

## SBML Model Report

# Model name: “Venkatraman2012 - Interplay between PLS and TSP1 in TGF-1 activation”



May 6, 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 Chelliah<sup>1</sup> and Huipeng Li<sup>2</sup> at March 26<sup>th</sup> 2013 at 1:34 p. m. and last time modified at April seventh 2014 at 2:42 a. 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	1
species types	0	species	13
events	0	constraints	0
reactions	32	function definitions	1
global parameters	23	unit definitions	1
rules	0	initial assignments	0

## Model Notes

Venkatraman2012 - Interplay between PLS and TSP1 in TGF-1 activation

The interplay between PLS (Plasmin) and TSP1 (Thrombospondin-1) in TGF-1 (Transforming growth factor-1) is shown using mathematical modelling and in vitro experimentents.

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This model is described in the article: [Plasmin triggers a switch-like decrease in thrombospondin-dependent activation of TGF-1](#). Venkatraman L, Chia SM, Narmada BC, White JK, Bhowmick SS, Forbes Dewey C Jr, So PT, Tucker-Kellogg L, Yu H. *Biophys J*. 2012 Sep 5;103(5):1060-8.

Abstract:

Transforming growth factor-1 (TGF-1) is a potent regulator of extracellular matrix production, wound healing, differentiation, and immune response, and is implicated in the progression of fibrotic diseases and cancer. Extracellular activation of TGF-1 from its latent form provides spatiotemporal control over TGF-1 signaling, but the current understanding of TGF-1 activation does not emphasize cross talk between activators. Plasmin (PLS) and thrombospondin-1 (TSP1) have been studied individually as activators of TGF-1, and in this work we used a systems-level approach with mathematical modeling and in vitro experiments to study the interplay between PLS and TSP1 in TGF-1 activation. Simulations and steady-state analysis predicted a switch-like bistable transition between two levels of active TGF-1, with an inverse correlation between PLS and TSP1. In particular, the model predicted that increasing PLS breaks a TSP1-TGF-1 positive feedback loop and causes an unexpected net decrease in TGF-1 activation. To test these predictions in vitro, we treated rat hepatocytes and hepatic stellate cells with PLS, which caused proteolytic cleavage of TSP1 and decreased activation of TGF-1. The TGF-1 activation levels showed a cooperative dose response, and a test of hysteresis in the cocultured cells validated that TGF-1 activation is bistable. We conclude that switch-like behavior arises from natural competition between two distinct modes of TGF-1 activation: a TSP1-mediated mode of high activation and a PLS-mediated mode of low activation. This switch suggests an explanation for the unexpected effects of the plasminogen activation system on TGF-1 in fibrotic diseases in vivo, as well as novel prognostic and therapeutic approaches for diseases with TGF- dysregulation.

This model is hosted on [BioModels Database](#) and identified by: [MODEL1303130000](#).

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## 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**  $\mu\text{mol}$

### 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<sup>2</sup>

### 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 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
compartment_1	compartment	0000290	3	1	litre	<input checked="" type="checkbox"/>	

### 3.1 Compartment compartment\_1

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

**Name** compartment

**SBO:0000290** physical compartment

## 4 Species

This model contains 13 species. Section 8 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
species_1	PLG	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_2	PLS	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_3	scUPA	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_4	tcUPA	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_5	LTGFb1	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_6	TGFb1	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_7	TSP1	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_8	PAI1	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_9	TSP1:PLS	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_10	A2M	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_11	A2M:PLS	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_12	PAI1:tcUPA	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$
species_13	PAI1:scUPA	compartment_1	$\mu\text{mol} \cdot \text{l}^{-1}$	$\square$	$\square$

## 5 Parameters

This model contains 23 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
parameter_1	keff1		0.035		✓
parameter_2	keff2		0.350		✓
parameter_3	keff3		1.400		✓
parameter_4	k1		0.035		✓
parameter_5	k2		24.500		✓
parameter_6	kothers		0.005		✓
parameter_7	kp1		0.350		✓
parameter_8	kp2		1.050		✓
parameter_9	k3		17.500		✓
parameter_10	k_3		0.025		✓
parameter_11	k4		0.350		✓
parameter_12	k5		24.500		✓
parameter_13	k_5		0.011		✓
parameter_14	k6		0.035		✓
parameter_15	k_6		0.004		✓
parameter_16	k7		0.070		✓
parameter_17	k_7		0.004		✓
parameter_18	k8		24.500		✓
parameter_19	k9		0.210		✓
parameter_20	u_edeg		0.053		✓
parameter_21	u_pdeg		0.018		✓
parameter_22	alpha1		0.004		✓
parameter_23	alpha2		0.035		✓

## 6 Function definition

This is an overview of one function definition.

