SBML Model Report

Model name: “Bianconi2012 - EGFR and IGF1R pathway in lung cancer”

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah[1] and Fortunato Bianconi[2] at November 20th 2012 at 6:31 p. m. and last time modified at October nineth 2014 at 5:31 p. m. Table 1 gives an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	21
events	0	constraints	0
reactions	22	function definitions	0
global parameters	5	unit definitions	0
rules	0	initial assignments	0

Model Notes

Bianconi2012 - EGFR and IGF1R pathway in lung cancer

EGFR and IGF1R pathways play a key role in various human cancers and are crucial for tumour transformation and survival of malignant cells. High EGFR and IGF1R expression and

[1] EMBL-EBI, viji@ebi.ac.uk

[2] Univeristy of Perugia, fortunato.bianconi@gmail.com

activity has been associated with multiple aspects of cancer progression including tumourigenesis, metastasis, resistance to chemotherapeutics and other molecularly targeted drugs. Here, the biological relationship between the proteins involved in EGFR and IGF1R pathways and the downstream MAPK and PIK3 networks has been modelled to study the time behaviour of the overall system, and the functional interdependencies among the receptors, the proteins and kinases involved.

This model is described in the article:Computational model of EGFR and IGF1R pathways in lung cancer: a Systems Biology approach for Translational Oncology.Bianconi F, Baldelli E, Ludovini V, Crin L, Flacco A, Valigi P.Biotechnol Adv. 2012 Jan-Feb;30(1):142-53.

Abstract:

In this paper we propose a Systems Biology approach to understand the molecular biology of the Epidermal Growth Factor Receptor (EGFR, also known as ErbB1/HER1) and type 1 Insulin-like Growth Factor (IGF1R) pathways in non-small cell lung cancer (NSCLC). This approach, combined with Translational Oncology methodologies, is used to address the experimental evidence of a close relationship among EGFR and IGF1R protein expression, by immunohistochemistry (IHC) and gene amplification, by in situ hybridization (FISH) and the corresponding ability to develop a more aggressive behavior. We develop a detailed in silico model, based on ordinary differential equations, of the pathways and study the dynamic implications of receptor alterations on the time behavior of the MAPK cascade down to ERK, which in turn governs proliferation and cell migration. In addition, an extensive sensitivity analysis of the proposed model is carried out and a simplified model is proposed which allows us to infer a similar relationship among EGFR and IGF1R activities and disease outcome.

This model is hosted on BioModels Database and identified by: MODEL1209230000 .

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 which are all predefined by SBML and not mentioned in the model.

2.1 Unit `substance`

Notes Mole is the predefined SBML unit for `substance`.

Definition mol

2.2 Unit `volume`

Notes Litre is the predefined SBML unit for `volume`.

Definition l

2.3 Unit `area`

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

Definition m^2

2.4 Unit `length`

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

Definition m

2.5 Unit `time`

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

Definition s

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

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

3.1 Compartment `cell_nsclc`

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

Name cell_nsclc

4 Species

This model contains 21 species. 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
EGFR_active	EGFR_active	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
D_SOS	D_SOS	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
A_SOS	A_SOS	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Raf	Raf	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Ras_active	Ras_active	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Mek_active	Mek_active	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ERK	ERK	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ERK_active	ERK_active	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
IGFR_active	IGFR_active	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
PI3KCA	PI3KCA	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
PI3KCA_active	PI3KCA_active	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
AKT_active	AKT_active	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
AKT	AKT	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
PP2A	PP2A	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Ras	Ras	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Raf_active	Raf_active	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Mek	Mek	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
RasGapActive	RasGapActive	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
RafPP	RafPP	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
P90RskInactive	P90RskInactive	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
P90Rsk_Active	P90Rsk_Active	cell_nsclc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains five global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
gamma_IGFR	gamma_IGFR		0.020		☑
kd_PI3K_a	kd_PI3K_a		0.005		☑
k_P90Rsk-_ERKActive	k_P90Rsk-_ERKActive		0.021		☑
KM_P90Rsk-_ERKActive	KM_P90Rsk-_ERKActive		763523.000		☑
gamma_EGFR	gamma_EGFR		0.020		☑

6 Reactions

This model contains 22 reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	SOS_conformational_activation	SOS conformational activation	$\mathrm{D\_SOS} + \mathrm{EGFR\_active} \xrightarrow{\mathrm{EGFR\_active,\ D\_SOS}} \mathrm{A\_SOS} + \mathrm{EGFR\_active}$	
2	kRas_Activation	kRas Activation	$\mathrm{A\_SOS} + \mathrm{Ras} \xrightarrow{\mathrm{A\_SOS,\ Ras}} \mathrm{Ras\_active} + \mathrm{A\_SOS}$	
3	EGFR_degradation	EGFR degradation	$\mathrm{EGFR\_active} \xrightarrow{\mathrm{EGFR\_active}} \emptyset$	
4	ERK_activationBy_Mek	ERK activation by Mek	$\mathrm{ERK} + \mathrm{Mek\_active} \xrightarrow{\mathrm{Mek\_active,\ ERK}} \mathrm{ERK\_active} + \mathrm{Mek\_active}$	
5	SOS_deactivationBy_P90	SOS deactivation by P90	$\mathrm{P90Rsk\_Active} + \mathrm{A\_SOS} \xrightarrow{\mathrm{P90Rsk\_Active,\ A\_SOS}} \mathrm{D\_SOS} + \mathrm{P90Rsk\_Active}$	
6	SOS_activationBy_IGF	SOS activation by IGF	$\mathrm{IGFR\_active} + \mathrm{D\_SOS} \xrightarrow{\mathrm{IGFR\_active,\ D\_SOS}} \mathrm{A\_SOS} + \mathrm{IGFR\_active}$	
7	PI3KCA_activationBy_IGF1R	PI3KCA activation by IGF1R	$\mathrm{PI3KCA} + \mathrm{IGFR\_active} \xrightarrow{\mathrm{IGFR\_active,\ PI3KCA}} \mathrm{PI3KCA\_active} + \mathrm{IGFR\_active}$	

