SBML Model Report

Model name: “Sarma2012 - Interaction topologies of MAPK cascade (M4_K2_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 3:47 p. m. and last time modified at May 30th 2014 at 6:19 p. m. Table 1 shows 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	27
events	0	constraints	0
reactions	28	function definitions	0
global parameters	1	unit definitions	2
rules	0	initial assignments	0

Model Notes

Sarma2012 - Interaction topologies of MAPK cascade (M4_K2_USEQ)

[1]EMBL-EBI, viji@ebi.ac.uk
[2]National Centre for Cell Science, uddipans@gmail.com

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 (MODEL1204280001-40). 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 [MODEL1204280020 - M4_K2_USEQ] correspond to type M4 with mass-action kinetics K2, in 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: MODEL1204280020 .

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resource for 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_1	compartment		3	1	litre	☑	

3.1 Compartment compartment_1

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

Name compartment

4 Species

This model contains 27 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_1	MK	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_2	MKK-PP	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_3	MK_MKK-PP	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_4	MK-P	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_5	MK-P_MKK-PP	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_6	MK-PP	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_7	MKK	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_8	MKKK-P	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_9	MKK_MKKK-P	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_10	MKK-P	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_11	MKK-P_MKKK-P	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_12	MKK-PP_P2	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_13	P2	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_14	MKK-P_P2	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_15	MKK_P2	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_16	MKKK	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_17	MKKK_Sig	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_18	Sig	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_19	MKKK-P_P1	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_20	P1	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_21	MK-PP_P2	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟
species_22	MK-P_P2	compartment_1	$\mathrm{nmol \cdot ml^{-1}}$	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
species_23	MK_P2	compartment_1	$\mathrm{nmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_24	MKK-PP_P1	compartment_1	$\mathrm{nmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_25	MKK-P_P1	compartment_1	$\mathrm{nmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_26	MKK_P1	compartment_1	$\mathrm{nmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
species_27	MKKK_P1	compartment_1	$\mathrm{nmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟

5 Parameter

This model contains one global parameter.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
parameter_1	quantity_1		0.0		☑

6 Reactions

This model contains 28 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	15	$\text{species\_1} + \text{species\_2} \overset{\text{species\_1, species\_2, species\_3}}{\rightleftharpoons} \text{species\_3}$	
2	reaction_2	16	$\text{species\_3} \xrightarrow{\text{species\_3}} \text{species\_4} + \text{species\_2}$	
3	reaction_3	17	$\text{species\_4} + \text{species\_2} \overset{\text{species\_4, species\_2, species\_5}}{\rightleftharpoons} \text{species\_5}$	
4	reaction_4	18	$\text{species\_5} \xrightarrow{\text{species\_5}} \text{species\_6} + \text{species\_2}$	
5	reaction_5	19	$\text{species\_6} + \text{species\_13} \overset{\text{species\_6, species\_13, species\_21}}{\rightleftharpoons} \text{species\_21}$	
6	reaction_6	20	$\text{species\_21} \xrightarrow{\text{species\_21}} \text{species\_4} + \text{species\_13}$	
7	reaction_7	21	$\text{species\_4} + \text{species\_13} \overset{\text{species\_4, species\_13, species\_22}}{\rightleftharpoons} \text{species\_22}$	
8	reaction_8	22	$\text{species\_22} \xrightarrow{\text{species\_22}} \text{species\_1} + \text{species\_13}$	
9	reaction_9	23	$\text{species\_23} \overset{\text{species\_23, species\_1, species\_13}}{\rightleftharpoons} \text{species\_1} + \text{species\_13}$	
10	reaction_10	6	$\text{species\_7} + \text{species\_8} \overset{\text{species\_7, species\_8, species\_9}}{\rightleftharpoons} \text{species\_9}$	
11	reaction_11	7	$\text{species\_9} \xrightarrow{\text{species\_9}} \text{species\_10} + \text{species\_8}$	
12	reaction_12	8	$\text{species\_10} + \text{species\_8} \overset{\text{species\_10, species\_8, species\_11}}{\rightleftharpoons} \text{species\_11}$	
13	reaction_13	9	$\text{species\_11} \xrightarrow{\text{species\_11}} \text{species\_2} + \text{species\_8}$	
14	reaction_14	10_P2	$\text{species\_2} + \text{species\_13} \overset{\text{species\_2, species\_13, species\_12}}{\rightleftharpoons} \text{species\_12}$	

