SBML Model Report

Model name: "Schmierer_2008_Smad_Tgfb"

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: Lukas Endler[1] and Bernhard Schmierer[2] at July 30th 2008 at 10:47 a. m. and last time modified at April eighth 2016 at 3:39 p. m. Table 1 gives an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	2
species types	0	species	26
events	0	constraints	0
reactions	26	function definitions	0
global parameters	17	unit definitions	5
rules	4	initial assignments	0

Model Notes

This sbml file describes the RECI model from:
„Mathematical modeling identifies Smad nucleocytoplasmic shuttling as a dynamic signal-interpreting system„ by Bernhard Schmierer, Alexander L. Tournier, Paul A. Bates and Caroline S. Hill, Proc Natl Acad Sci U S A. 2008 May 6;105(18):6608-13.
All parameter and species names are as in Figure S3 of the original publication. The original

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model was done in copasi.
SB-431542 addition to a concentration of 10000 nM is set at 2700 sec. The initial concentration of SB, the time point of addition and the final concentration can be set by altering the parameters **SB_0**, **t_SB** and **SB_end**.
This model file has been used to reproduce Figures 2D and 5A from the research paper using SBMLodesolver. To get the results for the figures, sum the corresponding concentrations:
fig 2D: nuclear EGFP-Smad2 = G_n + pG_n + G2_n + G4_n + 2* GG_n
fig 5A (either n or c for nucleus or cytosol):
monomeric Smad2 = S2_n/c + G_n/c
monomeric P-Smad2 = pS2_n/c + pG_n/c
Smad2/Smad4 complexes = S24_n/c + G4_n/c
Smad2/Smad2 complexes = S22_n/c + G2_n/c + GG_n/c

2 Unit Definitions

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

2.1 Unit `substance`

Definition nmol

2.2 Unit `nM`

Name nM

Definition $\mathrm{nmol} \cdot \mathrm{l}^{-1}$

2.3 Unit `ps`

Name persecond

Definition s^{-1}

2.4 Unit pnMps

Name pernMpersecond

Definition $\mathrm{nmol}^{-1} \cdot \mathrm{s}^{-1} \cdot \mathrm{l}$

2.5 Unit lps

Name litrepersecond

Definition $\mathrm{l} \cdot \mathrm{s}^{-1}$

2.6 Unit volume

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

Definition l

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

2.9 Unit time

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

Definition s

3 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
nucleus	Nuc		3	10^{-12}	l	☑	
cytosol	Cyt		3	$2.27 \cdot 10^{-12}$	l	☑	

3.1 Compartment `nucleus`

This is a three dimensional compartment with a constant size of 10^{-12} litre.

Name Nuc

3.2 Compartment `cytosol`

This is a three dimensional compartment with a constant size of $2.27 \cdot 10^{-12}$ litre.

Name Cyt

4 Species

This model contains 26 species. The boundary condition of three of these species is set to `true` so that these 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
PPase	PPase	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☑	☑
S2_n	Smad2_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
pS2_n	pSmad2_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
G_n	GFP-Smad2_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
pG_n	pGFP-Smad2_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
S22_n	pSmad2/pSmad2_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
S24_n	pSmad2/Smad4_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
S4_n	Smad4_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
G2_n	pGFP-Smad2/pSmad2_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
G4_n	pGFP-Smad2/Smad4_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
GG_n	pGFP-Smad2/pGFP_Smad2_n	nucleus	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
S22_c	pSmad2/pSmad2_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
S24_c	pSmad2/Smad4_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
S4_c	Smad4_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
S2_c	Smad2_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
pS2_c	pSmad2_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
G_c	GFP-Smad2_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
pG_c	pGFP-Smad2_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
G2_c	pGFP-Smad2/pSmad2_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
G4_c	pGFP-Smad2/Smad4_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
GG_c	pGFP-Smad2/pGFP-Smad2_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
TGFb_c	TGFb_c	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☑	☑
R_act	R_act	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
R	R	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
R_inact	R_inact	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☐
SB	SB-431542	cytosol	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☐	☑

