

SBML Model Report

Model name: “Zi2011_TGF-beta_Pathway”



May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah¹ and Zhike Zi² at July 14th 2011 at 12:23 a. m. and last time modified at February 24th 2014 at five o’ clock in the afternoon. 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	4
species types	0	species	21
events	1	constraints	0
reactions	29	function definitions	0
global parameters	34	unit definitions	12
rules	10	initial assignments	5

Model Notes

This model is from the article:

Quantitative analysis of transient and sustained transforming growth factor- signaling dynamics.

Zhike Zi, Zipei Feng, Douglas A Chapnick, Markus Dahl, Difan Deng, Edda Klipp, Aristidis Moustakas & Xuedong Liu Molecular Systems Biology 2011 May 24;7:492. [21613981](#) ,

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Abstract:

Mammalian cells can decode the concentration of extracellular transforming growth factor- (TGF-) and transduce this cue into appropriate cell fate decisions. How variable TGF- ligand doses quantitatively control intracellular signaling dynamics and how continuous ligand doses are translated into discontinuous cellular fate decisions remain poorly understood. Using a combined experimental and mathematical modeling approach, we discovered that cells respond differently to continuous and pulsating TGF- stimulation. The TGF- pathway elicits a transient signaling response to a single pulse of TGF- stimulation, whereas it is capable of integrating repeated pulses of ligand stimulation at short time interval, resulting in sustained phospho-Smad2 and transcriptional responses. Additionally, the TGF- pathway displays different sensitivities to ligand doses at different time scales. While ligand-induced short-term Smad2 phosphorylation is graded, long-term Smad2 phosphorylation is switch-like to a small change in TGF- levels. Correspondingly, the short-term Smad7 gene expression is graded, while long-term PAI-1 gene expression is switch-like, as is the long-term growth inhibitory response. Our results suggest that long-term switch-like signaling responses in the TGF- pathway might be critical for cell fate determination.

Note:

Developer of the model: Zhike Zi

Reference: Zi Z. et al., Quantitative Analysis of Transient and Sustained Transforming Growth Factor-beta Signaling Dynamics, Molecular Systems Biology, 2011

1. The global parameter that set the type of stimulation

(a) for sustained TGF-beta stimulation: set stimulation_type = 1.

(b) for single pulse of TGF-beta stimulation: set stimulation_type = 2.

parameter „single_pulse_duration,, is for the duration of stimulation, for example, single_pulse_duration = 0.5, for 0.5 min (30 seconds) of TGF-beta stimulation.

*Note: make sure that the time course cover the time point when the event is triggered.

(c) for single pulse of TGF-beta stimulation in COPASI

change the trigger of event „single_pulse_TGF_beta_washout,, from

„and(eq(stimulation_type, 2), eq(time, single_pulse_duration)),, (for SBML-SAT)

to

„and(eq(stimulation_type, 2), gt(time, single_pulse_duration)),, (for COPASI)

2. Notes for TGF-beta dose in terms of molecules per cell

(a) The following equation applies for conversion of TGF-beta dose in molecules per cell

$\text{TGF_beta_dose_mol_per_cell} = \text{initial TGF_beta_ex} \times 1\text{e-}9 \times V_{\text{med}} \times 6\text{e}23$

(b) for standard experimental setup 1e6 cells in 2 mL medium

0.001 nM initial TGF_beta_ex is approximately equal to the dose of 1200 TGF-beta molecules/cell

0.050 nM initial TGF_beta_ex is approximately equal to the dose of 60000 TGF-beta molecules/cell

(c) For 1e6 cells in 10 mL medium, please change the initial compartment size of Vmed and the corresponding assignment rule for Vmed.

initial Vmed = 1e-8 (1e6 cells in 10 mL medium)

$V_{\text{med}} = 0.010 / (1\text{e}6 \times \exp(\log(1.45) \times \text{time} / 1440))$ (1e6 cells in 10 mL medium)

3. Please note that this model contains events and the medium compartment size is varied.

4. For the model simulation in SBML-SAT, please remove initialAssignments and save it as SBML Level 2 Version 1 file.

2 Unit Definitions

This is an overview of twelve unit definitions.

2.1 Unit substance

Name substance

Definition nmol

2.2 Unit volume

Name volume

Definition l

2.3 Unit area

Name area

Definition m²

2.4 Unit length

Name length

Definition m

2.5 Unit time

Name min

Definition 60 s

2.6 Unit per_min

Name per min

Definition (60 s)⁻¹

2.7 Unit nM_per_min

Name nM per min

Definition nmol · (60 s)⁻¹

2.8 Unit `third_order`

Name third order rate constant

Definition $\text{nmol}^{-2} \cdot (60 \text{ s})^{-1}$

2.9 Unit `second_order`

Name second order rate constant

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

2.10 Unit `min`

Name minute

Definition 60 s

2.11 Unit `nM`

Name nanomolar

Definition nmol

2.12 Unit `molecules_per_cell`

Name molecules per cell

Definition dimensionless

3 Compartments

This model contains four compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
default			3	1	litre	<input checked="" type="checkbox"/>	
Vmed	Medium	0000290	3	$2 \cdot 10^{-9}$	l	<input type="checkbox"/>	default
Vcyt	Cytoplasm	0000290	3	$2.3 \cdot 10^{-12}$	l	<input checked="" type="checkbox"/>	Vmed
Vnuc	Nucleus	0000290	3	10^{-12}	l	<input checked="" type="checkbox"/>	Vcyt

3.1 Compartment `default`

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

3.2 Compartment V_{med}

This is a three dimensional compartment with a not constant size of $2 \cdot 10^{-9}$ litre, which is surrounded by default.

