

## SBML Model Report

# Model name: “Sarma2012 - Oscillations in MAPK cascade (S1n)”



March 18, 2013

## 1 General Overview

This is a document in SBML Level 2 Version 4 format. 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	19
events	0	constraints	0
reactions	22	function definitions	15
global parameters	0	unit definitions	2
rules	0	initial assignments	0

## Model Notes

Sarma2012 - Oscillations in MAPK cascade (S1n)

Two plausible designs (S1 and S2) of coupled positive and negative feedback loops of MAPK cascade has been described in this paper. Further these models were extended to S1n and S2n, to incorporate the nuclear-cytoplasmic translocation of the MK layer components of the cascade. This model corresponds to model S1n that comprises negative feedback from MK-PP to MKKK-P layer coupled to positive feedback from MK-PP to MKK-PP layer, with the inclusion of nuclear-cytoplasmic translocation.

This model is described in the article: [Oscillations in MAPK cascade triggered by two distinct designs of coupled positive and negative feedback loops](#). Sarma U, Ghosh I. BMC Res Notes. 2012 Jun 13;5:287.

Abstract:

#### BACKGROUND:

Feedback loops, both positive and negative are embedded in the Mitogen Activated Protein Kinase (MAPK) cascade. In the three layer MAPK cascade, both feedback loops originate from the terminal layer and their sites of action are either of the two upstream layers. Recent studies have shown that the cascade uses coupled positive and negative feedback loops in generating oscillations. Two plausible designs of coupled positive and negative feedback loops can be elucidated from the literature; in one design the positive feedback precedes the negative feedback in the direction of signal flow and vice-versa in another. But it remains unexplored how the two designs contribute towards triggering oscillations in MAPK cascade. Thus it is also not known how amplitude, frequency, robustness or nature (analogous/digital) of the oscillations would be shaped by these two designs.

#### RESULTS:

We built two models of MAPK cascade that exhibited oscillations as function of two underlying designs of coupled positive and negative feedback loops. Frequency, amplitude and nature (digital/analogous) of oscillations were found to be differentially determined by each design. It was observed that the positive feedback emerging from an oscillating MAPK cascade and functional in an external signal processing module can trigger oscillations in the target module, provided that the target module satisfy certain parametric requirements. The augmentation of the two models was done to incorporate the nuclear-cytoplasmic shuttling of cascade components followed by induction of a nuclear phosphatase. It revealed that the fate of oscillations in the MAPK cascade is governed by the feedback designs. Oscillations were unaffected due to nuclear compartmentalization owing to one design but were completely abolished in the other case.

#### CONCLUSION:

The MAPK cascade can utilize two distinct designs of coupled positive and negative feedback loops to trigger oscillations. The amplitude, frequency and robustness of the oscillations in presence or absence of nuclear compartmentalization were differentially determined by two designs of coupled positive and negative feedback loops. A positive feedback from an oscillating MAPK cascade was shown to induce oscillations in an external signal processing module, uncovering a novel regulatory aspect of MAPK signal processing.

This model is hosted on [BioModels Database](#) and identified by: [MODEL1112190006](#).

To cite BioModels Database, please use: [BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models](#).

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## 2 Unit Definitions

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

### 2.1 Unit volume

**Name** volume

**Definition** ml

### 2.2 Unit substance

**Name** substance

**Definition** nmol

### 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_0	compartment		3	1	litre	<input checked="" type="checkbox"/>	

### 3.1 Compartment `compartment_0`

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

**Name** `compartment`

## 4 Species

This model contains 19 species. Section 7 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_0	MKKK	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_1	MKKK_P	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_2	MKK	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_3	MKK_P	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_4	MKK_PP	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_5	M	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_6	M_P	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_7	M_PP	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_8	P1	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_9	P2	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_10	P3	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_11	M_PP_n	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_12	PreP3_mRNA	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_13	P3mRNA	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_14	P3_c	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_15	pP3_c	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_16	M_n	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_17	M_P_n	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$
species_18	P3_n	compartment_0	$\text{nmol} \cdot \text{ml}^{-1}$	$\square$	$\square$

## 5 Function definitions

This is an overview of 15 function definitions.

### 5.1 Function definition `function_4_1_1`

**Name** `function_4_1_1`

**Arguments** `K1`, `KI`, `V1`, `[species_0]`, `[species_7]`

**Mathematical Expression**

$$\frac{\frac{V1 \cdot [species\_0]}{K1}}{\left(1 + \frac{[species\_0]}{K1}\right) \cdot \left(1 + \frac{[species\_7]}{KI}\right)} \quad (1)$$

### 5.2 Function definition `function_4_3_1`

**Name** `function_4_3_1`

**Arguments** `A`, `K3`, `Ka`, `k3`, `[species_1]`, `[species_2]`, `[species_3]`, `[species_7]`

**Mathematical Expression**

$$\frac{\frac{k3 \cdot [species\_1] \cdot [species\_2]}{K3}}{1 + \frac{[species\_2]}{K3} + \frac{[species\_3]}{K3}} \cdot \frac{1 + \frac{A \cdot [species\_7]}{Ka}}{1 + \frac{[species\_7]}{Ka}} \quad (2)$$

### 5.3 Function definition `function_4_4_1`

**Name** `function_4_4_1`

**Arguments** `A`, `K4`, `Ka`, `k4`, `[species_1]`, `[species_2]`, `[species_3]`, `[species_7]`

**Mathematical Expression**

$$\frac{\frac{k4 \cdot [species\_1] \cdot [species\_3]}{K4}}{1 + \frac{[species\_3]}{K4} + \frac{[species\_2]}{K4}} \cdot \frac{1 + \frac{A \cdot [species\_7]}{Ka}}{1 + \frac{[species\_7]}{Ka}} \quad (3)$$

### 5.4 Function definition `function_4_7_1`

**Name** `function_4_7_1`

**Arguments** `K7`, `k7`, `[species_4]`, `[species_5]`, `[species_6]`

**Mathematical Expression**

$$\frac{\frac{k7 \cdot [species\_4] \cdot [species\_5]}{K7}}{1 + \frac{[species\_5]}{K7} + \frac{[species\_6]}{K7}} \quad (4)$$

### 5.5 Function definition [function\\_4\\_8\\_1](#)

**Name** function\_4\_8\_1

**Arguments** K8, k8, [species\_4], [species\_5], [species\_6]

**Mathematical Expression**

$$\frac{\frac{k8 \cdot [\text{species}_4] \cdot [\text{species}_6]}{K8}}{1 + \frac{[\text{species}_5]}{K8} + \frac{[\text{species}_6]}{K8}} \quad (5)$$

### 5.6 Function definition [function\\_4\\_2\\_1](#)

**Name** function\_4\_2\_1

**Arguments** K2, k2, [species\_1], [species\_8]

**Mathematical Expression**

$$\frac{\frac{k2 \cdot [\text{species}_8] \cdot [\text{species}_1]}{K2}}{1 + \frac{[\text{species}_1]}{K2}} \quad (6)$$

### 5.7 Function definition [function\\_4\\_5\\_1](#)

**Name** function\_4\_5\_1

**Arguments** K5, k5, [species\_3], [species\_4], [species\_9]

**Mathematical Expression**

$$\frac{\frac{k5 \cdot [\text{species}_9] \cdot [\text{species}_4]}{K5}}{1 + \frac{[\text{species}_4]}{K5} + \frac{[\text{species}_3]}{K5}} \quad (7)$$

### 5.8 Function definition [function\\_4\\_6\\_1](#)

**Name** function\_4\_6\_1

**Arguments** K6, k6, [species\_3], [species\_4], [species\_9]

**Mathematical Expression**

$$\frac{\frac{k6 \cdot [\text{species}_9] \cdot [\text{species}_3]}{K6}}{1 + \frac{[\text{species}_4]}{K6} + \frac{[\text{species}_3]}{K6}} \quad (8)$$