5 Parameters

This model contains 17 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kin	kin (import rate for monomeric Smads)		$5.93 \cdot 10^{-15}$	$1 \cdot s^{-1}$	☑
kex	kex (export rate for monomeric Smads)		$1.26 \cdot 10^{-14}$	$1 \cdot s^{-1}$	☑
kphos	kphos (phosphorylation rate)		$4.037081673984 \cdot 10^{-4}$	$nmol^{-1} \cdot s^{-1} \cdot 1$	☑
kdephos	kdephos (dephosphorylation rate)		0.007	$nmol^{-1} \cdot s^{-1} \cdot 1$	☑
kin_CIF	kin*CIF (Complex import rate)		$3.36347821 \cdot 10^{-14}$	$1 \cdot s^{-1}$	☑
kon	kon (Smad complex on-rate)		0.002	$nmol^{-1} \cdot s^{-1} \cdot 1$	☑
koff	koff (Smad complex off-rate)		0.016	s^{-1}	☑
CIF	CIF (complex import factor)		5.672	dimensionless	⊟
K_diss	Kdiss (dissociation constant of Smad complexes)		8.699	$nmol \cdot 1^{-1}$	⊟
kon_SB	kon_SB (on-rate of the SB/receptor interaction)		0.146	$nmol^{-1} \cdot s^{-1} \cdot 1$	☑
koff_SB	koff_SB (off-rate of the SB/receptor interaction)		100.000	s^{-1}	☑
k_TGFb	k_TGFb (rate of TGFb binding to receptors)		0.074	$nmol^{-1} \cdot s^{-1} \cdot 1$	☑
K_dissSB	Kdiss SB (dissociation constant of the SB/receptor interaction)		682.956	$nmol \cdot 1^{-1}$	⊟
ntoN	quantity to number factor		$6.0221415 \cdot 10^{14}$	dimensionless	☑
SB_0	SB conc at start		0.000	$nmol \cdot 1^{-1}$	☑

Id	Name	SBO	Value	Unit	Constant
SB_add	SB conc after addition		10000.000	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	☑
t_SB	time of SB addition		2700.000	s	☑

6 Rules

This is an overview of four rules.

6.1 Rule CIF

Rule CIF is an assignment rule for parameter CIF:

$$\mathrm{CIF} = \frac{\mathrm{kin\_CIF}}{\mathrm{kin}} \tag{1}$$

Derived unit dimensionless

6.2 Rule K_diss

Rule K_diss is an assignment rule for parameter K_diss:

$$\mathrm{K\_diss} = \frac{\mathrm{koff}}{\mathrm{kon}} \tag{2}$$

Derived unit $\mathrm{nmol} \cdot \mathrm{l}^{-1}$

6.3 Rule K_dissSB

Rule K_dissSB is an assignment rule for parameter K_dissSB:

$$\mathrm{K\_dissSB} = \frac{\mathrm{koff\_SB}}{\mathrm{kon\_SB}} \tag{3}$$

Derived unit $\mathrm{nmol} \cdot \mathrm{l}^{-1}$

6.4 Rule SB

Rule SB is an assignment rule for species SB:

$$\mathrm{SB} = \begin{cases} \mathrm{SB\_add} & \text{if time} > \mathrm{t\_SB} \\ \mathrm{SB\_0} & \text{otherwise} \end{cases} \tag{4}$$

