SBML Model Report

Model name: "Sarma2012 - Interaction topologies of MAPK cascade (M4_K2_QSS_USEQ)"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah[1] and Uddipan Sarma[2] at November 23rd 2012 at 4:17 p. m. and last time modified at May 30th 2014 at 6:21 p. m. Table 1 gives an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	2
species types	0	species	11
events	0	constraints	0
reactions	10	function definitions	10
global parameters	14	unit definitions	2
rules	0	initial assignments	0

Model Notes

Sarma2012 - Interaction topologies of MAPK cascade (M4_K2_QSS_USEQ)

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The paper presents the various interaction topologies between the kinases and phosphatases of MAPK cascade. They are represented as M1, M2, M3 and M4. The kinases of the cascades are MKKK, MKK and MK, and Phos1, Phos2 and Phos3 are phosphatases of the system. All three kinases in a M1 type network have specific phosphatases Phos1, Phos2 and Phos3 for the dephosphorylation process. In a M2 type system, kinases MKKK and MKK are dephosphorylated by Phos1 and MK is dephosphorylated by Phos2. The architecture of system like M3 is such that MKKK gets dephosphorylated by Phos1, whereas Phos2 dephosphorylates both MKK and MK. Finally, the MAPK cascade exhibiting more complex design of interaction such as M4 is such that MKKK and MKK are dephosphorylated by Phos1 whereas MKK and MK are dephosphorylated by Phos2. In addition, as it is plausible that the kinases can sequester their respective phosphatases by binding to them, this is considered in the design of the systems (PSEQ-sequestrated system; USEQ-Unsequestrated system). The robustness of different interaction designs of the systems is checked, considering both MichaelisMenten type kinetics (K1) and elementary mass action kinetics (K2). In the living systems, the MAPK cascade transmit both short and long duration signals where short duration signals trigger proliferation and long duration signals trigger cell differentiation. These signal variants are considered to interpret the systems behaviour. It is also tested how the robustness and signal response behaviour of K2 models are affected when K2 assumes quasi steady state (QSS). The combinations of the above variants resulted in 40 models (MODEL1204280001-MODEL1204280040). All these 40 models are available from BioModels Database .

Models that correspond to type M4 with mass-action kinetics K2, in four condition 1) USEQ [MODEL1204280020 - M4_K2_USEQ], 2) PSEQ [MODEL1204280024 - M4_K2_PSEQ], 3) QSS_USEQ [MODEL1204280036 - M4_K2_QSS_USEQ] and 4) QSS_PSEQ [MODEL1204280040 - M4_K2_QSS_PSEQ] are available from the curated branch. The remaining 36 models can be accessed from the non-curated branch.

This model [MODEL1204280036 - M4_K2_QSS_USEQ] correspond to type M4 with mass-action kinetics K2, in QSS (quasi steady state) and USEQ (Unsequestrated) condition. .

This model is described in the article:Different designs of kinase-phosphatase interactions and phosphatase sequestration shapes the robustness and signal flow in the MAPK cascade.Sarma U, Ghosh I.BMC Syst Biol. 2012 Jul 2;6(1):82.

Abstract:

BACKGROUND: The three layer mitogen activated protein kinase (MAPK) signaling cascade exhibits different designs of interactions between its kinases and phosphatases. While the sequential interactions between the three kinases of the cascade are tightly preserved, the phosphatases of the cascade, such as MKP3 and PP2A, exhibit relatively diverse interactions with their substrate kinases. Additionally, the kinases of the MAPK cascade can also sequester their phosphatases. Thus, each topologically distinct interaction design of kinases and phosphatases could exhibit unique signal processing characteristics, and the presence of phosphatase sequestration may lead to further fine tuning of the propagated signal.

RESULTS: We have built four models of the MAPK cascade, each model with identical kinase-kinase interactions but unique kinases-phosphatases interactions. Our simulations unravelled that MAPK cascade's robustness to external perturbations is a function of nature of interaction between its kinases and phosphatases. The cascade's output robustness was enhanced when

phosphatases were sequestrated by their target kinases. We uncovered a novel implicit/hidden negative feedback loop from the phosphatase MKP3 to its upstream kinase Raf-1, in a cascade resembling the B cell MAPK cascade. Notably, strength of the feedback loop was reciprocal to the strength of phosphatases' sequestration and stronger sequestration abolished the feedback loop completely. An experimental method to verify the presence of the feedback loop is also proposed. We further showed, when the models were activated by transient signal, memory (total time taken by the cascade output to reach its unstimulated level after removal of signal) of a cascade was determined by the specific designs of interaction among its kinases and phosphatases.

CONCLUSIONS: Differences in interaction designs among the kinases and phosphatases can differentially shape the robustness and signal response behaviour of the MAPK cascade and phosphatase sequestration dramatically enhances the robustness to perturbations in each of the cascade. An implicit negative feedback loop was uncovered from our analysis and we found that strength of the negative feedback loop is reciprocally related to the strength of phosphatase sequestration. Duration of output phosphorylation in response to a transient signal was also found to be determined by the individual cascade's kinase-phosphatase interaction design.

This model is hosted on BioModels Database and identified by: MODEL1204280036 .

