

## SBML Model Report

# Model name: “Besozzi2012 - Oscillatory regimes in the Ras/cAMP/PKA pathway in *S.cerevisiae*”



May 6, 2016

## 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah<sup>1</sup> and Daniela Besozzi<sup>2</sup> at September eleventh 2013 at 11:38 a. m. and last time modified at March tenth 2014 at 3:38 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	1
species types	0	species	33
events	0	constraints	0
reactions	39	function definitions	0
global parameters	39	unit definitions	3
rules	0	initial assignments	0

## Model Notes

Besozzi2012 - Oscillatory regimes in the Ras/cAMP/PKA pathway in *S.cerevisiae*

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Mechanistic model of the Ras/cAMP/PKA in yeast *S.cerevisiae*. The Ras/cAMP/PKA pathway plays a major role in the regulation of metabolism, stress resistance and cell cycle progress and is tightly regulated by multiple feedback loops, exerted by the protein kinase A (PKA). This model investigates the dynamics of the second messenger cAMP on Ras/cAMP/PKA pathway, to determine the effects of the feedback mechanisms on establishing stable oscillatory regimes.

The model has been defined according to the stochastic formulation of chemical kinetics [Gillespie DT, 1977], which requires to specify the set of molecular species occurring in the pathway and their respective interactions, formally described as a set of biochemical reactions.

The volume considered for this system is 30fL; this value can be used to convert the model into the deterministic formulation.

This model is described in the article: [The role of feedback control mechanisms on the establishment of oscillatory regimes in the Ras/cAMP/PKA pathway in \*S. cerevisiae\*](#). Besozzi D, Cazzaniga P, Pescini D, Mauri G, Colombo S, Martegani E. EURASIP J Bioinform Syst Biol. 2012 Jul 20;2012(1):10.

Abstract:

In the yeast *Saccharomyces cerevisiae*, the Ras/cAMP/PKA pathway is involved in the regulation of cell growth and proliferation in response to nutritional sensing and stress conditions. The pathway is tightly regulated by multiple feedback loops, exerted by the protein kinase A (PKA) on a few pivotal components of the pathway. In this article, we investigate the dynamics of the second messenger cAMP by performing stochastic simulations and parameter sweep analysis of a mechanistic model of the Ras/cAMP/PKA pathway, to determine the effects that the modulation of these feedback mechanisms has on the establishment of stable oscillatory regimes. In particular, we start by studying the role of phosphodiesterases, the enzymes that catalyze the degradation of cAMP, which represent the major negative feedback in this pathway. Then, we show the results on cAMP oscillations when perturbing the amount of protein Cdc25 coupled with the alteration of the intracellular ratio of the guanine nucleotides (GTP/GDP), which are known to regulate the switch of the GTPase Ras protein. This multi-level regulation of the amplitude and frequency of oscillations in the Ras/cAMP/PKA pathway might act as a fine tuning mechanism for the downstream targets of PKA, as also recently evidenced by some experimental investigations on the nucleocytoplasmic shuttling of the transcription factor Msn2 in yeast cells.

This model is hosted on [BioModels Database](#) and identified by: [BIOMD0000000478](#).

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## 2 Unit Definitions

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

## 2.1 Unit volume

**Name** volume

**Definition** dimensionless

## 2.2 Unit substance

**Name** substance

**Definition** dimensionless

## 2.3 Unit per\_second

**Definition**  $s^{-1}$

## 2.4 Unit area

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

**Definition**  $m^2$

## 2.5 Unit length

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

**Definition** m

## 2.6 Unit time

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

**Definition** s

# 3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
compartment01		0000290	3	1	dimensionless	<input checked="" type="checkbox"/>	

### 3.1 Compartment `compartment01`

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

**SBO:0000290** physical compartment

## 4 Species

This model contains 33 species. The boundary condition of three of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 7 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
Ras2_GDP		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
Cdc25		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
Ras2_GDP_Cdc25		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
Ras2_Cdc25		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
GDP		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
GTP		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Ras2_GTP_Cdc25		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
Ras2_GTP		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
Ira2		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>
Ras2_GTP_Ira2		compartment01	dimensionless · dimensionless <sup>-1</sup>	<input type="checkbox"/>	<input type="checkbox"/>

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
CYR1		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
Ras2_GTP_CYR1		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
ATP		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
cAMP		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
PKA		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
cAMP_PKA		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
IIcAMP_PKA		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
IIIcAMP_PKA		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
IVcAMP_PKA		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
C		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
R_2cAMP		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
R		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>
R_C		compartment01	dimensionless dimensionless <sup>-1</sup>	· <input type="checkbox"/>	<input type="checkbox"/>

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
Pde1		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞
Pde1f		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞
cAMP_Pde1f		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞
AMP		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞
PPA2		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞
Pde2		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞
cAMP_Pde2		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞
Cdc25f		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞
Ira2P		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞
Ras2_GTP_Ira2P		compartment01	dimensionless dimensionless <sup>-1</sup>	· ⊞	⊞

## 5 Parameters

This model contains 39 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K0			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K1			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K2			1.500	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K3			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K4			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K5			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K6			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K7			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K8			0.010	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K9			0.250	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K10			0.001	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K11			$2.1 \cdot 10^{-6}$	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K12			0.001	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K13			$10^{-5}$	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K14			$10^{-5}$	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K15			$10^{-5}$	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K16			$10^{-5}$	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K17			0.100	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K18			0.100	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K19			0.100	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K20			0.100	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K21			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K22			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K23			0.750	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K24			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K25			$10^{-6}$	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K26			0.100	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K27			0.100	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K28			7.500	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K29			$10^{-4}$	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K30			$10^{-4}$	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K31			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K32			1.700	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K33			1.000	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K34			0.010	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K35			0.001	s <sup>-1</sup>	<input checked="" type="checkbox"/>
K36			1.250	s <sup>-1</sup>	<input checked="" type="checkbox"/>



Id	Name	SBO	Value	Unit	Constant
K37			2.500	$s^{-1}$	<input checked="" type="checkbox"/>
K38			10.000	$s^{-1}$	<input checked="" type="checkbox"/>

## 6 Reactions

This model contains 39 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

Nº	Id	Name	Reaction Equation	SBO
1	R0		$\text{Ras2\_GDP} + \text{Cdc25} \xrightarrow{\text{Ras2\_GDP, Cdc25}} \text{Ras2\_GDP\_Cdc25}$	
2	R1		$\text{Ras2\_GDP\_Cdc25} \xrightarrow{\text{Ras2\_GDP\_Cdc25}} \text{Ras2\_GDP} + \text{Cdc25}$	
3	R2		$\text{Ras2\_GDP\_Cdc25} \xrightarrow{\text{Ras2\_GDP\_Cdc25}} \text{Ras2\_Cdc25} + \text{GDP}$	
4	R3		$\text{Ras2\_Cdc25} + \text{GDP} \xrightarrow{\text{Ras2\_Cdc25, GDP}} \text{Ras2\_GDP\_Cdc25}$	
5	R4		$\text{Ras2\_Cdc25} + \text{GTP} \xrightarrow{\text{Ras2\_Cdc25, GTP}} \text{Ras2\_GTP\_Cdc25}$	
6	R5		$\text{Ras2\_GTP\_Cdc25} \xrightarrow{\text{Ras2\_GTP\_Cdc25}} \text{Ras2\_Cdc25} + \text{GTP}$	
7	R6		$\text{Ras2\_GTP\_Cdc25} \xrightarrow{\text{Ras2\_GTP\_Cdc25}} \text{Cdc25} + \text{Ras2\_GTP}$	
8	R7		$\text{Cdc25} + \text{Ras2\_GTP} \xrightarrow{\text{Cdc25, Ras2\_GTP}} \text{Ras2\_GTP\_Cdc25}$	
9	R8		$\text{Ras2\_GTP} + \text{Ira2} \xrightarrow{\text{Ras2\_GTP, Ira2}} \text{Ras2\_GTP\_Ira2}$	
10	R9		$\text{Ras2\_GTP\_Ira2} \xrightarrow{\text{Ras2\_GTP\_Ira2}} \text{Ras2\_GDP} + \text{Ira2}$	
11	R10		$\text{Ras2\_GTP} + \text{CYR1} \xrightarrow{\text{Ras2\_GTP, CYR1}} \text{Ras2\_GTP\_CYR1}$	
12	R11		$\text{Ras2\_GTP\_CYR1} + \text{ATP} \xrightarrow{\text{Ras2\_GTP\_CYR1, ATP}} \text{Ras2\_GTP\_CYR1} + \text{cAMP}$	

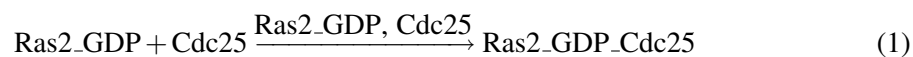
Nº	Id	Name	Reaction Equation	SBO
13	R12		$\text{Ira2} + \text{Ras2\_GTP\_CYR1} \xrightarrow{\text{Ira2, Ras2\_GTP\_CYR1}} \text{Ras2\_GDP} + \text{Ira2} + \text{CYR1}$	
14	R13		$\text{cAMP} + \text{PKA} \xrightarrow{\text{cAMP, PKA}} \text{cAMP\_PKA}$	
15	R14		$\text{cAMP} + \text{cAMP\_PKA} \xrightarrow{\text{cAMP, cAMP\_PKA}} \text{IIcAMP\_PKA}$	
16	R15		$\text{cAMP} + \text{IIcAMP\_PKA} \xrightarrow{\text{cAMP, IIcAMP\_PKA}} \text{IIIcAMP\_PKA}$	
17	R16		$\text{cAMP} + \text{IIIcAMP\_PKA} \xrightarrow{\text{cAMP, IIIcAMP\_PKA}} \text{IVcAMP\_PKA}$	
18	R17		$\text{IVcAMP\_PKA} \xrightarrow{\text{IVcAMP\_PKA}} \text{cAMP} + \text{IIIcAMP\_PKA}$	
19	R18		$\text{IIIcAMP\_PKA} \xrightarrow{\text{IIIcAMP\_PKA}} \text{cAMP} + \text{IIcAMP\_PKA}$	
20	R19		$\text{IIcAMP\_PKA} \xrightarrow{\text{IIcAMP\_PKA}} \text{cAMP} + \text{cAMP\_PKA}$	
21	R20		$\text{cAMP\_PKA} \xrightarrow{\text{cAMP\_PKA}} \text{cAMP} + \text{PKA}$	
22	R21		$\text{IVcAMP\_PKA} \xrightarrow{\text{IVcAMP\_PKA}} 2 \text{ C} + 2 \text{ R\_2cAMP}$	
23	R22		$\text{R\_2cAMP} \xrightarrow{\text{R\_2cAMP}} 2 \text{ cAMP} + \text{R}$	
24	R23		$\text{C} + \text{R} \xrightarrow{\text{C, R}} \text{R\_C}$	
25	R24		$2 \text{ R\_C} \xrightarrow{\text{R\_C}} \text{PKA}$	
26	R25		$\text{C} + \text{Pde1} \xrightarrow{\text{C, Pde1}} \text{C} + \text{Pde1f}$	
27	R26		$\text{cAMP} + \text{Pde1f} \xrightarrow{\text{cAMP, Pde1f}} \text{cAMP\_Pde1f}$	
28	R27		$\text{cAMP\_Pde1f} \xrightarrow{\text{cAMP\_Pde1f}} \text{cAMP} + \text{Pde1f}$	
29	R28		$\text{cAMP\_Pde1f} \xrightarrow{\text{cAMP\_Pde1f}} \text{Pde1f} + \text{AMP}$	
30	R29		$\text{Pde1f} + \text{PPA2} \xrightarrow{\text{Pde1f, PPA2}} \text{Pde1} + \text{PPA2}$	

Nº	Id	Name	Reaction Equation	SBO
31	R30		$\text{cAMP} + \text{Pde2} \xrightarrow{\text{cAMP, Pde2}} \text{cAMP\_Pde2}$	
32	R31		$\text{cAMP\_Pde2} \xrightarrow{\text{cAMP\_Pde2}} \text{cAMP} + \text{Pde2}$	
33	R32		$\text{cAMP\_Pde2} \xrightarrow{\text{cAMP\_Pde2}} \text{AMP} + \text{Pde2}$	
34	R33		$\text{Cdc25} + \text{C} \xrightarrow{\text{Cdc25, C}} \text{C} + \text{Cdc25f}$	
35	R34		$\text{PPA2} + \text{Cdc25f} \xrightarrow{\text{PPA2, Cdc25f}} \text{Cdc25} + \text{PPA2}$	
36	R35		$\text{Ira2} + \text{C} \xrightarrow{\text{Ira2, C}} \text{C} + \text{Ira2P}$	
37	R36		$\text{Ras2\_GTP} + \text{Ira2P} \xrightarrow{\text{Ras2\_GTP, Ira2P}} \text{Ras2\_GTP\_Ira2P}$	
38	R37		$\text{Ras2\_GTP\_Ira2P} \xrightarrow{\text{Ras2\_GTP\_Ira2P}} \text{Ras2\_GDP} + \text{Ira2P}$	
39	R38		$\text{Ira2P} \xrightarrow{\text{Ira2P}} \text{Ira2}$	

## 6.1 Reaction R0

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

### Reaction equation



### Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
Ras2_GDP		
Cdc25		

### Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
Ras2_GDP		
Cdc25		

### Product

Table 8: Properties of each product.