### 5.9 Function definition [function\\_4\\_9\\_1](#)

**Name** function\_4\_9\_1

**Arguments** K9, k9, [species\_10], [species\_6], [species\_7]

**Mathematical Expression**

$$\frac{\frac{k9 \cdot [\text{species}_{10}] \cdot [\text{species}_7]}{K9}}{1 + \frac{[\text{species}_7]}{K9} + \frac{[\text{species}_6]}{K9}} \quad (9)$$

### 5.10 Function definition [function\\_4\\_10\\_1](#)

**Name** function\_4\_10\_1

**Arguments** K10, k10, [species\_10], [species\_6], [species\_7]

**Mathematical Expression**

$$\frac{\frac{k10 \cdot [\text{species}_{10}] \cdot [\text{species}_6]}{K10}}{1 + \frac{[\text{species}_7]}{K10} + \frac{[\text{species}_6]}{K10}} \quad (10)$$

### 5.11 Function definition [function\\_1](#)

**Name** 11

**Arguments** k11f, ppERK\_c, k11b, ppERK\_n

**Mathematical Expression**

$$k11f \cdot \text{ppERK\_c} - k11b \cdot \text{ppERK\_n} \quad (11)$$

### 5.12 Function definition [function\\_2](#)

**Name** 12

**Arguments** V12, n12, K12, M\_PP\_n

**Mathematical Expression**

$$\frac{V12 \cdot M\_PP\_n^{n12}}{K12^{n12} + M\_PP\_n^{n12}} \quad (12)$$

### 5.13 Function definition [function\\_3](#)

**Name** 15

**Arguments** k15, P3mRNA

**Mathematical Expression**

$$k15 \cdot \text{P3mRNA} \quad (13)$$



#### 5.14 Function definition `function_4`

**Name** 21

**Arguments**  $M\_PP\_n$ ,  $M\_P\_n$ ,  $P3\_n$ ,  $k21$ ,  $K21$ ,  $K21i$

**Mathematical Expression**

$$\frac{\frac{k21 \cdot P3\_n \cdot M\_PP\_n}{K21}}{1 + \frac{M\_PP\_n}{K21} + \frac{M\_P\_n}{K21i}} \quad (14)$$

#### 5.15 Function definition `function_5`

**Name** 22

**Arguments**  $P3\_n$ ,  $M\_P\_n$ ,  $M\_PP\_n$ ,  $k22$ ,  $K22$ ,  $K22i$

**Mathematical Expression**

$$\frac{\frac{k22 \cdot P3\_n \cdot M\_P\_n}{K22}}{1 + \frac{M\_P\_n}{K22} + \frac{M\_PP\_n}{K22i}} \quad (15)$$

## 6 Reactions

This model contains 22 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 4: Overview of all reactions

Nº	Id	Name	Reaction Equation	SBO
1	reaction_0	1	species_0 $\xrightarrow{\text{species}_7, \text{species}_0, \text{species}_7, \text{species}_0, \text{species}_7}$ species_1	
2	reaction_1	3	species_2 $\xrightarrow{\text{species}_1, \text{species}_3, \text{species}_7, \text{species}_1, \text{species}_2, \text{species}_3, \text{species}_7, \text{species}_1}$ species_3	
3	reaction_2	4	species_3 $\xrightarrow{\text{species}_1, \text{species}_2, \text{species}_7, \text{species}_1, \text{species}_2, \text{species}_3, \text{species}_7, \text{species}_1}$ species_4	
4	reaction_3	7	species_5 $\xrightarrow{\text{species}_4, \text{species}_6, \text{species}_4, \text{species}_5, \text{species}_6, \text{species}_4, \text{species}_5, \text{species}_6}$ species_6	
5	reaction_4	8	species_6 $\xrightarrow{\text{species}_4, \text{species}_5, \text{species}_4, \text{species}_5, \text{species}_6, \text{species}_4, \text{species}_5, \text{species}_6}$ species_7	
6	reaction_5	2	species_1 $\xrightarrow{\text{species}_8, \text{species}_1, \text{species}_8, \text{species}_1, \text{species}_8}$ species_0	
7	reaction_6	5	species_4 $\xrightarrow{\text{species}_9, \text{species}_3, \text{species}_3, \text{species}_4, \text{species}_9, \text{species}_3, \text{species}_4, \text{species}_9}$ species_5	
8	reaction_7	6	species_3 $\xrightarrow{\text{species}_9, \text{species}_4, \text{species}_3, \text{species}_4, \text{species}_9, \text{species}_3, \text{species}_4, \text{species}_9}$ species_6	
9	reaction_8	9	species_7 $\xrightarrow{\text{species}_{10}, \text{species}_6, \text{species}_5, \text{species}_{10}, \text{species}_6, \text{species}_7, \text{species}_{10}}$ species_8	
10	reaction_9	10	species_6 $\xrightarrow{\text{species}_{10}, \text{species}_7, \text{species}_5, \text{species}_{10}, \text{species}_6, \text{species}_7, \text{species}_{10}}$ species_9	
11	reaction_10	11	species_7 $\xrightarrow{\text{species}_7, \text{species}_{11}, \text{species}_7, \text{species}_{11}}$ species_11	
12	reaction_11	12	$\emptyset \xrightarrow{\text{species}_{11}, \text{species}_{11}, \text{species}_{11}}$ species_12	
13	reaction_12	13	species_12 $\xrightarrow{\text{species}_{12}, \text{species}_{12}}$ species_13	
14	reaction_13	14	species_13 $\xrightarrow{\text{species}_{13}, \text{species}_{13}}$ $\emptyset$	
15	reaction_14	15	$\emptyset \xrightarrow{\text{species}_{13}, \text{species}_{13}, \text{species}_{13}}$ species_14	

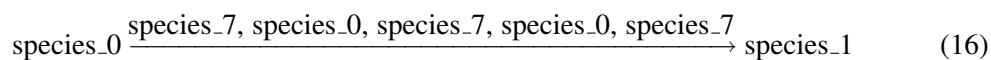
Nº	Id	Name	Reaction Equation	SBO
16	reaction_15	17	species_14 $\xrightarrow{\text{species\_14, species\_14}}$ $\emptyset$	
17	reaction_16	19	species_5 $\xleftrightarrow{\text{species\_5, species\_16, species\_5, species\_16}}$ species_16	
18	reaction_17	20	species_6 $\xleftrightarrow{\text{species\_6, species\_17, species\_6, species\_17}}$ species_17	
19	reaction_18	16	species_14 $\xleftrightarrow{\text{species\_14, species\_18, species\_14, species\_18}}$ species_18	
20	reaction_19	21	species_11 $\xrightarrow{\text{species\_17, species\_18, species\_11, species\_17, species\_18, species\_11, species\_17, species\_18, species\_11}}$ species_18	
21	reaction_20	22	species_17 $\xrightarrow{\text{species\_18, species\_11, species\_18, species\_17, species\_11, species\_18, species\_17, species\_18, species\_11}}$ species_18	
22	reaction_21	18	species_18 $\xrightarrow{\text{species\_18, species\_18}}$ $\emptyset$	

## 6.1 Reaction `reaction_0`

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

**Name** 1

### Reaction equation



### Reactant

Table 5: Properties of each reactant.

Id	Name	SBO
species_0	MKKK	

### Modifiers

Table 6: Properties of each modifier.

Id	Name	SBO
species_7	M_PP	
species_0	MKKK	
species_7	M_PP	
species_0	MKKK	
species_7	M_PP	

### Product

Table 7: Properties of each product.