№	Id	Name	Reaction Equation	SBO
15	reaction_15	11_P2	$\text{species\_12} \xrightarrow{\text{species\_12}} \text{species\_10} + \text{species\_13}$	
16	reaction_16	12_P2	$\text{species\_10} + \text{species\_13} \xrightleftharpoons{\text{species\_10, species\_13, species\_14}} \text{species\_14}$	
17	reaction_17	13_P2	$\text{species\_14} \xrightarrow{\text{species\_14}} \text{species\_7} + \text{species\_13}$	
18	reaction_18	14_P2	$\text{species\_15} \xrightleftharpoons{\text{species\_15, species\_7, species\_13}} \text{species\_7} + \text{species\_13}$	
19	reaction_19	1	$\text{species\_16} + \text{species\_18} \xrightleftharpoons{\text{species\_16, species\_18, species\_17}} \text{species\_17}$	
20	reaction_20	2	$\text{species\_17} \xrightarrow{\text{species\_17}} \text{species\_8} + \text{species\_18}$	
21	reaction_21	3	$\text{species\_8} + \text{species\_20} \xrightleftharpoons{\text{species\_8, species\_20, species\_19}} \text{species\_19}$	
22	reaction_22	4	$\text{species\_19} \xrightarrow{\text{species\_19}} \text{species\_16} + \text{species\_20}$	
23	reaction_23	10_P1	$\text{species\_2} + \text{species\_20} \xrightleftharpoons{\text{species\_2, species\_20, species\_24}} \text{species\_24}$	
24	reaction_25	11_P1	$\text{species\_24} \xrightarrow{\text{species\_24}} \text{species\_10} + \text{species\_20}$	
25	reaction_26	12_P1	$\text{species\_10} + \text{species\_20} \xrightleftharpoons{\text{species\_10, species\_20, species\_25}} \text{species\_25}$	
26	reaction_27	13_P1	$\text{species\_25} \xrightarrow{\text{species\_25}} \text{species\_7} + \text{species\_20}$	
27	reaction_28	14_P1	$\text{species\_26} \xrightleftharpoons{\text{species\_26, species\_7, species\_20}} \text{species\_7} + \text{species\_20}$	
28	reaction_24	5	$\text{species\_27} \xrightleftharpoons{\text{species\_27, species\_16, species\_20}} \text{species\_16} + \text{species\_20}$	

6.1 Reaction `reaction_1`

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

Name 15

Reaction equation

$$\text{species\_1} + \text{species\_2} \xrightleftharpoons{\text{species\_1, species\_2, species\_3}} \text{species\_3} \tag{1}$$

Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
`species_1`	MK	
`species_2`	MKK-PP	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
`species_1`	MK	
`species_2`	MKK-PP	
`species_3`	MK_MKK-PP	

Product

Table 8: Properties of each product.

Id	Name	SBO
`species_3`	MK_MKK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}\left(\text{compartment\_1}\right) \cdot \left(\text{k1} \cdot [\text{species\_1}] \cdot [\text{species\_2}] - \text{k2} \cdot [\text{species\_3}]\right) \tag{2}$$

Table 9: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.02		☑
k2	k2		1.00		☑

6.2 Reaction reaction_2

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

Name 16

Reaction equation

$$\text{species\_3} \xrightarrow{\text{species\_3}} \text{species\_4} + \text{species\_2} \tag{3}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
species_3	MK_MKK-PP	

Modifier

Table 11: Properties of each modifier.

Id	Name	SBO
species_3	MK_MKK-PP	

Products

Table 12: Properties of each product.

Id	Name	SBO
species_4	MK-P	
species_2	MKK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_3}] \tag{4}$$

Table 13: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.01		☑

6.3 Reaction reaction_3

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

Name 17

Reaction equation

$$\mathrm{species\_4} + \mathrm{species\_2} \xrightleftharpoons{\mathrm{species\_4,\ species\_2,\ species\_5}} \mathrm{species\_5} \tag{5}$$

Reactants

Table 14: Properties of each reactant.

Id	Name	SBO
species_4	MK-P	
species_2	MKK-PP	

Modifiers

Table 15: Properties of each modifier.

Id	Name	SBO
species_4	MK-P	
species_2	MKK-PP	
species_5	MK-P_MKK-PP	

Product

Table 16: Properties of each product.

Id	Name	SBO
species_5	MK-P_MKK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_4}] \cdot [\mathrm{species\_2}] - \mathrm{k2} \cdot [\mathrm{species\_5}]) \tag{6}$$

Table 17: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.032		☑
k2	k2		1.000		☑

6.4 Reaction reaction_4

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

Name 18

Reaction equation

$$\mathrm{species\_5} \xrightarrow{\mathrm{species\_5}} \mathrm{species\_6} + \mathrm{species\_2} \tag{7}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
species_5	MK-P_MKK-PP	

Modifier

Table 19: Properties of each modifier.

