SBML Model Report

Model name: "Levchenko2000_MAPK_noScaffold"



May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Bruce Shapiro¹ at February 15th 2005 at 0:12 a.m. and last time modified at June third 2013 at 1:36 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	22
events	0	constraints	0
reactions	30	function definitions	0
global parameters	0	unit definitions	1
rules	0	initial assignments	0

Model Notes

MAPK cascade in solution (no scaffold)

Description

¹NASA Jet Propulsion Laboratory, bshapiro@jpl.nasa.gov

This model describes a basic 3-stage Mitogen Activated Protein Kinase (MAPK) cascade in solution. This cascade is typically expressed as RAF==>MEK==>MAPK (alternative forms are K3==>K2==>K1 and KKK==>KK==>K). The input signal is RAFK (RAF Kinase) and the output signal is MAPKpp (doubly phosphorylated form of MAPK). RAFK phosphorylates RAF once to RAFp. RAFp, the phosphorylated form of RAF induces two phosphorylations of MEK, to MEKp and MEKpp. MEKpp, the doubly phosphorylated form of MEK, induces two phosphorylations of MAPK to MAPKp and MAPKpp.

Rateconstant	Reaction
a10=5.	MAPKPH+MAPKpp-
	>MAPKppMAPKPH
a1=1.	RAF+RAFK->RAFRAFK
a2=0.5	RAFp+RAFPH->RAFpRAFPH
a3=3.3	MEK+RAFp->MEKRAFp
a4=10.	MEKp+MEKPH->MEKpMEKPH
a5=3.3	MEKp+RAFp->MEKpRAFp
a6=10.	MEKPH+MEKpp->MEKppMEKPH
a7=20.	MAPK+MEKpp->MAPKMEKpp
a8=5.	MAPKp+MAPKPH->MAPKpMAPKPH
a9=20.	MAPKp+MEKpp->MAPKpMEKpp
d10=0.4	MAPKppMAPKPH-
	>MAPKPH+MAPKpp
d1=0.4	RAFRAFK->RAF+RAFK
d2=0.5	RAFpRAFPH->RAFp+RAFPH
d3=0.42	MEKRAFp->MEK+RAFp
d4=0.8	MEKpMEKPH->MEKp+MEKPH
d5=0.4	MEKpRAFp->MEKp+RAFp
d6=0.8	MEKppMEKPH->MEKPH+MEKpp
d7=0.6	MAPKMEKpp->MAPK+MEKpp
d8=0.4	MAPKpMAPKPH->MAPKp+MAPKPH
d9=0.6	MAPKpMEKpp->MAPKp+MEKpp
k10=0.1	MAPKppMAPKPH-
	>MAPKp+MAPKPH
k1=0.1	RAFRAFK->RAFK+RAFp
k2=0.1	RAFpRAFPH->RAF+RAFPH
k3=0.1	MEKRAFp->MEKp+RAFp
k4=0.1	MEKpMEKPH->MEK+MEKPH
k5=0.1	MEKpRAFp->MEKpp+RAFp
k6=0.1	MEKppMEKPH->MEKp+MEKPH
k7=0.1	MAPKMEKpp->MAPKp+MEKpp
k8=0.1	MAPKpMAPKPH->MAPK+MAPKPH

Variable	IC	ODE
MAPK	0.3	MAPK'[t] = d7*MAPKMEKpp[t] + k8*MAPKpMAPKpMAPKpMAPKpMAPKpMAPKpMAPKpMAPKp
		a7*MAPK[t]*MEKpp[t]
MAPKMEKpp	0	MAPKMEKpp'[t]==-
		(d7*MAPKMEKpp[t])-
		k7*MAPKMEKpp[t]+a7*MAPK[t]*MEKpp[t]
MAPKp	0	MAPKp'[t] == k7*MAPKMEKpp[t]-
		a8*MAPKp[t]*MAPKPH[t]+d8*MAPKpMAPKP
		a9*MAPKp[t]*MEKpp[t]
MAPKPH	0.3	MAPKPH'[t]==-
		(a8*MAPKp[t]*MAPKPH[t])+d8*MAPKpMAPK
		a10*MAPKPH[t]*MAPKpp[t]+d10*MAPKppMA
MAPKpMAPKPH	0	MAPKpMAPKPH'[t] == a8*MAPKp[t]*MAPKPH
1		d8*MAPKpMAPKPH[t]-
		k8*MAPKpMAPKPH[t]
MAPKpMEKpp	0	MAPKpMEKpp'[t]==-
1 11		(d9*MAPKpMEKpp[t])-
		k9*MAPKpMEKpp[t]+a9*MAPKp[t]*MEKpp[t]
MAPKpp	0	MAPKpp'[t]==k9*MAPKpMEKpp[t]-
11		a10*MAPKPH[t]*MAPKpp[t]+d10*MAPKppMA
MAPKppMAPKPH	0	MAPKppMAPKPH'[t]==a10*MAPKPH[t]*MAPI
11		d10*MAPKppMAPKPH[t]-
		k10*MAPKppMAPKPH[t]
MEK	0.2	MEK'[t]==k4*MEKpMEKPH[t]+d3*MEKRAFp[
		a3*MEK[t]*RAFp[t]
MEKp	0	MEKp'[t]==-
r		(a4*MEKp[t]*MEKPH[t])+d4*MEKpMEKPH[t]+
		a5*MEKp[t]*RAFp[t]
MEKPH	0.2	MEKPH'[t] = -
		(a4*MEKp[t]*MEKPH[t])+d4*MEKpMEKPH[t]+
		a6*MEKPH[t]*MEKpp[t]+d6*MEKppMEKPH[t]
MEKpMEKPH	0	MEKpMEKPH' $[t]$ ==a4*MEKp $[t]$ *MEKPH $[t]$ -
-	· ·	d4*MEKpMEKPH[t]-
		k4*MEKpMEKPH[t]
MEKpp	0	MEKpp'[t] == d7*MAPKMEKpp[t] + k7*MAPKME
rr	-	a7*MAPK[t]*MEKpp[t]-
		a9*MAPKp[t]*MEKpp[t]-
		a6*MEKPH[t]*MEKpp[t]+d6*MEKppMEKPH[t]-
		ao mining mininpp[t] too mininppminin ii[t]