Id	Name	SBO
species_1	MKKK_P	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_1 = \text{vol}(\text{compartment\_0}) \cdot \text{function\_4\_1\_1}(\text{K1}, \text{KI}, \text{V1}, [\text{species\_0}], [\text{species\_7}]) \quad (17)$$

$$\text{function\_4\_1\_1}(K1, KI, V1, [\text{species\_0}], [\text{species\_7}]) = \frac{\frac{V1 \cdot [\text{species\_0}]}{K1}}{\left(1 + \frac{[\text{species\_0}]}{K1}\right) \cdot \left(1 + \frac{[\text{species\_7}]}{KI}\right)} \quad (18)$$

$$\text{function\_4\_1\_1}(K1, KI, V1, [\text{species\_0}], [\text{species\_7}]) = \frac{\frac{V1 \cdot [\text{species\_0}]}{K1}}{\left(1 + \frac{[\text{species\_0}]}{K1}\right) \cdot \left(1 + \frac{[\text{species\_7}]}{KI}\right)} \quad (19)$$

Table 8: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K1	K1		20.0		<input checked="" type="checkbox"/>
KI	KI		9.0		<input checked="" type="checkbox"/>
V1	V1		2.5		<input checked="" type="checkbox"/>

## 6.2 Reaction `reaction_1`

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

**Name** 3

### Reaction equation

$$\text{species\_2} \xrightarrow{\text{species\_1, species\_3, species\_7, species\_1, species\_2, species\_3, species\_7, species\_1, species\_2, species\_3, species\_2}} \quad (20)$$

### Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
species_2	MKK	

### Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
species_1	MKKK_P	
species_3	MKK_P	

Id	Name	SBO
species_7	M_PP	
species_1	MKKK_P	
species_2	MKK	
species_3	MKK_P	
species_7	M_PP	
species_1	MKKK_P	
species_2	MKK	
species_3	MKK_P	
species_7	M_PP	

## Product

Table 11: Properties of each product.

Id	Name	SBO
species_3	MKK_P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_2 = \text{vol}(\text{compartment}_0) \cdot \text{function\_4\_3\_1}(A, K3, Ka, k3, [\text{species}_1], [\text{species}_2], [\text{species}_3], [\text{species}_7]) \quad (21)$$

$$\begin{aligned} & \text{function\_4\_3\_1}(A, K3, Ka, k3, [\text{species}_1], [\text{species}_2], [\text{species}_3], [\text{species}_7]) \\ &= \frac{\frac{k3 \cdot [\text{species}_1] \cdot [\text{species}_2]}{K3}}{1 + \frac{[\text{species}_2]}{K3} + \frac{[\text{species}_3]}{K3}} \cdot \frac{1 + \frac{A \cdot [\text{species}_7]}{Ka}}{1 + \frac{[\text{species}_7]}{Ka}} \end{aligned} \quad (22)$$

$$\begin{aligned} & \text{function\_4\_3\_1}(A, K3, Ka, k3, [\text{species}_1], [\text{species}_2], [\text{species}_3], [\text{species}_7]) \\ &= \frac{\frac{k3 \cdot [\text{species}_1] \cdot [\text{species}_2]}{K3}}{1 + \frac{[\text{species}_2]}{K3} + \frac{[\text{species}_3]}{K3}} \cdot \frac{1 + \frac{A \cdot [\text{species}_7]}{Ka}}{1 + \frac{[\text{species}_7]}{Ka}} \end{aligned} \quad (23)$$

Table 12: Properties of each parameter.

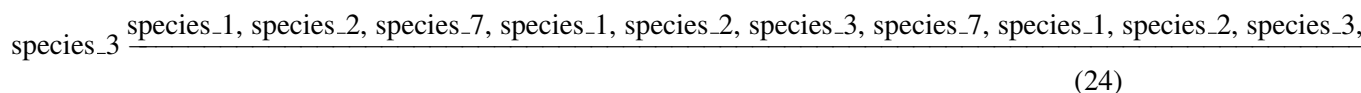
Id	Name	SBO	Value	Unit	Constant
A	A		10.0		✓
K3	K3		20.0		✓
Ka	Ka		500.0		✓
k3	k3		0.1		✓

### 6.3 Reaction `reaction_2`

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

**Name** 4

#### Reaction equation



#### Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
species_3	MKK_P	

#### Modifiers

Table 14: Properties of each modifier.

Id	Name	SBO
species_1	MKKK_P	
species_2	MKK	
species_7	M_PP	
species_1	MKKK_P	
species_2	MKK	
species_3	MKK_P	
species_7	M_PP	
species_1	MKKK_P	
species_2	MKK	
species_3	MKK_P	
species_7	M_PP	

#### Product

Table 15: Properties of each product.

Id	Name	SBO
species_4	MKK_PP	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_3 = \text{vol}(\text{compartment}_0) \cdot \text{function\_4\_4\_1}(A, K4, Ka, k4, [\text{species}_1], [\text{species}_2], [\text{species}_3], [\text{species}_7]) \quad (25)$$

$$\begin{aligned} & \text{function\_4\_4\_1}(A, K4, Ka, k4, [\text{species}_1], [\text{species}_2], [\text{species}_3], [\text{species}_7]) \\ &= \frac{\frac{k4 \cdot [\text{species}_1] \cdot [\text{species}_3]}{K4}}{1 + \frac{[\text{species}_3]}{K4} + \frac{[\text{species}_2]}{K4}} \cdot \frac{1 + \frac{A \cdot [\text{species}_7]}{Ka}}{1 + \frac{[\text{species}_7]}{Ka}} \end{aligned} \quad (26)$$

$$\begin{aligned} & \text{function\_4\_4\_1}(A, K4, Ka, k4, [\text{species}_1], [\text{species}_2], [\text{species}_3], [\text{species}_7]) \\ &= \frac{\frac{k4 \cdot [\text{species}_1] \cdot [\text{species}_3]}{K4}}{1 + \frac{[\text{species}_3]}{K4} + \frac{[\text{species}_2]}{K4}} \cdot \frac{1 + \frac{A \cdot [\text{species}_7]}{Ka}}{1 + \frac{[\text{species}_7]}{Ka}} \end{aligned} \quad (27)$$

Table 16: Properties of each parameter.

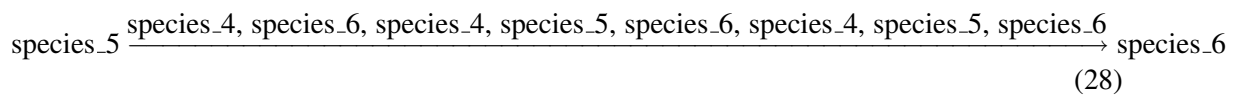
Id	Name	SBO	Value	Unit	Constant
A	A		10.0		<input checked="" type="checkbox"/>
K4	K4		20.0		<input checked="" type="checkbox"/>
Ka	Ka		500.0		<input checked="" type="checkbox"/>
k4	k4		0.1		<input checked="" type="checkbox"/>

## 6.4 Reaction `reaction_3`

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

**Name** 7

### Reaction equation



### Reactant



Table 17: Properties of each reactant.

Id	Name	SBO
species_5	M	

## Modifiers

Table 18: Properties of each modifier.

Id	Name	SBO
species_4	MKK_PP	
species_6	M_P	
species_4	MKK_PP	
species_5	M	
species_6	M_P	
species_4	MKK_PP	
species_5	M	
species_6	M_P	

## Product

Table 19: Properties of each product.