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^2

2.4 Unit `length`

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

Definition m

2.5 Unit `time`

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

Definition s

3 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
compartment_1	compartment		3	1	litre	☑	
compartment_2	No Name		3	1	litre	☑	

3.1 Compartment `compartment_1`

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

Name compartment

3.2 Compartment `compartment_2`

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

Name No Name

4 Species

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

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
species_1	MKKK	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_2	MKKK_P	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_3	MKK	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_4	MKK_P	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_5	MKK_PP	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_6	MK	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_7	MK_P	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_8	MK_PP	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_9	P1	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_10	P2	compartment_1	$nmol \cdot ml^{-1}$	☐	☐
species_11	Sig	compartment_1	$nmol \cdot ml^{-1}$	☐	☐

5 Parameters

This model contains 14 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
parameter_1	K1		100.000		☑
parameter_2	K2a		54.300		☑
parameter_3	K3		50.500		☑
parameter_4	K4		500.000		☑
parameter_5	K5a		24.300		☑
parameter_6	K6a		108.600		☑
parameter_7	K7		50.500		☑
parameter_8	K8		500.000		☑
parameter_9	K9b		24.300		☑
parameter_10	K10b		108.600		☑
parameter_11	Kse1		$3 \cdot 10^{51}$		☑
parameter_12	Kse2		$3 \cdot 10^{51}$		☑
parameter_13	K5b		24.300		☑
parameter_14	K6b		108.600		☑

6 Function definitions

This is an overview of ten function definitions.

6.1 Function definition `function_10`

Name 10

Arguments MK_P, MKK_PP, MKK_P, MK_PP, MKK, MK, P2, K10b, K5b, K6b, Kse2, K9b, k10b

Mathematical Expression

$$\frac{\frac{\text{k10b} \cdot \text{P2} \cdot \text{MK\_P}}{\text{K10b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}} \quad (1)$$

6.2 Function definition `function_2`

Name 2

Arguments MKKK_P, MKKK, P1, MKK_PP, MKK_P, MKK, Kse1, K2a, K5a, K6a, k2a

Mathematical Expression

$$\frac{\frac{\text{k2a} \cdot \text{MKKK\_P} \cdot \text{P1}}{\text{K2a}}}{1 + \frac{\text{MKKK\_P}}{\text{K2a}} + \frac{\text{MKKK}}{\text{Kse1}} + \frac{\text{MKK\_PP}}{\text{K5a}} + \frac{\text{MKK\_P}}{\text{K6a}} + \frac{\text{MKK}}{\text{Kse1}}} \tag{2}$$

6.3 Function definition `function_3`

Name 3

Arguments k3, MKKK_P, MKK, K3, MKK_P, K4

Mathematical Expression

$$\frac{\frac{\text{k3} \cdot \text{MKKK\_P} \cdot \text{MKK}}{\text{K3}}}{1 + \frac{\text{MKK}}{\text{K3}} + \frac{\text{MKK\_P}}{\text{K4}}} \tag{3}$$

6.4 Function definition `function_6`

Name 6

Arguments P1, MKK_P, MKK_PP, MK_P, MK_PP, MKK, MK, k6a, K6a, MKKK, MKKK_P, P2, K6b, K2a, Kse1, K5a, k6b, K5b, Kse2, K10b, K9b

Mathematical Expression

$$\frac{\frac{\text{k6a} \cdot \text{P1} \cdot \text{MKK\_P}}{\text{K6a}}}{1 + \frac{\text{MKKK\_P}}{\text{K2a}} + \frac{\text{MKKK}}{\text{Kse1}} + \frac{\text{MKK\_PP}}{\text{K5a}} + \frac{\text{MKK\_P}}{\text{K6a}} + \frac{\text{MKK}}{\text{Kse1}}}$$
$$+ \frac{\frac{\text{k6b} \cdot \text{P2} \cdot \text{MKK\_P}}{\text{K6b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}} \tag{4}$$

6.5 Function definition `function_1`

Name 1

Arguments MKKK, K1, k1, Sig

Mathematical Expression

$$\frac{\text{k1} \cdot \text{Sig} \cdot \text{MKKK}}{\text{K1} + \text{MKKK}} \tag{5}$$

6.6 Function definition `function_4`

Name 4

Arguments k4, MKKK_P, MKK_P, K4, MKK, K3

Mathematical Expression

$$\frac{\frac{k4 \cdot MKKK\_P \cdot MKK\_P}{K4}}{1 + \frac{MKK}{K3} + \frac{MKK\_P}{K4}} \tag{6}$$

6.7 Function definition `function_5`

Name 5

Arguments MKK_PP, MKK_P, MK_P, MK_PP, P1, MKK, MK, k5a, K5a, MKKK, MKKK_P, k5b, P2, K5b, K6a, Kse1, K2a, K6b, Kse2, K10b, K9b

Mathematical Expression

$$\frac{\frac{k5a \cdot P1 \cdot MKK\_PP}{K5a}}{1 + \frac{MKKK\_P}{K2a} + \frac{MKKK}{Kse1} + \frac{MKK\_PP}{K5a} + \frac{MKK\_P}{K6a} + \frac{MKK}{Kse1}} \\ + \frac{\frac{k5b \cdot P2 \cdot MKK\_PP}{K5b}}{1 + \frac{MKK\_PP}{K5b} + \frac{MKK\_P}{K6b} + \frac{MKK}{Kse2} + \frac{MK}{Kse2} + \frac{MK\_P}{K10b} + \frac{MK\_PP}{K9b}} \tag{7}$$

6.8 Function definition `function_7`

Name 7

Arguments k7, MKK_PP, MK, K7, MK_P, K8

Mathematical Expression

$$\frac{\frac{k7 \cdot MKK\_PP \cdot MK}{K7}}{1 + \frac{MK}{K7} + \frac{MK\_P}{K8}} \tag{8}$$

