SBML Model Report

Model name: "Reiterer2013 - pseudophosphatase STYX role in ERK signalling"

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1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah[1] and Dirk Fey[2] at November 25th 2014 at 3:32 p. m. and last time modified at December twelveth 2014 at 3:08 p. m. Table 1 provides an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	2
species types	0	species	25
events	0	constraints	0
reactions	22	function definitions	0
global parameters	50	unit definitions	0
rules	6	initial assignments	0

Model Notes

Reiterer2013 - pseudophosphatase STYX role inERK signalling

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This model is described in the article:Pseudophosphatase STYX modulates cell-fate decisions and cell migration by spatiotemporal regulation of ERK1/2.Reiterer V, Fey D, Kolch W, Kholodenko BN, Farhan H.Proc. Natl. Acad. Sci. U.S.A. 2013 Jul; 110(31): E2934-43

Abstract:

Serine/threonine/tyrosine-interacting protein (STYX) is a catalytically inactive member of the dual-specificity phosphatases (DUSPs) family. Whereas the role of DUSPs in cellular signaling is well explored, the function of STYX is still unknown. Here, we identify STYX as a spatial regulator of ERK signaling. We used predictive-model simulation to test several hypotheses for possible modes of STYX action. We show that STYX localizes to the nucleus, competes with nuclear DUSP4 for binding to ERK, and acts as a nuclear anchor that regulates ERK nuclear export. Depletion of STYX increases ERK activity in both cytosol and nucleus. Importantly, depletion of STYX causes an ERK-dependent fragmentation of the Golgi apparatus and inhibits Golgi polarization and directional cell migration. Finally, we show that overexpression of STYX reduces ERK1/2 activation, thereby blocking PC12 cell differentiation. Overall, our results identify STYX as an important regulator of ERK1/2 signaling critical for cell migration and PC12 cell differentiation.

2 Unit Definitions

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

2.1 Unit `substance`

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

Definition mol

2.2 Unit `volume`

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

Definition l

2.3 Unit `area`

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

Definition m^2

2.4 Unit `length`

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

Definition m

2.5 Unit `time`

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

Definition s

3 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`cytosol`	cytosol		3	0.94	l	☑	
`nucleus`	nucleus		3	0.22	l	☑	

3.1 Compartment `cytosol`

This is a three dimensional compartment with a constant size of 0.94 litre.

Name cytosol

3.2 Compartment `nucleus`

This is a three dimensional compartment with a constant size of 0.22 litre.

Name nucleus

4 Species

This model contains 25 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
ERKc	ERKc	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pERKc	pERKc	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ppERKc	ppERKc	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ERK_ppMEKc	ERK_ppMEKc	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pERK_ppMEKc	pERK_ppMEKc	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
DUSPc	DUSPc	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pERK_DUSPc	pERK_DUSPc	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ppERK_DUSPc	ppERK_DUSPc	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ERKn	ERKn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pERKn	pERKn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ppERKn	ppERKn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pERK_DUSPn	pERK_DUSPn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ppERK_DUSPn	ppERK_DUSPn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
STYXn	STYXn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ERK_STYXn	ERK_STYXn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pERK_STYXn	pERK_STYXn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ppERK_STYXn	ppERK_STYXn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
duspn	duspn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
DUSPn	DUSPn	nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
u_ppMEKc_tot	u_ppMEKc_tot	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ppMEKc_tot	ppMEKc_tot	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ERKc_obs	ERKc_obs	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
pERKc_obs	pERKc_obs	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ppERKc_obs	ppERKc_obs	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ERK_ppMEKc_obs	ERK_ppMEKc_obs	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 50 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k_ERKin			0.144		☑
k_ERKout			1.080		☑
k_pERKin			0.144		☑
k_pERKout			1.080		☑
k_ppERKin			0.660		☑
k_ppERKout			0.780		☑
k1_ES			1.000		☑
k2_ES			60.000		☑
k1_pES			1.000		☑
k2_pES			60.000		☑
k1_ppES			1.000		☑
k2_ppES			60.000		☑
k1_ERKc			1.000		☑
k2_ERKc			350.000		☑
k3_ERKc			13.200		☑
kd1_ppERKc			1.000		☑
kd2_ppERKc			60.000		☑
kd3_ppERKc			0.388		☑
kd1_pERKc			1.000		☑
kd2_pERKc			160.000		☑
kd3_pERKc			0.432		☑
kd1_ERKc			0.000		☑
kd2_ERKc			5160.000		☑
k1_ERKn			1.000		☑
k2_ERKn			350.000		☑
k3_ERKn			13.200		☑
kd1_ppERKn			1.000		☑
kd2_ppERKn			60.000		☑
kd3_ppERKn			38.880		☑
kd1_pERKn			1.000		☑
kd2_pERKn			160.000		☑
kd3_pERKn			43.200		☑
kd1_ERKn			0.000		☑
kd2_ERKn			160.000		☑
k_ppMEKc_tot			100.000		☑
actCompl			10^{-9}		☑
duspn_basal			1.000		☑

Id	Name	SBO	Value	Unit	Constant
duspn_ind			20.000		☑
Kduspn			1000.000		☑
Tduspn			10.000		☑
v2			10.000		☑
TDUSPn			45.000		☑
scale-_cytERK_tot			1.000		☑
scale-_nucERK_tot			1.000		☑
scale-_cellERK_tot			1.000		☑
scale-_cytppERK_tot			1.000		☑
scale-_nucppERK_tot			1.000		☑
scale-_cellppERK-_tot			0.019		☑
scale_tDUSPn			1.000		☑
scale_tERK-_STYXn			1.000		☑

6 Rules

This is an overview of six rules.

6.1 Rule ppMEKc_tot

Rule ppMEKc_tot is an assignment rule for species ppMEKc_tot:

$$\text{ppMEKc\_tot} = [\text{u\_ppMEKc\_tot}] \cdot \text{k\_ppMEKc\_tot} \tag{1}$$

6.2 Rule ERKc_obs

Rule ERKc_obs is an assignment rule for species ERKc_obs:

$$\text{ERKc\_obs} = [\text{ERKc}] \tag{2}$$

Derived unit $\text{mol} \cdot \text{l}^{-1}$

6.3 Rule pERKc_obs

Rule pERKc_obs is an assignment rule for species pERKc_obs:

$$\text{pERKc\_obs} = [\text{pERKc}] \tag{3}$$

Derived unit $\text{mol} \cdot \text{l}^{-1}$

6.4 Rule ppERKc_obs

Rule ppERKc_obs is an assignment rule for species ppERKc_obs:

$$\text{ppERKc\_obs} = [\text{ppERKc}] \tag{4}$$

Derived unit $\text{mol} \cdot \text{l}^{-1}$

6.5 Rule ERK_ppMEKc_obs

Rule ERK_ppMEKc_obs is an assignment rule for species ERK_ppMEKc_obs:

$$\text{ERK\_ppMEKc\_obs} = [\text{ERK\_ppMEKc}] \tag{5}$$

Derived unit $\text{mol} \cdot \text{l}^{-1}$

6.6 Rule u_ppMEKc_tot

Rule u_ppMEKc_tot is an assignment rule for species u_ppMEKc_tot:

$$\text{u\_ppMEKc\_tot} = \begin{cases} 0 & \text{if time} < -1 \\ 0 & \text{if time} < 0 \\ 1 & \text{if time} < 120 \\ 1 & \text{otherwise} \end{cases} \tag{6}$$

7 Reactions

This model contains 22 reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	reaction_1		$\mathrm{ERKc} \xrightleftharpoons{\mathrm{ppMEKc\_tot,\ pERK\_ppMEKc,\ ERKc,\ ppMEKc\_tot,\ ERK\_ppMEKc,\ pERK\_ppM}}$	
2	reaction_2		$\mathrm{ERK\_ppMEKc} \xrightarrow{\mathrm{ERK\_ppMEKc}} \mathrm{pERKc}$	
3	reaction_3		$\mathrm{pERKc} \xrightleftharpoons{\mathrm{ppMEKc\_tot,\ ERK\_ppMEKc,\ pERKc,\ ppMEKc\_tot,\ pERK\_ppMEKc,\ ERK\_pp}}$	
4	reaction_4		$\mathrm{pERK\_ppMEKc} \xrightarrow{\mathrm{pERK\_ppMEKc}} \mathrm{ppERKc}$	
5	reaction_5		$\mathrm{ERKc} \xrightarrow{\mathrm{ERKc,\ ERKn}} \mathrm{ERKn}$	
6	reaction_6		$\mathrm{pERKc} \xrightarrow{\mathrm{pERKc,\ pERKn}} \mathrm{pERKn}$	
7	reaction_7		$\mathrm{ppERKc} \xrightarrow{\mathrm{ppERKc,\ ppERKn}} \mathrm{ppERKn}$	
8	reaction_8		$\mathrm{ppERKc + DUSPc} \xrightleftharpoons{\mathrm{ppERKc,\ DUSPc,\ ppERK\_DUSPc}} \mathrm{ppERK\_DUSPc}$	
9	reaction_9		$\mathrm{ppERK\_DUSPc} \xrightarrow{\mathrm{ppERK\_DUSPc}} \mathrm{pERKc + DUSPc}$	
10	reaction_10		$\mathrm{pERKc + DUSPc} \xrightleftharpoons{\mathrm{pERKc,\ DUSPc,\ pERK\_DUSPc}} \mathrm{pERK\_DUSPc}$	
11	reaction_11		$\mathrm{pERK\_DUSPc} \xrightarrow{\mathrm{pERK\_DUSPc}} \mathrm{ERKc + DUSPc}$	
12	reaction_12		$\mathrm{ppERKn + DUSPn} \xrightleftharpoons{\mathrm{ppERKn,\ DUSPn,\ ppERK\_DUSPn}} \mathrm{ppERK\_DUSPn}$	
13	reaction_13		$\mathrm{ppERK\_DUSPn} \xrightarrow{\mathrm{ppERK\_DUSPn}} \mathrm{pERKn + DUSPn}$	
14	reaction_14		$\mathrm{pERKn + DUSPn} \xrightleftharpoons{\mathrm{pERKn,\ DUSPn,\ pERK\_DUSPn}} \mathrm{pERK\_DUSPn}$	
15	reaction_15		$\mathrm{pERK\_DUSPn} \xrightarrow{\mathrm{pERK\_DUSPn}} \mathrm{ERKn + DUSPn}$	

№	Id	Name	Reaction Equation	SBO
16	reaction_16		$\emptyset \xrightarrow{\text{ppERKn, ppERKn}} \text{duspn}$	
17	reaction_17		$\text{duspn} \xrightarrow{\text{duspn}} \emptyset$	
18	reaction_18		$\emptyset \xrightarrow{\text{duspn, duspn}} \text{DUSPn}$	
19	reaction_19		$\text{DUSPn} \xrightarrow{\text{DUSPn}} \emptyset$	
20	reaction_20		$\text{ERKn} + \text{STYXn} \xrightleftharpoons{\text{ERKn, STYXn, ERK\_STYXn}} \text{ERK\_STYXn}$	
21	reaction_21		$\text{pERKn} + \text{STYXn} \xrightleftharpoons{\text{pERKn, STYXn, pERK\_STYXn}} \text{pERK\_STYXn}$	
22	reaction_22		$\text{ppERKn} + \text{STYXn} \xrightleftharpoons{\text{ppERKn, STYXn, ppERK\_STYXn}} \text{ppERK\_STYXn}$	

7.1 Reaction reaction_1

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

Reaction equation

$$\text{ERKc} \xrightleftharpoons{\text{ppMEKc\_tot, pERK\_ppMEKc, ERKc, ppMEKc\_tot, ERK\_ppMEKc, pERK\_ppMEKc}} \text{ERK\_ppMEKc} \tag{7}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
ERKc	ERKc	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
ppMEKc_tot	ppMEKc_tot	
pERK_ppMEKc	pERK_ppMEKc	
ERKc	ERKc	
ppMEKc_tot	ppMEKc_tot	
ERK_ppMEKc	ERK_ppMEKc	
pERK_ppMEKc	pERK_ppMEKc	

Product

Table 8: Properties of each product.

Id	Name	SBO
ERK_ppMEKc	ERK_ppMEKc	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{k1\_ERKc} \cdot [\text{ERKc}] \cdot ([\text{ppMEKc\_tot}] \cdot \text{vol}(\text{cytosol}) - [\text{ERK\_ppMEKc}] \cdot \text{vol}(\text{cytosol}) - [\text{pERK\_ppMEKc}]) \cdot \text{vol}(\text{cytosol}) - \text{k2\_ERKc} \cdot [\text{ERK\_ppMEKc}] \cdot \text{vol}(\text{cytosol}) \tag{8}$$

7.2 Reaction `reaction_2`

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

Reaction equation

$$\text{ERK\_ppMEKc} \xrightarrow{\text{ERK\_ppMEKc}} \text{pERKc} \tag{9}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
`ERK_ppMEKc`	ERK_ppMEKc	

Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
`ERK_ppMEKc`	ERK_ppMEKc	

Product

Table 11: Properties of each product.

Id	Name	SBO
`pERKc`	pERKc	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{k3\_ERKc} \cdot [\text{ERK\_ppMEKc}] \cdot \text{vol}(\text{cytosol}) \tag{10}$$

7.3 Reaction reaction_3

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

Reaction equation

$$\text{pERKc} \xrightleftharpoons{\text{ppMEKc\_tot, ERK\_ppMEKc, pERKc, ppMEKc\_tot, pERK\_ppMEKc, ERK\_ppMEKc}} \text{pERK\_ppMEKc} \tag{11}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
pERKc	pERKc	

Modifiers

Table 13: Properties of each modifier.

Id	Name	SBO
ppMEKc_tot	ppMEKc_tot	
ERK_ppMEKc	ERK_ppMEKc	
pERKc	pERKc	
ppMEKc_tot	ppMEKc_tot	
pERK_ppMEKc	pERK_ppMEKc	
ERK_ppMEKc	ERK_ppMEKc	

Product

Table 14: Properties of each product.

Id	Name	SBO
pERK_ppMEKc	pERK_ppMEKc	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{k1\_ERKc} \cdot [\text{pERKc}] \cdot ([\text{ppMEKc\_tot}] \cdot \text{vol}(\text{cytosol}) - [\text{pERK\_ppMEKc}] \cdot \text{vol}(\text{cytosol}) - [\text{ERK\_ppMEKc}]) \cdot \text{vol}(\text{cytosol}) - \text{k2\_ERKc} \cdot [\text{pERK\_ppMEKc}] \cdot \text{vol}(\text{cytosol}) \tag{12}$$

7.4 Reaction `reaction_4`

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

Reaction equation

$$\text{pERK\_ppMEKc} \xrightarrow{\text{pERK\_ppMEKc}} \text{ppERKc} \tag{13}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
`pERK_ppMEKc`	pERK_ppMEKc	

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
`pERK_ppMEKc`	pERK_ppMEKc	

Product

Table 17: Properties of each product.

Id	Name	SBO
`ppERKc`	ppERKc	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{k3\_ERKc} \cdot [\text{pERK\_ppMEKc}] \cdot \text{vol}(\text{cytosol}) \tag{14}$$

7.5 Reaction reaction_5

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

Reaction equation

$$\mathrm{ERKc} \xrightarrow{\mathrm{ERKc,\ ERKn}} \mathrm{ERKn} \tag{15}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
ERKc	ERKc	

Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
ERKc	ERKc	
ERKn	ERKn	

Product

Table 20: Properties of each product.

Id	Name	SBO
ERKn	ERKn	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{k\_ERKin} \cdot [\mathrm{ERKc}] \cdot \mathrm{vol}\,(\mathrm{cytosol}) - \mathrm{k\_ERKout} \cdot [\mathrm{ERKn}] \cdot \mathrm{vol}\,(\mathrm{nucleus}) \tag{16}$$

7.6 Reaction reaction_6

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

Reaction equation

$$\text{pERKc} \xrightarrow{\text{pERKc, pERKn}} \text{pERKn} \tag{17}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
pERKc	pERKc	

Modifiers

Table 22: Properties of each modifier.

Id	Name	SBO
pERKc	pERKc	
pERKn	pERKn	

Product

Table 23: Properties of each product.

Id	Name	SBO
pERKn	pERKn	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{k\_pERKin} \cdot [\text{pERKc}] \cdot \text{vol}(\text{cytosol}) - \text{k\_pERKout} \cdot [\text{pERKn}] \cdot \text{vol}(\text{nucleus}) \tag{18}$$

7.7 Reaction reaction_7

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

Reaction equation

$$\text{ppERKc} \xrightarrow{\text{ppERKc, ppERKn}} \text{ppERKn} \tag{19}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
ppERKc	ppERKc	

Modifiers

Table 25: Properties of each modifier.

Id	Name	SBO
ppERKc	ppERKc	
ppERKn	ppERKn	

Product

Table 26: Properties of each product.

Id	Name	SBO
ppERKn	ppERKn	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{k\_ppERKin} \cdot [\text{ppERKc}] \cdot \text{vol}(\text{cytosol}) - \text{k\_ppERKout} \cdot [\text{ppERKn}] \cdot \text{vol}(\text{nucleus}) \quad (20)$$

7.8 Reaction reaction_8

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

Reaction equation

$$\text{ppERKc} + \text{DUSPc} \xrightleftharpoons{\text{ppERKc, DUSPc, ppERK\_DUSPc}} \text{ppERK\_DUSPc} \quad (21)$$

Reactants

Table 27: Properties of each reactant.

Id	Name	SBO
ppERKc	ppERKc	
DUSPc	DUSPc	

Modifiers

Table 28: Properties of each modifier.

Id	Name	SBO
ppERKc	ppERKc	
DUSPc	DUSPc	
ppERK_DUSPc	ppERK_DUSPc	

Product

Table 29: Properties of each product.

Id	Name	SBO
ppERK_DUSPc	ppERK_DUSPc	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \left(\frac{\text{kd1\_ppERKc} \cdot [\text{ppERKc}] \cdot [\text{DUSPc}]}{0.94} \cdot \text{vol}\,(\text{cytosol}) - \text{kd2\_ppERKc} \cdot [\text{ppERK\_DUSPc}] \right) \cdot \text{vol}\,(\text{cytosol}) \tag{22}$$

7.9 Reaction reaction_9

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

Reaction equation

$$\text{ppERK\_DUSPc} \xrightarrow{\text{ppERK\_DUSPc}} \text{pERKc} + \text{DUSPc} \tag{23}$$

Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
ppERK_DUSPc	ppERK_DUSPc	

Modifier

Table 31: Properties of each modifier.

Id	Name	SBO
ppERK_DUSPc	ppERK_DUSPc	

Products

Table 32: Properties of each product.

Id	Name	SBO
pERKc	pERKc	
DUSPc	DUSPc	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{kd3\_ppERKc} \cdot [\text{ppERK\_DUSPc}] \cdot \text{vol}(\text{cytosol}) \tag{24}$$

7.10 Reaction reaction_10

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

Reaction equation

$$\text{pERKc} + \text{DUSPc} \xrightleftharpoons{\text{pERKc, DUSPc, pERK\_DUSPc}} \text{pERK\_DUSPc} \tag{25}$$

Reactants

Table 33: Properties of each reactant.

Id	Name	SBO
pERKc	pERKc	
DUSPc	DUSPc	

Modifiers

Table 34: Properties of each modifier.

Id	Name	SBO
pERKc	pERKc	
DUSPc	DUSPc	
pERK_DUSPc	pERK_DUSPc	

Product

Table 35: Properties of each product.

Id	Name	SBO
pERK_DUSPc	pERK_DUSPc	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \left(\frac{\text{kd1\_pERKc} \cdot [\text{pERKc}] \cdot [\text{DUSPc}]}{0.94} \cdot \text{vol}\,(\text{cytosol}) - \text{kd2\_pERKc} \cdot [\text{pERK\_DUSPc}] \right) \cdot \text{vol}\,(\text{cytosol}) \tag{26}$$

7.11 Reaction reaction_11

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

Reaction equation

$$\text{pERK\_DUSPc} \xrightarrow{\text{pERK\_DUSPc}} \text{ERKc} + \text{DUSPc} \tag{27}$$

Reactant

Table 36: Properties of each reactant.

Id	Name	SBO
pERK_DUSPc	pERK_DUSPc	

Modifier

Table 37: Properties of each modifier.

Id	Name	SBO
pERK_DUSPc	pERK_DUSPc	

Products

Table 38: Properties of each product.

Id	Name	SBO
ERKc	ERKc	
DUSPc	DUSPc	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{kd3\_pERKc} \cdot [\text{pERK\_DUSPc}] \cdot \text{vol}(\text{cytosol}) \tag{28}$$

7.12 Reaction reaction_12

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

Reaction equation

$$\text{ppERKn} + \text{DUSPn} \xrightleftharpoons{\text{ppERKn, DUSPn, ppERK\_DUSPn}} \text{ppERK\_DUSPn} \tag{29}$$

Reactants

Table 39: Properties of each reactant.

Id	Name	SBO
ppERKn	ppERKn	
DUSPn	DUSPn	

Modifiers

Table 40: Properties of each modifier.

Id	Name	SBO
ppERKn	ppERKn	

Id	Name	SBO
DUSPn	DUSPn	
ppERK_DUSPn	ppERK_DUSPn	

Product

Table 41: Properties of each product.

Id	Name	SBO
ppERK_DUSPn	ppERK_DUSPn	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \left(\frac{\text{kd1\_ppERKn} \cdot [\text{ppERKn}] \cdot [\text{DUSPn}]}{0.22} \cdot \text{vol}\left(\text{nucleus}\right) - \text{kd2\_ppERKn} \cdot [\text{ppERK\_DUSPn}] \right) \cdot \text{vol}\left(\text{nucleus}\right) \tag{30}$$

7.13 Reaction reaction_13

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

Reaction equation

$$\text{ppERK\_DUSPn} \xrightarrow{\text{ppERK\_DUSPn}} \text{pERKn} + \text{DUSPn} \tag{31}$$

Reactant

Table 42: Properties of each reactant.

Id	Name	SBO
ppERK_DUSPn	ppERK_DUSPn	

Modifier

Table 43: Properties of each modifier.

Id	Name	SBO
ppERK_DUSPn	ppERK_DUSPn	

Products

Table 44: Properties of each product.

Id	Name	SBO
pERKn	pERKn	
DUSPn	DUSPn	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{kd3\_ppERKn} \cdot [\text{ppERK\_DUSPn}] \cdot \text{vol}(\text{nucleus}) \tag{32}$$

7.14 Reaction reaction_14

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

Reaction equation

$$\text{pERKn} + \text{DUSPn} \xrightleftharpoons{\text{pERKn, DUSPn, pERK\_DUSPn}} \text{pERK\_DUSPn} \tag{33}$$

Reactants

Table 45: Properties of each reactant.

Id	Name	SBO
pERKn	pERKn	
DUSPn	DUSPn	

Modifiers

Table 46: Properties of each modifier.

Id	Name	SBO
pERKn	pERKn	

Id	Name	SBO
DUSPn	DUSPn	
pERK_DUSPn	pERK_DUSPn	

Product

Table 47: Properties of each product.

Id	Name	SBO
pERK_DUSPn	pERK_DUSPn	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \left(\frac{\text{kd1\_pERKn} \cdot [\text{pERKn}] \cdot [\text{DUSPn}]}{0.22} \cdot \text{vol}\left(\text{nucleus}\right) - \text{kd2\_pERKn} \cdot [\text{pERK\_DUSPn}] \right) \cdot \text{vol}\left(\text{nucleus}\right) \tag{34}$$

7.15 Reaction reaction_15

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

Reaction equation

$$\text{pERK\_DUSPn} \xrightarrow{\text{pERK\_DUSPn}} \text{ERKn} + \text{DUSPn} \tag{35}$$

Reactant

Table 48: Properties of each reactant.

Id	Name	SBO
pERK_DUSPn	pERK_DUSPn	

Modifier

Table 49: Properties of each modifier.

Id	Name	SBO
pERK_DUSPn	pERK_DUSPn	

Products

Table 50: Properties of each product.

Id	Name	SBO
ERKn	ERKn	
DUSPn	DUSPn	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \text{kd3\_pERKn} \cdot [\text{pERK\_DUSPn}] \cdot \text{vol}(\text{nucleus}) \tag{36}$$

7.16 Reaction reaction_16

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

Reaction equation

$$\emptyset \xrightarrow{\text{ppERKn, ppERKn}} \text{duspn} \tag{37}$$

Modifiers

Table 51: Properties of each modifier.

Id	Name	SBO
ppERKn	ppERKn	
ppERKn	ppERKn	

Product

Table 52: Properties of each product.

Id	Name	SBO
duspn	duspn	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \frac{\text{duspn\_basal} \cdot \left(1 + \frac{\text{duspn\_ind} \cdot [\text{ppERKn}]^2}{[\text{ppERKn}]^2 \cdot \text{vol(nucleus)} + \text{Kduspn}^2}\right) \cdot 0.693}{\text{Tduspn}} \tag{38}$$

7.17 Reaction `reaction_17`

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

Reaction equation

$$\text{duspn} \xrightarrow{\text{duspn}} \emptyset \tag{39}$$

Reactant

Table 53: Properties of each reactant.

Id	Name	SBO
`duspn`	duspn	

Modifier

Table 54: Properties of each modifier.

Id	Name	SBO
`duspn`	duspn	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \frac{[\text{duspn}] \cdot 0.693}{\text{Tduspn}} \cdot \text{vol}\,(\text{nucleus}) \tag{40}$$

7.18 Reaction `reaction_18`

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

Reaction equation

$$\emptyset \xrightarrow{\text{duspn, duspn}} \text{DUSPn} \tag{41}$$

Modifiers

Table 55: Properties of each modifier.

Id	Name	SBO
duspn	duspn	
duspn	duspn	

Product

Table 56: Properties of each product.

Id	Name	SBO
DUSPn	DUSPn	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \frac{\frac{\text{v2} \cdot [\text{duspn}]}{0.22} \cdot 0.693}{\text{TDUSPn}} \cdot \text{vol}\left(\text{nucleus}\right) \tag{42}$$

7.19 Reaction reaction_19

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

Reaction equation

$$\text{DUSPn} \xrightarrow{\text{DUSPn}} \emptyset \tag{43}$$

Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
DUSPn	DUSPn	

Modifier

Table 58: Properties of each modifier.

Id	Name	SBO
DUSPn	DUSPn	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \frac{[\text{DUSPn}] \cdot 0.693}{\text{TDUSPn}} \cdot \text{vol}(\text{nucleus}) \tag{44}$$

7.20 Reaction reaction_20

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

Reaction equation

$$\text{ERKn} + \text{STYXn} \underset{}{\overset{\text{ERKn, STYXn, ERK\_STYXn}}{\rightleftharpoons}} \text{ERK\_STYXn} \tag{45}$$

Reactants

Table 59: Properties of each reactant.

Id	Name	SBO
ERKn	ERKn	
STYXn	STYXn	

Modifiers

Table 60: Properties of each modifier.

Id	Name	SBO
ERKn	ERKn	
STYXn	STYXn	
ERK_STYXn	ERK_STYXn	

Product

Table 61: Properties of each product.

Id	Name	SBO
ERK_STYXn	ERK_STYXn	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \left(\frac{\text{k1\_ES} \cdot [\text{ERKn}] \cdot [\text{STYXn}]}{0.22} \cdot \text{vol}\left(\text{nucleus}\right) - \text{k2\_ES} \cdot [\text{ERK\_STYXn}] \right) \cdot \text{vol}\left(\text{nucleus}\right) \tag{46}$$

7.21 Reaction reaction_21

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

Reaction equation

$$\text{pERKn} + \text{STYXn} \xrightleftharpoons{\text{pERKn, STYXn, pERK\_STYXn}} \text{pERK\_STYXn} \tag{47}$$

Reactants

Table 62: Properties of each reactant.

Id	Name	SBO
pERKn	pERKn	
STYXn	STYXn	

Modifiers

Table 63: Properties of each modifier.

Id	Name	SBO
pERKn	pERKn	
STYXn	STYXn	
pERK_STYXn	pERK_STYXn	

Product

Table 64: Properties of each product.

Id	Name	SBO
pERK_STYXn	pERK_STYXn	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \left(\frac{\text{k1\_pES} \cdot [\text{pERKn}] \cdot [\text{STYXn}]}{0.22} \cdot \text{vol}(\text{nucleus}) - \text{k2\_pES} \cdot [\text{pERK\_STYXn}] \right) \cdot \text{vol}(\text{nucleus}) \tag{48}$$

7.22 Reaction reaction_22

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

Reaction equation

$$\text{ppERKn} + \text{STYXn} \xrightleftharpoons{\text{ppERKn, STYXn, ppERK\_STYXn}} \text{ppERK\_STYXn} \tag{49}$$

Reactants

Table 65: Properties of each reactant.

Id	Name	SBO
ppERKn	ppERKn	
STYXn	STYXn	

Modifiers

Table 66: Properties of each modifier.

Id	Name	SBO
ppERKn	ppERKn	
STYXn	STYXn	
ppERK_STYXn	ppERK_STYXn	

Product

Table 67: Properties of each product.

Id	Name	SBO
ppERK_STYXn	ppERK_STYXn	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \left(\frac{\text{k1\_ppES} \cdot [\text{ppERKn}] \cdot [\text{STYXn}]}{0.22} \cdot \text{vol}\,(\text{nucleus}) - \text{k2\_ppES} \cdot [\text{ppERK\_STYXn}] \right) \cdot \text{vol}\,(\text{nucleus}) \tag{50}$$

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 ERKc

Name ERKc

Initial concentration $572.5\ \text{mol} \cdot \text{l}^{-1}$

This species takes part in five reactions (as a reactant in reaction_1, reaction_5 and as a product in reaction_11 and as a modifier in reaction_1, reaction_5).

$$\frac{\text{d}}{\text{d}t}\text{ERKc} = v_{11} - v_1 - v_5 \tag{51}$$

8.2 Species pERKc

Name pERKc

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pERKc} = v_2 + v_9 - v_3 - v_6 - v_{10} \tag{52}$$

8.3 Species ppERKc

Name ppERKc

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

This species takes part in five reactions (as a reactant in reaction_7, reaction_8 and as a product in reaction_4 and as a modifier in reaction_7, reaction_8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ppERKc} = v_4 - v_7 - v_8 \tag{53}$$

8.4 Species ERK_ppMEKc

Name ERK_ppMEKc

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

This species takes part in six reactions (as a reactant in reaction_2 and as a product in reaction_1 and as a modifier in reaction_1, reaction_2, reaction_3, reaction_3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ERK\_ppMEKc} = v_1 - v_2 \tag{54}$$

8.5 Species pERK_ppMEKc

Name pERK_ppMEKc

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

This species takes part in six reactions (as a reactant in reaction_4 and as a product in reaction_3 and as a modifier in reaction_1, reaction_1, reaction_3, reaction_4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pERK\_ppMEKc} = v_3 - v_4 \tag{55}$$

8.6 Species DUSPc

Name DUSPc

Initial concentration $100\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in six reactions (as a reactant in reaction_8, reaction_10 and as a product in reaction_9, reaction_11 and as a modifier in reaction_8, reaction_10).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{DUSPc} = v_9 + v_{11} - v_8 - v_{10} \tag{56}$$

8.7 Species pERK_DUSPc

Name pERK_DUSPc

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pERK\_DUSPc} = v_{10} - v_{11} \tag{57}$$

8.8 Species ppERK_DUSPc

Name ppERK_DUSPc

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ppERK\_DUSPc} = v_{8} - v_{9} \tag{58}$$

8.9 Species ERKn

Name ERKn

Initial concentration $1630.9\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in five reactions (as a reactant in reaction_20 and as a product in reaction_5, reaction_15 and as a modifier in reaction_5, reaction_20).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ERKn} = v_{5} + v_{15} - v_{20} \tag{59}$$

8.10 Species pERKn

Name pERKn

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

This species takes part in seven reactions (as a reactant in reaction_14, reaction_21 and as a product in reaction_6, reaction_13 and as a modifier in reaction_6, reaction_14, reaction_21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pERKn} = v_{6} + v_{13} - v_{14} - v_{21} \tag{60}$$

8.11 Species ppERKn

Name ppERKn

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

This species takes part in eight reactions (as a reactant in reaction_12, reaction_22 and as a product in reaction_7 and as a modifier in reaction_7, reaction_12, reaction_16, reaction_16, reaction_22).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ppERKn} = v_7 - v_{12} - v_{22} \tag{61}$$

8.12 Species pERK_DUSPn

Name pERK_DUSPn

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pERK\_DUSPn} = v_{14} - v_{15} \tag{62}$$

8.13 Species ppERK_DUSPn

Name ppERK_DUSPn

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ppERK\_DUSPn} = v_{12} - v_{13} \tag{63}$$

8.14 Species STYXn

Name STYXn

Initial concentration $3000\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in six reactions (as a reactant in reaction_20, reaction_21, reaction_22 and as a modifier in reaction_20, reaction_21, reaction_22).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{STYXn} = -v_{20} - v_{21} - v_{22} \tag{64}$$

8.15 Species ERK_STYXn

Name ERK_STYXn

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

This species takes part in two reactions (as a product in reaction_20 and as a modifier in reaction_20).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ERK\_STYXn} = v_{20} \tag{65}$$

8.16 Species pERK_STYXn

Name pERK_STYXn

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

This species takes part in two reactions (as a product in reaction_21 and as a modifier in reaction_21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pERK\_STYXn} = v_{21} \tag{66}$$

8.17 Species ppERK_STYXn

Name ppERK_STYXn

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

This species takes part in two reactions (as a product in reaction_22 and as a modifier in reaction_22).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ppERK\_STYXn} = v_{22} \tag{67}$$

8.18 Species duspn

Name duspn

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

This species takes part in five reactions (as a reactant in reaction_17 and as a product in reaction_16 and as a modifier in reaction_17, reaction_18, reaction_18).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{duspn} = v_{16} - v_{17} \tag{68}$$

8.19 Species DUSPn

Name DUSPn

Initial concentration $10\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in nine reactions (as a reactant in reaction_12, reaction_14, reaction_19 and as a product in reaction_13, reaction_15, reaction_18 and as a modifier in reaction_12, reaction_14, reaction_19).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{DUSPn} = v_{13} + v_{15} + v_{18} - v_{12} - v_{14} - v_{19} \tag{69}$$

8.20 Species u_ppMEKc_tot

Name u_ppMEKc_tot

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

Involved in rule u_ppMEKc_tot

One rule which determines this species' quantity.

8.21 Species ppMEKc_tot

Name ppMEKc_tot

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

Involved in rule ppMEKc_tot

This species takes part in four reactions (as a modifier in reaction_1, reaction_1, reaction_3, reaction_3) and is also involved in one rule which determines this species' quantity.

8.22 Species ERKc_obs

Name ERKc_obs

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

Involved in rule ERKc_obs

One rule which determines this species' quantity.

8.23 Species pERKc_obs

Name pERKc_obs

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

Involved in rule pERKc_obs

One rule which determines this species' quantity.

8.24 Species ppERKc_obs

Name ppERKc_obs

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

Involved in rule ppERKc_obs

One rule which determines this species' quantity.

8.25 Species ERK_ppMEKc_obs

Name ERK_ppMEKc_obs

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

Involved in rule ERK_ppMEKc_obs

One rule which determines this species' quantity.

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