№	Id	Name	Reaction Equation	SBO
8	PI3KCA_activationBy_EGF	PI3KCA activation by EGF	$\text{PI3KCA} + \text{EGFR\_active} \xrightarrow{\text{EGFR\_active, PI3KCA}} \text{PI3KCA\_active} + \text{EGFR\_active}$	
9	Akt_activationBy_PI3KCA	Akt activation by PI3KCA	$\text{AKT} + \text{PI3KCA\_active} \xrightarrow{\text{PI3KCA\_active, AKT}} \text{AKT\_active} + \text{PI3KCA\_active}$	
10	Akt_deactivation	Akt deactivation	$\text{AKT\_active} \xrightarrow{\text{AKT\_active}} \text{AKT}$	
11	ERK_deactivationBy_PP2A	ERK deactivation by PP2A	$\text{ERK\_active} + \text{PP2A} \xrightarrow{\text{PP2A, ERK\_active}} \text{ERK} + \text{PP2A}$	
12	PI3KCA_activationBy_kRas	PI3KCA activation by kRas	$\text{PI3KCA} + \text{Ras\_active} \xrightarrow{\text{Ras\_active, PI3KCA}} \text{PI3KCA\_active} + \text{Ras\_active}$	
13	Raf_activationBy_kRas	Raf activation by kRas	$\text{Ras\_active} + \text{Raf} \xrightarrow{\text{Ras\_active, Raf}} \text{Raf\_active} + \text{Ras\_active}$	
14	Mek_activationBy_Raf	Mek activation by Raf	$\text{Raf\_active} + \text{Mek} \xrightarrow{\text{Raf\_active, Mek}} \text{Mek\_active} + \text{Raf\_active}$	
15	Raf_deactivationBy_Akt	Raf deactivation by Akt	$\text{AKT\_active} + \text{Raf\_active} \xrightarrow{\text{AKT\_active, Raf\_active}} \text{Raf} + \text{AKT\_active}$	
16	Ras_deactivation	Ras deactivation by RasGab	$\text{RasGapActive} + \text{Ras\_active} \xrightarrow{\text{RasGapActive, Ras\_active}} \text{Ras} + \text{RasGapActive}$	

№	Id	Name	Reaction Equation	SBO
17	Mek_deactivation	Mek deactivation by PP2A	$\text{PP2A} + \text{Mek\_active} \xrightarrow{\text{PP2A, Mek\_active}} \text{Mek} + \text{PP2A}$	
18	IGFR_active_degradation	IGFR active degradation	$\text{IGFR\_active} \xrightarrow{\text{IGFR\_active}} \emptyset$	
19	PI3KCA_deactivation	PI3KCA deactivation	$\text{PI3KCA\_active} \xrightarrow{\text{PI3KCA\_active}} \text{PI3KCA}$	
20	Raf_deactivation	Raf deactivation by RafPP	$\text{RafPP} + \text{Raf\_active} \xrightarrow{\text{RafPP, Raf\_active}} \text{Raf} + \text{RafPP}$	
21	P90_activationBy_ERK	P90 activation by ERK	$\text{P90RskInactive} + \text{ERK\_active} \xrightarrow{\text{ERK\_active, P90RskInactive}} \text{P90Rsk\_Active} + \text{ERK\_active}$	
22	P90_deactivation	P90 deactivation	$\text{P90Rsk\_Active} \xrightarrow{\text{P90Rsk\_Active}} \text{P90RskInactive}$	

6.1 Reaction SOS_conformational_activation

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

Name SOS conformational activation

Reaction equation

$$\text{D\_SOS} + \text{EGFR\_active} \xrightarrow{\text{EGFR\_active, D\_SOS}} \text{A\_SOS} + \text{EGFR\_active} \tag{1}$$

Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
D_SOS	D_SOS	
EGFR_active	EGFR_active	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
EGFR_active	EGFR_active	
D_SOS	D_SOS	

Products

Table 8: Properties of each product.

Id	Name	SBO
A_SOS	A_SOS	
EGFR_active	EGFR_active	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{\text{k\_SOS\_E} \cdot [\text{EGFR\_active}] \cdot [\text{D\_SOS}]^{\text{n\_SOS}}}{\text{KM\_SOS\_E}^{\text{n\_SOS}} + [\text{D\_SOS}]^{\text{n\_SOS}}} \tag{2}$$

Table 9: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_SOS_E	k_SOS_E		694.731		☑
n_SOS	n_SOS		1.000		☑
KM_SOS_E	KM_SOS_E		6086070.000		☑

6.2 Reaction kRas_Activation

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

Name kRas Activation

Reaction equation

$$\text{A\_SOS} + \text{Ras} \xrightarrow{\text{A\_SOS, Ras}} \text{Ras\_active} + \text{A\_SOS} \tag{3}$$

Reactants

Table 10: Properties of each reactant.

