

SBML Model Report

Model name: “Clarke2006_Smad_signalling”



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: Harish Dharuri¹ and Katja Wegner² at November 29th 2006 at 11:35 a. m. and last time modified at October 29th 2010 at 1:55 p. m. Table 1 shows an overview of the quantities of all components of this model.

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

| Element | Quantity | Element | Quantity |
|-------------------|----------|----------------------|----------|
| compartment types | 0 | compartments | 2 |
| species types | 0 | species | 10 |
| events | 0 | constraints | 0 |
| reactions | 8 | function definitions | 0 |
| global parameters | 4 | unit definitions | 5 |
| rules | 4 | initial assignments | 0 |

Model Notes

The model reproduces the temporal evolution of four variables depicted in Fig 2a. The solution is generated for median parameter values as given in Table 3. Result shown was generated by MathSBML.

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To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler L, Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novre N, Laibe C (2010) BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

2 Unit Definitions

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

2.1 Unit `time`

Name minutes

Definition 60 s

2.2 Unit `substance`

Definition item

2.3 Unit `min_inv`

Name min_inv

Definition $(60\text{ s})^{-1}$

2.4 Unit `items_per_min`

Name items per min

Definition $\text{item} \cdot (60\text{ s})^{-1}$

2.5 Unit `per_item_min`

Name per item per min

Definition $\text{item}^{-1} \cdot (60\text{ s})^{-1}$

2.6 Unit `volume`

Notes Litre is the predefined SBML unit for volume.

Definition 1

2.7 Unit `area`

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

Definition m^2

2.8 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 | ✓ | cytoplasm |

3.1 Compartment `cytoplasm`

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

Name `cytoplasm`

3.2 Compartment `nucleus`

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

Name `nucleus`

4 Species

This model contains ten species. Section 8 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 |
|--------------------|--------------------|-------------|--------------|-----------|--------------------|
| receptor | receptors | cytoplasm | item | \square | \square |
| R_smad_cyt | R-Smad_cyt | cytoplasm | item | \square | \square |
| R_smad_P_cyt | R-Smad-P_cyt | cytoplasm | item | \square | \square |
| smad4_cyt | Smad4_cyt | cytoplasm | item | \square | \square |
| R_smad_P_smad4_cyt | R-Smad-P-Smad4_cyt | cytoplasm | item | \square | \square |
| R_smad_P_smad4_nuc | R-Smad-P-Smad4_nuc | nucleus | item | \square | \square |
| R_smad_nuc | R-Smad_nuc | nucleus | item | \square | \square |
| R_smad_P_nuc | R-Smad-P_nuc | nucleus | item | \square | \square |
| smad4_nuc | Smad4_nuc | nucleus | item | \square | \square |
| Pi | Pi | nucleus | item | \square | \square |

5 Parameters

This model contains four global parameters.

Table 4: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|-----------------|----------------|-----|-------|------|----------|
| sum_R_smad-_cyt | sum_R_smad_cyt | | 0.0 | | ☐ |
| sum_R_smad-_nuc | sum_R_smad_nuc | | 0.0 | | ☐ |
| sum_smad4-_cyt | sum_Smad4_cyt | | 0.0 | | ☐ |
| sum_smad4-_nuc | sum_Smad4_nuc | | 0.0 | | ☐ |

6 Rules

This is an overview of four rules.

6.1 Rule `sum_R_smad_nuc`

Rule `sum_R_smad_nuc` is an assignment rule for parameter `sum_R_smad_nuc`:

$$\text{sum_R_smad_nuc} = \text{R_smad_nuc} + \text{R_smad_P_nuc} + \text{R_smad_P_smad4_nuc} \quad (1)$$

Derived unit item

6.2 Rule `sum_smad4_nuc`

Rule `sum_smad4_nuc` is an assignment rule for parameter `sum_smad4_nuc`:

$$\text{sum_smad4_nuc} = \text{smad4_nuc} + \text{R_smad_P_smad4_nuc} \quad (2)$$

Derived unit item

6.3 Rule `sum_R_smad_cyt`

Rule `sum_R_smad_cyt` is an assignment rule for parameter `sum_R_smad_cyt`:

$$\text{sum_R_smad_cyt} = \text{R_smad_cyt} + \text{R_smad_P_cyt} + \text{R_smad_P_smad4_cyt} \quad (3)$$

Derived unit item

6.4 Rule `sum_smad4_cyt`

Rule `sum_smad4_cyt` is an assignment rule for parameter `sum_smad4_cyt`:

$$\text{sum_smad4_cyt} = \text{smad4_cyt} + \text{R_smad_P_smad4_cyt} \quad (4)$$