### 6.1 Function definition `function_1`

**Name** Constant flux (irreversible)

**Argument** `v`

**Mathematical Expression**

$$v \quad (1)$$

## 7 Reactions

This model contains 32 reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

Nº	Id	Name	Reaction Equation	SBO
1	reaction_1	reaction_1	$\text{species\_3} + \text{species\_1} \xrightarrow{\text{species\_3, species\_1}} \text{species\_2} + \text{species\_3}$	
2	reaction_2	reaction_2	$\text{species\_2} + \text{species\_3} \xrightarrow{\text{species\_2, species\_3}} \text{species\_4} + \text{species\_2}$	
3	reaction_3	reaction_3	$\text{species\_4} + \text{species\_1} \xrightarrow{\text{species\_4, species\_1}} \text{species\_2} + \text{species\_4}$	
4	reaction_4	reaction_4	$\text{species\_2} + \text{species\_5} \xrightarrow{\text{species\_2, species\_5}} \text{species\_6} + \text{species\_2}$	
5	reaction_5	reaction_5	$\text{species\_7} + \text{species\_5} \xrightarrow{\text{species\_7, species\_5}} \text{species\_6}$	
6	reaction_6	reaction_6	$\text{species\_5} \xrightarrow{\text{species\_5}} \text{species\_6}$	
7	reaction_7	reaction_7	$\text{species\_6} \xrightarrow{\text{species\_6}} \text{species\_6} + \text{species\_7}$	
8	reaction_8	reaction_8	$\text{species\_6} \xrightarrow{\text{species\_6}} \text{species\_6} + \text{species\_8}$	
9	reaction_9	reaction_9	$\text{species\_7} + \text{species\_2} \xrightleftharpoons{\text{species\_7, species\_2, species\_9}} \text{species\_9}$	
10	reaction_10	reaction_10	$\text{species\_9} \xrightarrow{\text{species\_9}} \text{species\_2}$	
11	reaction_11	reaction_11	$\text{species\_10} + \text{species\_2} \xrightleftharpoons{\text{species\_10, species\_2, species\_11}} \text{species\_11}$	
12	reaction_12	reaction_12	$\text{species\_8} + \text{species\_4} \xrightleftharpoons{\text{species\_8, species\_4, species\_12}} \text{species\_12}$	

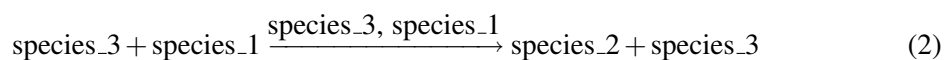
Nº	Id	Name	Reaction Equation	SBO
13	reaction_13	reaction_13	$\text{species\_8} + \text{species\_3} \xrightarrow{\text{species\_8, species\_3, species\_13}} \text{species\_13}$	
14	reaction_14	reaction_14	$\emptyset \longrightarrow \text{species\_3}$	
15	reaction_15	reaction_15	$\emptyset \longrightarrow \text{species\_5}$	
16	reaction_16	reaction_16	$\emptyset \longrightarrow \text{species\_10}$	
17	reaction_17	reaction_17	$\emptyset \longrightarrow \text{species\_1}$	
18	reaction_18	reaction_18	$\text{species\_3} \xrightarrow{\text{species\_3}} \emptyset$	
19	reaction_19	reaction_19	$\text{species\_4} \xrightarrow{\text{species\_4}} \emptyset$	
20	reaction_20	reaction_20	$\text{species\_2} \xrightarrow{\text{species\_2}} \emptyset$	
21	reaction_21	reaction_21	$\text{species\_7} \xrightarrow{\text{species\_7}} \emptyset$	
22	reaction_22	reaction_22	$\text{species\_8} \xrightarrow{\text{species\_8}} \emptyset$	
23	reaction_23	reaction_23	$\text{species\_5} \xrightarrow{\text{species\_5}} \emptyset$	
24	reaction_24	reaction_24	$\text{species\_6} \xrightarrow{\text{species\_6}} \emptyset$	
25	reaction_25	reaction_25	$\text{species\_1} \xrightarrow{\text{species\_1}} \emptyset$	
26	reaction_26	reaction_26	$\text{species\_10} \xrightarrow{\text{species\_10}} \emptyset$	
27	reaction_27	reaction_28	$\text{species\_11} \xrightarrow{\text{species\_11}} \emptyset$	
28	reaction_28	reaction_29	$\text{species\_12} \xrightarrow{\text{species\_12}} \emptyset$	
29	reaction_29	reaction_30	$\text{species\_13} \xrightarrow{\text{species\_13}} \emptyset$	
30	reaction_30	reaction_27	$\text{species\_9} \xrightarrow{\text{species\_9}} \emptyset$	
31	reaction_31	reaction_31	$\text{species\_9} \xrightarrow{\text{species\_9}} \emptyset$	
32	reaction_32	reaction_32	$\text{species\_6} \xrightarrow{\text{species\_6}} \emptyset$	