Derived unit $\mathrm{nmol} \cdot \mathrm{l}^{-1}$

7 Reactions

This model contains 26 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	reaction_1	Reaction 7 Shuttling S4	S4_c $\rightleftharpoons$ S4_n	
2	reaction_2	Reaction 5A Shuttling S2	S2_c $\rightleftharpoons$ S2_n	
3	reaction_3	Reaction 6A Shuttling pS2	pS2_c $\rightleftharpoons$ pS2_n	
4	reaction_4	Reaction 2A Phosphorylation S2	R_act + S2_c $\longrightarrow$ R_act + pS2_c	
5	reaction_5	Reaction 3A Formation S24_C	pS2_c + S4_c $\rightleftharpoons$ S24_c	
6	reaction_6	Reaction 3B Formation S24_N	pS2_n + S4_n $\rightleftharpoons$ S24_n	
7	reaction_7	Reaction 8A Import S24	S24_c $\longrightarrow$ S24_n	
8	reaction_8	Reaction 9A Import S22	S22_c $\longrightarrow$ S22_n	
9	reaction_9	Reaction 4A Formation S22_C	2 pS2_c $\rightleftharpoons$ S22_c	
10	reaction_10	Reaction 4B Formation S22_N	2 pS2_n $\rightleftharpoons$ S22_n	
11	reaction_11	Reaction 10A Dephos pS2 Nuc	pS2_n + PPase $\longrightarrow$ S2_n + PPase	
12	reaction_12	Reaction 1 TGFb Binding	R + TGFb_c $\longrightarrow$ R_act	
13	reaction_13	Reaction 11 Receptor Inhibition	R_act + SB $\rightleftharpoons$ R_inact	
14	reaction_14	Reaction 2B Phosphorylation GS2	G_c + R_act $\longrightarrow$ pG_c + R_act	
15	reaction_15	Reaction 10B Dephos pG Nuc	pG_n + PPase $\longrightarrow$ G_n + PPase	
16	reaction_16	Reaction 5B Shuttling G	G_c $\rightleftharpoons$ G_n	
17	reaction_17	Reaction 6B Shuttling pG	pG_c $\rightleftharpoons$ pG_n	
18	reaction_18	Reaction 4E Formation GG_C	2 pG_c $\rightleftharpoons$ GG_c	
19	reaction_19	Reaction 4F Formation GG_N	2 pG_n $\rightleftharpoons$ GG_n	
20	reaction_20	Reaction 4C Formation G2_C	pS2_c + pG_c $\rightleftharpoons$ G2_c	
21	reaction_21	Reaction 4D Formation G2_N	pS2_n + pG_n $\rightleftharpoons$ G2_n	
22	reaction_22	Reaction 3C Formation G4_C	pG_c + S4_c $\rightleftharpoons$ G4_c	
23	reaction_23	Reaction 3D Formation G4_N	pG_n + S4_n $\rightleftharpoons$ G4_n	

№	Id	Name	Reaction Equation	SBO
24	reaction_24	Reaction 9C Import GG	GG_c ⟶ GG_n	
25	reaction_25	Reaction 9B Import G2	G2_c ⟶ G2_n	
26	reaction_26	Reaction 8B Import G4	G4_c ⟶ G4_n	

7.1 Reaction reaction_1

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

Name Reaction 7 Shuttling S4

Reaction equation

$$\mathrm{S4\_c} \rightleftharpoons \mathrm{S4\_n} \tag{5}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
S4_c	Smad4_c	

Product

Table 7: Properties of each product.

Id	Name	SBO
S4_n	Smad4_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_1 = \mathrm{kin} \cdot [\mathrm{S4\_c}] - \mathrm{kin} \cdot [\mathrm{S4\_n}] \tag{6}$$

7.2 Reaction reaction_2

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

Name Reaction 5A Shuttling S2

Reaction equation

$$\mathrm{S2\_c} \rightleftharpoons \mathrm{S2\_n} \tag{7}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
S2_c	Smad2_c	

Product

Table 9: Properties of each product.

Id	Name	SBO
S2_n	Smad2_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_2 = \mathrm{kin} \cdot [\mathrm{S2\_c}] - \mathrm{kex} \cdot [\mathrm{S2\_n}] \tag{8}$$

7.3 Reaction `reaction_3`

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

Name Reaction 6A Shuttling pS2

Reaction equation

$$\mathrm{pS2\_c} \rightleftharpoons \mathrm{pS2\_n} \tag{9}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
pS2_c	pSmad2_c	

Product

Table 11: Properties of each product.

Id	Name	SBO
pS2_n	pSmad2_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_3 = \mathrm{kin} \cdot [\mathrm{pS2\_c}] - \mathrm{kex} \cdot [\mathrm{pS2\_n}] \tag{10}$$

7.4 Reaction `reaction_4`

This is an irreversible reaction of two reactants forming two products.

Name Reaction 2A Phosphorylation S2

Reaction equation

$$\mathrm{R\_act} + \mathrm{S2\_c} \longrightarrow \mathrm{R\_act} + \mathrm{pS2\_c} \tag{11}$$

Reactants

Table 12: Properties of each reactant.

Id	Name	SBO
`R_act`	R_act	
`S2_c`	Smad2_c	

Products

Table 13: Properties of each product.

Id	Name	SBO
`R_act`	R_act	
`pS2_c`	pSmad2_c	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_4 = \mathrm{vol}\,(\mathrm{cytosol}) \cdot \mathrm{kphos} \cdot [\mathrm{R\_act}] \cdot [\mathrm{S2\_c}] \tag{12}$$

7.5 Reaction `reaction_5`

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

Name Reaction 3A Formation S24_C

Reaction equation

$$\mathrm{pS2\_c} + \mathrm{S4\_c} \rightleftharpoons \mathrm{S24\_c} \tag{13}$$

Reactants

Table 14: Properties of each reactant.