Id	Name	SBO
A_SOS	A_SOS	
Ras	Ras	

Modifiers

Table 11: Properties of each modifier.

Id	Name	SBO
A_SOS	A_SOS	
Ras	Ras	

Products

Table 12: Properties of each product.

Id	Name	SBO
Ras_active	Ras_active	
A_SOS	A_SOS	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \frac{[\text{A\_SOS}] \cdot \text{k\_Ras\_SOS} \cdot [\text{Ras}]^{\text{n\_Ras\_SOS}}}{\text{KM\_Ras\_SOS}^{\text{n\_Ras\_SOS}} + [\text{Ras}]^{\text{n\_Ras\_SOS}}} \tag{4}$$

Table 13: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_Ras_SOS	k_Ras_SOS		32.344		☑
n_Ras_SOS	n_Ras_SOS		1.000		☑
KM_Ras_SOS	KM_Ras_SOS		35954.300		☑

6.3 Reaction EGFR_degradation

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

Name EGFR degradation

Reaction equation

$$\text{EGFR\_active} \xrightarrow{\text{EGFR\_active}} \emptyset \tag{5}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
EGFR_active	EGFR_active	

Modifier

Table 15: Properties of each modifier.

Id	Name	SBO
EGFR_active	EGFR_active	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{gamma\_EGFR} \cdot [\text{EGFR\_active}] \tag{6}$$

6.4 Reaction ERK_activationBy_Mek

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

Name ERK activation by Mek

Reaction equation

$$\text{ERK} + \text{Mek\_active} \xrightarrow{\text{Mek\_active, ERK}} \text{ERK\_active} + \text{Mek\_active} \tag{7}$$

Reactants

Table 16: Properties of each reactant.

Id	Name	SBO
ERK	ERK	
Mek_active	Mek_active	

Modifiers

Table 17: Properties of each modifier.

Id	Name	SBO
Mek_active	Mek_active	
ERK	ERK	

Products

Table 18: Properties of each product.

Id	Name	SBO
ERK_active	ERK_active	
Mek_active	Mek_active	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \frac{[\text{Mek\_active}] \cdot \text{k\_ERK\_MekActive} \cdot [\text{ERK}]}{\text{KM\_ERK\_MekActive} + [\text{ERK}]} \tag{8}$$

Table 19: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_ERK-_MekActive	k_ERK_MekActive		9.854		☑
KM_ERK-_MekActive	KM_ERK-_MekActive		1007340.000		☑

6.5 Reaction SOS_deactivationBy_P90

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

Name SOS deactivation by P90

Reaction equation

$$\text{P90Rsk\_Active} + \text{A\_SOS} \xrightarrow{\text{P90Rsk\_Active, A\_SOS}} \text{D\_SOS} + \text{P90Rsk\_Active} \tag{9}$$

Reactants

Table 20: Properties of each reactant.

Id	Name	SBO
P90Rsk_Active	P90Rsk_Active	
A_SOS	A_SOS	

Modifiers

Table 21: Properties of each modifier.

Id	Name	SBO
P90Rsk_Active	P90Rsk_Active	
A_SOS	A_SOS	

Products

Table 22: Properties of each product.

Id	Name	SBO
D_SOS	D_SOS	
P90Rsk_Active	P90Rsk_Active	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \frac{[\text{P90Rsk\_Active}] \cdot \text{k\_D\_SOS\_P90Rsk} \cdot [\text{A\_SOS}]^{\text{n\_D\_SOS}}}{\text{KM\_D\_SOS\_P90Rsk}^{\text{n\_D\_SOS}} + [\text{A\_SOS}]^{\text{n\_D\_SOS}}} \tag{10}$$

Table 23: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_D_SOS-_P90Rsk	k_D_SOS_P90Rsk		161197.0		☑
n_D_SOS	n_D_SOS		1.0		☑
KM_D_SOS-_P90Rsk	KM_D_SOS-_P90Rsk		896896.0		☑

6.6 Reaction SOS_activationBy_IGF

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

Name SOS activation by IGF

Reaction equation

$$\text{IGFR\_active} + \text{D\_SOS} \xrightarrow{\text{IGFR\_active, D\_SOS}} \text{A\_SOS} + \text{IGFR\_active} \tag{11}$$

Reactants

Table 24: Properties of each reactant.

Id	Name	SBO
IGFR_active	IGFR_active	
D_SOS	D_SOS	

Modifiers

Table 25: Properties of each modifier.

Id	Name	SBO
IGFR_active	IGFR_active	
D_SOS	D_SOS	

Products

Table 26: Properties of each product.

Id	Name	SBO
A_SOS	A_SOS	
IGFR_active	IGFR_active	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \frac{[\text{IGFR\_active}] \cdot \text{k\_A\_SOS\_I} \cdot [\text{D\_SOS}]^{\text{n\_A\_SOS\_I}}}{\text{KM\_A\_SOS\_I}^{\text{n\_A\_SOS\_I}} + [\text{D\_SOS}]^{\text{n\_A\_SOS\_I}}} \tag{12}$$

Table 27: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_A_SOS_I	k_A_SOS_I		500.0		☑
n_A_SOS_I	n_A_SOS_I		1.0		☑
KM_A_SOS_I	KM_A_SOS_I		100000.0		☑

6.7 Reaction PI3KCA_activationBy_IGF1R

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

Name PI3KCA activation by IGF1R

Reaction equation

$$\text{PI3KCA} + \text{IGFR\_active} \xrightarrow{\text{IGFR\_active, PI3KCA}} \text{PI3KCA\_active} + \text{IGFR\_active} \tag{13}$$

Reactants

Table 28: Properties of each reactant.