## 7.1 Reaction `reaction_1`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

**Name** `reaction_1`

### Reaction equation



### Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
<code>species_3</code>	scUPA	
<code>species_1</code>	PLG	

### Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
<code>species_3</code>	scUPA	
<code>species_1</code>	PLG	

### Products

Table 8: Properties of each product.

Id	Name	SBO
<code>species_2</code>	PLS	
<code>species_3</code>	scUPA	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_1 = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_1} \cdot [\text{species\_3}] \cdot [\text{species\_1}] \quad (3)$$

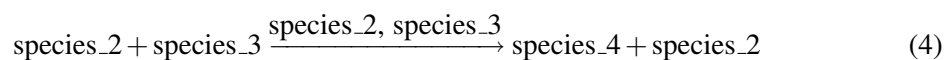


## 7.2 Reaction `reaction_2`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

**Name** `reaction_2`

### Reaction equation



### Reactants

Table 9: Properties of each reactant.

Id	Name	SBO
<code>species_2</code>	PLS	
<code>species_3</code>	scUPA	

### Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
<code>species_2</code>	PLS	
<code>species_3</code>	scUPA	

### Products

Table 11: Properties of each product.

Id	Name	SBO
<code>species_4</code>	tcUPA	
<code>species_2</code>	PLS	

### Kinetic Law

**Derived unit** contains undeclared units

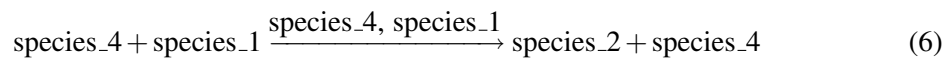
$$v_2 = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_2} \cdot [\text{species\_2}] \cdot [\text{species\_3}] \quad (5)$$

### 7.3 Reaction `reaction_3`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

**Name** `reaction_3`

#### Reaction equation



#### Reactants

Table 12: Properties of each reactant.

Id	Name	SBO
<code>species_4</code>	tcUPA	
<code>species_1</code>	PLG	

#### Modifiers

Table 13: Properties of each modifier.

Id	Name	SBO
<code>species_4</code>	tcUPA	
<code>species_1</code>	PLG	

#### Products

Table 14: Properties of each product.

Id	Name	SBO
<code>species_2</code>	PLS	
<code>species_4</code>	tcUPA	

#### Kinetic Law

**Derived unit** contains undeclared units

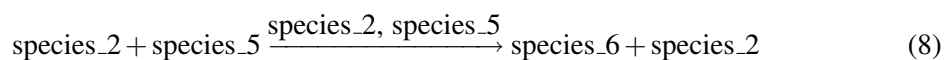
$$v_3 = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_3} \cdot [\text{species\_4}] \cdot [\text{species\_1}] \quad (7)$$

## 7.4 Reaction `reaction_4`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

**Name** `reaction_4`

### Reaction equation



### Reactants

Table 15: Properties of each reactant.

Id	Name	SBO
<code>species_2</code>	PLS	
<code>species_5</code>	LTGFb1	

### Modifiers

Table 16: Properties of each modifier.

Id	Name	SBO
<code>species_2</code>	PLS	
<code>species_5</code>	LTGFb1	

### Products

Table 17: Properties of each product.

Id	Name	SBO
<code>species_6</code>	TGFb1	
<code>species_2</code>	PLS	

### Kinetic Law

**Derived unit** contains undeclared units

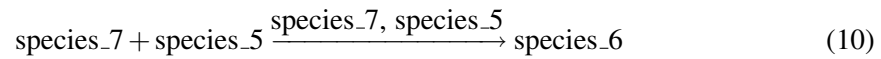
$$v_4 = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_4} \cdot [\text{species\_2}] \cdot [\text{species\_5}] \quad (9)$$

## 7.5 Reaction `reaction_5`

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

**Name** `reaction_5`

### Reaction equation



### Reactants

Table 18: Properties of each reactant.

Id	Name	SBO
<code>species_7</code>	TSP1	
<code>species_5</code>	LTGFb1	

### Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
<code>species_7</code>	TSP1	
<code>species_5</code>	LTGFb1	

### Product

Table 20: Properties of each product.