Id	Name	SBO
species_5	MK-P_MKK-PP	

Products

Table 20: Properties of each product.

Id	Name	SBO
species_6	MK-PP	
species_2	MKK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_5}] \tag{8}$$

Table 21: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		15.0		☑

6.5 Reaction reaction_5

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

Name 19

Reaction equation

$$\mathrm{species\_6} + \mathrm{species\_13} \xrightleftharpoons{\mathrm{species\_6,\ species\_13,\ species\_21}} \mathrm{species\_21} \tag{9}$$

Reactants

Table 22: Properties of each reactant.

Id	Name	SBO
species_6	MK-PP	
species_13	P2	

Modifiers

Table 23: Properties of each modifier.

Id	Name	SBO
species_6	MK-PP	

Id	Name	SBO
species_13	P2	
species_21	MK-PP_P2	

Product

Table 24: Properties of each product.

Id	Name	SBO
species_21	MK-PP_P2	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}(\text{compartment\_1}) \cdot (\text{k1} \cdot [\text{species\_6}] \cdot [\text{species\_13}] - \text{k2} \cdot [\text{species\_21}]) \quad (10)$$

Table 25: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.045		☑
k2	k2		1.000		☑

6.6 Reaction reaction_6

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

Name 20

Reaction equation

$$\text{species\_21} \xrightarrow{\text{species\_21}} \text{species\_4} + \text{species\_13} \quad (11)$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
species_21	MK-PP_P2	

Modifier

Table 27: Properties of each modifier.

Id	Name	SBO
species_21	MK-PP_P2	

Products

Table 28: Properties of each product.

Id	Name	SBO
species_4	MK-P	
species_13	P2	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_21}] \tag{12}$$

Table 29: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.092		☑

6.7 Reaction reaction_7

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

Name 21

Reaction equation

$$\mathrm{species\_4} + \mathrm{species\_13} \xrightleftharpoons{\mathrm{species\_4,\ species\_13,\ species\_22}} \mathrm{species\_22} \tag{13}$$

Reactants

Table 30: Properties of each reactant.

Id	Name	SBO
species_4	MK-P	
species_13	P2	

Modifiers

Table 31: Properties of each modifier.

Id	Name	SBO
species_4	MK-P	
species_13	P2	
species_22	MK-P_P2	

Product

Table 32: Properties of each product.

Id	Name	SBO
species_22	MK-P_P2	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_4}] \cdot [\mathrm{species\_13}] - \mathrm{k2} \cdot [\mathrm{species\_22}]) \qquad (14)$$

Table 33: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.01		☑
k2	k2		1.00		☑

6.8 Reaction reaction_8

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

Name 22

Reaction equation

$$\text{species\_22} \xrightarrow{\text{species\_22}} \text{species\_1} + \text{species\_13} \tag{15}$$

Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
species_22	MK-P_P2	

Modifier

Table 35: Properties of each modifier.

Id	Name	SBO
species_22	MK-P_P2	

Products

Table 36: Properties of each product.

Id	Name	SBO
species_1	MK	
species_13	P2	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{vol}\left(\text{compartment\_1}\right) \cdot \text{k1} \cdot [\text{species\_22}] \tag{16}$$

Table 37: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.086		☑

6.9 Reaction reaction_9

This is a reversible reaction of one reactant forming two products influenced by three modifiers.

Name 23

Reaction equation

$$\text{species\_23} \xrightleftharpoons{\text{species\_23, species\_1, species\_13}} \text{species\_1} + \text{species\_13} \tag{17}$$

Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
species_23	MK_P2	

Modifiers

Table 39: Properties of each modifier.

Id	Name	SBO
species_23	MK_P2	
species_1	MK	
species_13	P2	

Products

Table 40: Properties of each product.

Id	Name	SBO
species_1	MK	
species_13	P2	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{vol}(\text{compartment\_1}) \cdot (\text{k1} \cdot [\text{species\_23}] - \text{k2} \cdot [\text{species\_1}] \cdot [\text{species\_13}]) \tag{18}$$

Table 41: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.0		☑
k2	k2		0.0		☑

6.10 Reaction reaction_10

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

Name 6

Reaction equation

$$\text{species\_7} + \text{species\_8} \xrightleftharpoons{\text{species\_7, species\_8, species\_9}} \text{species\_9} \tag{19}$$

Reactants

Table 42: Properties of each reactant.