6.9 Function definition `function_9`

Name 9

Arguments MK_PP, MKK_PP, MKK_P, MK_P, MKK, MK, P2, K9b, K5b, K6b, Kse2, K10b, k9b

Mathematical Expression

$$\frac{\frac{k9b \cdot P2 \cdot MK\_PP}{K9b}}{1 + \frac{MKK\_PP}{K5b} + \frac{MKK\_P}{K6b} + \frac{MKK}{Kse2} + \frac{MK}{Kse2} + \frac{MK\_P}{K10b} + \frac{MK\_PP}{K9b}} \tag{9}$$

6.10 Function definition `function_8`

Name 8

Arguments k7, MKK_PP, MK_P, K8, MK, K7

Mathematical Expression

$$\frac{\frac{k7 \cdot MKK\_PP \cdot MK\_P}{K8}}{1 + \frac{MK}{K7} + \frac{MK\_P}{K8}} \tag{10}$$

7 Reactions

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

Table 5: Overview of all reactions

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

7.1 Reaction `reaction_1`

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

Name 1

Reaction equation

$$\text{species\_1} \xrightarrow{\text{species\_11, species\_1, species\_11}} \text{species\_2} \tag{11}$$
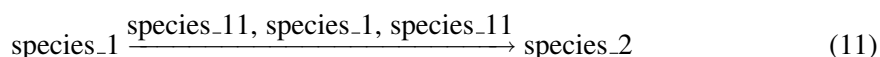
Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
species_1	MKKK	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
species_11	Sig	
species_1	MKKK	
species_11	Sig	

Product

Table 8: Properties of each product.

Id	Name	SBO
species_2	MKKK_P	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}\,(\text{compartment\_1}) \cdot \text{function\_1}\,([\text{species\_1}], \text{parameter\_1}, k1, [\text{species\_11}]) \tag{12}$$

$$\text{function\_1}\,(\text{MKKK}, \text{K1}, k1, \text{Sig}) = \frac{k1 \cdot \text{Sig} \cdot \text{MKKK}}{\text{K1} + \text{MKKK}} \tag{13}$$

$$\text{function\_1}(\text{MKKK}, \text{K1}, \text{k1}, \text{Sig}) = \frac{\text{k1} \cdot \text{Sig} \cdot \text{MKKK}}{\text{K1} + \text{MKKK}} \tag{14}$$

Table 9: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.0		☑

7.2 Reaction `reaction_2`

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

Name 2

Reaction equation

$$\text{species\_2} \; \frac{\text{species\_1, species\_9, species\_5, species\_4, species\_3, species\_2, species\_1, species\_9, species\_5, species\_4,}}{} \tag{15}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
species_2	MKKK_P	

Modifiers

Table 11: Properties of each modifier.

Id	Name	SBO
species_1	MKKK	
species_9	P1	
species_5	MKK_PP	
species_4	MKK_P	
species_3	MKK	
species_2	MKKK_P	
species_1	MKKK	
species_9	P1	
species_5	MKK_PP	

Produced by SBML2LATEX

Id	Name	SBO
species_4	MKK_P	
species_3	MKK	

Product

Table 12: Properties of each product.

Id	Name	SBO
species_1	MKKK	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}\,(\text{compartment\_1}) \cdot \text{function\_2}\,([\text{species\_2}], [\text{species\_1}], [\text{species\_9}], [\text{species\_5}], \\ [\text{species\_4}], [\text{species\_3}], \text{parameter\_11}, \text{parameter\_2}, \text{parameter\_5}, \text{parameter\_6}, \text{k2a}) \tag{16}$$

$$\text{function\_2}\,(\text{MKKK\_P}, \text{MKKK}, \text{P1}, \text{MKK\_PP}, \text{MKK\_P}, \text{MKK}, \text{Kse1}, \text{K2a}, \text{K5a}, \text{K6a}, \text{k2a}) \\ = \frac{\frac{\text{k2a} \cdot \text{MKKK\_P} \cdot \text{P1}}{\text{K2a}}}{1 + \frac{\text{MKKK\_P}}{\text{K2a}} + \frac{\text{MKKK}}{\text{Kse1}} + \frac{\text{MKK\_PP}}{\text{K5a}} + \frac{\text{MKK\_P}}{\text{K6a}} + \frac{\text{MKK}}{\text{Kse1}}} \tag{17}$$

$$\text{function\_2}\,(\text{MKKK\_P}, \text{MKKK}, \text{P1}, \text{MKK\_PP}, \text{MKK\_P}, \text{MKK}, \text{Kse1}, \text{K2a}, \text{K5a}, \text{K6a}, \text{k2a}) \\ = \frac{\frac{\text{k2a} \cdot \text{MKKK\_P} \cdot \text{P1}}{\text{K2a}}}{1 + \frac{\text{MKKK\_P}}{\text{K2a}} + \frac{\text{MKKK}}{\text{Kse1}} + \frac{\text{MKK\_PP}}{\text{K5a}} + \frac{\text{MKK\_P}}{\text{K6a}} + \frac{\text{MKK}}{\text{Kse1}}} \tag{18}$$

Table 13: Properties of each parameter.

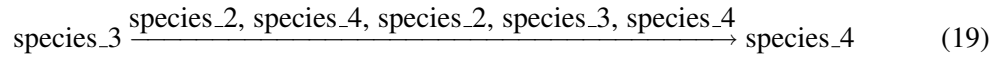| Id	Name	SBO	Value	Unit	Constant
k2a	k2a		0.086		☑

7.3 Reaction `reaction_3`

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

Name 3

Reaction equation

$$\text{species\_3} \xrightarrow{\text{species\_2, species\_4, species\_2, species\_3, species\_4}} \text{species\_4} \tag{19}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
species_3	MKK	

Modifiers

Table 15: Properties of each modifier.