MEKppMEKPH	0	MEKppMEKPH'[t] == a6*MEKPH[t]*MEKpp[t]-
		d6*MEKppMEKPH[t]-
		k6*MEKppMEKPH[t]
MEKpRAFp	0	MEKpRAFp'[t] ==
		(d5*MEKpRAFp[t])-
		k5*MEKpRAFp[t]+a5*MEKp[t]*RAFp[t]
MEKRAFp	0	MEKRAFp'[t] ==
		(d3*MEKRAFp[t])-
		k3*MEKRAFp[t]+a3*MEK[t]*RAFp[t]
RAF	0.4	RAF'[t]==-
		(a1*RAF[t]*RAFK[t])+k2*RAFpRAFPH[t]+d1*R
RAFK	0.1	RAFK'[t]==-
		(a1*RAF[t]*RAFK[t])+d1*RAFRAFK[t]+k1*RAF
RAFp	0	RAFp'[t] = d5*MEKpRAFp[t] + k5*MEKpRAFp[t]
		a3*MEK[t]*RAFp[t]-
		a5*MEKp[t]*RAFp[t]-
		a2*RAFp[t]*RAFPH[t]+d2*RAFpRAFPH[t]+k1*I
RAFPH	0.3	RAFPH'[t] ==-
		(a2*RAFp[t]*RAFPH[t])+d2*RAFpRAFPH[t]+k2
RAFpRAFPH	0	RAFpRAFPH'[t] == a2*RAFp[t]*RAFPH[t]-
_		d2*RAFpRAFPH[t]-
		k2*RAFpRAFPH[t]
RAFRAFK	0	RAFRAFK'[t] == a1*RAF[t]*RAFK[t]-
		d1*RAFRAFK[t]-
		k1*RAFRAFK[t]

Generated by Cellerator Version 1.4.3 (6-March-2004) using Mathematica 5.0 for Mac OS X (November 19, 2003), March 6, 2004 12:18:07, using (PowerMac,PowerPC,Mac OS X,MacOSX,Darwin) author=B.E.Shapiro

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To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler L, Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novre N, Laibe C (2010) BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

2 Unit Definitions

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

2.1 Unit substance

Name micromole

Definition µmol

2.2 Unit volume

Notes Litre is the predefined SBML unit for volume.

Definition 1

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 5: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
Cytoplasm			3	1	litre	Ø	

3.1 Compartment Cytoplasm

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

6

4 Species

This model contains 22 species. Section 6 provides further details and the derived rates of change of each species.

Table 6: Properties of each species.

		able 6: Properties of each species.		~	
Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
MAPK	MAPK	Cytoplasm	μmol		\Box
МАРКМЕКрр	MAPK_MEK-PP	Cytoplasm	μmol		
МАРКр	MAPK-P	Cytoplasm	μmol		
MAPKPH	MAPK phosphatase	Cytoplasm	μmol		\Box
МАРКрМАРКРН	MAPK-P_MAPKPase	Cytoplasm	μmol		\Box
МАРКрМЕКрр	MAPK-P_MEK-PP	Cytoplasm	μmol		
МАРКрр	MAPK-PP	Cytoplasm	μmol		
МАРКррМАРКРН	MAPK-PP_MAPKPase	Cytoplasm	μmol		\Box
MEK	MEK	Cytoplasm	μmol		\Box
МЕКр	MEK-P	Cytoplasm	μmol		\Box
MEKPH	MEK phosphatase	Cytoplasm	μmol		
МЕКрМЕКРН	MEK-P_MEKPase	Cytoplasm	μmol		
МЕКрр	MEK-PP	Cytoplasm	μmol		\Box
МЕКррМЕКРН	MEK-PP_MEKPase	Cytoplasm	μmol		
MEKpRAFp	MEK-P_RAF-P	Cytoplasm	μmol		\Box
MEKRAFp	MEK_RAF-P	Cytoplasm	μmol		\Box
RAF	RAF	Cytoplasm	μmol		
RAFK	RAFK	Cytoplasm	μmol		\Box
RAFp	RAF-P	Cytoplasm	μmol		\Box
RAFPH	RAF phosphatase	Cytoplasm	μmol		\Box
RAFpRAFPH	RAF-P_RAFPase	Cytoplasm	μmol		\Box
RAFRAFK	RAF_RAFK	Cytoplasm	μmol		

Id	Name	Compartment	Derived Unit	Constant	Boundary
					Condi-
					tion

5 Reactions

This model contains 30 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 7: Overview of all reactions

		Table 7. Overview of		~
Nº	Id	Name	Reaction Equation	SBO
1	Reaction1	binding of RAF and RAFK	$RAF + RAFK \longrightarrow RAFRAFK$	
2	Reaction2	dissociation of RAF_RAFK	$RAFRAFK \longrightarrow RAF + RAFK$	
3	Reaction3	phosphorylation of RAF	$RAFRAFK \longrightarrow RAFK + RAFp$	
4	Reaction4	binding of RAF-P and RAF phosphatase	$RAFp + RAFPH \longrightarrow RAFpRAFPH$	
5	Reaction5	dissociation of RAF-P_RAFPase	$RAFpRAFPH \longrightarrow RAFp + RAFPH$	
6	Reaction6	dephosphorylation of RAF-P	$RAFpRAFPH \longrightarrow RAF + RAFPH$	
7	Reaction7	binding of MEK and RAF-P	$MEK + RAFp \longrightarrow MEKRAFp$	
8	Reaction8	dissociation of MEK_RAF-P	$MEKRAFp \longrightarrow MEK + RAFp$	
9	Reaction9	phosphorylation of MEK	$MEKRAFp \longrightarrow MEKp + RAFp$	
10	Reaction10	binding of MEK-P and MEK phosphatase	$MEKp + MEKPH \longrightarrow MEKpMEKPH$	
11	Reaction11	dissociation of MEK-P_MEKPase	$MEKpMEKPH \longrightarrow MEKp + MEKPH$	
12	Reaction12	dephosphorylation of MEK-P	$MEKpMEKPH \longrightarrow MEK + MEKPH$	
13	Reaction13	binding of MEK-P and RAF-P	$MEKp + RAFp \longrightarrow MEKpRAFp$	
14	Reaction14	dissociation of MEK-P_RAF-P	$MEKpRAFp \longrightarrow MEKp + RAFp$	
15	Reaction15	phosphorylation of MEK-P	$MEKpRAFp \longrightarrow MEKpp + RAFp$	
16	Reaction16	binding of MEK-PP and MEK phosphatase	$MEKPH + MEKpp \longrightarrow MEKppMEKPH$	
17	Reaction17	dissociation of MEK-PP_MEKPase	$MEKppMEKPH \longrightarrow MEKPH + MEKpp$	
18	Reaction18	dephosphorylation of MEK-PP	$MEKppMEKPH \longrightarrow MEKp + MEKPH$	
19	Reaction19	binding of MAPK and MEK-PP	$MAPK + MEKpp \longrightarrow MAPKMEKpp$	
20	Reaction20	dissociation of MAPK_MEK-PP	$MAPKMEKpp \longrightarrow MAPK + MEKpp$	
21	Reaction21	phosphorylation of MAPK	$MAPKMEKpp \longrightarrow MAPKp + MEKpp$	
22	Reaction22	binding of MAPK-P and MAPK phosphatase	$MAPKp + MAPKPH \longrightarrow MAPKpMAPKPH$	
23	Reaction23	dissociation of MAPK-P_MAPKPase	$MAPKpMAPKPH \longrightarrow MAPKp + MAPKPH$	

No	Id	Name	Reaction Equation	SBO
24	Reaction24	dephosphorylation of MAPK-P	$MAPKpMAPKPH \longrightarrow MAPK + MAPKPH$	
25	Reaction25	binding of MAPK-P and MEK-PP	$MAPKp + MEKpp \longrightarrow MAPKpMEKpp$	
26	Reaction26	dissociation of MAPK-P_MEK-PP	$MAPKpMEKpp \longrightarrow MAPKp + MEKpp$	
27	Reaction27	phosphorylation of MAPK-P	$MAPKpMEKpp \longrightarrow MAPKpp + MEKpp$	
28	Reaction28	binding of MAPK-PP and MAPK phos-	$MAPKPH + MAPKpp \longrightarrow MAPKppMAPKPH$	
		phatase		
29	Reaction29	dissociation of MAPK-PP_MAPKPase	$MAPKppMAPKPH \longrightarrow MAPKPH + MAPKpp$	
30	Reaction30	dephosphorylation of MAPK-PP	$MAPKppMAPKPH \longrightarrow MAPKp + MAPKPH$	

5.1 Reaction Reaction1

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

Name binding of RAF and RAFK

Reaction equation

$$RAF + RAFK \longrightarrow RAFRAFK \tag{1}$$

Reactants

Table 8: Properties of each reactant.

Id	Name	SBO
RAF	RAF	
RAFK	RAFK	

Product

Table 9: Properties of each product.

	•	1
Id	Name	SBO
RAFRAFK	RAF_RAFK	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = a1 \cdot RAF \cdot RAFK \tag{2}$$

Table 10: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a1		1.0	

5.2 Reaction Reaction2

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

Name dissociation of RAF_RAFK

Reaction equation

$$RAFRAFK \longrightarrow RAF + RAFK \tag{3}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
RAFRAFK	RAF_RAFK	

Products

Table 12: Properties of each product.

Id	Name	SBO
RAF	RAF	
RAFK	RAFK	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = d1 \cdot RAFRAFK \tag{4}$$

Table 13: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
d1		0.4	

5.3 Reaction Reaction3

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

Name phosphorylation of RAF

Reaction equation

$$RAFRAFK \longrightarrow RAFK + RAFp \tag{5}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
RAFRAFK	RAF_RAFK	

Products

Table 15: Properties of each product.

Id	Name	SBO
RAFK	RAFK	
RAFp	RAF-P	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = k1 \cdot RAFRAFK \tag{6}$$

Table 16: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1		0.1	

5.4 Reaction Reaction4

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

Name binding of RAF-P and RAF phosphatase

Reaction equation

$$RAFp + RAFPH \longrightarrow RAFpRAFPH \tag{7}$$

Reactants

Table 17: Properties of each reactant.

	- I	
Id	Name	SBO
RAFPH	RAF-P RAF phosphatase	

Product

Table 18: Properties of each product.

Tueste Test Trepetities of euten products			
Id	Name	SBO	
RAFpRAFPH	RAF-P_RAFPase	_	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = a2 \cdot RAFp \cdot RAFPH \tag{8}$$

Table 19: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a2		0.5	

5.5 Reaction Reaction5

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

Name dissociation of RAF-P_RAFPase

Reaction equation

$$RAFpRAFPH \longrightarrow RAFp + RAFPH \tag{9}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
RAFpRAFPH	RAF-P_RAFPase	

Products

Table 21: Properties of each product.

Id	Name	SBO
RAFp	RAF-P	

Id	Name	SBO
RAFPH	RAF phosphatase	

Derived unit contains undeclared units

$$v_5 = d2 \cdot RAFpRAFPH \tag{10}$$

Table 22: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
d2		0.5	

5.6 Reaction Reaction6

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

Name dephosphorylation of RAF-P

Reaction equation

$$RAFpRAFPH \longrightarrow RAF + RAFPH \tag{11}$$

Reactant

Table 23: Properties of each reactant.

rable 25: Troperties of each reactant.			
Id	Name	SBO	
RAFpRAFPH	RAF-P_RAFPase		

Products

Table 24: Properties of each product.

Id	Name	SBO
RAF	RAF	
RAFPH	RAF phosphatase	

Derived unit contains undeclared units

$$v_6 = k2 \cdot RAFpRAFPH \tag{12}$$

Table 25: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k2		0.1	

5.7 Reaction Reaction 7

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

Name binding of MEK and RAF-P

Reaction equation

$$MEK + RAFp \longrightarrow MEKRAFp$$
 (13)

Reactants

Table 26: Properties of each reactant.

Id	Name	SBO
MEK	MEK	
RAFp	RAF-P	

Product

Table 27: Properties of each product.

Id	Name	SBO
MEKRAFp	MEK_RAF-P	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = a3 \cdot MEK \cdot RAFp \tag{14}$$

Table 28: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a3		3.3	

5.8 Reaction Reaction8

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

Name dissociation of MEK_RAF-P

Reaction equation

$$MEKRAFp \longrightarrow MEK + RAFp \tag{15}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
MEKRAFp	MEK_RAF-P	

Products

Table 30: Properties of each product.

Id	Name	SBO
MEK	MEK	
RAFp	RAF-P	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = d3 \cdot MEKRAFp \tag{16}$$

Table 31: Properties of each parameter.

		1			
Id	Name	SBO	Value	Unit	Constant
d3			0.42		\overline{Z}

5.9 Reaction Reaction9

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

Name phosphorylation of MEK

Reaction equation

$$MEKRAFp \longrightarrow MEKp + RAFp \tag{17}$$

Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
MEKRAFp	MEK_RAF-P	

Products

Table 33: Properties of each product.

Id	Name	SBO
МЕКр	MEK-P	
RAFp	RAF-P	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = k3 \cdot MEKRAFp \tag{18}$$

Table 34: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k3		0.1	

5.10 Reaction Reaction 10

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

Name binding of MEK-P and MEK phosphatase

Reaction equation

$$MEKp + MEKPH \longrightarrow MEKpMEKPH$$
 (19)

Reactants

Table 35: Properties of each reactant.

Id	Name	SBO
MEKp	MEK-P	
MEKPH	MEK phosphatase	

Product

Table 36: Properties of each product.

Id	Name	SBO
МЕКрМЕКРН	MEK-P_MEKPase	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = a4 \cdot MEKp \cdot MEKPH \tag{20}$$

Table 37: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a4		10.0	

5.11 Reaction Reaction11

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

Name dissociation of MEK-P_MEKPase

Reaction equation

$$MEKpMEKPH \longrightarrow MEKp + MEKPH$$
 (21)

Reactant

Table 38: Properties of each reactant.

Id	Name	SBO	
МЕКрМЕКРН	MEK-P_MEKPase		

Products

Table 39: Properties of each product.

	1	L .
Id	Name	SBO
MEKp MEKPH	MEK-P MEK phosphatase	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = d4 \cdot MEKpMEKPH \tag{22}$$

Table 40: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
d4		0.8	

5.12 Reaction Reaction 12

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

Name dephosphorylation of MEK-P

Reaction equation

$$MEKpMEKPH \longrightarrow MEK + MEKPH \tag{23}$$

Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
МЕКрМЕКРН	MEK-P_MEKPase	

Products

Table 42: Properties of each product.

	1 1	
Id	Name	SBO
MEK MEKPH	MEK MEK phosphatase	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = k4 \cdot MEKpMEKPH \tag{24}$$

Table 43: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k4		0.1	

5.13 Reaction Reaction 13

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

Name binding of MEK-P and RAF-P

Reaction equation

$$MEKp + RAFp \longrightarrow MEKpRAFp$$
 (25)

Reactants

Table 44: Properties of each reactant.

Id	Name	SBO
MEKp	MEK-P	
RAFp	RAF-P	

Product

Table 45: Properties of each product

Table 43. I Toperties of each product.		
Id Name		SBO
MEKpRAFp	MEK-P_RAF-P	

Derived unit contains undeclared units

$$v_{13} = a5 \cdot \text{MEKp} \cdot \text{RAFp} \tag{26}$$

Table 46: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a5		3.3	

5.14 Reaction Reaction 14

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

Name dissociation of MEK-P_RAF-P

Reaction equation

$$MEKpRAFp \longrightarrow MEKp + RAFp \tag{27}$$

Reactant

Table 47: Properties of each reactant.

Id	Name	SBO
MEKpRAFp	MEK-P_RAF-P	

Products

Table 48: Properties of each product.

Id	Name	SBO
MEKp	MEK-P	
RAFp	RAF-P	

Derived unit contains undeclared units

$$v_{14} = d5 \cdot MEKpRAFp \tag{28}$$

Table 49: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
d 5		0.4	\overline{Z}

5.15 Reaction Reaction 15

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

Name phosphorylation of MEK-P

Reaction equation

$$MEKpRAFp \longrightarrow MEKpp + RAFp \tag{29}$$

Reactant

Table 50: Properties of each reactant.

Id	Name	SBO
MEKpRAFp	MEK-P_RAF-P	

Products

Table 51: Properties of each product.

Id	Name	SBO
MEKpp RAFp	MEK-PP RAF-P	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = k5 \cdot MEKpRAFp \tag{30}$$

Table 52: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k5		0.1	

5.16 Reaction Reaction16

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

Name binding of MEK-PP and MEK phosphatase

Reaction equation

$$MEKPH + MEKpp \longrightarrow MEKppMEKPH$$
 (31)

Reactants

Table 53: Properties of each reactant.

Id	Name	SBO
MEKPH	MEK phosphatase	
MEKpp	MEK-PP	

Product

Table 54: Properties of each product.

Id	Name	SBO
МЕКррМЕКРН	MEK-PP_MEKPase	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = a6 \cdot MEKPH \cdot MEKpp \tag{32}$$

Table 55: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a6		10.0	Ø

5.17 Reaction Reaction17

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

Name dissociation of MEK-PP_MEKPase

Reaction equation

$$MEKppMEKPH \longrightarrow MEKPH + MEKpp$$
 (33)

Reactant

Table 56: Properties of each reactant.

Id	Name	SBO
МЕКррМЕКРН	MEK-PP_MEKPase	

Products

Table 57: Properties of each product.

Id	Name	SBO
MEKPH MEKpp	MEK phosphatase MEK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = d6 \cdot MEKppMEKPH$$
 (34)

Table 58: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
d6		0.8	

5.18 Reaction Reaction 18

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

Name dephosphorylation of MEK-PP

Reaction equation

$$MEKppMEKPH \longrightarrow MEKp + MEKPH$$
 (35)

Reactant

Table 59: Properties of each reactant.

Id	Name	SBO
МЕКррМЕКРН	MEK-PP_MEKPase	

Products

Table 60: Properties of each product.

Id	Name	SBO
MEKp MEKPH	MEK-P MEK phosphatase	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = k6 \cdot MEKppMEKPH \tag{36}$$

Table 61: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k6		0.1	

5.19 Reaction Reaction 19

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

Name binding of MAPK and MEK-PP

Reaction equation

$$MAPK + MEKpp \longrightarrow MAPKMEKpp$$
 (37)

Reactants

Table 62: Properties of each reactant.

Id	Name	SBO
MAPK	MAPK	
MEKpp	MEK-PP	

Product

Table 63: Properties of each product.

Id	Name	SBO
MAPKMEKpp	MAPK_MEK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = a7 \cdot MAPK \cdot MEKpp \tag{38}$$

Table 64: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a7		20.0	$ \mathcal{L} $

5.20 Reaction Reaction 20

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

Name dissociation of MAPK_MEK-PP

Reaction equation

$$MAPKMEKpp \longrightarrow MAPK + MEKpp$$
 (39)

Reactant

Table 65: Properties of each reactant.

Two is oct i repetition of swell reasonable			
Id	Name	SBO	
MAPKMEKpp	MAPK_MEK-PP		

Products

Table 66: Properties of each product.

Id	Name	SBO
MAPK	MAPK	
MEKpp	MEK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = d7 \cdot MAPKMEKpp \tag{40}$$

Table 67: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
d7		0.6	

5.21 Reaction Reaction21

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

Name phosphorylation of MAPK

Reaction equation

$$MAPKMEKpp \longrightarrow MAPKp + MEKpp$$
 (41)

Reactant

Table 68: Properties of each reactant.

Id	Name	SBO
МАРКМЕКрр	MAPK_MEK-PP	

Products

Table 69: Properties of each product.

Id	Name	SBO
МАРКр	MAPK-P	
MEKpp	MEK-PP	

Derived unit contains undeclared units

$$v_{21} = k7 \cdot MAPKMEKpp \tag{42}$$

Table 70: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k7		0.1	

5.22 Reaction Reaction22

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

Name binding of MAPK-P and MAPK phosphatase

Reaction equation

$$MAPKp + MAPKPH \longrightarrow MAPKpMAPKPH$$
 (43)

Reactants

Table 71: Properties of each reactant.

Id	Name	SBO
MAPKP MAPKPH	MAPK-P MAPK phosphatase	

Product

Table 72: Properties of each product.

	· · · · · · · · · · · · · · · · · · ·	1
Id	Name	SBO
MAPKpMA	PKPH MAPK-P_MA	PKPase

Derived unit contains undeclared units

$$v_{22} = a8 \cdot MAPKp \cdot MAPKPH \tag{44}$$

Table 73: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a8		5.0	

5.23 Reaction Reaction 23

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

Name dissociation of MAPK-P_MAPKPase

Reaction equation

$$MAPKpMAPKPH \longrightarrow MAPKp + MAPKPH$$
 (45)

Reactant

Table 74: Properties of each reactant.

Id	Name	SBO
МАРКрМАРКРН	MAPK-P_MAPKPase	

Products

Table 75: Properties of each product.

Id	Name	SBO
MAPKp MAPKPH	MAPK-P MAPK phosphatase	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = d8 \cdot MAPKpMAPKPH \tag{46}$$

Table 76: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
d8		0.4	

5.24 Reaction Reaction 24

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

Name dephosphorylation of MAPK-P

Reaction equation

$$MAPKpMAPKPH \longrightarrow MAPK + MAPKPH \tag{47}$$

Reactant

Table 77: Properties of each reactant.

Id	Name	SBO
МАРКрМАРКРН	MAPK-P_MAPKPase	

Products

Table 78: Properties of each product.

Id	Name	SBO
MAPK	MAPK	
MAPKPH	MAPK phosphatase	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = k8 \cdot MAPKpMAPKPH \tag{48}$$

Table 79: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k8		0.1	

5.25 Reaction Reaction 25

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

Name binding of MAPK-P and MEK-PP

Reaction equation

$$MAPKp + MEKpp \longrightarrow MAPKpMEKpp$$
 (49)

Reactants

Table 80: Properties of each reactant.

Id	Name	SBO
MAPKp	MAPK-P	
MEKpp	MEK-PP	

Product

Table 81: Properties of each product.

Id	Name	SBO
МАРКрМЕКрр	MAPK-P_MEK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = a9 \cdot MAPKp \cdot MEKpp \tag{50}$$

Table 82: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a 9		20.0	

5.26 Reaction Reaction 26

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

Name dissociation of MAPK-P_MEK-PP

Reaction equation

$$MAPKpMEKpp \longrightarrow MAPKp + MEKpp$$
 (51)

Reactant

Table 83: Properties of each reactant.

Id	Name	SBO
МАРКрМЕКрр	MAPK-P_MEK-PP	

Products

Table 84: Properties of each product.

Id	Name	SBO
MAPKp	MAPK-P	
MEKpp	MEK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = d9 \cdot MAPKpMEKpp \tag{52}$$

Table 85: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
d9		0.6	

5.27 Reaction Reaction 27

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

Name phosphorylation of MAPK-P

Reaction equation

$$MAPKpMEKpp \longrightarrow MAPKpp + MEKpp$$
 (53)

Reactant

Table 86: Properties of each reactant.

 Name	SBO
 MAPK-P_MEK-PP	

Products

Table 87: Properties of each product.

Id	Name	SBO
МАРКрр	MAPK-PP	
MEKpp	MEK-PP	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = k9 \cdot MAPKpMEKpp \tag{54}$$

Table 88: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k9		0.1	

5.28 Reaction Reaction 28

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

Name binding of MAPK-PP and MAPK phosphatase

Reaction equation

$$MAPKPH + MAPKpp \longrightarrow MAPKppMAPKPH$$
 (55)

Reactants

Table 89: Properties of each reactant.

Id	Name	SBO
MAPKPH MAPKpp	MAPK phosphatase MAPK-PP	

Product

Table 90: Properties of each product.

	1 1	
Id	Name	SBO
МАРКррМАРКРН	MAPK-PP_MAPKPase	

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = a10 \cdot MAPKPH \cdot MAPKpp \tag{56}$$

Table 91: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
a10		5.0	

5.29 Reaction Reaction 29

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

Name dissociation of MAPK-PP_MAPKPase

Reaction equation

$$MAPKppMAPKPH \longrightarrow MAPKPH + MAPKpp$$
 (57)

Reactant

Table 92: Properties of each reactant.

Id	Name	SBO
МАРКррМАРКРН	MAPK-PP_MAPKPase	

Products

Table 93: Properties of each product.

	1 1	
Id	Name	SBO
MAPKPH	MAPK phosphatase	•

Id	Name	SBO
МАРКрр	MAPK-PP	

Derived unit contains undeclared units

$$v_{29} = d10 \cdot MAPKppMAPKPH \tag{58}$$

Table 94: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
d10		0.4	

5.30 Reaction Reaction 30

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

Name dephosphorylation of MAPK-PP

Reaction equation

$$MAPKppMAPKPH \longrightarrow MAPKp + MAPKPH$$
 (59)

Reactant

Table 95: Properties of each reactant.

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Id	Name	SBO	
МАРКррМАРКРН	MAPK-PP_MAPKPase		

Products

Table 96: Properties of each product.

Id	Name	SBO
МАРКр	MAPK-P	
MAPKPH	MAPK phosphatase	

Derived unit contains undeclared units

$$v_{30} = k10 \cdot MAPKppMAPKPH \tag{60}$$

Table 97: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k10		0.1	Ø

6 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.

6.1 Species MAPK

Name MAPK

Initial amount 0.4 µmol

This species takes part in three reactions (as a reactant in Reaction19 and as a product in Reaction20, Reaction24).

$$\frac{d}{dt}MAPK = |v_{20}| + |v_{24}| - |v_{19}|$$
 (61)

6.2 Species MAPKMEKpp

Name MAPK_MEK-PP

Initial amount 0 µmol

This species takes part in three reactions (as a reactant in Reaction20, Reaction21 and as a product in Reaction19).

$$\frac{d}{dt}MAPKMEKpp = |v_{19} - v_{20}| - |v_{21}|$$
 (62)

6.3 Species MAPKp

Name MAPK-P

Initial amount 0 µmol

This species takes part in six reactions (as a reactant in Reaction22, Reaction25 and as a product in Reaction21, Reaction23, Reaction26, Reaction30).

$$\frac{d}{dt}MAPKp = |v_{21}| + |v_{23}| + |v_{26}| + |v_{30}| - |v_{22}| - |v_{25}|$$
(63)

6.4 Species MAPKPH

Name MAPK phosphatase

Initial amount 0.3 µmol

This species takes part in six reactions (as a reactant in Reaction22, Reaction28 and as a product in Reaction23, Reaction24, Reaction29, Reaction30).

$$\frac{d}{dt}MAPKPH = |v_{23}| + |v_{24}| + |v_{29}| + |v_{30}| - |v_{22}| - |v_{28}|$$
(64)

6.5 Species MAPKpMAPKPH

Name MAPK-P_MAPKPase

Initial amount 0 µmol

This species takes part in three reactions (as a reactant in Reaction23, Reaction24 and as a product in Reaction22).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MAPKpMAPKPH} = |v_{22}| - |v_{23}| - |v_{24}| \tag{65}$$

6.6 Species MAPKpMEKpp

Name MAPK-P_MEK-PP

Initial amount 0 μmol

This species takes part in three reactions (as a reactant in Reaction26, Reaction27 and as a product in Reaction25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MAPKpMEKpp} = |v_{25}| - |v_{26}| - |v_{27}| \tag{66}$$

6.7 Species MAPKpp

Name MAPK-PP

Initial amount 0 µmol

This species takes part in three reactions (as a reactant in Reaction28 and as a product in Reaction27, Reaction29).

$$\frac{d}{dt}MAPKpp = |v_{27}| + |v_{29}| - |v_{28}|$$
 (67)

6.8 Species MAPKppMAPKPH

Name MAPK-PP_MAPKPase

Initial amount 0 µmol

This species takes part in three reactions (as a reactant in Reaction29, Reaction30 and as a product in Reaction28).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MAPKppMAPKPH} = |v_{28}| - |v_{29}| - |v_{30}| \tag{68}$$

6.9 Species MEK

Name MEK

Initial amount 0.2 µmol

This species takes part in three reactions (as a reactant in Reaction7 and as a product in Reaction8, Reaction12).

$$\frac{d}{dt}MEK = |v_8| + |v_{12}| - |v_7| \tag{69}$$

6.10 Species MEKp

Name MEK-P

Initial amount 0 µmol

This species takes part in six reactions (as a reactant in Reaction10, Reaction13 and as a product in Reaction9, Reaction11, Reaction14, Reaction18).

$$\frac{d}{dt}MEKp = v_9 + v_{11} + v_{14} + v_{18} - v_{10} - v_{13}$$
 (70)

6.11 Species MEKPH

Name MEK phosphatase

Initial amount 0.2 µmol

This species takes part in six reactions (as a reactant in Reaction10, Reaction16 and as a product in Reaction11, Reaction12, Reaction17, Reaction18).

$$\frac{d}{dt}MEKPH = |v_{11}| + |v_{12}| + |v_{17}| + |v_{18}| - |v_{10}| - |v_{16}|$$
(71)

6.12 Species MEKpMEKPH

Name MEK-P_MEKPase

Initial amount 0 µmol

This species takes part in three reactions (as a reactant in Reaction11, Reaction12 and as a product in Reaction10).

$$\frac{d}{dt}MEKpMEKPH = |v_{10}| - |v_{11}| - |v_{12}|$$
 (72)

6.13 Species MEKpp

Name MEK-PP

Initial amount 0 μmol

This species takes part in nine reactions (as a reactant in Reaction16, Reaction19, Reaction25 and as a product in Reaction15, Reaction17, Reaction20, Reaction21, Reaction26, Reaction27).

$$\frac{d}{dt}MEKpp = v_{15} + v_{17} + v_{20} + v_{21} + v_{26} + v_{27} - v_{16} - v_{19} - v_{25}$$
 (73)

6.14 Species MEKppMEKPH

Name MEK-PP_MEKPase

Initial amount 0 µmol

This species takes part in three reactions (as a reactant in Reaction17, Reaction18 and as a product in Reaction16).

$$\frac{d}{dt}MEKppMEKPH = |v_{16}| - |v_{17}| - |v_{18}|$$
 (74)

6.15 Species MEKpRAFp

Name MEK-P_RAF-P

Initial amount 0 µmol

This species takes part in three reactions (as a reactant in Reaction14, Reaction15 and as a product in Reaction13).

$$\frac{d}{dt}MEKpRAFp = |v_{13}| - |v_{14}| - |v_{15}|$$
 (75)

6.16 Species MEKRAFp

Name MEK_RAF-P

Initial amount 0 µmol

This species takes part in three reactions (as a reactant in Reaction8, Reaction9 and as a product in Reaction7).

$$\frac{\mathrm{d}}{\mathrm{d}t} \mathrm{MEKRAFp} = |v_7| - |v_8| - |v_9| \tag{76}$$

6.17 Species RAF

Name RAF

Initial amount 0.3 µmol

This species takes part in three reactions (as a reactant in Reaction1 and as a product in Reaction2, Reaction6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{RAF} = |v_2| + |v_6| - |v_1| \tag{77}$$

6.18 Species RAFK

Name RAFK

Initial amount 0.2 μmol

This species takes part in three reactions (as a reactant in Reaction1 and as a product in Reaction2, Reaction3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{RAFK} = |v_2| + |v_3| - |v_1| \tag{78}$$

6.19 Species RAFp

Name RAF-P

Initial amount 0 µmol

This species takes part in nine reactions (as a reactant in Reaction4, Reaction7, Reaction13 and as a product in Reaction3, Reaction5, Reaction8, Reaction9, Reaction14, Reaction15).

$$\frac{d}{dt}RAFp = |v_3| + |v_5| + |v_8| + |v_9| + |v_{14}| + |v_{15}| - |v_4| - |v_7| - |v_{13}|$$
(79)

6.20 Species RAFPH

Name RAF phosphatase

Initial amount 0.3 µmol

This species takes part in three reactions (as a reactant in Reaction4 and as a product in Reaction5, Reaction6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{RAFPH} = |v_5| + |v_6| - |v_4| \tag{80}$$

6.21 Species RAFPRAFPH

Name RAF-P_RAFPase

Initial amount 0 µmol

This species takes part in three reactions (as a reactant in Reaction5, Reaction6 and as a product in Reaction4).

$$\frac{\mathrm{d}}{\mathrm{d}t} \mathrm{RAFPRAFPH} = |v_4| - |v_5| - |v_6| \tag{81}$$

6.22 Species RAFRAFK

Name RAF_RAFK

Initial amount $0 \mu mol$

This species takes part in three reactions (as a reactant in Reaction2, Reaction3 and as a product in Reaction1).

$$\frac{\mathrm{d}}{\mathrm{d}t} \mathrm{RAFRAFK} = |v_1| - |v_2| - |v_3| \tag{82}$$

SML2ATEX 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.

^aCenter for Bioinformatics Tübingen (ZBIT), Germany

^bCalifornia Institute of Technology, Beckman Institute BNMC, Pasadena, United States

^cEuropean Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom

^dEML Research gGmbH, Heidelberg, Germany