

## 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<sup>1</sup> at November 28<sup>th</sup> 2016 at 9:09 a. m. and last time modified at November 28<sup>th</sup> 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 in the EGFR/ERK pathway - EGF Model This model studies the aberrations in ERK signalling for different cancer mutations. The authors alter a previously existing EGF model (Brown et al 2004) to include new interactions that better fit empirical data. Predictions show that the ERK signalling is a robust mechanism taking different courses

<sup>1</sup>EMBL-EBI, [tvarusai@ebi.ac.uk](mailto:tvarusai@ebi.ac.uk)

for different cancer mutations. Most parameter values are used from the previous model and the new parameters are estimated using experimental data performed by the authors on PC12 cells (adrenal gland, rat). The authors provide 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 shut-down. 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](#).

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## 2 Unit Definitions

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

### 2.1 Unit volume

**Name** volume

**Definition** 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<sup>2</sup>

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

### 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 Condi- tion
species_0	boundEGFReceptor	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_1	freeEGFReceptor	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_2	SosActive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_3	SosInactive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_4	RasActive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_5	RasInactive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_6	Raf1Active	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_7	Raf1Inactive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_8	MekActive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_9	MekInactive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_10	ErkActive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_11	ErkInactive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_12	P90RskActive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_13	P90RskInactive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_14	PI3KActive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_15	PI3KInactive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_16	AktActive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_17	AktInactive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_18	degradedEGFReceptor	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_19	C3GActive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
species_20	C3GInactive	compartment_0	$\text{mmol} \cdot \text{ml}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
species_21	Rap1Active	compartment_0	mmol · ml <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
species_22	Rap1Inactive	compartment_0	mmol · ml <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
species_23	bRafActive	compartment_0	mmol · ml <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
species_24	bRafInactive	compartment_0	mmol · ml <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
species_25	EGF	compartment_0	mmol · ml <sup>-1</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
species_26	PP2AActive	compartment_0	mmol · ml <sup>-1</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
species_27	Raf1PPtase	compartment_0	mmol · ml <sup>-1</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
species_28	RasGapActive	compartment_0	mmol · ml <sup>-1</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
species_29	Rap1Gap	compartment_0	mmol · ml <sup>-1</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
species_30	proEGFReceptor	compartment_0	mmol · ml <sup>-1</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

## 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**

$$v \quad (1)$$

### 5.2 Function definition `Menten_Explicit_Enzyme_12`

**Name** `Menten_Explicit_Enzyme_12`

**Arguments**  $K_{cat}$ ,  $km$ ,  $[species\_0]$ ,  $[species\_15]$

**Mathematical Expression**

$$\frac{K_{cat} \cdot [species\_0] \cdot [species\_15]}{km + [species\_15]} \quad (2)$$

### 5.3 Function definition `MM_Explicit_Enzyme_5`

**Name** `MM Explicit Enzyme_5`

**Arguments**  $k_{cat}$ ,  $km$ ,  $[species\_23]$ ,  $[species\_27]$

**Mathematical Expression**

$$\frac{k_{cat} \cdot [species\_27] \cdot [species\_23]}{km + [species\_23]} \quad (3)$$

### 5.4 Function definition `Menten_Explicit_Enzyme_14`

**Name** `Menten_Explicit_Enzyme_14`

**Arguments**  $K_{cat}$ ,  $km$ ,  $[species\_14]$ ,  $[species\_17]$

**Mathematical Expression**

$$\frac{K_{cat} \cdot [species\_14] \cdot [species\_17]}{km + [species\_17]} \quad (4)$$

### 5.5 Function definition `Menten_Explicit_Enzyme_9`

**Name** `Menten_Explicit_Enzyme_9`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_26] \cdot [species\_10]}{km + [species\_10]} \quad (5)$$

### 5.6 Function definition `MM_Explicit_Enzyme_7`

**Name** `MM_Explicit_Enzyme_7`

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

**Mathematical Expression**

$$\frac{kcat \cdot [species\_4] \cdot [species\_24]}{km + [species\_24]} \quad (6)$$

### 5.7 Function definition `Menten_Explicit_Enzyme_4`

**Name** `Menten_Explicit_Enzyme_4`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_4] \cdot [species\_7]}{km + [species\_7]} \quad (7)$$

### 5.8 Function definition `Menten_Explicit_Enzyme_6`

**Name** `Menten_Explicit_Enzyme_6`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_6] \cdot [species\_9]}{km + [species\_9]} \quad (8)$$