Id	Name	SBO
species_2	MKKK_P	
species_4	MKK_P	
species_2	MKKK_P	
species_3	MKK	
species_4	MKK_P	

Product

Table 16: Properties of each product.

Id	Name	SBO
species_4	MKK_P	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{vol}\,(\text{compartment\_1})$$
$$\cdot \, \text{function\_3}\,(\text{k3}, [\text{species\_2}], [\text{species\_3}], \text{parameter\_3}, [\text{species\_4}], \text{parameter\_4}) \tag{20}$$

$$\text{function\_3}\,(\text{k3}, \text{MKKK\_P}, \text{MKK}, \text{K3}, \text{MKK\_P}, \text{K4}) = \frac{\frac{\text{k3}\cdot\text{MKKK\_P}\cdot\text{MKK}}{\text{K3}}}{1 + \frac{\text{MKK}}{\text{K3}} + \frac{\text{MKK\_P}}{\text{K4}}} \tag{21}$$

$$\text{function\_3}\,(\text{k3}, \text{MKKK\_P}, \text{MKK}, \text{K3}, \text{MKK\_P}, \text{K4}) = \frac{\frac{\text{k3}\cdot\text{MKKK\_P}\cdot\text{MKK}}{\text{K3}}}{1 + \frac{\text{MKK}}{\text{K3}} + \frac{\text{MKK\_P}}{\text{K4}}} \tag{22}$$
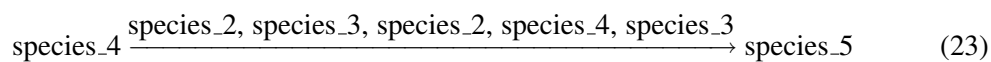
Table 17: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k3	k3		0.01		☑

7.4 Reaction `reaction_4`

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

Name 4

Reaction equation

$$\text{species\_4} \xrightarrow{\text{species\_2, species\_3, species\_2, species\_4, species\_3}} \text{species\_5} \qquad (23)$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
species_4	MKK_P	

Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
species_2	MKKK_P	
species_3	MKK	
species_2	MKKK_P	
species_4	MKK_P	
species_3	MKK	

Product

Table 20: Properties of each product.

Id	Name	SBO
species_5	MKK_PP	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}\,(\text{compartment\_1}) \\ \cdot \text{function\_4}\,(\text{k4}, [\text{species\_2}], [\text{species\_4}], \text{parameter\_4}, [\text{species\_3}], \text{parameter\_3}) \tag{24}$$

$$\text{function\_4}\,(\text{k4}, \text{MKKK\_P}, \text{MKK\_P}, \text{K4}, \text{MKK}, \text{K3}) = \frac{\frac{\text{k4}\cdot\text{MKKK\_P}\cdot\text{MKK\_P}}{\text{K4}}}{1 + \frac{\text{MKK}}{\text{K3}} + \frac{\text{MKK\_P}}{\text{K4}}} \tag{25}$$

$$\text{function\_4}\,(\text{k4}, \text{MKKK\_P}, \text{MKK\_P}, \text{K4}, \text{MKK}, \text{K3}) = \frac{\frac{\text{k4}\cdot\text{MKKK\_P}\cdot\text{MKK\_P}}{\text{K4}}}{1 + \frac{\text{MKK}}{\text{K3}} + \frac{\text{MKK\_P}}{\text{K4}}} \tag{26}$$

Table 21: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k4	k4		15.0		☑

7.5 Reaction `reaction_5`

This is an irreversible reaction of one reactant forming one product influenced by 19 modifiers.

Name 5

Reaction equation

$$\text{species\_5} \xrightarrow{\text{species\_4, species\_7, species\_8, species\_9, species\_3, species\_6, species\_1, species\_2, species\_10, species\_5}} \tag{27}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
species_5	MKK_PP	

Modifiers

Table 23: Properties of each modifier.

Id	Name	SBO
species_4	MKK_P	
species_7	MK_P	
species_8	MK_PP	
species_9	P1	
species_3	MKK	
species_6	MK	
species_1	MKKK	
species_2	MKKK_P	
species_10	P2	
species_5	MKK_PP	
species_4	MKK_P	
species_7	MK_P	
species_8	MK_PP	
species_9	P1	
species_3	MKK	
species_6	MK	
species_1	MKKK	
species_2	MKKK_P	
species_10	P2	

Product

Table 24: Properties of each product.

Id	Name	SBO
species_4	MKK_P	

Kinetic Law

Derived unit contains undeclared units

$$
\begin{aligned}
v_5 = \text{vol}\,(\text{compartment\_1}) \cdot \text{function\_5}\,([\text{species\_5}], [\text{species\_4}], [\text{species\_7}], [\text{species\_8}], \\
[\text{species\_9}], [\text{species\_3}], [\text{species\_6}], \text{k5a}, \text{parameter\_5}, [\text{species\_1}], [\text{species\_2}], \text{k5b}, \\
[\text{species\_10}], \text{parameter\_13}, \text{parameter\_6}, \text{parameter\_11}, \text{parameter\_2}, \text{parameter\_14}, \\
\text{parameter\_12}, \text{parameter\_10}, \text{parameter\_9})
\end{aligned} \tag{28}
$$

