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 identifiedby: MODEL1112190006 .

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resourcefor published quantitative kinetic models .

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^2

2.4 Unit `length`

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

Definition m

2.5 Unit `time`

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

Definition s

3 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	☑	

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	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_1	MKKK_P	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_2	MKK	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_3	MKK_P	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_4	MKK_PP	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_5	M	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_6	M_P	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_7	M_PP	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_8	P1	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_9	P2	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_10	P3	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_11	M_PP_n	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_12	PreP3_mRNA	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_13	P3mRNA	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_14	P3_c	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_15	pP3_c	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_16	M_n	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_17	M_P_n	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_18	P3_n	compartment_0	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟

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

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

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

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

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

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

5.4 Function definition `function_4_7_1`

Name function_4_7_1

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

Mathematical Expression

$$\frac{\frac{\mathrm{k7}\cdot[\mathrm{species\_4}]\cdot[\mathrm{species\_5}]}{\mathrm{K7}}}{1+\frac{[\mathrm{species\_5}]}{\mathrm{K7}}+\frac{[\mathrm{species\_6}]}{\mathrm{K7}}} \tag{4}$$

5.5 Function definition function_4_8_1

Name function_4_8_1

Arguments K8, k8, [species_4], [species_5], [species_6]

Mathematical Expression

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

5.6 Function definition function_4_2_1

Name function_4_2_1

Arguments K2, k2, [species_1], [species_8]

Mathematical Expression

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

5.7 Function definition function_4_5_1

Name function_4_5_1

Arguments K5, k5, [species_3], [species_4], [species_9]

Mathematical Expression

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

5.8 Function definition function_4_6_1

Name function_4_6_1

Arguments K6, k6, [species_3], [species_4], [species_9]

Mathematical Expression

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

5.9 Function definition function_4_9_1

Name function_4_9_1

Arguments K9, k9, [species_10], [species_6], [species_7]

Mathematical Expression

$$\frac{\frac{\text{k9} \cdot [\text{species\_10}] \cdot [\text{species\_7}]}{\text{K9}}}{1 + \frac{[\text{species\_7}]}{\text{K9}} + \frac{[\text{species\_6}]}{\text{K9}}} \tag{9}$$

5.10 Function definition function_4_10_1

Name function_4_10_1

Arguments K10, k10, [species_10], [species_6], [species_7]

Mathematical Expression

$$\frac{\frac{\text{k10} \cdot [\text{species\_10}] \cdot [\text{species\_6}]}{\text{K10}}}{1 + \frac{[\text{species\_7}]}{\text{K10}} + \frac{[\text{species\_6}]}{\text{K10}}} \tag{10}$$

5.11 Function definition function_1

Name 11

Arguments k11f, ppERK_c, k11b, ppERK_n

Mathematical Expression

$$\text{k11f} \cdot \text{ppERK\_c} - \text{k11b} \cdot \text{ppERK\_n} \tag{11}$$

5.12 Function definition function_2

Name 12

Arguments V12, n12, K12, M_PP_n

Mathematical Expression

$$\frac{\text{V12} \cdot \text{M\_PP\_n}^{\text{n12}}}{\text{K12}^{\text{n12}} + \text{M\_PP\_n}^{\text{n12}}} \tag{12}$$

5.13 Function definition function_3

Name 15

Arguments k15, P3mRNA

Mathematical Expression

$$\text{k15} \cdot \text{P3mRNA} \tag{13}$$

5.14 Function definition function_4

Name 21

Arguments M_PP_n, M_P_n, P3_n, k21, K21, K21i

Mathematical Expression

$$\frac{\frac{\text{k21}\cdot\text{P3\_n}\cdot\text{M\_PP\_n}}{\text{K21}}}{1+\frac{\text{M\_PP\_n}}{\text{K21}}+\frac{\text{M\_P\_n}}{\text{K21i}}} \tag{14}$$

