SBML Model Report

Model name: "Neves2008 - Role of cell shape and size in controlling intracellular signalling"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by Harish Dharuri[1] at August 20th 2008 at 9:35 a. m. and last time modified at April seventh 2014 at 0:39 a. 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	3
species types	0	species	37
events	0	constraints	0
reactions	32	function definitions	0
global parameters	28	unit definitions	14
rules	19	initial assignments	0

Model Notes

Neves2008 - Role of cell shape and size in controlling intracellular signalling

The role of cell shape and size in the flow of spatial information from the cell surface receptor to downstream components within the cell has been studied on the -adrenergic receptor to MAPK-signalling network.

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This model is described in the article:Cell shape and negative links in regulatory motifs together control spatial information flow in signaling networks.Neves SR, Tsokas P, Sarkar A, Grace EA, Rangamani P, Taubenfeld SM, Alberini CM, Schaff JC, Blitzer RD, Moraru II, Iyengar RCell. 2008, 133(4):666-680

Abstract:

The role of cell size and shape in controlling local intracellular signaling reactions, and how this spatial information originates and is propagated, is not well understood. We have used partial differential equations to model the flow of spatial information from the beta-adrenergic receptor to MAPK1,2 through the cAMP/PKA/B-Raf/MAPK1,2 network in neurons using real geometries. The numerical simulations indicated that cell shape controls the dynamics of local biochemical activity of signal-modulated negative regulators, such as phosphodiesterases and protein phosphatases within regulatory loops to determine the size of microdomains of activated signaling components. The model prediction that negative regulators control the flow of spatial information to downstream components was verified experimentally in rat hippocampal slices. These results suggest a mechanism by which cellular geometry, the presence of regulatory loops with negative regulators, and key reaction rates all together control spatial information transfer and microdomain characteristics within cells.

This model is hosted on BioModels Database and identifiedby: MODEL8609366518 .

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

2 Unit Definitions

This is an overview of 16 unit definitions of which two are predefined by SBML and not mentioned in the model.

2.1 Unit `substance`

Definition item

2.2 Unit `volume`

Definition $\left(10^{-6}\ \mathrm{m}\right)^3$

2.3 Unit `area`

Definition $\mu\mathrm{m}^2$

2.4 Unit `molecules`

Definition item

2.5 Unit um2

Definition μm^2

2.6 Unit uM_um3_molecules_1

Definition $item^{-1} \cdot \mu mol \cdot l^{-1} \cdot \mu m^{-3}$

2.7 Unit molecules_um_2_s_1

Definition $item \cdot \mu m^{-2} \cdot s^{-1}$

2.8 Unit pA_um_2

Definition $dimensionless \cdot A \cdot m^{-2}$

2.9 Unit s_1

Definition s^{-1}

2.10 Unit _one_000000_0_m6_mol_2_s_1

Definition $1000000\ dimensionless \cdot m^6 \cdot mol^{-2} \cdot s^{-1}$

2.11 Unit uM_s_1

Definition $0.0010\ dimensionless \cdot m^{-3} \cdot mol \cdot s^{-1}$

2.12 Unit uM

Definition $0.0010\ dimensionless \cdot m^{-3} \cdot mol$

2.13 Unit uM_1_s_1

Definition $1000\ dimensionless \cdot m^3 \cdot mol^{-1} \cdot s^{-1}$

2.14 Unit molecules_um_2

Definition $item \cdot \mu m^{-2}$

2.15 Unit length

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

Definition m

2.16 Unit time

Notes Second is the predefined SBML unit for time.

Definition s

3 Compartments

This model contains three compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
cyto	cyto		3	1	$(10^{-6}\ \mathrm{m})^3$	☑	cyto_mem
extra	extra		3	0.111111111111111	$(10^{-6}\ \mathrm{m})^3$	☑	
cyto_mem	cyto_mem		2	0.2	$\mu\mathrm{m}^2$	☑	extra

3.1 Compartment cyto

This is a three dimensional compartment with a constant size of one $(10^{-6}\ \mathrm{m})^3$, which is surrounded by cyto_mem (cyto_mem).

Name cyto

3.2 Compartment extra

This is a three dimensional compartment with a constant size of 0.111111111111111 $(10^{-6}\ \mathrm{m})^3$.

Name extra

3.3 Compartment cyto_mem

This is a two dimensional compartment with a constant size of 0.2 $\mu\mathrm{m}^2$, which is surrounded by extra (extra).

Name cyto_mem

4 Species

This model contains 37 species. Section 8 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
AC_active_cyto_mem		cyto_mem	$\mathrm{item} \cdot \mu\mathrm{m}^{-2}$	⊟	⊟
G_GDP_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
G_protein_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
G_a_s_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
GRK_bg_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
iso_BAR_p_cyto_mem		cyto_mem	$\mathrm{item} \cdot \mu\mathrm{m}^{-2}$	⊟	⊟
PDE4_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
ATP_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
AC_PKA_cyto_mem		cyto_mem	$\mathrm{item} \cdot \mu\mathrm{m}^{-2}$	⊟	⊟
R2C2_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
PP_PDE_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
BAR_cyto_mem		cyto_mem	$\mathrm{item} \cdot \mu\mathrm{m}^{-2}$	⊟	⊟
BAR_G_cyto_mem		cyto_mem	$\mathrm{item} \cdot \mu\mathrm{m}^{-2}$	⊟	⊟
iso_extra		extra	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
iso_BAR_cyto_mem		cyto_mem	$\mathrm{item} \cdot \mu\mathrm{m}^{-2}$	⊟	⊟
MAPK_active_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
MEK_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
MEK_active_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
B_Raf_active_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
bg_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
B_Raf_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
PKA_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
AC_cyto_mem		cyto_mem	$\mathrm{item} \cdot \mu\mathrm{m}^{-2}$	⊟	⊟
AMP_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
GRK_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
PP2A_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
MAPK_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
PTP_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
PTP_PKA_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
c_R2C2_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
c2_R2C2_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
c3_R2C2_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
iso_BAR_G_cyto_mem		cyto_mem	$\mathrm{item} \cdot \mu\mathrm{m}^{-2}$	⊟	⊟
PDE_high_km_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
cAMP_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
PTP_PP_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟
PDE4_P_cyto		cyto	$\mathrm{item} \cdot \left(10^{-6}\ \mathrm{m}\right)^{-3}$	⊟	⊟

5 Parameters

This model contains 28 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
KMOLE			0.002	$\text{item}^{-1} \cdot \mu\text{mol} \cdot \text{l}^{-1} \cdot \mu\text{m}^{-3}$	☑
Vmax_pde4_p-_pde4_p			0.000	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol} \cdot \text{s}^{-1}$	⊟
kcat_PPase-_Raf			5.000	s^{-1}	☑
Vmax_PPase-_Raf			0.000	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol} \cdot \text{s}^{-1}$	⊟
Vmax_PDE4-_PDE4			0.000	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol} \cdot \text{s}^{-1}$	⊟
Vmax_MEK-_activates-_MAPK			0.000	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol} \cdot \text{s}^{-1}$	⊟
kcat_PKA-_activates-_Raf			10.000	s^{-1}	☑
Vmax_PKA-_activates-_Raf			0.000	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol} \cdot \text{s}^{-1}$	⊟
Vmax_AC-_active_AC-_active			0.000	$\text{item} \cdot \mu\text{m}^{-2} \cdot \text{s}^{-1}$	⊟
Vmax_highKM-_PDE			0.000	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol} \cdot \text{s}^{-1}$	⊟
kcat_PKA_P-_PTP			0.200	s^{-1}	☑
Vmax_PKA_P-_PTP			0.000	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol} \cdot \text{s}^{-1}$	⊟
Vmax_AC-_basal_AC-_basal			0.000	$\text{item} \cdot \mu\text{m}^{-2} \cdot \text{s}^{-1}$	⊟
Vmax_grk_GRK			0.000	$\text{item} \cdot \mu\text{m}^{-2} \cdot \text{s}^{-1}$	⊟
Vmax_PKA_P-_PDE			0.000	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol} \cdot \text{s}^{-1}$	⊟
Vmax_Raf-_activates-_MEK			0.000	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol} \cdot \text{s}^{-1}$	⊟

Id	Name	SBO	Value	Unit	Constant
kcat_PTP_PKA			0.100	s^{-1}	☑
Vmax_PTP_PKA			0.000	$0.0010\,\text{dimensionless} \cdot m^{-3} \cdot mol \cdot s^{-1}$	☐
kcat_PTP			1.060	s^{-1}	☑
Vmax_PTP			0.000	$0.0010\,\text{dimensionless} \cdot m^{-3} \cdot mol \cdot s^{-1}$	☐
kcat_PPase_MAPK			0.636	s^{-1}	☑
Vmax_PPase_MAPK			0.000	$0.0010\,\text{dimensionless} \cdot m^{-3} \cdot mol \cdot s^{-1}$	☐
Vmax_pp2a_4_pp2a_4			0.000	$0.0010\,\text{dimensionless} \cdot m^{-3} \cdot mol \cdot s^{-1}$	☐
kcat_pp_ptp_pp_ptp			5.000	s^{-1}	☑
Vmax_pp_ptp			0.000	$0.0010\,\text{dimensionless} \cdot m^{-3} \cdot mol \cdot s^{-1}$	☐
Vmax_GRK_bg_GRK_bg			0.000	$\text{item} \cdot \mu m^{-2} \cdot s^{-1}$	☐
kcat_PPase_mek			5.000	s^{-1}	☑
Vmax_PPase_mek			0.000	$0.0010\,\text{dimensionless} \cdot m^{-3} \cdot mol \cdot s^{-1}$	☐

6 Rules

This is an overview of 19 rules.

6.1 Rule Vmax_pde4_p_pde4_p

Rule Vmax_pde4_p_pde4_p is an assignment rule for parameter Vmax_pde4_p_pde4_p:

$$\text{Vmax\_pde4\_p\_pde4\_p} = 20 \cdot 0.00166112956810631 \cdot [\text{PDE4\_P\_cyto}] \quad (1)$$

6.2 Rule Vmax_PPase_Raf

Rule Vmax_PPase_Raf is an assignment rule for parameter Vmax_PPase_Raf:

$$\text{Vmax\_PPase\_Raf} = \text{kcat\_PPase\_Raf} \cdot 0.00166112956810631 \cdot [\text{PP2A\_cyto}] \quad (2)$$

6.3 Rule Vmax_PDE4_PDE4

Rule Vmax_PDE4_PDE4 is an assignment rule for parameter Vmax_PDE4_PDE4:

$$\text{Vmax\_PDE4\_PDE4} = 8 \cdot 0.00166112956810631 \cdot [\text{PDE4\_cyto}] \quad (3)$$

6.4 Rule Vmax_MEK_activates_MAPK

Rule Vmax_MEK_activates_MAPK is an assignment rule for parameter Vmax_MEK_activates_MAPK:

$$\text{Vmax\_MEK\_activates\_MAPK} = 0.15 \cdot 0.00166112956810631 \cdot [\text{MEK\_active\_cyto}] \quad (4)$$

6.5 Rule Vmax_PKA_activates_Raf

Rule Vmax_PKA_activates_Raf is an assignment rule for parameter Vmax_PKA_activates_Raf:

$$\text{Vmax\_PKA\_activates\_Raf} = \text{kcat\_PKA\_activates\_Raf} \cdot 0.00166112956810631 \cdot [\text{PKA\_cyto}] \quad (5)$$

6.6 Rule Vmax_AC_active_AC_active

Rule Vmax_AC_active_AC_active is an assignment rule for parameter Vmax_AC_active_AC_active:

$$\text{Vmax\_AC\_active\_AC\_active} = 8.5 \cdot [\text{AC\_active\_cyto\_mem}] \quad (6)$$

6.7 Rule Vmax_highKM_PDE

Rule Vmax_highKM_PDE is an assignment rule for parameter Vmax_highKM_PDE:

$$\text{Vmax\_highKM\_PDE} = 8 \cdot 0.00166112956810631 \cdot [\text{PDE\_high\_km\_cyto}] \quad (7)$$

6.8 Rule Vmax_PKA_P_PTP

Rule Vmax_PKA_P_PTP is an assignment rule for parameter Vmax_PKA_P_PTP:

$$\text{Vmax\_PKA\_P\_PTP} = \text{kcat\_PKA\_P\_PTP} \cdot 0.00166112956810631 \cdot [\text{PKA\_cyto}] \quad (8)$$

6.9 Rule Vmax_AC_basal_AC_basal

Rule Vmax_AC_basal_AC_basal is an assignment rule for parameter Vmax_AC_basal_AC_basal:

$$\text{Vmax\_AC\_basal\_AC\_basal} = 0.2 \cdot [\text{AC\_cyto\_mem}] \quad (9)$$

6.10 Rule Vmax_grk_GRK

Rule Vmax_grk_GRK is an assignment rule for parameter Vmax_grk_GRK:

$$\text{Vmax\_grk\_GRK} = 0.104 \cdot 0.00166112956810631 \cdot [\text{GRK\_cyto}] \quad (10)$$

6.11 Rule Vmax_PKA_P_PDE

Rule Vmax_PKA_P_PDE is an assignment rule for parameter Vmax_PKA_P_PDE:

$$\text{Vmax\_PKA\_P\_PDE} = 10 \cdot 0.00166112956810631 \cdot [\text{PKA\_cyto}] \quad (11)$$

6.12 Rule Vmax_Raf_activates_MEK

Rule Vmax_Raf_activates_MEK is an assignment rule for parameter Vmax_Raf_activates_MEK:

$$\text{Vmax\_Raf\_activates\_MEK} = 0.105 \cdot 0.00166112956810631 \cdot [\text{B\_Raf\_active\_cyto}] \quad (12)$$

6.13 Rule Vmax_PTP_PKA

Rule Vmax_PTP_PKA is an assignment rule for parameter Vmax_PTP_PKA:

$$\text{Vmax\_PTP\_PKA} = \text{kcat\_PTP\_PKA} \cdot 0.00166112956810631 \cdot [\text{PTP\_PKA\_cyto}] \quad (13)$$

6.14 Rule Vmax_PTP

Rule Vmax_PTP is an assignment rule for parameter Vmax_PTP:

$$\text{Vmax\_PTP} = \text{kcat\_PTP} \cdot 0.00166112956810631 \cdot [\text{PTP\_cyto}] \quad (14)$$

6.15 Rule Vmax_PPase_MAPK

Rule Vmax_PPase_MAPK is an assignment rule for parameter Vmax_PPase_MAPK:

$$\text{Vmax\_PPase\_MAPK} = \text{kcat\_PPase\_MAPK} \cdot 0.00166112956810631 \cdot [\text{PP2A\_cyto}] \quad (15)$$

6.16 Rule Vmax_pp2a_4_pp2a_4

Rule Vmax_pp2a_4_pp2a_4 is an assignment rule for parameter Vmax_pp2a_4_pp2a_4:

$$\text{Vmax\_pp2a\_4\_pp2a\_4} = 5 \cdot 0.00166112956810631 \cdot [\text{PP\_PDE\_cyto}] \quad (16)$$

6.17 Rule Vmax_pp_ptp

Rule Vmax_pp_ptp is an assignment rule for parameter Vmax_pp_ptp:

$$\text{Vmax\_pp\_ptp} = \text{kcat\_pp\_ptp\_pp\_ptp} \cdot 0.00166112956810631 \cdot [\text{PTP\_PP\_cyto}] \quad (17)$$

6.18 Rule Vmax_GRK_bg_GRK_bg

Rule Vmax_GRK_bg_GRK_bg is an assignment rule for parameter Vmax_GRK_bg_GRK_bg:

$$\text{Vmax\_GRK\_bg\_GRK\_bg} = 1.34 \cdot 0.00166112956810631 \cdot [\text{GRK\_bg\_cyto}] \quad (18)$$

6.19 Rule Vmax_PPase_mek

Rule Vmax_PPase_mek is an assignment rule for parameter Vmax_PPase_mek:

$$\text{Vmax\_PPase\_mek} = \text{kcat\_PPase\_mek} \cdot 0.00166112956810631 \cdot [\text{PP2A\_cyto}] \quad (19)$$

7 Reactions

This model contains 32 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	activate_Gs	activate_Gs	$\text{iso\_BAR\_G\_cyto\_mem} \rightleftharpoons \text{iso\_BAR\_cyto\_mem} + \text{bg\_cyto} + \text{G\_a\_s\_cyto}$	
2	pde4_p	pde4_p	$\text{cAMP\_cyto} \overset{\text{PDE4\_P\_cyto}}{\rightleftharpoons} \text{AMP\_cyto}$	
3	PPase_Raf	PPase_Raf	$\text{B\_Raf\_active\_cyto} \overset{\text{PP2A\_cyto}}{\rightleftharpoons} \text{B\_Raf\_cyto}$	
4	iso_binds_BAR	iso_binds_BAR	$\text{BAR\_cyto\_mem} + \text{iso\_extra} \rightleftharpoons \text{iso\_BAR\_cyto\_mem}$	
5	PDE4	PDE4	$\text{cAMP\_cyto} \overset{\text{PDE4\_cyto}}{\rightleftharpoons} \text{AMP\_cyto}$	
6	bg_binds_GRK	bg_binds_GRK	$\text{GRK\_cyto} + \text{bg\_cyto} \rightleftharpoons \text{GRK\_bg\_cyto}$	
7	MEK_activates_MAPK	MEK_activates_MAPK	$\text{MAPK\_cyto} \overset{\text{MEK\_active\_cyto}}{\rightleftharpoons} \text{MAPK\_active\_cyto}$	
8	PKA_activates_Raf	PKA_activates_Raf	$\text{B\_Raf\_cyto} \overset{\text{PKA\_cyto}}{\rightleftharpoons} \text{B\_Raf\_active\_cyto}$	
9	AC_active	AC_active	$\text{ATP\_cyto} \overset{\text{AC\_active\_cyto\_mem}}{\rightleftharpoons} \text{cAMP\_cyto}$	
10	GTPase	GTPase	$\text{G\_a\_s\_cyto} \rightleftharpoons \text{G\_GDP\_cyto}$	
11	trimer	trimer	$\text{bg\_cyto} + \text{G\_GDP\_cyto} \rightleftharpoons \text{G\_protein\_cyto}$	
12	G_binds_iso_BAR	G_binds_iso_BAR	$\text{iso\_BAR\_cyto\_mem} + \text{G\_protein\_cyto} \rightleftharpoons \text{iso\_BAR\_G\_cyto\_mem}$	
13	A2	A2	$\text{c3\_R2C2\_cyto} + \text{cAMP\_cyto} \rightleftharpoons \text{PKA\_cyto}$	
14	highKM_PDE	highKM_PDE	$\text{cAMP\_cyto} \overset{\text{PDE\_high\_km\_cyto}}{\rightleftharpoons} \text{AMP\_cyto}$	

№	Id	Name	Reaction Equation	SBO
15	PKA_P_PTP	PKA_P_PTP	$\text{PTP\_cyto} \overset{\text{PKA\_cyto}}{\rightleftharpoons} \text{PTP\_PKA\_cyto}$	
16	AC_activation	AC_activation	$\text{G\_a\_s\_cyto} + \text{AC\_cyto\_mem} \rightleftharpoons \text{AC\_active\_cyto\_mem}$	
17	AC_basal	AC_basal	$\text{ATP\_cyto} \overset{\text{AC\_cyto\_mem}}{\rightleftharpoons} \text{cAMP\_cyto}$	
18	B1	B1	$\text{R2C2\_cyto} + \text{cAMP\_cyto} \rightleftharpoons \text{c\_R2C2\_cyto}$	
19	GRK	GRK	$\text{iso\_BAR\_cyto\_mem} \overset{\text{GRK\_cyto}}{\rightleftharpoons} \text{iso\_BAR\_p\_cyto\_mem}$	
20	PKA_P_PDE	PKA_P_PDE	$\text{PDE4\_cyto} \overset{\text{PKA\_cyto}}{\rightleftharpoons} \text{PDE4\_P\_cyto}$	
21	Raf_activates-_MEK	Raf_activates_MEK	$\text{MEK\_cyto} \overset{\text{B\_Raf\_active\_cyto}}{\rightleftharpoons} \text{MEK\_active\_cyto}$	
22	PTP_PKA	PTP_PKA	$\text{MAPK\_active\_cyto} \overset{\text{PTP\_PKA\_cyto}}{\rightleftharpoons} \text{MAPK\_cyto}$	
23	B2	B2	$\text{c\_R2C2\_cyto} + \text{cAMP\_cyto} \rightleftharpoons \text{c2\_R2C2\_cyto}$	
24	PTP	PTP	$\text{MAPK\_active\_cyto} \overset{\text{PTP\_cyto}}{\rightleftharpoons} \text{MAPK\_cyto}$	
25	iso_binds_BAR_g	iso_binds_BAR_g	$\text{iso\_extra} + \text{BAR\_G\_cyto\_mem} \rightleftharpoons \text{iso\_BAR\_G\_cyto\_mem}$	
26	PPase_MAPK	PPase_MAPK	$\text{MAPK\_active\_cyto} \overset{\text{PP2A\_cyto}}{\rightleftharpoons} \text{MAPK\_cyto}$	
27	pp2a_4	pp2a_4	$\text{PDE4\_P\_cyto} \overset{\text{PP\_PDE\_cyto}}{\rightleftharpoons} \text{PDE4\_cyto}$	
28	pp_ptp	pp_ptp	$\text{PTP\_PKA\_cyto} \overset{\text{PTP\_PP\_cyto}}{\rightleftharpoons} \text{PTP\_cyto}$	
29	GRK_bg	GRK_bg	$\text{iso\_BAR\_cyto\_mem} \overset{\text{GRK\_bg\_cyto}}{\rightleftharpoons} \text{iso\_BAR\_p\_cyto\_mem}$	
30	G_binds_BAR	G_binds_BAR	$\text{BAR\_cyto\_mem} + \text{G\_protein\_cyto} \rightleftharpoons \text{BAR\_G\_cyto\_mem}$	
31	PPase_mek	PPase_mek	$\text{MEK\_active\_cyto} \overset{\text{PP2A\_cyto}}{\rightleftharpoons} \text{MEK\_cyto}$	
32	A1	A1	$\text{c2\_R2C2\_cyto} + \text{cAMP\_cyto} \rightleftharpoons \text{c3\_R2C2\_cyto}$	

7.1 Reaction activate_Gs

This is a reversible reaction of one reactant forming three products.

Name activate_Gs

Reaction equation

$$\text{iso\_BAR\_G\_cyto\_mem} \rightleftharpoons \text{iso\_BAR\_cyto\_mem} + \text{bg\_cyto} + \text{G\_a\_s\_cyto} \tag{20}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
iso_BAR_G_cyto_mem		

Products

Table 7: Properties of each product.

Id	Name	SBO
iso_BAR_cyto_mem		
bg_cyto		
G_a_s_cyto		

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_1 = (&\text{Kf\_activate\_Gs} \cdot [\text{iso\_BAR\_G\_cyto\_mem}] - \text{Kr\_activate\_Gs} \cdot [\text{iso\_BAR\_cyto\_mem}] \\ &\cdot 0.00166112956810631 \cdot [\text{bg\_cyto}] \cdot 0.00166112956810631 \cdot [\text{G\_a\_s\_cyto}]) \\ &\cdot \text{area}(\text{cyto\_mem}) \end{aligned} \tag{21}$$

Table 8: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.000	dimensionless · A · m^{-2}	☑
Kf_activate_Gs			0.025	s^{-1}	☑

Id	Name	SBO	Value	Unit	Constant
Kr_activate-_Gs			0.000	1000000 dimensionless · $m^6 \cdot mol^{-2} \cdot s^{-1}$	☑

7.2 Reaction pde4_p

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

Name pde4_p

Reaction equation

$$\text{cAMP\_cyto} \xrightleftharpoons{\text{PDE4\_P\_cyto}} \text{AMP\_cyto} \tag{22}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
cAMP_cyto		

Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
PDE4_P_cyto		

Product

Table 11: Properties of each product.

Id	Name	SBO
AMP_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{Vmax\_pde4\_p\_pde4\_p} \cdot 0.00166112956810631 \cdot [\mathrm{cAMP\_cyto}] \cdot \frac{1}{\mathrm{Km\_pde4\_p} + 0.00166112956810631 \cdot [\mathrm{cAMP\_cyto}]} \cdot \mathrm{vol}\,(\mathrm{cyto}) \cdot 1 \cdot \frac{1}{\mathrm{KMOLE}} \tag{23}$$

Table 12: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Km_pde4_p`			1.3	$0.0010\,\mathrm{dimensionless} \cdot \mathrm{m}^{-3} \cdot \mathrm{mol}$	☑

7.3 Reaction `PPase_Raf`

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

Name PPase_Raf

Reaction equation

$$\mathrm{B\_Raf\_active\_cyto} \xrightleftharpoons{\mathrm{PP2A\_cyto}} \mathrm{B\_Raf\_cyto} \tag{24}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
`B_Raf_active_cyto`		

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
`PP2A_cyto`		

Product

Table 15: Properties of each product.

Id	Name	SBO
B_Raf_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{Vmax\_PPase\_Raf} \cdot 0.00166112956810631 \cdot [\text{B\_Raf\_active\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{B\_Raf\_active\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \quad (25)$$

Table 16: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			15.7	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol}$	☑

7.4 Reaction iso_binds_BAR

This is a reversible reaction of two reactants forming one product.

Name iso_binds_BAR

Reaction equation

$$\text{BAR\_cyto\_mem} + \text{iso\_extra} \rightleftharpoons \text{iso\_BAR\_cyto\_mem} \quad (26)$$

Reactants

Table 17: Properties of each reactant.

Id	Name	SBO
BAR_cyto_mem		
iso_extra		

Product

Table 18: Properties of each product.

Id	Name	SBO
iso_BAR_cyto_mem		

Kinetic Law

Derived unit contains undeclared units

$$v_4 = (\mathrm{Kf} \cdot [\mathrm{BAR\_cyto\_mem}] \cdot 0.00166112956810631 \cdot [\mathrm{iso\_extra}] + ((\mathrm{Kr} \cdot [\mathrm{iso\_BAR\_cyto\_mem}]))) \cdot \mathrm{area}(\mathrm{cyto\_mem}) \quad (27)$$

Table 19: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.0	dimensionless · A · m^{-2}	☑
Kf			1.0	1000 dimensionless · $m^3 \cdot mol^{-1} \cdot s^{-1}$	☑
Kr			0.2	s^{-1}	☑

7.5 Reaction PDE4

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

Name PDE4

Reaction equation

$$\mathrm{cAMP\_cyto} \xrightleftharpoons{\mathrm{PDE4\_cyto}} \mathrm{AMP\_cyto} \quad (28)$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
cAMP_cyto		

Modifier

Table 21: Properties of each modifier.

Id	Name	SBO
PDE4_cyto		

Product

Table 22: Properties of each product.

Id	Name	SBO
AMP_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{Vmax\_PDE4\_PDE4} \cdot 0.00166112956810631 \cdot [\text{cAMP\_cyto}] \cdot \frac{1}{\text{Km\_PDE4} + 0.00166112956810631 \cdot [\text{cAMP\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \tag{29}$$

Table 23: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km_PDE4			1.3	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol}$	☑

7.6 Reaction bg_binds_GRK

This is a reversible reaction of two reactants forming one product.

Name bg_binds_GRK

Reaction equation

$$\text{GRK\_cyto} + \text{bg\_cyto} \rightleftharpoons \text{GRK\_bg\_cyto} \tag{30}$$

Reactants

Table 24: Properties of each reactant.

Id	Name	SBO
GRK_cyto		
bg_cyto		

Product

Table 25: Properties of each product.

Id	Name	SBO
GRK_bg_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_6 = (\text{Kf\_bg\_binds\_GRK} \cdot 0.00166112956810631 \cdot [\text{GRK\_cyto}] \cdot 0.00166112956810631 \cdot [\text{bg\_cyto}] + ((\text{Kr\_bg\_binds\_GRK} \cdot 0.00166112956810631 \cdot [\text{GRK\_bg\_cyto}]))) \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \quad (31)$$

Table 26: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kf_bg_binds_GRK			1.00	$1000\,\text{dimensionless} \cdot \text{m}^3 \cdot \text{mol}^{-1} \cdot \text{s}^{-1}$	☑
Kr_bg_binds_GRK			0.25	s^{-1}	☑

7.7 Reaction MEK_activates_MAPK

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

Name MEK_activates_MAPK

Reaction equation

$$\text{MAPK\_cyto} \xrightleftharpoons{\text{MEK\_active\_cyto}} \text{MAPK\_active\_cyto} \quad (32)$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
MAPK_cyto		

Modifier

Table 28: Properties of each modifier.

Id	Name	SBO
MEK_active_cyto		

Product

Table 29: Properties of each product.

Id	Name	SBO
MAPK_active_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{Vmax\_MEK\_activates\_MAPK} \cdot 0.00166112956810631 \cdot [\text{MAPK\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{MAPK\_cyto}]} \cdot \text{vol}\,(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \tag{33}$$

Table 30: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			0.046	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol}$	☑

7.8 Reaction PKA_activates_Raf

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

Name PKA_activates_Raf

Reaction equation

$$\text{B\_Raf\_cyto} \xrightleftharpoons{\text{PKA\_cyto}} \text{B\_Raf\_active\_cyto} \tag{34}$$

Reactant

Table 31: Properties of each reactant.

Id	Name	SBO
B_Raf_cyto		

Modifier

Table 32: Properties of each modifier.

Id	Name	SBO
PKA_cyto		

Product

Table 33: Properties of each product.

Id	Name	SBO
B_Raf_active_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{Vmax\_PKA\_activates\_Raf} \cdot 0.00166112956810631 \cdot [\text{B\_Raf\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{B\_Raf\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \tag{35}$$

Table 34: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			0.5	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol}$	☑

7.9 Reaction AC_active

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

Name AC_active

Reaction equation

$$\mathrm{ATP\_cyto} \overset{\mathrm{AC\_active\_cyto\_mem}}{\rightleftharpoons} \mathrm{cAMP\_cyto} \tag{36}$$

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
ATP_cyto		

Modifier

Table 36: Properties of each modifier.

Id	Name	SBO
AC_active_cyto_mem		

Product

Table 37: Properties of each product.

Id	Name	SBO
cAMP_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{Vmax\_AC\_active\_AC\_active} \cdot 0.00166112956810631 \cdot [\mathrm{ATP\_cyto}] \cdot \frac{1}{\mathrm{Km\_AC\_active} + 0.00166112956810631 \cdot [\mathrm{ATP\_cyto}]} \cdot \mathrm{area}\,(\mathrm{cyto\_mem}) \tag{37}$$

Table 38: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.0	dimensionless · A · m^{-2}	☑
Km_AC_active			32.0	0.0010 dimensionless · m^{-3} · mol	☑

7.10 Reaction GTPase

This is a reversible reaction of one reactant forming one product.

Name GTPase

Reaction equation

$$\text{G\_a\_s\_cyto} \rightleftharpoons \text{G\_GDP\_cyto} \tag{38}$$

Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
G_a_s_cyto		

Product

Table 40: Properties of each product.

Id	Name	SBO
G_GDP_cyto		

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{10} = {} & (\text{Kf\_GTPase} \cdot 0.00166112956810631 \cdot [\text{G\_a\_s\_cyto}] \\ & + ((\text{Kr\_GTPase} \cdot 0.00166112956810631 \cdot [\text{G\_GDP\_cyto}]))) \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \end{aligned} \tag{39}$$

Table 41: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kf_GTPase			0.067	s^{-1}	☑
Kr_GTPase			0.000	s^{-1}	☑

7.11 Reaction trimer

This is a reversible reaction of two reactants forming one product.

Name trimer

Reaction equation

$$\text{bg\_cyto} + \text{G\_GDP\_cyto} \rightleftharpoons \text{G\_protein\_cyto} \tag{40}$$

Reactants

Table 42: Properties of each reactant.

Id	Name	SBO
bg_cyto		
G_GDP_cyto		

Product

Table 43: Properties of each product.

Id	Name	SBO
G_protein_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = (\text{Kf\_trimer} \cdot 0.00166112956810631 \cdot [\text{bg\_cyto}] \cdot 0.00166112956810631 \cdot [\text{G\_GDP\_cyto}] + ((\text{Kr\_trimer} \cdot 0.00166112956810631 \cdot [\text{G\_protein\_cyto}]))) \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \tag{41}$$

Table 44: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kf_trimer			6.0	1000 dimensionless · $m^3 \cdot mol^{-1} \cdot s^{-1}$	☑
Kr_trimer			0.0	s^{-1}	☑

7.12 Reaction G_binds_iso_BAR

This is a reversible reaction of two reactants forming one product.

Name G_binds_iso_BAR

Reaction equation

$$\text{iso\_BAR\_cyto\_mem} + \text{G\_protein\_cyto} \rightleftharpoons \text{iso\_BAR\_G\_cyto\_mem} \tag{42}$$

Reactants

Table 45: Properties of each reactant.

Id	Name	SBO
iso_BAR_cyto_mem		
G_protein_cyto		

Product

Table 46: Properties of each product.

Id	Name	SBO
iso_BAR_G_cyto_mem		

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = (\text{Kf\_G\_binds\_iso\_BAR} \cdot [\text{iso\_BAR\_cyto\_mem}] \cdot 0.00166112956810631 \cdot [\text{G\_protein\_cyto}] + ((\text{Kr\_G\_binds\_iso\_BAR} \cdot [\text{iso\_BAR\_G\_cyto\_mem}]))) \cdot \text{area}(\text{cyto\_mem}) \tag{43}$$

Table 47: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.0	dimensionless · A · m^{-2}	☑
Kf_G_binds_iso_BAR			10.0	1000 dimensionless · $m^3 \cdot mol^{-1} \cdot s^{-1}$	☑
Kr_G_binds_iso_BAR			0.1	s^{-1}	☑

7.13 Reaction A2

This is a reversible reaction of two reactants forming one product.

Name A2

Reaction equation

$$\text{c3\_R2C2\_cyto} + \text{cAMP\_cyto} \rightleftharpoons \text{PKA\_cyto} \tag{44}$$

Reactants

Table 48: Properties of each reactant.

Id	Name	SBO
c3_R2C2_cyto		
cAMP_cyto		

Product

Table 49: Properties of each product.

Id	Name	SBO
PKA_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = (\text{Kf} \cdot 0.00166112956810631 \cdot [\text{c3\_R2C2\_cyto}] \cdot 0.00166112956810631 \cdot [\text{cAMP\_cyto}] + ((\text{Kr} \cdot 0.00166112956810631 \cdot [\text{PKA\_cyto}]))) \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \tag{45}$$

Table 50: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kf			8.350	1000 dimensionless · $m^3 \cdot mol^{-1} \cdot s^{-1}$	☑
Kr			0.017	s^{-1}	☑

7.14 Reaction highKM_PDE

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

Name highKM_PDE

Reaction equation

$$\text{cAMP\_cyto} \overset{\text{PDE\_high\_km\_cyto}}{\rightleftharpoons} \text{AMP\_cyto} \tag{46}$$

Reactant

Table 51: Properties of each reactant.

Id	Name	SBO
cAMP_cyto		

Modifier

Table 52: Properties of each modifier.

Id	Name	SBO
PDE_high_km_cyto		

Product

Table 53: Properties of each product.

Id	Name	SBO
AMP_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \text{Vmax\_highKM\_PDE} \cdot 0.00166112956810631 \cdot [\text{cAMP\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{cAMP\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \quad (47)$$

Table 54: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			15.0	0.0010 dimensionless · $m^{-3} \cdot mol$	☑

7.15 Reaction PKA_P_PTP

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

Name PKA_P_PTP

Reaction equation

$$\text{PTP\_cyto} \xrightleftharpoons{\text{PKA\_cyto}} \text{PTP\_PKA\_cyto} \quad (48)$$

Reactant

Table 55: Properties of each reactant.

Id	Name	SBO
PTP_cyto		

Modifier

Table 56: Properties of each modifier.

Id	Name	SBO
PKA_cyto		

Product

Table 57: Properties of each product.

Id	Name	SBO
PTP_PKA_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \text{Vmax\_PKA\_P\_PTP} \cdot 0.00166112956810631 \cdot [\text{PTP\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{PTP\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \tag{49}$$

Table 58: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			0.1	0.0010 dimensionless $\cdot$ $\text{m}^{-3} \cdot \text{mol}$	☑

7.16 Reaction AC_activation

This is a reversible reaction of two reactants forming one product.

Name AC_activation

Reaction equation

$$\text{G\_a\_s\_cyto} + \text{AC\_cyto\_mem} \rightleftharpoons \text{AC\_active\_cyto\_mem} \tag{50}$$

Reactants

Table 59: Properties of each reactant.

Id	Name	SBO
G_a_s_cyto		
AC_cyto_mem		

Product

Table 60: Properties of each product.

Id	Name	SBO
AC_active_cyto_mem		

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = (\text{Kf\_AC\_activation} \cdot 0.00166112956810631 \cdot [\text{G\_a\_s\_cyto}] \cdot [\text{AC\_cyto\_mem}] + ((\text{Kr\_AC\_activation} \cdot [\text{AC\_active\_cyto\_mem}]))) \cdot \text{area}(\text{cyto\_mem}) \quad (51)$$

Table 61: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.0	dimensionless · A · m^{-2}	☑
Kf_AC_activation			500.0	1000 dimensionless · $m^3 \cdot mol^{-1} \cdot s^{-1}$	☑
Kr_AC_activation			1.0	s^{-1}	☑

7.17 Reaction AC_basal

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

Name AC_basal

Reaction equation

$$\text{ATP\_cyto} \xrightleftharpoons{\text{AC\_cyto\_mem}} \text{cAMP\_cyto} \quad (52)$$

Reactant

Table 62: Properties of each reactant.

Id	Name	SBO
ATP_cyto		

Modifier

Table 63: Properties of each modifier.

Id	Name	SBO
AC_cyto_mem		

Product

Table 64: Properties of each product.

Id	Name	SBO
cAMP_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \text{Vmax\_AC\_basal\_AC\_basal} \cdot 0.00166112956810631 \cdot [\text{ATP\_cyto}] \cdot \frac{1}{\text{Km\_AC\_basal} + 0.00166112956810631 \cdot [\text{ATP\_cyto}]} \cdot \text{area}\,(\text{cyto\_mem}) \tag{53}$$

Table 65: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.0	dimensionless · A · m^{-2}	☑
Km_AC_basal			1030.0	0.0010 dimensionless · m^{-3} · mol	☑

7.18 Reaction B1

This is a reversible reaction of two reactants forming one product.

Name B1

Reaction equation

$$\text{R2C2\_cyto} + \text{cAMP\_cyto} \rightleftharpoons \text{c\_R2C2\_cyto} \tag{54}$$

Reactants

Table 66: Properties of each reactant.

Id	Name	SBO
R2C2_cyto		
cAMP_cyto		

Product

Table 67: Properties of each product.

Id	Name	SBO
c_R2C2_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = (\mathrm{Kf} \cdot 0.00166112956810631 \cdot [\mathrm{R2C2\_cyto}] \cdot 0.00166112956810631 \cdot [\mathrm{cAMP\_cyto}] + ((\mathrm{Kr} \cdot 0.00166112956810631 \cdot [\mathrm{c\_R2C2\_cyto}]))) \cdot \mathrm{vol}(\mathrm{cyto}) \cdot 1 \cdot \frac{1}{\mathrm{KMOLE}} \quad (55)$$

Table 68: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kf			0.006	$1000\,\mathrm{dimensionless} \cdot \mathrm{m}^3 \cdot \mathrm{mol}^{-1} \cdot \mathrm{s}^{-1}$	☑
Kr			$2.8 \cdot 10^{-4}$	s^{-1}	☑

7.19 Reaction GRK

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

Name GRK

Reaction equation

$$\mathrm{iso\_BAR\_cyto\_mem} \xrightleftharpoons{\mathrm{GRK\_cyto}} \mathrm{iso\_BAR\_p\_cyto\_mem} \quad (56)$$

Reactant

Table 69: Properties of each reactant.

Id	Name	SBO
iso_BAR_cyto_mem		

Modifier

Table 70: Properties of each modifier.

Id	Name	SBO
GRK_cyto		

Product

Table 71: Properties of each product.

Id	Name	SBO
iso_BAR_p_cyto_mem		

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{Vmax\_grk\_GRK} \cdot [\text{iso\_BAR\_cyto\_mem}] \cdot \frac{1}{\text{Km\_grk} + [\text{iso\_BAR\_cyto\_mem}]} \cdot \text{area}\,(\text{cyto\_mem}) \tag{57}$$

Table 72: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.0	dimensionless · A · m^{-2}	☑
Km_grk			15.0	item · μm^{-2}	☑

7.20 Reaction PKA_P_PDE

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

Name PKA_P_PDE

Reaction equation

$$\text{PDE4\_cyto} \xrightleftharpoons{\text{PKA\_cyto}} \text{PDE4\_P\_cyto} \tag{58}$$

Reactant

Table 73: Properties of each reactant.

Id	Name	SBO
PDE4_cyto		

Modifier

Table 74: Properties of each modifier.

Id	Name	SBO
PKA_cyto		

Product

Table 75: Properties of each product.

Id	Name	SBO
PDE4_P_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \text{Vmax\_PKA\_P\_PDE} \cdot 0.00166112956810631 \cdot [\text{PDE4\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{PDE4\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \tag{59}$$

Table 76: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			0.5	0.0010 dimensionless · $\text{m}^{-3} \cdot \text{mol}$	☑

7.21 Reaction Raf_activates_MEK

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

Name Raf_activates_MEK

Reaction equation

$$\mathrm{MEK\_cyto} \xrightleftharpoons{\mathrm{B\_Raf\_active\_cyto}} \mathrm{MEK\_active\_cyto} \tag{60}$$

Reactant

Table 77: Properties of each reactant.

Id	Name	SBO
MEK_cyto		

Modifier

Table 78: Properties of each modifier.

Id	Name	SBO
B_Raf_active_cyto		

Product

Table 79: Properties of each product.

Id	Name	SBO
MEK_active_cyto		

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{21} = {} & \mathrm{Vmax\_Raf\_activates\_MEK} \cdot 0.00166112956810631 \cdot [\mathrm{MEK\_cyto}] \\ & \cdot \frac{1}{\mathrm{Km} + 0.00166112956810631 \cdot [\mathrm{MEK\_cyto}]} \cdot \mathrm{vol}\,(\mathrm{cyto}) \cdot 1 \cdot \frac{1}{\mathrm{KMOLE}} \end{aligned} \tag{61}$$

Table 80: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			0.159	0.0010 dimensionless · $m^{-3} \cdot mol$	☑

7.22 Reaction PTP_PKA

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

Name PTP_PKA

Reaction equation

$$\text{MAPK\_active\_cyto} \overset{\text{PTP\_PKA\_cyto}}{\rightleftharpoons} \text{MAPK\_cyto} \tag{62}$$

Reactant

Table 81: Properties of each reactant.

Id	Name	SBO
MAPK_active_cyto		

Modifier

Table 82: Properties of each modifier.

Id	Name	SBO
PTP_PKA_cyto		

Product

Table 83: Properties of each product.

Id	Name	SBO
MAPK_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \text{Vmax\_PTP\_PKA} \cdot 0.00166112956810631 \cdot [\text{MAPK\_active\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{MAPK\_active\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \quad (63)$$

Table 84: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			9.0	0.0010 dimensionless · $m^{-3} \cdot mol$	☑

7.23 Reaction B2

This is a reversible reaction of two reactants forming one product.

Name B2

Reaction equation

$$\text{c\_R2C2\_cyto} + \text{cAMP\_cyto} \rightleftharpoons \text{c2\_R2C2\_cyto} \quad (64)$$

Reactants

Table 85: Properties of each reactant.

Id	Name	SBO
c_R2C2_cyto		
cAMP_cyto		

Product

Table 86: Properties of each product.

Id	Name	SBO
c2_R2C2_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = (\mathrm{Kf} \cdot 0.00166112956810631 \cdot [\mathrm{c\_R2C2\_cyto}] \cdot 0.00166112956810631 \cdot [\mathrm{cAMP\_cyto}] + ((\mathrm{Kr} \cdot 0.00166112956810631 \cdot [\mathrm{c2\_R2C2\_cyto}]))) \cdot \mathrm{vol}(\mathrm{cyto}) \cdot 1 \cdot \frac{1}{\mathrm{KMOLE}} \quad (65)$$

Table 87: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kf			0.006	1000 dimensionless $\cdot$ $\mathrm{m}^3 \cdot \mathrm{mol}^{-1} \cdot \mathrm{s}^{-1}$	☑
Kr			$2.8 \cdot 10^{-4}$	s^{-1}	☑

7.24 Reaction PTP

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

Name PTP

Reaction equation

$$\mathrm{MAPK\_active\_cyto} \xrightleftharpoons{\mathrm{PTP\_cyto}} \mathrm{MAPK\_cyto} \quad (66)$$

Reactant

Table 88: Properties of each reactant.

Id	Name	SBO
MAPK_active_cyto		

Modifier

Table 89: Properties of each modifier.

Id	Name	SBO
PTP_cyto		

Product

Table 90: Properties of each product.

Id	Name	SBO
MAPK_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \text{Vmax\_PTP} \cdot 0.00166112956810631 \cdot [\text{MAPK\_active\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{MAPK\_active\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \quad (67)$$

Table 91: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			0.46	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol}$	☑

7.25 Reaction iso_binds_BAR_g

This is a reversible reaction of two reactants forming one product.

Name iso_binds_BAR_g

Reaction equation

$$\text{iso\_extra} + \text{BAR\_G\_cyto\_mem} \rightleftharpoons \text{iso\_BAR\_G\_cyto\_mem} \quad (68)$$

Reactants

Table 92: Properties of each reactant.

Id	Name	SBO
iso_extra		
BAR_G_cyto_mem		

Product

Table 93: Properties of each product.

Id	Name	SBO
iso_BAR_G_cyto_mem		

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = (\mathrm{Kf} \cdot 0.00166112956810631 \cdot [\mathrm{iso\_extra}] \cdot [\mathrm{BAR\_G\_cyto\_mem}] + ((\mathrm{Kr} \cdot [\mathrm{iso\_BAR\_G\_cyto\_mem}]))) \cdot \mathrm{area}(\mathrm{cyto\_mem}) \quad (69)$$

Table 94: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.000	dimensionless · A · m^{-2}	☑
Kf			1.000	1000 dimensionless · $m^3 \cdot mol^{-1} \cdot s^{-1}$	☑
Kr			0.062	s^{-1}	☑

7.26 Reaction PPase_MAPK

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

Name PPase_MAPK

Reaction equation

$$\mathrm{MAPK\_active\_cyto} \overset{\mathrm{PP2A\_cyto}}{\rightleftharpoons} \mathrm{MAPK\_cyto} \quad (70)$$

Reactant

Table 95: Properties of each reactant.

Id	Name	SBO
MAPK_active_cyto		

Modifier

Table 96: Properties of each modifier.

Id	Name	SBO
PP2A_cyto		

Product

Table 97: Properties of each product.

Id	Name	SBO
MAPK_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \text{Vmax\_PPase\_MAPK} \cdot 0.00166112956810631 \cdot [\text{MAPK\_active\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{MAPK\_active\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \quad (71)$$

Table 98: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			0.77	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol}$	☑

7.27 Reaction pp2a_4

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

Name pp2a_4

Reaction equation

$$\text{PDE4\_P\_cyto} \xrightleftharpoons{\text{PP\_PDE\_cyto}} \text{PDE4\_cyto} \quad (72)$$

Reactant

Table 99: Properties of each reactant.

Id	Name	SBO
PDE4_P_cyto		

Modifier

Table 100: Properties of each modifier.

Id	Name	SBO
PP_PDE_cyto		

Product

Table 101: Properties of each product.

Id	Name	SBO
PDE4_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \text{Vmax\_pp2a\_4\_pp2a\_4} \cdot 0.00166112956810631 \cdot [\text{PDE4\_P\_cyto}] \cdot \frac{1}{\text{Km\_pp2a\_4} + 0.00166112956810631 \cdot [\text{PDE4\_P\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \quad (73)$$

Table 102: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km_pp2a_4			8.0	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol}$	☑

7.28 Reaction pp_ptp

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

Name pp_ptp

Reaction equation

$$\text{PTP\_PKA\_cyto} \xrightleftharpoons{\text{PTP\_PP\_cyto}} \text{PTP\_cyto} \tag{74}$$

Reactant

Table 103: Properties of each reactant.

Id	Name	SBO
PTP_PKA_cyto		

Modifier

Table 104: Properties of each modifier.

Id	Name	SBO
PTP_PP_cyto		

Product

Table 105: Properties of each product.

Id	Name	SBO
PTP_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \text{Vmax\_pp\_ptp} \cdot 0.00166112956810631 \cdot [\text{PTP\_PKA\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{PTP\_PKA\_cyto}]} \cdot \text{vol}\,(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \tag{75}$$

Table 106: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			6.0	$0.0010\,\text{dimensionless} \cdot \text{m}^{-3} \cdot \text{mol}$	☑

7.29 Reaction GRK_bg

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

Name GRK_bg

Reaction equation

$$\text{iso\_BAR\_cyto\_mem} \xrightleftharpoons{\text{GRK\_bg\_cyto}} \text{iso\_BAR\_p\_cyto\_mem} \tag{76}$$

Reactant

Table 107: Properties of each reactant.

Id	Name	SBO
iso_BAR_cyto_mem		

Modifier

Table 108: Properties of each modifier.

Id	Name	SBO
GRK_bg_cyto		

Product

Table 109: Properties of each product.

Id	Name	SBO
iso_BAR_p_cyto_mem		

Kinetic Law

Derived unit contains undeclared units

$$v_{29} = \text{Vmax\_GRK\_bg\_GRK\_bg} \cdot [\text{iso\_BAR\_cyto\_mem}] \cdot \frac{1}{\text{Km\_GRK\_bg} + [\text{iso\_BAR\_cyto\_mem}]} \cdot \text{area}\,(\text{cyto\_mem}) \tag{77}$$

Table 110: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.0	dimensionless · A · m^{-2}	☑
Km_GRK_bg			4.0	item · μm^{-2}	☑

7.30 Reaction G_binds_BAR

This is a reversible reaction of two reactants forming one product.

Name G_binds_BAR

Reaction equation

$$\text{BAR\_cyto\_mem} + \text{G\_protein\_cyto} \rightleftharpoons \text{BAR\_G\_cyto\_mem} \tag{78}$$

Reactants

Table 111: Properties of each reactant.

Id	Name	SBO
BAR_cyto_mem		
G_protein_cyto		

Product

Table 112: Properties of each product.

Id	Name	SBO
BAR_G_cyto_mem		

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{30} = (&\text{Kf\_G\_binds\_BAR} \cdot [\text{BAR\_cyto\_mem}] \cdot 0.00166112956810631 \cdot [\text{G\_protein\_cyto}] \\ &+ ((\text{Kr\_G\_binds\_BAR} \cdot [\text{BAR\_G\_cyto\_mem}]))) \cdot \text{area}(\text{cyto\_mem}) \end{aligned} \tag{79}$$

Table 113: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
I			0.0	dimensionless · A · m^{-2}	☑
Kf_G_binds_BAR			0.3	1000 dimensionless · $m^3 \cdot mol^{-1} \cdot s^{-1}$	☑
Kr_G_binds_BAR			0.1	s^{-1}	☑

7.31 Reaction PPase_mek

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

Name PPase_mek

Reaction equation

$$\text{MEK\_active\_cyto} \overset{\text{PP2A\_cyto}}{\rightleftharpoons} \text{MEK\_cyto} \tag{80}$$

Reactant

Table 114: Properties of each reactant.

Id	Name	SBO
MEK_active_cyto		

Modifier

Table 115: Properties of each modifier.

Id	Name	SBO
PP2A_cyto		

Product

Table 116: Properties of each product.

Id	Name	SBO
MEK_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{31} = \text{Vmax\_PPase\_mek} \cdot 0.00166112956810631 \cdot [\text{MEK\_active\_cyto}] \cdot \frac{1}{\text{Km} + 0.00166112956810631 \cdot [\text{MEK\_active\_cyto}]} \cdot \text{vol}(\text{cyto}) \cdot 1 \cdot \frac{1}{\text{KMOLE}} \quad (81)$$

Table 117: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km			15.7	0.0010 dimensionless · $m^{-3} \cdot mol$	☑

7.32 Reaction A1

This is a reversible reaction of two reactants forming one product.

Name A1

Reaction equation

$$\text{c2\_R2C2\_cyto} + \text{cAMP\_cyto} \rightleftharpoons \text{c3\_R2C2\_cyto} \quad (82)$$

Reactants

Table 118: Properties of each reactant.

Id	Name	SBO
c2_R2C2_cyto		
cAMP_cyto		

Product

Table 119: Properties of each product.

Id	Name	SBO
c3_R2C2_cyto		

Kinetic Law

Derived unit contains undeclared units

$$v_{32} = (\mathrm{Kf} \cdot 0.00166112956810631 \cdot [\mathrm{c2\_R2C2\_cyto}] \cdot 0.00166112956810631 \cdot [\mathrm{cAMP\_cyto}] + ((\mathrm{Kr} \cdot 0.00166112956810631 \cdot [\mathrm{c3\_R2C2\_cyto}]))) \cdot \mathrm{vol}(\mathrm{cyto}) \cdot 1 \cdot \frac{1}{\mathrm{KMOLE}} \quad (83)$$

Table 120: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kf			8.350	$1000\,\mathrm{dimensionless} \cdot \mathrm{m}^3 \cdot \mathrm{mol}^{-1} \cdot \mathrm{s}^{-1}$	☑
Kr			0.017	s^{-1}	☑

8 Derived Rate Equations

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

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

- parameters without an unit definition are involved or
- volume correction is necessary because the `hasOnlySubstanceUnits` flag may be set to `false` and `spacialDimensions`> 0 for certain species.

8.1 Species AC_active_cyto_mem

Initial concentration $0\,\mathrm{item} \cdot \mu\mathrm{m}^{-2}$

This species takes part in two reactions (as a product in AC_activation and as a modifier in AC_active).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AC\_active\_cyto\_mem} = v_{16} \quad (84)$$

8.2 Species G_GDP_cyto

Initial concentration $0\,\mathrm{item} \cdot \left(10^{-6}\,\mathrm{m}\right)^{-3}$

This species takes part in two reactions (as a reactant in trimer and as a product in GTPase).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G\_GDP\_cyto} = v_{10} - v_{11} \quad (85)$$

8.3 Species G_protein_cyto

Initial concentration $2167.2\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a reactant in G_binds_iso_BAR, G_binds_BAR and as a product in trimer).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{G\_protein\_cyto} = v_{11} - v_{12} - v_{30} \tag{86}$$

8.4 Species G_a_s_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a reactant in GTPase, AC_activation and as a product in activate_Gs).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{G\_a\_s\_cyto} = v_{1} - v_{10} - v_{16} \tag{87}$$

8.5 Species GRK_bg_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in two reactions (as a product in bg_binds_GRK and as a modifier in GRK_bg).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{GRK\_bg\_cyto} = v_{6} \tag{88}$$

8.6 Species iso_BAR_p_cyto_mem

Initial concentration $0\ \text{item} \cdot \mu\text{m}^{-2}$

This species takes part in two reactions (as a product in GRK, GRK_bg).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{iso\_BAR\_p\_cyto\_mem} = v_{19} + v_{29} \tag{89}$$

8.7 Species PDE4_cyto

Initial concentration $240.8\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a reactant in PKA_P_PDE and as a product in pp2a_4 and as a modifier in PDE4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PDE4\_cyto} = v_{27} - v_{20} \tag{90}$$

8.8 Species ATP_cyto

Initial concentration $3010000\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in two reactions (as a reactant in AC_active, AC_basal).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{ATP\_cyto} = -v_9 - v_{17} \tag{91}$$

8.9 Species AC_PKA_cyto_mem

Initial concentration $0\ \text{item} \cdot \mu\text{m}^{-2}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{AC\_PKA\_cyto\_mem} = 0 \tag{92}$$

8.10 Species R2C2_cyto

Initial concentration $120.4\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in one reaction (as a reactant in B1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{R2C2\_cyto} = -v_{18} \tag{93}$$

8.11 Species PP_PDE_cyto

Initial concentration $120.4\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in one reaction (as a modifier in pp2a_4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PP\_PDE\_cyto} = 0 \tag{94}$$

8.12 Species BAR_cyto_mem

Initial concentration $94\ \text{item} \cdot \mu\text{m}^{-2}$

This species takes part in two reactions (as a reactant in iso_binds_BAR, G_binds_BAR).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{BAR\_cyto\_mem} = -v_4 - v_{30} \tag{95}$$

8.13 Species BAR_G_cyto_mem

Initial concentration $0\,\text{item}\cdot\mu\text{m}^{-2}$

This species takes part in two reactions (as a reactant in iso_binds_BAR_g and as a product in G_binds_BAR).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{BAR\_G\_cyto\_mem} = v_{30} - v_{25} \tag{96}$$

8.14 Species iso_extra

Initial concentration $6020\,\text{item}\cdot\left(10^{-6}\,\text{m}\right)^{-3}$

This species takes part in two reactions (as a reactant in iso_binds_BAR, iso_binds_BAR_g).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{iso\_extra} = -v_4 - v_{25} \tag{97}$$

8.15 Species iso_BAR_cyto_mem

Initial concentration $0\,\text{item}\cdot\mu\text{m}^{-2}$

This species takes part in five reactions (as a reactant in G_binds_iso_BAR, GRK, GRK_bg and as a product in activate_Gs, iso_binds_BAR).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{iso\_BAR\_cyto\_mem} = v_1 + v_4 - v_{12} - v_{19} - v_{29} \tag{98}$$

8.16 Species MAPK_active_cyto

Initial concentration $0\,\text{item}\cdot\left(10^{-6}\,\text{m}\right)^{-3}$

This species takes part in four reactions (as a reactant in PTP_PKA, PTP, PPase_MAPK and as a product in MEK_activates_MAPK).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{MAPK\_active\_cyto} = v_7 - v_{22} - v_{24} - v_{26} \tag{99}$$

8.17 Species MEK_cyto

Initial concentration $108.36\,\text{item}\cdot\left(10^{-6}\,\text{m}\right)^{-3}$

This species takes part in two reactions (as a reactant in Raf_activates_MEK and as a product in PPase_mek).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{MEK\_cyto} = v_{31} - v_{21} \tag{100}$$

8.18 Species MEK_active_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a reactant in PPase_mek and as a product in Raf_activates_MEK and as a modifier in MEK_activates_MAPK).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{MEK\_active\_cyto} = v_{21} - v_{31} \tag{101}$$

8.19 Species B_Raf_active_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a reactant in PPase_Raf and as a product in PKA_activates_Raf and as a modifier in Raf_activates_MEK).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{B\_Raf\_active\_cyto} = v_{8} - v_{3} \tag{102}$$

8.20 Species bg_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a reactant in bg_binds_GRK, trimer and as a product in activate_Gs).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{bg\_cyto} = v_{1} - v_{6} - v_{11} \tag{103}$$

8.21 Species B_Raf_cyto

Initial concentration $120.4\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in two reactions (as a reactant in PKA_activates_Raf and as a product in PPase_Raf).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{B\_Raf\_cyto} = v_{3} - v_{8} \tag{104}$$

8.22 Species PKA_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in four reactions (as a product in A2 and as a modifier in PKA_activates_Raf, PKA_P_PTP, PKA_P_PDE).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PKA\_cyto} = v_{13} \tag{105}$$

8.23 Species AC_cyto_mem

Initial concentration $300\ \text{item} \cdot \mu\text{m}^{-2}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{AC\_cyto\_mem} = -v_{16} \tag{106}$$

8.24 Species AMP_cyto

Initial concentration $3010000\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a product in pde4_p, PDE4, highKM_PDE).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{AMP\_cyto} = v_2 + v_5 + v_{14} \tag{107}$$

8.25 Species GRK_cyto

Initial concentration $0.602\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{GRK\_cyto} = -v_6 \tag{108}$$

8.26 Species PP2A_cyto

Initial concentration $60.2\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a modifier in PPase_Raf, PPase_MAPK, PPase_mek).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PP2A\_cyto} = 0 \tag{109}$$

8.27 Species MAPK_cyto

Initial concentration $216.72\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in four reactions (as a reactant in MEK_activates_MAPK and as a product in PTP_PKA, PTP, PPase_MAPK).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{MAPK\_cyto} = v_{22} + v_{24} + v_{26} - v_7 \tag{110}$$

8.28 Species PTP_cyto

Initial concentration $120.4\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a reactant in PKA_P_PTP and as a product in pp_ptp and as a modifier in PTP).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PTP\_cyto} = v_{28} - v_{15} \tag{111}$$

8.29 Species PTP_PKA_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a reactant in pp_ptp and as a product in PKA_P_PTP and as a modifier in PTP_PKA).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PTP\_PKA\_cyto} = v_{15} - v_{28} \tag{112}$$

8.30 Species c_R2C2_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in two reactions (as a reactant in B2 and as a product in B1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{c\_R2C2\_cyto} = v_{18} - v_{23} \tag{113}$$

8.31 Species c2_R2C2_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in two reactions (as a reactant in A1 and as a product in B2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{c2\_R2C2\_cyto} = v_{23} - v_{32} \tag{114}$$

8.32 Species c3_R2C2_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in two reactions (as a reactant in A2 and as a product in A1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{c3\_R2C2\_cyto} = v_{32} - v_{13} \tag{115}$$

8.33 Species iso_BAR_G_cyto_mem

Initial concentration $0\ \text{item} \cdot \mu\text{m}^{-2}$

This species takes part in three reactions (as a reactant in activate_Gs and as a product in G_binds_iso_BAR, iso_binds_BAR_g).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{iso\_BAR\_G\_cyto\_mem} = v_{12} + v_{25} - v_1 \tag{116}$$

8.34 Species PDE_high_km_cyto

Initial concentration $301\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in one reaction (as a modifier in highKM_PDE).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PDE\_high\_km\_cyto} = 0 \tag{117}$$

8.35 Species cAMP_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in nine reactions (as a reactant in pde4_p, PDE4, A2, highKM_PDE, B1, B2, A1 and as a product in AC_active, AC_basal).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{cAMP\_cyto} = v_9 + v_{17} - v_2 - v_5 - v_{13} - v_{14} - v_{18} - v_{23} - v_{32} \tag{118}$$

8.36 Species PTP_PP_cyto

Initial concentration $60.2\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in one reaction (as a modifier in pp_ptp).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PTP\_PP\_cyto} = 0 \tag{119}$$

8.37 Species PDE4_P_cyto

Initial concentration $0\ \text{item} \cdot \left(10^{-6}\ \text{m}\right)^{-3}$

This species takes part in three reactions (as a reactant in pp2a_4 and as a product in PKA_P_PDE and as a modifier in pde4_p).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{PDE4\_P\_cyto} = v_{20} - v_{27} \tag{120}$$

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