$$
\begin{aligned}
&\text{function\_5} \left(\text{MKK\_PP}, \text{MKK\_P}, \text{MK\_P}, \text{MK\_PP}, \text{P1}, \text{MKK}, \text{MK}, \text{k5a}, \right.\\
&\left. \text{K5a}, \text{MKKK}, \text{MKKK\_P}, \text{k5b}, \text{P2}, \text{K5b}, \text{K6a}, \text{Kse1}, \text{K2a}, \text{K6b}, \text{Kse2}, \right.\\
&\left. \text{K10b}, \text{K9b} \right) = \frac{\frac{\text{k5a} \cdot \text{P1} \cdot \text{MKK\_PP}}{\text{K5a}}}{1 + \frac{\text{MKKK\_P}}{\text{K2a}} + \frac{\text{MKKK}}{\text{Kse1}} + \frac{\text{MKK\_PP}}{\text{K5a}} + \frac{\text{MKK\_P}}{\text{K6a}} + \frac{\text{MKK}}{\text{Kse1}}} \\
&+ \frac{\frac{\text{k5b} \cdot \text{P2} \cdot \text{MKK\_PP}}{\text{K5b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}}
\end{aligned} \tag{29}
$$

$$
\begin{aligned}
&\text{function\_5} \left(\text{MKK\_PP}, \text{MKK\_P}, \text{MK\_P}, \text{MK\_PP}, \text{P1}, \text{MKK}, \text{MK}, \text{k5a}, \right.\\
&\left. \text{K5a}, \text{MKKK}, \text{MKKK\_P}, \text{k5b}, \text{P2}, \text{K5b}, \text{K6a}, \text{Kse1}, \text{K2a}, \text{K6b}, \text{Kse2}, \right.\\
&\left. \text{K10b}, \text{K9b} \right) = \frac{\frac{\text{k5a} \cdot \text{P1} \cdot \text{MKK\_PP}}{\text{K5a}}}{1 + \frac{\text{MKKK\_P}}{\text{K2a}} + \frac{\text{MKKK}}{\text{Kse1}} + \frac{\text{MKK\_PP}}{\text{K5a}} + \frac{\text{MKK\_P}}{\text{K6a}} + \frac{\text{MKK}}{\text{Kse1}}} \\
&+ \frac{\frac{\text{k5b} \cdot \text{P2} \cdot \text{MKK\_PP}}{\text{K5b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}}
\end{aligned} \tag{30}
$$

Table 25: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k5a	k5a		0.092		☑
k5b	k5b		0.092		☑

7.6 Reaction `reaction_6`

This is an irreversible reaction of one reactant forming one product influenced by 19 modifiers.

Name 6

Reaction equation

$$
\text{species\_4} \xrightarrow{\text{species\_9, species\_5, species\_7, species\_8, species\_3, species\_6, species\_1, species\_2, species\_10, species\_9}}
$$

$$\tag{31}$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
species_4	MKK_P	

Produced by SBML2LATEX

Modifiers

Table 27: Properties of each modifier.

Id	Name	SBO
species_9	P1	
species_5	MKK_PP	
species_7	MK_P	
species_8	MK_PP	
species_3	MKK	
species_6	MK	
species_1	MKKK	
species_2	MKKK_P	
species_10	P2	
species_9	P1	
species_4	MKK_P	
species_5	MKK_PP	
species_7	MK_P	
species_8	MK_PP	
species_3	MKK	
species_6	MK	
species_1	MKKK	
species_2	MKKK_P	
species_10	P2	

Product

Table 28: Properties of each product.

Id	Name	SBO
species_3	MKK	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{vol}(\text{compartment\_1}) \cdot \text{function\_6}([\text{species\_9}], [\text{species\_4}], [\text{species\_5}], [\text{species\_7}],$$
$$[\text{species\_8}], [\text{species\_3}], [\text{species\_6}], \text{k6a}, \text{parameter\_6}, [\text{species\_1}], [\text{species\_2}], [\text{species\_10}],$$
$$\text{parameter\_14}, \text{parameter\_2}, \text{parameter\_11}, \text{parameter\_5}, \text{k6b}, \text{parameter\_13}, \text{parameter\_12},$$
$$\text{parameter\_10}, \text{parameter\_9})$$
$$(32)$$

$$
\begin{aligned}
&\text{function\_6}\,(\text{P1}, \text{MKK\_P}, \text{MKK\_PP}, \text{MK\_P}, \text{MK\_PP}, \text{MKK}, \text{MK}, \text{k6a}, \\
&\text{K6a}, \text{MKKK}, \text{MKKK\_P}, \text{P2}, \text{K6b}, \text{K2a}, \text{Kse1}, \text{K5a}, \text{k6b}, \text{K5b}, \text{Kse2}, \\
&\text{K10b}, \text{K9b}) = \frac{\frac{\text{k6a}\cdot\text{P1}\cdot\text{MKK\_P}}{\text{K6a}}}{1 + \frac{\text{MKKK\_P}}{\text{K2a}} + \frac{\text{MKKK}}{\text{Kse1}} + \frac{\text{MKK\_PP}}{\text{K5a}} + \frac{\text{MKK\_P}}{\text{K6a}} + \frac{\text{MKK}}{\text{Kse1}}} \\
&\quad + \frac{\frac{\text{k6b}\cdot\text{P2}\cdot\text{MKK\_P}}{\text{K6b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}}
\end{aligned}
\tag{33}
$$

$$
\begin{aligned}
&\text{function\_6}\,(\text{P1}, \text{MKK\_P}, \text{MKK\_PP}, \text{MK\_P}, \text{MK\_PP}, \text{MKK}, \text{MK}, \text{k6a}, \\
&\text{K6a}, \text{MKKK}, \text{MKKK\_P}, \text{P2}, \text{K6b}, \text{K2a}, \text{Kse1}, \text{K5a}, \text{k6b}, \text{K5b}, \text{Kse2}, \\
&\text{K10b}, \text{K9b}) = \frac{\frac{\text{k6a}\cdot\text{P1}\cdot\text{MKK\_P}}{\text{K6a}}}{1 + \frac{\text{MKKK\_P}}{\text{K2a}} + \frac{\text{MKKK}}{\text{Kse1}} + \frac{\text{MKK\_PP}}{\text{K5a}} + \frac{\text{MKK\_P}}{\text{K6a}} + \frac{\text{MKK}}{\text{Kse1}}} \\
&\quad + \frac{\frac{\text{k6b}\cdot\text{P2}\cdot\text{MKK\_P}}{\text{K6b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}}
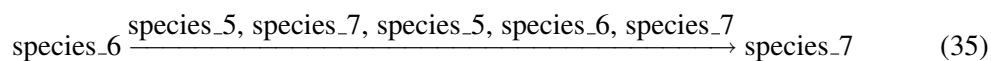\end{aligned}
\tag{34}
$$

Table 29: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k6a	k6a		0.086		☑
k6b	k6b		0.086		☑

7.7 Reaction `reaction_7`

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

Name 7

Reaction equation

$$
\text{species\_6} \xrightarrow{\text{species\_5, species\_7, species\_5, species\_6, species\_7}} \text{species\_7}
\tag{35}
$$

Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
species_6	MK	

Modifiers

Table 31: Properties of each modifier.

Id	Name	SBO
species_5	MKK_PP	
species_7	MK_P	
species_5	MKK_PP	
species_6	MK	
species_7	MK_P	

Product

Table 32: Properties of each product.

Id	Name	SBO
species_7	MK_P	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{vol}\,(\text{compartment\_1})$$
$$\cdot \text{function\_7}\,(\text{k7}, [\text{species\_5}], [\text{species\_6}], \text{parameter\_7}, [\text{species\_7}], \text{parameter\_8}) \tag{36}$$

$$\text{function\_7}\,(\text{k7}, \text{MKK\_PP}, \text{MK}, \text{K7}, \text{MK\_P}, \text{K8}) = \frac{\frac{\text{k7}\cdot\text{MKK\_PP}\cdot\text{MK}}{\text{K7}}}{1 + \frac{\text{MK}}{\text{K7}} + \frac{\text{MK\_P}}{\text{K8}}} \tag{37}$$

$$\text{function\_7}\,(\text{k7}, \text{MKK\_PP}, \text{MK}, \text{K7}, \text{MK\_P}, \text{K8}) = \frac{\frac{\text{k7}\cdot\text{MKK\_PP}\cdot\text{MK}}{\text{K7}}}{1 + \frac{\text{MK}}{\text{K7}} + \frac{\text{MK\_P}}{\text{K8}}} \tag{38}$$

Table 33: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k7	k7		0.01		☑

7.8 Reaction `reaction_8`

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

Name 8

Reaction equation

$$\text{species\_7} \xrightarrow{\text{species\_5, species\_6, species\_5, species\_7, species\_6}} \text{species\_8} \qquad (39)$$
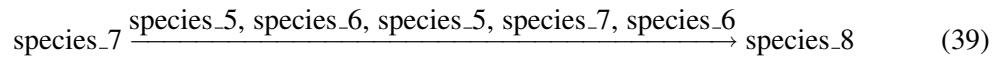
Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
species_7	MK_P	

Modifiers

Table 35: Properties of each modifier.

Id	Name	SBO
species_5	MKK_PP	
species_6	MK	
species_5	MKK_PP	
species_7	MK_P	
species_6	MK	

Product

Table 36: Properties of each product.

Id	Name	SBO
species_8	MK_PP	

Kinetic Law

Derived unit contains undeclared units

$$
\begin{aligned}
v_8 = {}& \text{vol}\,(\text{compartment\_1}) \\
& \cdot \text{function\_8}\,(k7, [\text{species\_5}], [\text{species\_7}], \text{parameter\_8}, [\text{species\_6}], \text{parameter\_7})
\end{aligned}
\qquad (40)
$$

$$\text{function\_8}\left(\text{k7}, \text{MKK\_PP}, \text{MK\_P}, \text{K8}, \text{MK}, \text{K7}\right) = \frac{\frac{\text{k7}\cdot\text{MKK\_PP}\cdot\text{MK\_P}}{\text{K8}}}{1 + \frac{\text{MK}}{\text{K7}} + \frac{\text{MK\_P}}{\text{K8}}} \tag{41}$$

$$\text{function\_8}\left(\text{k7}, \text{MKK\_PP}, \text{MK\_P}, \text{K8}, \text{MK}, \text{K7}\right) = \frac{\frac{\text{k7}\cdot\text{MKK\_PP}\cdot\text{MK\_P}}{\text{K8}}}{1 + \frac{\text{MK}}{\text{K7}} + \frac{\text{MK\_P}}{\text{K8}}} \tag{42}$$

Table 37: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k7	k7		15.0		☑

7.9 Reaction `reaction_9`

This is an irreversible reaction of one reactant forming one product influenced by 13 modifiers.

Name 9

Reaction equation

$$\text{species\_8} \, \frac{\text{species\_9, species\_4, species\_7, species\_3, species\_6, species\_10, species\_8, species\_9, species\_4, species\_7}}{}$$

$$\tag{43}$$

Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
species_8	MK_PP	

Modifiers

Table 39: Properties of each modifier.

Id	Name	SBO
species_9	P1	
species_4	MKK_P	
species_7	MK_P	
species_3	MKK	
species_6	MK	
species_10	P2	

Id	Name	SBO
species_8	MK_PP	
species_9	P1	
species_4	MKK_P	
species_7	MK_P	
species_3	MKK	
species_6	MK	
species_10	P2	

Product

Table 40: Properties of each product.

Id	Name	SBO
species_7	MK_P	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{vol}\,(\text{compartment\_1})$$
$$\cdot \text{function\_9}\,([\text{species\_8}], [\text{species\_9}], [\text{species\_4}], [\text{species\_7}], [\text{species\_3}], [\text{species\_6}],$$
$$[\text{species\_10}], \text{parameter\_9}, \text{parameter\_13}, \text{parameter\_14}, \text{parameter\_12}, \text{parameter\_10}, \text{k9b})$$

(44)

$$\text{function\_9}\,(\text{MK\_PP}, \text{MKK\_PP}, \text{MKK\_P}, \text{MK\_P}, \text{MKK}, \text{MK}, \text{P2}, \text{K9b}, \text{K5b}, \text{K6b},$$
$$\text{Kse2}, \text{K10b}, \text{k9b}) = \frac{\frac{\text{k9b}\cdot\text{P2}\cdot\text{MK\_PP}}{\text{K9b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}}$$

(45)

$$\text{function\_9}\,(\text{MK\_PP}, \text{MKK\_PP}, \text{MKK\_P}, \text{MK\_P}, \text{MKK}, \text{MK}, \text{P2}, \text{K9b}, \text{K5b}, \text{K6b},$$
$$\text{Kse2}, \text{K10b}, \text{k9b}) = \frac{\frac{\text{k9b}\cdot\text{P2}\cdot\text{MK\_PP}}{\text{K9b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}}$$

(46)

Table 41: Properties of each parameter.

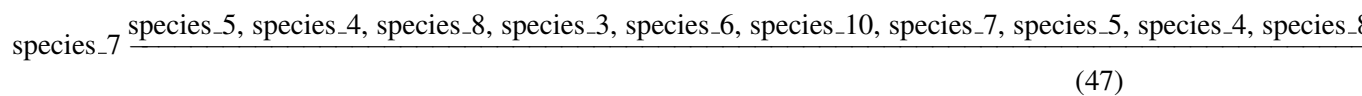| Id	Name	SBO	Value	Unit	Constant
k9b	k9b		0.092		☑

7.10 Reaction `reaction_10`

This is an irreversible reaction of one reactant forming one product influenced by 13 modifiers.

Name 10

Reaction equation

$$\text{species\_7} \xrightarrow{\text{species\_5, species\_4, species\_8, species\_3, species\_6, species\_10, species\_7, species\_5, species\_4, species\_8}}$$

(47)

Reactant

Table 42: Properties of each reactant.

Id	Name	SBO
species_7	MK_P	

Modifiers

Table 43: Properties of each modifier.

Id	Name	SBO
species_5	MKK_PP	
species_4	MKK_P	
species_8	MK_PP	
species_3	MKK	
species_6	MK	
species_10	P2	
species_7	MK_P	
species_5	MKK_PP	
species_4	MKK_P	
species_8	MK_PP	
species_3	MKK	
species_6	MK	
species_10	P2	

Product

Table 44: Properties of each product.

Id	Name	SBO
species_6	MK	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{vol}\,(\text{compartment\_1}) \cdot \text{function\_10}\,([\text{species\_7}], [\text{species\_5}], [\text{species\_4}], [\text{species\_8}],$$
$$[\text{species\_3}], [\text{species\_6}], [\text{species\_10}], \text{parameter\_10}, \text{parameter\_13}, \text{parameter\_14}, \quad (48)$$
$$\text{parameter\_12}, \text{parameter\_9}, \text{k10b})$$

$$\text{function\_10}\,(\text{MK\_P}, \text{MKK\_PP}, \text{MKK\_P}, \text{MK\_PP}, \text{MKK}, \text{MK}, \text{P2}, \text{K10b}, \text{K5b}, \text{K6b},$$
$$\text{Kse2}, \text{K9b}, \text{k10b}) = \frac{\frac{\text{k10b} \cdot \text{P2} \cdot \text{MK\_P}}{\text{K10b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}} \quad (49)$$

$$\text{function\_10}\,(\text{MK\_P}, \text{MKK\_PP}, \text{MKK\_P}, \text{MK\_PP}, \text{MKK}, \text{MK}, \text{P2}, \text{K10b}, \text{K5b}, \text{K6b},$$
$$\text{Kse2}, \text{K9b}, \text{k10b}) = \frac{\frac{\text{k10b} \cdot \text{P2} \cdot \text{MK\_P}}{\text{K10b}}}{1 + \frac{\text{MKK\_PP}}{\text{K5b}} + \frac{\text{MKK\_P}}{\text{K6b}} + \frac{\text{MKK}}{\text{Kse2}} + \frac{\text{MK}}{\text{Kse2}} + \frac{\text{MK\_P}}{\text{K10b}} + \frac{\text{MK\_PP}}{\text{K9b}}} \quad (50)$$

Table 45: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k10b	k10b		0.086		☑

8 Derived Rate Equations

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rates of change of each species.

Identifiers for kinetic laws highlighted in `gray` cannot be verified to evaluate to units of SBML `substance` per `time`. As a result, some SBML interpreters may not be able to verify the consistency of the units on quantities in the model. Please check if

- parameters without an unit definition are involved or

- volume correction is necessary because the `hasOnlySubstanceUnits` flag may be set to `false` and `spacialDimensions` > 0 for certain species.

8.1 Species `species_1`

Name MKKK

Initial concentration $300 \, \text{nmol} \cdot \text{ml}^{-1}$

This species takes part in nine reactions (as a reactant in `reaction_1` and as a product in `reaction_2` and as a modifier in `reaction_1`, `reaction_2`, `reaction_2`, `reaction_5`, `reaction_5`, `reaction_6`, `reaction_6`).

$$\frac{\text{d}}{\text{d}t}\text{species\_1} = v_2 - v_1 \tag{51}$$

8.2 Species `species_2`

Name MKKK_P

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

This species takes part in eleven reactions (as a reactant in `reaction_2` and as a product in `reaction_1` and as a modifier in `reaction_2`, `reaction_3`, `reaction_3`, `reaction_4`, `reaction_4`, `reaction_5`, `reaction_5`, `reaction_6`, `reaction_6`).

$$\frac{\text{d}}{\text{d}t}\text{species\_2} = v_1 - v_2 \tag{52}$$

8.3 Species `species_3`

Name MKK

Initial concentration $1199.99994221325 \, \text{nmol} \cdot \text{ml}^{-1}$

This species takes part in 15 reactions (as a reactant in `reaction_3` and as a product in `reaction_6` and as a modifier in `reaction_2`, `reaction_2`, `reaction_3`, `reaction_4`, `reaction_4`, `reaction_5`, `reaction_5`, `reaction_6`, `reaction_6`, `reaction_9`, `reaction_9`, `reaction_10`, `reaction_10`).

$$\frac{\text{d}}{\text{d}t}\text{species\_3} = v_6 - v_3 \tag{53}$$

8.4 Species `species_4`

Name MKK_P

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

This species takes part in 16 reactions (as a reactant in `reaction_4`, `reaction_6` and as a product in `reaction_3`, `reaction_5` and as a modifier in `reaction_2`, `reaction_2`, `reaction_3`, `reaction_3`, `reaction_4`, `reaction_5`, `reaction_5`, `reaction_6`, `reaction_9`, `reaction_9`, `reaction_10`, `reaction_10`).

$$\frac{\text{d}}{\text{d}t}\text{species\_4} = v_3 + v_5 - v_4 - v_6 \tag{54}$$

8.5 Species `species_5`

Name MKK_PP

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

This species takes part in 13 reactions (as a reactant in `reaction_5` and as a product in `reaction_4` and as a modifier in `reaction_2`, `reaction_2`, `reaction_5`, `reaction_6`, `reaction_6`, `reaction_7`, `reaction_7`, `reaction_8`, `reaction_8`, `reaction_10`, `reaction_10`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_5} = v_4 - v_5 \tag{55}$$

8.6 Species `species_6`

Name MK

Initial concentration $1199.99994221325 \, \text{nmol} \cdot \text{ml}^{-1}$

This species takes part in 13 reactions (as a reactant in `reaction_7` and as a product in `reaction_10` and as a modifier in `reaction_5`, `reaction_5`, `reaction_6`, `reaction_6`, `reaction_7`, `reaction_8`, `reaction_8`, `reaction_9`, `reaction_9`, `reaction_10`, `reaction_10`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_6} = v_{10} - v_7 \tag{56}$$

8.7 Species `species_7`

Name MK_P

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

This species takes part in 14 reactions (as a reactant in `reaction_8`, `reaction_10` and as a product in `reaction_7`, `reaction_9` and as a modifier in `reaction_5`, `reaction_5`, `reaction_6`, `reaction_6`, `reaction_7`, `reaction_7`, `reaction_8`, `reaction_9`, `reaction_9`, `reaction_10`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_7} = v_7 + v_9 - v_8 - v_{10} \tag{57}$$

8.8 Species `species_8`

Name MK_PP

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

This species takes part in nine reactions (as a reactant in `reaction_9` and as a product in `reaction_8` and as a modifier in `reaction_5`, `reaction_5`, `reaction_6`, `reaction_6`, `reaction_9`, `reaction_10`, `reaction_10`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_8} = v_8 - v_9 \tag{58}$$

8.9 Species `species_9`

Name P1

Initial concentration $100 \, \text{nmol} \cdot \text{ml}^{-1}$

This species takes part in eight reactions (as a modifier in `reaction_2`, `reaction_2`, `reaction-_5`, `reaction_5`, `reaction_6`, `reaction_6`, `reaction_9`, `reaction_9`).

$$\frac{\text{d}}{\text{d}t}\text{species\_9} = 0 \tag{59}$$

8.10 Species `species_10`

Name P2

Initial concentration $200 \, \text{nmol} \cdot \text{ml}^{-1}$

This species takes part in eight reactions (as a modifier in `reaction_5`, `reaction_5`, `reaction-_6`, `reaction_6`, `reaction_9`, `reaction_9`, `reaction_10`, `reaction_10`).

$$\frac{\text{d}}{\text{d}t}\text{species\_10} = 0 \tag{60}$$

8.11 Species `species_11`

Name Sig

Initial concentration $20 \, \text{nmol} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a modifier in `reaction_1`, `reaction_1`).

$$\frac{\text{d}}{\text{d}t}\text{species\_11} = 0 \tag{61}$$