Id	Name	SBO
species_6	M_P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_4 = \text{vol}(\text{compartment}_0) \cdot \text{function\_4\_7\_1}(K7, k7, [\text{species}_4], [\text{species}_5], [\text{species}_6]) \quad (29)$$

$$\text{function\_4\_7\_1}(K7, k7, [\text{species}_4], [\text{species}_5], [\text{species}_6]) = \frac{\frac{k7 \cdot [\text{species}_4] \cdot [\text{species}_5]}{K7}}{1 + \frac{[\text{species}_5]}{K7} + \frac{[\text{species}_6]}{K7}} \quad (30)$$

$$\text{function\_4\_7\_1}(K7, k7, [\text{species}_4], [\text{species}_5], [\text{species}_6]) = \frac{\frac{k7 \cdot [\text{species}_4] \cdot [\text{species}_5]}{K7}}{1 + \frac{[\text{species}_5]}{K7} + \frac{[\text{species}_6]}{K7}} \quad (31)$$

Table 20: Properties of each parameter.

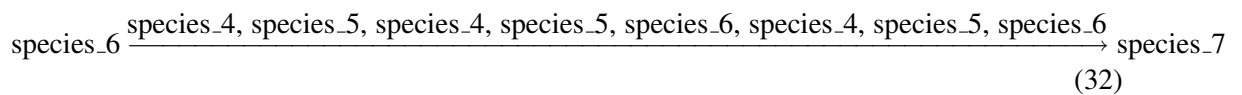
Id	Name	SBO	Value	Unit	Constant
K7	K7		20.0		<input checked="" type="checkbox"/>
k7	k7		0.1		<input checked="" type="checkbox"/>

## 6.5 Reaction `reaction_4`

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

**Name** 8

### Reaction equation



### Reactant

Table 21: Properties of each reactant.

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

### Modifiers

Table 22: Properties of each modifier.

Id	Name	SBO
<code>species_4</code>	MKK_PP	
<code>species_5</code>	M	
<code>species_4</code>	MKK_PP	
<code>species_5</code>	M	
<code>species_6</code>	M_P	
<code>species_4</code>	MKK_PP	
<code>species_5</code>	M	
<code>species_6</code>	M_P	

### Product

Table 23: Properties of each product.

Id	Name	SBO
species_7	M_PP	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_5 = \text{vol}(\text{compartment}_0) \cdot \text{function\_4\_8\_1}(\text{K8}, \text{k8}, [\text{species}_4], [\text{species}_5], [\text{species}_6]) \quad (33)$$

$$\text{function\_4\_8\_1}(\text{K8}, \text{k8}, [\text{species}_4], [\text{species}_5], [\text{species}_6]) = \frac{\frac{\text{k8} \cdot [\text{species}_4] \cdot [\text{species}_6]}{\text{K8}}}{1 + \frac{[\text{species}_5]}{\text{K8}} + \frac{[\text{species}_6]}{\text{K8}}} \quad (34)$$

$$\text{function\_4\_8\_1}(\text{K8}, \text{k8}, [\text{species}_4], [\text{species}_5], [\text{species}_6]) = \frac{\frac{\text{k8} \cdot [\text{species}_4] \cdot [\text{species}_6]}{\text{K8}}}{1 + \frac{[\text{species}_5]}{\text{K8}} + \frac{[\text{species}_6]}{\text{K8}}} \quad (35)$$

Table 24: Properties of each parameter.

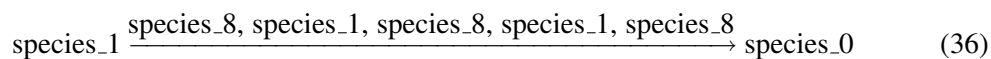
Id	Name	SBO	Value	Unit	Constant
K8	K8		20.0		<input checked="" type="checkbox"/>
k8	k8		0.1		<input checked="" type="checkbox"/>

## 6.6 Reaction reaction\_5

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

**Name** 2

### Reaction equation



### Reactant

Table 25: Properties of each reactant.

Id	Name	SBO
species_1	MKKK_P	

## Modifiers

Table 26: Properties of each modifier.

Id	Name	SBO
species_8	P1	
species_1	MKKK_P	
species_8	P1	
species_1	MKKK_P	
species_8	P1	

## Product

Table 27: Properties of each product.

Id	Name	SBO
species_0	MKKK	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_6 = \text{vol}(\text{compartment}_0) \cdot \text{function\_4\_2\_1}(K2, k2, [\text{species}_1], [\text{species}_8]) \quad (37)$$

$$\text{function\_4\_2\_1}(K2, k2, [\text{species}_1], [\text{species}_8]) = \frac{\frac{k2 \cdot [\text{species}_8] \cdot [\text{species}_1]}{K2}}{1 + \frac{[\text{species}_1]}{K2}} \quad (38)$$

$$\text{function\_4\_2\_1}(K2, k2, [\text{species}_1], [\text{species}_8]) = \frac{\frac{k2 \cdot [\text{species}_8] \cdot [\text{species}_1]}{K2}}{1 + \frac{[\text{species}_1]}{K2}} \quad (39)$$

Table 28: Properties of each parameter.

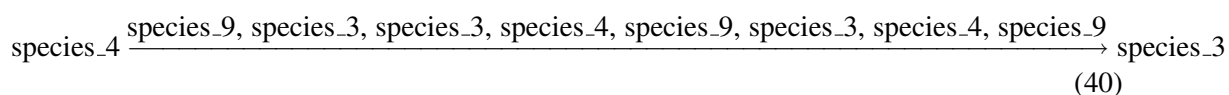
Id	Name	SBO	Value	Unit	Constant
K2	K2		200.000		✓
k2	k2		0.025		✓

## 6.7 Reaction `reaction_6`

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

**Name** 5

### Reaction equation



### Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
species_4	MKK_PP	

### Modifiers

Table 30: Properties of each modifier.

Id	Name	SBO
species_9	P2	
species_3	MKK_P	
species_3	MKK_P	
species_4	MKK_PP	
species_9	P2	
species_3	MKK_P	
species_4	MKK_PP	
species_9	P2	

### Product

Table 31: Properties of each product.

Id	Name	SBO
species_3	MKK_P	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_7 = \text{vol}(\text{compartment}_0) \cdot \text{function\_4\_5\_1}(K5, k5, [\text{species}_3], [\text{species}_4], [\text{species}_9]) \quad (41)$$

$$\text{function\_4\_5\_1}(K5, k5, [\text{species}_3], [\text{species}_4], [\text{species}_9]) = \frac{\frac{k5 \cdot [\text{species}_9] \cdot [\text{species}_4]}{K5}}{1 + \frac{[\text{species}_4]}{K5} + \frac{[\text{species}_3]}{K5}} \quad (42)$$

$$\text{function\_4\_5\_1}(K5, k5, [\text{species}_3], [\text{species}_4], [\text{species}_9]) = \frac{\frac{k5 \cdot [\text{species}_9] \cdot [\text{species}_4]}{K5}}{1 + \frac{[\text{species}_4]}{K5} + \frac{[\text{species}_3]}{K5}} \quad (43)$$

Table 32: Properties of each parameter.

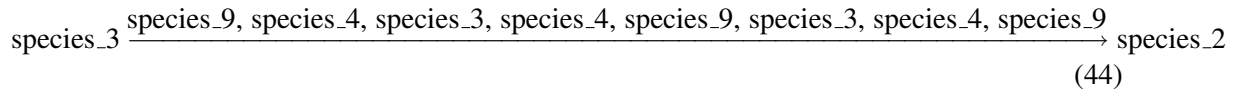
Id	Name	SBO	Value	Unit	Constant
K5	K5		200.0		<input checked="" type="checkbox"/>
k5	k5		0.1		<input checked="" type="checkbox"/>

## 6.8 Reaction `reaction_7`

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

**Name** 6

### Reaction equation



### Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
species_3	MKK_P	

### Modifiers

Table 34: Properties of each modifier.

Id	Name	SBO
species_9	P2	
species_4	MKK_PP	

Id	Name	SBO
species_3	MKK_P	
species_4	MKK_PP	
species_9	P2	
species_3	MKK_P	
species_4	MKK_PP	
species_9	P2	

## Product

Table 35: Properties of each product.