Name Medium

SBO:0000290 physical compartment

3.3 Compartment V_{cyt}

This is a three dimensional compartment with a constant size of $2.3 \cdot 10^{-12}$ litre, which is surrounded by V_{med} (Medium).

Name Cytoplasm

SBO:0000290 physical compartment

3.4 Compartment V_{nuc}

This is a three dimensional compartment with a constant size of 10^{-12} litre, which is surrounded by V_{cyt} (Cytoplasm).

Name Nucleus

SBO:0000290 physical compartment

4 Species

This model contains 21 species. The boundary condition of two of these species is set to true so that these 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
TGF_beta_ex	TGF_beta_ex	Vmed	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
T1R_surf	T1R_surf	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
T1R_endo	T1R_endo	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
T2R_surf	T2R_surf	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
T2R_endo	T2R_endo	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
LRC_surf	LRC_surf	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
LRC_endo	LRC_endo	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
Smad2c	Smad2c	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
Smad2n	Smad2n	Vnuc	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
Smad4c	Smad4c	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
Smad4n	Smad4n	Vnuc	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
PSmad2c	PSmad2c	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
PSmad2_PSmad2_c	PSmad2_PSmad2_c	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
PSmad2_Smad4_c	PSmad2_Smad4_c	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
PSmad2n	PSmad2n	Vnuc	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
PSmad2_PSmad2_n	PSmad2_PSmad2_n	Vnuc	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
PSmad2_Smad4_n	PSmad2_Smad4_n	Vnuc	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
TGF_beta_endo	TGF_beta_endo	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
TGF_beta_ns	TGF_beta_ns	Vmed	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
AA	AA	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
empty_degraded	empty_degraded	Vcyt	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion

5 Parameters

This model contains 34 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
stimulation-			1.000	dimensionless	<input checked="" type="checkbox"/>
_type					
single-			0.500	60 s	<input checked="" type="checkbox"/>
_pulse-					
_duration					
totalNumT1R			10005.000	dimensionless	<input type="checkbox"/>
totalNumT2R			2272.000	dimensionless	<input type="checkbox"/>
totalNumLRC			0.000	dimensionless	<input type="checkbox"/>
totalNumPSmad2			0.000	dimensionless	<input type="checkbox"/>
totalNuclearPSmad2			0.000	nmol	<input type="checkbox"/>
totalSmad2c			60.600	nmol	<input type="checkbox"/>
totalSmad2n			28.500	nmol	<input type="checkbox"/>
medium_TGF-			0.000	dimensionless	<input type="checkbox"/>
_beta_amount					
TGF_beta-			0.000	dimensionless	<input type="checkbox"/>
_dose_mol-					
_per_cell					
ki			0.333	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kr			0.033	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
k_T1R			0.017	$\text{nmol} \cdot (60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
k_T2R			0.019	$\text{nmol} \cdot (60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kdeg_T1R			0.003	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kdeg_T2R			0.013	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kdeg_LRC			0.003	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kdeg_TGF-			0.347	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
_beta					
klid			0.023	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
ka_LRC			117.897	$\text{nmol}^{-2} \cdot (60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kdiss_LRC			0.044	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kimp_Smad2			0.156	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kexp_Smad2			0.763	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kimp_Smad4			0.156	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kexp_Smad4			0.359	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kpho_Smad2			0.049	$\text{nmol}^{-1} \cdot (60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kon_Smads			0.198	$\text{nmol}^{-1} \cdot (60\text{ s})^{-1}$	<input checked="" type="checkbox"/>

Id	Name	SBO	Value	Unit	Constant
koff_Smads			1.000	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kimp_Smads			0.889	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kdepho_Smad2			0.394	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
kon_ns			0.051	$(60\text{ s})^{-1}$	<input checked="" type="checkbox"/>
koff_ns			2.033	$(60\text{ s})^{-1}$	<input type="checkbox"/>
KD_ns			40.226	dimensionless	<input checked="" type="checkbox"/>

6 Initialassignments

This is an overview of five initialassignments.

6.1 Initialassignment T1R_surf

Derived unit nmol

Math $\frac{k_T1R \cdot kdeg_T1R + k_T1R \cdot kr}{kdeg_T1R \cdot ki}$

6.2 Initialassignment T1R_endo

Derived unit nmol

Math $\frac{k_T1R}{kdeg_T1R}$

6.3 Initialassignment T2R_surf

Derived unit nmol

Math $\frac{k_T2R \cdot kdeg_T2R + k_T2R \cdot kr}{kdeg_T2R \cdot ki}$

6.4 Initialassignment T2R_endo

Derived unit nmol

Math $\frac{k_T2R}{kdeg_T2R}$

6.5 Initialassignment TGF_beta_dose_mol_per_cell

Derived unit contains undeclared units

Math $[TGF_beta_ex] \cdot 1.0E-9 \cdot vol(Vmed) \cdot 5.9999999999999995E23$

7 Rules

This is an overview of ten rules.

