

SBML Model Report

Model name: “Sivakumar2011 - EGF Receptor Signaling Pathway”



May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 1 format. This model was created by the following two authors: Vijayalakshmi Chelliah¹ and KC Sivakumar² at November second 2011 at 2:44 p. m. and last time modified at April eighth 2016 at 5:15 p. m. Table 1 provides an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	2
species types	0	species	23
events	0	constraints	0
reactions	10	function definitions	0
global parameters	38	unit definitions	0
rules	0	initial assignments	0

Model Notes

Sivakumar2011 - EGF Receptor Signaling Pathway

EGFR belongs to the human epidermal receptor (HER) family of receptor tyrosine kinases, which consists of four closely related receptors (EGFR (HER1, erbB1), HER2 (neu, erbB2), HER3 (erbB3), and HER4 (erbB4)) that mediate cellular signaling pathways involved in growth

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and proliferation in response to the binding of a variety of growth factor ligands. There are currently six known endogenous ligands for EGFR: EGF, transforming growth factor- (TGF-), amphiregulin, betacellulin, heparin-binding EGF (HB-EGF), and epiregulin. Upon ligand binding, the EGFR forms homo- or heterodimeric complexes (usually with HER2), which leads to activation of the receptor tyrosine kinase, via autophosphorylation.

References:

- The EGF receptor family—multiple roles in proliferation, differentiation, and neoplasia with an emphasis on HER4.
- An open-and-shut case? Recent insights into the activation of EGF/ErbB receptors.
- EGF receptor signaling: putting a new spin on eye development.
- Epidermal growth factor receptor: a promising target in solid tumours.

This model is described in the article: [A systems biology approach to model neural stem cell regulation by notch, shh, wnt, and EGF signaling pathways](#). Sivakumar KC, Dhanesh SB, Shobana S, James J, Mundayoor S. *Omics: a Journal of Integrative Biology*. 2011; 15(10):729-737

Abstract:

The Notch, Sonic Hedgehog (Shh), Wnt, and EGF pathways have long been known to influence cell fate specification in the developing nervous system. Here we attempted to evaluate the contemporary knowledge about neural stem cell differentiation promoted by various drug-based regulations through a systems biology approach. Our model showed the phenomenon of DAPT-mediated antagonism of Enhancer of split [E(spl)] genes and enhancement of Shh target genes by a SAG agonist that were effectively demonstrated computationally and were consistent with experimental studies. However, in the case of model simulation of Wnt and EGF pathways, the model network did not supply any concurrent results with experimental data despite the fact that drugs were added at the appropriate positions. This paves insight into the potential of crosstalks between pathways considered in our study. Therefore, we manually developed a map of signaling crosstalk, which included the species connected by representatives from Notch, Shh, Wnt, and EGF pathways and highlighted the regulation of a single target gene, Hes-1, based on drug-induced simulations. These simulations provided results that matched with experimental studies. Therefore, these signaling crosstalk models complement as a tool toward the discovery of novel regulatory processes involved in neural stem cell maintenance, proliferation, and differentiation during mammalian central nervous system development. To our knowledge, this is the first report of a simple crosstalk map that highlights the differential regulation of neural stem cell differentiation and underscores the flow of positive and negative regulatory signals modulated by drugs.

This model is hosted on [BioModels Database](#) and identified by: BIOMD0000000394.

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

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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 1

2.3 Unit area

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

Definition m²

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 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
default			3	1	litre	<input checked="" type="checkbox"/>	
c2	Cytosol		3	1	litre	<input checked="" type="checkbox"/>	default

3.1 Compartment default

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

3.2 Compartment c2

This is a three dimensional compartment with a constant size of one litre, which is surrounded by default.

Name Cytosol

4 Species

This model contains 23 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
s21	Akt	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s22	Akt	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s25	MEK1_minus_2	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s26	MEK1_minus_2	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s27	ERK1_minus_2	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s28	ERK1_minus_2	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s29	RKIP	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s30	RKIP	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s31	PP2A	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s33	14_minus_3_minus_3	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s34	Mitogenesis_br_Differentiation	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s23	Raf_minus_1	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s24	Raf_minus_1	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s3	EGF	default	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s123	EGFR	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s124	Ras	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s125	GDP	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s126	GTP	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s127	PKC	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s129	EGFR	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s142	erlotinib	default	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s144	Complex_br_(EGFR/.._br_GAP)	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
s147	Complex(Grb2/../PLC)	c2	$\text{mol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>