Id	Name	SBO
species_2	MKK	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_8 = \text{vol}(\text{compartment}_0) \cdot \text{function\_4\_6\_1}(K6, k6, [\text{species}_3], [\text{species}_4], [\text{species}_9]) \quad (45)$$

$$\text{function\_4\_6\_1}(K6, k6, [\text{species}_3], [\text{species}_4], [\text{species}_9]) = \frac{\frac{k6 \cdot [\text{species}_9] \cdot [\text{species}_3]}{K6}}{1 + \frac{[\text{species}_4]}{K6} + \frac{[\text{species}_3]}{K6}} \quad (46)$$

$$\text{function\_4\_6\_1}(K6, k6, [\text{species}_3], [\text{species}_4], [\text{species}_9]) = \frac{\frac{k6 \cdot [\text{species}_9] \cdot [\text{species}_3]}{K6}}{1 + \frac{[\text{species}_4]}{K6} + \frac{[\text{species}_3]}{K6}} \quad (47)$$

Table 36: Properties of each parameter.

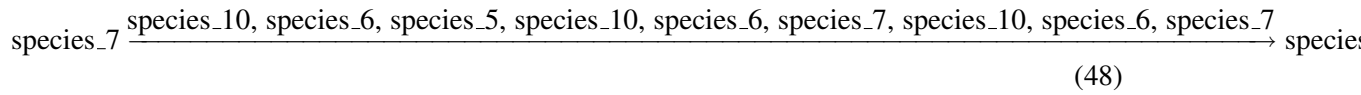
Id	Name	SBO	Value	Unit	Constant
K6	K6		200.0		<input checked="" type="checkbox"/>
k6	k6		0.1		<input checked="" type="checkbox"/>

## 6.9 Reaction `reaction_8`

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

**Name** 9

## Reaction equation



## Reactant

Table 37: Properties of each reactant.

Id	Name	SBO
species_7	M_PP	

## Modifiers

Table 38: Properties of each modifier.

Id	Name	SBO
species_10	P3	
species_6	M_P	
species_5	M	
species_10	P3	
species_6	M_P	
species_7	M_PP	
species_10	P3	
species_6	M_P	
species_7	M_PP	

## Product

Table 39: Properties of each product.

Id	Name	SBO
species_6	M_P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_9 = \text{vol}(\text{compartment\_0}) \cdot \text{function\_4\_9\_1}(K_9, k_9, [\text{species\_10}], [\text{species\_6}], [\text{species\_7}]) \quad (49)$$

$$\text{function\_4\_9\_1}(K_9, k_9, [\text{species\_10}], [\text{species\_6}], [\text{species\_7}]) = \frac{\frac{k_9 \cdot [\text{species\_10}] \cdot [\text{species\_7}]}{K_9}}{1 + \frac{[\text{species\_7}]}{K_9} + \frac{[\text{species\_6}]}{K_9}} \quad (50)$$



$$\text{function\_4\_9\_1}(K9, k9, [\text{species\_10}], [\text{species\_6}], [\text{species\_7}]) = \frac{\frac{k9 \cdot [\text{species\_10}] \cdot [\text{species\_7}]}{K9}}{1 + \frac{[\text{species\_7}]}{K9} + \frac{[\text{species\_6}]}{K9}} \quad (51)$$

Table 40: Properties of each parameter.

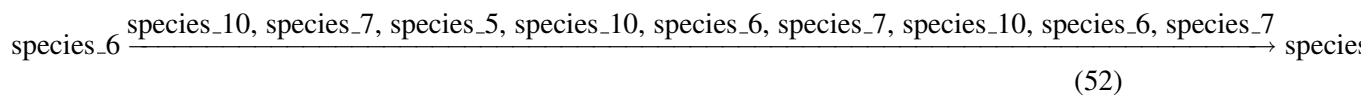
Id	Name	SBO	Value	Unit	Constant
K9	K9		200.0		<input checked="" type="checkbox"/>
k9	k9		0.1		<input checked="" type="checkbox"/>

## 6.10 Reaction `reaction_9`

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

**Name** 10

### Reaction equation



### Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
species_6	M_P	

### Modifiers

Table 42: Properties of each modifier.

Id	Name	SBO
species_10	P3	
species_7	M_PP	
species_5	M	
species_10	P3	
species_6	M_P	
species_7	M_PP	
species_10	P3	
species_6	M_P	
species_7	M_PP	

Id	Name	SBO
----	------	-----

## Product

Table 43: Properties of each product.

Id	Name	SBO
species_5	M	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{10} = \text{vol}(\text{compartment}_0) \cdot \text{function\_4\_10\_1}(K10, k10, [\text{species\_10}], [\text{species\_6}], [\text{species\_7}]) \quad (53)$$

$$\text{function\_4\_10\_1}(K10, k10, [\text{species\_10}], [\text{species\_6}], [\text{species\_7}]) = \frac{\frac{k10 \cdot [\text{species\_10}] \cdot [\text{species\_6}]}{K10}}{1 + \frac{[\text{species\_7}]}{K10} + \frac{[\text{species\_6}]}{K10}} \quad (54)$$

$$\text{function\_4\_10\_1}(K10, k10, [\text{species\_10}], [\text{species\_6}], [\text{species\_7}]) = \frac{\frac{k10 \cdot [\text{species\_10}] \cdot [\text{species\_6}]}{K10}}{1 + \frac{[\text{species\_7}]}{K10} + \frac{[\text{species\_6}]}{K10}} \quad (55)$$

Table 44: Properties of each parameter.

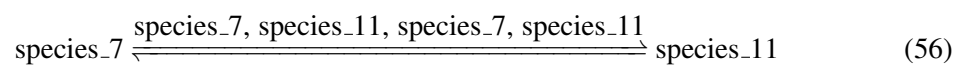
Id	Name	SBO	Value	Unit	Constant
K10	K10		200.0		<input checked="" type="checkbox"/>
k10	k10		0.1		<input checked="" type="checkbox"/>

### 6.11 Reaction `reaction_10`

This is a reversible reaction of one reactant forming one product influenced by four modifiers.

**Name** 11

#### Reaction equation



## Reactant

Table 45: Properties of each reactant.

Id	Name	SBO
species_7	M_PP	

## Modifiers

Table 46: Properties of each modifier.

Id	Name	SBO
species_7	M_PP	
species_11	M_PP_n	
species_7	M_PP	
species_11	M_PP_n	

## Product

Table 47: Properties of each product.

Id	Name	SBO
species_11	M_PP_n	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{11} = \text{vol}(\text{compartment}_0) \cdot \text{function}_1(k_{11f}, [\text{species}_7], k_{11b}, [\text{species}_{11}]) \quad (57)$$

$$\text{function}_1(k_{11f}, \text{ppERK}_c, k_{11b}, \text{ppERK}_n) = k_{11f} \cdot \text{ppERK}_c - k_{11b} \cdot \text{ppERK}_n \quad (58)$$

$$\text{function}_1(k_{11f}, \text{ppERK}_c, k_{11b}, \text{ppERK}_n) = k_{11f} \cdot \text{ppERK}_c - k_{11b} \cdot \text{ppERK}_n \quad (59)$$

Table 48: Properties of each parameter.

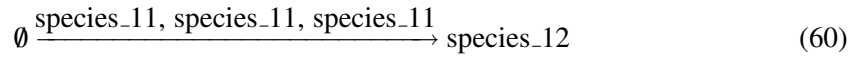
Id	Name	SBO	Value	Unit	Constant
k11f	k11f		10.34		✓
k11b	k11b		2.86		✓

## 6.12 Reaction `reaction_11`

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

**Name** 12

### Reaction equation



### Modifiers

Table 49: Properties of each modifier.