Id	Name	SBO
pS2_c	pSmad2_c	
S4_c	Smad4_c	

Product

Table 15: Properties of each product.

Id	Name	SBO
S24_c	pSmad2/Smad4_c	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_5 = \mathrm{vol}\,(\mathrm{cytosol}) \cdot (\mathrm{kon} \cdot [\mathrm{pS2\_c}] \cdot [\mathrm{S4\_c}] - \mathrm{koff} \cdot [\mathrm{S24\_c}]) \tag{14}$$

7.6 Reaction reaction_6

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

Name Reaction 3B Formation S24_N

Reaction equation

$$\mathrm{pS2\_n} + \mathrm{S4\_n} \rightleftharpoons \mathrm{S24\_n} \tag{15}$$

Reactants

Table 16: Properties of each reactant.

Id	Name	SBO
pS2_n	pSmad2_n	
S4_n	Smad4_n	

Product

Table 17: Properties of each product.

Id	Name	SBO
S24_n	pSmad2/Smad4_n	

Kinetic Law

Derived unit $s^{-1} \cdot nmol$

$$v_6 = \text{vol}(\text{nucleus}) \cdot (\text{kon} \cdot [\text{pS2\_n}] \cdot [\text{S4\_n}] - \text{koff} \cdot [\text{S24\_n}]) \tag{16}$$

7.7 Reaction reaction_7

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

Name Reaction 8A Import S24

Reaction equation

$$\text{S24\_c} \longrightarrow \text{S24\_n} \tag{17}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
S24_c	pSmad2/Smad4_c	

Product

Table 19: Properties of each product.

Id	Name	SBO
S24_n	pSmad2/Smad4_n	

Kinetic Law

Derived unit $s^{-1} \cdot nmol$

$$v_7 = \text{kin\_CIF} \cdot [\text{S24\_c}] \tag{18}$$

7.8 Reaction reaction_8

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

Name Reaction 9A Import S22

Reaction equation

$$\mathrm{S22\_c} \longrightarrow \mathrm{S22\_n} \tag{19}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
S22_c	pSmad2/pSmad2_c	

Product

Table 21: Properties of each product.

Id	Name	SBO
S22_n	pSmad2/pSmad2_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_8 = \mathrm{kin\_CIF} \cdot [\mathrm{S22\_c}] \tag{20}$$

7.9 Reaction reaction_9

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

Name Reaction 4A Formation S22_C

Reaction equation

$$2\,\mathrm{pS2\_c} \rightleftharpoons \mathrm{S22\_c} \tag{21}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
pS2_c	pSmad2_c	

Product

Table 23: Properties of each product.

Id	Name	SBO
S22_c	pSmad2/pSmad2_c	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_9 = \mathrm{vol}\,(\mathrm{cytosol}) \cdot (\mathrm{kon} \cdot [\mathrm{pS2\_c}] \cdot [\mathrm{pS2\_c}] - \mathrm{koff} \cdot [\mathrm{S22\_c}]) \tag{22}$$

7.10 Reaction `reaction_10`

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

Name Reaction 4B Formation S22_N

Reaction equation

$$2\,\mathrm{pS2\_n} \rightleftharpoons \mathrm{S22\_n} \tag{23}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
pS2_n	pSmad2_n	

Product

Table 25: Properties of each product.

Id	Name	SBO
S22_n	pSmad2/pSmad2_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{10} = \mathrm{vol}(\mathrm{nucleus}) \cdot (\mathrm{kon} \cdot [\mathrm{pS2\_n}] \cdot [\mathrm{pS2\_n}] - \mathrm{koff} \cdot [\mathrm{S22\_n}]) \tag{24}$$

7.11 Reaction `reaction_11`

This is an irreversible reaction of two reactants forming two products.

Name Reaction 10A Dephos pS2 Nuc

Reaction equation

$$\mathrm{pS2\_n} + \mathrm{PPase} \longrightarrow \mathrm{S2\_n} + \mathrm{PPase} \tag{25}$$

Reactants

Table 26: Properties of each reactant.

Id	Name	SBO
`pS2_n`	pSmad2_n	
`PPase`	PPase	

Products

Table 27: Properties of each product.