5 Parameters

This model contains 38 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcatp_r8- _s124			0.511		<input checked="" type="checkbox"/>
kM_r8_s124- _s23			0.470		<input checked="" type="checkbox"/>
kcatn_r8- _s124			1.083		<input checked="" type="checkbox"/>
kM_r8_s124- _s24			0.786		<input checked="" type="checkbox"/>
kcatp_r8_s31			0.727		<input checked="" type="checkbox"/>
kM_r8_s31_s23			0.614		<input checked="" type="checkbox"/>
kcatn_r8_s31			0.636		<input checked="" type="checkbox"/>
kM_r8_s31_s24			1.367		<input checked="" type="checkbox"/>
kI_r8_s22			0.583		<input checked="" type="checkbox"/>
kI_r8_s29			1.219		<input checked="" type="checkbox"/>
kI_r8_s33			0.293		<input checked="" type="checkbox"/>
kcatp_r9			2.000		<input checked="" type="checkbox"/>
kM_r9_s25			0.626		<input checked="" type="checkbox"/>
kcatn_r9			0.693		<input checked="" type="checkbox"/>
kM_r9_s26			0.463		<input checked="" type="checkbox"/>
kcatp_r11			0.787		<input checked="" type="checkbox"/>
kM_r11_s29			1.459		<input checked="" type="checkbox"/>
kcatn_r11			0.566		<input checked="" type="checkbox"/>
kM_r11_s30			1.021		<input checked="" type="checkbox"/>
kcatp_r14			0.558		<input checked="" type="checkbox"/>
kM_r14_s27			0.038		<input checked="" type="checkbox"/>
kcatn_r14			0.725		<input checked="" type="checkbox"/>
kM_r14_s28			1.650		<input checked="" type="checkbox"/>
kass_r15			2.000		<input checked="" type="checkbox"/>
kdiiss_r15			0.074		<input checked="" type="checkbox"/>
kass_r17_s3			0.730		<input checked="" type="checkbox"/>
kdiiss_r17_s3			1.130		<input checked="" type="checkbox"/>
kI_re11_s142			1.000		<input checked="" type="checkbox"/>
kass_r6_s144			1.000		<input checked="" type="checkbox"/>
kdiiss_r6- _s144			1.000		<input checked="" type="checkbox"/>
kass_r7_s144			1.000		<input checked="" type="checkbox"/>

Id	Name	SBO	Value	Unit	Constant
kdiss_r7-	1.000	<input checked="" type="checkbox"/>			
_s144					
kass_r4_s144	1.000	<input checked="" type="checkbox"/>			
kdiss_r4-	1.000	<input checked="" type="checkbox"/>			
_s144					
Vp_re11	1.000	<input checked="" type="checkbox"/>			
kM_re11_s129	1.000	<input checked="" type="checkbox"/>			
kM_re11_s147	1.000	<input checked="" type="checkbox"/>			
ki_re11_s129	1.000	<input checked="" type="checkbox"/>			

6 Reactions

This model contains ten 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

Nº	Id	Name	Reaction Equation	SBO
1	r8		$s23 \xrightleftharpoons[s22, s29, s124, s33, s31]{s24} s24$	
2	r9		$s25 \xrightleftharpoons[s24]{s26} s26$	
3	r11		$s29 \xrightleftharpoons[s127]{s30} s30$	
4	r14		$s27 \xrightleftharpoons[s26]{s28} s28$	
5	r15		$s28 \rightleftharpoons s34$	
6	r17		$2 s123 \xrightleftharpoons[s3]{s129} s129$	
7	r6		$s127 \xrightleftharpoons[s144]{s127} s127$	
8	r7		$s21 \xrightleftharpoons[s144]{s22} s22$	
9	r4		$s124 + s125 \xrightleftharpoons[s144]{s124 + s126} s124 + s126$	
10	re11		$s129 + s147 \xrightleftharpoons[s142]{s144} s144$	

6.1 Reaction r8

This is a reversible reaction of one reactant forming one product influenced by five modifiers.

Notes kinetics of unireactant enzymes

Reaction equation



Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
s23	Raf_minus_1	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
s22	Akt	
s29	RKIP	
s124	Ras	
s33	14_minus_3_minus_3	
s31	PP2A	

Product

Table 8: Properties of each product.

Id	Name	SBO
s24	Raf_minus_1	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{kI_r8_s22}{kI_r8_s22 + [s22]} \cdot \frac{kI_r8_s29}{kI_r8_s29 + [s29]} \cdot \frac{kI_r8_s33}{kI_r8_s33 + [s33]} \cdot \left([s124] \cdot \frac{\frac{kcatp_r8_s124}{kM_r8_s124_s23} \cdot [s23] - \frac{kcatn_r8_s124}{kM_r8_s124_s24} \cdot [s24]}{1 + \frac{[s23]}{kM_r8_s124_s23} + \frac{[s24]}{kM_r8_s124_s24}} + [s31] \cdot \frac{\frac{kcatp_r8_s31}{kM_r8_s31_s23} \cdot [s23] - \frac{kcatn_r8_s31}{kM_r8_s31_s24} \cdot [s24]}{1 + \frac{[s23]}{kM_r8_s31_s23} + \frac{[s24]}{kM_r8_s31_s24}} \right) \quad (2)$$

6.2 Reaction r9

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Notes kinetics of non-modulated unireactant enzymes

Reaction equation



Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
s25	MEK1_minus_2	

Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
s24	Raf_minus_1	

Product

Table 11: Properties of each product.

Id	Name	SBO
s26	MEK1_minus_2	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = [s24] \cdot \frac{\frac{kcatp_r9}{kM_r9_s25} \cdot [s25] - \frac{kcatn_r9}{kM_r9_s26} \cdot [s26]}{1 + \frac{[s25]}{kM_r9_s25} + \frac{[s26]}{kM_r9_s26}} \quad (4)$$

6.3 Reaction r11

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Notes kinetics of non-modulated unireactant enzymes

Reaction equation



Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
s29	RKIP	

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
s127	PKC	

Product

Table 14: Properties of each product.

Id	Name	SBO
s30	RKIP	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = [s127] \cdot \frac{\frac{kcatp_r11}{kM_r11_s29} \cdot [s29] - \frac{kcatn_r11}{kM_r11_s30} \cdot [s30]}{1 + \frac{[s29]}{kM_r11_s29} + \frac{[s30]}{kM_r11_s30}} \quad (6)$$

6.4 Reaction r14

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Notes kinetics of non-modulated unireactant enzymes

Reaction equation



Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
s27	ERK1_minus_2	

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
s26	MEK1_minus_2	

Product

Table 17: Properties of each product.

Id	Name	SBO
s28	ERK1_minus_2	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = [s26] \cdot \frac{\frac{kcatp_r14}{kM_r14_s27} \cdot [s27] - \frac{kcatn_r14}{kM_r14_s28} \cdot [s28]}{1 + \frac{[s27]}{kM_r14_s27} + \frac{[s28]}{kM_r14_s28}} \quad (8)$$

6.5 Reaction r15

This is a reversible reaction of one reactant forming one product.

Notes mass action rate law for first order forward, first order reverse, reversible reactions, continuous scheme

Reaction equation



Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
s28	ERK1_minus_2	

Product

Table 19: Properties of each product.

Id	Name	SBO
s34	Mitogenesis_br_Differentiation	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = k_{ass_r15} \cdot [s28] - k_{diss_r15} \cdot [s34] \quad (10)$$

6.6 Reaction r17

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Notes reversible rapid-equilibrium random order ternary-complex mechanism with one product

Reaction equation



Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
s123	EGFR	

Modifier

Table 21: Properties of each modifier.

Id	Name	SBO
s3	EGF	

Product

Table 22: Properties of each product.

Id	Name	SBO
s129	EGFR	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = [s3] \cdot (kass_r17_s3 \cdot [s123]^2 - kdiss_r17_s3 \cdot [s129]) \quad (12)$$

6.7 Reaction r6

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Notes kinetics of non-modulated unireactant enzymes

Reaction equation



Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
s127	PKC	

Modifier

Table 24: Properties of each modifier.

Id	Name	SBO
s144	Complex_br_(EGFR/../_br_GAP)	

Product

Table 25: Properties of each product.

Id	Name	SBO
s127	PKC	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = [s144] \cdot (kass_r6_s144 \cdot [s127] - kdiss_r6_s144 \cdot [s127]) \quad (14)$$

6.8 Reaction r7

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Notes kinetics of non-modulated unireactant enzymes

Reaction equation



Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
s21	Akt	

Modifier

Table 27: Properties of each modifier.

Id	Name	SBO
s144	Complex_br_(EGFR/../.br_GAP)	

Product

Table 28: Properties of each product.

Id	Name	SBO
s22	Akt	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = [s144] \cdot (kass_r7_s144 \cdot [s21] - kdiss_r7_s144 \cdot [s22]) \quad (16)$$

6.9 Reaction r4

This is a reversible reaction of two reactants forming two products influenced by one modifier.

Notes reversible rapid-equilibrium random order ternary-complex mechanism with two products

Reaction equation



Reactants

Table 29: Properties of each reactant.

Id	Name	SBO
s124	Ras	
s125	GDP	

Modifier

Table 30: Properties of each modifier.

Id	Name	SBO
s144	Complex_br_(EGFR/../.br_GAP)	

Products

Table 31: Properties of each product.

Id	Name	SBO
s124	Ras	
s126	GTP	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = [s144] \cdot (kass_r4_s144 \cdot [s124] \cdot [s125] - kdiss_r4_s144 \cdot [s124] \cdot [s126]) \quad (18)$$

6.10 Reaction re11

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

Notes mass action rate law for second order irreversible reactions, two reactants, continuous scheme

Reaction equation



Reactants

Table 32: Properties of each reactant.

Id	Name	SBO
s129	EGFR	
s147	Complex(Grb2/../.PLC)	

Modifier

Table 33: Properties of each modifier.

Id	Name	SBO
s142	erlotinib	

Product

Table 34: Properties of each product.

Id	Name	SBO
s144	Complex_br_(EGFR/../.br_GAP)	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \frac{kI_re11_s142}{kI_re11_s142 + [s142]} \cdot \frac{Vp_re11 \cdot [s129] \cdot [s147]}{ki_re11_s129 \cdot kM_re11_s147 + kM_re11_s147 \cdot [s129] + kM_re11_s129 \cdot [s147] + [s129] \cdot [s147]} \quad (20)$$

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 s21

Name Akt

Notes Long Name: Thymoma viral proto-oncogene
Synonym: PKB, RAC protein kinase, protein kinase B
Accession: P00551

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in [r7](#)).

$$\frac{d}{dt}s21 = - v_8 \quad (21)$$

7.2 Species s22

Name Akt

Notes Long Name: Thymoma viral proto-oncogene
Synonym: PKB,RAC protein kinase,protein kinase B
Accession: P00551

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a product in [r7](#) and as a modifier in [r8](#)).

$$\frac{d}{dt}s22 = v_8 \quad (22)$$

7.3 Species s25

Name MEK1_minus_2

Notes Long Name: MAP/ERK kinase
Synonym: Dual specificity mitogen-activated protein kinase kinase
Accession: P00559

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in [r9](#)).

$$\frac{d}{dt}s25 = - v_2 \quad (23)$$

7.4 Species s26

Name MEK1_minus_2

Notes Long Name: MAP/ERK kinase
Synonym: Dual specificity mitogen-activated protein kinase kinase
Accession: P00559

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a product in [r9](#) and as a modifier in [r14](#)).

$$\frac{d}{dt}s26 = v_2 \quad (24)$$

7.5 Species s27

Name ERK1_minus_2

Notes Long Name: Extracellular signal-regulated kinase
Synonym: MAPK,Mitogen-activated protein kinase,pp42/44
Accession: P00543

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in [r14](#)).

$$\frac{d}{dt}s27 = - \textcolor{blue}{v}_4 \quad (25)$$

7.6 Species s28

Name ERK1_minus_2

Notes Long Name: Extracellular signal-regulated kinase
Synonym: MAPK,Mitogen-activated protein kinase,pp42/44
Accession: P00543

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in [r15](#) and as a product in [r14](#)).

$$\frac{d}{dt}s28 = \textcolor{blue}{v}_4 - \textcolor{blue}{v}_5 \quad (26)$$

7.7 Species s29

Name RKIP

Notes Long Name: Raf-1 kinase inhibitor protein
Synonym: Hippocampal cholinergic stimulatory peptide precursor,PEBP,Phosphatidylethanolamine-binding protein,Terminal flower 1,neuropolypeptide h3,prostastic binding protein
Accession: P00548

Initial amount 5 mol

Charge 0

This species takes part in two reactions (as a reactant in [r11](#) and as a modifier in [r8](#)).

$$\frac{d}{dt}s29 = - \textcolor{blue}{v}_3 \quad (27)$$

7.8 Species s30

Name RKIP

Notes Long Name: Raf-1 kinase inhibitor protein
Synonym: Hippocampal cholinergic stimulatory peptide precursor,PEBP,Phosphatidylethanolamine-binding protein,Terminal flower 1,neuropolypeptide h3,prostactic binding protein
Accession: P00548

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in [r11](#)).

$$\frac{d}{dt}s30 = v_3 \quad (28)$$

7.9 Species s31

Name PP2A

Notes Long Name: protein phosphatase 2ASynonym: Serine/threonine protein phosphatase 2AAccession: P00547