### 5.9 Function definition `MM_Explicit_Enzyme_4`

**Name** `MM_Explicit_Enzyme_4`

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

**Mathematical Expression**

$$\frac{kcat \cdot [species\_21] \cdot [species\_24]}{km + [species\_24]} \quad (9)$$

### 5.10 Function definition `Menten_Explicit_Enzyme_2`

**Name** `Menten_Explicit_Enzyme_2`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_2] \cdot [species\_5]}{km + [species\_5]} \quad (10)$$

### 5.11 Function definition `Menten_Explicit_Enzyme_7`

**Name** `Menten_Explicit_Enzyme_7`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_26] \cdot [species\_8]}{km + [species\_8]} \quad (11)$$

### 5.12 Function definition `Menten_Explicit_Enzyme_11`

**Name** `Menten_Explicit_Enzyme_11`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_12] \cdot [species\_2]}{km + [species\_2]} \quad (12)$$

### 5.13 Function definition [Menten\\_Explicit\\_Enzyme\\_15](#)

**Name** Menten\_Explicit\_Enzyme\_15

**Arguments** Kcat, km, [species\_16], [species\_6]

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_16] \cdot [species\_6]}{km + [species\_6]} \quad (13)$$

### 5.14 Function definition [MM\\_Explicit\\_Enzyme\\_1](#)

**Name** MM Explicit Enzyme\_1

**Arguments** kcat, km, [species\_0], [species\_20]

**Mathematical Expression**

$$\frac{kcat \cdot [species\_0] \cdot [species\_20]}{km + [species\_20]} \quad (14)$$

### 5.15 Function definition [Menten\\_Explicit\\_Enzyme\\_10](#)

**Name** Menten\_Explicit\_Enzyme\_10

**Arguments** Kcat, km, [species\_10], [species\_13]

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_10] \cdot [species\_13]}{km + [species\_13]} \quad (15)$$

### 5.16 Function definition [Menten\\_Explicit\\_Enzyme\\_5](#)

**Name** Menten\_Explicit\_Enzyme\_5

**Arguments** Kcat, km, [species\_27], [species\_6]

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_27] \cdot [species\_6]}{km + [species\_6]} \quad (16)$$

### 5.17 Function definition `Menten_Explicit_Enzyme_8`

**Name** `Menten_Explicit_Enzyme_8`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_8] \cdot [species\_11]}{km + [species\_11]} \quad (17)$$

### 5.18 Function definition `Menten_Explicit_Enzyme_13`

**Name** `Menten_Explicit_Enzyme_13`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_4] \cdot [species\_15]}{km + [species\_15]} \quad (18)$$

### 5.19 Function definition `Menten_Explicit_Enzyme_3`

**Name** `Menten_Explicit_Enzyme_3`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_28] \cdot [species\_4]}{km + [species\_4]} \quad (19)$$

### 5.20 Function definition `MM_Explicit_Enzyme_2`

**Name** `MM_Explicit_Enzyme_2`

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

**Mathematical Expression**

$$\frac{kcat \cdot [species\_19] \cdot [species\_22]}{km + [species\_22]} \quad (20)$$

### 5.21 Function definition `Menten_Explicit_Enzyme_1`

**Name** `Menten_Explicit_Enzyme_1`

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

**Mathematical Expression**

$$\frac{Kcat \cdot [species\_0] \cdot [species\_3]}{km + [species\_3]} \quad (21)$$

### 5.22 Function definition `MM_Explicit_Enzyme_3`

**Name** `MM_Explicit_Enzyme_3`

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

**Mathematical Expression**

$$\frac{kcat \cdot [species\_29] \cdot [species\_21]}{km + [species\_21]} \quad (22)$$

### 5.23 Function definition `MM_Explicit_Enzyme_6`

**Name** `MM_Explicit_Enzyme_6`

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

**Mathematical Expression**

$$\frac{kcat \cdot [species\_23] \cdot [species\_9]}{km + [species\_9]} \quad (23)$$

## 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

Nº	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	$\text{species\_15} \xrightarrow{\text{species\_4}} \text{species\_14}$	

Nº	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	

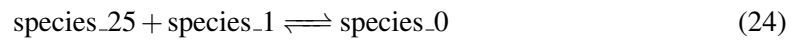
## 6.1 Reaction `reaction_0`

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



### 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

$$v_1 = \text{vol}(\text{compartment\_0}) \cdot (k_1 \cdot [\text{species\_25}] \cdot [\text{species\_1}] - k_2 \cdot [\text{species\_0}]) \quad (25)$$

Table 7: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$2.18503 \cdot 10^{-5}$		<input checked="" type="checkbox"/>
k2	k2		0.121		<input checked="" type="checkbox"/>

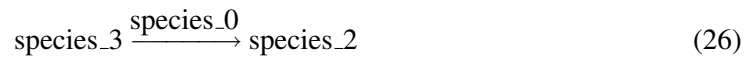
## 6.2 Reaction `reaction_1`

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



### 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

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

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

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



Table 11: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		694.731		<input checked="" type="checkbox"/>
km	km		6086070.000		<input checked="" type="checkbox"/>

### 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



#### Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
<code>species_2</code>	<code>SosActive</code>	

#### Product

Table 13: Properties of each product.

Id	Name	SBO
<code>species_3</code>	<code>SosInactive</code>	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_3 = \text{vol}(\text{compartment}_0) \cdot k_1 \cdot [\text{species}_2] \quad (31)$$

Table 14: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		2.5		<input checked="" type="checkbox"/>

## 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



### Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
<code>species_5</code>	RasInactive	

### Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
<code>species_2</code>	SosActive	

### Product

Table 17: Properties of each product.

Id	Name	SBO
<code>species_4</code>	RasActive	

### Kinetic Law

**Derived unit** contains undeclared units

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

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

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

Table 18: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		32.344		<input checked="" type="checkbox"/>
km	km		35954.300		<input checked="" type="checkbox"/>

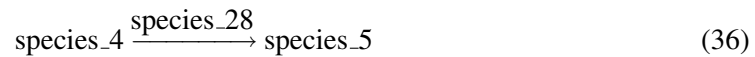
## 6.5 Reaction [reaction\\_4](#)

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



### 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

$$v_5 = \text{vol}(\text{compartment}_0) \cdot \text{Menten\_Explicit\_Enzyme}_3(\text{Kcat}, \text{km}, [\text{species}_{28}], [\text{species}_4]) \quad (37)$$

$$\begin{aligned} & \text{Menten\_Explicit\_Enzyme}_3(\text{Kcat}, \text{km}, [\text{species}_{28}], [\text{species}_4]) \\ &= \frac{\text{Kcat} \cdot [\text{species}_{28}] \cdot [\text{species}_4]}{\text{km} + [\text{species}_4]} \end{aligned} \quad (38)$$

$$\begin{aligned} & \text{Menten\_Explicit\_Enzyme}_3(\text{Kcat}, \text{km}, [\text{species}_{28}], [\text{species}_4]) \\ &= \frac{\text{Kcat} \cdot [\text{species}_{28}] \cdot [\text{species}_4]}{\text{km} + [\text{species}_4]} \end{aligned} \quad (39)$$

Table 22: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		1509.36		<input checked="" type="checkbox"/>
km	km		1432410.00		<input checked="" type="checkbox"/>

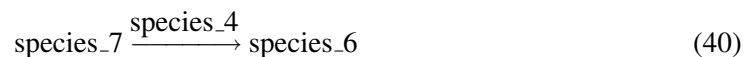
## 6.6 Reaction [reaction\\_5](#)

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



### 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

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

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

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

Table 26: Properties of each parameter.

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

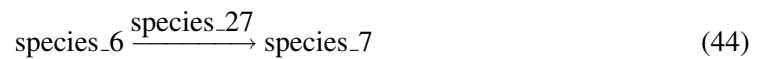
## 6.7 Reaction `reaction_6`

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



### Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
<code>species_6</code>	<code>Raf1Active</code>	

### Modifier

Table 28: Properties of each modifier.

Id	Name	SBO
<code>species_27</code>	<code>Raf1PPtase</code>	

### Product

Table 29: Properties of each product.

Id	Name	SBO
<code>species_7</code>	<code>Raf1Inactive</code>	

### Kinetic Law

**Derived unit** contains undeclared units

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

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

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

Table 30: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.126		<input checked="" type="checkbox"/>
km	km		1061.710		<input checked="" type="checkbox"/>

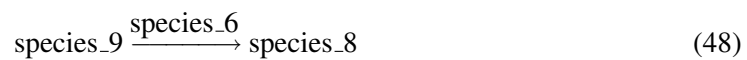
## 6.8 Reaction `reaction_7`

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



### 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

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

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

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

Table 34: Properties of each parameter.

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

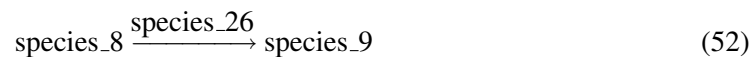
## 6.9 Reaction `reaction_8`

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



### 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

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

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

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

Table 38: Properties of each parameter.

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

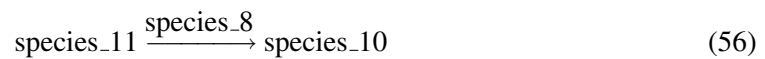
## 6.10 Reaction `reaction_9`

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



### Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
<code>species_11</code>	<code>ErkInactive</code>	

### Modifier

Table 40: Properties of each modifier.

Id	Name	SBO
<code>species_8</code>	<code>MekActive</code>	

### Product

Table 41: Properties of each product.

Id	Name	SBO
<code>species_10</code>	<code>ErkActive</code>	

### Kinetic Law

**Derived unit** contains undeclared units

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

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

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

Table 42: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		9.854		<input checked="" type="checkbox"/>
km	km		1007340.000		<input checked="" type="checkbox"/>

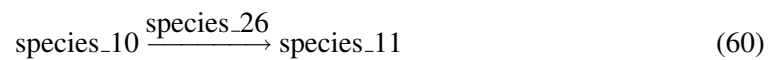
### 6.11 Reaction [reaction\\_10](#)

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



#### 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

$$v_{11} = \text{vol}(\text{compartment}_0) \cdot \text{Menten\_Explicit\_Enzyme}_9(\text{Kcat}, \text{km}, [\text{species}_{10}], [\text{species}_{26}]) \quad (61)$$

$$\begin{aligned} & \text{Menten\_Explicit\_Enzyme}_9(\text{Kcat}, \text{km}, [\text{species}_{10}], [\text{species}_{26}]) \\ &= \frac{\text{Kcat} \cdot [\text{species}_{26}] \cdot [\text{species}_{10}]}{\text{km} + [\text{species}_{10}]} \end{aligned} \quad (62)$$

$$\begin{aligned} & \text{Menten\_Explicit\_Enzyme}_9(\text{Kcat}, \text{km}, [\text{species}_{10}], [\text{species}_{26}]) \\ &= \frac{\text{Kcat} \cdot [\text{species}_{26}] \cdot [\text{species}_{10}]}{\text{km} + [\text{species}_{10}]} \end{aligned} \quad (63)$$

Table 46: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		8.891		<input checked="" type="checkbox"/>
km	km		3496490.000		<input checked="" type="checkbox"/>

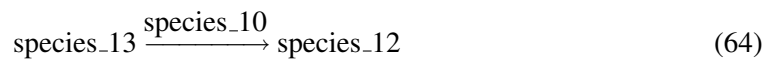
### 6.12 Reaction [reaction\\_11](#)

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



### 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

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

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

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

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



#### 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

$$v_{13} = \text{vol}(\text{compartment\_0}) \cdot k_1 \cdot [\text{species\_12}] \quad (69)$$

Table 53: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.005		<input checked="" type="checkbox"/>

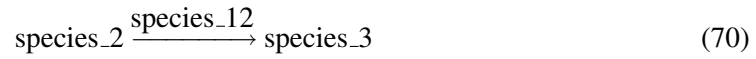
### 6.14 Reaction [reaction\\_13](#)

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



## 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

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

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

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

Table 57: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		1611.97		<input checked="" type="checkbox"/>
km	km		896896.00		<input checked="" type="checkbox"/>

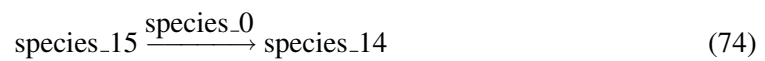
### 6.15 Reaction [reaction\\_14](#)

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



#### 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

$$v_{15} = \text{vol}(\text{compartment}_0) \cdot \text{Menten\_Explicit\_Enzyme\_12}(\text{Kcat}, \text{km}, [\text{species}_0], [\text{species}_{15}]) \quad (75)$$

$$\begin{aligned} & \text{Menten\_Explicit\_Enzyme\_12}(\text{Kcat}, \text{km}, [\text{species}_0], [\text{species}_{15}]) \\ &= \frac{\text{Kcat} \cdot [\text{species}_0] \cdot [\text{species}_{15}]}{\text{km} + [\text{species}_{15}]} \end{aligned} \quad (76)$$

$$\begin{aligned} & \text{Menten\_Explicit\_Enzyme\_12}(\text{Kcat}, \text{km}, [\text{species}_0], [\text{species}_{15}]) \\ &= \frac{\text{Kcat} \cdot [\text{species}_0] \cdot [\text{species}_{15}]}{\text{km} + [\text{species}_{15}]} \end{aligned} \quad (77)$$

Table 61: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		10.674		<input checked="" type="checkbox"/>
km	km		184912.000		<input checked="" type="checkbox"/>

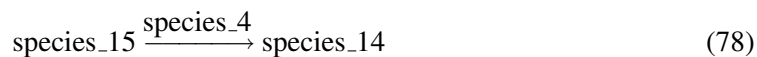
## 6.16 Reaction `reaction_15`

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



### Reactant

Table 62: Properties of each reactant.

Id	Name	SBO
<code>species_15</code>	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

$$v_{16} = \text{vol}(\text{compartment}_0) \cdot \text{Menten\_Explicit\_Enzyme\_13}(\text{Kcat}, \text{km}, [\text{species}_{15}], [\text{species}_4]) \quad (79)$$

$$\begin{aligned} & \text{Menten\_Explicit\_Enzyme\_13}(\text{Kcat}, \text{km}, [\text{species}_{15}], [\text{species}_4]) \\ &= \frac{\text{Kcat} \cdot [\text{species}_4] \cdot [\text{species}_{15}]}{\text{km} + [\text{species}_{15}]} \end{aligned} \quad (80)$$

$$\begin{aligned} & \text{Menten\_Explicit\_Enzyme\_13}(\text{Kcat}, \text{km}, [\text{species}_{15}], [\text{species}_4]) \\ &= \frac{\text{Kcat} \cdot [\text{species}_4] \cdot [\text{species}_{15}]}{\text{km} + [\text{species}_{15}]} \end{aligned} \quad (81)$$

Table 65: Properties of each parameter.

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

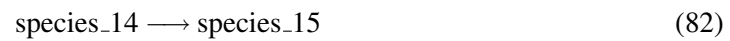
## 6.17 Reaction `reaction_16`

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

**Name** PI3K\_Deactivation

**Notes** Parameters taken from Brown et al 2004

### Reaction equation



### 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

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

Table 68: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.005		<input checked="" type="checkbox"/>

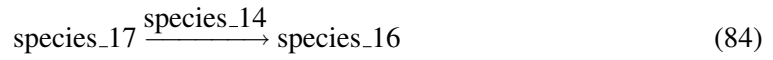
## 6.18 Reaction [reaction\\_17](#)

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



## 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

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

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

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

Table 72: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		0.057		<input checked="" type="checkbox"/>
km	km		653951.000		<input checked="" type="checkbox"/>

### 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



#### 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

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

Table 75: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.005		<input checked="" type="checkbox"/>

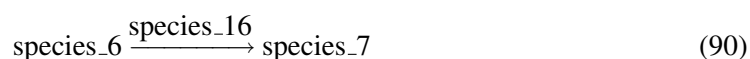
## 6.20 Reaction `reaction_19`

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



### Reactant

Table 76: Properties of each reactant.

Id	Name	SBO
<code>species_6</code>	<code>Raf1Active</code>	

### Modifier

Table 77: Properties of each modifier.

Id	Name	SBO
<code>species_16</code>	<code>AktActive</code>	

### Product

Table 78: Properties of each product.

Id	Name	SBO
<code>species_7</code>	<code>Raf1Inactive</code>	

### Kinetic Law

**Derived unit** contains undeclared units

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

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

$$\text{Menten\_Explicit\_Enzyme\_15}(\text{Kcat}, \text{km}, [\text{species\_16}], [\text{species\_6}]) = \frac{\text{Kcat} \cdot [\text{species\_16}] \cdot [\text{species\_6}]}{\text{km} + [\text{species\_6}]} \quad (93)$$

Table 79: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kcat	Kcat		15.121		<input checked="" type="checkbox"/>
km	km		119355.000		<input checked="" type="checkbox"/>

## 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



### 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

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

Table 82: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.2		<input checked="" type="checkbox"/>

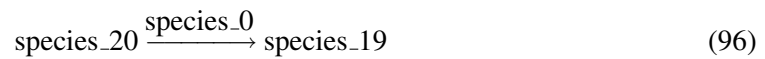
## 6.22 Reaction [reaction\\_21](#)

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



### 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



$$v_{22} = \text{vol}(\text{compartment}_0) \cdot \text{MM\_Explicit\_Enzyme}_1(\text{kcat}, \text{km}, [\text{species}_0], [\text{species}_{20}]) \quad (97)$$

$$\text{MM\_Explicit\_Enzyme}_1(\text{kcat}, \text{km}, [\text{species}_0], [\text{species}_{20}]) = \frac{\text{kcat} \cdot [\text{species}_0] \cdot [\text{species}_{20}]}{\text{km} + [\text{species}_{20}]} \quad (98)$$

$$\text{MM\_Explicit\_Enzyme}_1(\text{kcat}, \text{km}, [\text{species}_0], [\text{species}_{20}]) = \frac{\text{kcat} \cdot [\text{species}_0] \cdot [\text{species}_{20}]}{\text{km} + [\text{species}_{20}]} \quad (99)$$

Table 86: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcat	kcat		694.731		<input checked="" type="checkbox"/>
km	km		6086070.000		<input checked="" type="checkbox"/>

### 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



#### Reactant

Table 87: Properties of each reactant.

Id	Name	SBO
species <sub>19</sub>	C3GActive	

#### Product

Table 88: Properties of each product.

Id	Name	SBO
species <sub>20</sub>	C3GInactive	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{23} = \text{vol}(\text{compartment}_0) \cdot k1 \cdot [\text{species}_{19}] \quad (101)$$

Table 89: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		2.5		<input checked="" type="checkbox"/>

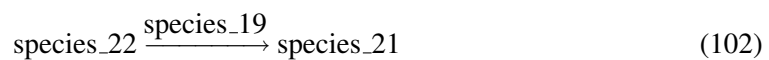
## 6.24 Reaction [reaction\\_23](#)

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



## 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

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

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

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

Table 93: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcat	kcat		32.344		<input checked="" type="checkbox"/>
km	km		35954.300		<input checked="" type="checkbox"/>

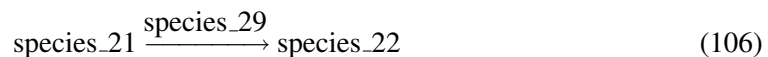
### 6.25 Reaction [reaction\\_24](#)

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



### 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

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

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

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

Table 97: Properties of each parameter.

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

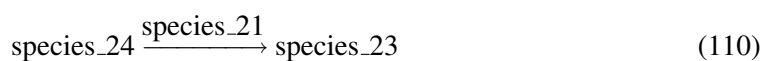
## 6.26 Reaction `reaction_25`

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



### Reactant

Table 98: Properties of each reactant.

Id	Name	SBO
<code>species_24</code>	<code>bRafInactive</code>	

### Modifier

Table 99: Properties of each modifier.

Id	Name	SBO
<code>species_21</code>	<code>Rap1Active</code>	

### Product

Table 100: Properties of each product.

Id	Name	SBO
<code>species_23</code>	<code>bRafActive</code>	

### Kinetic Law

**Derived unit** contains undeclared units

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

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

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

Table 101: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcat	kcat		0.884		<input checked="" type="checkbox"/>
km	km		62464.600		<input checked="" type="checkbox"/>

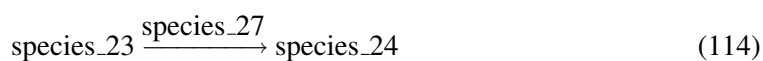
## 6.27 Reaction [reaction\\_26](#)

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



### 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

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

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

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

Table 105: Properties of each parameter.

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

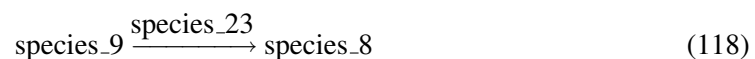
## 6.28 Reaction [reaction\\_27](#)

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



## 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

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

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

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

Table 109: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcat	kcat		185.759		<input checked="" type="checkbox"/>
km	km		4768350.000		<input checked="" type="checkbox"/>



## 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



### Reactant

Table 110: Properties of each reactant.

Id	Name	SBO
<code>species_30</code>	<code>proEGFReceptor</code>	

### Product

Table 111: Properties of each product.

Id	Name	SBO
<code>species_1</code>	<code>freeEGFReceptor</code>	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{29} = \text{vol}(\text{compartment\_0}) \cdot \text{Constant\_flux\_irreversible}(v) \quad (123)$$

$$\text{Constant\_flux\_irreversible}(v) = v \quad (124)$$

$$\text{Constant\_flux\_irreversible}(v) = v \quad (125)$$

Table 112: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
<code>v</code>	<code>v</code>		100.0		<input checked="" type="checkbox"/>

### 6.30 Reaction [reaction\\_29](#)

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

**Name** EGFRceptor\_Degradation\_Free

**Notes** Parameters were estimated from experiments

#### Reaction equation



#### Reactant

Table 113: Properties of each reactant.

Id	Name	SBO
species_1	freeEGFRceptor	

#### Product

Table 114: Properties of each product.

Id	Name	SBO
species_18	degradedEGFRceptor	

#### Kinetic Law

**Derived unit** contains undeclared units

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

Table 115: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.001		<input checked="" type="checkbox"/>

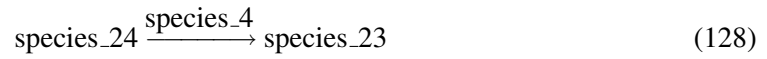
### 6.31 Reaction [reaction\\_30](#)

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



## 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

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

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

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

Table 119: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcat	kcat		0.884		<input checked="" type="checkbox"/>
km	km		62464.600		<input checked="" type="checkbox"/>

## 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**  $0 \text{ mmol} \cdot \text{ml}^{-1}$

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](#)).

$$\frac{d}{dt}\text{species}_0 = v_1 - v_{21} \quad (132)$$

### 7.2 Species `species_1`

**Name** freeEGFReceptor

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

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

This species takes part in three reactions (as a reactant in [reaction\\_0](#), [reaction\\_29](#) and as a product in [reaction\\_28](#)).

$$\frac{d}{dt}\text{species}_1 = v_{29} - v_1 - v_{30} \quad (133)$$

### 7.3 Species `species_2`

**Name** SosActive

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_2} = v_2 - v_3 - v_{14} \quad (134)$$

### 7.4 Species `species_3`

**Name** SosInactive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

This species takes part in three reactions (as a reactant in [reaction\\_1](#) and as a product in [reaction\\_2](#), [reaction\\_13](#)).

$$\frac{d}{dt}\text{species\_3} = v_3 + v_{14} - v_2 \quad (135)$$

### 7.5 Species `species_4`

**Name** RasActive

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_4} = v_4 - v_5 \quad (136)$$

### 7.6 Species `species_5`

**Name** RasInactive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

This species takes part in two reactions (as a reactant in [reaction\\_3](#) and as a product in [reaction\\_4](#)).

$$\frac{d}{dt}\text{species\_5} = v_5 - v_4 \quad (137)$$

## 7.7 Species `species_6`

**Name** Raf1Active

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_6} = v_6 - v_7 - v_{20} \quad (138)$$

## 7.8 Species `species_7`

**Name** Raf1Inactive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

This species takes part in three reactions (as a reactant in [reaction\\_5](#) and as a product in [reaction\\_6](#), [reaction\\_19](#)).

$$\frac{d}{dt}\text{species\_7} = v_7 + v_{20} - v_6 \quad (139)$$

## 7.9 Species `species_8`

**Name** MekActive

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_8} = v_8 + v_{28} - v_9 \quad (140)$$

## 7.10 Species `species_9`

**Name** MekInactive

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

**Initial concentration** 600000 mmol · ml<sup>-1</sup>

This species takes part in three reactions (as a reactant in [reaction\\_7](#), [reaction\\_27](#) and as a product in [reaction\\_8](#)).

$$\frac{d}{dt}\text{species\_9} = v_9 - v_8 - v_{28} \quad (141)$$

### 7.11 Species `species_10`

**Name** ErkActive

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_10} = v_{10} - v_{11} \quad (142)$$

### 7.12 Species `species_11`

**Name** ErkInactive

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

**Initial concentration** 600000 mmol · ml<sup>-1</sup>

This species takes part in two reactions (as a reactant in [reaction\\_9](#) and as a product in [reaction\\_10](#)).

$$\frac{d}{dt}\text{species\_11} = v_{11} - v_{10} \quad (143)$$

### 7.13 Species `species_12`

**Name** P90RskActive

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_12} = v_{12} - v_{13} \quad (144)$$

### 7.14 Species `species_13`

**Name** P90RskInactive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

This species takes part in two reactions (as a reactant in [reaction\\_11](#) and as a product in [reaction\\_12](#)).

$$\frac{d}{dt}\text{species\_13} = v_{13} - v_{12} \quad (145)$$

### 7.15 Species `species_14`

**Name** PI3KActive

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_14} = v_{15} + v_{16} - v_{17} \quad (146)$$

### 7.16 Species `species_15`

**Name** PI3KInactive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

This species takes part in three reactions (as a reactant in [reaction\\_14](#), [reaction\\_15](#) and as a product in [reaction\\_16](#)).

$$\frac{d}{dt}\text{species\_15} = v_{17} - v_{15} - v_{16} \quad (147)$$

### 7.17 Species `species_16`

**Name** AktActive

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_16} = v_{18} - v_{19} \quad (148)$$

### 7.18 Species `species_17`

**Name** AktInactive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

This species takes part in two reactions (as a reactant in [reaction\\_17](#) and as a product in [reaction\\_18](#)).

$$\frac{d}{dt}\text{species\_17} = v_{19} - v_{18} \quad (149)$$



### 7.19 Species `species_18`

**Name** degradedEGFReceptor

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

This species takes part in two reactions (as a product in [reaction\\_20](#), [reaction\\_29](#)).

$$\frac{d}{dt}\text{species\_18} = v_{21} + v_{30} \quad (150)$$

### 7.20 Species `species_19`

**Name** C3GActive

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_19} = v_{22} - v_{23} \quad (151)$$

### 7.21 Species `species_20`

**Name** C3GInactive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

This species takes part in two reactions (as a reactant in [reaction\\_21](#) and as a product in [reaction\\_22](#)).

$$\frac{d}{dt}\text{species\_20} = v_{23} - v_{22} \quad (152)$$

### 7.22 Species `species_21`

**Name** Rap1Active

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_21} = v_{24} - v_{25} \quad (153)$$

### 7.23 Species `species_22`

**Name** Rap1Inactive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

This species takes part in two reactions (as a reactant in [reaction\\_23](#) and as a product in [reaction\\_24](#)).

$$\frac{d}{dt}\text{species\_22} = v_{25} - v_{24} \quad (154)$$

### 7.24 Species `species_23`

**Name** bRafActive

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

**Initial concentration** 0 mmol · ml<sup>-1</sup>

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](#)).

$$\frac{d}{dt}\text{species\_23} = v_{26} + v_{31} - v_{27} \quad (155)$$

### 7.25 Species `species_24`

**Name** bRafInactive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

This species takes part in three reactions (as a reactant in [reaction\\_25](#), [reaction\\_30](#) and as a product in [reaction\\_26](#)).

$$\frac{d}{dt}\text{species\_24} = v_{27} - v_{26} - v_{31} \quad (156)$$

### 7.26 Species `species_25`

**Name** EGF

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

**Initial concentration** 1.0002 · 10<sup>7</sup> mmol · ml<sup>-1</sup>

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:

$$\frac{d}{dt}\text{species\_25} = 0 \quad (157)$$

### 7.27 Species `species_26`

**Name** PP2AActive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

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:

$$\frac{d}{dt}\text{species\_26} = 0 \quad (158)$$

### 7.28 Species `species_27`

**Name** Raf1PPtase

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

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:

$$\frac{d}{dt}\text{species\_27} = 0 \quad (159)$$

### 7.29 Species `species_28`

**Name** RasGapActive

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

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:

$$\frac{d}{dt}\text{species\_28} = 0 \quad (160)$$

### 7.30 Species `species_29`

**Name** Rap1Gap

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

**Initial concentration** 120000 mmol · ml<sup>-1</sup>

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:

$$\frac{d}{dt}\text{species\_29} = 0 \quad (161)$$

### 7.31 Species `species_30`

**Name** `proEGFReceptor`

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

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

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:

$$\frac{d}{dt}\text{species\_30} = 0 \quad (162)$$

SBML2<sup>A</sup>TeX was developed by Andreas Dräger<sup>a</sup>, Hannes Planatscher<sup>a</sup>, Dieudonné M Wouamba<sup>a</sup>, Adrian Schröder<sup>a</sup>, Michael Hucka<sup>b</sup>, Lukas Endler<sup>c</sup>, Martin Golebiewski<sup>d</sup> and Andreas Zell<sup>a</sup>. Please see <http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX> for more information.

<sup>a</sup>Center for Bioinformatics Tübingen (ZBIT), Germany

<sup>b</sup>California Institute of Technology, Beckman Institute BNMC, Pasadena, United States

<sup>c</sup>European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom

<sup>d</sup>EML Research gGmbH, Heidelberg, Germany