7.1 Rule `Vmed`

Rule `Vmed` is an assignment rule for compartment `Vmed`:

$$\text{vol}(\text{Vmed}) = \frac{0.0020}{1000000.0 \cdot \exp\left(\frac{\ln 1.45 \cdot \text{time}}{1440}\right)} \quad (1)$$

7.2 Rule `totalNumPSmad2`

Rule `totalNumPSmad2` is an assignment rule for parameter `totalNumPSmad2`:

$$\begin{aligned} \text{totalNumPSmad2} = & ([\text{PSmad2c}] + [\text{PSmad2_PSmad2_c}] \cdot 2 + [\text{PSmad2_Smad4_c}]) \cdot 2.3 \cdot 602 \\ & + ([\text{PSmad2n}] + [\text{PSmad2_PSmad2_n}] \cdot 2 + [\text{PSmad2_Smad4_n}]) \cdot 602 \end{aligned} \quad (2)$$

7.3 Rule `totalNuclearPSmad2`

Rule `totalNuclearPSmad2` is an assignment rule for parameter `totalNuclearPSmad2`:

$$\text{totalNuclearPSmad2} = [\text{PSmad2n}] + 2 \cdot [\text{PSmad2_PSmad2_n}] + [\text{PSmad2_Smad4_n}] \quad (3)$$

7.4 Rule `totalNumT1R`

Rule `totalNumT1R` is an assignment rule for parameter `totalNumT1R`:

$$\text{totalNumT1R} = ([\text{T1R_surf}] + [\text{T1R_endo}] + [\text{LRC_surf}] + [\text{LRC_endo}]) \cdot 2.3 \cdot 602 \quad (4)$$

7.5 Rule `totalNumT2R`

Rule `totalNumT2R` is an assignment rule for parameter `totalNumT2R`:

$$\text{totalNumT2R} = ([\text{T2R_surf}] + [\text{T2R_endo}] + [\text{LRC_surf}] + [\text{LRC_endo}]) \cdot 2.3 \cdot 602 \quad (5)$$

7.6 Rule `totalNumLRC`

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

$$\text{totalNumLRC} = ([\text{LRC_surf}] + [\text{LRC_endo}]) \cdot 2.3 \cdot 602 \quad (6)$$

7.7 Rule `totalSmad2c`

Rule `totalSmad2c` is an assignment rule for parameter `totalSmad2c`:

$$\text{totalSmad2c} = [\text{Smad2c}] + [\text{PSmad2c}] + 2 \cdot [\text{PSmad2_PSmad2_c}] + [\text{PSmad2_Smad4_c}] \quad (7)$$

7.8 Rule `totalSmad2n`

Rule `totalSmad2n` is an assignment rule for parameter `totalSmad2n`:

$$\text{totalSmad2n} = [\text{Smad2n}] + [\text{PSmad2n}] + 2 \cdot [\text{PSmad2_PSmad2_n}] + [\text{PSmad2_Smad4_n}] \quad (8)$$

7.9 Rule koff_ns

Rule koff_ns is an assignment rule for parameter koff_ns:

$$\text{koff_ns} = \text{kon_ns} \cdot \text{KD_ns} \quad (9)$$

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

7.10 Rule medium_TGF_beta_amount

Rule medium_TGF_beta_amount is an assignment rule for parameter medium_TGF_beta_amount:

$$\text{medium_TGF_beta_amount} = [\text{TGF_beta_ex}] \cdot 1.0E-9 \cdot \text{vol}(\text{Vmed}) \cdot 5.9999999999999995E23 \quad (10)$$

8 Event

This is an overview of one event. Each event is initiated whenever its trigger condition switches from false to true. A delay function postpones the effects of an event to a later time point. At the time of execution, an event can assign values to species, parameters or compartments if these are not set to constant.

8.1 Event single_pulse_TGF_beta_washout

Name TGF-beta washout in singel pulse stimulation

Trigger condition

$$(\text{stimulation_type} = 2) \wedge (\text{time} = \text{single_pulse_duration}) \quad (11)$$

Delay

$$0 \quad (12)$$

Assignment

$$\text{TGF_beta_ex} = 0 \quad (13)$$

9 Reactions

This model contains 29 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	re1	T1R production	$AA \longrightarrow T1R_surf$	
2	re2	T1R internalization to early endosome	$T1R_surf \longrightarrow T1R_endo$	
3	re3	T1R recycling from early endosome	$T1R_endo \longrightarrow T1R_surf$	
4	re4	T1R constitutive degradation	$T1R_endo \longrightarrow empty_degraded$	
5	re5	T2R production	$AA \longrightarrow T2R_surf$	
6	re6	T2R internalization to early endosome	$T2R_surf \longrightarrow T2R_endo$	
7	re7	T2R recycling from early endosome	$T2R_endo \longrightarrow T2R_surf$	
8	re8	T2R constitutive degradation	$T2R_endo \longrightarrow empty_degraded$	
9	re9	LRC activation	$TGF_beta_ex + T2R_surf + T1R_surf \longrightarrow LRC_surf$	
10	re10	LRC internalization to early endosome	$LRC_surf \longrightarrow LRC_endo$	
11	re11	LRC constitutive degradation	$LRC_endo \longrightarrow empty_degraded$	
12	re12	dissociation of LRC in endosome	$LRC_endo \longrightarrow T1R_endo + T2R_endo + TGF_beta_endo$	
13	re13	TGF-beta constitutive degradation	$TGF_beta_endo \longrightarrow empty_degraded$	
14	re14	Smad2 nuclear import	$Smad2c \longrightarrow Smad2n$	
15	re15	Smad2 nuclear export	$Smad2n \longrightarrow Smad2c$	
16	re16	Smad4 nuclear import	$Smad4c \longrightarrow Smad4n$	
17	re17	Smad4 nuclear export	$Smad4n \longrightarrow Smad4c$	
18	re18	Smad2 phosphorylation	$Smad2c \xrightarrow{LRC_endo} PSmad2c$	
19	re19	PSmad2 nuclear import	$PSmad2c \longrightarrow PSmad2n$	
20	re20	PSmad2 nuclear export	$PSmad2n \longrightarrow PSmad2c$	
21	re21	Smad2-Smad4 complex formation	$PSmad2c + Smad4c \rightleftharpoons PSmad2_Smad4_c$	