Id	Name	SBO
Ras2_GDP_Cdc25		

### Kinetic Law

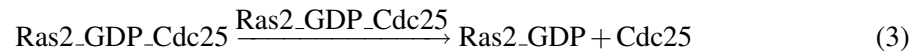
**Derived unit**  $\text{s}^{-1}$

$$v_1 = K_0 \cdot [\text{Ras2\_GDP}] \cdot [\text{Cdc25}] \quad (2)$$

## 6.2 Reaction R1

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

### Reaction equation



### Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
Ras2_GDP_Cdc25		

### Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
Ras2_GDP_Cdc25		

### Products

Table 11: Properties of each product.

Id	Name	SBO
Ras2_GDP		
Cdc25		

### Kinetic Law

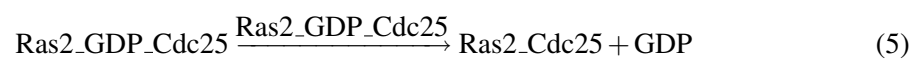
**Derived unit**  $\text{s}^{-1}$

$$v_2 = K1 \cdot [\text{Ras2\_GDP\_Cdc25}] \quad (4)$$

## 6.3 Reaction R2

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

### Reaction equation



### Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
Ras2_GDP_Cdc25		

## Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
Ras2_GDP_Cdc25		

## Products

Table 14: Properties of each product.

Id	Name	SBO
Ras2_Cdc25		
GDP		

## Kinetic Law

**Derived unit**  $s^{-1}$

$$v_3 = K2 \cdot [\text{Ras2\_GDP\_Cdc25}] \quad (6)$$

## 6.4 Reaction R3

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

## Reaction equation



## Reactants

Table 15: Properties of each reactant.

Id	Name	SBO
Ras2_Cdc25		
GDP		

## Modifiers

Table 16: Properties of each modifier.

Id	Name	SBO
Ras2_Cdc25		
GDP		

## Product

Table 17: Properties of each product.

Id	Name	SBO
Ras2_GDP_Cdc25		

## Kinetic Law

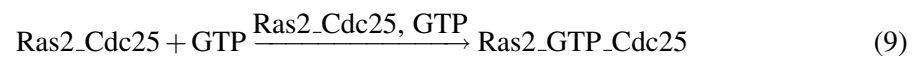
**Derived unit**  $\text{s}^{-1}$

$$v_4 = K3 \cdot [\text{Ras2\_Cdc25}] \cdot [\text{GDP}] \quad (8)$$

## 6.5 Reaction R4

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

### Reaction equation



## Reactants

Table 18: Properties of each reactant.

Id	Name	SBO
Ras2_Cdc25		
GTP		

## Modifiers



Table 19: Properties of each modifier.

Id	Name	SBO
Ras2_Cdc25		
GTP		

## Product

Table 20: Properties of each product.

Id	Name	SBO
Ras2_GTP_Cdc25		

## Kinetic Law

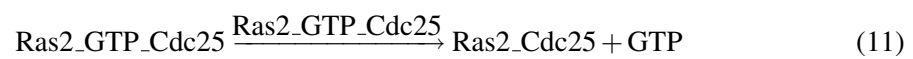
Derived unit  $\text{s}^{-1}$

$$v_5 = K4 \cdot [\text{Ras2\_Cdc25}] \cdot [\text{GTP}] \quad (10)$$

## 6.6 Reaction R5

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

### Reaction equation



## Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
Ras2_GTP_Cdc25		

## Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
Ras2_GTP_Cdc25		

## Products

Table 23: Properties of each product.

Id	Name	SBO
Ras2_Cdc25		
GTP		

## Kinetic Law

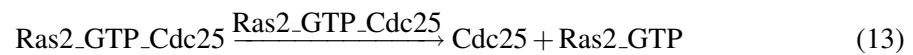
**Derived unit**  $s^{-1}$

$$v_6 = K5 \cdot [\text{Ras2\_GTP\_Cdc25}] \quad (12)$$

## 6.7 Reaction R6

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

### Reaction equation



## Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
Ras2_GTP_Cdc25		

## Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
Ras2_GTP_Cdc25		

## Products

Table 26: Properties of each product.

Id	Name	SBO
Cdc25		
Ras2_GTP		

### Kinetic Law

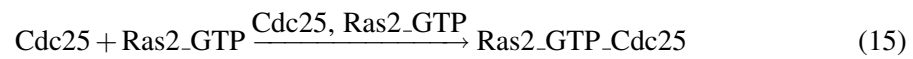
**Derived unit**  $s^{-1}$

$$v_7 = K6 \cdot [\text{Ras2\_GTP\_Cdc25}] \quad (14)$$

### 6.8 Reaction R7

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

### Reaction equation



### Reactants

Table 27: Properties of each reactant.

Id	Name	SBO
Cdc25		
Ras2_GTP		

### Modifiers

Table 28: Properties of each modifier.

Id	Name	SBO
Cdc25		
Ras2_GTP		

### Product

Table 29: Properties of each product.

Id	Name	SBO
Ras2_GTP_Cdc25		

### Kinetic Law

**Derived unit**  $\text{s}^{-1}$

$$v_8 = K7 \cdot [\text{Cdc25}] \cdot [\text{Ras2\_GTP}] \quad (16)$$

### 6.9 Reaction R8

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

### Reaction equation



### Reactants

Table 30: Properties of each reactant.

Id	Name	SBO
Ras2_GTP		
Ira2		

### Modifiers

Table 31: Properties of each modifier.

Id	Name	SBO
Ras2_GTP		
Ira2		

### Product

Table 32: Properties of each product.

Id	Name	SBO
Ras2_GTP_Ira2		

### Kinetic Law

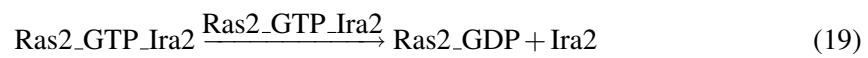
**Derived unit**  $\text{s}^{-1}$

$$v_9 = K8 \cdot [\text{Ras2\_GTP}] \cdot [\text{Ira2}] \quad (18)$$

### 6.10 Reaction R9

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

### Reaction equation



### Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
Ras2_GTP_Ira2		

### Modifier

Table 34: Properties of each modifier.

Id	Name	SBO
Ras2_GTP_Ira2		

### Products

Table 35: Properties of each product.

Id	Name	SBO
Ras2_GDP		
Ira2		

### Kinetic Law

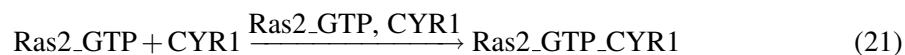
**Derived unit**  $\text{s}^{-1}$

$$v_{10} = K9 \cdot [\text{Ras2\_GTP\_Ira2}] \quad (20)$$

### 6.11 Reaction R10

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

#### Reaction equation



#### Reactants

Table 36: Properties of each reactant.

Id	Name	SBO
Ras2_GTP		
CYR1		

#### Modifiers

Table 37: Properties of each modifier.

Id	Name	SBO
Ras2_GTP		
CYR1		

#### Product

Table 38: Properties of each product.

Id	Name	SBO
Ras2_GTP_CYR1		

#### Kinetic Law

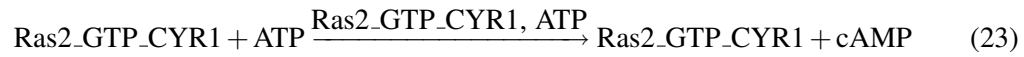
**Derived unit**  $\text{s}^{-1}$

$$v_{11} = K10 \cdot [\text{Ras2\_GTP}] \cdot [\text{CYR1}] \quad (22)$$

### 6.12 Reaction R11

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation



### Reactants

Table 39: Properties of each reactant.

Id	Name	SBO
Ras2_GTP_CYR1		
ATP		

### Modifiers

Table 40: Properties of each modifier.

Id	Name	SBO
Ras2_GTP_CYR1		
ATP		

### Products

Table 41: Properties of each product.

Id	Name	SBO
Ras2_GTP_CYR1		
cAMP		

### Kinetic Law

Derived unit  $\text{s}^{-1}$

$$v_{12} = K_{11} \cdot [\text{Ras2\_GTP\_CYR1}] \cdot [\text{ATP}] \quad (24)$$

## 6.13 Reaction R12

This is an irreversible reaction of two reactants forming three products influenced by two modifiers.

### Reaction equation



## Reactants

Table 42: Properties of each reactant.

Id	Name	SBO
Ira2		
Ras2_GTP_CYR1		

## Modifiers

Table 43: Properties of each modifier.

Id	Name	SBO
Ira2		
Ras2_GTP_CYR1		

## Products

Table 44: Properties of each product.

Id	Name	SBO
Ras2_GDP		
Ira2		
CYR1		

## Kinetic Law

**Derived unit**  $s^{-1}$

$$v_{13} = K_{12} \cdot [\text{Ira2}] \cdot [\text{Ras2\_GTP\_CYR1}] \quad (26)$$

### 6.14 Reaction R13

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

#### Reaction equation



## Reactants



Table 45: Properties of each reactant.

Id	Name	SBO
cAMP		
PKA		

Modifiers

Table 46: Properties of each modifier.

Id	Name	SBO
cAMP		
PKA		

Product

Table 47: Properties of each product.

Id	Name	SBO
cAMP_PKA		

Kinetic Law

Derived unit  $s^{-1}$

$$v_{14} = K13 \cdot [cAMP] \cdot [PKA] \tag{28}$$

6.15 Reaction R14

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

Reaction equation



Reactants

Table 48: Properties of each reactant.

Id	Name	SBO
cAMP		
cAMP_PKA		

## Modifiers

Table 49: Properties of each modifier.

Id	Name	SBO
cAMP		
cAMP_PKA		

## Product

Table 50: Properties of each product.

Id	Name	SBO
IIcAMP_PKA		

## Kinetic Law

Derived unit  $\text{s}^{-1}$

$$v_{15} = K_{14} \cdot [\text{cAMP}] \cdot [\text{cAMP\_PKA}] \quad (30)$$

### 6.16 Reaction R15

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

#### Reaction equation



## Reactants

Table 51: Properties of each reactant.

Id	Name	SBO
cAMP		
IIcAMP_PKA		

## Modifiers

Table 52: Properties of each modifier.

Id	Name	SBO
cAMP		
IIcAMP_PKA		

## Product

Table 53: Properties of each product.

Id	Name	SBO
IIIcAMP_PKA		

## Kinetic Law

Derived unit  $\text{s}^{-1}$

$$v_{16} = K_{15} \cdot [\text{cAMP}] \cdot [\text{IIcAMP\_PKA}] \quad (32)$$

## 6.17 Reaction R16

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

## Reaction equation



## Reactants

Table 54: Properties of each reactant.

Id	Name	SBO
cAMP		
IIIcAMP_PKA		

## Modifiers

Table 55: Properties of each modifier.

Id	Name	SBO
cAMP		

Id	Name	SBO
IIIcAMP_PKA		

## Product

Table 56: Properties of each product.

Id	Name	SBO
IVcAMP_PKA		

## Kinetic Law

**Derived unit**  $\text{s}^{-1}$

$$v_{17} = K16 \cdot [\text{cAMP}] \cdot [\text{IIIcAMP\_PKA}] \quad (34)$$

## 6.18 Reaction R17

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

## Reaction equation



## Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
IVcAMP_PKA		

## Modifier

Table 58: Properties of each modifier.

Id	Name	SBO
IVcAMP_PKA		

## Products

Table 59: Properties of each product.

Id	Name	SBO
cAMP		
IIIcAMP_PKA		

### Kinetic Law

**Derived unit**  $\text{s}^{-1}$

$$v_{18} = K17 \cdot [\text{IVcAMP\_PKA}] \quad (36)$$

### 6.19 Reaction R18

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

### Reaction equation



### Reactant

Table 60: Properties of each reactant.

Id	Name	SBO
IIIcAMP_PKA		

### Modifier

Table 61: Properties of each modifier.

Id	Name	SBO
IIIcAMP_PKA		

### Products

Table 62: Properties of each product.

Id	Name	SBO
cAMP		
IIcAMP_PKA		

### Kinetic Law

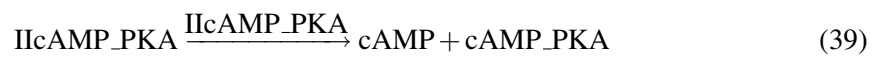
Derived unit  $s^{-1}$

$$v_{19} = K18 \cdot [IIIcAMP\_PKA] \quad (38)$$

### 6.20 Reaction R19

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

### Reaction equation



### Reactant

Table 63: Properties of each reactant.

Id	Name	SBO
IIcAMP_PKA		

### Modifier

Table 64: Properties of each modifier.

Id	Name	SBO
IIcAMP_PKA		

### Products

Table 65: Properties of each product.

Id	Name	SBO
cAMP		
cAMP_PKA		

### Kinetic Law

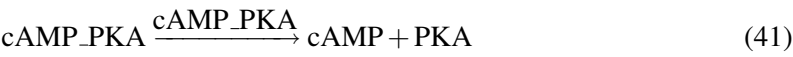
Derived unit  $s^{-1}$

$$v_{20} = K19 \cdot [IIcAMP\_PKA] \quad (40)$$

6.21 Reaction R20

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

Reaction equation



Reactant

Table 66: Properties of each reactant.

Id	Name	SBO
cAMP_PKA		

Modifier

Table 67: Properties of each modifier.

Id	Name	SBO
cAMP_PKA		

Products

Table 68: Properties of each product.

Id	Name	SBO
cAMP		
PKA		

Kinetic Law

Derived unit s<sup>-1</sup>

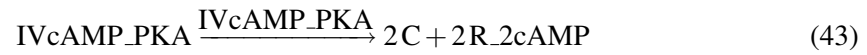
$$v_{21} = K20 \cdot [\text{cAMP\_PKA}]$$

(42)

6.22 Reaction R21

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

### Reaction equation



### Reactant

Table 69: Properties of each reactant.

Id	Name	SBO
IVcAMP_PKA		

### Modifier

Table 70: Properties of each modifier.

Id	Name	SBO
IVcAMP_PKA		

### Products

Table 71: Properties of each product.

Id	Name	SBO
C		
R_2cAMP		

### Kinetic Law

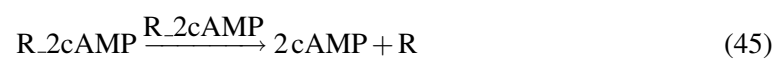
**Derived unit**  $\text{s}^{-1}$

$$v_{22} = K_{21} \cdot [\text{IVcAMP\_PKA}] \quad (44)$$

## 6.23 Reaction R22

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

### Reaction equation



### Reactant



Table 72: Properties of each reactant.

Id	Name	SBO
R_2cAMP		

## Modifier

Table 73: Properties of each modifier.

Id	Name	SBO
R_2cAMP		

## Products

Table 74: Properties of each product.

Id	Name	SBO
cAMP		
R		

## Kinetic Law

**Derived unit**  $s^{-1}$

$$v_{23} = K_{22} \cdot [R\_2cAMP] \quad (46)$$

## 6.24 Reaction R23

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

## Reaction equation



## Reactants

Table 75: Properties of each reactant.

Id	Name	SBO
C		
R		

## Modifiers

Table 76: Properties of each modifier.

Id	Name	SBO
C		
R		

## Product

Table 77: Properties of each product.

Id	Name	SBO
R_C		

## Kinetic Law

Derived unit  $\text{s}^{-1}$

$$v_{24} = K_{23} \cdot [C] \cdot [R] \quad (48)$$

### 6.25 Reaction R24

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

#### Reaction equation



## Reactant

Table 78: Properties of each reactant.

Id	Name	SBO
R_C		

## Modifier

Table 79: Properties of each modifier.

Id	Name	SBO
R_C		

## Product

Table 80: Properties of each product.

Id	Name	SBO
PKA		

## Kinetic Law

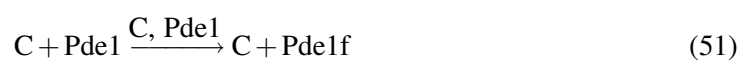
**Derived unit** contains undeclared units

$$v_{25} = K_{24} \cdot \frac{[R\_C] \cdot ([R\_C] - 1)}{2} \quad (50)$$

## 6.26 Reaction R25

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

## Reaction equation



## Reactants

Table 81: Properties of each reactant.

Id	Name	SBO
C		
Pde1		

## Modifiers

Table 82: Properties of each modifier.

Id	Name	SBO
C		
Pde1		

## Products

Table 83: Properties of each product.

Id	Name	SBO
C		
Pde1f		

## Kinetic Law

**Derived unit**  $\text{s}^{-1}$

$$v_{26} = K25 \cdot [C] \cdot [Pde1] \quad (52)$$

## 6.27 Reaction R26

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

## Reaction equation



## Reactants

Table 84: Properties of each reactant.

Id	Name	SBO
cAMP		
Pde1f		

## Modifiers

Table 85: Properties of each modifier.

Id	Name	SBO
cAMP		
Pde1f		

## Product

Table 86: Properties of each product.

Id	Name	SBO
cAMP_Pde1f		

## Kinetic Law

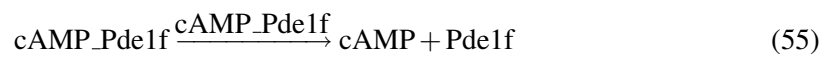
**Derived unit**  $\text{s}^{-1}$

$$v_{27} = K_{26} \cdot [\text{cAMP}] \cdot [\text{Pde1f}] \quad (54)$$

## 6.28 Reaction R27

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

## Reaction equation



## Reactant

Table 87: Properties of each reactant.

Id	Name	SBO
cAMP_Pde1f		

## Modifier

Table 88: Properties of each modifier.

Id	Name	SBO
cAMP_Pde1f		

## Products

Table 89: Properties of each product.

Id	Name	SBO
cAMP		
Pde1f		

## Kinetic Law

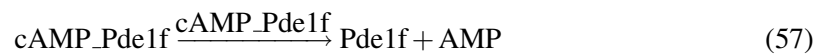
**Derived unit**  $s^{-1}$

$$v_{28} = K27 \cdot [cAMP\_Pde1f] \quad (56)$$

## 6.29 Reaction R28

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

## Reaction equation



## Reactant

Table 90: Properties of each reactant.

Id	Name	SBO
cAMP_Pde1f		

## Modifier

Table 91: Properties of each modifier.

Id	Name	SBO
cAMP_Pde1f		

## Products

Table 92: Properties of each product.

Id	Name	SBO
Pde1f		
AMP		

## Kinetic Law

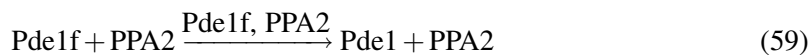
**Derived unit**  $\text{s}^{-1}$

$$v_{29} = K28 \cdot [\text{cAMP\_Pde1f}] \quad (58)$$

## 6.30 Reaction R29

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

## Reaction equation



## Reactants

Table 93: Properties of each reactant.

Id	Name	SBO
Pde1f		
PPA2		

## Modifiers

Table 94: Properties of each modifier.

Id	Name	SBO
Pde1f		
PPA2		

## Products

Table 95: Properties of each product.

Id	Name	SBO
Pde1		
PPA2		

## Kinetic Law

**Derived unit**  $s^{-1}$

$$v_{30} = K29 \cdot [Pde1f] \cdot [PPA2] \quad (60)$$

## 6.31 Reaction R30

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

## Reaction equation



## Reactants

Table 96: Properties of each reactant.

Id	Name	SBO
cAMP		
Pde2		

## Modifiers

Table 97: Properties of each modifier.

Id	Name	SBO
cAMP		
Pde2		

## Product



Table 98: Properties of each product.

Id	Name	SBO
cAMP_Pde2		

**Kinetic Law****Derived unit** s<sup>-1</sup>

$$v_{31} = K30 \cdot [\text{cAMP}] \cdot [\text{Pde2}] \quad (62)$$

**6.32 Reaction R31**

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

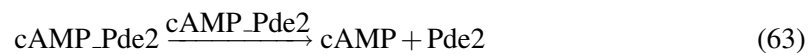
**Reaction equation****Reactant**

Table 99: Properties of each reactant.

Id	Name	SBO
cAMP_Pde2		

**Modifier**

Table 100: Properties of each modifier.

Id	Name	SBO
cAMP_Pde2		

**Products**

Table 101: Properties of each product.

Id	Name	SBO
cAMP		
Pde2		

### Kinetic Law

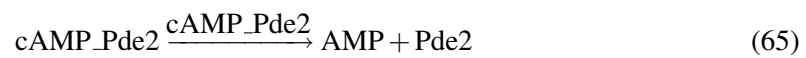
**Derived unit**  $\text{s}^{-1}$

$$v_{32} = K31 \cdot [\text{cAMP\_Pde2}] \quad (64)$$

### 6.33 Reaction R32

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

### Reaction equation



### Reactant

Table 102: Properties of each reactant.

Id	Name	SBO
cAMP_Pde2		

### Modifier

Table 103: Properties of each modifier.

Id	Name	SBO
cAMP_Pde2		

### Products

Table 104: Properties of each product.

Id	Name	SBO
AMP		
Pde2		

### Kinetic Law

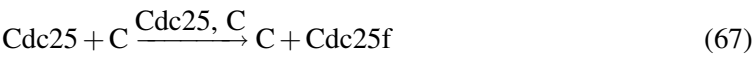
**Derived unit**  $\text{s}^{-1}$

$$v_{33} = K32 \cdot [\text{cAMP\_Pde2}] \quad (66)$$

6.34 Reaction R33

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Reaction equation



Reactants

Table 105: Properties of each reactant.

Id	Name	SBO
Cdc25		
C		

Modifiers

Table 106: Properties of each modifier.

Id	Name	SBO
Cdc25		
C		

Products

Table 107: Properties of each product.

Id	Name	SBO
C		
Cdc25f		

Kinetic Law

Derived unit s<sup>-1</sup>

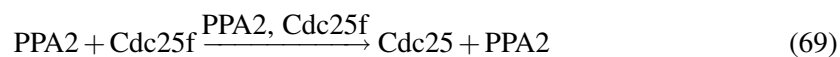
$$v_{34} = K33 \cdot [\text{Cdc25}] \cdot [\text{C}]$$

(68)

### 6.35 Reaction R34

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



#### Reactants

Table 108: Properties of each reactant.

Id	Name	SBO
PPA2		
Cdc25f		

#### Modifiers

Table 109: Properties of each modifier.

Id	Name	SBO
PPA2		
Cdc25f		

#### Products

Table 110: Properties of each product.

Id	Name	SBO
Cdc25		
PPA2		

#### Kinetic Law

**Derived unit**  $\text{s}^{-1}$

$$v_{35} = K_{34} \cdot [\text{PPA2}] \cdot [\text{Cdc25f}] \quad (70)$$

6.36 Reaction R35

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Reaction equation



Reactants

Table 111: Properties of each reactant.

Id	Name	SBO
Ira2		
C		

Modifiers

Table 112: Properties of each modifier.

Id	Name	SBO
Ira2		
C		

Products

Table 113: Properties of each product.

Id	Name	SBO
C		
Ira2P		

Kinetic Law

Derived unit s<sup>-1</sup>

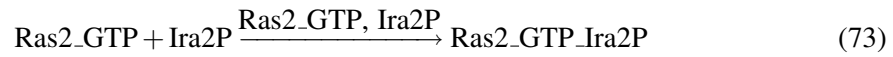
$$v_{36} = K35 \cdot [\text{Ira2}] \cdot [\text{C}]$$

(72)

6.37 Reaction R36

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

### Reaction equation



### Reactants

Table 114: Properties of each reactant.

Id	Name	SBO
Ras2_GTP		
Ira2P		

### Modifiers

Table 115: Properties of each modifier.

Id	Name	SBO
Ras2_GTP		
Ira2P		

### Product

Table 116: Properties of each product.

Id	Name	SBO
Ras2_GTP_Ira2P		

### Kinetic Law

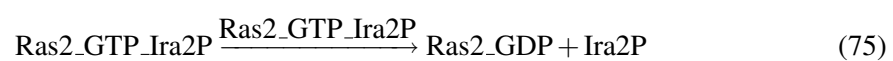
**Derived unit**  $\text{s}^{-1}$

$$v_{37} = K36 \cdot [\text{Ras2\_GTP}] \cdot [\text{Ira2P}] \quad (74)$$

## 6.38 Reaction R37

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

### Reaction equation



**Reactant**

Table 117: Properties of each reactant.

Id	Name	SBO
Ras2_GTP_Ira2P		

## Modifier

Table 118: Properties of each modifier.

Id	Name	SBO
Ras2_GTP_Ira2P		

## Products

Table 119: Properties of each product.

Id	Name	SBO
Ras2_GDP		
Ira2P		

## Kinetic Law

**Derived unit**  $\text{s}^{-1}$

$$v_{38} = K_{37} \cdot [\text{Ras2\_GTP\_Ira2P}] \quad (76)$$

## 6.39 Reaction R38

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

## Reaction equation



## Reactant

Table 120: Properties of each reactant.

Id	Name	SBO
Ira2P		



## Modifier

Table 121: Properties of each modifier.

Id	Name	SBO
Ira2P		

## Product

Table 122: Properties of each product.

Id	Name	SBO
Ira2		

## Kinetic Law

**Derived unit** s<sup>-1</sup>

$$v_{39} = K38 \cdot [\text{Ira2P}] \quad (78)$$

## 7 Derived Rate Equations

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

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

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

### 7.1 Species Ras2\_GDP

**Initial amount** 20000 dimensionless

This species takes part in six reactions (as a reactant in R0 and as a product in R1, R9, R12, R37 and as a modifier in R0).

$$\frac{d}{dt} \text{Ras2\_GDP} = v_2 + v_{10} + v_{13} + v_{38} - v_1 \quad (79)$$

## 7.2 Species Cdc25

**Initial amount** 300 dimensionless

This species takes part in nine reactions (as a reactant in R0, R7, R33 and as a product in R1, R6, R34 and as a modifier in R0, R7, R33).

$$\frac{d}{dt}\text{Cdc25} = v_2 + v_7 + v_{35} - v_1 - v_8 - v_{34} \quad (80)$$

## 7.3 Species Ras2\_GDP\_Cdc25

**Initial amount** 0 dimensionless

This species takes part in six reactions (as a reactant in R1, R2 and as a product in R0, R3 and as a modifier in R1, R2).

$$\frac{d}{dt}\text{Ras2\_GDP\_Cdc25} = v_1 + v_4 - v_2 - v_3 \quad (81)$$

## 7.4 Species Ras2\_Cdc25

**Initial amount** 0 dimensionless

This species takes part in six reactions (as a reactant in R3, R4 and as a product in R2, R5 and as a modifier in R3, R4).

$$\frac{d}{dt}\text{Ras2\_Cdc25} = v_3 + v_6 - v_4 - v_5 \quad (82)$$

## 7.5 Species GDP

**Initial amount** 1500000 dimensionless

This species takes part in three reactions (as a reactant in R3 and as a product in R2 and as a modifier in R3), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{GDP} = 0 \quad (83)$$

## 7.6 Species GTP

**Initial amount** 5000000 dimensionless

This species takes part in three reactions (as a reactant in R4 and as a product in R5 and as a modifier in R4), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{GTP} = 0 \quad (84)$$

### 7.7 Species Ras2\_GTP\_Cdc25

**Initial amount** 0 dimensionless

This species takes part in six reactions (as a reactant in R5, R6 and as a product in R4, R7 and as a modifier in R5, R6).

$$\frac{d}{dt}\text{Ras2\_GTP\_Cdc25} = v_5 + v_8 - v_6 - v_7 \quad (85)$$

### 7.8 Species Ras2\_GTP

**Initial amount** 0 dimensionless

This species takes part in nine reactions (as a reactant in R7, R8, R10, R36 and as a product in R6 and as a modifier in R7, R8, R10, R36).

$$\frac{d}{dt}\text{Ras2\_GTP} = v_7 - v_8 - v_9 - v_{11} - v_{37} \quad (86)$$

### 7.9 Species Ira2

**Initial amount** 200 dimensionless

This species takes part in nine reactions (as a reactant in R8, R12, R35 and as a product in R9, R12, R38 and as a modifier in R8, R12, R35).

$$\frac{d}{dt}\text{Ira2} = v_{10} + v_{13} + v_{39} - v_9 - v_{13} - v_{36} \quad (87)$$

### 7.10 Species Ras2\_GTP\_Ira2

**Initial amount** 0 dimensionless

This species takes part in three reactions (as a reactant in R9 and as a product in R8 and as a modifier in R9).

$$\frac{d}{dt}\text{Ras2\_GTP\_Ira2} = v_9 - v_{10} \quad (88)$$

### 7.11 Species CYR1

**Initial amount** 200 dimensionless

This species takes part in three reactions (as a reactant in R10 and as a product in R12 and as a modifier in R10).

$$\frac{d}{dt}\text{CYR1} = v_{13} - v_{11} \quad (89)$$

### 7.12 Species Ras2\_GTP\_CYR1

**Initial amount** 0 dimensionless

This species takes part in six reactions (as a reactant in R11, R12 and as a product in R10, R11 and as a modifier in R11, R12).

$$\frac{d}{dt}\text{Ras2\_GTP\_CYR1} = v_{11} + v_{12} - v_{12} - v_{13} \quad (90)$$

### 7.13 Species ATP

**Initial amount**  $2.4 \cdot 10^7$  dimensionless

This species takes part in two reactions (as a reactant in R11 and as a modifier in R11), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{ATP} = 0 \quad (91)$$

### 7.14 Species cAMP

**Initial amount** 0 dimensionless

This species takes part in 20 reactions (as a reactant in R13, R14, R15, R16, R26, R30 and as a product in R11, R17, R18, R19, R20, R22, R27, R31 and as a modifier in R13, R14, R15, R16, R26, R30).

$$\begin{aligned} \frac{d}{dt}\text{cAMP} = & v_{12} + v_{18} + v_{19} + v_{20} + v_{21} + 2 v_{23} + v_{28} \\ & + v_{32} - v_{14} - v_{15} - v_{16} - v_{17} - v_{27} - v_{31} \end{aligned} \quad (92)$$

### 7.15 Species PKA

**Initial amount** 2500 dimensionless

This species takes part in four reactions (as a reactant in R13 and as a product in R20, R24 and as a modifier in R13).

$$\frac{d}{dt}\text{PKA} = v_{21} + v_{25} - v_{14} \quad (93)$$

### 7.16 Species cAMP\_PKA

**Initial amount** 0 dimensionless

This species takes part in six reactions (as a reactant in R14, R20 and as a product in R13, R19 and as a modifier in R14, R20).

$$\frac{d}{dt}\text{cAMP\_PKA} = v_{14} + v_{20} - v_{15} - v_{21} \quad (94)$$

### 7.17 Species IIcAMP\_PKA

**Initial amount** 0 dimensionless

This species takes part in six reactions (as a reactant in R15, R19 and as a product in R14, R18 and as a modifier in R15, R19).

$$\frac{d}{dt}\text{IIcAMP\_PKA} = v_{15} + v_{19} - v_{16} - v_{20} \quad (95)$$

### 7.18 Species IIIcAMP\_PKA

**Initial amount** 0 dimensionless

This species takes part in six reactions (as a reactant in R16, R18 and as a product in R15, R17 and as a modifier in R16, R18).

$$\frac{d}{dt}\text{IIIcAMP\_PKA} = v_{16} + v_{18} - v_{17} - v_{19} \quad (96)$$

### 7.19 Species IVcAMP\_PKA

**Initial amount** 0 dimensionless

This species takes part in five reactions (as a reactant in R17, R21 and as a product in R16 and as a modifier in R17, R21).

$$\frac{d}{dt}\text{IVcAMP\_PKA} = v_{17} - v_{18} - v_{22} \quad (97)$$

### 7.20 Species C

**Initial amount** 0 dimensionless

This species takes part in twelve reactions (as a reactant in R23, R25, R33, R35 and as a product in R21, R25, R33, R35 and as a modifier in R23, R25, R33, R35).

$$\frac{d}{dt}C = 2v_{22} + v_{26} + v_{34} + v_{36} - v_{24} - v_{26} - v_{34} - v_{36} \quad (98)$$

### 7.21 Species R\_2cAMP

**Initial amount** 0 dimensionless

This species takes part in three reactions (as a reactant in R22 and as a product in R21 and as a modifier in R22).

$$\frac{d}{dt}R\_2cAMP = 2v_{22} - v_{23} \quad (99)$$

## 7.22 Species R

**Initial amount** 0 dimensionless

This species takes part in three reactions (as a reactant in R23 and as a product in R22 and as a modifier in R23).

$$\frac{d}{dt}R = v_{23} - v_{24} \quad (100)$$

## 7.23 Species R\_C

**Initial amount** 0 dimensionless

This species takes part in three reactions (as a reactant in R24 and as a product in R23 and as a modifier in R24).

$$\frac{d}{dt}R_C = v_{24} - 2 v_{25} \quad (101)$$

## 7.24 Species Pde1

**Initial amount** 1400 dimensionless

This species takes part in three reactions (as a reactant in R25 and as a product in R29 and as a modifier in R25).

$$\frac{d}{dt}Pde1 = v_{30} - v_{26} \quad (102)$$

## 7.25 Species Pde1f

**Initial amount** 0 dimensionless

This species takes part in seven reactions (as a reactant in R26, R29 and as a product in R25, R27, R28 and as a modifier in R26, R29).

$$\frac{d}{dt}Pde1f = v_{26} + v_{28} + v_{29} - v_{27} - v_{30} \quad (103)$$

## 7.26 Species cAMP\_Pde1f

**Initial amount** 0 dimensionless

This species takes part in five reactions (as a reactant in R27, R28 and as a product in R26 and as a modifier in R27, R28).

$$\frac{d}{dt}cAMP\_Pde1f = v_{27} - v_{28} - v_{29} \quad (104)$$

### 7.27 Species AMP

**Initial amount** 0 dimensionless

This species takes part in two reactions (as a product in R28, R32).

$$\frac{d}{dt}\text{AMP} = v_{29} + v_{33} \quad (105)$$

### 7.28 Species PPA2

**Initial amount** 4000 dimensionless

This species takes part in six reactions (as a reactant in R29, R34 and as a product in R29, R34 and as a modifier in R29, R34).

$$\frac{d}{dt}\text{PPA2} = v_{30} + v_{35} - v_{30} - v_{35} \quad (106)$$

### 7.29 Species Pde2

**Initial amount** 6500 dimensionless

This species takes part in four reactions (as a reactant in R30 and as a product in R31, R32 and as a modifier in R30).

$$\frac{d}{dt}\text{Pde2} = v_{32} + v_{33} - v_{31} \quad (107)$$

### 7.30 Species cAMP\_Pde2

**Initial amount** 0 dimensionless

This species takes part in five reactions (as a reactant in R31, R32 and as a product in R30 and as a modifier in R31, R32).

$$\frac{d}{dt}\text{cAMP\_Pde2} = v_{31} - v_{32} - v_{33} \quad (108)$$

### 7.31 Species Cdc25f

**Initial amount** 0 dimensionless

This species takes part in three reactions (as a reactant in R34 and as a product in R33 and as a modifier in R34).

$$\frac{d}{dt}\text{Cdc25f} = v_{34} - v_{35} \quad (109)$$

### 7.32 Species Ira2P

**Initial amount** 0 dimensionless

This species takes part in six reactions (as a reactant in R36, R38 and as a product in R35, R37 and as a modifier in R36, R38).

$$\frac{d}{dt}\text{Ira2P} = v_{36} + v_{38} - v_{37} - v_{39} \quad (110)$$

### 7.33 Species Ras2\_GTP\_Ira2P

**Initial amount** 0 dimensionless

This species takes part in three reactions (as a reactant in R37 and as a product in R36 and as a modifier in R37).

$$\frac{d}{dt}\text{Ras2\_GTP\_Ira2P} = v_{37} - v_{38} \quad (111)$$

## A Glossary of Systems Biology Ontology Terms

**SBO:0000290 physical compartment:** Specific location of space, that can be bounded or not.

A physical compartment can have 1, 2 or 3 dimensions

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