Id	Name	SBO
species_11	M_PP_n	
species_11	M_PP_n	
species_11	M_PP_n	

### Product

Table 50: Properties of each product.

Id	Name	SBO
species_12	PreP3_mRNA	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{12} = \text{vol}(\text{compartment\_0}) \cdot \text{function\_2}(V_{12}, n_{12}, K_{12}, [\text{species\_11}]) \quad (61)$$

$$\text{function\_2}(V_{12}, n_{12}, K_{12}, M_{PP\_n}) = \frac{V_{12} \cdot M_{PP\_n}^{n_{12}}}{K_{12}^{n_{12}} + M_{PP\_n}^{n_{12}}} \quad (62)$$

$$\text{function\_2}(V_{12}, n_{12}, K_{12}, M_{PP\_n}) = \frac{V_{12} \cdot M_{PP\_n}^{n_{12}}}{K_{12}^{n_{12}} + M_{PP\_n}^{n_{12}}} \quad (63)$$

Table 51: Properties of each parameter.

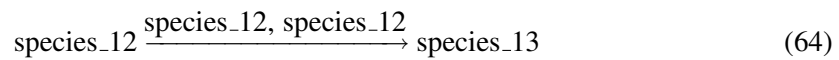
Id	Name	SBO	Value	Unit	Constant
V12	V12		29.24		<input checked="" type="checkbox"/>
n12	n12		3.97		<input checked="" type="checkbox"/>
K12	K12		169.00		<input checked="" type="checkbox"/>

### 6.13 Reaction [reaction\\_12](#)

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

**Name** 13

#### Reaction equation



#### Reactant

Table 52: Properties of each reactant.

Id	Name	SBO
species_12	PreP3_mRNA	

#### Modifiers

Table 53: Properties of each modifier.

Id	Name	SBO
species_12	PreP3_mRNA	
species_12	PreP3_mRNA	

#### Product

Table 54: Properties of each product.

Id	Name	SBO
species_13	P3mRNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{13} = \text{vol}(\text{compartment\_0}) \cdot k1 \cdot [\text{species\_12}] \quad (65)$$

Table 55: Properties of each parameter.

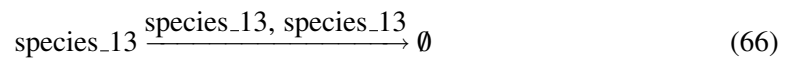
Id	Name	SBO	Value	Unit	Constant
k1	k1		0.022		<input checked="" type="checkbox"/>

## 6.14 Reaction `reaction_13`

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

**Name** 14

## Reaction equation



## Reactant

Table 56: Properties of each reactant.

Id	Name	SBO
species_13	P3mRNA	

## Modifiers

Table 57: Properties of each modifier.

Id	Name	SBO
species_13	P3mRNA	
species_13	P3mRNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{14} = \text{vol}(\text{compartment\_0}) \cdot k1 \cdot [\text{species\_13}] \quad (67)$$

Table 58: Properties of each parameter.

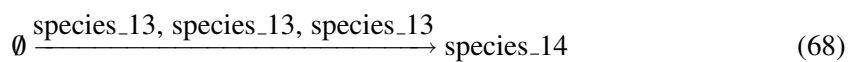
Id	Name	SBO	Value	Unit	Constant
k1	k1		0.008		<input checked="" type="checkbox"/>

### 6.15 Reaction [reaction\\_14](#)

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

**Name** 15

#### Reaction equation



#### Modifiers

Table 59: Properties of each modifier.

Id	Name	SBO
species_13	P3mRNA	
species_13	P3mRNA	
species_13	P3mRNA	

#### Product

Table 60: Properties of each product.

Id	Name	SBO
species_14	P3_c	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{15} = \text{vol}(\text{compartment\_0}) \cdot \text{function\_3}(k15, [\text{species\_13}]) \quad (69)$$

$$\text{function\_3}(k15, \text{P3mRNA}) = k15 \cdot \text{P3mRNA} \quad (70)$$

$$\text{function\_3}(k15, \text{P3mRNA}) = k15 \cdot \text{P3mRNA} \quad (71)$$

Table 61: Properties of each parameter.

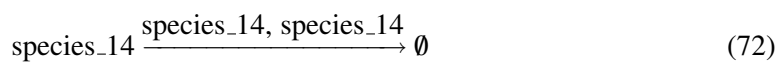
Id	Name	SBO	Value	Unit	Constant
k15	k15		0.001		<input checked="" type="checkbox"/>

## 6.16 Reaction [reaction\\_15](#)

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

**Name** 17

### Reaction equation



### Reactant

Table 62: Properties of each reactant.

Id	Name	SBO
species_14	P3_c	

### Modifiers

Table 63: Properties of each modifier.

Id	Name	SBO
species_14	P3_c	
species_14	P3_c	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{16} = \text{vol}(\text{compartment}_0) \cdot k1 \cdot [\text{species\_14}] \quad (73)$$

Table 64: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$2.5 \cdot 10^{-4}$		<input checked="" type="checkbox"/>

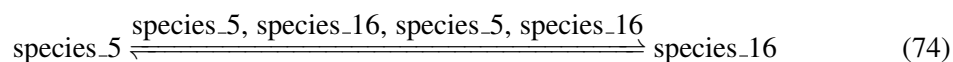


## 6.17 Reaction `reaction_16`

This is a reversible reaction of one reactant forming one product influenced by four modifiers.

**Name** 19

### Reaction equation



### Reactant

Table 65: Properties of each reactant.

Id	Name	SBO
species_5	M	

### Modifiers

Table 66: Properties of each modifier.

Id	Name	SBO
species_5	M	
species_16	M_n	
species_5	M	
species_16	M_n	

### Product

Table 67: Properties of each product.

Id	Name	SBO
species_16	M_n	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{17} = \text{vol}(\text{compartment}_0) \cdot (k_1 \cdot [\text{species}_5] - k_2 \cdot [\text{species}_{16}]) \quad (75)$$

Table 68: Properties of each parameter.

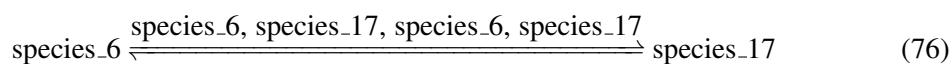
Id	Name	SBO	Value	Unit	Constant
k1	k1		10.34		<input checked="" type="checkbox"/>
k2	k2		2.86		<input checked="" type="checkbox"/>

### 6.18 Reaction [reaction\\_17](#)

This is a reversible reaction of one reactant forming one product influenced by four modifiers.

**Name** 20

#### Reaction equation



#### Reactant

Table 69: Properties of each reactant.

Id	Name	SBO
species_6	M_P	

#### Modifiers

Table 70: Properties of each modifier.

Id	Name	SBO
species_6	M_P	
species_17	M_P_n	
species_6	M_P	
species_17	M_P_n	

#### Product

Table 71: Properties of each product.

Id	Name	SBO
species_17	M_P_n	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{18} = \text{vol}(\text{compartment}_0) \cdot (k1 \cdot [\text{species}_6] - k2 \cdot [\text{species}_{17}]) \quad (77)$$

Table 72: Properties of each parameter.

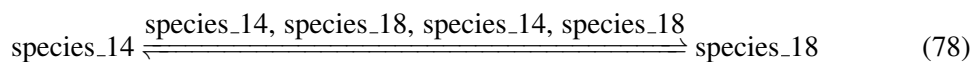
Id	Name	SBO	Value	Unit	Constant
k1	k1		10.34		<input checked="" type="checkbox"/>
k2	k2		2.86		<input checked="" type="checkbox"/>

## 6.19 Reaction `reaction_18`

This is a reversible reaction of one reactant forming one product influenced by four modifiers.

**Name** 16

### Reaction equation



### Reactant

Table 73: Properties of each reactant.

Id	Name	SBO
<code>species_14</code>	P3.c	

### Modifiers

Table 74: Properties of each modifier.

Id	Name	SBO
<code>species_14</code>	P3.c	
<code>species_18</code>	P3.n	
<code>species_14</code>	P3.c	
<code>species_18</code>	P3.n	

### Product

Table 75: Properties of each product.

Id	Name	SBO
species_18	P3_n	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{19} = \text{vol}(\text{compartment}_0) \cdot (k_1 \cdot [\text{species}_{14}] - k_2 \cdot [\text{species}_{18}]) \quad (79)$$

Table 76: Properties of each parameter.

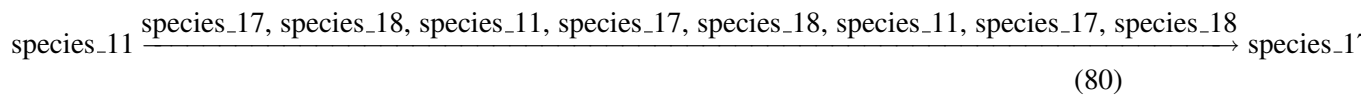
Id	Name	SBO	Value	Unit	Constant
k1	k1		22.56		<input checked="" type="checkbox"/>
k2	k2		15.40		<input checked="" type="checkbox"/>

## 6.20 Reaction [reaction\\_19](#)

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

**Name** 21

## Reaction equation



## Reactant

Table 77: Properties of each reactant.

Id	Name	SBO
species_11	M_PP_n	

## Modifiers

Table 78: Properties of each modifier.

Id	Name	SBO
species_17	M_P_n	

Id	Name	SBO
species_18	P3_n	
species_11	M_PP_n	
species_17	M_P_n	
species_18	P3_n	
species_11	M_PP_n	
species_17	M_P_n	
species_18	P3_n	

## Product

Table 79: Properties of each product.

Id	Name	SBO
species_17	M_P_n	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{20} = \text{vol}(\text{compartment}_0) \cdot \text{function\_4}([\text{species\_11}], [\text{species\_17}], [\text{species\_18}], k21, K21, K21i) \quad (81)$$

$$\text{function\_4}(M\_PP\_n, M\_P\_n, P3\_n, k21, K21, K21i) = \frac{\frac{k21 \cdot P3\_n \cdot M\_PP\_n}{K21}}{1 + \frac{M\_PP\_n}{K21} + \frac{M\_P\_n}{K21i}} \quad (82)$$

$$\text{function\_4}(M\_PP\_n, M\_P\_n, P3\_n, k21, K21, K21i) = \frac{\frac{k21 \cdot P3\_n \cdot M\_PP\_n}{K21}}{1 + \frac{M\_PP\_n}{K21} + \frac{M\_P\_n}{K21i}} \quad (83)$$

Table 80: Properties of each parameter.

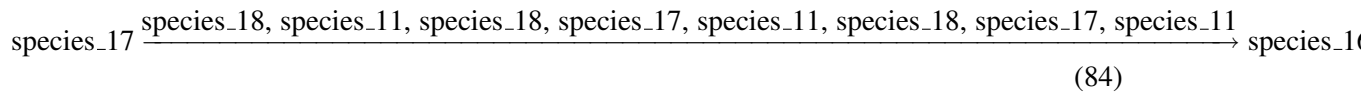
Id	Name	SBO	Value	Unit	Constant
k21	k21		0.68		✓
K21	K21		10300.00		✓
K21i	K21i		87.00		✓

### 6.21 Reaction `reaction_20`

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

**Name** 22

### Reaction equation



### Reactant

Table 81: Properties of each reactant.

Id	Name	SBO
species_17	M_P_n	

### Modifiers

Table 82: Properties of each modifier.

Id	Name	SBO
species_18	P3_n	
species_11	M_PP_n	
species_18	P3_n	
species_17	M_P_n	
species_11	M_PP_n	
species_18	P3_n	
species_17	M_P_n	
species_11	M_PP_n	

### Product

Table 83: Properties of each product.

Id	Name	SBO
species_16	M_n	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{21} = \text{vol}(\text{compartment}_0) \cdot \text{function\_5}([\text{species\_18}], [\text{species\_17}], [\text{species\_11}], k22, K22, K22i) \quad (85)$$

$$\text{function\_5}(P3\_n, M\_P\_n, M\_PP\_n, k22, K22, K22i) = \frac{\frac{k22 \cdot P3\_n \cdot M\_P\_n}{K22}}{1 + \frac{M\_P\_n}{K22} + \frac{M\_PP\_n}{K22i}} \quad (86)$$

$$\text{function\_5}(P3\_n, M\_P\_n, M\_PP\_n, k22, K22, K22i) = \frac{\frac{k22 \cdot P3\_n \cdot M\_P\_n}{K22}}{1 + \frac{M\_P\_n}{K22} + \frac{M\_PP\_n}{K22i}} \quad (87)$$

Table 84: Properties of each parameter.

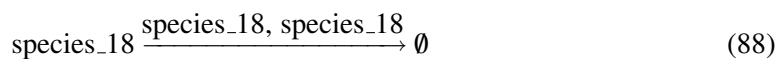
Id	Name	SBO	Value	Unit	Constant
k22	k22		0.31		<input checked="" type="checkbox"/>
K22	K22		87.00		<input checked="" type="checkbox"/>
K22i	K22i		10300.00		<input checked="" type="checkbox"/>

## 6.22 Reaction [reaction\\_21](#)

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

**Name** 18

### Reaction equation



### Reactant

Table 85: Properties of each reactant.

Id	Name	SBO
species_18	P3.n	

### Modifiers

Table 86: Properties of each modifier.

Id	Name	SBO
species_18	P3.n	
species_18	P3.n	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{22} = \text{vol}(\text{compartment}_0) \cdot k1 \cdot [\text{species}_{18}] \quad (89)$$

Table 87: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$2.5 \cdot 10^{-4}$		✓

## 7 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.

### 7.1 Species `species_0`

**Name** MKKK

**Initial concentration** 999.999903688753 nmol · ml<sup>-1</sup>

This species takes part in four reactions (as a reactant in [reaction\\_0](#) and as a product in [reaction\\_5](#) and as a modifier in [reaction\\_0](#), [reaction\\_0](#)).

$$\frac{d}{dt}\text{species}_0 = v_6 - v_1 \quad (90)$$

### 7.2 Species `species_1`

**Name** MKKK\_P

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in ten reactions (as a reactant in [reaction\\_5](#) and as a product in [reaction\\_0](#) and as a modifier in [reaction\\_1](#), [reaction\\_1](#), [reaction\\_1](#), [reaction\\_2](#), [reaction\\_2](#), [reaction\\_2](#), [reaction\\_5](#), [reaction\\_5](#)).



$$\frac{d}{dt}\text{species\_1} = v_1 - v_6 \quad (91)$$

### 7.3 Species species\_2

**Name** MKK

**Initial concentration** 3999.99961475501 nmol · ml<sup>-1</sup>

This species takes part in seven reactions (as a reactant in [reaction\\_1](#) and as a product in [reaction\\_7](#) and as a modifier in [reaction\\_1](#), [reaction\\_1](#), [reaction\\_2](#), [reaction\\_2](#), [reaction\\_2](#)).

$$\frac{d}{dt}\text{species\_2} = v_8 - v_2 \quad (92)$$

### 7.4 Species species\_3

**Name** MKK\_P

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in 14 reactions (as a reactant in [reaction\\_2](#), [reaction\\_7](#) and as a product in [reaction\\_1](#), [reaction\\_6](#) and as a modifier in [reaction\\_1](#), [reaction\\_1](#), [reaction\\_1](#), [reaction\\_2](#), [reaction\\_2](#), [reaction\\_6](#), [reaction\\_6](#), [reaction\\_6](#), [reaction\\_7](#), [reaction\\_7](#)).