Nº	Id	Name	Reaction Equation	SBO
22	re22	Smad2-Smad4 nuclear import	$\text{PSmad2_Smad4_c} \longrightarrow \text{PSmad2_Smad4_n}$	
23	re23	Smad2-Smad4 dissociation	$\text{PSmad2_Smad4_n} \rightleftharpoons \text{PSmad2n} + \text{Smad4n}$	
24	re24	Smad2 dephosphorylation	$\text{PSmad2n} \longrightarrow \text{Smad2n}$	
25	re25	PSmad2 dimer formation	$2 \text{PSmad2c} \rightleftharpoons \text{PSmad2_PSmad2_c}$	
26	re26	PSmad2 dimer nuclear import	$\text{PSmad2_PSmad2_c} \longrightarrow \text{PSmad2_PSmad2_n}$	
27	re27	PSmad2 dimer dissociation	$\text{PSmad2_PSmad2_n} \rightleftharpoons 2 \text{PSmad2n}$	
28	re28	negative feedback induced LRC degradation	$\text{LRC_surf} \longrightarrow \text{empty_degraded}$	
29	re29	non-specific binding of TGF-beta	$\text{TGF_beta_ex} \rightleftharpoons \text{TGF_beta_ns}$	

9.1 Reaction re1

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

Name T1R production

Reaction equation



Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
AA	AA	

Product

Table 7: Properties of each product.

Id	Name	SBO
T1R_surf	T1R_surf	

Kinetic Law

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

$$v_1 = \text{vol}(\text{Vcyt}) \cdot k_T1R \quad (15)$$

9.2 Reaction re2

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

Name T1R internalization to early endosome

Reaction equation



Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
T1R_surf	T1R_surf	

Product

Table 9: Properties of each product.

Id	Name	SBO
T1R_endo	T1R_endo	

Kinetic Law

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

$$v_2 = \text{vol}(\text{Vcyt}) \cdot k_i \cdot [\text{T1R_surf}] \quad (17)$$

9.3 Reaction re3

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

Name T1R recycling from early endosome

Reaction equation



Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
T1R_endo	T1R_endo	

Product

Table 11: Properties of each product.

Id	Name	SBO
T1R_surf	T1R_surf	

Kinetic Law

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

$$v_3 = \text{vol}(\text{Vcyt}) \cdot \text{kr} \cdot [\text{T1R_endo}] \quad (19)$$

9.4 Reaction re4

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

Name T1R constitutive degradation

Reaction equation



Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
T1R_endo	T1R_endo	

Product

Table 13: Properties of each product.

Id	Name	SBO
empty_degraded	empty_degraded	

Kinetic Law

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

$$v_4 = \text{vol}(\text{Vcyt}) \cdot \text{kdeg_T1R} \cdot [\text{T1R_endo}] \quad (21)$$

9.5 Reaction re5

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

Name T2R production

Reaction equation



Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
AA	AA	

Product

Table 15: Properties of each product.

Id	Name	SBO
T2R_surf	T2R_surf	

Kinetic Law

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

$$v_5 = \text{vol}(\text{Vcyt}) \cdot k_T2R \quad (23)$$

9.6 Reaction re6

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

Name T2R internalization to early endosome

Reaction equation



Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
T2R_surf	T2R_surf	

Product

Table 17: Properties of each product.

Id	Name	SBO
T2R_endo	T2R_endo	

Kinetic Law

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

$$v_6 = \text{vol}(\text{Vcyt}) \cdot k_i \cdot [\text{T2R_surf}] \quad (25)$$

9.7 Reaction re7

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

Name T2R recycling from early endosome

Reaction equation



Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
T2R_endo	T2R_endo	

Product

Table 19: Properties of each product.

Id	Name	SBO
T2R_surf	T2R_surf	

Kinetic Law

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

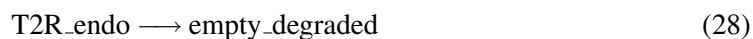
$$v_7 = \text{vol}(\text{Vcyt}) \cdot k_r \cdot [\text{T2R_endo}] \quad (27)$$

9.8 Reaction re8

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

Name T2R constitutive degradation

Reaction equation



Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
T2R_endo	T2R_endo	

Product

Table 21: Properties of each product.

Id	Name	SBO
empty_degraded	empty_degraded	

Kinetic Law

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

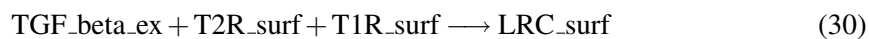
$$v_8 = \text{vol}(\text{Vcyt}) \cdot \text{kdeg_T2R} \cdot [\text{T2R_endo}] \quad (29)$$

9.9 Reaction re9

This is an irreversible reaction of three reactants forming one product.

Name LRC activation

Reaction equation



Reactants

Table 22: Properties of each reactant.

Id	Name	SBO
TGF_beta_ex	TGF_beta_ex	
T2R_surf	T2R_surf	
T1R_surf	T1R_surf	

Product

Table 23: Properties of each product.

Id	Name	SBO
LRC_surf	LRC_surf	

Kinetic Law

Derived unit $(60\text{ s})^{-1} \cdot \text{l}^{-2} \cdot \text{nmol}$

$$v_9 = \text{vol}(\text{Vcyt}) \cdot \text{ka_LRC} \cdot [\text{TGF_beta_ex}] \cdot [\text{T2R_surf}] \cdot [\text{T1R_surf}] \quad (31)$$

9.10 Reaction re10

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

Name LRC internalization to early endosome

Reaction equation



Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
LRC_surf	LRC_surf	

Product

Table 25: Properties of each product.

Id	Name	SBO
LRC_endo	LRC_endo	

Kinetic Law**Derived unit** $(60\text{ s})^{-1} \cdot \text{nmol}$

$$v_{10} = \text{vol}(\text{Vcyt}) \cdot k_i \cdot [\text{LRC_surf}] \quad (33)$$

9.11 Reaction re11

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

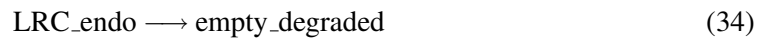
Name LRC constitutive degradation**Reaction equation****Reactant**

Table 26: Properties of each reactant.

Id	Name	SBO
LRC_endo	LRC_endo	

Product

Table 27: Properties of each product.

Id	Name	SBO
empty_degraded	empty_degraded	

Kinetic Law**Derived unit** $(60\text{ s})^{-1} \cdot \text{nmol}$

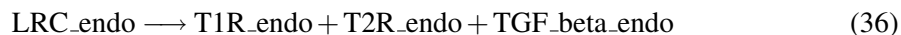
$$v_{11} = \text{vol}(\text{Vcyt}) \cdot k_{\text{deg_LRC}} \cdot [\text{LRC_endo}] \quad (35)$$

9.12 Reaction re12

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

Name dissociation of LRC in endosome

Reaction equation



Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
LRC_endo	LRC_endo	

Products

Table 29: Properties of each product.

Id	Name	SBO
T1R_endo	T1R_endo	
T2R_endo	T2R_endo	
TGF_beta_endo	TGF_beta_endo	

Kinetic Law

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

$$v_{12} = \text{vol}(\text{Vcyt}) \cdot \text{kdiss_LRC} \cdot [\text{LRC_endo}] \quad (37)$$

9.13 Reaction re13

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

Name TGF-beta constitutive degradation

Reaction equation



Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
TGF_beta_endo	TGF_beta_endo	

Product

Table 31: Properties of each product.

Id	Name	SBO
empty_degraded	empty_degraded	

Kinetic Law

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

$$v_{13} = \text{vol}(\text{Vcyt}) \cdot \text{kdeg_TGF_beta} \cdot [\text{TGF_beta_endo}] \quad (39)$$

9.14 Reaction re14

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

Name Smad2 nuclear import

Reaction equation



Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
Smad2c	Smad2c	

Product

Table 33: Properties of each product.

Id	Name	SBO
Smad2n	Smad2n	

Kinetic Law

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

$$v_{14} = \text{vol}(\text{Vcyt}) \cdot \text{kimp_Smad2} \cdot [\text{Smad2c}] \quad (41)$$

9.15 Reaction re15

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

Name Smad2 nuclear export

Reaction equation



Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
Smad2n	Smad2n	

Product

Table 35: Properties of each product.

Id	Name	SBO
Smad2c	Smad2c	

Kinetic Law

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

$$v_{15} = \text{vol}(\text{Vnuc}) \cdot \text{kexp_Smad2} \cdot [\text{Smad2n}] \quad (43)$$

9.16 Reaction re16

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

Name Smad4 nuclear import

Reaction equation



Reactant

Table 36: Properties of each reactant.

Id	Name	SBO
Smad4c	Smad4c	

Product

Table 37: Properties of each product.

Id	Name	SBO
Smad4n	Smad4n	

Kinetic Law

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

$$v_{16} = \text{vol}(\text{Vcyt}) \cdot \text{kimp_Smad4} \cdot [\text{Smad4c}] \quad (45)$$

9.17 Reaction re17

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

Name Smad4 nuclear export

Reaction equation



Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
Smad4n	Smad4n	

Product

Table 39: Properties of each product.

Id	Name	SBO
Smad4c	Smad4c	

Kinetic Law

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

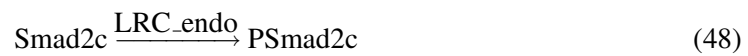
$$v_{17} = \text{vol}(\text{Vnuc}) \cdot k_{\text{exp_Smad4}} \cdot [\text{Smad4n}] \quad (47)$$

9.18 Reaction re18

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

Name Smad2 phosphorylation

Reaction equation



Reactant

Table 40: Properties of each reactant.

Id	Name	SBO
Smad2c	Smad2c	

Modifier

Table 41: Properties of each modifier.

Id	Name	SBO
LRC_endo	LRC_endo	

Product

Table 42: Properties of each product.

Id	Name	SBO
PSmad2c	PSmad2c	

Kinetic Law**Derived unit** $(60\text{ s})^{-1} \cdot \text{nmol} \cdot \text{l}^{-1}$

$$v_{18} = \text{vol}(\text{Vcyt}) \cdot \text{kpho_Smad2} \cdot [\text{Smad2c}] \cdot [\text{LRC_endo}] \quad (49)$$

9.19 Reaction re19

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

Name PSmad2 nuclear import**Reaction equation****Reactant**

Table 43: Properties of each reactant.

Id	Name	SBO
PSmad2c	PSmad2c	

Product

Table 44: Properties of each product.

Id	Name	SBO
PSmad2n	PSmad2n	

Kinetic Law**Derived unit** $(60\text{ s})^{-1} \cdot \text{nmol}$

$$v_{19} = \text{vol}(\text{Vcyt}) \cdot \text{kimp_Smad2} \cdot [\text{PSmad2c}] \quad (51)$$

9.20 Reaction re20

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

Name PSmad2 nuclear export

Reaction equation



Reactant

Table 45: Properties of each reactant.

Id	Name	SBO
PSmad2n	PSmad2n	

Product

Table 46: Properties of each product.

Id	Name	SBO
PSmad2c	PSmad2c	

Kinetic Law

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

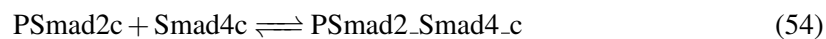
$$v_{20} = \text{vol}(\text{Vnuc}) \cdot k_{\text{exp_Smad2}} \cdot [\text{PSmad2n}] \quad (53)$$

9.21 Reaction re21

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

Name Smad2-Smad4 complex formation

Reaction equation



Reactants

Table 47: Properties of each reactant.

Id	Name	SBO
PSmad2c	PSmad2c	
Smad4c	Smad4c	

Product

Table 48: Properties of each product.

Id	Name	SBO
PSmad2_Smad4_c	PSmad2_Smad4_c	

Kinetic Law

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

$$v_{21} = \text{vol}(\text{Vcyt}) \cdot (\text{kon_Smads} \cdot [\text{PSmad2c}] \cdot [\text{Smad4c}] - \text{koff_Smads} \cdot [\text{PSmad2_Smad4_c}]) \quad (55)$$

9.22 Reaction re22

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

Name Smad2-Smad4 nuclear import

Reaction equation



Reactant

Table 49: Properties of each reactant.

Id	Name	SBO
PSmad2_Smad4_c	PSmad2_Smad4_c	

Product

Table 50: Properties of each product.

Id	Name	SBO
PSmad2_Smad4_n	PSmad2_Smad4_n	

Id	Name	SBO
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Kinetic Law

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

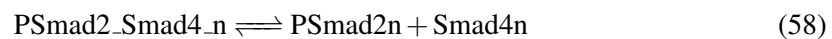
$$v_{22} = \text{vol}(\text{Vcyt}) \cdot \text{kimp_Smads} \cdot [\text{PSmad2_Smad4_c}] \quad (57)$$

9.23 Reaction re23

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

Name Smad2-Smad4 dissociation

Reaction equation



Reactant

Table 51: Properties of each reactant.

Id	Name	SBO
PSmad2_Smad4_n	PSmad2_Smad4_n	

Products

Table 52: Properties of each product.

Id	Name	SBO
PSmad2n	PSmad2n	
Smad4n	Smad4n	

Kinetic Law

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

$$v_{23} = \text{vol}(\text{Vnuc}) \cdot (\text{koff_Smads} \cdot [\text{PSmad2_Smad4_n}] - \text{kon_Smads} \cdot [\text{PSmad2n}] \cdot [\text{Smad4n}]) \quad (59)$$

9.24 Reaction re24

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

Name Smad2 dephosphorylation

Reaction equation



Reactant

Table 53: Properties of each reactant.

Id	Name	SBO
PSmad2n	PSmad2n	

Product

Table 54: Properties of each product.

Id	Name	SBO
Smad2n	Smad2n	

Kinetic Law

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

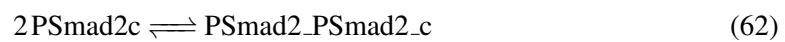
$$v_{24} = \text{vol}(\text{Vnuc}) \cdot \text{kdepho_Smad2} \cdot [\text{PSmad2n}] \quad (61)$$

9.25 Reaction re25

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

Name PSmad2 dimer formation

Reaction equation



Reactant

Table 55: Properties of each reactant.

Id	Name	SBO
PSmad2c	PSmad2c	

Product

Table 56: Properties of each product.

Id	Name	SBO
PSmad2_PSmad2_c	PSmad2_PSmad2_c	

Kinetic Law

Derived unit $1^{-1} \cdot 9.999999999999998 \cdot 10^{-10} \text{ mol} \cdot (60 \text{ s})^{-1}$

$$v_{25} = \text{vol}(\text{Vcyt}) \cdot (\text{kon_Smads} \cdot [\text{PSmad2c}]^2 - \text{koff_Smads} \cdot [\text{PSmad2_PSmad2_c}]) \quad (63)$$

9.26 Reaction re26

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

Name PSmad2 dimer nuclear import

Reaction equation



Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
PSmad2_PSmad2_c	PSmad2_PSmad2_c	

Product

Table 58: Properties of each product.

Id	Name	SBO
PSmad2_PSmad2_n	PSmad2_PSmad2_n	

Kinetic Law

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

$$v_{26} = \text{vol}(\text{Vcyt}) \cdot \text{kimp_Smads} \cdot [\text{PSmad2_PSmad2_c}] \quad (65)$$

9.27 Reaction re27

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

Name PSmad2 dimmer dissociation

Reaction equation



Reactant

Table 59: Properties of each reactant.

