SBML Model Report

Model name: "Sivakumar2011-_NeuralStemCellDifferentiation_Crosstalk"

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 Chelliah[1] and KC Sivakumar[2] at November second 2011 at 2:54 p. m. and last time modified at April eighth 2016 at 5:17 p. 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	2
species types	0	species	27
events	0	constraints	0
reactions	12	function definitions	0
global parameters	37	unit definitions	0
rules	0	initial assignments	0

Model Notes

Sivakumar2011_NeuralStemCellDifferentiation_CrosstalkThis model is generated by integrating BIOMD0000000394(EGFR), BIOMD0000000395(Hedgehog), BIOMD0000000396(Notch) and BIOMD0000000397(Wnt), to investigate the signalling crosstalk between the fourpathways.

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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 2011 Oct; 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: BIOMD0000000398.

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 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	☑	
`c1`	nucleus		3	1	litre	☑	`default`

3.1 Compartment `default`

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

3.2 Compartment `c1`

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

Name nucleus

4 Species

This model contains 27 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
s53	NICD	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s57	Notch	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s58	Notch TM	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s60	Gamma secretase	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s61	DAPT	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s68	RBP-jk	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s72	Complex NICD-RBP	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s73	Hes-1	c1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s81	Shh	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s83	Ptch1	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s85	Complex Shh Ptch1	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s88	smo	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s89	SAG	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s96	EGF	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s98	EGFR	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s100	Complex EGF-EGFR	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s101	Erlotinib	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s107	Wnt	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s109	Frzzl	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s111	Complex Wnt-Frzzl	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s122	Dishevelled	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s124	FRAT-CK2	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
s135	Complex Dishevelled-FRAT-CK2	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s142	GSK3B	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s144	Beta-catenin	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s146	Complex GSK3B-Bcatenin	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s147	6 bromoindirubin 3‘oxime	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 37 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kV_re29_s60			1.0		☑
kM_re29_s60-_s57			1.0		☑
kG_s57			1.0		☑
kM_re29_s60-_s53			1.0		☑
kG_s53			1.0		☑
kM_re29_s60-_s58			1.0		☑
kG_s58			1.0		☑
kI_re29_s61			1.0		☑
kass_re31			1.0		☑
kdiss_re31			1.0		☑
kass_re32			1.0		☑
kdiss_re32			1.0		☑
kass_re33			1.0		☑
kdiss_re33			1.0		☑
kass_re36			1.0		☑
kdiss_re36			1.0		☑
kI_re36_s101			1.0		☑
kass_re37			1.0		☑
kdiss_re37			1.0		☑
kass_re38			1.0		☑
kdiss_re38			1.0		☑
kcatp_re40			1.0		☑
kcatn_re40			1.0		☑
kM_re40_s124			1.0		☑
ki_re40_s124			1.0		☑
kass_re42			1.0		☑
kdiss_re42			1.0		☑
kI_re42_s147			1.0		☑
kI_re42_s135			1.0		☑
kass_re43			1.0		☑
kdiss_re43			1.0		☑
kass_re34-_s85			1.0		☑

Id	Name	SBO	Value	Unit	Constant
kdiss_re34_s85			1.0		☑
kass_re34_s89			1.0		☑
kdiss_re34_s89			1.0		☑
kass_re35_s89			1.0		☑
kdiss_re35_s89			1.0		☑

6 Reactions

This model contains twelve 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	re29		$s57 \xrightleftharpoons{s60,\ s61} s53 + s58$	
2	re31		$s53 + s68 \rightleftharpoons s72$	
3	re32		$s72 \rightleftharpoons s73$	
4	re33		$s81 + s83 \rightleftharpoons s85$	
5	re36		$s96 + s98 \xrightleftharpoons{s101} s100$	
6	re37		$s100 \rightleftharpoons s73$	
7	re38		$s107 + s109 \rightleftharpoons s111$	
8	re40		$s122 + s124 \xrightleftharpoons{s111} s135$	
9	re42		$s142 + s144 \xrightleftharpoons{s147,\ s135} s146$	
10	re43		$s144 \rightleftharpoons s73$	
11	re34		$s88 \xrightleftharpoons{s85,\ s89} s88$	
12	re35		$s88 \xrightleftharpoons{s89} s73$	

6.1 Reaction re29

This is a reversible reaction of one reactant forming two products influenced by two modifiers.

Notes reversible thermodynamically independent convenience kinetics

Reaction equation

$$\mathrm{s57} \overset{\mathrm{s60,\ s61}}{\rightleftharpoons} \mathrm{s53} + \mathrm{s58} \tag{1}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
s57	Notch	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
s60	Gamma secretase	
s61	DAPT	

Products

Table 8: Properties of each product.

Id	Name	SBO
s53	NICD	
s58	Notch TM	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{\mathrm{kI\_re29\_s61}}{\mathrm{kI\_re29\_s61} + [\mathrm{s61}]} \cdot [\mathrm{s60}] \cdot \mathrm{kV\_re29\_s60} \cdot \frac{\frac{[\mathrm{s57}]}{\mathrm{kM\_re29\_s60\_s57}} \cdot \sqrt{2} - \frac{[\mathrm{s53}]}{\mathrm{kM\_re29\_s60\_s53}} \cdot \frac{[\mathrm{s58}]}{\mathrm{kM\_re29\_s60\_s58}} \cdot \sqrt{2}}{\frac{[\mathrm{s57}]}{\mathrm{kM\_re29\_s60\_s57}} + \left(1 + \frac{[\mathrm{s53}]}{\mathrm{kM\_re29\_s60\_s53}}\right) \cdot \left(1 + \frac{[\mathrm{s58}]}{\mathrm{kM\_re29\_s60\_s58}}\right)} \tag{2}$$

6.2 Reaction re31

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

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

Reaction equation

$$\mathrm{s53} + \mathrm{s68} \rightleftharpoons \mathrm{s72} \tag{3}$$

Reactants

Table 9: Properties of each reactant.

Id	Name	SBO
s53	NICD	
s68	RBP-jk	

Product

Table 10: Properties of each product.

Id	Name	SBO
s72	Complex NICD-RBP	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{kass\_re31} \cdot [\mathrm{s53}] \cdot [\mathrm{s68}] - \mathrm{kdiss\_re31} \cdot [\mathrm{s72}] \tag{4}$$

6.3 Reaction re32

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

$$\mathrm{s72} \rightleftharpoons \mathrm{s73} \tag{5}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
s72	Complex NICD-RBP	

Product

Table 12: Properties of each product.

Id	Name	SBO
s73	Hes-1	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{kass\_re32} \cdot [\text{s72}] - \text{kdiss\_re32} \cdot [\text{s73}] \tag{6}$$

6.4 Reaction re33

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

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

Reaction equation

$$\text{s81} + \text{s83} \rightleftharpoons \text{s85} \tag{7}$$

Reactants

Table 13: Properties of each reactant.

Id	Name	SBO
s81	Shh	
s83	Ptch1	

Product

Table 14: Properties of each product.

Id	Name	SBO
s85	Complex Shh Ptch1	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{kass\_re33} \cdot [\text{s81}] \cdot [\text{s83}] - \text{kdiss\_re33} \cdot [\text{s85}] \tag{8}$$

6.5 Reaction re36

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

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

Reaction equation

$$\text{s96} + \text{s98} \overset{\text{s101}}{\rightleftharpoons} \text{s100} \tag{9}$$

Reactants

Table 15: Properties of each reactant.

Id	Name	SBO
s96	EGF	
s98	EGFR	

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
s101	Erlotinib	

Product

Table 17: Properties of each product.

Id	Name	SBO
s100	Complex EGF-EGFR	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \frac{\text{kI\_re36\_s101}}{\text{kI\_re36\_s101} + [\text{s101}]} \cdot (\text{kass\_re36} \cdot [\text{s96}] \cdot [\text{s98}] - \text{kdiss\_re36} \cdot [\text{s100}]) \tag{10}$$

6.6 Reaction re37

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

$$\text{s100} \rightleftharpoons \text{s73} \tag{11}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
s100	Complex EGF-EGFR	

Product

Table 19: Properties of each product.

Id	Name	SBO
s73	Hes-1	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{kass\_re37} \cdot [\text{s100}] - \text{kdiss\_re37} \cdot [\text{s73}] \tag{12}$$

6.7 Reaction re38

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

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

Reaction equation

$$\mathrm{s107} + \mathrm{s109} \rightleftharpoons \mathrm{s111} \tag{13}$$

Reactants

Table 20: Properties of each reactant.

Id	Name	SBO
s107	Wnt	
s109	Frzzl	

Product

Table 21: Properties of each product.

Id	Name	SBO
s111	Complex Wnt-Frzzl	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{kass\_re38} \cdot [\mathrm{s107}] \cdot [\mathrm{s109}] - \mathrm{kdiss\_re38} \cdot [\mathrm{s111}] \tag{14}$$

6.8 Reaction re40

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

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

Reaction equation

$$\mathrm{s122} + \mathrm{s124} \overset{\mathrm{s111}}{\rightleftharpoons} \mathrm{s135} \tag{15}$$

Reactants

Table 22: Properties of each reactant.

Id	Name	SBO
s122	Dishevelled	
s124	FRAT-CK2	

Modifier

Table 23: Properties of each modifier.

Id	Name	SBO
s111	Complex Wnt-Frzzl	

Product

Table 24: Properties of each product.

Id	Name	SBO
s135	Complex Dishevelled-FRAT-CK2	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \frac{\frac{\text{kcatp\_re40}}{\text{ki\_re40\_s124}\cdot\text{kM\_re40\_s124}} \cdot [\text{s111}] \cdot [\text{s122}] \cdot [\text{s124}] - \frac{\text{kcatn\_re40}}{\text{kM\_re40\_s124}} \cdot [\text{s111}] \cdot [\text{s135}]}{1 + \frac{[\text{s122}]}{\text{ki\_re40\_s124}} + \frac{[\text{s124}]}{\text{ki\_re40\_s124}} + \frac{[\text{s122}]\cdot[\text{s124}]}{\text{ki\_re40\_s124}\cdot\text{kM\_re40\_s124}} + \frac{[\text{s135}]}{\text{kM\_re40\_s124}}} \tag{16}$$

6.9 Reaction re42

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

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

Reaction equation

$$\text{s142} + \text{s144} \underset{}{\overset{\text{s147, s135}}{\rightleftharpoons}} \text{s146} \tag{17}$$

Reactants

Table 25: Properties of each reactant.

Id	Name	SBO
s142	GSK3B	
s144	Beta-catenin	

Modifiers

Table 26: Properties of each modifier.

Id	Name	SBO
s147	6 bromoindirubin 3‘oxime	
s135	Complex Dishevelled-FRAT-CK2	

Product

Table 27: Properties of each product.

Id	Name	SBO
s146	Complex GSK3B-Bcatenin	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \frac{\text{kI\_re42\_s147}}{\text{kI\_re42\_s147} + [\text{s147}]} \cdot \frac{\text{kI\_re42\_s135}}{\text{kI\_re42\_s135} + [\text{s135}]} \cdot (\text{kass\_re42} \cdot [\text{s142}] \cdot [\text{s144}] - \text{kdiss\_re42} \cdot [\text{s146}]) \tag{18}$$

6.10 Reaction re43

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

$$\text{s144} \rightleftharpoons \text{s73} \tag{19}$$

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
s144	Beta-catenin	

Product

Table 29: Properties of each product.

Id	Name	SBO
s73	Hes-1	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{kass\_re43} \cdot [\text{s144}] - \text{kdiss\_re43} \cdot [\text{s73}] \tag{20}$$

6.11 Reaction re34

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

Notes kinetics of non-modulated unireactant enzymes

Reaction equation

$$\text{s88} \overset{\text{s85, s89}}{\rightleftharpoons} \text{s88} \tag{21}$$

Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
s88	smo	

Modifiers

Table 31: Properties of each modifier.

Id	Name	SBO
s85	Complex Shh Ptch1	

Id	Name	SBO
s89	SAG	

Product

Table 32: Properties of each product.

Id	Name	SBO
s88	smo	

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{11} = {} & [\text{s85}] \cdot (\text{kass\_re34\_s85} \cdot [\text{s88}] - \text{kdiss\_re34\_s85} \cdot [\text{s88}]) \\ & + [\text{s89}] \cdot (\text{kass\_re34\_s89} \cdot [\text{s88}] - \text{kdiss\_re34\_s89} \cdot [\text{s88}]) \end{aligned} \tag{22}$$

6.12 Reaction re35

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

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

Reaction equation

$$\text{s88} \overset{\text{s89}}{\rightleftharpoons} \text{s73} \tag{23}$$

Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
s88	smo	

Modifier

Table 34: Properties of each modifier.

Id	Name	SBO
s89	SAG	

Id	Name	SBO

Product

Table 35: Properties of each product.

Id	Name	SBO
s73	Hes-1	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = [\text{s89}] \cdot (\text{kass\_re35\_s89} \cdot [\text{s88}] - \text{kdiss\_re35\_s89} \cdot [\text{s73}]) \tag{24}$$

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 s53

Name NICD

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in re31 and as a product in re29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{s53} = v_1 - v_2 \tag{25}$$

7.2 Species s57

Name Notch

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s57} = -v_1 \tag{26}$$

7.3 Species s58

Name Notch TM

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in re29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s58} = v_1 \tag{27}$$

7.4 Species s60

Name Gamma secretase

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a modifier in re29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s60} = 0 \tag{28}$$

7.5 Species s61

Name DAPT

Initial amount 100 mol

Charge 0

This species takes part in one reaction (as a modifier in re29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s61} = 0 \tag{29}$$

7.6 Species s68

Name RBP-jk

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re31).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s68} = -v_2 \tag{30}$$

7.7 Species s72

Name Complex NICD-RBP

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in re32 and as a product in re31).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s72} = v_2 - v_3 \tag{31}$$

7.8 Species s73

Name Hes-1

Initial amount 0 mol

Charge 0

This species takes part in four reactions (as a product in re32, re37, re43, re35).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s73} = v_3 + v_6 + v_{10} + v_{12} \tag{32}$$

7.9 Species s81

Name Shh

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re33).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s81} = -v_4 \tag{33}$$

7.10 Species s83

Name Ptch1

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re33).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s83} = -v_4 \tag{34}$$

7.11 Species s85

Name Complex Shh Ptch1

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a product in re33 and as a modifier in re34).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s85} = v_4 \tag{35}$$

7.12 Species s88

Name smo

Initial amount 5 mol

Charge 0

This species takes part in three reactions (as a reactant in re34, re35 and as a product in re34).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s88} = v_{11} - v_{11} - v_{12} \tag{36}$$

7.13 Species s89

Name SAG

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a modifier in re34, re35).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s89} = 0 \tag{37}$$

7.14 Species s96

Name EGF

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re36).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s96} = -v_5 \tag{38}$$

7.15 Species s98

Name EGFR

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re36).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s98} = -v_5 \tag{39}$$

7.16 Species s100

Name Complex EGF-EGFR

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in re37 and as a product in re36).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s100} = v_5 - v_6 \tag{40}$$

7.17 Species s101

Name Erlotinib

Initial amount 100 mol

Charge 0

This species takes part in one reaction (as a modifier in re36).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s101} = 0 \tag{41}$$

7.18 Species s107

Name Wnt

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re38).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s107} = -v_7 \tag{42}$$

7.19 Species s109

Name Frzzl

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re38).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s109} = -v_7 \tag{43}$$

7.20 Species s111

Name Complex Wnt-Frzzl

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a product in re38 and as a modifier in re40).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s111} = v_7 \tag{44}$$

7.21 Species s122

Name Dishevelled

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re40).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s122} = -v_8 \tag{45}$$

7.22 Species s124

Name FRAT-CK2

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re40).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s124} = -v_8 \tag{46}$$

7.23 Species s135

Name Complex Dishevelled-FRAT-CK2

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a product in re40 and as a modifier in re42).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s135} = v_8 \tag{47}$$

7.24 Species s142

Name GSK3B

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re42).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s142} = -v_9 \tag{48}$$

7.25 Species s144

Name Beta-catenin

Initial amount 5 mol

Charge 0

This species takes part in two reactions (as a reactant in re42, re43).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s144} = -v_9 - v_{10} \tag{49}$$

7.26 Species s146

Name Complex GSK3B-Bcatenin

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in re42).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s146} = v_9 \tag{50}$$

7.27 Species s147

Name 6 bromoindirubin 3‘oxime

Initial amount 100 mol

Charge 0

This species takes part in one reaction (as a modifier in re42).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s147} = 0 \tag{51}$$

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