

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 Kothamachu¹ and Matthew Grant Roberts² 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)

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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.](#)

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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 | <input checked="" type="checkbox"/> | |
| Nucleus | Nucleus | | 3 | 1 | litre | <input checked="" type="checkbox"/> | |

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 | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| Dsh_a | Dsh_a | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| APC_axin_GSK3 | APC*/axin*/GSK3 | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| APC_axin_GSK3 | APC/axin/GSK3 | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| GSK3 | GSK3 | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| APC_axin | APC/axin | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| APC | APC | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| B_catenin_APC-_axin_GSK3 | B_catenin/APC*/axin*/GSK3 | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| B_catenin_APC-_axin_GSK3 | B_catenin*/APC*/axin*/GSK3 | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| B_catenin | B_catenin* | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| B_catenin_0 | B_catenin | Nucleus | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| Axin | Axin | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| TCF | TCF | Nucleus | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| B_catenin_TCF | B_catenin/TCF | Nucleus | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| B_catenin_APC | B_catenin/APC | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| W | W | Cytoplasm | $\mu\text{mol} \cdot \text{ml}^{-1}$ | <input type="checkbox"/> | <input checked="" type="checkbox"/> |

5. Parameters

This model contains 31 global parameters.

Table 4: Properties of each parameter.

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

6. Initialassignment

This is an overview of one initialassignment.

6.1. Initialassignment `Dsh_i`

Derived unit contains undeclared units

Math $Dsh0 - [Dsh_a]$

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

$$v \quad (1)$$

7.2. Function definition `function_for_v1`

Name function for $v1$

Arguments $k1, x1, [W]$

Mathematical Expression

$$k1 \cdot x1 \cdot [W] \quad (2)$$

7.3. Function definition `function_for_v3`

Name function for $v3$

Arguments $k3, x2, x4$

Mathematical Expression

$$k3 \cdot x2 \cdot x4 \quad (3)$$

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:

$$\begin{aligned} \text{Total_B_Catenin} = & [\text{B_catenin_APC_axin_GSK3}] + [\text{B_catenin_APC_axin_GSK3}] \\ & + [\text{B_catenin}] + [\text{B_catenin}_0] + [\text{B_catenin_TCF}] + [\text{B_catenin_APC}] \end{aligned} \quad (4)$$

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:

$$\begin{aligned} \text{Total_Axin} = & [\text{APC_axin_GSK3}] + [\text{APC_axin_GSK3}] + [\text{APC_axin}] \\ & + [\text{B_catenin_APC_axin_GSK3}] + [\text{B_catenin_APC_axin_GSK3}] + [\text{Axin}] \end{aligned} \quad (5)$$

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:

$$k_{16} = k_{16} \cdot K_{16} \quad (6)$$

8.4. Rule k_7

Rule k_7 is an assignment rule for parameter k_7:

$$k_7 = k_7 \cdot K_7 \quad (7)$$

8.5. Rule k_17

Rule k_17 is an assignment rule for parameter k_17:

$$k_{17} = k_{17} \cdot K_{17} \quad (8)$$

8.6. Rule k_8

Rule k_8 is an assignment rule for parameter k_8:

$$k_8 = k_8 \cdot K_8 \quad (9)$$

8.7. Rule W

Rule W is an assignment rule for species W:

$$W = \begin{cases} 0 & \text{if time} < t_0 \\ \exp(1 \cdot \text{lambda} \cdot (\text{time} - t_0)) & \text{otherwise} \end{cases} \quad (10)$$

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

| Nº | 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 | $\text{APC_axin_GSK3} \rightleftharpoons \text{B_catenin_APC_axin_GSK3}$ | + |
| 9 | v9 | v9 | $\text{B_catenin_APC_axin_GSK3} \longrightarrow \text{B_catenin_APC_axin_GSK3}$ | |
| 10 | v10 | v10 | $\text{B_catenin_APC_axin_GSK3} \longrightarrow \text{B_catenin_APC_axin_GSK3}$ | + |
| 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 v_1