Derived unit item

7 Reactions

This model contains eight 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

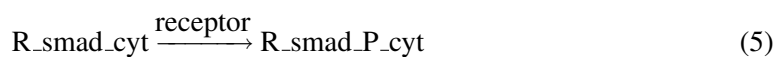
| Nº | Id | Name | Reaction Equation | SBO |
|----|------------|-----------------------|--|-----|
| 1 | reaction_1 | Phosphorylation | $R_smad_cyt \xrightarrow{\text{receptor}} R_smad_P_cyt$ | |
| 2 | reaction_5 | R-Smad translocation | $R_smad_nuc \rightleftharpoons R_smad_cyt$ | |
| 3 | reaction_4 | Smad4 translocation | $smad4_nuc \rightleftharpoons smad4_cyt$ | |
| 4 | reaction_2 | Complex formation | $R_smad_P_cyt + smad4_cyt \rightleftharpoons R_smad_P_smad4_cyt$ | |
| 5 | reaction_3 | Complex translocation | $R_smad_P_smad4_cyt \longrightarrow R_smad_P_smad4_nuc$ | |
| 6 | reaction_6 | Complex in nucleus | $R_smad_P_smad4_nuc \rightleftharpoons smad4_nuc + R_smad_P_nuc$ | |
| 7 | reaction_7 | Dephosphorylation | $R_smad_P_nuc \longrightarrow R_smad_nuc + Pi$ | |
| 8 | reaction_0 | Receptor degradation | $\text{receptor} \longrightarrow \emptyset$ | |

7.1 Reaction `reaction_1`

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

Name Phosphorylation

Reaction equation



Reactant

Table 6: Properties of each reactant.

| Id | Name | SBO |
|------------|------------|-----|
| R_smad_cyt | R-Smad_cyt | |

Modifier

Table 7: Properties of each modifier.

| Id | Name | SBO |
|----------|-----------|-----|
| receptor | receptors | |

Product

Table 8: Properties of each product.

| Id | Name | SBO |
|--------------|--------------|-----|
| R_smad_P_cyt | R-Smad-P_cyt | |

Kinetic Law

Derived unit $(60 \text{ s})^{-1} \cdot \text{item}$

$$v_1 = \frac{\text{KCAT} \cdot \text{receptor} \cdot \text{R_smad_cyt}}{\text{K1} + \text{R_smad_cyt}} \quad (6)$$

Table 9: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|------|------|-----|-----------|----------------------|-------------------------------------|
| KCAT | | | 3.51 | $(60\text{ s})^{-1}$ | <input checked="" type="checkbox"/> |
| K1 | | | 289000.00 | item | <input checked="" type="checkbox"/> |

7.2 Reaction `reaction_5`

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

Name R-Smad translocation

Reaction equation



Reactant

Table 10: Properties of each reactant.

| Id | Name | SBO |
|------------|------------|-----|
| R_smad_nuc | R-Smad_nuc | |

Product

Table 11: Properties of each product.

| Id | Name | SBO |
|------------|------------|-----|
| R_smad_cyt | R-Smad_cyt | |

Kinetic Law

Derived unit $(60\text{ s})^{-1} \cdot \text{item}$

$$v_2 = k5nc \cdot \text{R_smad_nuc} - k5cn \cdot \text{R_smad_cyt} \quad (8)$$

Table 12: Properties of each parameter.

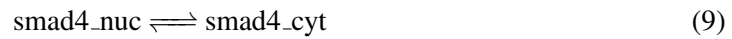
| Id | Name | SBO | Value | Unit | Constant |
|------|------|-----|-------|----------------------|-------------------------------------|
| k5nc | | | 5.630 | $(60\text{ s})^{-1}$ | <input checked="" type="checkbox"/> |
| k5cn | | | 0.563 | $(60\text{ s})^{-1}$ | <input checked="" type="checkbox"/> |

7.3 Reaction `reaction_4`

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

Name Smad4 translocation

Reaction equation



Reactant

Table 13: Properties of each reactant.

| Id | Name | SBO |
|-----------|-----------|-----|
| smad4_nuc | Smad4_nuc | |

Product

Table 14: Properties of each product.

| Id | Name | SBO |
|-----------|-----------|-----|
| smad4_cyt | Smad4_cyt | |

Kinetic Law

Derived unit $(60 \text{ s})^{-1} \cdot \text{item}$

$$v_3 = k4nc \cdot \text{smad4_nuc} - k4cn \cdot \text{smad4_cyt} \quad (10)$$

Table 15: Properties of each parameter.

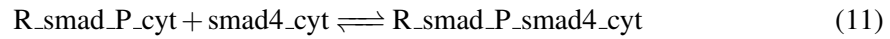
| Id | Name | SBO | Value | Unit | Constant |
|------|------|-----|-------|-----------------------|-------------------------------------|
| k4nc | | | 0.783 | $(60 \text{ s})^{-1}$ | <input checked="" type="checkbox"/> |
| k4cn | | | 0.005 | $(60 \text{ s})^{-1}$ | <input checked="" type="checkbox"/> |

7.4 Reaction `reaction_2`

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

Name Complex formation

Reaction equation



Reactants

Table 16: Properties of each reactant.

| Id | Name | SBO |
|--------------|--------------|-----|
| R_smad_P_cyt | R-Smad-P_cyt | |
| smad4_cyt | Smad4_cyt | |

Product

Table 17: Properties of each product.

| Id | Name | SBO |
|--------------------|--------------------|-----|
| R_smad_P_smad4_cyt | R-Smad-P-Smad4_cyt | |

Kinetic Law

Derived unit $(60 \text{ s})^{-1} \cdot \text{item}$

$$v_4 = k2a \cdot \text{R_smad_P_cyt} \cdot \text{smad4_cyt} - k2d \cdot \text{R_smad_P_smad4_cyt} \quad (12)$$

Table 18: Properties of each parameter.

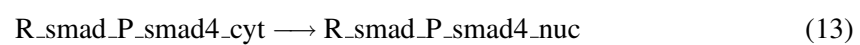
| Id | Name | SBO | Value | Unit | Constant |
|-----|------|-----|---------------------|--|-------------------------------------|
| k2a | | | $6.5 \cdot 10^{-5}$ | $\text{item}^{-1} \cdot (60 \text{ s})^{-1}$ | <input checked="" type="checkbox"/> |
| k2d | | | 0.040 | $(60 \text{ s})^{-1}$ | <input checked="" type="checkbox"/> |

7.5 Reaction `reaction_3`

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

Name Complex translocation

Reaction equation



Reactant

Table 19: Properties of each reactant.

| Id | Name | SBO |
|--------------------|--------------------|-----|
| R_smad_P_smad4_cyt | R-Smad-P-Smad4_cyt | |

Product

Table 20: Properties of each product.

| Id | Name | SBO |
|--------------------|--------------------|-----|
| R_smad_P_smad4_nuc | R-Smad-P-Smad4_nuc | |

Kinetic Law

Derived unit $(60\text{ s})^{-1} \cdot \text{item}$

$$v_5 = k_3 \cdot \text{R_smad_P_smad4_cyt} \quad (14)$$

Table 21: Properties of each parameter.

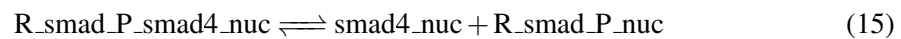
| Id | Name | SBO | Value | Unit | Constant |
|----|------|-----|-------|----------------------|-------------------------------------|
| k3 | | | 16.6 | $(60\text{ s})^{-1}$ | <input checked="" type="checkbox"/> |

7.6 Reaction `reaction_6`

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

Name Complex in nucleus

Reaction equation



Reactant

Table 22: Properties of each reactant.

| Id | Name | SBO |
|--------------------|--------------------|-----|
| R_smad_P_smad4_nuc | R-Smad-P-Smad4_nuc | |

Products

Table 23: Properties of each product.

| Id | Name | SBO |
|--------------|--------------|-----|
| smad4_nuc | Smad4_nuc | |
| R_smad_P_nuc | R-Smad-P_nuc | |

Kinetic Law

Derived unit $(60\text{ s})^{-1} \cdot \text{item}$

$$v_6 = k6d \cdot R_smad_P_smad4_nuc - k6a \cdot smad4_nuc \cdot R_smad_P_nuc \quad (16)$$

Table 24: Properties of each parameter.

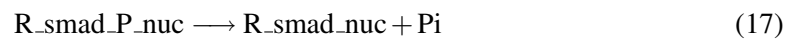
| Id | Name | SBO | Value | Unit | Constant |
|-----|------|-----|----------------------|---|-------------------------------------|
| k6d | | | 0.049 | $(60\text{ s})^{-1}$ | <input checked="" type="checkbox"/> |
| k6a | | | $1.44 \cdot 10^{-4}$ | $\text{item}^{-1} \cdot (60\text{ s})^{-1}$ | <input checked="" type="checkbox"/> |

7.7 Reaction [reaction_7](#)

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

Name Dephosphorylation

Reaction equation



Reactant

Table 25: Properties of each reactant.

| Id | Name | SBO |
|--------------|--------------|-----|
| R_smad_P_nuc | R-Smad-P_nuc | |

Products

Table 26: Properties of each product.

| Id | Name | SBO |
|------------|------------|-----|
| R_smad_nuc | R-Smad_nuc | |
| Pi | Pi | |

Kinetic Law

Derived unit $\text{item} \cdot (60 \text{ s})^{-1}$

$$v_7 = \frac{V_{\max 7} \cdot R_smad_P_nuc}{K7 + R_smad_P_nuc} \quad (18)$$

Table 27: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|-------|------|-----|---------|---|-------------------------------------|
| Vmax7 | | | 17100.0 | $\text{item} \cdot (60 \text{ s})^{-1}$ | <input checked="" type="checkbox"/> |
| K7 | | | 8950.0 | item | <input checked="" type="checkbox"/> |

7.8 Reaction `reaction_0`

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

Name Receptor degradation

Reaction equation



Reactant

Table 28: Properties of each reactant.

| Id | Name | SBO |
|----------|-----------|-----|
| receptor | receptors | |

Kinetic Law

Derived unit contains undeclared units

$$v_8 = 100 \cdot \exp\left(\frac{\text{time}}{90}\right) \quad (20)$$

8 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.

8.1 Species `receptor`

Name `receptors`

Initial amount 10000 item

This species takes part in two reactions (as a reactant in `reaction_0` and as a modifier in `reaction_1`).

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

8.2 Species `R_smad_cyt`

Name `R-Smad_cyt`

Initial amount 162000 item

This species takes part in two reactions (as a reactant in `reaction_1` and as a product in `reaction_5`).

$$\frac{d}{dt}\text{R_smad_cyt} = v_2 - v_1 \quad (22)$$

8.3 Species `R_smad_P_cyt`

Name `R-Smad-P_cyt`

Initial amount 0 item

This species takes part in two reactions (as a reactant in `reaction_2` and as a product in `reaction_1`).

$$\frac{d}{dt}\text{R_smad_P_cyt} = v_1 - v_4 \quad (23)$$

8.4 Species `smad4_cyt`

Name `Smad4_cyt`

Initial amount 120000 item

This species takes part in two reactions (as a reactant in [reaction_2](#) and as a product in [reaction_4](#)).

$$\frac{d}{dt}\text{smad4_cyt} = v_3 - v_4 \quad (24)$$

8.5 Species `R_smad_P_smad4_cyt`

Name `R-Smad-P-Smad4_cyt`

Initial amount 0 item

This species takes part in two reactions (as a reactant in [reaction_3](#) and as a product in [reaction_2](#)).

$$\frac{d}{dt}\text{R_smad_P_smad4_cyt} = v_4 - v_5 \quad (25)$$

8.6 Species `R_smad_P_smad4_nuc`

Name `R-Smad-P-Smad4_nuc`

Initial amount 0 item

This species takes part in two reactions (as a reactant in [reaction_6](#) and as a product in [reaction_3](#)).

$$\frac{d}{dt}\text{R_smad_P_smad4_nuc} = v_5 - v_6 \quad (26)$$

8.7 Species `R_smad_nuc`

Name `R-Smad_nuc`

Initial amount 18000 item

This species takes part in two reactions (as a reactant in [reaction_5](#) and as a product in [reaction_7](#)).

$$\frac{d}{dt}\text{R_smad_nuc} = v_7 - v_2 \quad (27)$$

8.8 Species `R_smad_P_nuc`

Name R-Smad-P_nuc

Initial amount 0 item

This species takes part in two reactions (as a reactant in [reaction_7](#) and as a product in [reaction_6](#)).

$$\frac{d}{dt}R_smad_P_nuc = v_6 - v_7 \quad (28)$$

8.9 Species `smad4_nuc`

Name Smad4_nuc

Initial amount 30000 item

This species takes part in two reactions (as a reactant in [reaction_4](#) and as a product in [reaction_6](#)).

$$\frac{d}{dt}smad4_nuc = v_6 - v_3 \quad (29)$$

8.10 Species `Pi`

Name Pi

Initial amount 0 item

This species takes part in one reaction (as a product in [reaction_7](#)).

$$\frac{d}{dt}Pi = v_7 \quad (30)$$

SBML2^{LaTeX} 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.

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