SBML Model Report

Model name: "Cellire2011 - Plasticity of TGF- Signalling"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following eight authors: Nick Juty[1], Vijayalakshmi Chelliah[2], Ryan Gutenkunst[3], Rachel Wellington[4], Benjamin Zaepfel[5], Dinah Davison[6], Travis Struck[7] and Georgios Fengos[8] at April 18th 2016 at 12:54 a. m. and last time modified at April 18th 2016 at 2:56 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	3
species types	0	species	18
events	0	constraints	0
reactions	29	function definitions	4
global parameters	20	unit definitions	1
rules	0	initial assignments	0

[1]EMBL-EBI, juty@ebi.ac.uk
[2]EMBL-EBI, viji@ebi.ac.uk
[3]University of Arizona, rgutenk@email.arizona.edu
[4]University of Arizona, rwellington@email.arizona.edu
[5]University of Arizona, benzaepfel@email.arizona.edu
[6]University of Arizona, dinahdavison@email.arizona.edu
[7]University of Arizona, tjstruck@email.arizona.edu
[8]Eidgenssische Technische Hochschule Zurich (ETHZ), georgios.fengos@bsse.ethz.ch

Model Notes

Cellire2011 - Plasticity of TGF- Signalling

Transforming growth factor beta (TGF-) signalling has been implicated as an important regulator of almost all major cell behaviours, including proliferation, differentiation, cell death, and motility. It remains unclear that how the TGF- signalling pathway accomplishes the flexibility in its responses. What and how many parameters have to be altered for cells to respond differently to perform complex tasks? This canonical response has been explored in this model, by considering the core signalling architecture of TGF- pathway.

This model is described in the article:Plasticity of TGF- signalingCellire G, Fengos G, Herv M, Iber D.BMC Syst Biol. 2011 Nov 3;5:184.

Abstract:

The family of TGF- ligands is large and its members are involved in many different signaling processes. These signaling processes strongly differ in type with TGF- ligands eliciting both sustained or transient responses. Members of the TGF- family can also act as morphogen and cellular responses would then be expected to provide a direct read-out of the extracellular ligand concentration. A number of different models have been proposed to reconcile these different behaviours. We were interested to define the set of minimal modifications that are required to change the type of signal processing in the TGF- signaling network.RESULTS:To define the key aspects for signaling plasticity we focused on the core of the TGF- signaling network. With the help of a parameter screen we identified ranges of kinetic parameters and protein concentrations that give rise to transient, sustained, or oscillatory responses to constant stimuli, as well as those parameter ranges that enable a proportional response to time-varying ligand concentrations (as expected in the read-out of morphogens). A combination of a strong negative feedback and fast shuttling to the nucleus biases signaling to a transient rather than a sustained response, while oscillations were obtained if ligand binding to the receptor is weak and the turn-over of the I-Smad is fast. A proportional read-out required inefficient receptor activation in addition to a low affinity of receptor-ligand binding. We find that targeted modification of single parameters suffices to alter the response type. The intensity of a constant signal (i.e. the ligand concentration), on the other hand, affected only the strength but not the type of the response.CONCLUSIONS:The architecture of the TGF- pathway enables the observed signaling plasticity. The observed range of signaling outputs to TGF- ligand in different cell types and under different conditions can be explained with differences in cellular protein concentrations and with changes in effective rate constants due to cross-talk with other signaling pathways. It will be interesting to uncover the exact cellular differences as well as the details of the cross-talks in future work.

This model is hosted on BioModels Database and identified by: MODEL1208280000 .

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. PMID: 20587024 .

2 Unit Definitions

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

2.1 Unit `substance`

Name substance

Definition pmol

2.2 Unit `volume`

Notes Litre is the predefined SBML unit for `volume`.

Definition l

2.3 Unit `area`

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

Definition m^2

2.4 Unit `length`

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

Definition m

2.5 Unit `time`

Notes Second is the predefined SBML unit for `time`.

Definition s

3 Compartments

This model contains three compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`c`	cytoplasm		3	2.3	l	☑	
`n`	nucleus		3	1	litre	☑	
`extracellular`	extracellular		3	1	litre	☑	

3.1 Compartment c

This is a three dimensional compartment with a constant size of 2.3 litre.

Name cytoplasm

Notes Defined by provided Gene Ontology annotation.

3.2 Compartment n

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

Name nucleus

Notes Gene Ontology GO:0005634 encompasses the term information for the nucleus compartme

3.3 Compartment extracellular

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

Name extracellular

Notes Defined by provided Gene Ontology annotation.

4 Species

This model contains 18 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 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
TGFbR	TGFbR	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
TGFb_TGFbR	TGFb_TGFbR	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
TGFb_TGFbR_P	TGFb_TGFbR_P	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
I_Smad_TGFb_TGFbR_P	I_Smad_TGFb_TGFbR_P	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Smad	Smad	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Smad_P	Smad_P	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
CoSmad	CoSmad	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Smad_P_Smad_P	Smad_P_Smad_P	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Smad_P_CoSmad	Smad_P_CoSmad	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
I_Smad_mRNA2	I_Smad_mRNA2	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
I_Smad	I_Smad	c	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Smad_N	Smad_N	n	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Smad_P_Smad_P_N	Smad_P_Smad_P_N	n	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Smad_P_N	Smad_P_N	n	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Smad_P_CoSmad_N	Smad_P_CoSmad_N	n	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
CoSmad_N	CoSmad_N	n	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
I_Smad_mRNA1	I_Smad_mRNA1	n	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
TGFb	TGFb	extracellular	$\mathrm{pmol} \cdot \mathrm{l}^{-1}$	☑	☑

5 Parameters

This model contains 20 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
h	h		2.060		☑
k1	k1		0.004		☑
k2	k2		$4.39 \cdot 10^{-6}$		☑
k3	k3		0.324		☑
k4	k4		0.002		☑
k7	k7		$9.35 \cdot 10^{-6}$		☑
k8	k8		0.010		☑
k9	k9		$7.5 \cdot 10^{-4}$		☑
k10	k10		$5.12 \cdot 10^{-8}$		☑
k11	k11		0.009		☑
k12	k12		0.051		☑
k13	k13		0.002		☑
k5	k5		$5.49 \cdot 10^{-4}$		☑
k6	k6		$1.29 \cdot 10^{-5}$		☑
k14	k14		0.038		☑
k15	k15		28.520		☑
k16	k16		0.021		☑
k17	k17		$8.05 \cdot 10^{-5}$		☑
k18	k18		0.043		☑
k19	k19		$4.12 \cdot 10^{-4}$		☑

6 Function definitions

This is an overview of four function definitions.

6.1 Function definition Function_for_r25__1

Name Function for r25 [1]

Arguments [Smad_P_CoSmad_N], h, k14, k15

Mathematical Expression

$$\frac{\mathrm{k14} \cdot [\mathrm{Smad\_P\_CoSmad\_N}]^{\mathrm{h}}}{[\mathrm{Smad\_P\_CoSmad\_N}]^{\mathrm{h}} + \mathrm{k15}^{\mathrm{h}}} \tag{1}$$

6.2 Function definition Function_for_r16__1

Name Function for r16 [1]

Arguments [Smad_P_Smad_P], k12, k8

Mathematical Expression

$$k12 \cdot k8 \cdot [Smad\_P\_Smad\_P] \tag{2}$$

6.3 Function definition Function_for_r28__1

Name Function for r28 [1]

Arguments [I_Smad_mRNA2], k18

Mathematical Expression

$$k18 \cdot [I\_Smad\_mRNA2] \tag{3}$$

6.4 Function definition Function_for_r7__1

Name Function for r7 [1]

Arguments k7, [Smad], [TGFb_TGFbR_P]

Mathematical Expression

$$k7 \cdot [Smad] \cdot [TGFb\_TGFbR\_P] \tag{4}$$

7 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

№	Id	Name	Reaction Equation	SBO
1	r1	r1	TGFb_TGFbR $\longrightarrow$ TGFbR	
2	r2	r2	TGFbR + TGFb $\longrightarrow$ TGFb_TGFbR	
3	r3	r3	TGFb_TGFbR $\longrightarrow$ TGFb_TGFbR_P	
4	r4	r4	TGFb_TGFbR_P $\longrightarrow$ TGFb_TGFbR	
5	r5	r5	TGFb_TGFbR_P + I_Smad $\longrightarrow$ I_Smad_TGFb_TGFbR_P	
6	r6	r6	I_Smad_TGFb_TGFbR_P $\longrightarrow$ TGFb_TGFbR + I_Smad	
7	r7	r7	Smad $\xrightarrow{\text{TGFb\_TGFbR\_P, Smad}}$ Smad_P	
8	r8	r8	Smad $\longrightarrow$ Smad_N	
9	r9	r9	Smad_N $\longrightarrow$ Smad	
10	r10	r10	2 Smad_P $\longrightarrow$ Smad_P_Smad_P	
11	r11	r11	Smad_P_Smad_P $\longrightarrow$ 2 Smad_P	
12	r12	r12	Smad_P + CoSmad $\longrightarrow$ Smad_P_CoSmad	
13	r13	r13	Smad_P_CoSmad $\longrightarrow$ Smad_P + CoSmad	
14	r14	r14	CoSmad $\longrightarrow$ CoSmad_N	
15	r15	r15	CoSmad_N $\longrightarrow$ CoSmad	
16	r16	r16	Smad_P_Smad_P $\longrightarrow$ Smad_P_Smad_P_N	
17	r17	r17	Smad_P $\longrightarrow$ Smad_P_N	
18	r18	r18	Smad_P_N $\longrightarrow$ Smad_P	
19	r19	r19	Smad_P_CoSmad $\longrightarrow$ Smad_P_CoSmad_N	
20	r20	r20	Smad_P_N $\longrightarrow$ Smad_N	

№	Id	Name	Reaction Equation	SBO
21	r21	r21	$2\,\text{Smad\_P\_N} \longrightarrow \text{Smad\_P\_Smad\_P\_N}$	
22	r22	r22	$\text{Smad\_P\_Smad\_P\_N} \longrightarrow 2\,\text{Smad\_P\_N}$	
23	r23	r23	$\text{Smad\_P\_N} + \text{CoSmad\_N} \longrightarrow \text{Smad\_P\_CoSmad\_N}$	
24	r24	r24	$\text{Smad\_P\_CoSmad\_N} \longrightarrow \text{Smad\_P\_N} + \text{CoSmad\_N}$	
25	r25	r25	$\emptyset \xrightarrow{\text{Smad\_P\_CoSmad\_N}} \text{I\_Smad\_mRNA1}$	
26	r26	r26	$\text{I\_Smad\_mRNA1} \longrightarrow \text{I\_Smad\_mRNA2}$	
27	r27	r27	$\text{I\_Smad\_mRNA2} \longrightarrow \emptyset$	
28	r28	r28	$\emptyset \xrightarrow{\text{I\_Smad\_mRNA2}} \text{I\_Smad}$	
29	r29	r29	$\text{I\_Smad} \longrightarrow \emptyset$	

7.1 Reaction r1

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

Name r1

Notes This reaction represents dissociation of the ligand TGF-beta from the TGF-beta rece

Reaction equation

$$\text{TGFb\_TGFbR} \longrightarrow \text{TGFbR} \tag{5}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
TGFb_TGFbR	TGFb_TGFbR	

Product

Table 7: Properties of each product.

Id	Name	SBO
TGFbR	TGFbR	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{c}) \cdot \text{k1} \cdot [\text{TGFb\_TGFbR}] \tag{6}$$

7.2 Reaction r2

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

Name r2

Notes TGF-beta binds to the TGF-beta receptor. Annotations are for TGF-beta receptor binc

Reaction equation

$$\text{TGFbR} + \text{TGFb} \longrightarrow \text{TGFb\_TGFbR} \tag{7}$$

Reactants

Table 8: Properties of each reactant.

Id	Name	SBO
TGFbR	TGFbR	
TGFb	TGFb	

Product

Table 9: Properties of each product.

Id	Name	SBO
TGFb_TGFbR	TGFb_TGFbR	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{k2} \cdot [\mathrm{TGFbR}] \cdot [\mathrm{TGFb}] \tag{8}$$

7.3 Reaction r3

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

Name r3

Notes Phosphorylation of TGF-Beta type 1 receptor bound to TGF-Beta by protein serine/thr

Reaction equation

$$\mathrm{TGFb\_TGFbR} \longrightarrow \mathrm{TGFb\_TGFbR\_P} \tag{9}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
TGFb_TGFbR	TGFb_TGFbR	

Product

Table 11: Properties of each product.

Id	Name	SBO
TGFb_TGFbR_P	TGFb_TGFbR_P	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}(\mathrm{c}) \cdot \mathrm{k3} \cdot [\mathrm{TGFb\_TGFbR}] \tag{10}$$

7.4 Reaction r4

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

Name r4

Notes Dephosphorylation of TGF-Beta type 1 receptor bound to TGF-Beta.

Reaction equation

$$\mathrm{TGFb\_TGFbR\_P} \longrightarrow \mathrm{TGFb\_TGFbR} \tag{11}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
TGFb_TGFbR_P	TGFb_TGFbR_P	

Product

Table 13: Properties of each product.

Id	Name	SBO
TGFb_TGFbR	TGFb_TGFbR	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}(\mathrm{c}) \cdot \mathrm{k4} \cdot [\mathrm{TGFb\_TGFbR\_P}] \tag{12}$$

7.5 Reaction r5

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

Name r5

Notes I-Smad sequestering and dephosphorylating TGF-Beta type 1 receptor.

Reaction equation

$$\text{TGFb\_TGFbR\_P} + \text{I\_Smad} \longrightarrow \text{I\_Smad\_TGFb\_TGFbR\_P} \tag{13}$$

Reactants

Table 14: Properties of each reactant.

Id	Name	SBO
TGFb_TGFbR_P	TGFb_TGFbR_P	
I_Smad	I_Smad	

Product

Table 15: Properties of each product.

Id	Name	SBO
I_Smad_TGFb_TGFbR_P	I_Smad_TGFb_TGFbR_P	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}(\text{c}) \cdot \text{k5} \cdot [\text{TGFb\_TGFbR\_P}] \cdot [\text{I\_Smad}] \tag{14}$$

7.6 Reaction r6

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

Name r6

Notes I-Smad and TGF-Beta type 1 receptor dissociate from each other.

Reaction equation

$$\text{I\_Smad\_TGFb\_TGFbR\_P} \longrightarrow \text{TGFb\_TGFbR} + \text{I\_Smad} \tag{15}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
I_Smad_TGFb_TGFbR_P	I_Smad_TGFb_TGFbR_P	

Products

Table 17: Properties of each product.

Id	Name	SBO
TGFb_TGFbR	TGFb_TGFbR	
I_Smad	I_Smad	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{c}) \cdot \mathrm{k6} \cdot [\mathrm{I\_Smad\_TGFb\_TGFbR\_P}] \tag{16}$$

7.7 Reaction r7

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

Name r7

Notes Phosphorylation of Smad 2 or Smad 3.

Reaction equation

$$\mathrm{Smad} \xrightarrow{\mathrm{TGFb\_TGFbR\_P,\ Smad}} \mathrm{Smad\_P} \tag{17}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
Smad	Smad	

Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
TGFb_TGFbR_P	TGFb_TGFbR_P	
Smad	Smad	

Product

Table 20: Properties of each product.

Id	Name	SBO
Smad_P	Smad_P	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}(\mathrm{c}) \cdot \mathrm{Function\_for\_r7\_\_1}(\mathrm{k7}, [\mathrm{Smad}], [\mathrm{TGFb\_TGFbR\_P}]) \tag{18}$$

$$\mathrm{Function\_for\_r7\_\_1}(\mathrm{k7}, [\mathrm{Smad}], [\mathrm{TGFb\_TGFbR\_P}]) = \mathrm{k7} \cdot [\mathrm{Smad}] \cdot [\mathrm{TGFb\_TGFbR\_P}] \tag{19}$$

$$\mathrm{Function\_for\_r7\_\_1}(\mathrm{k7}, [\mathrm{Smad}], [\mathrm{TGFb\_TGFbR\_P}]) = \mathrm{k7} \cdot [\mathrm{Smad}] \cdot [\mathrm{TGFb\_TGFbR\_P}] \tag{20}$$

7.8 Reaction r8

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

Name r8

Notes Unphosphorylated Smad 2 or Smad 3 import into the nucleus.

Reaction equation

$$\mathrm{Smad} \longrightarrow \mathrm{Smad\_N} \tag{21}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
Smad	Smad	

Product

Table 22: Properties of each product.

Id	Name	SBO
Smad_N	Smad_N	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{k8} \cdot [\mathrm{Smad}] \tag{22}$$

7.9 Reaction r9

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

Name r9

Notes Unphosphorylated Smad 2 or Smad 3 export from the nucleus.

Reaction equation

$$\mathrm{Smad\_N} \longrightarrow \mathrm{Smad} \tag{23}$$

Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
Smad_N	Smad_N	

Product

Table 24: Properties of each product.

Id	Name	SBO
Smad	Smad	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{k9} \cdot [\mathrm{Smad\_N}] \tag{24}$$

7.10 Reaction r10

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

Name r10

Notes Smad_P represents phosphorylated Smad.

Smad_P_Smad_P represents a homodimer of phosporylated Smads.

This reaction represents homodimerization of phosphorylated Smads.

Reaction equation

$$2\,\mathrm{Smad\_P} \longrightarrow \mathrm{Smad\_P\_Smad\_P} \tag{25}$$

Reactant

Table 25: Properties of each reactant.

Id	Name	SBO
Smad_P	Smad_P	

Product

Table 26: Properties of each product.

Id	Name	SBO
Smad_P_Smad_P	Smad_P_Smad_P	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}(\mathrm{c}) \cdot \mathrm{k10} \cdot [\mathrm{Smad\_P}]^2 \tag{26}$$

7.11 Reaction r11

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

Name r11

Notes Smad_P represents phosphorylated Smad.

Smad_P_Smad_P represents a homodimer of phosporylated Smads.

This reaction represents dissociation of the homodimer Smad_P_Smad_P into two phosph

Reaction equation

$$\text{Smad\_P\_Smad\_P} \longrightarrow 2\,\text{Smad\_P} \tag{27}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
Smad_P_Smad_P	Smad_P_Smad_P	

Product

Table 28: Properties of each product.

Id	Name	SBO
Smad_P	Smad_P	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{vol}\,(\text{c}) \cdot \text{k11} \cdot [\text{Smad\_P\_Smad\_P}] \tag{28}$$

7.12 Reaction r12

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

Name r12

Notes Smad_P represents phosphorylated Smad.

Smad_P_CoSmad represents the heterodimer containing Smad_P and CoSmad.

This reaction represents the binding of Smad_P and CoSmad to form the heterodimer Sm

Reaction equation

$$\text{Smad\_P} + \text{CoSmad} \longrightarrow \text{Smad\_P\_CoSmad} \tag{29}$$

Reactants

Table 29: Properties of each reactant.

Id	Name	SBO
Smad_P	Smad_P	
CoSmad	CoSmad	

Product

Table 30: Properties of each product.

Id	Name	SBO
Smad_P_CoSmad	Smad_P_CoSmad	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{vol}(\text{c}) \cdot \text{k10} \cdot [\text{Smad\_P}] \cdot [\text{CoSmad}] \tag{30}$$

7.13 Reaction r13

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

Name r13

Notes Smad_P represents phosphorylated Smad.

Smad_P_CoSmad represents the heterodimer containing Smad_P and CoSmad.

This reaction represents the dissociation of the Smad_P_CoSmad heterodimer into Smad

Reaction equation

$$\text{Smad\_P\_CoSmad} \longrightarrow \text{Smad\_P} + \text{CoSmad} \tag{31}$$

Reactant

Table 31: Properties of each reactant.

Id	Name	SBO
Smad_P_CoSmad	Smad_P_CoSmad	

Products

Table 32: Properties of each product.

Id	Name	SBO
Smad_P	Smad_P	
CoSmad	CoSmad	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}\,(\mathrm{c}) \cdot \mathrm{k11} \cdot [\mathrm{Smad\_P\_CoSmad}] \tag{32}$$

7.14 Reaction r14

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

Name r14

Notes CoSmad_N represents CoSmad located in the nucleus.

This reaction represents the transport of CoSmad to the nucleus from the cytoplasm.

Reaction equation

$$\mathrm{CoSmad} \longrightarrow \mathrm{CoSmad\_N} \tag{33}$$

Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
CoSmad	CoSmad	

Product

Table 34: Properties of each product.

Id	Name	SBO
CoSmad_N	CoSmad_N	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{k8} \cdot [\mathrm{CoSmad}] \tag{34}$$

7.15 Reaction r15

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

Name r15

Notes CoSmad_N represents CoSmad located in the nucleus.

This reaction represents the transport of CoSmad from the nucleus to the cytoplasm.

Reaction equation

$$\mathrm{CoSmad\_N} \longrightarrow \mathrm{CoSmad} \tag{35}$$

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
CoSmad_N	CoSmad_N	

Product

Table 36: Properties of each product.

Id	Name	SBO
CoSmad	CoSmad	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{k9} \cdot [\mathrm{CoSmad\_N}] \tag{36}$$

7.16 Reaction r16

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

Name r16

Notes The phosphorylated Smad complex is shuttled into the nucleus. GO annotation corresp

Reaction equation

$$\mathrm{Smad\_P\_Smad\_P} \longrightarrow \mathrm{Smad\_P\_Smad\_P\_N} \tag{37}$$

Reactant

Table 37: Properties of each reactant.

Id	Name	SBO
Smad_P_Smad_P	Smad_P_Smad_P	

Product

Table 38: Properties of each product.

Id	Name	SBO
Smad_P_Smad_P_N	Smad_P_Smad_P_N	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{Function\_for\_r16\_\_1}\left([\mathrm{Smad\_P\_Smad\_P}], \mathrm{k12}, \mathrm{k8}\right) \tag{38}$$

$$\mathrm{Function\_for\_r16\_\_1}\left([\mathrm{Smad\_P\_Smad\_P}], \mathrm{k12}, \mathrm{k8}\right) = \mathrm{k12} \cdot \mathrm{k8} \cdot [\mathrm{Smad\_P\_Smad\_P}] \tag{39}$$

7.17 Reaction r17

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

Name r17

Notes Phosphorylated Smad is shuttled into the nucleus. Annotations correspond to the SMA

Reaction equation

$$\text{Smad\_P} \longrightarrow \text{Smad\_P\_N} \tag{40}$$

Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
Smad_P	Smad_P	

Product

Table 40: Properties of each product.

Id	Name	SBO
Smad_P_N	Smad_P_N	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \text{k8} \cdot [\text{Smad\_P}] \tag{41}$$

7.18 Reaction r18

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

Name r18

Notes Phosphorylated Smad is shuttled from the nucleus and the cytoplasm. Annotations are

Reaction equation

$$\text{Smad\_P\_N} \longrightarrow \text{Smad\_P} \tag{42}$$

Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
Smad_P_N	Smad_P_N	

Product

Table 42: Properties of each product.

Id	Name	SBO
Smad_P	Smad_P	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{k9} \cdot [\mathrm{Smad\_P\_N}] \tag{43}$$

7.19 Reaction r19

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

Name r19

Notes The phosphorylated Smad/Co-Smad complex is shuttled into the nucleus. Annotations a

Reaction equation

$$\mathrm{Smad\_P\_CoSmad} \longrightarrow \mathrm{Smad\_P\_CoSmad\_N} \tag{44}$$

Reactant

Table 43: Properties of each reactant.

Id	Name	SBO
Smad_P_CoSmad	Smad_P_CoSmad	

Product

Table 44: Properties of each product.

Id	Name	SBO
Smad_P_CoSmad_N	Smad_P_CoSmad_N	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{Function\_for\_r16\_\_1}\left([\text{Smad\_P\_CoSmad}], \text{k12}, \text{k8}\right) \tag{45}$$

$$\text{Function\_for\_r16\_\_1}\left([\text{Smad\_P\_Smad\_P}], \text{k12}, \text{k8}\right) = \text{k12} \cdot \text{k8} \cdot [\text{Smad\_P\_Smad\_P}] \tag{46}$$

7.20 Reaction r20

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

Name r20

Notes `Nuclear Smad is dephosphorylated. Annotations are for the SMAD domain and for prote`

Reaction equation

$$\text{Smad\_P\_N} \longrightarrow \text{Smad\_N} \tag{47}$$

Reactant

Table 45: Properties of each reactant.

Id	Name	SBO
Smad_P_N	Smad_P_N	

Product

Table 46: Properties of each product.

Id	Name	SBO
Smad_N	Smad_N	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \text{vol}\left(\text{n}\right) \cdot \text{k13} \cdot [\text{Smad\_P\_N}] \tag{48}$$

7.21 Reaction r21

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

Name r21

Notes `Phosphorylated nuclear Smads form a dimer. Annotations are for Smad protein comple`

Reaction equation

$$2\,\text{Smad\_P\_N} \longrightarrow \text{Smad\_P\_Smad\_P\_N} \tag{49}$$

Reactant

Table 47: Properties of each reactant.

Id	Name	SBO
Smad_P_N	Smad_P_N	

Product

Table 48: Properties of each product.

Id	Name	SBO
Smad_P_Smad_P_N	Smad_P_Smad_P_N	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \text{vol}\,(\text{n}) \cdot \text{k10} \cdot [\text{Smad\_P\_N}]^2 \tag{50}$$

7.22 Reaction r22

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

Name r22

Notes Nuclear phosphorylated Smad homodimer dissociated into nuclear phosphorylated Smad

InterPro annotation gives details on and source information for general Smads (inclu

Gene Ontology GO:0043241 reference outlines terms associated with protein complex di

Gene Ontology GO:0010862 reference outlines terms associated with SMAD protein phosp

This reaction occurs in the nucleus.

All annotations are generalized as the model details general TGFb pathway dynamics a

Reaction equation

$$\text{Smad\_P\_Smad\_P\_N} \longrightarrow 2\,\text{Smad\_P\_N} \tag{51}$$

Reactant

Table 49: Properties of each reactant.

Id	Name	SBO
Smad_P_Smad_P_N	Smad_P_Smad_P_N	

Product

Table 50: Properties of each product.

Id	Name	SBO
Smad_P_N	Smad_P_N	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \text{vol}\,(\text{n}) \cdot \text{k11} \cdot [\text{Smad\_P\_Smad\_P\_N}] \tag{52}$$

7.23 Reaction r23

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

Name r23

Notes Nuclear phosphorylated Smad and Co-Smad heterodimerize.

InterPro annotation gives details on and source information for general Smads (inclu

GeneOntology GO:0070412 reference outlines terms associated with R-Smad binding, whi

Gene Ontology GO:0010862 reference outlines terms associated with SMAD protein phosp

Gene Ontology GO:0070410 references outlines terms associated with Co-Smad binding,

Uniprot Q13485 is a Homo sapien version of Smad4, the Smad indicated as a Co-Smad by

This reaction occurs in the nucleus.

Most annotations are generalized as the model details general TGFb pathway dynamics

Reaction equation

$$\text{Smad\_P\_N} + \text{CoSmad\_N} \longrightarrow \text{Smad\_P\_CoSmad\_N} \tag{53}$$

Reactants

Table 51: Properties of each reactant.

Id	Name	SBO
Smad_P_N	Smad_P_N	
CoSmad_N	CoSmad_N	

Product

Table 52: Properties of each product.

Id	Name	SBO
Smad_P_CoSmad_N	Smad_P_CoSmad_N	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = \text{vol}(\text{n}) \cdot \text{k10} \cdot [\text{Smad\_P\_N}] \cdot [\text{CoSmad\_N}] \tag{54}$$

7.24 Reaction r24

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

Name r24

Notes Nuclear phosphorylated Smad and Co-Smad disocciate into phosphorylated Smad and Co-

InterPro annotation gives details on and source information for general Smads (inclu

Gene Ontology GO:0043241 reference outlines terms associated with protein complex di

Gene Ontology GO:0010862 reference outlines terms associated with SMAD protein phosp

Gene Ontology GO:0070410 references outlines terms associated with Co-Smad binding,

Uniprot Q13485 is a Homo sapien version of Smad4, the Smad indicated as a Co-Smad by

This reaction occurs in nucleus.

All annotations are generalized as the model details general TGFb pathway dynamics a

Reaction equation

$$\text{Smad\_P\_CoSmad\_N} \longrightarrow \text{Smad\_P\_N} + \text{CoSmad\_N} \tag{55}$$

Reactant

Table 53: Properties of each reactant.

Id	Name	SBO
Smad_P_CoSmad_N	Smad_P_CoSmad_N	

Products

Table 54: Properties of each product.

Id	Name	SBO
Smad_P_N	Smad_P_N	
CoSmad_N	CoSmad_N	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \text{vol}(\text{n}) \cdot \text{k11} \cdot [\text{Smad\_P\_CoSmad\_N}] \tag{56}$$

7.25 Reaction r25

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

Name r25

Notes I-Smad mRNA is created in the nucleus, a process which is inhibited by the nuclear

InterPro annotation gives details on and source information for general Smads (inclu

This reaction occurs in the nucleus.

All annotations are generalized as the model details general TGFb pathway dynamics a

Reaction equation

$$\emptyset \xrightarrow{\text{Smad\_P\_CoSmad\_N}} \text{I\_Smad\_mRNA1} \tag{57}$$

Modifier

Table 55: Properties of each modifier.

Id	Name	SBO
Smad_P_CoSmad_N	Smad_P_CoSmad_N	

Product

Table 56: Properties of each product.

Id	Name	SBO
I_Smad_mRNA1	I_Smad_mRNA1	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \text{vol}(\text{n}) \cdot \text{Function\_for\_r25\_\_1}([\text{Smad\_P\_CoSmad\_N}], \text{h}, \text{k14}, \text{k15}) \tag{58}$$

$$\text{Function\_for\_r25\_\_1}([\text{Smad\_P\_CoSmad\_N}], \text{h}, \text{k14}, \text{k15}) = \frac{\text{k14} \cdot [\text{Smad\_P\_CoSmad\_N}]^{\text{h}}}{[\text{Smad\_P\_CoSmad\_N}]^{\text{h}} + \text{k15}^{\text{h}}} \tag{59}$$

$$\text{Function\_for\_r25\_\_1}([\text{Smad\_P\_CoSmad\_N}], \text{h}, \text{k14}, \text{k15}) = \frac{\text{k14} \cdot [\text{Smad\_P\_CoSmad\_N}]^{\text{h}}}{[\text{Smad\_P\_CoSmad\_N}]^{\text{h}} + \text{k15}^{\text{h}}} \tag{60}$$

7.26 Reaction r26

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

Name r26

Notes Nuclear I-Smad mRNA is shuttled to the cytoplasm.

InterPro annotation gives details on and source information for general Smads (inclu

Gene Ontology GO:0006913 gives terms associated with nuclear export; this reaction i

All annotations are generalized as the model details general TGFb pathway dynamics a

Reaction equation

$$\text{I\_Smad\_mRNA1} \longrightarrow \text{I\_Smad\_mRNA2} \tag{61}$$

Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
I_Smad_mRNA1	I_Smad_mRNA1	

Product

Table 58: Properties of each product.

Id	Name	SBO
I_Smad_mRNA2	I_Smad_mRNA2	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \text{k16} \cdot [\text{I\_Smad\_mRNA1}] \tag{62}$$

7.27 Reaction r27

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

Name r27

Notes Cytoplasmic I-Smad mRNA is degraded.

InterPro annotation gives details on and source information for general Smads (inclu

Gene Ontology GO:0006401 gives the terms associated with RNA catabolic processes; th

This reaction occurs in the cytoplasm.

All annotations are generalized as the model details general TGFb pathway dynamics a

Reaction equation

$$\text{I\_Smad\_mRNA2} \longrightarrow \emptyset \tag{63}$$

Reactant

Table 59: Properties of each reactant.

Id	Name	SBO
I_Smad_mRNA2	I_Smad_mRNA2	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \text{vol}(\text{c}) \cdot \text{k17} \cdot [\text{I\_Smad\_mRNA2}] \tag{64}$$

7.28 Reaction r28

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

Name r28

Notes I-Smad is generated, a process which is limited by cytoplasmi I-Smad mRNA.

InterPro annotation gives details on and source information for general Smads (inclu

This reaction occurs in the cytoplasm.

All annotations are generalized as the model details general TGFb pathway dynamics a

Reaction equation

$$\emptyset \xrightarrow{\text{I\_Smad\_mRNA2}} \text{I\_Smad} \tag{65}$$

Modifier

Table 60: Properties of each modifier.

Id	Name	SBO
I_Smad_mRNA2	I_Smad_mRNA2	

Product

Table 61: Properties of each product.

Id	Name	SBO
I_Smad	I_Smad	

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \mathrm{vol}(\mathrm{c}) \cdot \mathrm{Function\_for\_r28\_\_1}([\mathrm{I\_Smad\_mRNA2}], \mathrm{k18}) \tag{66}$$

$$\mathrm{Function\_for\_r28\_\_1}([\mathrm{I\_Smad\_mRNA2}], \mathrm{k18}) = \mathrm{k18} \cdot [\mathrm{I\_Smad\_mRNA2}] \tag{67}$$

$$\mathrm{Function\_for\_r28\_\_1}([\mathrm{I\_Smad\_mRNA2}], \mathrm{k18}) = \mathrm{k18} \cdot [\mathrm{I\_Smad\_mRNA2}] \tag{68}$$

7.29 Reaction r29

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

Name r29

Notes Degradation of I-Smad.

Reaction equation

$$\mathrm{I\_Smad} \longrightarrow \emptyset \tag{69}$$

Reactant

Table 62: Properties of each reactant.

Id	Name	SBO
I_Smad	I_Smad	

Kinetic Law

Derived unit contains undeclared units

$$v_{29} = \mathrm{vol}(\mathrm{c}) \cdot \mathrm{k19} \cdot [\mathrm{I\_Smad}] \tag{70}$$

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 TGFbR

Name TGFbR

Notes `Authors specified the receptor in the model is TGF-Beta type 1 receptor.`

Initial concentration $1010\,\mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in r2 and as a product in r1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{TGFbR} = v_1 - v_2 \tag{71}$$

8.2 Species TGFb_TGFbR

Name TGFb_TGFbR

Notes `A complex of a ligand withing the TGF-Beta family and TGF-Beta type 1 receptor.`

`The authors did not specify the exact ligand that they wanted in their model and onl`

Initial concentration $0\,\mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in five reactions (as a reactant in r1, r3 and as a product in r2, r4, r6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{TGFb\_TGFbR} = v_2 + v_4 + v_6 - v_1 - v_3 \tag{72}$$

8.3 Species TGFb_TGFbR_P

Name TGFb_TGFbR_P

SBO:0000216 phosphorylation

Notes A complex of a ligand withing the TGF-Beta family and TGF-Beta type 1 receptor.

Receptor is phosphorylated.

The authors did not specify the exact ligand that they wanted in their model and onl

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in r4, r5 and as a product in r3 and as a modifier in r7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{TGFb\_TGFbR\_P} = v_3 - v_4 - v_5 \tag{73}$$

8.4 Species I_Smad_TGFb_TGFbR_P

Name I_Smad_TGFb_TGFbR_P

SBO:0000216 phosphorylation

Notes This complex consists of an inhibitory Smad with a SMAD domain, a TGF-beta ligand a

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in r6 and as a product in r5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{I\_Smad\_TGFb\_TGFbR\_P} = v_5 - v_6 \tag{74}$$

8.5 Species Smad

Name Smad

Notes InterPro annotation gives details on and source information for general Smads (incl

GeneOntology GO:0070412 reference outlines terms associated with R-Smad binding, whi

Gene Ontology GO:0010862 reference outlines terms associated with SMAD protein phosp

Most annotations are generalized as the model details general TGFb pathway dynamics

Initial concentration $7000\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in r7, r8 and as a product in r9 and as a modifier in r7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Smad} = v_9 - v_7 - v_8 \tag{75}$$

8.6 Species Smad_P

Name Smad_P

Notes InterPro annotation gives details on and source information for general Smads (incl

GeneOntology GO:0070412 reference outlines terms associated with R-Smad binding, whi

Gene Ontology GO:0010862 reference outlines terms associated with SMAD protein phosp

Most annotations are generalized as the model details general TGFb pathway dynamics

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in seven reactions (as a reactant in r10, r12, r17 and as a product in r7, r11, r13, r18).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Smad\_P} = v_7 + 2\,v_{11} + v_{13} + v_{18} - 2\,v_{10} - v_{12} - v_{17} \tag{76}$$

8.7 Species CoSmad

Name CoSmad

Notes Annotation provides information on the general Smad family.

Initial concentration $12000\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in r12, r14 and as a product in r13, r15).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CoSmad} = v_{13} + v_{15} - v_{12} - v_{14} \tag{77}$$

8.8 Species Smad_P_Smad_P

Name Smad_P_Smad_P

Notes Phosphorylated version of Smad 2 or 3 complex (either homomer or heteromer).

Localized to the cytoplasm.

The authors were interested in Smad 2 and 3, since they are involved in the TGF-Beta

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Smad\_P\_Smad\_P} = v_{10} - v_{11} - v_{16} \tag{78}$$

8.9 Species Smad_P_CoSmad

Name Smad_P_CoSmad

Notes InterPro annotation gives details on and source information for general Smads (incl

GeneOntology GO:0070412 reference outlines terms associated with R-Smad binding, whi

Gene Ontology GO:0010862 reference outlines terms associated with SMAD protein phosp

Gene Ontology GO:0070410 references outlines terms associated with Co-Smad binding,

Uniprot Q13485 is a Homo sapien version of Smad4, the Smad indicated as a Co-Smad us

Most annotations are generalized as the model details general TGFb pathway dynamics

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in r13, r19 and as a product in r12).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Smad\_P\_CoSmad} = v_{12} - v_{13} - v_{19} \tag{79}$$

8.10 Species I_Smad_mRNA2

Name I_Smad_mRNA2

Notes Annotation provides information on the general Smad family.

mRNA coding for I_Smad localized to the cytoplasm.

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in r27 and as a product in r26 and as a modifier in r28).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{I\_Smad\_mRNA2} = v_{26} - v_{27} \tag{80}$$

8.11 Species I_Smad

Name I_Smad

Notes Annotation provides information on the general Smad family.

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in r5, r29 and as a product in r6, r28).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{I\_Smad} = v_6 + v_{28} - v_5 - v_{29} \tag{81}$$

8.12 Species Smad_N

Name Smad_N

Notes InterPro annotation gives details on and source information for general Smads (incl

GeneOntology GO:0070412 reference outlines terms associated with R-Smad binding, whi

Gene Ontology GO:0010862 reference outlines terms associated with SMAD protein phosp

Most annotations are generalized as the model details general TGFb pathway dynamics

Initial concentration $82000\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in r9 and as a product in r8, r20).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Smad\_N} = v_8 + v_{20} - v_9 \tag{82}$$

8.13 Species Smad_P_Smad_P_N

Name Smad_P_Smad_P_N

Notes Phosphorylated version of Smad 2 or 3 complex (either homomer or heteromer).

Localized to the nucleus.

The authors were interested in Smad 2 and 3, since they are involved in the TGF-Beta

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in r22 and as a product in r16, r21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Smad\_P\_Smad\_P\_N} = v_{16} + v_{21} - v_{22} \tag{83}$$

8.14 Species Smad_P_N

Name Smad_P_N

Notes InterPro annotation gives details on and source information for general Smads (incl

GeneOntology GO:0070412 reference outlines terms associated with R-Smad binding, whi

Gene Ontology GO:0010862 reference outlines terms associated with SMAD protein phosp

Most annotations are generalized as the model details general TGFb pathway dynamics

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in seven reactions (as a reactant in r18, r20, r21, r23 and as a product in r17, r22, r24).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Smad\_P\_N} = v_{17} + 2\,v_{22} + v_{24} - v_{18} - v_{20} - 2\,v_{21} - v_{23} \tag{84}$$

8.15 Species Smad_P_CoSmad_N

Name Smad_P_CoSmad_N

Notes InterPro annotation gives details on and source information for general Smads (incl

GeneOntology GO:0070412 reference outlines terms associated with R-Smad binding, whi

Gene Ontology GO:0010862 reference outlines terms associated with SMAD protein phosp

Gene Ontology GO:0070410 references outlines terms associated with Co-Smad binding,

Uniprot Q13485 is a Homo sapien version of Smad4, the Smad indicated as the Co-Smad

Most annotations are generalized as the model details general TGFb pathway dynamics

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in r24 and as a product in r19, r23 and as a modifier in r25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Smad\_P\_CoSmad\_N} = v_{19} + v_{23} - v_{24} \tag{85}$$

8.16 Species CoSmad_N

Name CoSmad_N

Notes Annotation provides information on the general Smad family.

CoSmad localized to the nucleus.

Initial concentration $135000\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in r15, r23 and as a product in r14, r24).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CoSmad\_N} = v_{14} + v_{24} - v_{15} - v_{23} \tag{86}$$

8.17 Species I_Smad_mRNA1

Name I_Smad_mRNA1

Notes Annotation provides information on the general Smad family.

mRNA coding for I_Smad localized to the nucleus.

Initial concentration $0\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in r26 and as a product in r25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{I\_Smad\_mRNA1} = v_{25} - v_{26} \tag{87}$$

8.18 Species TGFb

Name TGFb

Notes TGF-Beta ligand.

Pulled from the paper Constraint-based modeling and kinetic analysis of the Smad dep

Deviated from published value.

Initial concentration $460\ \mathrm{pmol}\cdot\mathrm{l}^{-1}$

This species takes part in one reaction (as a reactant in r2), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{TGFb} = 0 \tag{88}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000216 phosphorylation: Addition of a phosphate group (-H2PO4) to a chemical entity

SBML2LaTeX was developed by Andreas Dräger[a], Hannes Planatscher[a], Dieudonné M Wouamba[a], Adrian Schröder[a], Michael Hucka[b], Lukas Endler[c], Martin Golebiewski[d] and Andreas Zell[a]. Please see http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX for more information.

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany