SBML Model Report

Model name: "Sivakumar2011 - Notch 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 Chelliah[1] and KC Sivakumar[2] at November second 2011 at 2:45 p.m. and last time modified at April eighth 2016 at 5:16 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	3
species types	0	species	36
events	0	constraints	0
reactions	16	function definitions	0
global parameters	56	unit definitions	0
rules	0	initial assignments	0

Model Notes

Sivakumar2011 - Notch Signaling Pathway

Notch is a transmembrane receptor that mediates local cell-cell communication and coordinates a signaling cascade. It plays a key role in modulating cell fate decisions throughout the

[1]EMBL-EBI, `viji@ebi.ac.uk`
[2]Rajiv Gandhi Centre for Biotechnology, `sivakumar.kc@gmail.com`

development of invertebrate and vertebrate species and the misregulation leads to a number of human diseases.

References:

- Notch signaling: from the outside in.

- Notch signaling in hematopoiesis and early lymphocyte development.

- An overview of the Notch signalling pathway.

- Notch and cancer: best to avoid the ups and downs.

- Notch signaling: control of cell communication and cell fate.

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: BIOMD0000000396.

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 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 three compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
default			3	1	litre	☑	
c1	cytosol		3	1	litre	☑	default
c5	nucleus		3	1	litre	☑	c1

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 cytosol

3.3 Compartment `c5`

This is a three dimensional compartment with a constant size of one litre, which is surrounded by `c1` (cytosol).

Name nucleus

4 Species

This model contains 36 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
s2	Fringe	default	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s4	fucose	default	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s7	Delta	default	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s15	NI_sub_c_sub_t	c1	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s19	N_sub_tm	c1	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s21	TACE	c1	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s22	a7_degraded	default	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s23	Neuralized	default	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s25	Numb	c1	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s27	Mastermind	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s26	Su(H)	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s28	CoR	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s32	Complex_br_(Su(H)/CoR)	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s29	CoA	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s24	NI_sub_c_sub_s	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s35	Complex_br_(Mastermind/Su(H)/_br-_CoA/NI_sub_c_sub_s)	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s37	NI_sub_c_sub_s	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s38	Sel 10	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s39	Ub	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s40	a46_degraded	c5	$\text{mol} \cdot \text{l}^{-1}$	☐	☐
s1	Notch	c1	$\text{mol} \cdot \text{l}^{-1}$	☐	☐

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
s18	Complex_br_(Delta/N_sub_ext)	default	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s41	Notch	c1	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s42	Neurotic	default	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s48	Serrate	default	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s53	Complex_br_(Serrate/Notch)	c1	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s60	Complex_br_(Serrate/N_sub_ext)	default	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s63	NI_sub_c_sub_s	c1	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s64	a25_degraded	c1	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s65	LNXp80	c1	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s67	Complex_br_(Notch/Delta)	c1	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s75	E(spl)-C genes	c5	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s76	s76	default	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s77	s77	default	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s81	dapt	default	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟
s82	gama secretase	default	$\mathrm{mol}\cdot\mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 56 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcatp_r8			0.500		✓
kM_r8_s15			1.000		✓
kcatn_r8			1.500		✓
kM_r8_s19			2.000		✓
kM_r8_s63			1.500		✓
kcatp_r9			1.500		✓
kM_r9_s7			1.000		✓
kcatn_r9			0.040		✓
kM_r9_s22			0.050		✓
kass_r10			2.000		✓
kdiss_r10			0.010		✓
kI_r10_s25			1.000		✓
kcatp_r11			0.500		✓
kM_r11_s32			1.000		✓
kcatn_r11			0.500		✓
kM_r11_s26			1.500		✓
kM_r11_s28			1.000		✓
kass_r13			0.500		✓
kdiss_r13			2.000		✓
kcatp_r16			1.000		✓
kcatn_r16			1.000		✓
kM_r16_s39			1.000		✓
ki_r16_s39			1.000		✓
kass_r17			1.500		✓
kdiss_r17			1.500		✓
kcatp_r18			1.000		✓
kcatn_r18			1.500		✓
kM_r18_s4			1.000		✓
ki_r18_s4			1.500		✓
kass_r21			1.500		✓
kdiss_r21			1.500		✓
kI_r21_s2			1.500		✓
kcatp_r25			1.000		✓
kM_r25_s53			1.500		✓
kcatn_r25			1.500		✓
kM_r25_s60			1.250		✓
kM_r25_s15			1.500		✓

Id	Name	SBO	Value	Unit	Constant
kcatp_r26			0.500		☑
kM_r26_s25			1.700		☑
kcatn_r26			1.000		☑
kM_r26_s64			1.610		☑
kcatp_r28			1.710		☑
kcatn_r28			1.480		☑
kM_r28_s41			1.640		☑
ki_r28_s41			1.280		☑
kcatp_r29			1.860		☑
kM_r29_s67			1.610		☑
kcatn_r29			1.780		☑
kM_r29_s18			0.150		☑
kM_r29_s15			1.870		☑
kass_r30			1.950		☑
kass_r31			0.055		☑
kdiss_r31			2.000		☑
kass_re16			0.004		☑
kdiss_re16			2.000		☑
kI_re16_s81			0.006		☑

6 Reactions

This model contains 16 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	r30		$s32 \longrightarrow s75$	
2	r31		$s35 \longrightarrow s75$	
3	r8		$s15 \xrightarrow{s82} s19 + s63$	
4	r9		$s7 \xrightarrow{s23} s22$	
5	r10		$s63 \xrightarrow{s25} s24$	
6	r11		$s32 \xrightarrow{s24} s26 + s28$	
7	r13		$s24 + s26 + s27 + s29 \rightleftharpoons s35$	
8	r16		$s24 + s39 \xrightarrow{s38} s37$	
9	r17		$s37 \rightleftharpoons s40$	
10	r18		$s1 + s4 \xrightarrow{s42} s41$	
11	r21		$s41 + s48 \xrightarrow{s2} s53$	
12	r25		$s53 \xrightarrow{s21} s60 + s15$	
13	r26		$s25 \xrightarrow{s65} s64$	
14	r28		$s7 + s41 \xrightarrow{s2} s67$	
15	r29		$s67 \xrightarrow{s21} s18 + s15$	
16	re16		$s76 + s77 \xrightarrow{s81} s82$	

6.1 Reaction r30

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

Reaction equation

$$s32 \longrightarrow s75 \tag{1}$$
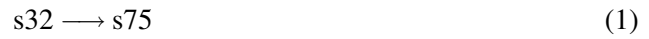
Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
s32	Complex_br_(Su(H)/CoR)	

Product

Table 7: Properties of each product.

Id	Name	SBO
s75	E(spl)-C genes	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{kass\_r30} \cdot [\text{s32}] \tag{2}$$

6.2 Reaction r31

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

Reaction equation

$$s35 \longrightarrow s75 \tag{3}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
s35	Complex_br_(Mastermind/Su(H)/_br_CoA/NI_sub_c_sub_s)	

Product

Table 9: Properties of each product.

Id	Name	SBO
s75	E(spl)-C genes	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{kass\_r31} \cdot [s35] - \text{kdiss\_r31} \cdot [s75] \tag{4}$$

6.3 Reaction r8

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

Notes reversible simple convenience kinetics

Reaction equation

$$s15 \overset{s82}{\rightleftharpoons} s19 + s63 \tag{5}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
s15	NI_sub_c_sub_t	

Modifier

Table 11: Properties of each modifier.

Id	Name	SBO
s82	gama secretase	

Products

Table 12: Properties of each product.

Id	Name	SBO
s19	N_sub_tm	
s63	NI_sub_c_sub_s	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = [s82] \cdot \frac{\text{kcatp\_r8} \cdot \frac{[s15]}{\text{kM\_r8\_s15}} - \text{kcatn\_r8} \cdot \frac{[s19]}{\text{kM\_r8\_s19}} \cdot \frac{[s63]}{\text{kM\_r8\_s63}}}{\frac{[s15]}{\text{kM\_r8\_s15}} + \left(1 + \frac{[s19]}{\text{kM\_r8\_s19}}\right) \cdot \left(1 + \frac{[s63]}{\text{kM\_r8\_s63}}\right)} \tag{6}$$

6.4 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

$$s7 \xrightleftharpoons{s23} s22 \tag{7}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
s7	Delta	

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
s23	Neuralized	

Product

Table 15: Properties of each product.

Id	Name	SBO
s22	a7_degraded	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = [\text{s23}] \cdot \frac{\frac{\text{kcatp\_r9}}{\text{kM\_r9\_s7}} \cdot [\text{s7}] - \frac{\text{kcatn\_r9}}{\text{kM\_r9\_s22}} \cdot [\text{s22}]}{1 + \frac{[\text{s7}]}{\text{kM\_r9\_s7}} + \frac{[\text{s22}]}{\text{kM\_r9\_s22}}} \tag{8}$$

6.5 Reaction `r10`

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

$$\text{s63} \xrightleftharpoons{\text{s25}} \text{s24} \tag{9}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
s63	NI_sub_c_sub_s	

Modifier

Table 17: Properties of each modifier.

Id	Name	SBO
s25	Numb	

Product

Table 18: Properties of each product.

Id	Name	SBO
s24	NI_sub_c_sub_s	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \frac{kI\_r10\_s25}{kI\_r10\_s25 + [s25]} \cdot (kass\_r10 \cdot [s63] - kdiss\_r10 \cdot [s24]) \tag{10}$$

6.6 Reaction r11

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

Notes reversible simple convenience kinetics

Reaction equation

$$s32 \overset{s24}{\rightleftharpoons} s26 + s28 \tag{11}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
s32	Complex_br_(Su(H)/CoR)	

Modifier

Table 20: Properties of each modifier.

Id	Name	SBO
s24	NI_sub_c_sub_s	

Products

Table 21: Properties of each product.

Id	Name	SBO
s26	Su(H)	

Id	Name	SBO
s28	CoR	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = [s24] \cdot \frac{\text{kcatp\_r11} \cdot \frac{[s32]}{\text{kM\_r11\_s32}} - \text{kcatn\_r11} \cdot \frac{[s26]}{\text{kM\_r11\_s26}} \cdot \frac{[s28]}{\text{kM\_r11\_s28}}}{\frac{[s32]}{\text{kM\_r11\_s32}} + \left(1 + \frac{[s26]}{\text{kM\_r11\_s26}}\right) \cdot \left(1 + \frac{[s28]}{\text{kM\_r11\_s28}}\right)} \tag{12}$$

6.7 Reaction r13

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

Notes mass action rate law for , reversible reactions, continuous scheme

Reaction equation

$$s24 + s26 + s27 + s29 \rightleftharpoons s35 \tag{13}$$

Reactants

Table 22: Properties of each reactant.

Id	Name	SBO
s24	NI_sub_c_sub_s	
s26	Su(H)	
s27	Mastermind	
s29	CoA	

Product

Table 23: Properties of each product.

Id	Name	SBO
s35	Complex_br_(Mastermind/Su(H)/_br_CoA/NI_sub_c_sub_s)	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{kass\_r13} \cdot [s24] \cdot [s26] \cdot [s27] \cdot [s29] - \text{kdiss\_r13} \cdot [s35] \tag{14}$$

6.8 Reaction r16

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

$$s24 + s39 \xrightleftharpoons{s38} s37 \tag{15}$$

Reactants

Table 24: Properties of each reactant.

Id	Name	SBO
s24	NI_sub_c_sub_s	
s39	Ub	

Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
s38	Sel 10	

Product

Table 26: Properties of each product.

Id	Name	SBO
s37	NI_sub_c_sub_s	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \frac{\frac{\text{kcatp\_r16}}{\text{ki\_r16\_s39} \cdot \text{kM\_r16\_s39}} \cdot [s38] \cdot [s24] \cdot [s39] - \frac{\text{kcatn\_r16}}{\text{kM\_r16\_s39}} \cdot [s38] \cdot [s37]}{1 + \frac{[s24]}{\text{ki\_r16\_s39}} + \frac{[s39]}{\text{ki\_r16\_s39}} + \frac{[s24] \cdot [s39]}{\text{ki\_r16\_s39} \cdot \text{kM\_r16\_s39}} + \frac{[s37]}{\text{kM\_r16\_s39}}} \tag{16}$$

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6.9 Reaction r17

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

$$s37 \rightleftharpoons s40 \tag{17}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
s37	NI_sub_c_sub_s	

Product

Table 28: Properties of each product.

Id	Name	SBO
s40	a46_degraded	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{kass\_r17} \cdot [\text{s37}] - \text{kdiss\_r17} \cdot [\text{s40}] \tag{18}$$

6.10 Reaction r18

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

$$s1 + s4 \overset{s42}{\rightleftharpoons} s41 \tag{19}$$

Reactants

Table 29: Properties of each reactant.

Id	Name	SBO
s1	Notch	
s4	fucose	

Modifier

Table 30: Properties of each modifier.

Id	Name	SBO
s42	Neurotic	

Product

Table 31: Properties of each product.

Id	Name	SBO
s41	Notch	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \frac{\frac{\text{kcatp\_r18}}{\text{ki\_r18\_s4} \cdot \text{kM\_r18\_s4}} \cdot [s42] \cdot [s1] \cdot [s4] - \frac{\text{kcatn\_r18}}{\text{kM\_r18\_s4}} \cdot [s42] \cdot [s41]}{1 + \frac{[s1]}{\text{ki\_r18\_s4}} + \frac{[s4]}{\text{ki\_r18\_s4}} + \frac{[s1] \cdot [s4]}{\text{ki\_r18\_s4} \cdot \text{kM\_r18\_s4}} + \frac{[s41]}{\text{kM\_r18\_s4}}} \tag{20}$$

6.11 Reaction r21

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

$$s41 + s48 \underset{}{\overset{s2}{\rightleftharpoons}} s53 \tag{21}$$

Reactants

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Table 32: Properties of each reactant.

Id	Name	SBO
s41	Notch	
s48	Serrate	

Modifier

Table 33: Properties of each modifier.

Id	Name	SBO
s2	Fringe	

Product

Table 34: Properties of each product.

Id	Name	SBO
s53	Complex_br_(Serrate/Notch)	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \frac{\text{kI\_r21\_s2}}{\text{kI\_r21\_s2} + [\text{s2}]} \cdot (\text{kass\_r21} \cdot [\text{s41}] \cdot [\text{s48}] - \text{kdiss\_r21} \cdot [\text{s53}]) \tag{22}$$

6.12 Reaction r25

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

Notes reversible simple convenience kinetics

Reaction equation

$$\text{s53} \underset{\longleftarrow}{\overset{\text{s21}}{\rightleftharpoons}} \text{s60} + \text{s15} \tag{23}$$

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
s53	Complex_br_(Serrate/Notch)	

Modifier

Table 36: Properties of each modifier.

Id	Name	SBO
s21	TACE	

Products

Table 37: Properties of each product.

Id	Name	SBO
s60	Complex_br_(Serrate/N_sub_ext)	
s15	NI_sub_c_sub_t	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = [\text{s21}] \cdot \frac{\text{kcatp\_r25} \cdot \frac{[\text{s53}]}{\text{kM\_r25\_s53}} - \text{kcatn\_r25} \cdot \frac{[\text{s60}]}{\text{kM\_r25\_s60}} \cdot \frac{[\text{s15}]}{\text{kM\_r25\_s15}}}{\frac{[\text{s53}]}{\text{kM\_r25\_s53}} + \left(1 + \frac{[\text{s60}]}{\text{kM\_r25\_s60}}\right) \cdot \left(1 + \frac{[\text{s15}]}{\text{kM\_r25\_s15}}\right)} \tag{24}$$

6.13 Reaction r26

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

Notes kinetics of non-modulated unireactant enzymes

Reaction equation

$$\text{s25} \xrightleftharpoons{\text{s65}} \text{s64} \tag{25}$$

Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
s25	Numb	

Modifier

Table 39: Properties of each modifier.

Id	Name	SBO
s65	LNXp80	

Product

Table 40: Properties of each product.

Id	Name	SBO
s64	a25_degraded	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = [\text{s65}] \cdot \frac{\frac{\text{kcatp\_r26}}{\text{kM\_r26\_s25}} \cdot [\text{s25}] - \frac{\text{kcatn\_r26}}{\text{kM\_r26\_s64}} \cdot [\text{s64}]}{1 + \frac{[\text{s25}]}{\text{kM\_r26\_s25}} + \frac{[\text{s64}]}{\text{kM\_r26\_s64}}} \tag{26}$$

6.14 Reaction r28

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

$$\text{s7} + \text{s41} \underset{\overset{\text{s2}}{\rightleftharpoons}}{} \text{s67} \tag{27}$$

Reactants

Table 41: Properties of each reactant.

Id	Name	SBO
s7	Delta	
s41	Notch	

Modifier

Table 42: Properties of each modifier.

Id	Name	SBO
s2	Fringe	

Product

Table 43: Properties of each product.

Id	Name	SBO
s67	Complex_br_(Notch/Delta)	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \frac{\frac{\text{kcatp\_r28}}{\text{ki\_r28\_s41}\cdot\text{kM\_r28\_s41}} \cdot [s2] \cdot [s7] \cdot [s41] - \frac{\text{kcatn\_r28}}{\text{kM\_r28\_s41}} \cdot [s2] \cdot [s67]}{1 + \frac{[s7]}{\text{ki\_r28\_s41}} + \frac{[s41]}{\text{ki\_r28\_s41}} + \frac{[s7]\cdot[s41]}{\text{ki\_r28\_s41}\cdot\text{kM\_r28\_s41}} + \frac{[s67]}{\text{kM\_r28\_s41}}} \tag{28}$$

6.15 Reaction r29

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

Notes reversible simple convenience kinetics

Reaction equation

$$s67 \underset{}{\overset{s21}{\rightleftharpoons}} s18 + s15 \tag{29}$$

Reactant

Table 44: Properties of each reactant.

Id	Name	SBO
s67	Complex_br_(Notch/Delta)	

Modifier

Table 45: Properties of each modifier.

Id	Name	SBO
s21	TACE	

Products

Table 46: Properties of each product.

Id	Name	SBO
s18	Complex_br_(Delta/N_sub_ext)	
s15	NI_sub_c_sub_t	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = [s21] \cdot \frac{\text{kcatp\_r29} \cdot \frac{[s67]}{\text{kM\_r29\_s67}} - \text{kcatn\_r29} \cdot \frac{[s18]}{\text{kM\_r29\_s18}} \cdot \frac{[s15]}{\text{kM\_r29\_s15}}}{\frac{[s67]}{\text{kM\_r29\_s67}} + \left(1 + \frac{[s18]}{\text{kM\_r29\_s18}}\right) \cdot \left(1 + \frac{[s15]}{\text{kM\_r29\_s15}}\right)} \tag{30}$$

6.16 Reaction `re16`

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

$$s76 + s77 \xrightleftharpoons{s81} s82 \tag{31}$$

Reactants

Table 47: Properties of each reactant.

Id	Name	SBO
s76	s76	
s77	s77	

Modifier

Table 48: Properties of each modifier.

Id	Name	SBO
s81	dapt	

Product

Table 49: Properties of each product.

Id	Name	SBO
s82	gama secretase	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \frac{\text{kI\_re16\_s81}}{\text{kI\_re16\_s81} + [\text{s81}]} \cdot (\text{kass\_re16} \cdot [\text{s76}] \cdot [\text{s77}] - \text{kdiss\_re16} \cdot [\text{s82}]) \tag{32}$$

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 s2

Name Fringe

Notes Long Name: FringeSynonym: Lunatic Fringe,Manic Fringe,Radical FringeAccession: P01107

Initial amount 5 mol

Charge 0

This species takes part in two reactions (as a modifier in r21, r28).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}2 = 0 \tag{33}$$

7.2 Species s4

Name fucose

Notes Long Name: FucoseSynonym: Synonym not specifiedAccession: S01795

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in r18).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}4 = -\ v_{10} \tag{34}$$

7.3 Species s7

Name Delta

Notes Long Name: DeltaSynonym: Delta-like1,Delta-like3,Delta-like4,DeltaC,LAG-2Accession: P01116

Initial amount 5 mol

Charge 0

This species takes part in two reactions (as a reactant in r9, r28).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}7 = -\ v_4\ -\ v_{14} \tag{35}$$

7.4 Species s15

Name NI_sub_c_sub_t

Notes Long Name: Notch intracellular tethered fragmentSynonym: Synonym not specifiedAccession: P01119

Initial amount 5 mol

Charge 0

This species takes part in three reactions (as a reactant in r8 and as a product in r25, r29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{s15} = v_{12} + v_{15} - v_3 \tag{36}$$

7.5 Species s19

Name N_sub_tm

Notes Long Name: Notch transmembrane domain fragmentSynonym: Synonym not specifiedAccession: P01114

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in r8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{s19} = v_3 \tag{37}$$

7.6 Species s21

Name TACE

Notes Long Name: TACESynonym: A disintegrin and metalloproteinase domain 17,ADAM17,Tumor necrosis factor alpha converting enzymeAccession: P01105

Initial amount 0.5 mol

Charge 0

This species takes part in two reactions (as a modifier in r25, r29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{s21} = 0 \tag{38}$$

7.7 Species s22

Name a7_degraded

Notes Long Name: a7_degradedSynonym: Synonym not specifiedAccession: U02511

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in r9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}22 = v_4 \tag{39}$$

7.8 Species s23

Name Neuralized

Notes Long Name: NeuralizedSynonym: NeuAccession: P01117

Initial amount 0.5 mol

Charge 0

This species takes part in one reaction (as a modifier in r9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}23 = 0 \tag{40}$$

7.9 Species s25

Name Numb

Notes Long Name: NumbSynonym: Synonym not specifiedAccession: P01118

Initial amount 0.64 mol

Charge 0

This species takes part in two reactions (as a reactant in r26 and as a modifier in r10).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}25 = - v_{13} \tag{41}$$

7.10 Species s27

Name Mastermind

Notes Long Name: MastermindSynonym: MECT-1,Mastermind-like 1 (MAML1),Mastermind-like2 (MAML2),Mastermind-like3(MAML3),mucoepidermoid carcinoma-translocated 1Accession: P01106

Initial amount 0.5 mol

Charge 0

This species takes part in one reaction (as a reactant in r13).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s27} = -\,v_7 \tag{42}$$

7.11 Species s26

Name Su(H)

Notes Long Name: Suppressor of Hairless [Su(H)]Synonym: C-promoter binding factor 1,CBF1,IKJRB1,Immunog Kappa J region recombination signal-binding protein 1,LAG-1Accession: P01101

Initial amount 5 mol

Charge 0

This species takes part in two reactions (as a reactant in r13 and as a product in r11).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s26} = v_6 - v_7 \tag{43}$$

7.12 Species s28

Name CoR

Notes Long Name: Co-repressorsSynonym: Synonym not specifiedAccession: P01112

Initial amount 5 mol

Charge 0

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s28} = v_6 \tag{44}$$

7.13 Species s32

Name Complex_br_(Su(H)/CoR)

Notes Long Name: Long Name: Suppressor of Hairless and Co-repressorsSynonym: Synonym not specifiedAccession: U05412Heterodimer Member Info: Su(H)#PROTEIN#Suppressor of Hairless [Su(H)]#P01101#C-promoter binding factor 1—CBF1—IKJRB1—Immunoglobulin Kappa J region recombination signal-binding protein 1—LAG-1#;CoR#PROTEIN#Co-repressors#P01112##

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in r30, r11).

$$\frac{d}{dt}s32 = -\,v_1\,-\,v_6 \tag{45}$$

7.14 Species s29

Name CoA

Notes Long Name: Co-ActivatorsSynonym: Synonym not specifiedAccession: P01100

Initial amount 0.5 mol

Charge 0

This species takes part in one reaction (as a reactant in r13).

$$\frac{d}{dt}s29 = -\,v_7 \tag{46}$$

7.15 Species s24

Name NI_sub_c_sub_s

Notes Long Name: Notch intracellular soluble fragmentSynonym: Synonym not specifiedAccession: P01120

Initial amount 0 mol

Charge 0

This species takes part in four reactions (as a reactant in r13, r16 and as a product in r10 and as a modifier in r11).

$$\frac{d}{dt}s24 = v_5\,-\,v_7\,-\,v_8 \tag{47}$$

7.16 Species s35

Name Complex_br_(Mastermind/Su(H)/_br_CoA/NI_sub_c_sub_s)

Notes Long Name: Long Name: Long name not specifiedSynonym: Synonym not specifiedAccession: U05413Heterodimer Member Info: CoA#PROTEIN#Co-Activators#P01100##;Su(H)#PROTE
of Hairless [Su(H)]#P01101#C-promoter binding factor 1—CBF1—IKJRB1—Immunoglobulin
Kappa J region recombination signal-binding protein 1—LAG-1#;Mastermind#PROTEIN#Mastermind#P011
1—Mastermind-like 1 (MAML1)—Mastermind-like2 (MAML2)—Mastermind-like3(MAML3)—mucoepider
carcinoma-translocated 1#;NIcs#PROTEIN#Notch intracellular soluble fragment#P01120##

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in r31 and as a product in r13).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}35 = v_7 - v_2 \tag{48}$$

7.17 Species s37

Name NI_sub_c_sub_s

Notes Long Name: Notch intracellular soluble fragmentSynonym: Synonym not specifiedAccession: P01120

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in r17 and as a product in r16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}37 = v_8 - v_9 \tag{49}$$

7.18 Species s38

Name Sel 10

Notes Long Name: Sel 10Synonym: Synonym not specifiedAccession: P01102

Initial amount 0.6 mol

Charge 0

This species takes part in one reaction (as a modifier in r16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}38 = 0 \tag{50}$$

7.19 Species s39

Name Ub

Notes Long Name: UbiquitinSynonym: Synonym not specifiedAccession: S01796

Initial amount 0.5 mol

Charge 0

This species takes part in one reaction (as a reactant in r16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}39 = -\ v_8 \tag{51}$$

7.20 Species s40

Name a46_degraded

Notes Long Name: a46_degradedSynonym: Synonym not specifiedAccession: U02510

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in r17).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}40 = v_9 \tag{52}$$

7.21 Species s1

Name Notch

Notes Long Name: NotchSynonym: GLP-1,LIN-12,Notch1,Notch2,Notch3,Notch4Accession: P01099

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in r18).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}1 = -\ v_{10} \tag{53}$$

7.22 Species s18

Name Complex_br_(Delta/N_sub_ext)

Notes Long Name: Long Name: Delta and Notch extracellular fragmentSynonym: Synonym not specifiedAccession: U05409Heterodimer Member Info: Next#PROTEIN#Serrate and Notch extracellular fragment#P01103##;Delta#PROTEIN#Delta#P01116#Delta-like1—Delta-like3—Delta-like4—DeltaC—LAG-2#

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in r29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{s18} = v_{15} \tag{54}$$

7.23 Species s41

Name Notch

Notes Long Name: NotchSynonym: GLP-1,LIN-12,Notch1,Notch2,Notch3,Notch4Accession: P01099

Initial amount 0 mol

Charge 0

This species takes part in three reactions (as a reactant in r21, r28 and as a product in r18).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{s41} = v_{10} - v_{11} - v_{14} \tag{55}$$

7.24 Species s42

Name Neurotic

Notes Long Name: NeuroticSynonym: O-fucosyltransferase 1,O-fut1,OFUT1,Ofut1Accession: P01115

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a modifier in r18).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{s42} = 0 \tag{56}$$

7.25 Species s48

Name Serrate

Notes Long Name: SerrateSynonym: APX-1,F16B12.2,Jagged1,Jagged2Accession: P01104

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in r21).

$$\frac{d}{dt}s48 = -\ v_{11} \tag{57}$$

7.26 Species s53

Name Complex_br_(Serrate/Notch)

Notes Long Name: Long Name: Serrate and Notch (fucosylated)Synonym: Synonym not specifiedAccession: U05410Heterodimer Member Info: Notch#PROTEIN#Notch#P01099#GLP-1—LIN-12—Notch1—Notch2—Notch3—Notch4#;Serrate#PROTEIN#Serrate#P01104#APX-1—F16B12.2—Jagged1—Jagged2#

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in r25 and as a product in r21).

$$\frac{d}{dt}s53 = v_{11} - v_{12} \tag{58}$$

7.27 Species s60

Name Complex_br_(Serrate/N_sub_ext)

Notes Long Name: Long Name: Serrate and Notch extracellular fragmentSynonym: Synonym not specifiedAccession: U05414Heterodimer Member Info: Next#PROTEIN#Serrate and Notch extracellular fragment#P01103##;Serrate#PROTEIN#Serrate#P01104#APX-1—F16B12.2—Jagged1—

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in r25).

$$\frac{d}{dt}s60 = v_{12} \tag{59}$$

7.28 Species s63

Name NI_sub_c_sub_s

Notes Long Name: Notch intracellular soluble fragmentSynonym: Synonym not specifiedAccession: P01120

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in r10 and as a product in r8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}63 = v_3 - v_5 \tag{60}$$

7.29 Species s64

Name a25_degraded

Notes Long Name: a25_degradedSynonym: Synonym not specifiedAccession: U02509

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a product in r26).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}64 = v_{13} \tag{61}$$

7.30 Species s65

Name LNXp80

Notes Long Name: LNXp80Synonym: Ligand of Numb-protein X 80 kDaAccession: P01111

Initial amount 0.33 mol

Charge 0

This species takes part in one reaction (as a modifier in r26).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}65 = 0 \tag{62}$$

Produced by SBML2LATEX

7.31 Species s67

Name Complex_br_(Notch/Delta)

Notes Long Name: Long Name: Delta and Notch (fucosylated)Synonym: Synonym not specifiedAccession: U05411Heterodimer Member Info: Notch#PROTEIN#Notch#P01099#GLP-1—LIN-12—Notch1—Notch2—Notch3—Notch4#;Delta#PROTEIN#Delta#P01116#Delta-like1—Delta-like3—Delta-like4—DeltaC—LAG-2#

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a reactant in r29 and as a product in r28).

$$\frac{d}{dt}s67 = v_{14} - v_{15} \tag{63}$$

7.32 Species s75

Name E(spl)-C genes

Notes Long Name: Enhancer of Split complex genesSynonym: Synonym not specifiedAccession: G01541

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a product in r30, r31).

$$\frac{d}{dt}s75 = v_1 + v_2 \tag{64}$$

7.33 Species s76

Name s76

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in re16).

$$\frac{d}{dt}s76 = -v_{16} \tag{65}$$

7.34 Species s77

Name s77

Initial amount 5 mol

Charge 0

This species takes part in one reaction (as a reactant in `re16`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}77 = -v_{16} \tag{66}$$

7.35 Species s81

Name dapt

Initial amount 0 mol

Charge 0

This species takes part in one reaction (as a modifier in `re16`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}81 = 0 \tag{67}$$

7.36 Species s82

Name gama secretase

Initial amount 0 mol

Charge 0

This species takes part in two reactions (as a product in `re16` and as a modifier in `r8`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s}82 = v_{16} \tag{68}$$