Id	Name	SBO
<code>species_6</code>	TGFb1	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_5 = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_5} \cdot [\text{species\_7}] \cdot [\text{species\_5}] \quad (11)$$

## 7.6 Reaction `reaction_6`

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

**Name** reaction\_6

### Reaction equation



### Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
species_5	LTGFb1	

### Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
species_5	LTGFb1	

### Product

Table 23: Properties of each product.

Id	Name	SBO
species_6	TGFb1	

### Kinetic Law

**Derived unit** contains undeclared units

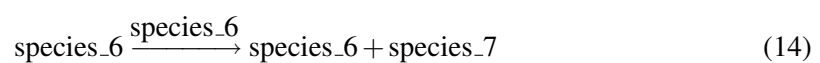
$$v_6 = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_6} \cdot [\text{species\_5}] \quad (13)$$

## 7.7 Reaction reaction\_7

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

**Name** reaction\_7

### Reaction equation



## Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
species_6	TGFb1	

## Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
species_6	TGFb1	

## Products

Table 26: Properties of each product.

Id	Name	SBO
species_6	TGFb1	
species_7	TSP1	

## Kinetic Law

**Derived unit** contains undeclared units

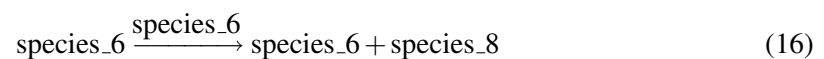
$$v_7 = \text{vol}(\text{compartment}_1) \cdot \text{parameter}_7 \cdot [\text{species}_6] \quad (15)$$

### 7.8 Reaction `reaction_8`

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

**Name** `reaction_8`

#### Reaction equation



## Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
species_6	TGFb1	

## Modifier

Table 28: Properties of each modifier.

Id	Name	SBO
species_6	TGFb1	

## Products

Table 29: Properties of each product.

Id	Name	SBO
species_6	TGFb1	
species_8	PAI1	

## Kinetic Law

**Derived unit** contains undeclared units

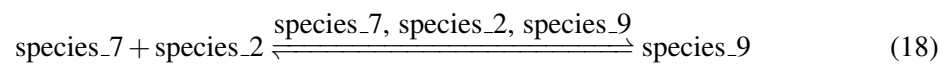
$$v_8 = \text{vol}(\text{compartment}_1) \cdot \text{parameter}_8 \cdot [\text{species}_6] \quad (17)$$

## 7.9 Reaction `reaction_9`

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** `reaction_9`

### Reaction equation



## Reactants

Table 30: Properties of each reactant.

Id	Name	SBO
species_7	TSP1	
species_2	PLS	

## Modifiers

Table 31: Properties of each modifier.

Id	Name	SBO
species_7	TSP1	
species_2	PLS	
species_9	TSP1:PLS	

## Product

Table 32: Properties of each product.

Id	Name	SBO
species_9	TSP1:PLS	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_9 = \text{vol}(\text{compartment}_1) \cdot (\text{parameter}_9 \cdot [\text{species}_7] \cdot [\text{species}_2] - \text{parameter}_{10} \cdot [\text{species}_9]) \quad (19)$$

### 7.10 Reaction `reaction_10`

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

**Name** `reaction_10`

#### Reaction equation



## Reactant



Table 33: Properties of each reactant.

Id	Name	SBO
species_9	TSP1:PLS	

## Modifier

Table 34: Properties of each modifier.

Id	Name	SBO
species_9	TSP1:PLS	

## Product

Table 35: Properties of each product.

Id	Name	SBO
species_2	PLS	

## Kinetic Law

**Derived unit** contains undeclared units

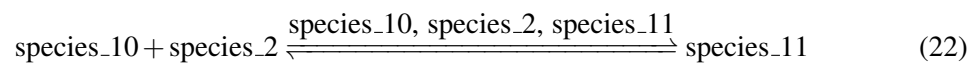
$$v_{10} = \text{vol}(\text{compartment}_1) \cdot \text{parameter}_{11} \cdot [\text{species}_9] \quad (21)$$

### 7.11 Reaction `reaction_11`

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** `reaction_11`

### Reaction equation



## Reactants

Table 36: Properties of each reactant.

Id	Name	SBO
species_10	A2M	
species_2	PLS	

## Modifiers

Table 37: Properties of each modifier.

Id	Name	SBO
species_10	A2M	
species_2	PLS	
species_11	A2M:PLS	

## Product

Table 38: Properties of each product.