Id	Name	SBO
PSmad2_PSmad2_n	PSmad2_PSmad2_n	

Product

Table 60: Properties of each product.

Id	Name	SBO
PSmad2n	PSmad2n	

Kinetic Law

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

$$v_{27} = \text{vol}(\text{Vnuc}) \cdot (\text{koff_Smads} \cdot [\text{PSmad2_PSmad2_n}] - \text{kon_Smads} \cdot [\text{PSmad2n}]^2) \quad (67)$$

9.28 Reaction re28

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

Name negative feedback induced LRC degradation

Reaction equation



Reactant

Table 61: Properties of each reactant.

Id	Name	SBO
LRC_surf	LRC_surf	

Product

Table 62: Properties of each product.

Id	Name	SBO
empty_degraded	empty_degraded	

Kinetic Law

Derived unit $(60\text{ s})^{-1} \cdot (10^{-9}\text{ mol})^2$

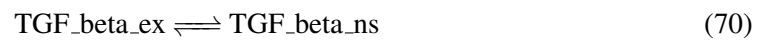
$$v_{28} = \text{vol}(\text{Vcyt}) \cdot \text{klid} \cdot [\text{LRC_surf}] \cdot \text{totalNuclearPSmad2} \quad (69)$$

9.29 Reaction re29

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

Name non-specific binding of TGF-beta

Reaction equation



Reactant

Table 63: Properties of each reactant.

Id	Name	SBO
TGF_beta_ex	TGF_beta_ex	

Product

Table 64: Properties of each product.

Id	Name	SBO
TGF_beta_ns	TGF_beta_ns	

Kinetic Law

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

$$v_{29} = \text{vol}(\text{Vmed}) \cdot (\text{kon_ns} \cdot [\text{TGF_beta_ex}] - \text{koff_ns} \cdot [\text{TGF_beta_ns}]) \quad (71)$$

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 TGF_beta_ex

Name TGF_beta_ex

SBO:0000252 polypeptide chain

Initial concentration $0.05\text{ nmol} \cdot \text{l}^{-1}$

Charge 0

Involved in event [single_pulse_TGF_beta_washout](#)

This species takes part in two reactions (as a reactant in [re9](#), [re29](#)).

$$\frac{d}{dt} \text{TGF_beta_ex} = -v_9 - v_{29} \quad (72)$$

Furthermore, one event influences this species' rate of change.

10.2 Species T1R_surf

Name T1R_surf

SBO:0000244 receptor

Initial concentration $0.702494\text{ nmol} \cdot \text{l}^{-1}$

Charge 0

Initial assignment T1R_surf

This species takes part in four reactions (as a reactant in [re2](#), [re9](#) and as a product in [re1](#), [re3](#)).

$$\frac{d}{dt}T1R_surf = v_1 + v_3 - v_2 - v_9 \quad (73)$$

10.3 Species T1R_endo

Name T1R_endo

SBO:0000244 receptor

Initial concentration 6.52344 nmol · l⁻¹

Charge 0

Initial assignment T1R_endo

This species takes part in four reactions (as a reactant in [re3](#), [re4](#) and as a product in [re2](#), [re12](#)).

$$\frac{d}{dt}T1R_endo = v_2 + v_{12} - v_3 - v_4 \quad (74)$$

10.4 Species T2R_surf

Name T2R_surf

SBO:0000244 receptor

Initial concentration 0.201077 nmol · l⁻¹

Charge 0

Initial assignment T2R_surf

This species takes part in four reactions (as a reactant in [re6](#), [re9](#) and as a product in [re5](#), [re7](#)).

$$\frac{d}{dt}T2R_surf = v_5 + v_7 - v_6 - v_9 \quad (75)$$

10.5 Species T2R_endo

Name T2R_endo

SBO:0000244 receptor

Initial concentration 1.43997 nmol · l⁻¹

Charge 0

Initial assignment T2R_endo

This species takes part in four reactions (as a reactant in [re7](#), [re8](#) and as a product in [re6](#), [re12](#)).

$$\frac{d}{dt}T2R_endo = v_6 + v_{12} - v_7 - v_8 \quad (76)$$

10.6 Species LRC_surf

Name LRC_surf

SBO:0000297 protein complex

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in three reactions (as a reactant in [re10](#), [re28](#) and as a product in [re9](#)).

$$\frac{d}{dt}LRC_surf = v_9 - v_{10} - v_{28} \quad (77)$$

10.7 Species LRC_endo

Name LRC_endo

SBO:0000297 protein complex

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in four reactions (as a reactant in [re11](#), [re12](#) and as a product in [re10](#) and as a modifier in [re18](#)).

$$\frac{d}{dt}LRC_endo = v_{10} - v_{11} - v_{12} \quad (78)$$

10.8 Species Smad2c

Name Smad2c

SBO:0000252 polypeptide chain

Initial concentration 60.6 nmol · l⁻¹

Charge 0

This species takes part in three reactions (as a reactant in [re14](#), [re18](#) and as a product in [re15](#)).

$$\frac{d}{dt}Smad2c = v_{15} - v_{14} - v_{18} \quad (79)$$

10.9 Species *Smad2n*

Name *Smad2n*

SBO:0000252 polypeptide chain

Initial concentration $28.5 \text{ nmol} \cdot \text{l}^{-1}$

Charge 0

This species takes part in three reactions (as a reactant in [re15](#) and as a product in [re14](#), [re24](#)).