Id	Name	SBO
species_7	MKK	
species_8	MKKK-P	

Modifiers

Table 43: Properties of each modifier.

Id	Name	SBO
species_7	MKK	
species_8	MKKK-P	
species_9	MKK_MKKK-P	

Product

Table 44: Properties of each product.

Id	Name	SBO
species_9	MKK_MKKK-P	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_7}] \cdot [\mathrm{species\_8}] - \mathrm{k2} \cdot [\mathrm{species\_9}]) \qquad (20)$$

Table 45: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.02		☑
k2	k2		1.00		☑

6.11 Reaction reaction_11

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

Name 7

Reaction equation

$$\mathrm{species\_9} \xrightarrow{\mathrm{species\_9}} \mathrm{species\_10} + \mathrm{species\_8} \qquad (21)$$

Reactant

Table 46: Properties of each reactant.

Id	Name	SBO
species_9	MKK_MKKK-P	

Modifier

Table 47: Properties of each modifier.

Id	Name	SBO
species_9	MKK_MKKK-P	

Products

Table 48: Properties of each product.

Id	Name	SBO
species_10	MKK-P	
species_8	MKKK-P	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_9}] \tag{22}$$

Table 49: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.01		☑

6.12 Reaction reaction_12

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

Name 8

Reaction equation

$$\mathrm{species\_10} + \mathrm{species\_8} \xrightleftharpoons{\mathrm{species\_10},\ \mathrm{species\_8},\ \mathrm{species\_11}} \mathrm{species\_11} \tag{23}$$

Reactants

Table 50: Properties of each reactant.

Id	Name	SBO
species_10	MKK-P	
species_8	MKKK-P	

Modifiers

Table 51: Properties of each modifier.

Id	Name	SBO
species_10	MKK-P	

Id	Name	SBO
species_8	MKKK-P	
species_11	MKK-P_MKKK-P	

Product

Table 52: Properties of each product.

Id	Name	SBO
species_11	MKK-P_MKKK-P	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_10}] \cdot [\mathrm{species\_8}] - \mathrm{k2} \cdot [\mathrm{species\_11}]) \qquad (24)$$

Table 53: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.032		☑
k2	k2		1.000		☑

6.13 Reaction reaction_13

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

Name 9

Reaction equation

$$\mathrm{species\_11} \xrightarrow{\mathrm{species\_11}} \mathrm{species\_2} + \mathrm{species\_8} \qquad (25)$$

Reactant

Table 54: Properties of each reactant.

Id	Name	SBO
species_11	MKK-P_MKKK-P	

Modifier

Table 55: Properties of each modifier.

Id	Name	SBO
species_11	MKK-P_MKKK-P	

Products

Table 56: Properties of each product.

Id	Name	SBO
species_2	MKK-PP	
species_8	MKKK-P	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_11}] \tag{26}$$

Table 57: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		15.0		☑

6.14 Reaction reaction_14

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

Name 10_P2

Reaction equation

$$\mathrm{species\_2} + \mathrm{species\_13} \xrightleftharpoons{\mathrm{species\_2,\ species\_13,\ species\_12}} \mathrm{species\_12} \tag{27}$$

Reactants

Table 58: Properties of each reactant.

Id	Name	SBO
species_2	MKK-PP	
species_13	P2	

Modifiers

Table 59: Properties of each modifier.

Id	Name	SBO
species_2	MKK-PP	
species_13	P2	
species_12	MKK-PP_P2	

Product

Table 60: Properties of each product.

Id	Name	SBO
species_12	MKK-PP_P2	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_2}] \cdot [\mathrm{species\_13}] - \mathrm{k2} \cdot [\mathrm{species\_12}]) \qquad (28)$$

Table 61: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.045		☑
k2	k2		1.000		☑

6.15 Reaction reaction_15

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

Name 11_P2

Reaction equation

$$\text{species\_12} \xrightarrow{\text{species\_12}} \text{species\_10} + \text{species\_13} \tag{29}$$

Reactant

Table 62: Properties of each reactant.

Id	Name	SBO
species_12	MKK-PP_P2	

Modifier

Table 63: Properties of each modifier.

Id	Name	SBO
species_12	MKK-PP_P2	

Products

Table 64: Properties of each product.

Id	Name	SBO
species_10	MKK-P	
species_13	P2	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \text{vol}(\text{compartment\_1}) \cdot \text{k1} \cdot [\text{species\_12}] \tag{30}$$

Table 65: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.092		☑

6.16 Reaction reaction_16

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

Name 12_P2

Reaction equation

$$\text{species\_10} + \text{species\_13} \xrightleftharpoons{\text{species\_10, species\_13, species\_14}} \text{species\_14} \tag{31}$$

Reactants

Table 66: Properties of each reactant.