Id	Name	SBO
species_11	A2M:PLS	

## Kinetic Law

**Derived unit** contains undeclared units

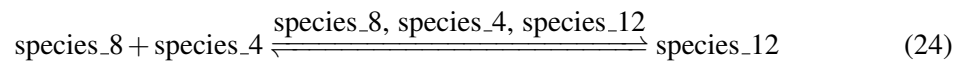
$$v_{11} = \text{vol}(\text{compartment}_1) \cdot (\text{parameter}_{12} \cdot [\text{species}_{10}] \cdot [\text{species}_2] - \text{parameter}_{13} \cdot [\text{species}_{11}]) \quad (23)$$

### 7.12 Reaction `reaction_12`

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** `reaction_12`

#### Reaction equation



## Reactants

Table 39: Properties of each reactant.

Id	Name	SBO
species_8	PAI1	
species_4	tcUPA	

## Modifiers

Table 40: Properties of each modifier.

Id	Name	SBO
species_8	PAI1	
species_4	tcUPA	
species_12	PAI1:tcUPA	

## Product

Table 41: Properties of each product.

Id	Name	SBO
species_12	PAI1:tcUPA	

## Kinetic Law

**Derived unit** contains undeclared units

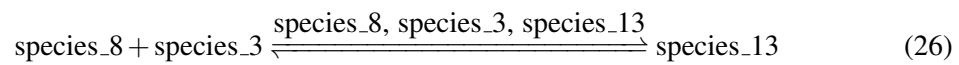
$$v_{12} = \text{vol}(\text{compartment}_1) \cdot (\text{parameter}_{14} \cdot [\text{species}_8] \cdot [\text{species}_4] - \text{parameter}_{15} \cdot [\text{species}_{12}]) \quad (25)$$

### 7.13 Reaction `reaction_13`

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** `reaction_13`

#### Reaction equation



## Reactants

Table 42: Properties of each reactant.

Id	Name	SBO
species_8	PAI1	
species_3	scUPA	

## Modifiers

Table 43: Properties of each modifier.

Id	Name	SBO
species_8	PAI1	
species_3	scUPA	
species_13	PAI1:scUPA	

## Product

Table 44: Properties of each product.

Id	Name	SBO
species_13	PAI1:scUPA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{13} = \text{vol}(\text{compartment\_1}) \cdot (\text{parameter\_16} \cdot [\text{species\_8}] \cdot [\text{species\_3}] - \text{parameter\_17} \cdot [\text{species\_13}]) \quad (27)$$

### 7.14 Reaction `reaction_14`

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

**Name** `reaction_14`

#### Reaction equation



## Product

Table 45: Properties of each product.

Id	Name	SBO
species_3	scUPA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{14} = \text{vol}(\text{compartment\_1}) \cdot \text{function\_1}(\text{parameter\_22}) \quad (29)$$

$$\text{function\_1}(v) = v \quad (30)$$

$$\text{function\_1}(v) = v \quad (31)$$

### 7.15 Reaction `reaction_15`

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

**Name** `reaction_15`

#### Reaction equation



#### Product

Table 46: Properties of each product.

Id	Name	SBO
<code>species_5</code>	LTGFb1	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{15} = \text{vol}(\text{compartment\_1}) \cdot \text{function\_1}(\text{parameter\_22}) \quad (33)$$

$$\text{function\_1}(v) = v \quad (34)$$

$$\text{function\_1}(v) = v \quad (35)$$

### 7.16 Reaction `reaction_16`

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

**Name** `reaction_16`

### Reaction equation



### Product

Table 47: Properties of each product.

Id	Name	SBO
species_10	A2M	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{16} = \text{vol}(\text{compartment\_1}) \cdot \text{function\_1}(\text{parameter\_22}) \quad (37)$$

$$\text{function\_1}(v) = v \quad (38)$$

$$\text{function\_1}(v) = v \quad (39)$$

## 7.17 Reaction `reaction_17`

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

**Name** `reaction_17`

### Reaction equation



### Product

Table 48: Properties of each product.

Id	Name	SBO
species_1	PLG	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{17} = \text{vol}(\text{compartment\_1}) \cdot \text{function\_1}(\text{parameter\_23}) \quad (41)$$

$$\text{function\_1}(v) = v \quad (42)$$

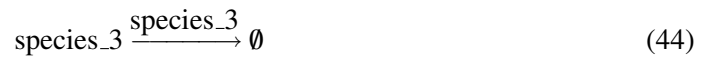
$$\text{function\_1}(v) = v \quad (43)$$

### 7.18 Reaction `reaction_18`

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

**Name** `reaction_18`

#### Reaction equation



#### Reactant

Table 49: Properties of each reactant.

Id	Name	SBO
<code>species_3</code>	<code>scUPA</code>	

#### Modifier

Table 50: Properties of each modifier.

Id	Name	SBO
<code>species_3</code>	<code>scUPA</code>	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{18} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_20} \cdot [\text{species\_3}] \quad (45)$$

### 7.19 Reaction `reaction_19`

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

**Name** `reaction_19`

#### Reaction equation



## Reactant

Table 51: Properties of each reactant.

Id	Name	SBO
species_4	tcUPA	

## Modifier

Table 52: Properties of each modifier.

Id	Name	SBO
species_4	tcUPA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{19} = \text{vol}(\text{compartment}_1) \cdot \text{parameter}_{20} \cdot [\text{species}_4] \quad (47)$$

## 7.20 Reaction `reaction_20`

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

**Name** `reaction_20`

## Reaction equation



## Reactant

Table 53: Properties of each reactant.

Id	Name	SBO
species_2	PLS	

## Modifier



Table 54: Properties of each modifier.

Id	Name	SBO
species_2	PLS	

**Kinetic Law****Derived unit** contains undeclared units

$$v_{20} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_20} \cdot [\text{species\_2}] \quad (49)$$

**7.21 Reaction** reaction\_21

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

**Name** reaction\_21**Reaction equation****Reactant**

Table 55: Properties of each reactant.

Id	Name	SBO
species_7	TSP1	

**Modifier**

Table 56: Properties of each modifier.

Id	Name	SBO
species_7	TSP1	

**Kinetic Law****Derived unit** contains undeclared units

$$v_{21} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_21} \cdot [\text{species\_7}] \quad (51)$$

## 7.22 Reaction `reaction_22`

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

**Name** `reaction_22`

### Reaction equation



### Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
<code>species_8</code>	PAI1	

### Modifier

Table 58: Properties of each modifier.

Id	Name	SBO
<code>species_8</code>	PAI1	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{22} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_21} \cdot [\text{species\_8}] \quad (53)$$

## 7.23 Reaction `reaction_23`

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

**Name** `reaction_23`

### Reaction equation



### Reactant

Table 59: Properties of each reactant.

Id	Name	SBO
species_5	LTGFb1	

### Modifier

Table 60: Properties of each modifier.

Id	Name	SBO
species_5	LTGFb1	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{23} = \text{vol}(\text{compartment}_1) \cdot \text{parameter}_{21} \cdot [\text{species}_5] \quad (55)$$

## 7.24 Reaction [reaction\\_24](#)

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

**Name** [reaction\\_24](#)

### Reaction equation



### Reactant

Table 61: Properties of each reactant.

Id	Name	SBO
species_6	TGFb1	

### Modifier

Table 62: Properties of each modifier.

Id	Name	SBO
species_6	TGFb1	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{24} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_21} \cdot [\text{species\_6}] \quad (57)$$

## 7.25 Reaction `reaction_25`

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

**Name** `reaction_25`

### Reaction equation



### Reactant

Table 63: Properties of each reactant.

Id	Name	SBO
<code>species_1</code>	PLG	

### Modifier

Table 64: Properties of each modifier.

Id	Name	SBO
<code>species_1</code>	PLG	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{25} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_21} \cdot [\text{species\_1}] \quad (59)$$

## 7.26 Reaction `reaction_26`

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

**Name** `reaction_26`

### Reaction equation



### Reactant

Table 65: Properties of each reactant.

Id	Name	SBO
species_10	A2M	

### Modifier

Table 66: Properties of each modifier.

Id	Name	SBO
species_10	A2M	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{26} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_21} \cdot [\text{species\_10}] \quad (61)$$

## 7.27 Reaction `reaction_27`

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

**Name** `reaction_28`

### Reaction equation



### Reactant

Table 67: Properties of each reactant.

Id	Name	SBO
species_11	A2M:PLS	

## Modifier

Table 68: Properties of each modifier.

Id	Name	SBO
species_11	A2M:PLS	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{27} = \text{vol}(\text{compartment}_1) \cdot \text{parameter}_{21} \cdot [\text{species}_{11}] \quad (63)$$

## 7.28 Reaction [reaction\\_28](#)

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

**Name** [reaction\\_29](#)

## Reaction equation



## Reactant

Table 69: Properties of each reactant.

Id	Name	SBO
species_12	PAI1:tcUPA	

## Modifier

Table 70: Properties of each modifier.

Id	Name	SBO
species_12	PAI1:tcUPA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{28} = \text{vol}(\text{compartment}_1) \cdot \text{parameter}_{21} \cdot [\text{species}_{12}] \quad (65)$$

### 7.29 Reaction `reaction_29`

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

**Name** `reaction_30`

#### Reaction equation



#### Reactant

Table 71: Properties of each reactant.

Id	Name	SBO
<code>species_13</code>	PAI1:scUPA	

#### Modifier

Table 72: Properties of each modifier.

Id	Name	SBO
<code>species_13</code>	PAI1:scUPA	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{29} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_21} \cdot [\text{species\_13}] \quad (67)$$

### 7.30 Reaction `reaction_30`

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

**Name** `reaction_27`

#### Reaction equation



#### Reactant

Table 73: Properties of each reactant.

Id	Name	SBO
species_9	TSP1:PLS	

### Modifier

Table 74: Properties of each modifier.

Id	Name	SBO
species_9	TSP1:PLS	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{30} = \text{vol}(\text{compartment}_1) \cdot \text{parameter}_{21} \cdot [\text{species}_9] \quad (69)$$

### 7.31 Reaction `reaction_31`

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

**Name** `reaction_31`

### Reaction equation



### Reactant

Table 75: Properties of each reactant.

Id	Name	SBO
species_9	TSP1:PLS	

### Modifier

Table 76: Properties of each modifier.

Id	Name	SBO
species_9	TSP1:PLS	



### Kinetic Law

**Derived unit** contains undeclared units

$$v_{31} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_18} \cdot [\text{species\_9}] \quad (71)$$

### 7.32 Reaction `reaction_32`

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

**Name** `reaction_32`

### Reaction equation



### Reactant

Table 77: Properties of each reactant.

Id	Name	SBO
<code>species_6</code>	TGFb1	

### Modifier

Table 78: Properties of each modifier.

Id	Name	SBO
<code>species_6</code>	TGFb1	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{32} = \text{vol}(\text{compartment\_1}) \cdot \text{parameter\_19} \cdot [\text{species\_6}] \quad (73)$$

## 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 `species_1`

**Name** PLG

**Initial concentration**  $0.0030 \mu\text{mol} \cdot \text{l}^{-1}$

This species takes part in seven reactions (as a reactant in [reaction\\_1](#), [reaction\\_3](#), [reaction\\_25](#) and as a product in [reaction\\_17](#) and as a modifier in [reaction\\_1](#), [reaction\\_3](#), [reaction\\_25](#)).

$$\frac{d}{dt}\text{species}_1 = v_{17} - v_1 - v_3 - v_{25} \quad (74)$$

### 8.2 Species `species_2`

**Name** PLS

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

This species takes part in 15 reactions (as a reactant in [reaction\\_2](#), [reaction\\_4](#), [reaction\\_9](#), [reaction\\_11](#), [reaction\\_20](#) and as a product in [reaction\\_1](#), [reaction\\_2](#), [reaction\\_3](#), [reaction\\_4](#), [reaction\\_10](#) and as a modifier in [reaction\\_2](#), [reaction\\_4](#), [reaction\\_9](#), [reaction\\_11](#), [reaction\\_20](#)).

$$\frac{d}{dt}\text{species}_2 = v_1 + v_2 + v_3 + v_4 + v_{10} - v_2 - v_4 - v_9 - v_{11} - v_{20} \quad (75)$$

### 8.3 Species `species_3`

**Name** scUPA

**Initial concentration**  $0.0010 \mu\text{mol} \cdot \text{l}^{-1}$

This species takes part in ten reactions (as a reactant in [reaction\\_1](#), [reaction\\_2](#), [reaction\\_13](#), [reaction\\_18](#) and as a product in [reaction\\_1](#), [reaction\\_14](#) and as a modifier in [reaction\\_1](#), [reaction\\_2](#), [reaction\\_13](#), [reaction\\_18](#)).

$$\frac{d}{dt}\text{species}_3 = v_1 + v_{14} - v_1 - v_2 - v_{13} - v_{18} \quad (76)$$

#### 8.4 Species `species_4`

**Name** tcUPA

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

This species takes part in eight reactions (as a reactant in [reaction\\_3](#), [reaction\\_12](#), [reaction\\_19](#) and as a product in [reaction\\_2](#), [reaction\\_3](#) and as a modifier in [reaction\\_3](#), [reaction\\_12](#), [reaction\\_19](#)).

$$\frac{d}{dt}\text{species\_4} = v_2 + v_3 - v_3 - v_{12} - v_{19} \quad (77)$$

#### 8.5 Species `species_5`

**Name** LTGFb1

**Initial concentration**  $0.0010 \mu\text{mol} \cdot \text{l}^{-1}$

This species takes part in nine reactions (as a reactant in [reaction\\_4](#), [reaction\\_5](#), [reaction\\_6](#), [reaction\\_23](#) and as a product in [reaction\\_15](#) and as a modifier in [reaction\\_4](#), [reaction\\_5](#), [reaction\\_6](#), [reaction\\_23](#)).

$$\frac{d}{dt}\text{species\_5} = v_{15} - v_4 - v_5 - v_6 - v_{23} \quad (78)$$

#### 8.6 Species `species_6`

**Name** TGFb1

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

This species takes part in 13 reactions (as a reactant in [reaction\\_7](#), [reaction\\_8](#), [reaction\\_24](#), [reaction\\_32](#) and as a product in [reaction\\_4](#), [reaction\\_5](#), [reaction\\_6](#), [reaction\\_7](#), [reaction\\_8](#) and as a modifier in [reaction\\_7](#), [reaction\\_8](#), [reaction\\_24](#), [reaction\\_32](#)).

$$\frac{d}{dt}\text{species\_6} = v_4 + v_5 + v_6 + v_7 + v_8 - v_7 - v_8 - v_{24} - v_{32} \quad (79)$$

#### 8.7 Species `species_7`

**Name** TSP1

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

This species takes part in seven reactions (as a reactant in [reaction\\_5](#), [reaction\\_9](#), [reaction\\_21](#) and as a product in [reaction\\_7](#) and as a modifier in [reaction\\_5](#), [reaction\\_9](#), [reaction\\_21](#)).

$$\frac{d}{dt}\text{species\_7} = v_7 - v_5 - v_9 - v_{21} \quad (80)$$

## 8.8 Species `species_8`

**Name** PAI1

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

This species takes part in seven reactions (as a reactant in [reaction\\_12](#), [reaction\\_13](#), [reaction\\_22](#) and as a product in [reaction\\_8](#) and as a modifier in [reaction\\_12](#), [reaction\\_13](#), [reaction\\_22](#)).

$$\frac{d}{dt}\text{species\_8} = v_8 - v_{12} - v_{13} - v_{22} \quad (81)$$

## 8.9 Species `species_9`

**Name** TSP1:PLS

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

This species takes part in eight reactions (as a reactant in [reaction\\_10](#), [reaction\\_30](#), [reaction\\_31](#) and as a product in [reaction\\_9](#) and as a modifier in [reaction\\_9](#), [reaction\\_10](#), [reaction\\_30](#), [reaction\\_31](#)).

$$\frac{d}{dt}\text{species\_9} = v_9 - v_{10} - v_{30} - v_{31} \quad (82)$$

## 8.10 Species `species_10`

**Name** A2M

**Initial concentration**  $0.0050 \mu\text{mol} \cdot \text{l}^{-1}$

This species takes part in five reactions (as a reactant in [reaction\\_11](#), [reaction\\_26](#) and as a product in [reaction\\_16](#) and as a modifier in [reaction\\_11](#), [reaction\\_26](#)).

$$\frac{d}{dt}\text{species\_10} = v_{16} - v_{11} - v_{26} \quad (83)$$

## 8.11 Species `species_11`

**Name** A2M:PLS

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

This species takes part in four reactions (as a reactant in [reaction\\_27](#) and as a product in [reaction\\_11](#) and as a modifier in [reaction\\_11](#), [reaction\\_27](#)).

$$\frac{d}{dt}\text{species\_11} = v_{11} - v_{27} \quad (84)$$

## 8.12 Species `species_12`

**Name** PAI1:tcUPA

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

This species takes part in four reactions (as a reactant in [reaction\\_28](#) and as a product in [reaction\\_12](#) and as a modifier in [reaction\\_12](#), [reaction\\_28](#)).

$$\frac{d}{dt}\text{species\_12} = v_{12} - v_{28} \quad (85)$$

## 8.13 Species `species_13`

**Name** PAI1:scUPA

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

This species takes part in four reactions (as a reactant in [reaction\\_29](#) and as a product in [reaction\\_13](#) and as a modifier in [reaction\\_13](#), [reaction\\_29](#)).

$$\frac{d}{dt}\text{species\_13} = v_{13} - v_{29} \quad (86)$$

# A Glossary of Systems Biology Ontology Terms

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

SBML2<sup>LaTeX</sup> was developed by Andreas Dräger<sup>a</sup>, Hannes Planatscher<sup>a</sup>, Dieudonné M Wouamba<sup>a</sup>, Adrian Schröder<sup>a</sup>, Michael Hucka<sup>b</sup>, Lukas Endler<sup>c</sup>, Martin Golebiewski<sup>d</sup> and Andreas Zell<sup>a</sup>. Please see <http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX> for more information.

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