Id	Name	SBO
`S2_n`	Smad2_n	
`PPase`	PPase	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{11} = \mathrm{vol}(\mathrm{nucleus}) \cdot \mathrm{kdephos} \cdot [\mathrm{pS2\_n}] \cdot [\mathrm{PPase}] \tag{26}$$

7.12 Reaction `reaction_12`

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

Name Reaction 1 TGFb Binding

Reaction equation

$$\mathrm{R} + \mathrm{TGFb\_c} \longrightarrow \mathrm{R\_act} \tag{27}$$

Reactants

Table 28: Properties of each reactant.

Id	Name	SBO
R	R	
TGFb_c	TGFb_c	

Product

Table 29: Properties of each product.

Id	Name	SBO
R_act	R_act	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{12} = \mathrm{vol}\,(\mathrm{cytosol}) \cdot \mathrm{k\_TGFb} \cdot [\mathrm{R}] \cdot [\mathrm{TGFb\_c}] \tag{28}$$

7.13 Reaction reaction_13

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

Name Reaction 11 Receptor Inhibition

Reaction equation

$$\mathrm{R\_act} + \mathrm{SB} \rightleftharpoons \mathrm{R\_inact} \tag{29}$$

Reactants

Table 30: Properties of each reactant.

Id	Name	SBO
R_act	R_act	
SB	SB-431542	

Product

Table 31: Properties of each product.

Id	Name	SBO
R_inact	R_inact	

Kinetic Law

Derived unit $s^{-1} \cdot nmol$

$$v_{13} = \text{vol}(\text{cytosol}) \cdot (\text{kon\_SB} \cdot [\text{R\_act}] \cdot [\text{SB}] - \text{koff\_SB} \cdot [\text{R\_inact}]) \tag{30}$$

7.14 Reaction reaction_14

This is an irreversible reaction of two reactants forming two products.

Name Reaction 2B Phosphorylation GS2

Reaction equation

$$\text{G\_c} + \text{R\_act} \longrightarrow \text{pG\_c} + \text{R\_act} \tag{31}$$

Reactants

Table 32: Properties of each reactant.

Id	Name	SBO
G_c	GFP-Smad2_c	
R_act	R_act	

Products

Table 33: Properties of each product.

Id	Name	SBO
pG_c	pGFP-Smad2_c	
R_act	R_act	

Kinetic Law

Derived unit $s^{-1} \cdot nmol$

$$v_{14} = \mathrm{vol}\,(\mathrm{cytosol}) \cdot \mathrm{kphos} \cdot [\mathrm{G\_c}] \cdot [\mathrm{R\_act}] \tag{32}$$

7.15 Reaction `reaction_15`

This is an irreversible reaction of two reactants forming two products.

Name Reaction 10B Dephos pG Nuc

Reaction equation

$$\mathrm{pG\_n} + \mathrm{PPase} \longrightarrow \mathrm{G\_n} + \mathrm{PPase} \tag{33}$$

Reactants

Table 34: Properties of each reactant.

Id	Name	SBO
`pG_n`	pGFP-Smad2_n	
`PPase`	PPase	

Products

Table 35: Properties of each product.

Id	Name	SBO
`G_n`	GFP-Smad2_n	
`PPase`	PPase	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{15} = \mathrm{vol}\,(\mathrm{nucleus}) \cdot \mathrm{kdephos} \cdot [\mathrm{pG\_n}] \cdot [\mathrm{PPase}] \tag{34}$$

7.16 Reaction `reaction_16`

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

Name Reaction 5B Shuttling G

Reaction equation

$$\mathrm{G\_c} \rightleftharpoons \mathrm{G\_n} \tag{35}$$

Reactant

Table 36: Properties of each reactant.

Id	Name	SBO
G_c	GFP-Smad2_c	

Product

Table 37: Properties of each product.

Id	Name	SBO
G_n	GFP-Smad2_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{16} = \mathrm{kin} \cdot [\mathrm{G\_c}] - \mathrm{kex} \cdot [\mathrm{G\_n}] \tag{36}$$

7.17 Reaction reaction_17

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

Name Reaction 6B Shuttling pG

Reaction equation

$$\mathrm{pG\_c} \rightleftharpoons \mathrm{pG\_n} \tag{37}$$

Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
pG_c	pGFP-Smad2_c	

Product

Table 39: Properties of each product.