$$\frac{d}{dt}\text{species\_3} = v_2 + v_7 - v_3 - v_8 \quad (93)$$

### 7.5 Species species\_4

**Name** MKK\_PP

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in 13 reactions (as a reactant in [reaction\\_6](#) and as a product in [reaction\\_2](#) and as a modifier in [reaction\\_3](#), [reaction\\_3](#), [reaction\\_3](#), [reaction\\_4](#), [reaction\\_4](#), [reaction\\_4](#), [reaction\\_6](#), [reaction\\_6](#), [reaction\\_7](#), [reaction\\_7](#), [reaction\\_7](#)).

$$\frac{d}{dt}\text{species\_4} = v_3 - v_7 \quad (94)$$

## 7.6 Species species\_5

**Name** M

**Initial concentration** 999.999903688753 nmol · ml<sup>-1</sup>

This species takes part in twelve reactions (as a reactant in [reaction\\_3](#), [reaction\\_16](#) and as a product in [reaction\\_9](#) and as a modifier in [reaction\\_3](#), [reaction\\_3](#), [reaction\\_4](#), [reaction\\_4](#), [reaction\\_4](#), [reaction\\_8](#), [reaction\\_9](#), [reaction\\_16](#), [reaction\\_16](#)).

$$\frac{d}{dt}\text{species}_5 = v_{10} - v_4 - v_{17} \quad (95)$$

## 7.7 Species species\_6

**Name** M\_P

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in 17 reactions (as a reactant in [reaction\\_4](#), [reaction\\_9](#), [reaction\\_17](#) and as a product in [reaction\\_3](#), [reaction\\_8](#) and as a modifier in [reaction\\_3](#), [reaction\\_3](#), [reaction\\_3](#), [reaction\\_4](#), [reaction\\_4](#), [reaction\\_4](#), [reaction\\_8](#), [reaction\\_8](#), [reaction\\_8](#), [reaction\\_9](#), [reaction\\_9](#), [reaction\\_17](#), [reaction\\_17](#)).

$$\frac{d}{dt}\text{species}_6 = v_4 + v_9 - v_5 - v_{10} - v_{18} \quad (96)$$

## 7.8 Species species\_7

**Name** M\_PP

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in 19 reactions (as a reactant in [reaction\\_8](#), [reaction\\_10](#) and as a product in [reaction\\_4](#) and as a modifier in [reaction\\_0](#), [reaction\\_0](#), [reaction\\_0](#), [reaction\\_1](#), [reaction\\_1](#), [reaction\\_1](#), [reaction\\_2](#), [reaction\\_2](#), [reaction\\_2](#), [reaction\\_8](#), [reaction\\_8](#), [reaction\\_9](#), [reaction\\_9](#), [reaction\\_9](#), [reaction\\_10](#), [reaction\\_10](#)).

$$\frac{d}{dt}\text{species}_7 = v_5 - v_9 - v_{11} \quad (97)$$

## 7.9 Species species\_8

**Name** P1

**Initial concentration** 99.9999903688752 nmol · ml<sup>-1</sup>

This species takes part in three reactions (as a modifier in [reaction\\_5](#), [reaction\\_5](#), [reaction\\_5](#)).

$$\frac{d}{dt}\text{species}_8 = 0 \quad (98)$$

## 7.10 Species `species_9`

**Name** P2

**Initial concentration** 499.999951844377 nmol · ml<sup>-1</sup>

This species takes part in six reactions (as a modifier in [reaction\\_6](#), [reaction\\_6](#), [reaction\\_6](#), [reaction\\_7](#), [reaction\\_7](#), [reaction\\_7](#)).

$$\frac{d}{dt}\text{species}_9 = 0 \quad (99)$$

## 7.11 Species `species_10`

**Name** P3

**Initial concentration** 499.999975922188 nmol · ml<sup>-1</sup>

This species takes part in six reactions (as a modifier in [reaction\\_8](#), [reaction\\_8](#), [reaction\\_8](#), [reaction\\_9](#), [reaction\\_9](#), [reaction\\_9](#)).

$$\frac{d}{dt}\text{species}_{10} = 0 \quad (100)$$

## 7.12 Species `species_11`

**Name** M\_PP\_n

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in twelve reactions (as a reactant in [reaction\\_19](#) and as a product in [reaction\\_10](#) and as a modifier in [reaction\\_10](#), [reaction\\_10](#), [reaction\\_11](#), [reaction\\_11](#), [reaction\\_11](#), [reaction\\_19](#), [reaction\\_19](#), [reaction\\_20](#), [reaction\\_20](#), [reaction\\_20](#)).

$$\frac{d}{dt}\text{species}_{11} = v_{11} - v_{20} \quad (101)$$

## 7.13 Species `species_12`

**Name** PreP3\_mRNA

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in four reactions (as a reactant in [reaction\\_12](#) and as a product in [reaction\\_11](#) and as a modifier in [reaction\\_12](#), [reaction\\_12](#)).

$$\frac{d}{dt}\text{species}_{12} = v_{12} - v_{13} \quad (102)$$

### 7.14 Species `species_13`

**Name** P3mRNA

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in seven reactions (as a reactant in [reaction\\_13](#) and as a product in [reaction\\_12](#) and as a modifier in [reaction\\_13](#), [reaction\\_13](#), [reaction\\_14](#), [reaction\\_14](#), [reaction\\_14](#)).

$$\frac{d}{dt}\text{species\_13} = v_{13} - v_{14} \quad (103)$$

### 7.15 Species `species_14`

**Name** P3\_c

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in seven reactions (as a reactant in [reaction\\_15](#), [reaction\\_18](#) and as a product in [reaction\\_14](#) and as a modifier in [reaction\\_15](#), [reaction\\_15](#), [reaction\\_18](#), [reaction\\_18](#)).

$$\frac{d}{dt}\text{species\_14} = v_{15} - v_{16} - v_{19} \quad (104)$$

### 7.16 Species `species_15`

**Name** pP3\_c

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species does not take part in any reactions. Its quantity does hence not change over time:

$$\frac{d}{dt}\text{species\_15} = 0 \quad (105)$$

### 7.17 Species `species_16`

**Name** M\_n

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in four reactions (as a product in [reaction\\_16](#), [reaction\\_20](#) and as a modifier in [reaction\\_16](#), [reaction\\_16](#)).

$$\frac{d}{dt}\text{species\_16} = v_{17} + v_{21} \quad (106)$$

## 7.18 Species `species_17`

**Name** M\_P\_n

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in ten reactions (as a reactant in [reaction\\_20](#) and as a product in [reaction\\_17](#), [reaction\\_19](#) and as a modifier in [reaction\\_17](#), [reaction\\_17](#), [reaction\\_19](#), [reaction\\_19](#), [reaction\\_19](#), [reaction\\_20](#), [reaction\\_20](#)).

$$\frac{d}{dt}\text{species\_17} = v_{18} + v_{20} - v_{21} \quad (107)$$

## 7.19 Species `species_18`

**Name** P3\_n

**Initial concentration** 0 nmol · ml<sup>-1</sup>

This species takes part in twelve reactions (as a reactant in [reaction\\_21](#) and as a product in [reaction\\_18](#) and as a modifier in [reaction\\_18](#), [reaction\\_18](#), [reaction\\_19](#), [reaction\\_19](#), [reaction\\_19](#), [reaction\\_20](#), [reaction\\_20](#), [reaction\\_20](#), [reaction\\_21](#), [reaction\\_21](#)).

$$\frac{d}{dt}\text{species\_18} = v_{19} - v_{22} \quad (108)$$

SBML<sup>2</sup>TeX 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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