5.15 Function definition function_5

Name 22

Arguments P3_n, M_P_n, M_PP_n, k22, K22, K22i

Mathematical Expression

$$\frac{\frac{\text{k22}\cdot\text{P3\_n}\cdot\text{M\_P\_n}}{\text{K22}}}{1+\frac{\text{M\_P\_n}}{\text{K22}}+\frac{\text{M\_PP\_n}}{\text{K22i}}} \tag{15}$$

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

№	Id	Name	Reaction Equation	SBO
1	reaction_0	1	$\text{species\_0} \xrightarrow{\text{species\_7, species\_0, species\_7, species\_0, species\_7}} \text{species\_1}$	
2	reaction_1	3	$\text{species\_2} \xrightarrow{\text{species\_1, species\_3, species\_7, species\_1, species\_2, species\_3, species\_7, sp}}$	
3	reaction_2	4	$\text{species\_3} \xrightarrow{\text{species\_1, species\_2, species\_7, species\_1, species\_2, species\_3, species\_7, sp}}$	
4	reaction_3	7	$\text{species\_5} \xrightarrow{\text{species\_4, species\_6, species\_4, species\_5, species\_6, species\_4, species\_5, sp}}$	
5	reaction_4	8	$\text{species\_6} \xrightarrow{\text{species\_4, species\_5, species\_4, species\_5, species\_6, species\_4, species\_5, sp}}$	
6	reaction_5	2	$\text{species\_1} \xrightarrow{\text{species\_8, species\_1, species\_8, species\_1, species\_8}} \text{species\_0}$	
7	reaction_6	5	$\text{species\_4} \xrightarrow{\text{species\_9, species\_3, species\_3, species\_4, species\_9, species\_3, species\_4, sp}}$	
8	reaction_7	6	$\text{species\_3} \xrightarrow{\text{species\_9, species\_4, species\_3, species\_4, species\_9, species\_3, species\_4, sp}}$	
9	reaction_8	9	$\text{species\_7} \xrightarrow{\text{species\_10, species\_6, species\_5, species\_10, species\_6, species\_7, species\_10}}$	
10	reaction_9	10	$\text{species\_6} \xrightarrow{\text{species\_10, species\_7, species\_5, species\_10, species\_6, species\_7, species\_10}}$	
11	reaction_10	11	$\text{species\_7} \xrightleftharpoons{\text{species\_7, species\_11, species\_7, species\_11}} \text{species\_11}$	
12	reaction_11	12	$\emptyset \xrightarrow{\text{species\_11, species\_11, species\_11}} \text{species\_12}$	
13	reaction_12	13	$\text{species\_12} \xrightarrow{\text{species\_12, species\_12}} \text{species\_13}$	
14	reaction_13	14	$\text{species\_13} \xrightarrow{\text{species\_13, species\_13}} \emptyset$	
15	reaction_14	15	$\emptyset \xrightarrow{\text{species\_13, species\_13, species\_13}} \text{species\_14}$	

№	Id	Name	Reaction Equation	SBO
16	reaction_15	17	$\mathrm{species\_14} \xrightarrow{\mathrm{species\_14,\ species\_14}} \emptyset$	
17	reaction_16	19	$\mathrm{species\_5} \xrightleftharpoons{\mathrm{species\_5,\ species\_16,\ species\_5,\ species\_16}} \mathrm{species\_16}$	
18	reaction_17	20	$\mathrm{species\_6} \xrightleftharpoons{\mathrm{species\_6,\ species\_17,\ species\_6,\ species\_17}} \mathrm{species\_17}$	
19	reaction_18	16	$\mathrm{species\_14} \xrightleftharpoons{\mathrm{species\_14,\ species\_18,\ species\_14,\ species\_18}} \mathrm{species\_18}$	
20	reaction_19	21	$\mathrm{species\_11} \xrightarrow{\mathrm{species\_17,\ species\_18,\ species\_11,\ species\_17,\ species\_18,\ species\_11,\ spec}$	
21	reaction_20	22	$\mathrm{species\_17} \xrightarrow{\mathrm{species\_18,\ species\_11,\ species\_18,\ species\_17,\ species\_11,\ species\_18,\ spec}$	
22	reaction_21	18	$\mathrm{species\_18} \xrightarrow{\mathrm{species\_18,\ species\_18}} \emptyset$	

6.1 Reaction `reaction_0`

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

Name 1

Reaction equation

$$\text{species\_0} \xrightarrow{\text{species\_7, species\_0, species\_7, species\_0, species\_7}} \text{species\_1} \tag{16}$$

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

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

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

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

Table 8: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K1	K1		20.0		☑
KI	KI		9.0		☑
V1	V1		2.5		☑

6.2 Reaction reaction_1

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

Name 3

Reaction equation

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

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

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

$$\mathrm{function\_4\_3\_1}\,(\mathrm{A}, \mathrm{K3}, \mathrm{Ka}, \mathrm{k3}, [\mathrm{species\_1}], [\mathrm{species\_2}], [\mathrm{species\_3}], [\mathrm{species\_7}]) = \frac{\frac{\mathrm{k3} \cdot [\mathrm{species\_1}] \cdot [\mathrm{species\_2}]}{\mathrm{K3}}}{1 + \frac{[\mathrm{species\_2}]}{\mathrm{K3}} + \frac{[\mathrm{species\_3}]}{\mathrm{K3}}} \cdot \frac{1 + \frac{\mathrm{A} \cdot [\mathrm{species\_7}]}{\mathrm{Ka}}}{1 + \frac{[\mathrm{species\_7}]}{\mathrm{Ka}}} \tag{22}$$

$$\mathrm{function\_4\_3\_1}\,(\mathrm{A}, \mathrm{K3}, \mathrm{Ka}, \mathrm{k3}, [\mathrm{species\_1}], [\mathrm{species\_2}], [\mathrm{species\_3}], [\mathrm{species\_7}]) = \frac{\frac{\mathrm{k3} \cdot [\mathrm{species\_1}] \cdot [\mathrm{species\_2}]}{\mathrm{K3}}}{1 + \frac{[\mathrm{species\_2}]}{\mathrm{K3}} + \frac{[\mathrm{species\_3}]}{\mathrm{K3}}} \cdot \frac{1 + \frac{\mathrm{A} \cdot [\mathrm{species\_7}]}{\mathrm{Ka}}}{1 + \frac{[\mathrm{species\_7}]}{\mathrm{Ka}}} \tag{23}$$

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

$$\text{species\_3} \xrightarrow{\text{species\_1, species\_2, species\_7, species\_1, species\_2, species\_3, species\_7, species\_1, species\_2, species\_3,}} \tag{24}$$

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

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

$$\mathrm{function\_4\_4\_1}\left(\mathrm{A}, \mathrm{K4}, \mathrm{Ka}, \mathrm{k4}, [\mathrm{species\_1}], [\mathrm{species\_2}], [\mathrm{species\_3}], [\mathrm{species\_7}]\right) = \frac{\frac{\mathrm{k4} \cdot [\mathrm{species\_1}] \cdot [\mathrm{species\_3}]}{\mathrm{K4}}}{1 + \frac{[\mathrm{species\_3}]}{\mathrm{K4}} + \frac{[\mathrm{species\_2}]}{\mathrm{K4}}} \cdot \frac{1 + \frac{\mathrm{A} \cdot [\mathrm{species\_7}]}{\mathrm{Ka}}}{1 + \frac{[\mathrm{species\_7}]}{\mathrm{Ka}}} \tag{26}$$

$$\mathrm{function\_4\_4\_1}\left(\mathrm{A}, \mathrm{K4}, \mathrm{Ka}, \mathrm{k4}, [\mathrm{species\_1}], [\mathrm{species\_2}], [\mathrm{species\_3}], [\mathrm{species\_7}]\right) = \frac{\frac{\mathrm{k4} \cdot [\mathrm{species\_1}] \cdot [\mathrm{species\_3}]}{\mathrm{K4}}}{1 + \frac{[\mathrm{species\_3}]}{\mathrm{K4}} + \frac{[\mathrm{species\_2}]}{\mathrm{K4}}} \cdot \frac{1 + \frac{\mathrm{A} \cdot [\mathrm{species\_7}]}{\mathrm{Ka}}}{1 + \frac{[\mathrm{species\_7}]}{\mathrm{Ka}}} \tag{27}$$