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

Name v_1

Reaction equation



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

$$v_1 = \text{vol}(\text{Cytoplasm}) \cdot \text{function_for_v1}(k_1, [\text{Dsh_i}], [W]) \quad (12)$$

$$\text{function_for_v1}(k_1, x_1, [W]) = k_1 \cdot x_1 \cdot [W] \quad (13)$$

$$\text{function_for_v1}(k_1, x_1, [W]) = k_1 \cdot x_1 \cdot [W] \quad (14)$$

9.2. Reaction v2

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

Name v2

Reaction equation



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

$$v_2 = \text{vol}(\text{Cytoplasm}) \cdot k_2 \cdot [\text{Dsh_a}] \quad (16)$$

9.3. Reaction v3

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

Name v3

Reaction equation



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

$$v_3 = \text{vol}(\text{Cytoplasm}) \cdot \text{function_for_v3}(k_3, [\text{Dsh_a}], [\text{APC_axin_GSK3}]) \quad (18)$$

$$\text{function_for_v3}(k_3, x_2, x_4) = k_3 \cdot x_2 \cdot x_4 \quad (19)$$

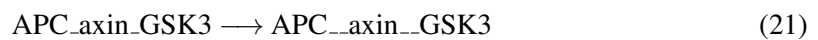
$$\text{function_for_v3}(k_3, x_2, x_4) = k_3 \cdot x_2 \cdot x_4 \quad (20)$$

9.4. Reaction v4

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

Name v4

Reaction equation



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

$$v_4 = \text{vol}(\text{Cytoplasm}) \cdot k_4 \cdot [\text{APC_axin_GSK3}] \quad (22)$$

9.5. Reaction v5

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

Name v5

Reaction equation



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

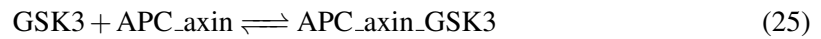
$$v_5 = \text{vol}(\text{Cytoplasm}) \cdot k_5 \cdot [\text{APC_axin_GSK3}] \quad (24)$$

9.6. Reaction v6

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

Name v6

Reaction equation



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

$$v_6 = \text{vol}(\text{Cytoplasm}) \cdot (k_6 \cdot [\text{GSK3}] \cdot [\text{APC_axin}] - k_{-6} \cdot [\text{APC_axin_GSK3}]) \quad (26)$$

9.7. Reaction v7

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

Name v7

Reaction equation



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

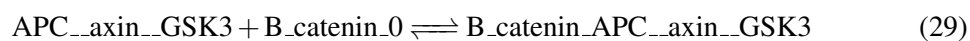
$$v_7 = \text{vol}(\text{Cytoplasm}) \cdot (k_7 \cdot [\text{APC}] \cdot [\text{Axin}] - k_{-7} \cdot [\text{APC_axin}]) \quad (28)$$

9.8. Reaction v8

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

Name v8

Reaction equation



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

$$v_8 = k_8 \cdot [\text{APC_axin_GSK3}] \cdot [\text{B_catenin}_0] - k_{-8} \cdot [\text{B_catenin_APC_axin_GSK3}] \quad (30)$$

9.9. Reaction v9

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

Name v9

Reaction equation



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

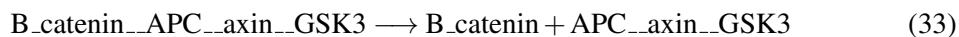
$$v_9 = \text{vol}(\text{Cytoplasm}) \cdot k_9 \cdot [\text{B_catenin_APC_axin_GSK3}] \quad (32)$$

9.10. Reaction v10

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

Name v10

Reaction equation



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

$$v_{10} = \text{vol}(\text{Cytoplasm}) \cdot k_{10} \cdot [\text{B_catenin_APC_axin_GSK3}] \quad (34)$$

9.11. Reaction v11

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

Name v11

Reaction equation



Reactant

Table 28: Properties of each reactant.

| Id | Name | SBO |
|-----------|------------|-----|
| B_catenin | B_catenin* | |

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{vol}(\text{Cytoplasm}) \cdot k_{11} \cdot [\text{B_catenin}] \quad (36)$$

9.12. Reaction v12

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

Name v12

Reaction equation



Product

Table 29: Properties of each product.

| Id | Name | SBO |
|-------------|-----------|-----|
| B_catenin_0 | B_catenin | |

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{vol}(\text{Nucleus}) \cdot \text{Constant_flux_irreversible}(k_{12}) \quad (38)$$

$$\text{Constant_flux_irreversible}(v) = v \quad (39)$$

$$\text{Constant_flux_irreversible}(v) = v \quad (40)$$

9.13. Reaction v_{13}

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

Name v_{13}

Reaction equation



Reactant

Table 30: Properties of each reactant.

| Id | Name | SBO |
|-------------|-----------|-----|
| B_catenin_0 | B_catenin | |

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{vol}(\text{Nucleus}) \cdot k_{13} \cdot [\text{B_catenin}_0] \quad (42)$$

9.14. Reaction v_{14}

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

Name v_{14}

Reaction equation



Product

Table 31: Properties of each product.

| Id | Name | SBO |
|-------------------|-------------------|-----|
| <code>Axin</code> | <code>Axin</code> | |

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \text{vol}(\text{Cytoplasm}) \cdot \text{Constant_flux_irreversible}(k_{14}) \quad (44)$$

$$\text{Constant_flux_irreversible}(v) = v \quad (45)$$

$$\text{Constant_flux_irreversible}(v) = v \quad (46)$$

9.15. Reaction `v15`

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

Name `v15`

Reaction equation



Reactant

Table 32: Properties of each reactant.

| Id | Name | SBO |
|-------------------|-------------------|-----|
| <code>Axin</code> | <code>Axin</code> | |

Kinetic Law

Derived unit contains undeclared units

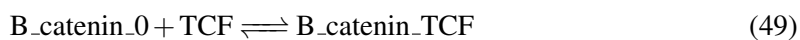
$$v_{15} = \text{vol}(\text{Cytoplasm}) \cdot k_{15} \cdot [\text{Axin}] \quad (48)$$

9.16. Reaction `v16`

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

Name v16

Reaction equation



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

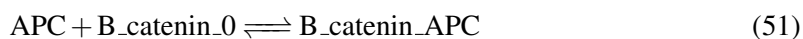
$$v_{16} = \text{vol}(\text{Nucleus}) \cdot (k_{16} \cdot [\text{B_catenin_0}] \cdot [\text{TCF}] - k_{-16} \cdot [\text{B_catenin_TCF}]) \quad (50)$$

9.17. Reaction v17

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

Name v17

Reaction equation



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

$$v_{17} = k_{17} \cdot [\text{APC}] \cdot [\text{B_catenin_0}] - k_{-17} \cdot [\text{B_catenin_APC}] \quad (52)$$

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 $100 \mu\text{mol} \cdot \text{ml}^{-1}$

Initial assignment Dsh_i

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

$$\frac{d}{dt} \text{Dsh_i} = v_2 - v_1 \quad (53)$$

10.2. Species Dsh_a

Name Dsh_a

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

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

$$\frac{d}{dt}\text{Dsh.a} = v_1 - v_2 \quad (54)$$

10.3. Species APC__axin__GSK3

Name APC*/axin*/GSK3

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

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

$$\frac{d}{dt}\text{APC_axin_GSK3} = v_4 + v_{10} - v_5 - v_8 \quad (55)$$

10.4. Species APC_axin_GSK3

Name APC/axin/GSK3

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

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

$$\frac{d}{dt}\text{APC_axin_GSK3} = v_5 + v_6 - v_3 - v_4 \quad (56)$$

10.5. Species GSK3

Name GSK3

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

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

$$\frac{d}{dt}\text{GSK3} = v_3 - v_6 \quad (57)$$

10.6. Species APC_axin

Name APC/axin

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

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

$$\frac{d}{dt}\text{APC_axin} = v_3 + v_7 - v_6 \quad (58)$$

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).

$$\frac{d}{dt}\text{APC} = -v_7 - v_{17} \quad (59)$$

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).

$$\frac{d}{dt}\text{B_catenin_APC_axin_GSK3} = v_8 - v_9 \quad (60)$$

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).

$$\frac{d}{dt}\text{B_catenin_APC_axin_GSK3} = v_9 - v_{10} \quad (61)$$

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).

$$\frac{d}{dt}\text{B_catenin} = v_{10} - v_{11} \quad (62)$$

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).

$$\frac{d}{dt}\text{B_catenin}_0 = v_{12} - v_8 - v_{13} - v_{16} - v_{17} \quad (63)$$

10.12. Species Axin

Name Axin

Initial concentration $4.93 \cdot 10^{-4} \mu\text{mol} \cdot \text{ml}^{-1}$

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

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

10.13. Species TCF

Name TCF

Initial concentration $8.17 \mu\text{mol} \cdot \text{ml}^{-1}$

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

$$\frac{d}{dt}\text{TCF} = -v_{16} \quad (65)$$

10.14. Species B_catenin_TCF

Name B_catenin/TCF

Initial concentration $6.83 \mu\text{mol} \cdot \text{ml}^{-1}$

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

$$\frac{d}{dt}\text{B_catenin_TCF} = v_{16} \quad (66)$$

10.15. Species B_catenin_APC

Name B_catenin/APC

Initial concentration $2.05 \mu\text{mol} \cdot \text{ml}^{-1}$

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

$$\frac{d}{dt}\text{B_catenin_APC} = v_{17} \quad (67)$$

10.16. Species W

Name W

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

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 K_d 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”.

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