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a modifier in [r8](#)).

$$\frac{d}{dt}s31 = 0 \quad (29)$$

7.10 Species s33

Name 14_minus_3_minus_3

Notes Long Name: 14-3-3Synonym: PAR-5,Stratifin,protein kinase C inhibitor protein-1 (KCIP-1)Accession: P00539

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a modifier in [r8](#)).

$$\frac{d}{dt}s33 = 0 \quad (30)$$

7.11 Species s34

Name Mitogenesis_br_Differentiation

Notes Long Name: Mitogenesis DifferentiationSynonym: Synonym not specifiedAccession: U02228

Initial amount 1 mol

Charge 0

This species takes part in one reaction (as a product in [r15](#)).

$$\frac{d}{dt}s34 = \textcolor{blue}{v_5} \quad (31)$$

7.12 Species s23

Name Raf_minus_1

Notes Long Name: RAF proto-oncogene serine/threonine-protein kinaseSynonym: C-Raf,MAP kinase kinase kinase,Raf-1Accession: P00560

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in [r8](#)).

$$\frac{d}{dt}s23 = - \textcolor{blue}{v_1} \quad (32)$$

7.13 Species s24

Name Raf_minus_1

Notes Long Name: RAF proto-oncogene serine/threonine-protein kinaseSynonym: C-Raf,MAP kinase kinase kinase,Raf-1Accession: P00560

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a product in [r8](#) and as a modifier in [r9](#)).

$$\frac{d}{dt}s24 = \textcolor{blue}{v_1} \quad (33)$$

7.14 Species s3

Name EGF

Notes Long Name: Epidermal growth factorSynonym: gurken,transforming growth factor al-phaAccession: P00549

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a modifier in [r17](#)).

$$\frac{d}{dt}s3 = 0 \quad (34)$$

7.15 Species s123

Name EGFR

Notes Long Name: EGFRSynonym: Gurken receptor, Erb, Neu, neuregulinAccession: P00542

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in [r17](#)).

$$\frac{d}{dt}s123 = -2 \text{ } v_6 \quad (35)$$

7.16 Species s124

Name Ras

Notes Long Name: RasSynonym: Synonym not specifiedAccession: P00552

Initial amount 5 mol

Charge 0

This species takes part in three reactions (as a reactant in [r4](#) and as a product in [r4](#) and as a modifier in [r8](#)).

$$\frac{d}{dt}s124 = v_9 - v_9 \quad (36)$$

7.17 Species s125

Name GDP

Notes Long Name: GDPSynonym: Synonym not specifiedAccession: S01652

Initial amount 0.5 mol

Charge 0

This species takes part in one reaction (as a reactant in [r4](#)).

$$\frac{d}{dt}s125 = - \boxed{v_9} \quad (37)$$

7.18 Species s126

Name GTP

Notes Long Name: GTPSynonym: Synonym not specifiedAccession: S01653

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in [r4](#)).

$$\frac{d}{dt}s126 = \boxed{v_9} \quad (38)$$

7.19 Species s127

Name PKC

Notes Long Name: PKCSynonym: Synonym not specifiedAccession: P00565

Initial amount 2 mol

Charge 0

This species takes part in three reactions (as a reactant in [r6](#) and as a product in [r6](#) and as a modifier in [r11](#)).

$$\frac{d}{dt}s127 = \boxed{v_7} - \boxed{v_7} \quad (39)$$

7.20 Species s129

Name EGFR

Notes Long Name: EGFR
Synonym: Gurken receptor, Erb, Neu, neuregulin
Accession: P00542

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in [re11](#) and as a product in [r17](#)).

$$\frac{d}{dt}s129 = \textcolor{blue}{v_6} - \textcolor{blue}{v_{10}} \quad (40)$$

7.21 Species s142

Name erlotinib

Initial amount 0.5 mol

Charge 0

This species takes part in one reaction (as a modifier in [re11](#)).

$$\frac{d}{dt}s142 = 0 \quad (41)$$

7.22 Species s144

Name Complex_br_(EGFR/./_br_GAP)

Initial amount 0 mol

Charge 0

This species takes part in four reactions (as a product in [re11](#) and as a modifier in [r6](#), [r7](#), [r4](#)).

$$\frac{d}{dt}s144 = \textcolor{blue}{v_{10}} \quad (42)$$

7.23 Species s147

Name Complex(Grb2/./PLC)

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in [re11](#)).

$$\frac{d}{dt}s147 = -\textcolor{blue}{v_{10}} \quad (43)$$

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