Table 16: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
A	A		10.0		☑
K4	K4		20.0		☑
Ka	Ka		500.0		☑
k4	k4		0.1		☑

6.4 Reaction reaction_3

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

Name 7

Reaction equation

$$\mathrm{species\_5} \xrightarrow{\mathrm{species\_4},\ \mathrm{species\_6},\ \mathrm{species\_4},\ \mathrm{species\_5},\ \mathrm{species\_6},\ \mathrm{species\_4},\ \mathrm{species\_5},\ \mathrm{species\_6}} \mathrm{species\_6} \tag{28}$$

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

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

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

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

Table 20: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K7	K7		20.0		☑
k7	k7		0.1		☑

6.5 Reaction reaction_4

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

Name 8

Reaction equation

$$\text{species\_6} \xrightarrow{\text{species\_4, species\_5, species\_4, species\_5, species\_6, species\_4, species\_5, species\_6}} \text{species\_7} \quad (32)$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
species_6	M_P	

Modifiers

Table 22: Properties of each modifier.

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

Product

Table 23: Properties of each product.

Id	Name	SBO
species_7	M_PP	

Kinetic Law

Derived unit contains undeclared units

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

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

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

Table 24: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K8	K8		20.0		☑
k8	k8		0.1		☑

6.6 Reaction reaction_5

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

Name 2

Reaction equation

$$\mathrm{species\_1} \xrightarrow{\mathrm{species\_8,\ species\_1,\ species\_8,\ species\_1,\ species\_8}} \mathrm{species\_0} \quad (36)$$

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

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

$$\mathrm{function\_4\_2\_1}\left(\mathrm{K2}, \mathrm{k2}, [\mathrm{species\_1}], [\mathrm{species\_8}]\right) = \frac{\frac{\mathrm{k2} \cdot [\mathrm{species\_8}] \cdot [\mathrm{species\_1}]}{\mathrm{K2}}}{1 + \frac{[\mathrm{species\_1}]}{\mathrm{K2}}} \tag{38}$$

$$\mathrm{function\_4\_2\_1}\left(\mathrm{K2}, \mathrm{k2}, [\mathrm{species\_1}], [\mathrm{species\_8}]\right) = \frac{\frac{\mathrm{k2} \cdot [\mathrm{species\_8}] \cdot [\mathrm{species\_1}]}{\mathrm{K2}}}{1 + \frac{[\mathrm{species\_1}]}{\mathrm{K2}}} \tag{39}$$

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

$$\text{species\_4} \xrightarrow{\text{species\_9, species\_3, species\_3, species\_4, species\_9, species\_3, species\_4, species\_9}} \text{species\_3} \quad (40)$$

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

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

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

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

Table 32: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K5	K5		200.0		☑
k5	k5		0.1		☑

6.8 Reaction reaction_7

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

Name 6

Reaction equation

$$\mathrm{species\_3} \xrightarrow{\mathrm{species\_9},\ \mathrm{species\_4},\ \mathrm{species\_3},\ \mathrm{species\_4},\ \mathrm{species\_9},\ \mathrm{species\_3},\ \mathrm{species\_4},\ \mathrm{species\_9}} \mathrm{species\_2} \quad (44)$$

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

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

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

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

Table 36: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K6	K6		200.0		☑
k6	k6		0.1		☑

6.9 Reaction reaction_8

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

Name 9

Reaction equation

$$\text{species\_7} \xrightarrow{\text{species\_10, species\_6, species\_5, species\_10, species\_6, species\_7, species\_10, species\_6, species\_7}} \text{species} \tag{48}$$

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

$$v_9 = \text{vol}\left(\text{compartment\_0}\right) \cdot \text{function\_4\_9\_1}\left(\text{K9}, \text{k9}, [\text{species\_10}], [\text{species\_6}], [\text{species\_7}]\right) \tag{49}$$

$$\text{function\_4\_9\_1}\left(\text{K9}, \text{k9}, [\text{species\_10}], [\text{species\_6}], [\text{species\_7}]\right) = \frac{\frac{\text{k9} \cdot [\text{species\_10}] \cdot [\text{species\_7}]}{\text{K9}}}{1 + \frac{[\text{species\_7}]}{\text{K9}} + \frac{[\text{species\_6}]}{\text{K9}}} \tag{50}$$

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

Table 40: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K9	K9		200.0		☑
k9	k9		0.1		☑

6.10 Reaction reaction_9

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

Name 10

Reaction equation

$$\text{species\_6} \xrightarrow{\text{species\_10, species\_7, species\_5, species\_10, species\_6, species\_7, species\_10, species\_6, species\_7}} \text{species} \quad (52)$$

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

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

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

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

Table 44: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K10	K10		200.0		☑
k10	k10		0.1		☑

6.11 Reaction reaction_10

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

Name 11

Reaction equation

$$\mathrm{species\_7} \underset{\mathrm{species\_7},\ \mathrm{species\_11},\ \mathrm{species\_7},\ \mathrm{species\_11}}{\rightleftharpoons} \mathrm{species\_11} \tag{56}$$

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

$$v_{11} = \mathrm{vol}\left(\mathrm{compartment\_0}\right) \cdot \mathrm{function\_1}\left(\mathrm{k11f}, [\mathrm{species\_7}], \mathrm{k11b}, [\mathrm{species\_11}]\right) \quad (57)$$

$$\mathrm{function\_1}\left(\mathrm{k11f}, \mathrm{ppERK\_c}, \mathrm{k11b}, \mathrm{ppERK\_n}\right) = \mathrm{k11f} \cdot \mathrm{ppERK\_c} - \mathrm{k11b} \cdot \mathrm{ppERK\_n} \quad (58)$$

$$\mathrm{function\_1}\left(\mathrm{k11f}, \mathrm{ppERK\_c}, \mathrm{k11b}, \mathrm{ppERK\_n}\right) = \mathrm{k11f} \cdot \mathrm{ppERK\_c} - \mathrm{k11b} \cdot \mathrm{ppERK\_n} \quad (59)$$

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

$$\emptyset \xrightarrow{\text{species\_11, species\_11, species\_11}} \text{species\_12} \tag{60}$$

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

$$v_{12} = \text{vol}(\text{compartment\_0}) \cdot \text{function\_2}(\text{V12}, \text{n12}, \text{K12}, [\text{species\_11}]) \tag{61}$$

$$\text{function\_2}(\text{V12}, \text{n12}, \text{K12}, \text{M\_PP\_n}) = \frac{\text{V12} \cdot \text{M\_PP\_n}^{\text{n12}}}{\text{K12}^{\text{n12}} + \text{M\_PP\_n}^{\text{n12}}} \tag{62}$$

$$\text{function\_2}(\text{V12}, \text{n12}, \text{K12}, \text{M\_PP\_n}) = \frac{\text{V12} \cdot \text{M\_PP\_n}^{\text{n12}}}{\text{K12}^{\text{n12}} + \text{M\_PP\_n}^{\text{n12}}} \tag{63}$$

Table 51: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
V12	V12		29.24		☑
n12	n12		3.97		☑
K12	K12		169.00		☑

6.13 Reaction reaction_12

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

Name 13

Reaction equation

$$\text{species\_12} \xrightarrow{\text{species\_12, species\_12}} \text{species\_13} \tag{64}$$

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

$$v_{13} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot \mathrm{k1} \cdot [\mathrm{species\_12}] \tag{65}$$

Table 55: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.022		☑

6.14 Reaction reaction_13

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

Name 14

Reaction equation

$$\mathrm{species\_13} \xrightarrow{\mathrm{species\_13},\ \mathrm{species\_13}} \emptyset \tag{66}$$

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

$$v_{14} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot \mathrm{k1} \cdot [\mathrm{species\_13}] \tag{67}$$

Table 58: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.008		☑

6.15 Reaction reaction_14

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

Name 15

Reaction equation

$$\emptyset \xrightarrow{\text{species\_13, species\_13, species\_13}} \text{species\_14} \tag{68}$$

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

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

$$\text{function\_3}\left(\text{k15}, \text{P3mRNA}\right) = \text{k15} \cdot \text{P3mRNA} \tag{70}$$

$$\text{function\_3}\left(\text{k15}, \text{P3mRNA}\right) = \text{k15} \cdot \text{P3mRNA} \tag{71}$$

Table 61: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k15	k15		0.001		☑

6.16 Reaction reaction_15

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

Name 17

Reaction equation

$$\text{species\_14} \xrightarrow{\text{species\_14, species\_14}} \emptyset \tag{72}$$

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

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

Table 64: Properties of each parameter.

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

6.17 Reaction reaction_16

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

Name 19

Reaction equation

$$\text{species\_5} \xrightleftharpoons{\text{species\_5, species\_16, species\_5, species\_16}} \text{species\_16} \tag{74}$$

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

$$v_{17} = \text{vol}\left(\text{compartment\_0}\right) \cdot \left(\text{k1} \cdot [\text{species\_5}] - \text{k2} \cdot [\text{species\_16}]\right) \tag{75}$$

Table 68: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		10.34		☑
k2	k2		2.86		☑

6.18 Reaction reaction_17

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

Name 20

Reaction equation

$$\text{species\_6} \xrightleftharpoons{\text{species\_6, species\_17, species\_6, species\_17}} \text{species\_17} \tag{76}$$

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

$$v_{18} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_6}] - \mathrm{k2} \cdot [\mathrm{species\_17}]) \tag{77}$$

Table 72: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		10.34		☑
k2	k2		2.86		☑

6.19 Reaction reaction_18

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

Name 16

Reaction equation

$$\mathrm{species\_14} \xrightleftharpoons{\mathrm{species\_14},\ \mathrm{species\_18},\ \mathrm{species\_14},\ \mathrm{species\_18}} \mathrm{species\_18} \tag{78}$$

Reactant

Table 73: Properties of each reactant.

Id	Name	SBO
species_14	P3_c	

Modifiers

Table 74: Properties of each modifier.

Id	Name	SBO
species_14	P3_c	
species_18	P3_n	
species_14	P3_c	
species_18	P3_n	

Product

Table 75: Properties of each product.

Id	Name	SBO
species_18	P3_n	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \mathrm{vol}(\mathrm{compartment\_0}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_14}] - \mathrm{k2} \cdot [\mathrm{species\_18}]) \tag{79}$$

Table 76: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		22.56		☑
k2	k2		15.40		☑

6.20 Reaction reaction_19

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

Name 21

Reaction equation

$$\mathrm{species\_11} \xrightarrow{\mathrm{species\_17},\ \mathrm{species\_18},\ \mathrm{species\_11},\ \mathrm{species\_17},\ \mathrm{species\_18},\ \mathrm{species\_11},\ \mathrm{species\_17},\ \mathrm{species\_18}} \mathrm{species\_1}$$

(80)

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

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

$$\mathrm{function\_4}\left(\mathrm{M\_PP\_n}, \mathrm{M\_P\_n}, \mathrm{P3\_n}, \mathrm{k21}, \mathrm{K21}, \mathrm{K21i}\right) = \frac{\frac{\mathrm{k21} \cdot \mathrm{P3\_n} \cdot \mathrm{M\_PP\_n}}{\mathrm{K21}}}{1 + \frac{\mathrm{M\_PP\_n}}{\mathrm{K21}} + \frac{\mathrm{M\_P\_n}}{\mathrm{K21i}}} \tag{82}$$

$$\mathrm{function\_4}\left(\mathrm{M\_PP\_n}, \mathrm{M\_P\_n}, \mathrm{P3\_n}, \mathrm{k21}, \mathrm{K21}, \mathrm{K21i}\right) = \frac{\frac{\mathrm{k21} \cdot \mathrm{P3\_n} \cdot \mathrm{M\_PP\_n}}{\mathrm{K21}}}{1 + \frac{\mathrm{M\_PP\_n}}{\mathrm{K21}} + \frac{\mathrm{M\_P\_n}}{\mathrm{K21i}}} \tag{83}$$

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

$$\text{species\_17} \xrightarrow{\text{species\_18, species\_11, species\_18, species\_17, species\_11, species\_18, species\_17, species\_11}} \text{species\_1}$$

(84)

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

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

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

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

Table 84: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k22	k22		0.31		☑
K22	K22		87.00		☑
K22i	K22i		10300.00		☑

6.22 Reaction reaction_21

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

Name 18

Reaction equation

$$\text{species\_18} \xrightarrow{\text{species\_18, species\_18}} \emptyset \tag{88}$$

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

$$v_{22} = \mathrm{vol}\,(\mathrm{compartment\_0}) \cdot \mathrm{k1} \cdot [\mathrm{species\_18}] \tag{89}$$

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 $999.999903688753\ \mathrm{nmol} \cdot \mathrm{ml}^{-1}$

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_0} = v_6 - v_1 \tag{90}$$

7.2 Species species_1

Name MKKK_P

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_1} = v_1 - v_6 \tag{91}$$

7.3 Species species_2

Name MKK

Initial concentration 3999.99961475501 $\mathrm{nmol \cdot ml^{-1}}$

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_2} = v_8 - v_2 \tag{92}$$

7.4 Species species_3

Name MKK_P

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_3} = v_2 + v_7 - v_3 - v_8 \tag{93}$$

7.5 Species species_4

Name MKK_PP

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_4} = v_3 - v_7 \tag{94}$$

7.6 Species species_5

Name M

Initial concentration 999.999903688753 $\mathrm{nmol} \cdot \mathrm{ml}^{-1}$

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_5} = v_{10} - v_4 - v_{17} \tag{95}$$

7.7 Species species_6

Name M_P

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

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_8, reaction_8, reaction_8, reaction_9, reaction_9, reaction_17, reaction_17).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_6} = v_4 + v_9 - v_5 - v_{10} - v_{18} \tag{96}$$

7.8 Species species_7

Name M_PP

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_7} = v_5 - v_9 - v_{11} \tag{97}$$

7.9 Species species_8

Name P1

Initial concentration 99.9999903688752 $\mathrm{nmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a modifier in reaction_5, reaction_5, reaction_5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_8} = 0 \tag{98}$$

7.10 Species species_9

Name P2

Initial concentration 499.999951844377 $\mathrm{nmol} \cdot \mathrm{ml}^{-1}$

This species takes part in six reactions (as a modifier in reaction_6, reaction_6, reaction_6, reaction_7, reaction_7, reaction_7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_9} = 0 \tag{99}$$

7.11 Species species_10

Name P3

Initial concentration 499.999975922188 $\mathrm{nmol} \cdot \mathrm{ml}^{-1}$

This species takes part in six reactions (as a modifier in reaction_8, reaction_8, reaction_8, reaction_9, reaction_9, reaction_9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_10} = 0 \tag{100}$$

7.12 Species species_11

Name M_PP_n

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_11} = v_{11} - v_{20} \tag{101}$$

7.13 Species species_12

Name PreP3_mRNA

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_12} = v_{12} - v_{13} \tag{102}$$

7.14 Species species_13

Name P3mRNA

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_13} = v_{13} - v_{14} \tag{103}$$

7.15 Species species_14

Name P3_c

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_14} = v_{15} - v_{16} - v_{19} \tag{104}$$

7.16 Species species_15

Name pP3_c

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_15} = 0 \tag{105}$$

7.17 Species species_16

Name M_n

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

This species takes part in four reactions (as a product in reaction_16, reaction_20 and as a modifier in reaction_16, reaction_16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_16} = v_{17} + v_{21} \tag{106}$$

7.18 Species species_17

Name M_P_n

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_17} = v_{18} + v_{20} - v_{21} \tag{107}$$

7.19 Species species_18

Name P3_n

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_18} = v_{19} - v_{22} \tag{108}$$

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