Id	Name	SBO
species_10	MKK-P	
species_13	P2	

Modifiers

Table 67: Properties of each modifier.

Id	Name	SBO
species_10	MKK-P	
species_13	P2	
species_14	MKK-P_P2	

Product

Table 68: Properties of each product.

Id	Name	SBO
species_14	MKK-P_P2	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \text{vol}\,(\text{compartment\_1}) \cdot (\text{k1} \cdot [\text{species\_10}] \cdot [\text{species\_13}] - \text{k2} \cdot [\text{species\_14}]) \tag{32}$$

Table 69: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.01		☑
k2	k2		1.00		☑

6.17 Reaction reaction_17

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

Name 13_P2

Reaction equation

$$\text{species\_14} \xrightarrow{\text{species\_14}} \text{species\_7} + \text{species\_13} \tag{33}$$

Reactant

Table 70: Properties of each reactant.

Id	Name	SBO
species_14	MKK-P_P2	

Modifier

Table 71: Properties of each modifier.

Id	Name	SBO
species_14	MKK-P_P2	

Products

Table 72: Properties of each product.

Id	Name	SBO
species_7	MKK	
species_13	P2	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_14}] \tag{34}$$

Table 73: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.086		☑

6.18 Reaction reaction_18

This is a reversible reaction of one reactant forming two products influenced by three modifiers.

Name 14_P2

Reaction equation

$$\mathrm{species\_15} \xrightleftharpoons{\mathrm{species\_15,\ species\_7,\ species\_13}} \mathrm{species\_7} + \mathrm{species\_13} \tag{35}$$

Reactant

Table 74: Properties of each reactant.

Id	Name	SBO
species_15	MKK_P2	

Modifiers

Table 75: Properties of each modifier.

Id	Name	SBO
species_15	MKK_P2	
species_7	MKK	
species_13	P2	

Products

Table 76: Properties of each product.

Id	Name	SBO
species_7	MKK	
species_13	P2	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_15}] - \mathrm{k2} \cdot [\mathrm{species\_7}] \cdot [\mathrm{species\_13}]) \qquad (36)$$

Table 77: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.0		☑
k2	k2		0.0		☑

6.19 Reaction reaction_19

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

Name 1

Reaction equation

$$\mathrm{species\_16} + \mathrm{species\_18} \underset{\leftarrow}{\overset{\mathrm{species\_16,\ species\_18,\ species\_17}}{\rightarrow}} \mathrm{species\_17} \qquad (37)$$

Reactants

Table 78: Properties of each reactant.

Id	Name	SBO
species_16	MKKK	
species_18	Sig	

Modifiers

Table 79: Properties of each modifier.

Id	Name	SBO
species_16	MKKK	
species_18	Sig	
species_17	MKKK_Sig	

Product

Table 80: Properties of each product.

Id	Name	SBO
species_17	MKKK_Sig	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_16}] \cdot [\mathrm{species\_18}] - \mathrm{k2} \cdot [\mathrm{species\_17}]) \quad (38)$$

Table 81: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.02		☑
k2	k2		1.00		☑

6.20 Reaction reaction_20

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

Name 2

Reaction equation

$$\mathrm{species\_17} \xrightarrow{\mathrm{species\_17}} \mathrm{species\_8} + \mathrm{species\_18} \quad (39)$$

Reactant

Table 82: Properties of each reactant.

Id	Name	SBO
species_17	MKKK_Sig	

Modifier

Table 83: Properties of each modifier.

Id	Name	SBO
species_17	MKKK_Sig	

Products

Table 84: Properties of each product.

Id	Name	SBO
species_8	MKKK-P	
species_18	Sig	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_17}] \tag{40}$$

Table 85: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.0		☑

6.21 Reaction reaction_21

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

Name 3

Reaction equation

$$\mathrm{species\_8} + \mathrm{species\_20} \xrightleftharpoons{\mathrm{species\_8},\ \mathrm{species\_20},\ \mathrm{species\_19}} \mathrm{species\_19} \tag{41}$$

Reactants

Table 86: Properties of each reactant.

Id	Name	SBO
species_8	MKKK-P	
species_20	P1	

Modifiers

Table 87: Properties of each modifier.

Id	Name	SBO
species_8	MKKK-P	
species_20	P1	
species_19	MKKK-P_P1	

Product

Table 88: Properties of each product.