$$\frac{d}{dt} \text{Smad2n} = v_{14} + v_{24} - v_{15} \quad (80)$$

10.10 Species *Smad4c*

Name *Smad4c*

SBO:0000252 polypeptide chain

Initial concentration $50.8 \text{ nmol} \cdot \text{l}^{-1}$

Charge 0

This species takes part in three reactions (as a reactant in [re16](#), [re21](#) and as a product in [re17](#)).

$$\frac{d}{dt} \text{Smad4c} = v_{17} - v_{16} - v_{21} \quad (81)$$

10.11 Species *Smad4n*

Name *Smad4n*

SBO:0000252 polypeptide chain

Initial concentration $50.8 \text{ nmol} \cdot \text{l}^{-1}$

Charge 0

This species takes part in three reactions (as a reactant in [re17](#) and as a product in [re16](#), [re23](#)).

$$\frac{d}{dt} \text{Smad4n} = v_{16} + v_{23} - v_{17} \quad (82)$$

10.12 Species PSmad2c

Name PSmad2c

SBO:0000252 polypeptide chain

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in five reactions (as a reactant in [re19](#), [re21](#), [re25](#) and as a product in [re18](#), [re20](#)).

$$\frac{d}{dt}\text{PSmad2c} = v_{18} + v_{20} - v_{19} - v_{21} - 2 v_{25} \quad (83)$$

10.13 Species PSmad2_PSmad2_c

Name PSmad2_PSmad2_c

SBO:0000286 multimer

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in two reactions (as a reactant in [re26](#) and as a product in [re25](#)).

$$\frac{d}{dt}\text{PSmad2_PSmad2_c} = v_{25} - v_{26} \quad (84)$$

10.14 Species PSmad2_Smad4_c

Name PSmad2_Smad4_c

SBO:0000297 protein complex

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in two reactions (as a reactant in [re22](#) and as a product in [re21](#)).

$$\frac{d}{dt}\text{PSmad2_Smad4_c} = v_{21} - v_{22} \quad (85)$$

10.15 Species PSmad2n

Name PSmad2n

SBO:0000252 polypeptide chain

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in five reactions (as a reactant in [re20](#), [re24](#) and as a product in [re19](#), [re23](#), [re27](#)).

$$\frac{d}{dt}\text{PSmad2n} = v_{19} + v_{23} + 2v_{27} - v_{20} - v_{24} \quad (86)$$

10.16 Species PSmad2_PSmad2_n

Name PSmad2_PSmad2_n

SBO:0000286 multimer

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in two reactions (as a reactant in [re27](#) and as a product in [re26](#)).

$$\frac{d}{dt}\text{PSmad2_PSmad2_n} = v_{26} - v_{27} \quad (87)$$

10.17 Species PSmad2_Smad4_n

Name PSmad2_Smad4_n

SBO:0000297 protein complex

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in two reactions (as a reactant in [re23](#) and as a product in [re22](#)).

$$\frac{d}{dt}\text{PSmad2_Smad4_n} = v_{22} - v_{23} \quad (88)$$

10.18 Species TGF_beta_endo

Name TGF_beta_endo

SBO:0000252 polypeptide chain

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in two reactions (as a reactant in [re13](#) and as a product in [re12](#)).

$$\frac{d}{dt} \text{TGF_beta_endo} = v_{12} - v_{13} \quad (89)$$

10.19 Species TGF_beta_ns

Name TGF_beta_ns

SBO:0000252 polypeptide chain

Initial concentration 0 nmol · l⁻¹

Charge 0

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

$$\frac{d}{dt} \text{TGF_beta_ns} = v_{29} \quad (90)$$

10.20 Species AA

Name AA

SBO:0000291 empty set

Initial concentration 0 nmol · l⁻¹

Charge 0

This species takes part in two reactions (as a reactant in [re1](#), [re5](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt} \text{AA} = 0 \quad (91)$$

10.21 Species `empty_degraded`

Name `empty_degraded`

SBO:0000291 `empty set`

Initial concentration $0 \text{ nmol} \cdot \text{l}^{-1}$

Charge 0

This species takes part in five reactions (as a product in [re4](#), [re8](#), [re11](#), [re13](#), [re28](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt} \text{empty_degraded} = 0 \quad (92)$$

A Glossary of Systems Biology Ontology Terms

SBO:0000244 receptor: Participating entity that binds to a specific physical entity and initiates the response to that physical entity. The original concept of the receptor was introduced independently at the end of the 19th century by John Newport Langley (1852-1925) and Paul Ehrlich (1854-1915). Langley JN. On the reaction of cells and of nerve-endings to certain poisons, chiefly as regards the reaction of striated muscle to nicotine and to curari. J Physiol. 1905 Dec 30;33(4-5):374-413

SBO:0000252 polypeptide chain: Naturally occurring macromolecule formed by the repetition of amino-acid residues linked by peptidic bonds. A polypeptide chain is synthesized by the ribosome. CHEBI:1654

SBO:0000286 multimer: Non-covalent association of identical, or pseudo-identical, entities. By pseudo-identical entities, we mean biochemical elements that differ chemically, although remaining globally identical in structure and/or function. Examples are homologous subunits in an hetero-oligomeric receptor

SBO:0000290 physical compartment: Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions

SBO:0000291 empty set: Entity defined by the absence of any actual object. An empty set is often used to represent the source of a creation process or the result of a degradation process.

SBO:0000297 protein complex: Macromolecular complex containing one or more polypeptide chains possibly associated with simple chemicals. CHEBI:3608

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