Id	Name	SBO
PI3KCA	PI3KCA	
IGFR_active	IGFR_active	

Modifiers

Table 29: Properties of each modifier.

Id	Name	SBO
IGFR_active	IGFR_active	
PI3KCA	PI3KCA	

Products

Table 30: Properties of each product.

Id	Name	SBO
PI3KCA_active	PI3KCA_active	
IGFR_active	IGFR_active	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \frac{[\text{IGFR\_active}] \cdot \text{k\_PI3K\_IGF1R} \cdot [\text{PI3KCA}]^{\text{n\_PI3K\_I}}}{\text{KM\_PI3K\_IGF1R}^{\text{n\_PI3K\_I}} + [\text{PI3KCA}]^{\text{n\_PI3K\_I}}} \tag{14}$$

Table 31: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_PI3K_IGF1R	k_PI3K_IGF1R		10.674		☑
n_PI3K_I	n_PI3K_I		1.000		☑
KM_PI3K_IGF1R	KM_PI3K_IGF1R		184912.000		☑

6.8 Reaction PI3KCA_activationBy_EGF

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

Name PI3KCA activation by EGF

Reaction equation

$$\text{PI3KCA} + \text{EGFR\_active} \xrightarrow{\text{EGFR\_active, PI3KCA}} \text{PI3KCA\_active} + \text{EGFR\_active} \tag{15}$$

Reactants

Table 32: Properties of each reactant.

Id	Name	SBO
PI3KCA	PI3KCA	
EGFR_active	EGFR_active	

Modifiers

Table 33: Properties of each modifier.

Id	Name	SBO
EGFR_active	EGFR_active	
PI3KCA	PI3KCA	

Products

Table 34: Properties of each product.

Id	Name	SBO
PI3KCA_active	PI3KCA_active	
EGFR_active	EGFR_active	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \frac{[\text{EGFR\_active}] \cdot \text{k\_PI3K\_EGF1R} \cdot [\text{EGFR\_active}] \cdot [\text{PI3KCA}]^{\text{n\_PI3K\_E}}}{\text{KM\_PI3K\_EGF1R}^{\text{n\_PI3K\_E}} + [\text{PI3KCA}]^{\text{n\_PI3K\_E}}} \tag{16}$$

Table 35: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_PI3K_EGF1R	k_PI3K_EGF1R		10.674		☑
n_PI3K_E	n_PI3K_E		1.000		☑
KM_PI3K-_EGF1R	KM_PI3K_EGF1R		184912.000		☑

6.9 Reaction Akt_activationBy_PI3KCA

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

Name Akt activation by PI3KCA

Reaction equation

$$\mathrm{AKT} + \mathrm{PI3KCA\_active} \xrightarrow{\mathrm{PI3KCA\_active,\ AKT}} \mathrm{AKT\_active} + \mathrm{PI3KCA\_active} \qquad (17)$$

Reactants

Table 36: Properties of each reactant.

Id	Name	SBO
AKT	AKT	
PI3KCA_active	PI3KCA_active	

Modifiers

Table 37: Properties of each modifier.

Id	Name	SBO
PI3KCA_active	PI3KCA_active	
AKT	AKT	

Products

Table 38: Properties of each product.

Id	Name	SBO
AKT_active	AKT_active	

Id	Name	SBO
PI3KCA_active	PI3KCA_active	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \frac{[\text{PI3KCA\_active}] \cdot \text{k\_AKT\_PI3K} \cdot [\text{AKT}]^{\text{n\_AKT\_PI3K}}}{\text{KM\_AKT\_PI3K}^{\text{n\_AKT\_PI3K}} + [\text{AKT}]^{\text{n\_AKT\_PI3K}}} \tag{18}$$

Table 39: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_AKT_PI3K	k_AKT_PI3K		0.057		☑
n_AKT_PI3K	n_AKT_PI3K		1.000		☑
KM_AKT_PI3K	KM_AKT_PI3K		653951.000		☑

6.10 Reaction Akt_deactivation

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

Name Akt deactivation

Reaction equation

$$\text{AKT\_active} \xrightarrow{\text{AKT\_active}} \text{AKT} \tag{19}$$

Reactant

Table 40: Properties of each reactant.

Id	Name	SBO
AKT_active	AKT_active	

Modifier

Table 41: Properties of each modifier.

Id	Name	SBO
AKT_active	AKT_active	

Product

Table 42: Properties of each product.

Id	Name	SBO
AKT	AKT	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{kd\_AKT} \cdot [\text{AKT\_active}] \tag{20}$$

Table 43: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kd_AKT	kd_AKT		0.005		☑

6.11 Reaction ERK_deactivationBy_PP2A

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

Name ERK deactivation by PP2A

Reaction equation

$$\text{ERK\_active} + \text{PP2A} \xrightarrow{\text{PP2A, ERK\_active}} \text{ERK} + \text{PP2A} \tag{21}$$

Reactants

Table 44: Properties of each reactant.

Id	Name	SBO
ERK_active	ERK_active	
PP2A	PP2A	

Modifiers

Table 45: Properties of each modifier.