Id	Name	SBO
pG_n	pGFP-Smad2_n	

Kinetic Law

Derived unit $s^{-1} \cdot nmol$

$$v_{17} = kin \cdot [pG\_c] - kex \cdot [pG\_n] \tag{38}$$

7.18 Reaction reaction_18

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

Name Reaction 4E Formation GG_C

Reaction equation

$$2\,pG\_c \rightleftharpoons GG\_c \tag{39}$$

Reactant

Table 40: Properties of each reactant.

Id	Name	SBO
pG_c	pGFP-Smad2_c	

Product

Table 41: Properties of each product.

Id	Name	SBO
GG_c	pGFP-Smad2/pGFP-Smad2_c	

Kinetic Law

Derived unit $s^{-1} \cdot nmol$

$$v_{18} = vol\,(cytosol) \cdot (kon \cdot [pG\_c] \cdot [pG\_c] - koff \cdot [GG\_c]) \tag{40}$$

7.19 Reaction reaction_19

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

Name Reaction 4F Formation GG_N

Reaction equation

$$2\,\mathrm{pG\_n} \rightleftharpoons \mathrm{GG\_n} \tag{41}$$

Reactant

Table 42: Properties of each reactant.

Id	Name	SBO
pG_n	pGFP-Smad2_n	

Product

Table 43: Properties of each product.

Id	Name	SBO
GG_n	pGFP-Smad2/pGFP_Smad2_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{19} = \mathrm{vol}\,(\mathrm{nucleus}) \cdot (\mathrm{kon} \cdot [\mathrm{pG\_n}] \cdot [\mathrm{pG\_n}] - \mathrm{koff} \cdot [\mathrm{GG\_n}]) \tag{42}$$

7.20 Reaction reaction_20

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

Name Reaction 4C Formation G2_C

Reaction equation

$$\mathrm{pS2\_c} + \mathrm{pG\_c} \rightleftharpoons \mathrm{G2\_c} \tag{43}$$

Reactants

Table 44: Properties of each reactant.

Id	Name	SBO
pS2_c	pSmad2_c	
pG_c	pGFP-Smad2_c	

Product

Table 45: Properties of each product.

Id	Name	SBO
G2_c	pGFP-Smad2/pSmad2_c	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{20} = \mathrm{vol}\,(\mathrm{cytosol}) \cdot (\mathrm{kon} \cdot [\mathrm{pS2\_c}] \cdot [\mathrm{pG\_c}] - \mathrm{koff} \cdot [\mathrm{G2\_c}]) \tag{44}$$

7.21 Reaction reaction_21

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

Name Reaction 4D Formation G2_N

Reaction equation

$$\mathrm{pS2\_n} + \mathrm{pG\_n} \rightleftharpoons \mathrm{G2\_n} \tag{45}$$

Reactants

Table 46: Properties of each reactant.

Id	Name	SBO
pS2_n	pSmad2_n	
pG_n	pGFP-Smad2_n	

Product

Table 47: Properties of each product.

Id	Name	SBO
G2_n	pGFP-Smad2/pSmad2_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{21} = \mathrm{vol}(\mathrm{nucleus}) \cdot (\mathrm{kon} \cdot [\mathrm{pS2\_n}] \cdot [\mathrm{pG\_n}] - \mathrm{koff} \cdot [\mathrm{G2\_n}]) \tag{46}$$

7.22 Reaction reaction_22

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

Name Reaction 3C Formation G4_C

Reaction equation

$$\mathrm{pG\_c} + \mathrm{S4\_c} \rightleftharpoons \mathrm{G4\_c} \tag{47}$$

Reactants

Table 48: Properties of each reactant.

Id	Name	SBO
pG_c	pGFP-Smad2_c	
S4_c	Smad4_c	

Product

Table 49: Properties of each product.

Id	Name	SBO
G4_c	pGFP-Smad2/Smad4_c	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{22} = \mathrm{vol}(\mathrm{cytosol}) \cdot (\mathrm{kon} \cdot [\mathrm{pG\_c}] \cdot [\mathrm{S4\_c}] - \mathrm{koff} \cdot [\mathrm{G4\_c}]) \tag{48}$$

7.23 Reaction reaction_23

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

Name Reaction 3D Formation G4_N

Reaction equation

$$\mathrm{pG\_n} + \mathrm{S4\_n} \rightleftharpoons \mathrm{G4\_n} \tag{49}$$

Reactants

Table 50: Properties of each reactant.

Id	Name	SBO
pG_n	pGFP-Smad2_n	
S4_n	Smad4_n	

Product

Table 51: Properties of each product.

Id	Name	SBO
G4_n	pGFP-Smad2/Smad4_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{23} = \mathrm{vol}\,(\mathrm{nucleus}) \cdot (\mathrm{kon} \cdot [\mathrm{pG\_n}] \cdot [\mathrm{S4\_n}] - \mathrm{koff} \cdot [\mathrm{G4\_n}]) \tag{50}$$

7.24 Reaction reaction_24

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

Name Reaction 9C Import GG

Reaction equation

$$\mathrm{GG\_c} \longrightarrow \mathrm{GG\_n} \tag{51}$$

Reactant

Table 52: Properties of each reactant.

Id	Name	SBO
GG_c	pGFP-Smad2/pGFP-Smad2_c	

Product

Table 53: Properties of each product.

Id	Name	SBO
GG_n	pGFP-Smad2/pGFP_Smad2_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{24} = \mathrm{kin\_CIF} \cdot [\mathrm{GG\_c}] \tag{52}$$

7.25 Reaction reaction_25

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

Name Reaction 9B Import G2

Reaction equation

$$\mathrm{G2\_c} \longrightarrow \mathrm{G2\_n} \tag{53}$$

Reactant

Table 54: Properties of each reactant.

Id	Name	SBO
G2_c	pGFP-Smad2/pSmad2_c	

Product

Table 55: Properties of each product.

Id	Name	SBO
G2_n	pGFP-Smad2/pSmad2_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{25} = \mathrm{kin\_CIF} \cdot [\mathrm{G2\_c}] \tag{54}$$

7.26 Reaction `reaction_26`

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

Name Reaction 8B Import G4

Reaction equation

$$\mathrm{G4\_c} \longrightarrow \mathrm{G4\_n} \tag{55}$$

Reactant

Table 56: Properties of each reactant.

Id	Name	SBO
`G4_c`	pGFP-Smad2/Smad4_c	

Product

Table 57: Properties of each product.

Id	Name	SBO
`G4_n`	pGFP-Smad2/Smad4_n	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{nmol}$

$$v_{26} = \mathrm{kin\_CIF} \cdot [\mathrm{G4\_c}] \tag{56}$$

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.

8.1 Species PPase

Name PPase

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

This species takes part in four reactions (as a reactant in reaction_11, reaction_15 and as a product in reaction_11, reaction_15), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{PPase} = 0 \tag{57}$$

8.2 Species S2_n

Name Smad2_n

Initial concentration $28.514773357617\ \mathrm{nmol} \cdot \mathrm{l}^{-1}$

This species takes part in two reactions (as a product in reaction_2, reaction_11).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S2\_n} = v_2 + v_{11} \tag{58}$$

8.3 Species pS2_n

Name pSmad2_n

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

This species takes part in five reactions (as a reactant in reaction_6, reaction_10, reaction_11, reaction_21 and as a product in reaction_3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pS2\_n} = v_3 - v_6 - 2v_{10} - v_{11} - v_{21} \tag{59}$$

8.4 Species G_n

Name GFP-Smad2_n

Initial concentration $28.514773357617\ \mathrm{nmol} \cdot \mathrm{l}^{-1}$

This species takes part in two reactions (as a product in reaction_15, reaction_16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G\_n} = v_{15} + v_{16} \tag{60}$$

8.5 Species pG_n

Name pGFP-Smad2_n

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

This species takes part in five reactions (as a reactant in reaction_15, reaction_19, reaction_21, reaction_23 and as a product in reaction_17).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pG\_n} = v_{17} - v_{15} - 2v_{19} - v_{21} - v_{23} \tag{61}$$

8.6 Species S22_n

Name pSmad2/pSmad2_n

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

This species takes part in two reactions (as a product in reaction_8, reaction_10).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S22\_n} = v_8 + v_{10} \tag{62}$$

8.7 Species S24_n

Name pSmad2/Smad4_n

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

This species takes part in two reactions (as a product in reaction_6, reaction_7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S24\_n} = v_6 + v_7 \tag{63}$$

8.8 Species S4_n

Name Smad4_n

Initial concentration $50.78093897\ \mathrm{nmol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in reaction_6, reaction_23 and as a product in reaction_1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S4\_n} = v_1 - v_6 - v_{23} \tag{64}$$

