SBML Model Report

Model name: "Swat2004_Mammalian_G1_S_Transition"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Lukas Endler[1] at August 17th 2009 at 2:15 p. m. and last time modified at August nineth 2012 at 4:28 p. m. Table 1 shows an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	9
events	0	constraints	0
reactions	22	function definitions	0
global parameters	40	unit definitions	3
rules	0	initial assignments	0

Model Notes

This is the extended model described the article:
Bifurcation analysis of the regulatory modules of the mammalian G1/S transition.
Swat M, Kel A, Herzel H. Bioinformatics 2004 Jul 10;20(10):1506-11. PMID: 15231543 , doi: 10.1093/bioinformatics/bth110
Abstract:
MOTIVATION: Mathematical models of the cell cycle can contribute to an understanding of

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its basic mechanisms. Modern simulation tools make the analysis of key components and their interactions very effective. This paper focuses on the role of small modules and feedbacks in the gene-protein network governing the G1/S transition in mammalian cells. Mutations in this network may lead to uncontrolled cell proliferation. Bifurcation analysis helps to identify the key components of this extremely complex interaction network.
RESULTS: We identify various positive and negative feedback loops in the network controlling the G1/S transition. It is shown that the positive feedback regulation of E2F1 and a double activator-inhibitor module can lead to bistability. Extensions of the core module preserve the essential features such as bistability. The complete model exhibits a transcritical bifurcation in addition to bistability. We relate these bifurcations to the cell cycle checkpoint and the G1/S phase transition point. Thus, core modules can explain major features of the complex G1/S network and have a robust decision taking function.

2 Unit Definitions

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

2.1 Unit `time`

Name norm. time

Definition dimensionless

2.2 Unit `volume`

Name norm. volume

Definition dimensionless

2.3 Unit substance

Name norm substance

Definition dimensionless

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

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
cell	cell		3	1	dimensionless	☑	

3.1 Compartment cell

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

Name cell

4 Species

This model contains nine species. 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
pRB	pRB	cell	dimensionless · dimensionless^{-1}	⊟	⊟
pRBp	pRBp	cell	dimensionless · dimensionless^{-1}	⊟	⊟
E2F1	E2F1	cell	dimensionless · dimensionless^{-1}	⊟	⊟
CycDi	CycD/cdk4,6(i)	cell	dimensionless · dimensionless^{-1}	⊟	⊟
CycDa	CycD/cdk4,6(a)	cell	dimensionless · dimensionless^{-1}	⊟	⊟
AP1	AP1	cell	dimensionless · dimensionless^{-1}	⊟	⊟
pRBpp	pRBpp	cell	dimensionless · dimensionless^{-1}	⊟	⊟
CycEi	CycE/cdk2(i)	cell	dimensionless · dimensionless^{-1}	⊟	⊟
CycEa	CycEa/cdk2(a)	cell	dimensionless · dimensionless^{-1}	⊟	⊟

5 Parameters

This model contains 40 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.000		☑
Km1	Km1		0.500		☑
J11	J11		0.500		☑
J61	J61		5.000		☑
k16	k16		0.400		☑
k61	k61		0.300		☑
phi_pRB	phi_pRB		0.005		☑
kp	kp		0.050		☑
k2	k2		1.600		☑
a	a		0.040		☑
Km2	Km2		4.000		☑
J12	J12		5.000		☑
J62	J62		8.000		☑
phi_E2F1	phi_E2F1		0.100		☑
k3	k3		0.050		☑
k23	k23		0.300		☑
J13	J13		0.002		☑
J63	J63		2.000		☑
k34	k34		0.040		☑
Km4	Km4		0.300		☑
phi_CycDi	phi_CycDi		0.023		☑
k43	k43		0.010		☑
phi_CycDa	phi_CycDa		0.030		☑
Fm	Fm		0.005		☑
k25	k25		0.900		☑
J15	J15		0.001		☑
J65	J65		6.000		☑
phi_AP1	phi_AP1		0.010		☑
k67	k67		0.700		☑
k76	k76		0.100		☑
phi_pRBpp	phi_pRBpp		0.040		☑
phi_pRBp	phi_pRBp		0.060		☑
k28	k28		0.060		☑
J18	J18		0.600		☑
J68	J68		7.000		☑
k89	k89		0.070		☑
Km9	Km9		0.005		☑

Id	Name	SBO	Value	Unit	Constant
k98	k98		0.010		☑
phi_CycEi	phi_CycEi		0.060		☑
phi_CycEa	phi_CycEa		0.050		☑

6 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	pRB_synthesis	pRB synthesis	$\emptyset \xrightarrow{\text{pRB, pRBp, E2F1}} \text{pRB}$	
2	pRB_phosphorylation	pRB phosphorylation	$\text{pRB} \xrightarrow{\text{pRB, CycDa}} \text{pRBp}$	
3	pRBp_dephosphorylation	pRBp dephosphorylation	$\text{pRBp} \longrightarrow \text{pRB}$	
4	pRB_degradation	pRB degradation	$\text{pRB} \longrightarrow \emptyset$	
5	E2F1_synthesis	E2F1 synthesis	$\emptyset \xrightarrow{\text{E2F1, pRB, pRBp}} \text{E2F1}$	
6	E2F1_degradation	E2F1 degradation	$\text{E2F1} \longrightarrow \emptyset$	
7	CycD_synthesis	CycD synthesis	$\emptyset \xrightarrow{\text{E2F1, pRB, pRBp, AP1}} \text{CycDi}$	
8	CycD_inibition	CycD inibition	$\text{CycDa} \longrightarrow \text{CycDi}$	
9	CycD_activation	CycD activation	$\text{CycDi} \xrightarrow{\text{CycDi, CycDa}} \text{CycDa}$	
10	CycD_degradation	CycD degradation	$\text{CycDi} \longrightarrow \emptyset$	
11	CycD_degradation2	CycD degradation2	$\text{CycDa} \longrightarrow \emptyset$	
12	AP1_synthesis	AP1 synthesis	$\emptyset \xrightarrow{\text{E2F1, pRB, pRBp}} \text{AP1}$	
13	Ap1_degradation	Ap1 degradation	$\text{AP1} \longrightarrow \emptyset$	
14	pRBp_phosphorylation	pRBp phosphorylation	$\text{pRBp} \xrightarrow{\text{pRBp, CycEa}} \text{pRBpp}$	

№	Id	Name	Reaction Equation	SBO
15	pRBpp-_dephosphorylation	pRBpp dephosphorylation	pRBpp $\longrightarrow$ pRBp	
16	pRBpp-_degradation	pRBpp degradation	pRBpp $\longrightarrow \emptyset$	
17	pRBp-_degradation	pRBp degradation	pRBp $\longrightarrow \emptyset$	
18	CycE_synthesis	CycE synthesis	$\emptyset \xrightarrow{\text{E2F1, pRB, pRBp}}$ CycEi	
19	CycE_activation	CycE activation	CycEi $\xrightarrow{\text{CycEi, CycEa}}$ CycEa	
20	CycE_inibition	CycE inibition	CycEa $\longrightarrow$ CycEi	
21	CycE-_degradation	CycE degradation	CycEi $\longrightarrow \emptyset$	
22	CycE-_degradation2	CycE degradation2	CycEa $\longrightarrow \emptyset$	

6.1 Reaction pRB_synthesis

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

Name pRB synthesis

Reaction equation

$$\emptyset \xrightarrow{\text{pRB, pRBp, E2F1}} \text{pRB} \tag{1}$$

Modifiers

Table 6: Properties of each modifier.

Id	Name	SBO
pRB	pRB	
pRBp	pRBp	
E2F1	E2F1	

Product

Table 7: Properties of each product.

Id	Name	SBO
pRB	pRB	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{cell}) \cdot \text{k1} \cdot \frac{[\text{E2F1}]}{\text{Km1} + [\text{E2F1}]} \cdot \frac{\text{J11}}{\text{J11} + [\text{pRB}]} \cdot \frac{\text{J61}}{\text{J61} + [\text{pRBp}]} \tag{2}$$

6.2 Reaction pRB_phosphorylation

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

Name pRB phosphorylation

Reaction equation

$$\text{pRB} \xrightarrow{\text{pRB, CycDa}} \text{pRBp} \tag{3}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
pRB	pRB	

Modifiers

Table 9: Properties of each modifier.

Id	Name	SBO
pRB	pRB	
CycDa	CycD/cdk4,6(a)	

Product

Table 10: Properties of each product.

Id	Name	SBO
pRBp	pRBp	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k16} \cdot [\mathrm{pRB}] \cdot [\mathrm{CycDa}] \tag{4}$$

6.3 Reaction pRBp_dephosphorylation

This is an irreversible reaction of one reactant forming one product.

Name pRBp dephosphorylation

Reaction equation

$$\mathrm{pRBp} \longrightarrow \mathrm{pRB} \tag{5}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
pRBp	pRBp	

Product

Table 12: Properties of each product.

Id	Name	SBO
pRB	pRB	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k61} \cdot [\mathrm{pRBp}] \tag{6}$$

6.4 Reaction pRB_degradation

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

Name pRB degradation

Reaction equation

$$\mathrm{pRB} \longrightarrow \emptyset \tag{7}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
pRB	pRB	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{phi\_pRB} \cdot [\mathrm{pRB}] \tag{8}$$

6.5 Reaction E2F1_synthesis

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

Name E2F1 synthesis

Reaction equation

$$\emptyset \xrightarrow{\text{E2F1, pRB, pRBp}} \text{E2F1} \tag{9}$$

Modifiers

Table 14: Properties of each modifier.

Id	Name	SBO
E2F1	E2F1	
pRB	pRB	
pRBp	pRBp	

Product

Table 15: Properties of each product.

Id	Name	SBO
E2F1	E2F1	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}(\text{cell}) \cdot \left(\text{kp} + \frac{\text{k2} \cdot \left(\text{a}^2 + [\text{E2F1}]^2\right)}{\text{Km2}^2 + [\text{E2F1}]^2} \cdot \frac{\text{J12}}{\text{J12} + [\text{pRB}]} \cdot \frac{\text{J62}}{\text{J62} + [\text{pRBp}]} \right) \tag{10}$$

6.6 Reaction E2F1_degradation

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

Name E2F1 degradation

Reaction equation

$$\text{E2F1} \longrightarrow \emptyset \tag{11}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
E2F1	E2F1	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{phi\_E2F1} \cdot [\mathrm{E2F1}] \tag{12}$$

6.7 Reaction CycD_synthesis

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

Name CycD synthesis

Reaction equation

$$\emptyset \xrightarrow{\text{E2F1, pRB, pRBp, AP1}} \text{CycDi} \tag{13}$$

Modifiers

Table 17: Properties of each modifier.

Id	Name	SBO
E2F1	E2F1	
pRB	pRB	
pRBp	pRBp	
AP1	AP1	

Product

Table 18: Properties of each product.

Id	Name	SBO
CycDi	CycD/cdk4,6(i)	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\,(\mathrm{cell}) \cdot \left(\mathrm{k3} \cdot [\mathrm{AP1}] + \mathrm{k23} \cdot [\mathrm{E2F1}] \cdot \frac{\mathrm{J13}}{\mathrm{J13} + [\mathrm{pRB}]} \cdot \frac{\mathrm{J63}}{\mathrm{J63} + [\mathrm{pRBp}]} \right) \tag{14}$$

6.8 Reaction `CycD_inibition`

This is an irreversible reaction of one reactant forming one product.

Name CycD inibition

Reaction equation

$$\mathrm{CycDa} \longrightarrow \mathrm{CycDi} \tag{15}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
`CycDa`	CycD/cdk4,6(a)	

Product

Table 20: Properties of each product.

Id	Name	SBO
`CycDi`	CycD/cdk4,6(i)	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k43} \cdot [\mathrm{CycDa}] \tag{16}$$

6.9 Reaction `CycD_activation`

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

Name CycD activation

Reaction equation

$$\mathrm{CycDi} \xrightarrow{\mathrm{CycDi,\ CycDa}} \mathrm{CycDa} \tag{17}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
CycDi	CycD/cdk4,6(i)	

Modifiers

Table 22: Properties of each modifier.

Id	Name	SBO
CycDi	CycD/cdk4,6(i)	
CycDa	CycD/cdk4,6(a)	

Product

Table 23: Properties of each product.

Id	Name	SBO
CycDa	CycD/cdk4,6(a)	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k34} \cdot [\mathrm{CycDi}] \cdot \frac{[\mathrm{CycDa}]}{\mathrm{Km4} + [\mathrm{CycDa}]} \tag{18}$$

6.10 Reaction CycD_degradation

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

Name CycD degradation

Reaction equation

$$\mathrm{CycDi} \longrightarrow \emptyset \tag{19}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
CycDi	CycD/cdk4,6(i)	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{phi\_CycDi} \cdot [\mathrm{CycDi}] \tag{20}$$

6.11 Reaction CycD_degradation2

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

Name CycD degradation2

Reaction equation

$$\mathrm{CycDa} \longrightarrow \emptyset \tag{21}$$

Reactant

Table 25: Properties of each reactant.

Id	Name	SBO
CycDa	CycD/cdk4,6(a)	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{phi\_CycDa} \cdot [\mathrm{CycDa}] \tag{22}$$

6.12 Reaction AP1_synthesis

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

Name AP1 synthesis

Reaction equation

$$\emptyset \xrightarrow{\mathrm{E2F1,\ pRB,\ pRBp}} \mathrm{AP1} \tag{23}$$

Modifiers

Table 26: Properties of each modifier.

Id	Name	SBO
E2F1	E2F1	
pRB	pRB	
pRBp	pRBp	

Product

Table 27: Properties of each product.

Id	Name	SBO
AP1	AP1	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\,(\mathrm{cell}) \cdot \left(\mathrm{Fm} + \mathrm{k25} \cdot [\mathrm{E2F1}] \cdot \frac{\mathrm{J15}}{\mathrm{J15} + [\mathrm{pRB}]} \cdot \frac{\mathrm{J65}}{\mathrm{J65} + [\mathrm{pRBp}]} \right) \tag{24}$$

6.13 Reaction Ap1_degradation

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

Name Ap1 degradation

Reaction equation

$$\mathrm{AP1} \longrightarrow \emptyset \tag{25}$$

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
AP1	AP1	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{phi\_AP1} \cdot [\mathrm{AP1}] \tag{26}$$

6.14 Reaction pRBp_phosphorylation

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

Name pRBp phosphorylation

Reaction equation

$$\mathrm{pRBp} \xrightarrow{\mathrm{pRBp,\ CycEa}} \mathrm{pRBpp} \tag{27}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
pRBp	pRBp	

Modifiers

Table 30: Properties of each modifier.

Id	Name	SBO
pRBp	pRBp	
CycEa	CycEa/cdk2(a)	

Product

Table 31: Properties of each product.

Id	Name	SBO
pRBpp	pRBpp	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k67} \cdot [\mathrm{pRBp}] \cdot [\mathrm{CycEa}] \tag{28}$$

6.15 Reaction pRBpp_dephosphorylation

This is an irreversible reaction of one reactant forming one product.

Name pRBpp dephosphorylation

Reaction equation

$$\mathrm{pRBpp} \longrightarrow \mathrm{pRBp} \tag{29}$$

Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
pRBpp	pRBpp	

Product

Table 33: Properties of each product.

Id	Name	SBO
pRBp	pRBp	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k76} \cdot [\mathrm{pRBpp}] \tag{30}$$

6.16 Reaction pRBpp_degradation

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

Name pRBpp degradation

Reaction equation

$$\mathrm{pRBpp} \longrightarrow \emptyset \tag{31}$$

Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
pRBpp	pRBpp	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{phi\_pRBpp} \cdot [\mathrm{pRBpp}] \tag{32}$$

6.17 Reaction pRBp_degradation

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

Name pRBp degradation

Reaction equation

$$\mathrm{pRBp} \longrightarrow \emptyset \tag{33}$$

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
pRBp	pRBp	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{phi\_pRBp} \cdot [\mathrm{pRBp}] \tag{34}$$

6.18 Reaction CycE_synthesis

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

Name CycE synthesis

Reaction equation

$$\emptyset \xrightarrow{\mathrm{E2F1,\ pRB,\ pRBp}} \mathrm{CycEi} \tag{35}$$

Modifiers

Table 36: Properties of each modifier.

Id	Name	SBO
E2F1	E2F1	
pRB	pRB	
pRBp	pRBp	

Product

Table 37: Properties of each product.

Id	Name	SBO
CycEi	CycE/cdk2(i)	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k28} \cdot [\mathrm{E2F1}] \cdot \frac{\mathrm{J18}}{\mathrm{J18} + [\mathrm{pRB}]} \cdot \frac{\mathrm{J68}}{\mathrm{J68} + [\mathrm{pRBp}]} \tag{36}$$

6.19 Reaction CycE_activation

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

Name CycE activation

Reaction equation

$$\mathrm{CycEi} \xrightarrow{\mathrm{CycEi,\ CycEa}} \mathrm{CycEa} \tag{37}$$

Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
CycEi	CycE/cdk2(i)	

Modifiers

Table 39: Properties of each modifier.

Id	Name	SBO
CycEi	CycE/cdk2(i)	
CycEa	CycEa/cdk2(a)	

Product

Table 40: Properties of each product.

Id	Name	SBO
CycEa	CycEa/cdk2(a)	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \frac{\mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k89} \cdot [\mathrm{CycEi}] \cdot [\mathrm{CycEa}]}{\mathrm{Km9} + [\mathrm{CycEa}]} \tag{38}$$

6.20 Reaction CycE_inibition

This is an irreversible reaction of one reactant forming one product.

Name CycE inibition

Reaction equation

$$\mathrm{CycEa} \longrightarrow \mathrm{CycEi} \tag{39}$$

Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
CycEa	CycEa/cdk2(a)	

Product

Table 42: Properties of each product.

Id	Name	SBO
CycEi	CycE/cdk2(i)	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k98} \cdot [\mathrm{CycEa}] \tag{40}$$

6.21 Reaction CycE_degradation

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

Name CycE degradation

Reaction equation

$$\mathrm{CycEi} \longrightarrow \emptyset \tag{41}$$

Reactant

Table 43: Properties of each reactant.

Id	Name	SBO
CycEi	CycE/cdk2(i)	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{phi\_CycEi} \cdot [\mathrm{CycEi}] \tag{42}$$

6.22 Reaction CycE_degradation2

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

Name CycE degradation2

Reaction equation

$$\mathrm{CycEa} \longrightarrow \emptyset \tag{43}$$

Reactant

Table 44: Properties of each reactant.

Id	Name	SBO
CycEa	CycEa/cdk2(a)	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{phi\_CycEa} \cdot [\mathrm{CycEa}] \tag{44}$$

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 pRB

Name pRB

Notes retinoblastoma tumor suppressor protein

Initial concentration $0.1\ \mathrm{dimensionless} \cdot \mathrm{dimensionless}^{-1}$

This species takes part in ten reactions (as a reactant in pRB_phosphorylation, pRB_degradation and as a product in pRB_synthesis, pRBp_dephosphorylation and as a modifier in pRB_synthesis, pRB_phosphorylation, E2F1_synthesis, CycD_synthesis, AP1_synthesis, CycE_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pRB} = v_1 + v_3 - v_2 - v_4 \tag{45}$$

7.2 Species pRBp

Name pRBp

Notes monophosphorlyated pRB

Initial concentration $0.1\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in eleven reactions (as a reactant in pRBp_dephosphorylation, pRBp_phosphorylation, pRBp_degradation and as a product in pRB_phosphorylation, pRBpp_dephosphorylation and as a modifier in pRB_synthesis, E2F1_synthesis, CycD_synthesis, AP1_synthesis, pRBp_phosphorylation, CycE_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pRBp} = v_2 + v_{15} - v_3 - v_{14} - v_{17} \tag{46}$$

7.3 Species E2F1

Name E2F1

Notes dimers of E2F1-6 and DP1,2

Initial concentration $0.1\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in seven reactions (as a reactant in E2F1_degradation and as a product in E2F1_synthesis and as a modifier in pRB_synthesis, E2F1_synthesis, CycD_synthesis, AP1_synthesis, CycE_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E2F1} = v_5 - v_6 \tag{47}$$

7.4 Species CycDi

Name CycD/cdk4,6(i)

Initial concentration $0.1\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in five reactions (as a reactant in CycD_activation, CycD_degradation and as a product in CycD_synthesis, CycD_inibition and as a modifier in CycD_activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CycDi} = v_7 + v_8 - v_9 - v_{10} \tag{48}$$

7.5 Species CycDa

Name CycD/cdk4,6(a)

Initial concentration $0.1\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in five reactions (as a reactant in CycD_inibition, CycD_degradation2 and as a product in CycD_activation and as a modifier in pRB_phosphorylation, CycD_activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CycDa} = v_9 - v_8 - v_{11} \tag{49}$$

7.6 Species AP1

Name AP1

Notes c-Jun/Fos dimers

Initial concentration $0.1\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in three reactions (as a reactant in Ap1_degradation and as a product in AP1_synthesis and as a modifier in CycD_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AP1} = v_{12} - v_{13} \tag{50}$$

7.7 Species pRBpp

Name pRBpp

Notes diphosphorylated form of pRB

Initial concentration $0.1\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in three reactions (as a reactant in pRBpp_dephosphorylation, pRBpp_degradation and as a product in pRBp_phosphorylation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pRBpp} = v_{14} - v_{15} - v_{16} \tag{51}$$

7.8 Species CycEi

Name CycE/cdk2(i)

Initial concentration $0.1\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in five reactions (as a reactant in CycE_activation, CycE_degradation and as a product in CycE_synthesis, CycE_inibition and as a modifier in CycE_activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CycEi} = v_{18} + v_{20} - v_{19} - v_{21} \tag{52}$$

7.9 Species CycEa

Name CycEa/cdk2(a)

Initial concentration $0.1\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in five reactions (as a reactant in CycE_inibition, CycE_degradation2 and as a product in CycE_activation and as a modifier in pRBp_phosphorylation, CycE_activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CycEa} = v_{19} - v_{20} - v_{22} \tag{53}$$

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