Id	Name	SBO
species_19	MKKK-P_P1	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_8}] \cdot [\mathrm{species\_20}] - \mathrm{k2} \cdot [\mathrm{species\_19}]) \quad (42)$$

Table 89: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.02		☑
k2	k2		1.00		☑

6.22 Reaction reaction_22

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

Name 4

Reaction equation

$$\mathrm{species\_19} \xrightarrow{\mathrm{species\_19}} \mathrm{species\_16} + \mathrm{species\_20} \quad (43)$$

Reactant

Table 90: Properties of each reactant.

Id	Name	SBO
species_19	MKKK-P_P1	

Modifier

Table 91: Properties of each modifier.

Id	Name	SBO
species_19	MKKK-P_P1	

Products

Table 92: Properties of each product.

Id	Name	SBO
species_16	MKKK	
species_20	P1	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_19}] \tag{44}$$

Table 93: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.086		☑

6.23 Reaction reaction_23

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

Name 10_P1

Reaction equation

$$\mathrm{species\_2} + \mathrm{species\_20} \xrightleftharpoons{\mathrm{species\_2,\ species\_20,\ species\_24}} \mathrm{species\_24} \tag{45}$$

Reactants

Table 94: Properties of each reactant.

Id	Name	SBO
species_2	MKK-PP	
species_20	P1	

Modifiers

Table 95: Properties of each modifier.

Id	Name	SBO
species_2	MKK-PP	
species_20	P1	
species_24	MKK-PP_P1	

Product

Table 96: Properties of each product.

Id	Name	SBO
species_24	MKK-PP_P1	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_2}] \cdot [\mathrm{species\_20}] - \mathrm{k2} \cdot [\mathrm{species\_24}]) \qquad (46)$$

Table 97: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.045		☑
k2	k2		1.000		☑

6.24 Reaction reaction_25

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

Name 11_P1

Reaction equation

$$\text{species\_24} \xrightarrow{\text{species\_24}} \text{species\_10} + \text{species\_20} \tag{47}$$

Reactant

Table 98: Properties of each reactant.

Id	Name	SBO
species_24	MKK-PP_P1	

Modifier

Table 99: Properties of each modifier.

Id	Name	SBO
species_24	MKK-PP_P1	

Products

Table 100: Properties of each product.

Id	Name	SBO
species_10	MKK-P	
species_20	P1	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \text{vol}(\text{compartment\_1}) \cdot \text{k1} \cdot [\text{species\_24}] \tag{48}$$

Table 101: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.092		☑

6.25 Reaction reaction_26

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

Name 12_P1

Reaction equation

$$\text{species\_10} + \text{species\_20} \xrightleftharpoons{\text{species\_10, species\_20, species\_25}} \text{species\_25} \tag{49}$$

Reactants

Table 102: Properties of each reactant.

Id	Name	SBO
species_10	MKK-P	
species_20	P1	

Modifiers

Table 103: Properties of each modifier.

Id	Name	SBO
species_10	MKK-P	
species_20	P1	
species_25	MKK-P_P1	

Product

Table 104: Properties of each product.

Id	Name	SBO
species_25	MKK-P_P1	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \text{vol}\,(\text{compartment\_1}) \cdot (\text{k1} \cdot [\text{species\_10}] \cdot [\text{species\_20}] - \text{k2} \cdot [\text{species\_25}]) \tag{50}$$

Table 105: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.01		☑
k2	k2		1.00		☑

6.26 Reaction reaction_27

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

Name 13_P1

Reaction equation

$$\text{species\_25} \xrightarrow{\text{species\_25}} \text{species\_7} + \text{species\_20} \tag{51}$$

Reactant

Table 106: Properties of each reactant.

Id	Name	SBO
species_25	MKK-P_P1	

Modifier

Table 107: Properties of each modifier.

Id	Name	SBO
species_25	MKK-P_P1	

Products

Table 108: Properties of each product.

Id	Name	SBO
species_7	MKK	
species_20	P1	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot \mathrm{k1} \cdot [\mathrm{species\_25}] \tag{52}$$

Table 109: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.086		☑

6.27 Reaction reaction_28

This is a reversible reaction of one reactant forming two products influenced by three modifiers.

Name 14_P1

Reaction equation

$$\mathrm{species\_26} \xrightleftharpoons{\mathrm{species\_26,\ species\_7,\ species\_20}} \mathrm{species\_7} + \mathrm{species\_20} \tag{53}$$

Reactant

Table 110: Properties of each reactant.

Id	Name	SBO
species_26	MKK_P1	

Modifiers

Table 111: Properties of each modifier.

Id	Name	SBO
species_26	MKK_P1	
species_7	MKK	
species_20	P1	

Products

Table 112: Properties of each product.

Id	Name	SBO
species_7	MKK	
species_20	P1	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_26}] - \mathrm{k2} \cdot [\mathrm{species\_7}] \cdot [\mathrm{species\_20}]) \qquad (54)$$

Table 113: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.0		☑
k2	k2		0.0		☑

6.28 Reaction reaction_24

This is a reversible reaction of one reactant forming two products influenced by three modifiers.

Name 5

Reaction equation

$$\mathrm{species\_27} \xrightleftharpoons{\mathrm{species\_27,\ species\_16,\ species\_20}} \mathrm{species\_16} + \mathrm{species\_20} \qquad (55)$$

Reactant

Table 114: Properties of each reactant.

Id	Name	SBO
species_27	MKKK_P1	

Modifiers

Table 115: Properties of each modifier.

Id	Name	SBO
species_27	MKKK_P1	
species_16	MKKK	
species_20	P1	

Products

Table 116: Properties of each product.

Id	Name	SBO
species_16	MKKK	
species_20	P1	

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \mathrm{vol}\,(\mathrm{compartment\_1}) \cdot (\mathrm{k1} \cdot [\mathrm{species\_27}] - \mathrm{k2} \cdot [\mathrm{species\_16}] \cdot [\mathrm{species\_20}]) \quad (56)$$

Table 117: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.0		☑
k2	k2		0.0		☑

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_1

Name MK

Initial concentration $1200\ \mathrm{nmol} \cdot \mathrm{ml}^{-1}$

This species takes part in five reactions (as a reactant in reaction_1 and as a product in reaction_8, reaction_9 and as a modifier in reaction_1, reaction_9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_1} = v_8 + v_9 - v_1 \quad (57)$$

7.2 Species species_2

Name MKK-PP

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

This species takes part in eleven reactions (as a reactant in reaction_1, reaction_3, reaction_14, reaction_23 and as a product in reaction_2, reaction_4, reaction_13 and as a modifier in reaction_1, reaction_3, reaction_14, reaction_23).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_2} = v_2 + v_4 + v_{13} - v_1 - v_3 - v_{14} - v_{23} \tag{58}$$

7.3 Species species_3

Name MK_MKK-PP

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

This species takes part in four reactions (as a reactant in reaction_2 and as a product in reaction_1 and as a modifier in reaction_1, reaction_2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_3} = v_1 - v_2 \tag{59}$$

7.4 Species species_4

Name MK-P

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

This species takes part in six reactions (as a reactant in reaction_3, reaction_7 and as a product in reaction_2, reaction_6 and as a modifier in reaction_3, reaction_7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_4} = v_2 + v_6 - v_3 - v_7 \tag{60}$$

7.5 Species species_5

Name MK-P_MKK-PP

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

This species takes part in four reactions (as a reactant in reaction_4 and as a product in reaction_3 and as a modifier in reaction_3, reaction_4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_5} = v_3 - v_4 \tag{61}$$

7.6 Species species_6

Name MK-PP

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

This species takes part in three reactions (as a reactant in reaction_5 and as a product in reaction_4 and as a modifier in reaction_5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_6} = v_4 - v_5 \tag{62}$$

7.7 Species species_7

Name MKK

Initial concentration $1200\ \mathrm{nmol} \cdot \mathrm{ml}^{-1}$

This species takes part in eight reactions (as a reactant in reaction_10 and as a product in reaction_17, reaction_18, reaction_27, reaction_28 and as a modifier in reaction_10, reaction_18, reaction_28).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_7} = v_{17} + v_{18} + v_{26} + v_{27} - v_{10} \tag{63}$$

7.8 Species species_8

Name MKKK-P

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

This species takes part in nine reactions (as a reactant in reaction_10, reaction_12, reaction_21 and as a product in reaction_11, reaction_13, reaction_20 and as a modifier in reaction_10, reaction_12, reaction_21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_8} = v_{11} + v_{13} + v_{20} - v_{10} - v_{12} - v_{21} \tag{64}$$

7.9 Species species_9

Name MKK_MKKK-P

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

This species takes part in four reactions (as a reactant in reaction_11 and as a product in reaction_10 and as a modifier in reaction_10, reaction_11).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_9} = v_{10} - v_{11} \tag{65}$$

7.10 Species species_10

Name MKK-P

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

This species takes part in nine reactions (as a reactant in reaction_12, reaction_16, reaction_26 and as a product in reaction_11, reaction_15, reaction_25 and as a modifier in reaction_12, reaction_16, reaction_26).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_10} = v_{11} + v_{15} + v_{24} - v_{12} - v_{16} - v_{25} \tag{66}$$

7.11 Species species_11

Name MKK-P_MKKK-P

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

This species takes part in four reactions (as a reactant in reaction_13 and as a product in reaction_12 and as a modifier in reaction_12, reaction_13).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_11} = v_{12} - v_{13} \tag{67}$$

7.12 Species species_12

Name MKK-PP_P2

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

This species takes part in four reactions (as a reactant in reaction_15 and as a product in reaction_14 and as a modifier in reaction_14, reaction_15).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_12} = v_{14} - v_{15} \tag{68}$$

7.13 Species species_13

Name P2

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

This species takes part in 16 reactions (as a reactant in reaction_5, reaction_7, reaction_14, reaction_16 and as a product in reaction_6, reaction_8, reaction_9, reaction_15, reaction_17, reaction_18 and as a modifier in reaction_5, reaction_7, reaction_9, reaction_14, reaction_16, reaction_18).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_13} = v_{6} + v_{8} + v_{9} + v_{15} + v_{17} + v_{18} - v_{5} - v_{7} - v_{14} - v_{16} \tag{69}$$

7.14 Species species_14

Name MKK-P_P2

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

This species takes part in four reactions (as a reactant in reaction_17 and as a product in reaction_16 and as a modifier in reaction_16, reaction_17).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_14} = v_{16} - v_{17} \tag{70}$$

7.15 Species species_15

Name MKK_P2

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_15} = -v_{18} \tag{71}$$

7.16 Species species_16

Name MKKK

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

This species takes part in five reactions (as a reactant in reaction_19 and as a product in reaction_22, reaction_24 and as a modifier in reaction_19, reaction_24).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_16} = v_{22} + v_{28} - v_{19} \tag{72}$$

7.17 Species species_17

Name MKKK_Sig

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

This species takes part in four reactions (as a reactant in reaction_20 and as a product in reaction_19 and as a modifier in reaction_19, reaction_20).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_17} = v_{19} - v_{20} \tag{73}$$

7.18 Species species_18

Name Sig

Initial concentration $10\ \mathrm{nmol \cdot ml^{-1}}$

This species takes part in three reactions (as a reactant in reaction_19 and as a product in reaction_20 and as a modifier in reaction_19).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_18} = v_{20} - v_{19} \tag{74}$$

7.19 Species species_19

Name MKKK-P_P1

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

This species takes part in four reactions (as a reactant in reaction_22 and as a product in reaction_21 and as a modifier in reaction_21, reaction_22).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_19} = v_{21} - v_{22} \tag{75}$$

7.20 Species species_20

Name P1

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

This species takes part in 13 reactions (as a reactant in reaction_21, reaction_23, reaction_26 and as a product in reaction_22, reaction_25, reaction_27, reaction_28, reaction_24 and as a modifier in reaction_21, reaction_23, reaction_26, reaction_28, reaction_24).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_20} = v_{22} + v_{24} + v_{26} + v_{27} + v_{28} - v_{21} - v_{23} - v_{25} \tag{76}$$

7.21 Species species_21

Name MK-PP_P2

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

This species takes part in four reactions (as a reactant in reaction_6 and as a product in reaction_5 and as a modifier in reaction_5, reaction_6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_21} = v_{5} - v_{6} \tag{77}$$

7.22 Species species_22

Name MK-P_P2

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

This species takes part in four reactions (as a reactant in reaction_8 and as a product in reaction_7 and as a modifier in reaction_7, reaction_8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_22} = v_7 - v_8 \tag{78}$$

7.23 Species species_23

Name MK_P2

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_23} = -v_9 \tag{79}$$

7.24 Species species_24

Name MKK-PP_P1

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

This species takes part in four reactions (as a reactant in reaction_25 and as a product in reaction_23 and as a modifier in reaction_23, reaction_25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_24} = v_{23} - v_{24} \tag{80}$$

7.25 Species species_25

Name MKK-P_P1

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

This species takes part in four reactions (as a reactant in reaction_27 and as a product in reaction_26 and as a modifier in reaction_26, reaction_27).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_25} = v_{25} - v_{26} \tag{81}$$

7.26 Species species_26

Name MKK_P1

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

This species takes part in two reactions (as a reactant in reaction_28 and as a modifier in reaction_28).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_26} = -\ v_{27} \tag{82}$$

7.27 Species species_27

Name MKKK_P1

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_27} = -\ v_{28} \tag{83}$$

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

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany