SBML Model Report

Model name: "Lee2003 - Roles of APC and Axin in Wnt Pathway (without regulatory loop)"

May 17, 2018

1. General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Varun Kothamachu Kothamachu[1] and Matthew Grant Roberts[2] at March 20th 2018 at 3:52 p. m. and last time modified at March 20th 2018 at 3:52 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	2
species types	0	species	16
events	0	constraints	0
reactions	17	function definitions	3
global parameters	31	unit definitions	3
rules	7	initial assignments	1

Model Notes

Lee2003 - Roles of APC and Axin in WntPathway (without regulatory loop)

[1]Babraham Institute, kothamav@babraham.ac.uk
[2]EMBL-EBI, mroberts@ebi.ac.uk

This model is described in the article:The roles of APC and Axin derived from experimental and theoretical analysis of the Wnt pathway.Lee E, Salic A, Krger R, Heinrich R, Kirschner MW.PLoS Biol. 2003 Oct; 1(1): E10

Abstract:

Wnt signaling plays an important role in both oncogenesis and development. Activation of the Wnt pathway results in stabilization of the transcriptional coactivator beta-catenin. Recent studies have demonstrated that axin, which coordinates beta-catenin degradation, is itself degraded. Although the key molecules required for transducing a Wnt signal have been identified, a quantitative understanding of this pathway has been lacking. We have developed a mathematical model for the canonical Wnt pathway that describes the interactions among the core components: Wnt, Frizzled, Dishevelled, GSK3beta, APC, axin, beta-catenin, and TCF. Using a system of differential equations, the model incorporates the kinetics of protein-protein interactions, protein synthesis/degradation, and phosphorylation/dephosphorylation. We initially defined a reference state of kinetic, thermodynamic, and flux data from experiments using Xenopus extracts. Predictions based on the analysis of the reference state were used iteratively to develop a more refined model from which we analyzed the effects of prolonged and transient Wnt stimulation on beta-catenin and axin turnover. We predict several unusual features of the Wnt pathway, some of which we tested experimentally. An insight from our model, which we confirmed experimentally, is that the two scaffold proteins axin and APC promote the formation of degradation complexes in very different ways. We can also explain the importance of axin degradation in amplifying and sharpening the Wnt signal, and we show that the dependence of axin degradation on APC is an essential part of an unappreciated regulatory loop that prevents the accumulation of beta-catenin at decreased APC concentrations. By applying control analysis to our mathematical model, we demonstrate the modular design, sensitivity, and robustness of the Wnt pathway and derive an explicit expression for tumor suppression and oncogenicity.

This model is hosted on BioModels Database and identified by: BIOMD0000000658.

To cite BioModels Database, please use: Chelliah V et al. BioModels: ten-year anniversary. Nucl. Acids Res. 2015, 43(Database issue):D542-8.

2. Unit Definitions

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

2.1. Unit `volume`

Name volume

Definition ml

2.2. Unit `time`

Name time

Definition 60 s

2.3. Unit `substance`

Name substance

Definition µmol

2.4. Unit `area`

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

Definition m^2

2.5. Unit `length`

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

Definition m

3. Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

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

3.1. Compartment `Cytoplasm`

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

Name Cytoplasm

3.2. Compartment `Nucleus`

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

Name Nucleus

4. Species

This model contains 16 species. The boundary condition of one of these species is set to `true` so that this species' amount cannot be changed by any reaction. Section 10 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
`Dsh_i`	Dsh_i	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`Dsh_a`	Dsh_a	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`APC__axin__GSK3`	APC*/axin*/GSK3	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`APC_axin_GSK3`	APC/axin/GSK3	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`GSK3`	GSK3	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`APC_axin`	APC/axin	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`APC`	APC	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`B_catenin_APC__axin__GSK3`	B_catenin/APC*/axin*/GSK3	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`B_catenin__APC__axin__GSK3`	B_catenin*/APC*/axin*/GSK3	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`B_catenin`	B_catenin*	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`B_catenin_0`	B_catenin	`Nucleus`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`Axin`	Axin	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`TCF`	TCF	`Nucleus`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`B_catenin_TCF`	B_catenin/TCF	`Nucleus`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`B_catenin_APC`	B_catenin/APC	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☐
`W`	W	`Cytoplasm`	$\mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$	☐	☑

5. Parameters

This model contains 31 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.182		☑
k2	k2		0.018		☑
k3	k3		0.050		☑
k4	k4		0.267		☑
k5	k5		0.133		☑
k6	k6		0.091		☑
k_6	k_6		0.909		☑
k7	k7		500.000		☑
k_7	k_7		25000.000		☐
k8	k8		500.000		☑
k_8	k_8		60000.000		☐
k9	k9		206.000		☑
k10	k10		206.000		☑
k11	k11		0.417		☑
k12	k12		0.423		☑
k13	k13		$2.57 \cdot 10^{-4}$		☑
k14	k14		$8.22 \cdot 10^{-5}$		☑
k15	k15		0.167		☑
k16	k16		500.000		☑
k_16	k_16		15000.000		☐
k17	k17		500.000		☑
k_17	k_17		600000.000		☐
K_7	K_7	0000282	50.000		☑
K_8	K_8	0000282	120.000		☑
K_16	K_16	0000282	30.000		☑
K_17	K_17	0000282	1200.000		☑
lambda	lambda	0000356	0.050		☑
t0	t0		40.000		☑
Dsh0	Dsh0		100.000		☑
Total_B-_Catenin	Total_B_Catenin		34.984		☐
Total_Axin	Total_Axin		0.020		☐

6. Initialassignment

This is an overview of one initialassignment.

6.1. Initialassignment `Dsh_i`

Derived unit contains undeclared units

Math $\mathrm{Dsh0} - [\mathrm{Dsh\_a}]$

7. Function definitions

This is an overview of three function definitions.

7.1. Function definition `Constant_flux__irreversible`

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$\mathrm{v} \tag{1}$$

7.2. Function definition `function_for_v1`

Name function for v1

Arguments k1, x1, [W]

Mathematical Expression

$$\mathrm{k1} \cdot \mathrm{x1} \cdot [\mathrm{W}] \tag{2}$$

7.3. Function definition `function_for_v3`

Name function for v3

Arguments k3, x2, x4

Mathematical Expression

$$\mathrm{k3} \cdot \mathrm{x2} \cdot \mathrm{x4} \tag{3}$$

8. Rules

This is an overview of seven rules.

8.1. Rule Total_B_Catenin

Rule Total_B_Catenin is an assignment rule for parameter Total_B_Catenin:

$$\begin{aligned}\text{Total\_B\_Catenin} = {} & [\text{B\_catenin\_APC\_\_axin\_\_GSK3}] + [\text{B\_catenin\_\_APC\_\_axin\_\_GSK3}] \\ & + [\text{B\_catenin}] + [\text{B\_catenin\_0}] + [\text{B\_catenin\_TCF}] + [\text{B\_catenin\_APC}]\end{aligned} \tag{4}$$

Derived unit $\mu\text{mol} \cdot \text{ml}^{-1}$

8.2. Rule Total_Axin

Rule Total_Axin is an assignment rule for parameter Total_Axin:

$$\begin{aligned}\text{Total\_Axin} = {} & [\text{APC\_\_axin\_\_GSK3}] + [\text{APC\_axin\_GSK3}] + [\text{APC\_axin}] \\ & + [\text{B\_catenin\_APC\_\_axin\_\_GSK3}] + [\text{B\_catenin\_\_APC\_\_axin\_\_GSK3}] + [\text{Axin}]\end{aligned} \tag{5}$$

Derived unit $\mu\text{mol} \cdot \text{ml}^{-1}$

8.3. Rule k_16

Rule k_16 is an assignment rule for parameter k_16:

$$\text{k\_16} = \text{k16} \cdot \text{K\_16} \tag{6}$$

8.4. Rule k_7

Rule k_7 is an assignment rule for parameter k_7:

$$\text{k\_7} = \text{k7} \cdot \text{K\_7} \tag{7}$$

8.5. Rule k_17

Rule k_17 is an assignment rule for parameter k_17:

$$\text{k\_17} = \text{k17} \cdot \text{K\_17} \tag{8}$$

8.6. Rule k_8

Rule k_8 is an assignment rule for parameter k_8:

$$\text{k\_8} = \text{k8} \cdot \text{K\_8} \tag{9}$$

8.7. Rule W

Rule W is an assignment rule for species W:

$$\text{W} = \begin{cases} 0 & \text{if time} < \text{t0} \\ \exp\left(1 \cdot \text{lambda} \cdot (\text{time} - \text{t0})\right) & \text{otherwise} \end{cases} \tag{10}$$

9. Reactions

This model contains 17 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	`v1`	v1	$\text{Dsh\_i} \xrightarrow{\text{W}} \text{Dsh\_a}$	
2	`v2`	v2	$\text{Dsh\_a} \longrightarrow \text{Dsh\_i}$	
3	`v3`	v3	$\text{APC\_axin\_GSK3} \xrightarrow{\text{Dsh\_a}} \text{GSK3} + \text{APC\_axin}$	
4	`v4`	v4	$\text{APC\_axin\_GSK3} \longrightarrow \text{APC\_\_axin\_\_GSK3}$	
5	`v5`	v5	$\text{APC\_\_axin\_\_GSK3} \longrightarrow \text{APC\_axin\_GSK3}$	
6	`v6`	v6	$\text{GSK3} + \text{APC\_axin} \rightleftharpoons \text{APC\_axin\_GSK3}$	
7	`v7`	v7	$\text{APC} + \text{Axin} \rightleftharpoons \text{APC\_axin}$	
8	`v8`	v8	$\text{APC\_\_axin\_\_GSK3} + \text{B\_catenin\_0} \rightleftharpoons \text{B\_catenin\_APC\_\_axin\_\_GSK3}$	
9	`v9`	v9	$\text{B\_catenin\_APC\_\_axin\_\_GSK3} \longrightarrow \text{B\_catenin\_\_APC\_\_axin\_\_GSK3}$	
10	`v10`	v10	$\text{B\_catenin\_\_APC\_\_axin\_\_GSK3} \longrightarrow \text{B\_catenin} + \text{APC\_\_axin\_\_GSK3}$	
11	`v11`	v11	$\text{B\_catenin} \longrightarrow \emptyset$	
12	`v12`	v12	$\emptyset \longrightarrow \text{B\_catenin\_0}$	
13	`v13`	v13	$\text{B\_catenin\_0} \longrightarrow \emptyset$	
14	`v14`	v14	$\emptyset \longrightarrow \text{Axin}$	
15	`v15`	v15	$\text{Axin} \longrightarrow \emptyset$	
16	`v16`	v16	$\text{B\_catenin\_0} + \text{TCF} \rightleftharpoons \text{B\_catenin\_TCF}$	
17	`v17`	v17	$\text{APC} + \text{B\_catenin\_0} \rightleftharpoons \text{B\_catenin\_APC}$	

9.1. Reaction v1

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

Name v1

Reaction equation

$$\mathrm{Dsh\_i} \xrightarrow{\mathrm{W}} \mathrm{Dsh\_a} \tag{11}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
Dsh_i	Dsh_i	

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
W	W	

Product

Table 8: Properties of each product.

Id	Name	SBO
Dsh_a	Dsh_a	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \mathrm{vol}(\mathrm{Cytoplasm}) \cdot \mathrm{function\_for\_v1}(\mathrm{k1}, [\mathrm{Dsh\_i}], [\mathrm{W}]) \tag{12}$$

$$\mathrm{function\_for\_v1}(\mathrm{k1}, \mathrm{x1}, [\mathrm{W}]) = \mathrm{k1} \cdot \mathrm{x1} \cdot [\mathrm{W}] \tag{13}$$

$$\mathrm{function\_for\_v1}(\mathrm{k1}, \mathrm{x1}, [\mathrm{W}]) = \mathrm{k1} \cdot \mathrm{x1} \cdot [\mathrm{W}] \tag{14}$$

9.2. Reaction v2

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

Name v2

Reaction equation

$$\text{Dsh\_a} \longrightarrow \text{Dsh\_i} \tag{15}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
Dsh_a	Dsh_a	

Product

Table 10: Properties of each product.

Id	Name	SBO
Dsh_i	Dsh_i	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}\left(\text{Cytoplasm}\right) \cdot \text{k2} \cdot [\text{Dsh\_a}] \tag{16}$$

9.3. Reaction v3

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

Name v3

Reaction equation

$$\text{APC\_axin\_GSK3} \xrightarrow{\text{Dsh\_a}} \text{GSK3} + \text{APC\_axin} \tag{17}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
APC_axin_GSK3	APC/axin/GSK3	

Modifier

Table 12: Properties of each modifier.

Id	Name	SBO
Dsh_a	Dsh_a	

Products

Table 13: Properties of each product.

Id	Name	SBO
GSK3	GSK3	
APC_axin	APC/axin	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{Cytoplasm}\right) \cdot \mathrm{function\_for\_v3}\left(\mathrm{k3}, [\mathrm{Dsh\_a}], [\mathrm{APC\_axin\_GSK3}]\right) \tag{18}$$

$$\mathrm{function\_for\_v3}\left(\mathrm{k3}, \mathrm{x2}, \mathrm{x4}\right) = \mathrm{k3} \cdot \mathrm{x2} \cdot \mathrm{x4} \tag{19}$$

$$\mathrm{function\_for\_v3}\left(\mathrm{k3}, \mathrm{x2}, \mathrm{x4}\right) = \mathrm{k3} \cdot \mathrm{x2} \cdot \mathrm{x4} \tag{20}$$

9.4. Reaction v4

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

Name v4

Reaction equation

$$\mathrm{APC\_axin\_GSK3} \longrightarrow \mathrm{APC\_\_axin\_\_GSK3} \tag{21}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
APC_axin_GSK3	APC/axin/GSK3	

Product

Table 15: Properties of each product.

Id	Name	SBO
APC__axin__GSK3	APC*/axin*/GSK3	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\left(\mathrm{Cytoplasm}\right) \cdot \mathrm{k4} \cdot [\mathrm{APC\_axin\_GSK3}] \tag{22}$$

9.5. Reaction v5

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

Name v5

Reaction equation

$$\mathrm{APC\_\_axin\_\_GSK3} \longrightarrow \mathrm{APC\_axin\_GSK3} \tag{23}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
APC__axin__GSK3	APC*/axin*/GSK3	

Product

Table 17: Properties of each product.

Id	Name	SBO
APC_axin_GSK3	APC/axin/GSK3	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\left(\mathrm{Cytoplasm}\right) \cdot \mathrm{k5} \cdot [\mathrm{APC\_\_axin\_\_GSK3}] \tag{24}$$

9.6. Reaction v6

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

Name v6

Reaction equation

$$\mathrm{GSK3} + \mathrm{APC\_axin} \rightleftharpoons \mathrm{APC\_axin\_GSK3} \tag{25}$$

Reactants

Table 18: Properties of each reactant.

Id	Name	SBO
GSK3	GSK3	
APC_axin	APC/axin	

Product

Table 19: Properties of each product.

Id	Name	SBO
APC_axin_GSK3	APC/axin/GSK3	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\left(\mathrm{Cytoplasm}\right) \cdot \left(\mathrm{k6} \cdot [\mathrm{GSK3}] \cdot [\mathrm{APC\_axin}] - \mathrm{k\_6} \cdot [\mathrm{APC\_axin\_GSK3}]\right) \tag{26}$$

9.7. Reaction v7

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

Name v7

Reaction equation

$$\mathrm{APC} + \mathrm{Axin} \rightleftharpoons \mathrm{APC\_axin} \tag{27}$$

Reactants

Table 20: Properties of each reactant.

Id	Name	SBO
APC	APC	
Axin	Axin	

Product

Table 21: Properties of each product.

Id	Name	SBO
APC_axin	APC/axin	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{Cytoplasm}\right) \cdot \left(\mathrm{k7} \cdot [\mathrm{APC}] \cdot [\mathrm{Axin}] - \mathrm{k\_7} \cdot [\mathrm{APC\_axin}]\right) \tag{28}$$

9.8. Reaction v8

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

Name v8

Reaction equation

$$\mathrm{APC\_\_axin\_\_GSK3} + \mathrm{B\_catenin\_0} \rightleftharpoons \mathrm{B\_catenin\_APC\_\_axin\_\_GSK3} \tag{29}$$

Reactants

Table 22: Properties of each reactant.

Id	Name	SBO
APC__axin__GSK3	APC*/axin*/GSK3	
B_catenin_0	B_catenin	

Product

Table 23: Properties of each product.

Id	Name	SBO
B_catenin_APC__axin__GSK3	B_catenin/APC*/axin*/GSK3	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{k8} \cdot [\mathrm{APC\_\_axin\_\_GSK3}] \cdot [\mathrm{B\_catenin\_0}] - \mathrm{k\_8} \cdot [\mathrm{B\_catenin\_APC\_\_axin\_\_GSK3}] \quad (30)$$

9.9. Reaction v9

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

Name v9

Reaction equation

$$\mathrm{B\_catenin\_APC\_\_axin\_\_GSK3} \longrightarrow \mathrm{B\_catenin\_\_APC\_\_axin\_\_GSK3} \quad (31)$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
B_catenin_APC__axin__GSK3	B_catenin/APC*/axin*/GSK3	

Product

Table 25: Properties of each product.

Id	Name	SBO
B_catenin__APC__axin__GSK3	B_catenin*/APC*/axin*/GSK3	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\,(\mathrm{Cytoplasm}) \cdot \mathrm{k9} \cdot [\mathrm{B\_catenin\_APC\_\_axin\_\_GSK3}] \qquad (32)$$

9.10. Reaction v10

This is an irreversible reaction of one reactant forming two products.

Name v10

Reaction equation

$$\mathrm{B\_catenin\_\_APC\_\_axin\_\_GSK3} \longrightarrow \mathrm{B\_catenin} + \mathrm{APC\_\_axin\_\_GSK3} \qquad (33)$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
B_catenin__APC__axin__GSK3	B_catenin*/APC*/axin*/GSK3	

Products

Table 27: Properties of each product.

Id	Name	SBO
B_catenin	B_catenin*	
APC__axin__GSK3	APC*/axin*/GSK3	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\,(\mathrm{Cytoplasm}) \cdot \mathrm{k10} \cdot [\mathrm{B\_catenin\_\_APC\_\_axin\_\_GSK3}] \qquad (34)$$

9.11. Reaction v11

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

Name v11

Reaction equation

$$\text{B\_catenin} \longrightarrow \emptyset \tag{35}$$

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
B_catenin	B_catenin*	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\left(\mathrm{Cytoplasm}\right) \cdot \mathrm{k11} \cdot [\mathrm{B\_catenin}] \tag{36}$$

9.12. Reaction v12

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

Name v12

Reaction equation

$$\emptyset \longrightarrow \text{B\_catenin\_0} \tag{37}$$

Product

Table 29: Properties of each product.

Id	Name	SBO
B_catenin_0	B_catenin	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\left(\mathrm{Nucleus}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{k12}\right) \quad (38)$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \quad (39)$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \quad (40)$$

9.13. Reaction v13

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

Name v13

Reaction equation

$$\mathrm{B\_catenin\_0} \longrightarrow \emptyset \quad (41)$$

Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
B_catenin_0	B_catenin	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}\left(\mathrm{Nucleus}\right) \cdot \mathrm{k13} \cdot [\mathrm{B\_catenin\_0}] \quad (42)$$

9.14. Reaction v14

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

Name v14

Reaction equation

$$\emptyset \longrightarrow \mathrm{Axin} \quad (43)$$

Product

Table 31: Properties of each product.

Id	Name	SBO
Axin	Axin	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\left(\mathrm{Cytoplasm}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{k14}\right) \tag{44}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{45}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{46}$$

9.15. Reaction v15

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

Name v15

Reaction equation

$$\mathrm{Axin} \longrightarrow \emptyset \tag{47}$$

Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
Axin	Axin	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\left(\mathrm{Cytoplasm}\right) \cdot \mathrm{k15} \cdot [\mathrm{Axin}] \tag{48}$$

9.16. Reaction v16

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

Name v16

Reaction equation

$$\text{B\_catenin\_0} + \text{TCF} \rightleftharpoons \text{B\_catenin\_TCF} \tag{49}$$

Reactants

Table 33: Properties of each reactant.

Id	Name	SBO
B_catenin_0	B_catenin	
TCF	TCF	

Product

Table 34: Properties of each product.

Id	Name	SBO
B_catenin_TCF	B_catenin/TCF	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \text{vol}\left(\text{Nucleus}\right) \cdot \left(\text{k16} \cdot [\text{B\_catenin\_0}] \cdot [\text{TCF}] - \text{k\_16} \cdot [\text{B\_catenin\_TCF}]\right) \tag{50}$$

9.17. Reaction v17

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

Name v17

Reaction equation

$$\text{APC} + \text{B\_catenin\_0} \rightleftharpoons \text{B\_catenin\_APC} \tag{51}$$

Reactants

Table 35: Properties of each reactant.

Id	Name	SBO
APC	APC	
B_catenin_0	B_catenin	

Product

Table 36: Properties of each product.

Id	Name	SBO
B_catenin_APC	B_catenin/APC	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{k17} \cdot [\mathrm{APC}] \cdot [\mathrm{B\_catenin\_0}] - \mathrm{k\_17} \cdot [\mathrm{B\_catenin\_APC}] \tag{52}$$

10. 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.

10.1. Species `Dsh_i`

Name Dsh_i

Initial concentration $100\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

Initial assignment `Dsh_i`

This species takes part in two reactions (as a reactant in `v1` and as a product in `v2`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Dsh\_i} = v_2 - v_1 \tag{53}$$

10.2. Species Dsh_a

Name Dsh_a

Initial concentration $0\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in v2 and as a product in v1 and as a modifier in v3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Dsh\_a} = v_1 - v_2 \tag{54}$$

10.3. Species APC__axin__GSK3

Name APC*/axin*/GSK3

Initial concentration $0.00966\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in v5, v8 and as a product in v4, v10).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{APC\_\_axin\_\_GSK3} = v_4 + v_{10} - v_5 - v_8 \tag{55}$$

10.4. Species APC_axin_GSK3

Name APC/axin/GSK3

Initial concentration $0.00483\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in v3, v4 and as a product in v5, v6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{APC\_axin\_GSK3} = v_5 + v_6 - v_3 - v_4 \tag{56}$$

10.5. Species GSK3

Name GSK3

Initial concentration $50\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a reactant in v6 and as a product in v3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GSK3} = v_3 - v_6 \tag{57}$$

10.6. Species APC_axin

Name APC/axin

Initial concentration $9.8065 \cdot 10^{-4}\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in v6 and as a product in v3, v7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{APC\_axin} = v_3 + v_7 - v_6 \tag{58}$$

10.7. Species APC

Name APC

Initial concentration $98\ \mu\text{mol} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a reactant in v7, v17).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{APC} = -v_7 - v_{17} \tag{59}$$

10.8. Species B_catenin_APC__axin__GSK3

Name B_catenin/APC*/axin*/GSK3

Initial concentration $0.00202\ \mu\text{mol} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a reactant in v9 and as a product in v8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{B\_catenin\_APC\_\_axin\_\_GSK3} = v_8 - v_9 \tag{60}$$

10.9. Species B_catenin__APC__axin__GSK3

Name B_catenin*/APC*/axin*/GSK3

Initial concentration $0.00202\ \mu\text{mol} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a reactant in v10 and as a product in v9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{B\_catenin\_\_APC\_\_axin\_\_GSK3} = v_9 - v_{10} \tag{61}$$

10.10. Species B_catenin

Name B_catenin*

Initial concentration $1\ \mu\text{mol} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a reactant in v11 and as a product in v10).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{B\_catenin} = v_{10} - v_{11} \tag{62}$$

10.11. Species B_catenin_0

Name B_catenin

Initial concentration $25.1\ \mu\text{mol} \cdot \text{ml}^{-1}$

This species takes part in five reactions (as a reactant in v8, v13, v16, v17 and as a product in v12).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{B\_catenin\_0} = v_{12} - v_8 - v_{13} - v_{16} - v_{17} \tag{63}$$

10.12. Species Axin

Name Axin

Initial concentration $4.93 \cdot 10^{-4}$ µmol · ml^{-1}

This species takes part in three reactions (as a reactant in v7, v15 and as a product in v14).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Axin} = v_{14} - v_7 - v_{15} \quad (64)$$

10.13. Species TCF

Name TCF

Initial concentration 8.17 µmol · ml^{-1}

This species takes part in one reaction (as a reactant in v16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{TCF} = -v_{16} \quad (65)$$

10.14. Species B_catenin_TCF

Name B_catenin/TCF

Initial concentration 6.83 µmol · ml^{-1}

This species takes part in one reaction (as a product in v16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{B\_catenin\_TCF} = v_{16} \quad (66)$$

10.15. Species B_catenin_APC

Name B_catenin/APC

Initial concentration 2.05 µmol · ml^{-1}

This species takes part in one reaction (as a product in v17).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{B\_catenin\_APC} = v_{17} \quad (67)$$

10.16. Species W

Name W

Initial concentration 0 µmol · ml^{-1}

Involved in rule W

This species takes part in one reaction (as a modifier in v1). Not this but one rule determines the species' quantity because this species is on the boundary of the reaction system.

A. Glossary of Systems Biology Ontology Terms

SBO:0000282 dissociation constant: Equilibrium constant that measures the propensity of a larger object to separate (dissociate) reversibly into smaller components, as when a complex falls apart into its component molecules, or when a salt splits up into its component ions. The dissociation constant is usually denoted Kd and is the inverse of the affinity constant.

SBO:0000356 decay constant: Kinetic constant characterising a mono-exponential decay. It is the inverse of the mean lifetime of the continuant being decayed. Its unit is"per tim".

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