} = v_{18} - v_{19} \tag{148}$$

7.18 Species species_17

Name AktInactive

Notes `Inactive species of Akt; Initial value taken from Brown et al 2004`

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_17} = v_{19} - v_{18} \tag{149}$$

7.19 Species species_18

Name degradedEGFReceptor

Notes `Degraded species of EGFR; Initial value estimated from experiments`

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

This species takes part in two reactions (as a product in reaction_20, reaction_29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_18} = v_{21} + v_{30} \tag{150}$$

7.20 Species species_19

Name C3GActive

Notes `Active species of C3G; Initial value taken from Brown et al 2004`

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_19} = v_{22} - v_{23} \tag{151}$$

7.21 Species species_20

Name C3GInactive

Notes `Inactive species of C3G; Initial value taken from Brown et al 2004`

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_20} = v_{23} - v_{22} \tag{152}$$

7.22 Species species_21

Name Rap1Active

Notes `Active species of Rap1; Initial value taken from Brown et al 2004`

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

This species takes part in three reactions (as a reactant in reaction_24 and as a product in reaction_23 and as a modifier in reaction_25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_21} = v_{24} - v_{25} \tag{153}$$

7.23 Species species_22

Name Rap1Inactive

Notes `Inactive species of Rap1; Initial value taken from Brown et al 2004`

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_22} = v_{25} - v_{24} \tag{154}$$

7.24 Species species_23

Name bRafActive

Notes `Active species of BRaf; Initial value taken from Brown et al 2004`

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

This species takes part in four reactions (as a reactant in reaction_26 and as a product in reaction_25, reaction_30 and as a modifier in reaction_27).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_23} = v_{26} + v_{31} - v_{27} \tag{155}$$

7.25 Species species_24

Name bRafInactive

Notes `Inactive species of BRaf; Initial value taken from Brown et al 2004`

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

This species takes part in three reactions (as a reactant in reaction_25, reaction_30 and as a product in reaction_26).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_24} = v_{27} - v_{26} - v_{31} \tag{156}$$

7.26 Species species_25

Name EGF

Notes `Epidermal Growth Factor; Initial value taken from Brown et al 2004`

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:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_25} = 0 \tag{157}$$

7.27 Species species_26

Name PP2AActive

Notes `Active species of PP2A; Initial value taken from Brown et al 2004`

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_26} = 0 \tag{158}$$

7.28 Species species_27

Name Raf1PPtase

Notes `Raf1 phosphatase; Initial value taken from Brown et al 2004`

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

This species takes part in two reactions (as a modifier in reaction_6, reaction_26), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_27} = 0 \tag{159}$$

7.29 Species species_28

Name RasGapActive

Notes `Active GTPase of Ras; Initial value taken from Brown et al 2004`

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:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_28} = 0 \tag{160}$$

7.30 Species species_29

Name Rap1Gap

Notes `GTPase of Rap1; Initial value taken from Brown et al 2004`

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:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_29} = 0 \tag{161}$$

7.31 Species species_30

Name proEGFReceptor

Notes `Species preceding active EGF receptor; Initial value estimated from experiments`

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:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_30} = 0 \tag{162}$$

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