SBML Model Report

Model name: “Muller2008 - Simplified MAPK activation Dynamics (Model B)”

May 17, 2018

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Matthew Grant Roberts[1] at January 26th 2018 at 12:13 a. m. and last time modified at January 29th 2018 at 11:15 a. 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	1
species types	0	species	8
events	0	constraints	0
reactions	15	function definitions	9
global parameters	20	unit definitions	4
rules	4	initial assignments	0

Model Notes

Muller2008 - Simplified MAPK activation Dynamics (Model B)Simplified mathematical model (model B)for predicting MAPK signal expression.

This model is described in the article:Network topology determines dynamics of the mammalian MAPK1,2 signaling network: bifan motif regulation of C-Raf and B-Raf isoforms by

[1]EMBL-EBI, mroberts@ebi.ac.uk

FGFR and MC1R.Muller M, Obeyesekere M, Mills GB, Ram PT.FASEB J. 2008 May; 22(5): 1393-1403

Abstract:

Activation of the fibroblast growth factor (FGFR) and melanocyte stimulating hormone (MC1R) receptors stimulates B-Raf and C-Raf isoforms that regulate the dynamics of MAPK1,2 signaling. Network topology motifs in mammalian cells include feed-forward and feedback loops and bifans where signals from two upstream molecules integrate to modulate the activity of two downstream molecules. We computationally modeled and experimentally tested signal processing in the FGFR/MC1R/B-Raf/C-Raf/MAPK1,2 network in human melanoma cells; identifying 7 regulatory loops and a bifan motif. Signaling from FGFR leads to sustained activation of MAPK1,2, whereas signaling from MC1R results in transient activation of MAPK1,2. The dynamics of MAPK activation depends critically on the expression level and connectivity to C-Raf, which is critical for a sustained MAPK1,2 response. A partially incoherent bifan motif with a feedback loop acts as a logic gate to integrate signals and regulate duration of activation of the MAPK signaling cascade. Further reducing a 106-node ordinary differential equations network encompassing the complete network to a 6-node network encompassing rate-limiting processes sustains the feedback loops and the bifan, providing sufficient information to predict biological responses.

2 Unit Definitions

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

2.1 Unit `time`

Name time

Definition 60 s

2.2 Unit `unit_0`

Name 0.06*mmol/(l*s)

Definition $0.06\ \mathrm{mmol} \cdot \mathrm{l}^{-1} \cdot \mathrm{s}^{-1}$

2.3 Unit unit_1

Name 1/(59.9999*s)

Definition $(59.9999\ \mathrm{s})^{-1}$

2.4 Unit unit_2

Name 0.06*ml/(mol*s)

Definition $\mathrm{mol}^{-1} \cdot 0.06\ \mathrm{ml} \cdot \mathrm{s}^{-1}$

2.5 Unit substance

Notes Mole is the predefined SBML unit for `substance`.

Definition mol

2.6 Unit volume

Notes Litre is the predefined SBML unit for `volume`.

Definition l

2.7 Unit area

Notes Square metre is the predefined SBML unit for `area` since SBML Level 2 Version 1.

Definition m^2

2.8 Unit length

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

Definition m

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
Compartment	Compartment		3	1	litre	☑	

3.1 Compartment `Compartment`

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

Name Compartment

4 Species

This model contains eight species. The boundary condition of two of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 9 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
FGFR	FGFR	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
MSH	MSH	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
B_Raf	B-Raf	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
MAPK	MAPK	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
C_Raf_inactive	C-Raf inactive	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
g2_0	g2	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
C_Raf	C-Raf	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
g1_0	g1	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑

5 Parameters

This model contains 20 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
a1	a1		10.000	$0.06\,\mathrm{mmol}\cdot\mathrm{l}^{-1}\cdot\mathrm{s}^{-1}$	☑
g1	g1		0.000		⊟
b1	b1		10.000		☑
d1	d1		0.200	$(59.9999\,\mathrm{s})^{-1}$	☑
a2	a2		10.000	$0.06\,\mathrm{mmol}\cdot\mathrm{l}^{-1}\cdot\mathrm{s}^{-1}$	☑
g2	g2		1.000		⊟
b2	b2		10.000		☑
d2	d2		0.100	$(59.9999\,\mathrm{s})^{-1}$	☑
f53	f53		1.500	$\mathrm{mol}^{-1}\cdot 0.06\,\mathrm{ml}\cdot\mathrm{s}^{-1}$	☑
f13	f13		0.600	$\mathrm{mol}^{-1}\cdot 0.06\,\mathrm{ml}\cdot\mathrm{s}^{-1}$	☑
h36_y3	h36		0.100	$\mathrm{mol}^{-1}\cdot 0.06\,\mathrm{ml}\cdot\mathrm{s}^{-1}$	☑
d3	d3		1.000	$(59.9999\,\mathrm{s})^{-1}$	☑
E	E		10.000		☑
f14	f14		0.100	$(59.9999\,\mathrm{s})^{-1}$	☑
f24	f24		0.800	$(59.9999\,\mathrm{s})^{-1}$	☑
d4	d4		1.100	$(59.9999\,\mathrm{s})^{-1}$	☑
f35	f35		0.300	$(59.9999\,\mathrm{s})^{-1}$	☑
f45	f45		0.100	$(59.9999\,\mathrm{s})^{-1}$	☑
d5	d5		1.000	$(59.9999\,\mathrm{s})^{-1}$	☑
d6	d6		0.001	$(59.9999\,\mathrm{s})^{-1}$	☑

6 Function definitions

This is an overview of nine function definitions.

6.1 Function definition function_1_1

Name function 1_1

Arguments a1, b1, g1

Mathematical Expression

$$\mathrm{a1}\cdot\frac{\mathrm{g1}}{\mathrm{b1}+\mathrm{g1}} \tag{1}$$

6.2 Function definition function_1_2

Name function 1_2

Arguments a2, b2, g2

Mathematical Expression

$$\mathrm{a2} \cdot \frac{\mathrm{g2}}{\mathrm{b2} + \mathrm{g2}} \tag{2}$$

6.3 Function definition function_2_1

Name function 2_1

Arguments [C_Raf], [C_Raf_inactive], E, [FGFR], f13

Mathematical Expression

$$\mathrm{f13} \cdot (\mathrm{E} - [\mathrm{C\_Raf}] - [\mathrm{C\_Raf\_inactive}]) \cdot [\mathrm{FGFR}] \tag{3}$$

6.4 Function definition function_3_1

Name function 3_1

Arguments [C_Raf], [C_Raf_inactive], E, [MAPK], f53

Mathematical Expression

$$\mathrm{f53} \cdot (\mathrm{E} - [\mathrm{C\_Raf}] - [\mathrm{C\_Raf\_inactive}]) \cdot [\mathrm{MAPK}] \tag{4}$$

6.5 Function definition function_4_1

Name function 4_1

Arguments [FGFR], f14

Mathematical Expression

$$\mathrm{f14} \cdot [\mathrm{FGFR}] \tag{5}$$

6.6 Function definition function_4_2

Name function 4_2

Arguments [MSH], f24

Mathematical Expression

$$\mathrm{f24} \cdot [\mathrm{MSH}] \tag{6}$$

6.7 Function definition function_4_3

Name function 4_3

Arguments [C_Raf], f35

Mathematical Expression

$$\mathrm{f35} \cdot [\mathrm{C\_Raf}] \tag{7}$$

6.8 Function definition function_4_4

Name function 4_4

Arguments [B_Raf], f45

Mathematical Expression

$$\mathrm{f45} \cdot [\mathrm{B\_Raf}] \tag{8}$$

6.9 Function definition function_5_1

Name function 5_1

Arguments [C_Raf], [MSH], h36_y3

Mathematical Expression

$$\mathrm{h36\_y3} \cdot [\mathrm{MSH}] \cdot [\mathrm{C\_Raf}] \tag{9}$$

7 Rules

This is an overview of four rules.

7.1 Rule g1

Rule g1 is an assignment rule for parameter g1:

$$\mathrm{g1} = \begin{cases} 0 & \text{if } (\mathrm{time} \geq 0) \wedge (\mathrm{time} < 5) \\ \begin{cases} 1 & \text{if } (\mathrm{time} \geq 5) \wedge (\mathrm{time} < 10) \\ 0 & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{10}$$

7.2 Rule g1_0

Rule g1_0 is an assignment rule for species g1_0:

$$\mathrm{g1\_0} = \mathrm{g1} \tag{11}$$

7.3 Rule g2

Rule g2 is an assignment rule for parameter g2:

$$\mathrm{g2} = \begin{cases} 1 & \text{if } (\mathrm{time} \geq 0) \wedge (\mathrm{time} < 5) \\ 0 & \text{otherwise} \end{cases} \tag{12}$$

7.4 Rule g2_0

Rule g2_0 is an assignment rule for species g2_0:

$$\mathrm{g2\_0} = \mathrm{g2} \tag{13}$$

8 Reactions

This model contains 15 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	FGFR_Activation	FGFR Stimulus	$\emptyset \xrightarrow{\text{g1\_0}} \text{FGFR}$	
2	FGFR_Degradation	FGFR Degradation	$\text{FGFR} \longrightarrow \emptyset$	
3	MSH_Activation	MSH Stimulus	$\emptyset \xrightarrow{\text{g2\_0}} \text{MSH}$	
4	MSH_Degradation	MSH Degradation	$\text{MSH} \longrightarrow \emptyset$	
5	C_Raf_Activation_1	C-Raf Activation 1	$\emptyset \xrightarrow{\text{C\_Raf\_inactive, FGFR}} \text{C\_Raf}$	
6	C_Raf_Activation_2	C_Raf Activation 2	$\emptyset \xrightarrow{\text{C\_Raf\_inactive, MAPK}} \text{C\_Raf}$	
7	C_Raf_Degradation	C-Raf Degradation	$\text{C\_Raf} \longrightarrow \emptyset$	
8	B_Raf_Activation_1	B-Raf Activation 1	$\emptyset \xrightarrow{\text{FGFR}} \text{B\_Raf}$	
9	B_Raf_Activation_2	B-Raf Activation 2	$\emptyset \xrightarrow{\text{MSH}} \text{B\_Raf}$	
10	B_Raf_Degradation	B-Raf Degradation	$\text{B\_Raf} \longrightarrow \emptyset$	
11	MAPK_Activation_1	MAPK Activation 1	$\emptyset \xrightarrow{\text{C\_Raf}} \text{MAPK}$	

№	Id	Name	Reaction Equation	SBO
12	MAPK_Activation_2	MAPK Activation 2	$\emptyset \xrightarrow{\text{B\_Raf}} \text{MAPK}$	
13	MAPK_Degradation	MAPK Degradation	$\text{MAPK} \longrightarrow \emptyset$	
14	C_Raf_Inactivation	C-Raf Inactivation	$\text{C\_Raf} \xrightarrow{\text{MSH}} \text{C\_Raf\_inactive}$	
15	Inactive_C_Raf_degradation	Inactive C-Raf degradation	$\text{C\_Raf\_inactive} \longrightarrow \emptyset$	

8.1 Reaction FGFR_Activation

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

Name FGFR Stimulus

Reaction equation

$$\emptyset \xrightarrow{\text{g1\_0}} \text{FGFR} \tag{14}$$

Modifier

Table 6: Properties of each modifier.

Id	Name	SBO
g1_0	g1	

Product

Table 7: Properties of each product.

Id	Name	SBO
FGFR	FGFR	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{Compartment}) \cdot \text{function\_1\_1}(\text{a1}, \text{b1}, \text{g1}) \tag{15}$$

$$\text{function\_1\_1}(\text{a1}, \text{b1}, \text{g1}) = \text{a1} \cdot \frac{\text{g1}}{\text{b1} + \text{g1}} \tag{16}$$

$$\text{function\_1\_1}(\text{a1}, \text{b1}, \text{g1}) = \text{a1} \cdot \frac{\text{g1}}{\text{b1} + \text{g1}} \tag{17}$$

8.2 Reaction FGFR_Degradation

This is an irreversible reaction of one reactant forming no product.

Name FGFR Degradation

Reaction equation

$$\text{FGFR} \longrightarrow \emptyset \tag{18}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
FGFR	FGFR	

Kinetic Law

Derived unit $(59.9999\ \text{s})^{-1} \cdot \text{mol}$

$$v_2 = \text{vol}\,(\text{Compartment}) \cdot \text{d1} \cdot [\text{FGFR}] \tag{19}$$

8.3 Reaction MSH_Activation

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

Name MSH Stimulus

Reaction equation

$$\emptyset \xrightarrow{\text{g2\_0}} \text{MSH} \tag{20}$$

Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
g2_0	g2	

Product

Table 10: Properties of each product.

Id	Name	SBO
MSH	MSH	

Id	Name	SBO

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\,(\mathrm{Compartment}) \cdot \mathrm{function\_1\_2}\,(\mathrm{a2}, \mathrm{b2}, \mathrm{g2}) \tag{21}$$

$$\mathrm{function\_1\_2}\,(\mathrm{a2}, \mathrm{b2}, \mathrm{g2}) = \mathrm{a2} \cdot \frac{\mathrm{g2}}{\mathrm{b2} + \mathrm{g2}} \tag{22}$$

$$\mathrm{function\_1\_2}\,(\mathrm{a2}, \mathrm{b2}, \mathrm{g2}) = \mathrm{a2} \cdot \frac{\mathrm{g2}}{\mathrm{b2} + \mathrm{g2}} \tag{23}$$

8.4 Reaction MSH_Degradation

This is an irreversible reaction of one reactant forming no product.

Name MSH Degradation

Reaction equation

$$\mathrm{MSH} \longrightarrow \emptyset \tag{24}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
MSH	MSH	

Kinetic Law

Derived unit $(59.9999\ \mathrm{s})^{-1} \cdot \mathrm{mol}$

$$v_4 = \mathrm{vol}\,(\mathrm{Compartment}) \cdot \mathrm{d2} \cdot [\mathrm{MSH}] \tag{25}$$

8.5 Reaction C_Raf_Activation_1

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

Name C-Raf Activation 1

Reaction equation

$$\emptyset \xrightarrow{\text{C\_Raf\_inactive, FGFR}} \text{C\_Raf} \tag{26}$$

Modifiers

Table 12: Properties of each modifier.

Id	Name	SBO
C_Raf_inactive	C-Raf inactive	
FGFR	FGFR	

Product

Table 13: Properties of each product.

Id	Name	SBO
C_Raf	C-Raf	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}\,(\text{Compartment}) \cdot \text{function\_2\_1}\,([\text{C\_Raf}], [\text{C\_Raf\_inactive}], \text{E}, [\text{FGFR}], \text{f13}) \tag{27}$$

$$\begin{aligned} &\text{function\_2\_1}\,([\text{C\_Raf}], [\text{C\_Raf\_inactive}], \text{E}, [\text{FGFR}], \text{f13}) \\ &\quad = \text{f13} \cdot (\text{E} - [\text{C\_Raf}] - [\text{C\_Raf\_inactive}]) \cdot [\text{FGFR}] \end{aligned} \tag{28}$$

$$\begin{aligned} &\text{function\_2\_1}\,([\text{C\_Raf}], [\text{C\_Raf\_inactive}], \text{E}, [\text{FGFR}], \text{f13}) \\ &\quad = \text{f13} \cdot (\text{E} - [\text{C\_Raf}] - [\text{C\_Raf\_inactive}]) \cdot [\text{FGFR}] \end{aligned} \tag{29}$$

8.6 Reaction C_Raf_Activation_2

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

Name C_Raf Activation 2

Reaction equation

$$\emptyset \xrightarrow{\text{C\_Raf\_inactive, MAPK}} \text{C\_Raf} \tag{30}$$

Modifiers

Table 14: Properties of each modifier.

Id	Name	SBO
C_Raf_inactive	C-Raf inactive	
MAPK	MAPK	

Product

Table 15: Properties of each product.

Id	Name	SBO
C_Raf	C-Raf	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{Compartment}) \cdot \mathrm{function\_3\_1}\,([\mathrm{C\_Raf}], [\mathrm{C\_Raf\_inactive}], \mathrm{E}, [\mathrm{MAPK}], \mathrm{f53}) \quad (31)$$

$$\begin{aligned} &\mathrm{function\_3\_1}\,([\mathrm{C\_Raf}], [\mathrm{C\_Raf\_inactive}], \mathrm{E}, [\mathrm{MAPK}], \mathrm{f53}) \\ &= \mathrm{f53} \cdot (\mathrm{E} - [\mathrm{C\_Raf}] - [\mathrm{C\_Raf\_inactive}]) \cdot [\mathrm{MAPK}] \end{aligned} \quad (32)$$

$$\begin{aligned} &\mathrm{function\_3\_1}\,([\mathrm{C\_Raf}], [\mathrm{C\_Raf\_inactive}], \mathrm{E}, [\mathrm{MAPK}], \mathrm{f53}) \\ &= \mathrm{f53} \cdot (\mathrm{E} - [\mathrm{C\_Raf}] - [\mathrm{C\_Raf\_inactive}]) \cdot [\mathrm{MAPK}] \end{aligned} \quad (33)$$

8.7 Reaction C_Raf_Degradation

This is an irreversible reaction of one reactant forming no product.

Name C-Raf Degradation

Reaction equation

$$\mathrm{C\_Raf} \longrightarrow \emptyset \quad (34)$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
C_Raf	C-Raf	

Kinetic Law

Derived unit $(59.9999\ \mathrm{s})^{-1} \cdot \mathrm{mol}$

$$v_7 = \mathrm{vol}(\mathrm{Compartment}) \cdot \mathrm{d3} \cdot [\mathrm{C\_Raf}] \tag{35}$$

8.8 Reaction B_Raf_Activation_1

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

Name B-Raf Activation 1

Reaction equation

$$\emptyset \xrightarrow{\mathrm{FGFR}} \mathrm{B\_Raf} \tag{36}$$

Modifier

Table 17: Properties of each modifier.

Id	Name	SBO
FGFR	FGFR	

Product

Table 18: Properties of each product.

Id	Name	SBO
B_Raf	B-Raf	

Kinetic Law

Derived unit $(59.9999\ \mathrm{s})^{-1} \cdot \mathrm{mol}$

$$v_8 = \mathrm{vol}(\mathrm{Compartment}) \cdot \mathrm{function\_4\_1}([\mathrm{FGFR}], \mathrm{f14}) \tag{37}$$

$$\text{function\_4\_1}\left([\text{FGFR}], \text{f14}\right) = \text{f14} \cdot [\text{FGFR}] \tag{38}$$

$$\text{function\_4\_1}\left([\text{FGFR}], \text{f14}\right) = \text{f14} \cdot [\text{FGFR}] \tag{39}$$

8.9 Reaction B_Raf_Activation_2

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

Name B-Raf Activation 2

Reaction equation

$$\emptyset \xrightarrow{\text{MSH}} \text{B\_Raf} \tag{40}$$

Modifier

Table 19: Properties of each modifier.

Id	Name	SBO
MSH	MSH	

Product

Table 20: Properties of each product.

Id	Name	SBO
B_Raf	B-Raf	

Kinetic Law

Derived unit $(59.9999\ \text{s})^{-1} \cdot \text{mol}$

$$v_9 = \text{vol}\left(\text{Compartment}\right) \cdot \text{function\_4\_2}\left([\text{MSH}], \text{f24}\right) \tag{41}$$

$$\text{function\_4\_2}\left([\text{MSH}], \text{f24}\right) = \text{f24} \cdot [\text{MSH}] \tag{42}$$

$$\text{function\_4\_2}\left([\text{MSH}], \text{f24}\right) = \text{f24} \cdot [\text{MSH}] \tag{43}$$

8.10 Reaction B_Raf_Degradation

This is an irreversible reaction of one reactant forming no product.

Name B-Raf Degradation

Reaction equation

$$\text{B\_Raf} \longrightarrow \emptyset \tag{44}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
B_Raf	B-Raf	

Kinetic Law

Derived unit $(59.9999\ \text{s})^{-1} \cdot \text{mol}$

$$v_{10} = \text{vol}\,(\text{Compartment}) \cdot \text{d4} \cdot [\text{B\_Raf}] \tag{45}$$

8.11 Reaction MAPK_Activation_1

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

Name MAPK Activation 1

Reaction equation

$$\emptyset \xrightarrow{\text{C\_Raf}} \text{MAPK} \tag{46}$$

Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
C_Raf	C-Raf	

Product

Table 23: Properties of each product.

Id	Name	SBO
MAPK	MAPK	

Id	Name	SBO

Kinetic Law

Derived unit $(59.9999\ \mathrm{s})^{-1} \cdot \mathrm{mol}$

$$v_{11} = \mathrm{vol}\,(\mathrm{Compartment}) \cdot \mathrm{function\_4\_3}\,([\mathrm{C\_Raf}], \mathrm{f35}) \tag{47}$$

$$\mathrm{function\_4\_3}\,([\mathrm{C\_Raf}], \mathrm{f35}) = \mathrm{f35} \cdot [\mathrm{C\_Raf}] \tag{48}$$

$$\mathrm{function\_4\_3}\,([\mathrm{C\_Raf}], \mathrm{f35}) = \mathrm{f35} \cdot [\mathrm{C\_Raf}] \tag{49}$$

8.12 Reaction MAPK_Activation_2

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

Name MAPK Activation 2

Reaction equation

$$\emptyset \xrightarrow{\mathrm{B\_Raf}} \mathrm{MAPK} \tag{50}$$

Modifier

Table 24: Properties of each modifier.

Id	Name	SBO
B_Raf	B-Raf	

Product

Table 25: Properties of each product.

Id	Name	SBO
MAPK	MAPK	

Kinetic Law

Derived unit $(59.9999\ \mathrm{s})^{-1} \cdot \mathrm{mol}$

$$v_{12} = \mathrm{vol}\,(\mathrm{Compartment}) \cdot \mathrm{function\_4\_4}\,([\mathrm{B\_Raf}], \mathrm{f45}) \tag{51}$$

$$\mathrm{function\_4\_4}\,([\mathrm{B\_Raf}], \mathrm{f45}) = \mathrm{f45} \cdot [\mathrm{B\_Raf}] \tag{52}$$

$$\mathrm{function\_4\_4}\,([\mathrm{B\_Raf}], \mathrm{f45}) = \mathrm{f45} \cdot [\mathrm{B\_Raf}] \tag{53}$$

8.13 Reaction `MAPK_Degradation`

This is an irreversible reaction of one reactant forming no product.

Name MAPK Degradation

Reaction equation

$$\mathrm{MAPK} \longrightarrow \emptyset \tag{54}$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
`MAPK`	MAPK	

Kinetic Law

Derived unit $(59.9999\ \mathrm{s})^{-1} \cdot \mathrm{mol}$

$$v_{13} = \mathrm{vol}\,(\mathrm{Compartment}) \cdot \mathrm{d5} \cdot [\mathrm{MAPK}] \tag{55}$$

8.14 Reaction `C_Raf_Inactivation`

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

Name C-Raf Inactivation

Reaction equation

$$\mathrm{C\_Raf} \xrightarrow{\mathrm{MSH}} \mathrm{C\_Raf\_inactive} \tag{56}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
C_Raf	C-Raf	

Modifier

Table 28: Properties of each modifier.

Id	Name	SBO
MSH	MSH	

Product

Table 29: Properties of each product.

Id	Name	SBO
C_Raf_inactive	C-Raf inactive	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{14} = \mathrm{vol}\left(\mathrm{Compartment}\right) \cdot \mathrm{function\_5\_1}\left(\left[\mathrm{C\_Raf}\right], \left[\mathrm{MSH}\right], \mathrm{h36\_y3}\right) \tag{57}$$

$$\mathrm{function\_5\_1}\left(\left[\mathrm{C\_Raf}\right], \left[\mathrm{MSH}\right], \mathrm{h36\_y3}\right) = \mathrm{h36\_y3} \cdot \left[\mathrm{MSH}\right] \cdot \left[\mathrm{C\_Raf}\right] \tag{58}$$

$$\mathrm{function\_5\_1}\left(\left[\mathrm{C\_Raf}\right], \left[\mathrm{MSH}\right], \mathrm{h36\_y3}\right) = \mathrm{h36\_y3} \cdot \left[\mathrm{MSH}\right] \cdot \left[\mathrm{C\_Raf}\right] \tag{59}$$

8.15 Reaction Inactive_C_Raf_degradation

This is an irreversible reaction of one reactant forming no product.

Name Inactive C-Raf degradation

Reaction equation

$$\mathrm{C\_Raf\_inactive} \longrightarrow \emptyset \tag{60}$$

Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
C_Raf_inactive	C-Raf inactive	

Kinetic Law

Derived unit $(59.9999\ \mathrm{s})^{-1} \cdot \mathrm{mol}$

$$v_{15} = \mathrm{vol}\,(\mathrm{Compartment}) \cdot \mathrm{d6} \cdot [\mathrm{C\_Raf\_inactive}] \tag{61}$$

9 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.

9.1 Species FGFR

Name FGFR

Initial concentration $0\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in FGFR_Degradation and as a product in FGFR_Activation and as a modifier in C_Raf_Activation_1, B_Raf_Activation_1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{FGFR} = v_1 - v_2 \tag{62}$$

9.2 Species MSH

Name MSH

Initial concentration $0\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in MSH_Degradation and as a product in MSH_Activation and as a modifier in B_Raf_Activation_2, C_Raf_Inactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MSH} = v_3 - v_4 \tag{63}$$

9.3 Species B_Raf

Name B-Raf

Initial concentration $0\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in B_Raf_Degradation and as a product in B_Raf_Activation_1, B_Raf_Activation_2 and as a modifier in MAPK_Activation_2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{B\_Raf} = v_8 + v_9 - v_{10} \tag{64}$$

9.4 Species MAPK

Name MAPK

Initial concentration $0\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in MAPK_Degradation and as a product in MAPK_Activation_1, MAPK_Activation_2 and as a modifier in C_Raf_Activation_2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MAPK} = v_{11} + v_{12} - v_{13} \tag{65}$$

9.5 Species C_Raf_inactive

Name C-Raf inactive

Initial concentration $0\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in Inactive_C_Raf_degradation and as a product in C_Raf_Inactivation and as a modifier in C_Raf_Activation_1, C_Raf_Activation_2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C\_Raf\_inactive} = v_{14} - v_{15} \tag{66}$$

9.6 Species g2_0

Name g2

Initial concentration $1\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Involved in rule g2_0

This species takes part in one reaction (as a modifier in MSH_Activation). Not this but one rule determines the species' quantity because this species is on the boundary of the reaction system.

9.7 Species C_Raf

Name C-Raf

Initial concentration $0\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in five reactions (as a reactant in C_Raf_Degradation, C_Raf_Inactivation and as a product in C_Raf_Activation_1, C_Raf_Activation_2 and as a modifier in MAPK-_Activation_1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C\_Raf} = v_5 + v_6 - v_7 - v_{14} \tag{67}$$

9.8 Species g1_0

Name g1

Initial concentration $0\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Involved in rule g1_0

This species takes part in one reaction (as a modifier in FGFR_Activation). Not this but one rule determines the species' quantity because this species is on the boundary of the reaction system.

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