8.9 Species G2_n

Name pGFP-Smad2/pSmad2_n

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

This species takes part in two reactions (as a product in reaction_21, reaction_25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G2\_n} = v_{21} + v_{25} \tag{65}$$

8.10 Species G4_n

Name pGFP-Smad2/Smad4_n

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

This species takes part in two reactions (as a product in reaction_23, reaction_26).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G4\_n} = v_{23} + v_{26} \tag{66}$$

8.11 Species GG_n

Name pGFP-Smad2/pGFP_Smad2_n

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

This species takes part in two reactions (as a product in reaction_19, reaction_24).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GG\_n} = v_{19} + v_{24} \tag{67}$$

8.12 Species S22_c

Name pSmad2/pSmad2_c

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

This species takes part in two reactions (as a reactant in reaction_8 and as a product in reaction_9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S22\_c} = v_{9} - v_{8} \tag{68}$$

8.13 Species S24_c

Name pSmad2/Smad4_c

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S24\_c} = v_5 - v_7 \tag{69}$$

8.14 Species S4_c

Name Smad4_c

Initial concentration $50.78103407\ \mathrm{nmol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in reaction_1, reaction_5, reaction_22).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S4\_c} = -v_1 - v_5 - v_{22} \tag{70}$$

8.15 Species S2_c

Name Smad2_c

Initial concentration $60.5899176013587\ \mathrm{nmol}\cdot\mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in reaction_2, reaction_4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S2\_c} = -v_2 - v_4 \tag{71}$$

8.16 Species pS2_c

Name pSmad2_c

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

This species takes part in five reactions (as a reactant in reaction_3, reaction_5, reaction_9, reaction_20 and as a product in reaction_4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pS2\_c} = v_4 - v_3 - v_5 - 2v_9 - v_{20} \tag{72}$$

8.17 Species G_c

Name GFP-Smad2_c

Initial concentration 60.5899176013587 nmol · l^{-1}

This species takes part in two reactions (as a reactant in reaction_14, reaction_16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G\_c} = -v_{14} - v_{16} \tag{73}$$

8.18 Species pG_c

Name pGFP-Smad2_c

Initial concentration 0 nmol · l^{-1}

This species takes part in five reactions (as a reactant in reaction_17, reaction_18, reaction_20, reaction_22 and as a product in reaction_14).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pG\_c} = v_{14} - v_{17} - 2v_{18} - v_{20} - v_{22} \tag{74}$$

8.19 Species G2_c

Name pGFP-Smad2/pSmad2_c

Initial concentration 0 nmol · l^{-1}

This species takes part in two reactions (as a reactant in reaction_25 and as a product in reaction_20).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G2\_c} = v_{20} - v_{25} \tag{75}$$

8.20 Species G4_c

Name pGFP-Smad2/Smad4_c

Initial concentration 0 nmol · l^{-1}

This species takes part in two reactions (as a reactant in reaction_26 and as a product in reaction_22).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G4\_c} = v_{22} - v_{26} \tag{76}$$

8.21 Species GG_c

Name pGFP-Smad2/pGFP-Smad2_c

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

This species takes part in two reactions (as a reactant in reaction_24 and as a product in reaction_18).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GG\_c} = v_{18} - v_{24} \tag{77}$$

8.22 Species TGFb_c

Name TGFb_c

Initial concentration $0.0659999824780232\ \mathrm{nmol}\cdot\mathrm{l}^{-1}$

This species takes part in one reaction (as a reactant in reaction_12), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{TGFb\_c} = 0 \tag{78}$$

8.23 Species R_act

Name R_act

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

This species takes part in six reactions (as a reactant in reaction_4, reaction_13, reaction_14 and as a product in reaction_4, reaction_12, reaction_14).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{R\_act} = v_4 + v_{12} + v_{14} - v_4 - v_{13} - v_{14} \tag{79}$$

8.24 Species R

Name R

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

This species takes part in one reaction (as a reactant in reaction_12).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{R} = -v_{12} \tag{80}$$

8.25 Species R_inact

Name R_inact

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

This species takes part in one reaction (as a product in reaction_13).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{R\_inact} = v_{13} \tag{81}$$

8.26 Species SB

Name SB-431542

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

Involved in rule SB

This species takes part in one reaction (as a reactant in reaction_13). Not this but one rule determines the species' quantity because this species is on the boundary of the reaction system.

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