Id	Name	SBO
PP2A	PP2A	
ERK_active	ERK_active	

Products

Table 46: Properties of each product.

Id	Name	SBO
ERK	ERK	
PP2A	PP2A	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \frac{[\text{PP2A}] \cdot \text{k\_ERKactive\_PP2A} \cdot [\text{ERK\_active}]^{\text{n\_ERKactive\_PP2A}}}{\text{KM\_ERKactive\_PP2A}^{\text{n\_ERKactive\_PP2A}} + [\text{ERK\_active}]^{\text{n\_ERKactive\_PP2A}}} \tag{22}$$

Table 47: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_ERKactive_PP2A	k_ERKactive_PP2A		8.891		☑
n_ERKactive_PP2A	n_ERKactive_PP2A		1.000		☑
KM_ERKactive_PP2A	KM_ERKactive_PP2A		3496490.000		☑

6.12 Reaction PI3KCA_activationBy_kRas

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

Name PI3KCA activation by kRas

Reaction equation

$$\text{PI3KCA} + \text{Ras\_active} \xrightarrow{\text{Ras\_active, PI3KCA}} \text{PI3KCA\_active} + \text{Ras\_active} \tag{23}$$

Reactants

Table 48: Properties of each reactant.

Id	Name	SBO
PI3KCA	PI3KCA	
Ras_active	Ras_active	

Modifiers

Table 49: Properties of each modifier.

Id	Name	SBO
Ras_active	Ras_active	
PI3KCA	PI3KCA	

Products

Table 50: Properties of each product.

Id	Name	SBO
PI3KCA_active	PI3KCA_active	
Ras_active	Ras_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \frac{[\text{Ras\_active}] \cdot \text{k\_PI3K\_Ras} \cdot [\text{PI3KCA}]^{\text{n\_PI3K\_Ras}}}{\text{KM\_PI3K\_Ras}^{\text{n\_PI3K\_Ras}} + [\text{PI3KCA}]^{\text{n\_PI3K\_Ras}}} \tag{24}$$

Table 51: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_PI3K_Ras	k_PI3K_Ras		0.077		☑
n_PI3K_Ras	n_PI3K_Ras		1.000		☑
KM_PI3K_Ras	KM_PI3K_Ras		272056.000		☑

6.13 Reaction Raf_activationBy_kRas

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

Name Raf activation by kRas

Reaction equation

$$\text{Ras\_active} + \text{Raf} \xrightarrow{\text{Ras\_active, Raf}} \text{Raf\_active} + \text{Ras\_active} \tag{25}$$

Reactants

Table 52: Properties of each reactant.

Id	Name	SBO
Ras_active	Ras_active	
Raf	Raf	

Modifiers

Table 53: Properties of each modifier.

Id	Name	SBO
Ras_active	Ras_active	
Raf	Raf	

Products

Table 54: Properties of each product.

Id	Name	SBO
Raf_active	Raf_active	
Ras_active	Ras_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \frac{[\text{Ras\_active}] \cdot \text{k\_Raf\_RasActive} \cdot [\text{Raf}]^{\text{n\_Raf\_RasActive}}}{\text{KM\_Raf\_RasActive} + [\text{Raf}]^{\text{n\_Raf\_RasActive}}} \tag{26}$$

Table 55: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_Raf_RasActive	k_Raf_RasActive		0.884		☑
n_Raf_RasActive	n_Raf_RasActive		1.000		☑
KM_Raf_RasActive	KM_Raf_RasActive		62464.600		☑

6.14 Reaction Mek_activationBy_Raf

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

Name Mek activation by Raf

Reaction equation

$$\text{Raf\_active} + \text{Mek} \xrightarrow{\text{Raf\_active, Mek}} \text{Mek\_active} + \text{Raf\_active} \tag{27}$$

Reactants

Table 56: Properties of each reactant.

Id	Name	SBO
Raf_active	Raf_active	
Mek	Mek	

Modifiers

Table 57: Properties of each modifier.

Id	Name	SBO
Raf_active	Raf_active	
Mek	Mek	

Products

Table 58: Properties of each product.

Id	Name	SBO
Mek_active	Mek_active	
Raf_active	Raf_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \frac{[\text{Raf\_active}] \cdot \text{k\_Mek\_PP2A} \cdot [\text{Mek}]^{\text{n\_Mek\_PP2A}}}{\text{KM\_MekPP2A}^{\text{n\_Mek\_PP2A}} + [\text{Mek}]^{\text{n\_Mek\_PP2A}}} \tag{28}$$

Table 59: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_Mek_PP2A	k_Mek_PP2A		185.759		☑
n_Mek_PP2A	n_Mek_PP2A		1.000		☑
KM_MekPP2A	KM_MekPP2A		4768350.000		☑

6.15 Reaction Raf_deactivationBy_Akt

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

Name Raf deactivation by Akt

Reaction equation

$$\text{AKT\_active} + \text{Raf\_active} \xrightarrow{\text{AKT\_active, Raf\_active}} \text{Raf} + \text{AKT\_active} \tag{29}$$

Reactants

Table 60: Properties of each reactant.

Id	Name	SBO
AKT_active	AKT_active	
Raf_active	Raf_active	

Modifiers

Table 61: Properties of each modifier.

Id	Name	SBO
AKT_active	AKT_active	
Raf_active	Raf_active	

Products

Table 62: Properties of each product.

Id	Name	SBO
Raf	Raf	
AKT_active	AKT_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \frac{[\text{AKT\_active}] \cdot \text{k\_Raf\_AKT} \cdot [\text{Raf\_active}]^{\text{n\_Raf\_AKT}}}{\text{KM\_Raf\_AKT}^{\text{n\_Raf\_AKT}} + [\text{Raf\_active}]^{\text{n\_Raf\_AKT}}} \tag{30}$$

Table 63: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_Raf_AKT	k_Raf_AKT		15.121		☑
n_Raf_AKT	n_Raf_AKT		1.000		☑
KM_Raf_AKT	KM_Raf_AKT		119355.000		☑

6.16 Reaction Ras_deactivation

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

Name Ras deactivation by RasGab

Reaction equation

$$\text{RasGapActive} + \text{Ras\_active} \xrightarrow{\text{RasGapActive, Ras\_active}} \text{Ras} + \text{RasGapActive} \tag{31}$$

Reactants

Table 64: Properties of each reactant.

Id	Name	SBO
RasGapActive	RasGapActive	
Ras_active	Ras_active	

Modifiers

Table 65: Properties of each modifier.

Id	Name	SBO
RasGapActive	RasGapActive	
Ras_active	Ras_active	

Products

Table 66: Properties of each product.

Id	Name	SBO
Ras	Ras	
RasGapActive	RasGapActive	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \frac{[\text{RasGapActive}] \cdot \text{k\_RasActiveRasGap} \cdot [\text{Ras\_active}]^{\text{n\_RasActiveRasGap}}}{\text{KM\_RasActiveRasGap}^{\text{n\_RasActiveRasGap}} + [\text{Ras\_active}]^{\text{n\_RasActiveRasGap}}} \tag{32}$$

Table 67: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_RasActiveRasGap	k_RasActiveRasGap		1509.36		☑
n_RasActiveRasGap	n_RasActiveRasGap		1.00		☑
KM_RasActiveRasGap	KM_RasActiveRasGap		1432410.00		☑

6.17 Reaction `Mek_deactivation`

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

Name Mek deactivation by PP2A

Reaction equation

$$\mathrm{PP2A} + \mathrm{Mek\_active} \xrightarrow{\mathrm{PP2A,\ Mek\_active}} \mathrm{Mek} + \mathrm{PP2A} \tag{33}$$

Reactants

Table 68: Properties of each reactant.

Id	Name	SBO
`PP2A`	PP2A	
`Mek_active`	Mek_active	

Modifiers

Table 69: Properties of each modifier.

Id	Name	SBO
`PP2A`	PP2A	
`Mek_active`	Mek_active	

Products

Table 70: Properties of each product.

Id	Name	SBO
`Mek`	Mek	
`PP2A`	PP2A	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \frac{[\mathrm{PP2A}] \cdot \mathrm{k\_MekActivePP2A} \cdot [\mathrm{Mek\_active}]^{\mathrm{n\_MekActivePP2A}}}{\mathrm{KM\_MekActivePP2A}^{\mathrm{n\_MekActivePP2A}} + [\mathrm{Mek\_active}]^{\mathrm{n\_MekActivePP2A}}} \tag{34}$$

Table 71: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_MekActivePP2A	k_MekActivePP2A		2.832		☑
n_MekActivePP2A	n_MekActivePP2A		1.000		☑
KM_MekActivePP2A	KM_MekActivePP2A		518753.000		☑

6.18 Reaction IGFR_active_degradation

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

Name IGFR active degradation

Reaction equation

$$\text{IGFR\_active} \xrightarrow{\text{IGFR\_active}} \emptyset \tag{35}$$

Reactant

Table 72: Properties of each reactant.

Id	Name	SBO
IGFR_active	IGFR_active	

Modifier

Table 73: Properties of each modifier.

Id	Name	SBO
IGFR_active	IGFR_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \text{gamma\_IGFR} \cdot [\text{IGFR\_active}] \tag{36}$$

6.19 Reaction PI3KCA_deactivation

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

Name PI3KCA deactivation

Reaction equation

$$\text{PI3KCA\_active} \xrightarrow{\text{PI3KCA\_active}} \text{PI3KCA} \tag{37}$$

Reactant

Table 74: Properties of each reactant.

Id	Name	SBO
PI3KCA_active	PI3KCA_active	

Modifier

Table 75: Properties of each modifier.

Id	Name	SBO
PI3KCA_active	PI3KCA_active	

Product

Table 76: Properties of each product.

Id	Name	SBO
PI3KCA	PI3KCA	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{kd\_PI3K\_a} \cdot [\text{PI3KCA\_active}] \tag{38}$$

6.20 Reaction Raf_deactivation

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

Name Raf deactivation by RafPP

Reaction equation

$$\text{RafPP} + \text{Raf\_active} \xrightarrow{\text{RafPP, Raf\_active}} \text{Raf} + \text{RafPP} \tag{39}$$

Reactants

Table 77: Properties of each reactant.

Id	Name	SBO
RafPP	RafPP	
Raf_active	Raf_active	

Modifiers

Table 78: Properties of each modifier.

Id	Name	SBO
RafPP	RafPP	
Raf_active	Raf_active	

Products

Table 79: Properties of each product.

Id	Name	SBO
Raf	Raf	
RafPP	RafPP	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \frac{[\text{RafPP}] \cdot \text{k\_RasActive\_RafPP} \cdot [\text{Raf\_active}]^{\text{n\_RasActive\_RafPP}}}{\text{KM\_RasActive\_RafPP}^{\text{n\_RasActive\_RafPP}} + [\text{Raf\_active}]^{\text{n\_RasActive\_RafPP}}} \tag{40}$$

Table 80: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_RasActive_RafPP	k_RasActive_RafPP		0.126		☑
n_RasActive_RafPP	n_RasActive_RafPP		1.000		☑
KM_RasActive_RafPP	KM_RasActive_RafPP		1061.710		☑

6.21 Reaction P90_activationBy_ERK

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

Name P90 activation by ERK

Reaction equation

$$\text{P90RskInactive} + \text{ERK\_active} \xrightarrow{\text{ERK\_active, P90RskInactive}} \text{P90Rsk\_Active} + \text{ERK\_active} \tag{41}$$

Reactants

Table 81: Properties of each reactant.

Id	Name	SBO
P90RskInactive	P90RskInactive	
ERK_active	ERK_active	

Modifiers

Table 82: Properties of each modifier.

Id	Name	SBO
ERK_active	ERK_active	
P90RskInactive	P90RskInactive	

Products

Table 83: Properties of each product.

Id	Name	SBO
P90Rsk_Active	P90Rsk_Active	
ERK_active	ERK_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \frac{[\text{ERK\_active}] \cdot \text{k\_P90Rsk\_ERKActive} \cdot [\text{P90RskInactive}]}{\text{KM\_P90Rsk\_ERKActive} + [\text{P90RskInactive}]} \tag{42}$$

6.22 Reaction P90_deactivation

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

Name P90 deactivation

Reaction equation

$$\text{P90Rsk\_Active} \xrightarrow{\text{P90Rsk\_Active}} \text{P90RskInactive} \tag{43}$$

Reactant

Table 84: Properties of each reactant.

Id	Name	SBO
P90Rsk_Active	P90Rsk_Active	

Modifier

Table 85: Properties of each modifier.

Id	Name	SBO
P90Rsk_Active	P90Rsk_Active	

Product

Table 86: Properties of each product.

Id	Name	SBO
P90RskInactive	P90RskInactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \text{kd\_P90Rsk} \cdot [\text{P90Rsk\_Active}] \tag{44}$$

Table 87: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kd_P90Rsk	kd_P90Rsk		0.005		☑

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 EGFR_active

Name EGFR_active

Initial amount 8000 mol

This species takes part in eight reactions (as a reactant in SOS_conformational_activation, EGFR_degradation, PI3KCA_activationBy_EGF and as a product in SOS_conformational_activation, PI3KCA_activationBy_EGF and as a modifier in SOS_conformational_activation, EGFR_degradation, PI3KCA_activationBy_EGF).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{EGFR\_active} = v_1 + v_8 - v_1 - v_3 - v_8 \tag{45}$$

7.2 Species D_SOS

Name D_SOS

Initial amount 120000 mol

This species takes part in five reactions (as a reactant in SOS_conformational_activation, SOS_activationBy_IGF and as a product in SOS_deactivationBy_P90 and as a modifier in SOS_conformational_activation, SOS_activationBy_IGF).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{D\_SOS} = v_5 - v_1 - v_6 \tag{46}$$

7.3 Species A_SOS

Name A_SOS

Initial amount 0 mol

This species takes part in seven reactions (as a reactant in kRas_Activation, SOS_deactivationBy_P90 and as a product in SOS_conformational_activation, kRas_Activation, SOS_activationBy_IGF and as a modifier in kRas_Activation, SOS_deactivationBy_P90).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{A\_SOS} = v_1 + v_2 + v_6 - v_2 - v_5 \tag{47}$$

7.4 Species Raf

Name Raf

Initial amount 120000 mol

This species takes part in four reactions (as a reactant in Raf_activationBy_kRas and as a product in Raf_deactivationBy_Akt, Raf_deactivation and as a modifier in Raf_activationBy_kRas).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Raf} = v_{15} + v_{20} - v_{13} \tag{48}$$

7.5 Species Ras_active

Name Ras_active

Initial amount 0 mol

This species takes part in nine reactions (as a reactant in PI3KCA_activationBy_kRas, Raf_activationBy_kRas, Ras_deactivation and as a product in kRas_Activation, PI3KCA_activationBy_kRas, Raf_activationBy_kRas and as a modifier in PI3KCA_activationBy_kRas, Raf_activationBy_kRas, Ras_deactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ras\_active} = v_2 + v_{12} + v_{13} - v_{12} - v_{13} - v_{16} \tag{49}$$

7.6 Species Mek_active

Name Mek_active

Initial amount 0 mol

This species takes part in six reactions (as a reactant in ERK_activationBy_Mek, Mek_deactivation and as a product in ERK_activationBy_Mek, Mek_activationBy_Raf and as a modifier in ERK_activationBy_Mek, Mek_deactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mek\_active} = v_4 + v_{14} - v_4 - v_{17} \tag{50}$$

7.7 Species ERK

Name ERK

Initial amount 600000 mol

This species takes part in three reactions (as a reactant in ERK_activationBy_Mek and as a product in ERK_deactivationBy_PP2A and as a modifier in ERK_activationBy_Mek).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ERK} = v_{11} - v_4 \tag{51}$$

7.8 Species ERK_active

Name ERK_active

Initial amount 0 mol

This species takes part in six reactions (as a reactant in ERK_deactivationBy_PP2A, P90_activationBy_ERK and as a product in ERK_activationBy_Mek, P90_activationBy_ERK and as a modifier in ERK_deactivationBy_PP2A, P90_activationBy_ERK).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ERK\_active} = v_4 + v_{21} - v_{11} - v_{21} \tag{52}$$

7.9 Species IGFR_active

Name IGFR_active

Initial amount 800 mol

This species takes part in eight reactions (as a reactant in SOS_activationBy_IGF, PI3KCA_activationBy_IGF1R, IGFR_active_degradation and as a product in SOS_activationBy_IGF, PI3KCA_activationBy_IGF1R and as a modifier in SOS_activationBy_IGF, PI3KCA_activationBy_IGF1R, IGFR_active_degradation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IGFR\_active} = v_6 + v_7 - v_6 - v_7 - v_{18} \tag{53}$$

7.10 Species PI3KCA

Name PI3KCA

Initial amount 120000 mol

This species takes part in seven reactions (as a reactant in PI3KCA_activationBy_IGF1R, PI3KCA_activationBy_EGF, PI3KCA_activationBy_kRas and as a product in PI3KCA_deactivation and as a modifier in PI3KCA_activationBy_IGF1R, PI3KCA_activationBy_EGF, PI3KCA_activationBy_kRas).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PI3KCA} = v_{19} - v_7 - v_8 - v_{12} \tag{54}$$

7.11 Species PI3KCA_active

Name PI3KCA_active

Initial amount 0 mol

This species takes part in eight reactions (as a reactant in Akt_activationBy_PI3KCA, PI3KCA_deactivation and as a product in PI3KCA_activationBy_IGF1R, PI3KCA_activationBy_EGF, Akt_activationBy_PI3KCA, PI3KCA_activationBy_kRas and as a modifier in Akt_activationBy_PI3KCA, PI3KCA_deactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PI3KCA\_active} = v_7 + v_8 + v_9 + v_{12} - v_9 - v_{19} \tag{55}$$

7.12 Species AKT_active

Name AKT_active

Initial amount 0 mol

This species takes part in six reactions (as a reactant in Akt_deactivation, Raf_deactivationBy_Akt and as a product in Akt_activationBy_PI3KCA, Raf_deactivationBy_Akt and as a modifier in Akt_deactivation, Raf_deactivationBy_Akt).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AKT\_active} = v_9 + v_{15} - v_{10} - v_{15} \tag{56}$$

7.13 Species AKT

Name AKT

Notes The initial concentration of AKT has been corrected from 120000 to 600000 after refering the matlab file

Initial amount 600000 mol

This species takes part in three reactions (as a reactant in Akt_activationBy_PI3KCA and as a product in Akt_deactivation and as a modifier in Akt_activationBy_PI3KCA).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AKT} = v_{10} - v_9 \tag{57}$$

7.14 Species PP2A

Name PP2A

Initial amount 120000 mol

This species takes part in six reactions (as a reactant in ERK_deactivationBy_PP2A, Mek_deactivation and as a product in ERK_deactivationBy_PP2A, Mek_deactivation and as a modifier in ERK_deactivationBy_PP2A, Mek_deactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PP2A} = v_{11} + v_{17} - v_{11} - v_{17} \tag{58}$$

7.15 Species Ras

Name Ras

Initial amount 120000 mol

This species takes part in three reactions (as a reactant in kRas_Activation and as a product in Ras_deactivation and as a modifier in kRas_Activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ras} = v_{16} - v_2 \tag{59}$$

7.16 Species Raf_active

Name Raf_active

Initial amount 0 mol

This species takes part in eight reactions (as a reactant in Mek_activationBy_Raf, Raf_deactivationBy_Akt, Raf_deactivation and as a product in Raf_activationBy_kRas, Mek_activationBy_Raf and as a modifier in Mek_activationBy_Raf, Raf_deactivationBy_Akt, Raf_deactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Raf\_active} = v_{13} + v_{14} - v_{14} - v_{15} - v_{20} \tag{60}$$

7.17 Species Mek

Name Mek

Initial amount 600000 mol

This species takes part in three reactions (as a reactant in Mek_activationBy_Raf and as a product in Mek_deactivation and as a modifier in Mek_activationBy_Raf).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mek} = v_{17} - v_{14} \tag{61}$$

7.18 Species RasGapActive

Name RasGapActive

Initial amount 120000 mol

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{RasGapActive} = v_{16} - v_{16} \tag{62}$$

7.19 Species RafPP

Name RafPP

Initial amount 120000 mol

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{RafPP} = v_{20} - v_{20} \tag{63}$$

7.20 Species P90RskInactive

Name P90RskInactive

Initial amount 120000 mol

This species takes part in three reactions (as a reactant in P90_activationBy_ERK and as a product in P90_deactivation and as a modifier in P90_activationBy_ERK).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P90RskInactive} = v_{22} - v_{21} \tag{64}$$

7.21 Species P90Rsk_Active

Name P90Rsk_Active

Initial amount 0 mol

This species takes part in six reactions (as a reactant in SOS_deactivationBy_P90, P90_deactivation and as a product in SOS_deactivationBy_P90, P90_activationBy_ERK and as a modifier in SOS_deactivationBy_P90, P90_deactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P90Rsk\_Active} = v_5 + v_{21} - v_5 - v_{22} \tag{65}$$

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

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany