SBML Model Report

Model name: "Heldt2018 - Proliferation-quiescence decision in response to DNA damage"

May 17, 2018

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Frank Stefan Heldt[1] and Matthieu MAIRE[2] at March first 2017 at 11:13 a. m. and last time modified at May 17th 2018 at 4:39 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	30
events	0	constraints	0
reactions	49	function definitions	24
global parameters	56	unit definitions	3
rules	7	initial assignments	0

Model Notes

Heldt2018 - Proliferation-quiescence decisionin response to DNA damage

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This model is described in the article:A comprehensive model for the proliferation-quiescence decision in response to endogenous DNA damage in human cells.Heldt FS, Barr AR, Cooper S, Bakal C, Novk B.Proc. Natl. Acad. Sci. U.S.A. 2018 Feb; :

Abstract:

Human cells that suffer mild DNA damage can enter a reversible state of growth arrest known as quiescence. This decision to temporarily exit the cell cycle is essential to prevent the propagation of mutations, and most cancer cells harbor defects in the underlying control system. Here we present a mechanistic mathematical model to study the proliferation-quiescence decision in nontransformed human cells. We show that two bistable switches, the restriction point (RP) and the G1/S transition, mediate this decision by integrating DNA damage and mitogen signals. In particular, our data suggest that the cyclin-dependent kinase inhibitor p21 (Cip1/Waf1), which is expressed in response to DNA damage, promotes quiescence by blocking positive feedback loops that facilitate G1 progression downstream of serum stimulation. Intriguingly, cells exploit bistability in the RP to convert graded p21 and mitogen signals into an all-or-nothing cell-cycle response. The same mechanism creates a window of opportunity where G1 cells that have passed the RP can revert to quiescence if exposed to DNA damage. We present experimental evidence that cells gradually lose this ability to revert to quiescence as they progress through G1 and that the onset of rapid p21 degradation at the G1/S transition prevents this response altogether, insulating S phase from mild, endogenous DNA damage. Thus, two bistable switches conspire in the early cell cycle to provide both sensitivity and robustness to external stimuli.

This model is hosted on BioModels Database and identified by: MODEL1703030000.

To cite BioModels Database, please use: Chelliah V et al. BioModels: ten-year anniversary. Nucl. Acids Res. 2015, 43(Database issue):D542-8.

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 `volume`

Name volume

Definition ml

2.2 Unit `time`

Name time

Definition 60 s

2.3 Unit `substance`

Name substance

Definition mmol

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	litre	☑	

3.1 Compartment `Cell`

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

Name cell

4 Species

This model contains 30 species. The boundary condition of seven of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 9 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
`Rb`	Retinoblastoma_protein	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`pRb`	Retinoblastoma_protein-_hyperphosphorylated	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`E2f`	E2f_active	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`RbE2f`	Retinoblastoma_protein_E2f_complex-_inactive	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`E1`	Emi1	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`C1`	Cdh1_C_APC_active	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`pC1`	C_Cdh1_APC_phosphorylated_inactive	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`E1C1`	Emi1_C_Cdh1_complex_inactive	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`P21`	P21	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`Ce`	CyclinE_Cdk2_active	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`Ca`	CyclinA_Cdk2	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`CeP21`	CyclinE_Cdk2_P21_complex_inactive	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`CaP21`	CyclinA_Cdk2_P21_complex_inactive	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`aPcna`	Pcna_nuclear_active	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`iPcna`	PCNA_Nuclear_inactive	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`Rc`	Pre_Replication_complex	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`pRc`	Pre_Replication_complex_primed	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$
`aRc`	Pre_Replication_complex_active	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	$\boxminus$	$\boxminus$

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
iRc	Pre_Replication_complex_inactive	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
Dna	Dna	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
P53	P53	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
Dam	Dna_damage	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
Pr	Activity_probe_of_APC_C_Cdh1	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
tRb	Retinoblastoma_protein_total	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	☑
tE2f	E2f_total	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	☑
tE1	Emi1_total	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	☑
tC1	C_Cdh1_APC_total	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	☑
tCe	CyclinE_Cdk2_total	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	☑
tCa	CyclinA_Cdk2_total	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	☑
tP21	P21_total	Cell	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	☑

5 Parameters

This model contains 56 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Cd	Cd		0.650		☑
Skp2	Skp2		1.000		☑
Cdt2	Cdt2		1.000		☑
kSyE2f	kSyE2f		0.030		☑
kSyE2fE2f	kSyE2fE2f		0.040		☑
jSyE2f	jSyE2f		0.200		☑
kAsRbE2f	kAsRbE2f		5.000		☑
kDsRbE2f	kDsRbE2f		0.005		☑
kDeE2f	kDeE2f		0.050		☑
kPhRbCd	kPhRbCd		0.200		☑
kPhRbCe	kPhRbCe		0.300		☑
kPhRbCa	kPhRbCa		0.300		☑
kDpRb	kDpRb		0.050		☑
kSyE1	kSyE1		0.005		☑
kDeE1C1	kDeE1C1		0.005		☑
kDeE1	kDeE1		$5 \cdot 10^{-4}$		☑
kPhC1	kPhC1		0.000		☑
kPhC1Ce	kPhC1Ce		0.010		☑
kPhC1Ca	kPhC1Ca		1.000		☑
kDpC1	kDpC1		0.050		☑
kAsE1C1	kAsE1C1		10.000		☑
kDsE1C1	kDsE1C1		0.010		☑
kSyP21	kSyP21		0.002		☑
kSyP21P53	kSyP21P53		0.008		☑
kDeP21	kDeP21		0.003		☑
kDeP21Cy	kDeP21Cy		0.007		☑
kDeP21aRc	kDeP21aRc		1.000		☑
kSyCe	kSyCe		0.010		☑
kSyCa	kSyCa		0.020		☑
kAsCyP21	kAsCyP21		1.000		☑
kDsCyP21	kDsCyP21		0.050		☑
kDeCe	kDeCe		0.004		☑
kDeCa	kDeCa		0.010		☑
kDeCeCa	kDeCeCa		0.015		☑
kDeCaC1	kDeCaC1		2.000		☑
kImPc	kImPc		0.003		☑

Id	Name	SBO	Value	Unit	Constant
kExPc	kExPc		0.006		☑
kPhRc	kPhRc		0.100		☑
kDpRc	kDpRc		0.050		☑
jCy	jCy		1.800		☑
n	n		6.000		☑
kAsRcPc	kAsRcPc		0.010		☑
kDsRcPc	kDsRcPc		0.001		☑
kAsPcP21	kAsPcP21		100.000		☑
kDsPcP21	kDsPcP21		0.010		☑
kSyDna	kSyDna		0.009		☑
kSyP53	kSyP53		0.050		☑
kDeP53	kDeP53		0.050		☑
jP53	jP53		0.010		☑
kGeDam	kGeDam		0.001		☑
kGeDamArc	kGeDamArc		0.012		☑
kReDam	kReDam		0.001		☑
kReDamP53	kReDamP53		0.005		☑
jDam	jDam		0.500		☑
kSyPr	kSyPr		0.010		☑
kDePr	kDePr		10^{-4}		☑

6 Function definitions

This is an overview of 24 function definitions.

6.1 Function definition Constant_flux__irreversible

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$v \tag{1}$$

6.2 Function definition rPhRb_2

Name rPhRb_2

Arguments [Ca], Cd, [Ce], [RbE2f], kPhRbCa, kPhRbCd, kPhRbCe

Mathematical Expression

$$(\mathrm{kPhRbCd} \cdot \mathrm{Cd} + \mathrm{kPhRbCe} \cdot [\mathrm{Ce}] + \mathrm{kPhRbCa} \cdot [\mathrm{Ca}]) \cdot [\mathrm{RbE2f}] \tag{2}$$

6.3 Function definition rSyE2f_1

Name rSyE2f_1

Arguments [E2f], jSyE2f, kSyE2f, kSyE2fE2f

Mathematical Expression

$$\mathrm{kSyE2f} + \frac{\mathrm{kSyE2fE2f} \cdot [\mathrm{E2f}]}{\mathrm{jSyE2f} + [\mathrm{E2f}]} \tag{3}$$

6.4 Function definition rDeP21_1

Name rDeP21_1

Arguments [Ca], Cdt2, [Ce], [CeP21], Skp2, [aRc], kDeP21, kDeP21Cy, kDeP21aRc

Mathematical Expression

$$(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot ([\mathrm{Ce}] + [\mathrm{Ca}]) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]) \cdot [\mathrm{CeP21}] \tag{4}$$

6.5 Function definition rDeP53_1

Name rDeP53_1

Arguments [Dam], [P53], jP53, kDeP53

Mathematical Expression

$$\frac{\mathrm{kDeP53}}{\mathrm{jP53} + [\mathrm{Dam}]} \cdot [\mathrm{P53}] \tag{5}$$

6.6 Function definition rDeCa_2

Name rDeCa_2

Arguments [C1], [CaP21], kDeCa, kDeCaC1

Mathematical Expression

$$(\mathrm{kDeCa} + \mathrm{kDeCaC1} \cdot [\mathrm{C1}]) \cdot [\mathrm{CaP21}] \tag{6}$$

6.7 Function definition rDeP21_5

Name rDeP21_5

Arguments [Ca], Cdt2, [Ce], Skp2, [aRc], [iRc], kDeP21, kDeP21Cy, kDeP21aRc

Mathematical Expression

$$(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot ([\mathrm{Ce}] + [\mathrm{Ca}]) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]) \cdot [\mathrm{iRc}] \tag{7}$$

6.8 Function definition rPhRb_1

Name rPhRb_1

Arguments [Ca], Cd, [Ce], [Rb], kPhRbCa, kPhRbCd, kPhRbCe

Mathematical Expression

$$(\mathrm{kPhRbCd} \cdot \mathrm{Cd} + \mathrm{kPhRbCe} \cdot [\mathrm{Ce}] + \mathrm{kPhRbCa} \cdot [\mathrm{Ca}]) \cdot [\mathrm{Rb}] \tag{8}$$

6.9 Function definition rSyP21_1

Name rSyP21_1

Arguments [P53], kSyP21, kSyP21P53

Mathematical Expression

$$\mathrm{kSyP21} + \mathrm{kSyP21P53} \cdot [\mathrm{P53}] \tag{9}$$

6.10 Function definition rPhC1_1

Name rPhC1_1

Arguments [C1], [Ca], [Ce], kPhC1, kPhC1Ca, kPhC1Ce

Mathematical Expression

$$(\mathrm{kPhC1} + \mathrm{kPhC1Ce} \cdot [\mathrm{Ce}] + \mathrm{kPhC1Ca} \cdot [\mathrm{Ca}]) \cdot [\mathrm{C1}] \tag{10}$$

6.11 Function definition rDeP21_3

Name rDeP21_3

Arguments [Ca], Cdt2, [Ce], [P21], Skp2, [aRc], kDeP21, kDeP21Cy, kDeP21aRc

Mathematical Expression

$$(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot ([\mathrm{Ce}] + [\mathrm{Ca}]) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]) \cdot [\mathrm{P21}] \tag{11}$$

6.12 Function definition rDsRc_3

Name rDsRc_3

Arguments [Dna], [aRc]

Mathematical Expression

$$\begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{aRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{aRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{12}$$

6.13 Function definition rDeCe_2

Name rDeCe_2

Arguments [Ca], [CeP21], kDeCe, kDeCeCa

Mathematical Expression

$$(\mathrm{kDeCe} + \mathrm{kDeCeCa} \cdot [\mathrm{Ca}]) \cdot [\mathrm{CeP21}] \tag{13}$$

6.14 Function definition rDeCe_1

Name rDeCe_1

Arguments [Ca], [Ce], kDeCe, kDeCeCa

Mathematical Expression

$$(\mathrm{kDeCe} + \mathrm{kDeCeCa} \cdot [\mathrm{Ca}]) \cdot [\mathrm{Ce}] \tag{14}$$

6.15 Function definition rReDam_1

Name rReDam_1

Arguments [Dam], [P53], jDam, kReDam, kReDamP53

Mathematical Expression

$$\left(\mathrm{kReDam} + \frac{\mathrm{kReDamP53} \cdot [\mathrm{P53}]}{\mathrm{jDam} + [\mathrm{Dam}]}\right) \cdot [\mathrm{Dam}] \tag{15}$$

6.16 Function definition rPhC1_2

Name rPhC1_2

Arguments [Ca], [Ce], [E1C1], kPhC1, kPhC1Ca, kPhC1Ce

Mathematical Expression

$$(\mathrm{kPhC1} + \mathrm{kPhC1Ce} \cdot [\mathrm{Ce}] + \mathrm{kPhC1Ca} \cdot [\mathrm{Ca}]) \cdot [\mathrm{E1C1}] \tag{16}$$

6.17 Function definition rDeP21_2

Name rDeP21_2

Arguments [Ca], [CaP21], Cdt2, [Ce], Skp2, [aRc], kDeP21, kDeP21Cy, kDeP21aRc

Mathematical Expression

$$(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot ([\mathrm{Ce}] + [\mathrm{Ca}]) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]) \cdot [\mathrm{CaP21}] \tag{17}$$

6.18 Function definition rPhRc_1

Name rPhRc_1

Arguments [Ca], [Ce], [Rc], jCy, kPhRc, n

Mathematical Expression

$$\frac{\mathrm{kPhRc} \cdot ([\mathrm{Ce}] + [\mathrm{Ca}])^{\mathrm{n}}}{\mathrm{jCy}^{\mathrm{n}} + ([\mathrm{Ce}] + [\mathrm{Ca}])^{\mathrm{n}}} \cdot [\mathrm{Rc}] \tag{18}$$

6.19 Function definition rDeCa_1

Name rDeCa_1

Arguments [C1], [Ca], kDeCa, kDeCaC1

Mathematical Expression

$$(\mathrm{kDeCa} + \mathrm{kDeCaC1} \cdot [\mathrm{C1}]) \cdot [\mathrm{Ca}] \tag{19}$$

6.20 Function definition rDsRc_4

Name rDsRc_4

Arguments [Dna], [iRc]

Mathematical Expression

$$\begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{iRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{iRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{20}$$

6.21 Function definition rDeP21_4

Name rDeP21_4

Arguments [Ca], Cdt2, [Ce], Skp2, [aRc], [iPcna], kDeP21, kDeP21Cy, kDeP21aRc

Mathematical Expression

$$(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot ([\mathrm{Ce}] + [\mathrm{Ca}]) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]) \cdot [\mathrm{iPcna}] \tag{21}$$

6.22 Function definition rDsRc_1

Name rDsRc_1

Arguments [Dna], [Rc]

Mathematical Expression

$$\begin{cases} 0 & \text{if } [\text{Dna}] < 1 \\ \begin{cases} 1 \cdot [\text{Rc}] & \text{if } [\text{Dna}] > 1 \\ 0.5 \cdot [\text{Rc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{22}$$

6.23 Function definition rDePr_1

Name rDePr_1

Arguments [C1], [Pr], kDeCaC1, kDePr

Mathematical Expression

$$(\text{kDePr} + \text{kDeCaC1} \cdot [\text{C1}]) \cdot [\text{Pr}] \tag{23}$$

6.24 Function definition rDsRc_2

Name rDsRc_2

Arguments [Dna], [pRc]

Mathematical Expression

$$\begin{cases} 0 & \text{if } [\text{Dna}] < 1 \\ \begin{cases} 1 \cdot [\text{pRc}] & \text{if } [\text{Dna}] > 1 \\ 0.5 \cdot [\text{pRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{24}$$

7 Rules

This is an overview of seven rules.

7.1 Rule tRb

Rule tRb is an assignment rule for species tRb:

$$\text{tRb} = [\text{Rb}] + [\text{pRb}] + [\text{RbE2f}] \tag{25}$$

Derived unit $\text{mmol} \cdot \text{ml}^{-1}$

7.2 Rule tE2f

Rule `tE2f` is an assignment rule for species `tE2f`:

$$\mathrm{tE2f} = [\mathrm{E2f}] + [\mathrm{RbE2f}] \tag{26}$$

Derived unit $\mathrm{mmol} \cdot \mathrm{ml}^{-1}$

7.3 Rule tE1

Rule `tE1` is an assignment rule for species `tE1`:

$$\mathrm{tE1} = [\mathrm{E1}] + [\mathrm{E1C1}] \tag{27}$$

Derived unit $\mathrm{mmol} \cdot \mathrm{ml}^{-1}$

7.4 Rule tC1

Rule `tC1` is an assignment rule for species `tC1`:

$$\mathrm{tC1} = [\mathrm{C1}] + [\mathrm{pC1}] + [\mathrm{E1C1}] \tag{28}$$

Derived unit $\mathrm{mmol} \cdot \mathrm{ml}^{-1}$

7.5 Rule tCe

Rule `tCe` is an assignment rule for species `tCe`:

$$\mathrm{tCe} = [\mathrm{Ce}] + [\mathrm{CeP21}] \tag{29}$$

Derived unit $\mathrm{mmol} \cdot \mathrm{ml}^{-1}$

7.6 Rule tCa

Rule `tCa` is an assignment rule for species `tCa`:

$$\mathrm{tCa} = [\mathrm{Ca}] + [\mathrm{CaP21}] \tag{30}$$

Derived unit $\mathrm{mmol} \cdot \mathrm{ml}^{-1}$

7.7 Rule tP21

Rule `tP21` is an assignment rule for species `tP21`:

$$\mathrm{tP21} = [\mathrm{P21}] + [\mathrm{CeP21}] + [\mathrm{CaP21}] + [\mathrm{iPcna}] + [\mathrm{iRc}] \tag{31}$$

Derived unit $\mathrm{mmol} \cdot \mathrm{ml}^{-1}$

8 Reactions

This model contains 49 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	`Phosphorylation_of_Rb`	Phosphorylation of Rb	$\text{Rb} \xrightarrow{\text{Ce, Ca}} \text{pRb}$	
2	`Phosphorylation_Rb_in_Rb_E2F_complexes`	Phosphorylation Rb in Rb:E2F complexes	$\text{RbE2f} \xrightarrow{\text{Ce, Ca}} \text{pRb} + \text{E2f}$	
3	`Dephosphorylation_of_Rb`	Dephosphorylation of Rb	$\text{pRb} \longrightarrow \text{Rb}$	
4	`Synthesis_of_E2F`	Synthesis of E2F	$\emptyset \xrightarrow{\text{E2f}} \text{E2f}$	
5	`Degradation_of_E2F`	Degradation of E2F	$\text{E2f} \longrightarrow \emptyset$	
6	`Degradation_of_E2F_in_Rb_E2F_complexes`	Degradation of E2F in Rb:E2F complexes	$\text{RbE2f} \longrightarrow \text{Rb}$	
7	`Association_dissociation_of_Rb_and_E2F`	Association/dissociation of Rb and E2F	$\text{Rb} + \text{E2f} \rightleftharpoons \text{RbE2f}$	
8	`Synthesis_of_p21`	Synthesis of p21	$\emptyset \xrightarrow{\text{P53}} \text{P21}$	
9	`Synthesis_of_CycE`	Synthesis of CycE	$\text{E2f} \longrightarrow \text{E2f} + \text{Ce}$	

№	Id	Name	Reaction Equation	SBO
10	Synthesis_of_CycA	Synthesis of CycA	$\mathrm{E2f} \longrightarrow \mathrm{E2f} + \mathrm{Ca}$	
11	Association_dissociation_of_CycE_Cdk2_and_p21	Association/dissociation of CycE:Cdk2 and p21	$\mathrm{Ce} + \mathrm{P21} \rightleftharpoons \mathrm{CeP21}$	
12	Association_dissociation_of_CycA_Cdk2_and_p21	Association/dissociation of CycA:Cdk2 and p21	$\mathrm{Ca} + \mathrm{P21} \rightleftharpoons \mathrm{CaP21}$	
13	Degradation_of_p21_in_CycE_Cdk2_p21_complexes	Degradation of p21 in CycE:Cdk2:p21 complexes	$\mathrm{CeP21} \xrightarrow{\mathrm{Ce,\ Ca,\ aRc}} \mathrm{Ce}$	
14	Degradation_of_p21_in_CycA_Cdk2_p21_complexes	Degradation of p21 in CycA:Cdk2:p21 complexes	$\mathrm{CaP21} \xrightarrow{\mathrm{Ce,\ Ca,\ aRc}} \mathrm{Ca}$	
15	Degradation_of_CycE_in_CycE_Cdk2_complexes	Degradation of CycE in CycE:Cdk2 complexes	$\mathrm{Ce} \xrightarrow{\mathrm{Ca}} \emptyset$	
16	Degradation_of_CycE_in_CycE_Cdk2_p21_complexes	Degradation of CycE in CycE:Cdk2:p21 complexes	$\mathrm{CeP21} \xrightarrow{\mathrm{Ca}} \mathrm{P21}$	

№	Id	Name	Reaction Equation	SBO
17	Degradation_of_CycA_in_CycA_Cdk2_complexes	Degradation of CycA in CycA:Cdk2 complexes	$\mathrm{Ca} \xrightarrow{\mathrm{C1}} \emptyset$	
18	Degradation_of_CycA_in_CycA_Cdk2_p21_complexes	Degradation of CycA in CycA:Cdk2:p21 complexes	$\mathrm{CaP21} \xrightarrow{\mathrm{C1}} \mathrm{P21}$	
19	Degradation_of_free_p21	Degradation of free p21	$\mathrm{P21} \xrightarrow{\mathrm{Ce,\ Ca,\ aRc}} \emptyset$	
20	Synthesis_of_Emi1	Synthesis of Emi1	$\mathrm{E2f} \longrightarrow \mathrm{E2f} + \mathrm{E1}$	
21	Degradation_of_Emi1	Degradation of Emi1	$\mathrm{E1} \longrightarrow \emptyset$	
22	Association_dissociation_of_Emi1_APC_C_Cdh1_complexes	Association/dissociation of Emi1:APC/C-Ĉdh1 complexes	$\mathrm{E1} + \mathrm{C1} \rightleftharpoons \mathrm{E1C1}$	
23	Degradation_of_Emi1_in_Emi1_APC_C_Cdh1_complexes	Degradation of Emi1 in Emi1:APC/CĈdh1 complexes	$\mathrm{E1C1} \longrightarrow \mathrm{C1}$	
24	Phosphorylation_of_free_APC_C_Cdh1	Phosphorylation of free APC/CĈdh1	$\mathrm{C1} \xrightarrow{\mathrm{Ce,\ Ca}} \mathrm{pC1}$	

№	Id	Name	Reaction Equation	SBO
25	Phosphorylation_of_APC_C_Cdh1_in_Emi1_APC_C_Cdh1_complexes	Phosphorylation of APC/CĈdh1 in Emi1:APC/CĈdh1 complexes	$\mathrm{E1C1} \xrightarrow{\mathrm{Ce,\ Ca}} \mathrm{E1} + \mathrm{pC1}$	
26	Dephosphorylation_of_APC_C_Cdh1	Dephosphorylation of APC/CĈdh1	$\mathrm{pC1} \longrightarrow \mathrm{C1}$	
27	Nuclear_import_of_active_PCNA	Nuclear import of active PCNA	$\emptyset \longrightarrow \mathrm{aPcna}$	
28	Nuclear_export_of_active_PCNA	Nuclear export of active PCNA	$\mathrm{aPcna} \longrightarrow \emptyset$	
29	Nuclear_export_of_inactive_PCNA	Nuclear export of inactive PCNA	$\mathrm{iPcna} \longrightarrow \mathrm{P21}$	
30	Association_dissociation_of_PCNA_and_p21	Association/dissociation of PCNA and p21	$\mathrm{aPcna} + \mathrm{P21} \rightleftharpoons \mathrm{iPcna}$	
31	Degradation_of_p21_in_PCNA_p21_complexes	Degradation of p21 in PCNA:p21 complexes	$\mathrm{iPcna} \xrightarrow{\mathrm{Ce,\ Ca,\ aRc}} \mathrm{aPcna}$	
32	Association_dissociation_of_active_PCNA_and_replication_complexes	Association/dissociation of active PCNA and replication complexes	$\mathrm{aPcna} + \mathrm{pRc} \rightleftharpoons \mathrm{aRc}$	

№	Id	Name	Reaction Equation	SBO
33	Association-_dissociation-_of_inactive-_PCNA_and-_replication-_complexes	Association/dissociation of inactive PCNA and replication complexes	$\mathrm{iPcna} + \mathrm{pRc} \rightleftharpoons \mathrm{iRc}$	
34	Phosphorylation-_priming_of-_replication-_complexes	Phosphorylation/priming of replication complexes	$\mathrm{Rc} \xrightarrow{\mathrm{Ce},\,\mathrm{Ca}} \mathrm{pRc}$	
35	Dephosphorylation-_of-_replication-_complexes	Dephosphorylation of replication complexes	$\mathrm{pRc} \longrightarrow \mathrm{Rc}$	
36	Association-_dissociation-_of_p21_and-_replication-_complexes	Association/dissociation of p21 and replication complexes	$\mathrm{aRc} + \mathrm{P21} \rightleftharpoons \mathrm{iRc}$	
37	Degradation-_of_p21_in-_inactive-_replication-_complexes	Degradation of p21 in inactive replication complexes	$\mathrm{iRc} \xrightarrow{\mathrm{Ce},\,\mathrm{Ca},\,\mathrm{aRc}} \mathrm{aRc}$	
38	Dissassembly-_of_RC	Dissassembly of RC	$\mathrm{Rc} \xrightarrow{\mathrm{Dna}} \emptyset$	

№	Id	Name	Reaction Equation	SBO
39	`Dissassembly-_of_pRC`	Dissassembly of pRC	$\mathrm{pRc} \xrightarrow{\mathrm{Dna}} \emptyset$	
40	`Dissassembly-_of_aRC`	Dissassembly of aRC	$\mathrm{aRc} \xrightarrow{\mathrm{Dna}} \mathrm{aPcna}$	
41	`Dissassembly-_of_iRC`	Dissassembly of iRC	$\mathrm{iRc} \xrightarrow{\mathrm{Dna}} \mathrm{iPcna}$	
42	`Synthesis_of-_DNA`	Synthesis of DNA	$\mathrm{aRc} \longrightarrow \mathrm{aRc} + \mathrm{Dna}$	
43	`Synthesis_of-_p53`	Synthesis of p53	$\emptyset \longrightarrow \mathrm{P53}$	
44	`Degradation_of-_p53`	Degradation of p53	$\mathrm{P53} \xrightarrow{\mathrm{Dam}} \emptyset$	
45	`Induction_of-_DNA_damage`	Induction of DNA damage	$\emptyset \longrightarrow \mathrm{Dam}$	
46	`Induction_of-_DNA_damage_by-_replication`	Induction of DNA damage by replication	$\mathrm{aRc} \longrightarrow \mathrm{aRc} + \mathrm{Dam}$	
47	`Synthesis_of-_APC_C_Cdh1-_activity_probe`	Synthesis of APC/CĈdh1 activity probe	$\emptyset \longrightarrow \mathrm{Pr}$	
48	`Degradation-_of_APC_C_Cdh1-_activity_probe`	Degradation of APC/CĈdh1 activity probe	$\mathrm{Pr} \xrightarrow{\mathrm{C1}} \emptyset$	
49	`Repair_of_DNA-_damage`	Repair of DNA damage	$\mathrm{Dam} \xrightarrow{\mathrm{P53}} \emptyset$	

8.1 Reaction `Phosphorylation_of_Rb`

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

Name Phosphorylation of Rb

Reaction equation

$$\mathrm{Rb} \xrightarrow{\mathrm{Ce},\,\mathrm{Ca}} \mathrm{pRb} \tag{32}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
`Rb`	Retinoblastoma_protein	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
`Ce`	CyclinE_Cdk2_active	
`Ca`	CyclinA_Cdk2	

Product

Table 8: Properties of each product.

Id	Name	SBO
`pRb`	Retinoblastoma_protein_hyperphosphorylated	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rPhRb\_1}\left([\mathrm{Ca}], \mathrm{Cd}, [\mathrm{Ce}], [\mathrm{Rb}], \mathrm{kPhRbCa}, \mathrm{kPhRbCd}, \mathrm{kPhRbCe}\right) \tag{33}$$

$$\begin{aligned} &\mathrm{rPhRb\_1}\left([\mathrm{Ca}], \mathrm{Cd}, [\mathrm{Ce}], [\mathrm{Rb}], \mathrm{kPhRbCa}, \mathrm{kPhRbCd}, \mathrm{kPhRbCe}\right) \\ &\quad = \left(\mathrm{kPhRbCd} \cdot \mathrm{Cd} + \mathrm{kPhRbCe} \cdot [\mathrm{Ce}] + \mathrm{kPhRbCa} \cdot [\mathrm{Ca}]\right) \cdot [\mathrm{Rb}] \end{aligned} \tag{34}$$

$$\begin{aligned} &\mathrm{rPhRb\_1}\left([\mathrm{Ca}], \mathrm{Cd}, [\mathrm{Ce}], [\mathrm{Rb}], \mathrm{kPhRbCa}, \mathrm{kPhRbCd}, \mathrm{kPhRbCe}\right) \\ &\quad = \left(\mathrm{kPhRbCd} \cdot \mathrm{Cd} + \mathrm{kPhRbCe} \cdot [\mathrm{Ce}] + \mathrm{kPhRbCa} \cdot [\mathrm{Ca}]\right) \cdot [\mathrm{Rb}] \end{aligned} \tag{35}$$

8.2 Reaction `Phosphorylation_Rb_in_Rb_E2F_complexes`

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

Name Phosphorylation Rb in Rb:E2F complexes

Reaction equation

$$\mathrm{RbE2f} \xrightarrow{\mathrm{Ce,\ Ca}} \mathrm{pRb} + \mathrm{E2f} \tag{36}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
`RbE2f`	Retinoblastoma_protein_E2f_complex_inactive	

Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
`Ce`	CyclinE_Cdk2_active	
`Ca`	CyclinA_Cdk2	

Products

Table 11: Properties of each product.

Id	Name	SBO
`pRb`	Retinoblastoma_protein_hyperphosphorylated	
`E2f`	E2f_active	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rPhRb\_2}\left([\mathrm{Ca}], \mathrm{Cd}, [\mathrm{Ce}], [\mathrm{RbE2f}], \mathrm{kPhRbCa}, \mathrm{kPhRbCd}, \mathrm{kPhRbCe}\right) \tag{37}$$

$$\begin{aligned} &\mathrm{rPhRb\_2}\left([\mathrm{Ca}], \mathrm{Cd}, [\mathrm{Ce}], [\mathrm{RbE2f}], \mathrm{kPhRbCa}, \mathrm{kPhRbCd}, \mathrm{kPhRbCe}\right) \\ &\quad = \left(\mathrm{kPhRbCd} \cdot \mathrm{Cd} + \mathrm{kPhRbCe} \cdot [\mathrm{Ce}] + \mathrm{kPhRbCa} \cdot [\mathrm{Ca}]\right) \cdot [\mathrm{RbE2f}] \end{aligned} \tag{38}$$

$$\begin{aligned} &\mathrm{rPhRb\_2}\left([\mathrm{Ca}], \mathrm{Cd}, [\mathrm{Ce}], [\mathrm{RbE2f}], \mathrm{kPhRbCa}, \mathrm{kPhRbCd}, \mathrm{kPhRbCe}\right) \\ &\quad = \left(\mathrm{kPhRbCd} \cdot \mathrm{Cd} + \mathrm{kPhRbCe} \cdot [\mathrm{Ce}] + \mathrm{kPhRbCa} \cdot [\mathrm{Ca}]\right) \cdot [\mathrm{RbE2f}] \end{aligned} \tag{39}$$

8.3 Reaction `Dephosphorylation_of_Rb`

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

Name Dephosphorylation of Rb

Reaction equation

$$\mathrm{pRb} \longrightarrow \mathrm{Rb} \tag{40}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
`pRb`	Retinoblastoma_protein_hyperphosphorylated	

Product

Table 13: Properties of each product.

Id	Name	SBO
`Rb`	Retinoblastoma_protein	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{kDpRb} \cdot [\mathrm{pRb}] \tag{41}$$

8.4 Reaction `Synthesis_of_E2F`

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

Name Synthesis of E2F

Reaction equation

$$\emptyset \xrightarrow{\mathrm{E2f}} \mathrm{E2f} \tag{42}$$

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
`E2f`	E2f_active	

Product

Table 15: Properties of each product.

Id	Name	SBO
`E2f`	E2f_active	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{rSyE2f\_1}([\mathrm{E2f}], \mathrm{jSyE2f}, \mathrm{kSyE2f}, \mathrm{kSyE2fE2f}) \tag{43}$$

$$\mathrm{rSyE2f\_1}([\mathrm{E2f}], \mathrm{jSyE2f}, \mathrm{kSyE2f}, \mathrm{kSyE2fE2f}) = \mathrm{kSyE2f} + \frac{\mathrm{kSyE2fE2f} \cdot [\mathrm{E2f}]}{\mathrm{jSyE2f} + [\mathrm{E2f}]} \tag{44}$$

$$\mathrm{rSyE2f\_1}([\mathrm{E2f}], \mathrm{jSyE2f}, \mathrm{kSyE2f}, \mathrm{kSyE2fE2f}) = \mathrm{kSyE2f} + \frac{\mathrm{kSyE2fE2f} \cdot [\mathrm{E2f}]}{\mathrm{jSyE2f} + [\mathrm{E2f}]} \tag{45}$$

8.5 Reaction `Degradation_of_E2F`

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

Name Degradation of E2F

Reaction equation

$$\mathrm{E2f} \longrightarrow \emptyset \tag{46}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
E2f	E2f_active	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kDeE2f} \cdot [\mathrm{E2f}] \tag{47}$$

8.6 Reaction Degradation_of_E2F_in_Rb_E2F_complexes

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

Name Degradation of E2F in Rb:E2F complexes

Reaction equation

$$\mathrm{RbE2f} \longrightarrow \mathrm{Rb} \tag{48}$$

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
RbE2f	Retinoblastoma_protein_E2f_complex_inactive	

Product

Table 18: Properties of each product.

Id	Name	SBO
Rb	Retinoblastoma_protein	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{kDeE2f} \cdot [\mathrm{RbE2f}] \quad (49)$$

8.7 Reaction `Association_dissociation_of_Rb_and_E2F`

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

Name Association/dissociation of Rb and E2F

Reaction equation

$$\mathrm{Rb} + \mathrm{E2f} \rightleftharpoons \mathrm{RbE2f} \quad (50)$$

Reactants

Table 19: Properties of each reactant.

Id	Name	SBO
`Rb`	Retinoblastoma_protein	
`E2f`	E2f_active	

Product

Table 20: Properties of each product.

Id	Name	SBO
`RbE2f`	Retinoblastoma_protein_E2f_complex_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\,(\mathrm{Cell}) \cdot (\mathrm{kAsRbE2f} \cdot [\mathrm{Rb}] \cdot [\mathrm{E2f}] - \mathrm{kDsRbE2f} \cdot [\mathrm{RbE2f}]) \quad (51)$$

8.8 Reaction `Synthesis_of_p21`

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

Name Synthesis of p21

Reaction equation

$$\emptyset \xrightarrow{\text{P53}} \text{P21} \tag{52}$$

Modifier

Table 21: Properties of each modifier.

Id	Name	SBO
P53	P53	

Product

Table 22: Properties of each product.

Id	Name	SBO
P21	P21	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{vol}\,(\text{Cell}) \cdot \text{rSyP21\_1}\,([\text{P53}], \text{kSyP21}, \text{kSyP21P53}) \tag{53}$$

$$\text{rSyP21\_1}\,([\text{P53}], \text{kSyP21}, \text{kSyP21P53}) = \text{kSyP21} + \text{kSyP21P53} \cdot [\text{P53}] \tag{54}$$

$$\text{rSyP21\_1}\,([\text{P53}], \text{kSyP21}, \text{kSyP21P53}) = \text{kSyP21} + \text{kSyP21P53} \cdot [\text{P53}] \tag{55}$$

8.9 Reaction Synthesis_of_CycE

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

Name Synthesis of CycE

Reaction equation

$$\text{E2f} \longrightarrow \text{E2f} + \text{Ce} \tag{56}$$

Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
E2f	E2f_active	

Products

Table 24: Properties of each product.

Id	Name	SBO
E2f	E2f_active	
Ce	CyclinE_Cdk2_active	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kSyCe} \cdot [\mathrm{E2f}] \tag{57}$$

8.10 Reaction Synthesis_of_CycA

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

Name Synthesis of CycA

Reaction equation

$$\mathrm{E2f} \longrightarrow \mathrm{E2f} + \mathrm{Ca} \tag{58}$$

Reactant

Table 25: Properties of each reactant.

Id	Name	SBO
E2f	E2f_active	

Products

Table 26: Properties of each product.

Id	Name	SBO
E2f	E2f_active	
Ca	CyclinA_Cdk2	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{kSyCa} \cdot [\mathrm{E2f}] \tag{59}$$

8.11 Reaction Association_dissociation_of_CycE_Cdk2_and_p21

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

Name Association/dissociation of CycE:Cdk2 and p21

Reaction equation

$$\mathrm{Ce} + \mathrm{P21} \rightleftharpoons \mathrm{CeP21} \tag{60}$$

Reactants

Table 27: Properties of each reactant.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	
P21	P21	

Product

Table 28: Properties of each product.

Id	Name	SBO
CeP21	CyclinE_Cdk2_P21_complex_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\,(\mathrm{Cell}) \cdot (\mathrm{kAsCyP21} \cdot [\mathrm{Ce}] \cdot [\mathrm{P21}] - \mathrm{kDsCyP21} \cdot [\mathrm{CeP21}]) \quad (61)$$

8.12 Reaction Association_dissociation_of_CycA_Cdk2_and_p21

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

Name Association/dissociation of CycA:Cdk2 and p21

Reaction equation

$$\mathrm{Ca} + \mathrm{P21} \rightleftharpoons \mathrm{CaP21} \quad (62)$$

Reactants

Table 29: Properties of each reactant.

Id	Name	SBO
Ca	CyclinA_Cdk2	
P21	P21	

Product

Table 30: Properties of each product.

Id	Name	SBO
CaP21	CyclinA_Cdk2_P21_complex_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\,(\mathrm{Cell}) \cdot (\mathrm{kAsCyP21} \cdot [\mathrm{Ca}] \cdot [\mathrm{P21}] - \mathrm{kDsCyP21} \cdot [\mathrm{CaP21}]) \quad (63)$$

8.13 Reaction Degradation_of_p21_in_CycE_Cdk2_p21_complexes

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

Name Degradation of p21 in CycE:Cdk2:p21 complexes

Reaction equation

$$\mathrm{CeP21} \xrightarrow{\mathrm{Ce},\ \mathrm{Ca},\ \mathrm{aRc}} \mathrm{Ce} \quad (64)$$

Reactant

Table 31: Properties of each reactant.

Id	Name	SBO
CeP21	CyclinE_Cdk2_P21_complex_inactive	

Modifiers

Table 32: Properties of each modifier.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	
Ca	CyclinA_Cdk2	
aRc	Pre_Replication_complex_active	

Product

Table 33: Properties of each product.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{rDeP21\_1}([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], [\mathrm{CeP21}], \mathrm{Skp2}, [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}) \tag{65}$$

$$\begin{aligned} &\mathrm{rDeP21\_1}([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], [\mathrm{CeP21}], \mathrm{Skp2}, [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}) \\ &= (\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot ([\mathrm{Ce}] + [\mathrm{Ca}]) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]) \cdot [\mathrm{CeP21}] \end{aligned} \tag{66}$$

$$\begin{aligned} &\mathrm{rDeP21\_1}([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], [\mathrm{CeP21}], \mathrm{Skp2}, [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}) \\ &= (\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot ([\mathrm{Ce}] + [\mathrm{Ca}]) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]) \cdot [\mathrm{CeP21}] \end{aligned} \tag{67}$$

8.14 Reaction `Degradation_of_p21_in_CycA_Cdk2_p21_complexes`

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

Name Degradation of p21 in CycA:Cdk2:p21 complexes

Reaction equation

$$\mathrm{CaP21} \xrightarrow{\mathrm{Ce},\ \mathrm{Ca},\ \mathrm{aRc}} \mathrm{Ca} \tag{68}$$

Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
CaP21	CyclinA_Cdk2_P21_complex_inactive	

Modifiers

Table 35: Properties of each modifier.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	
Ca	CyclinA_Cdk2	
aRc	Pre_Replication_complex_active	

Product

Table 36: Properties of each product.

Id	Name	SBO
Ca	CyclinA_Cdk2	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDeP21\_2}\left([\mathrm{Ca}], [\mathrm{CaP21}], \mathrm{Cdt2}, [\mathrm{Ce}], \mathrm{Skp2}, [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \tag{69}$$

$$\begin{aligned} &\mathrm{rDeP21\_2}\left([\mathrm{Ca}], [\mathrm{CaP21}], \mathrm{Cdt2}, [\mathrm{Ce}], \mathrm{Skp2}, [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \\ &\quad = \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot \left([\mathrm{Ce}] + [\mathrm{Ca}]\right) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{CaP21}] \end{aligned} \tag{70}$$

$$\begin{aligned} &\mathrm{rDeP21\_2}\left([\mathrm{Ca}], [\mathrm{CaP21}], \mathrm{Cdt2}, [\mathrm{Ce}], \mathrm{Skp2}, [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \\ &\quad = \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot \left([\mathrm{Ce}] + [\mathrm{Ca}]\right) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{CaP21}] \end{aligned} \tag{71}$$

8.15 Reaction Degradation_of_CycE_in_CycE_Cdk2_complexes

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

Name Degradation of CycE in CycE:Cdk2 complexes

Reaction equation

$$\mathrm{Ce} \xrightarrow{\mathrm{Ca}} \emptyset \tag{72}$$

Reactant

Table 37: Properties of each reactant.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	

Modifier

Table 38: Properties of each modifier.

Id	Name	SBO
Ca	CyclinA_Cdk2	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDeCe\_1}\left([\mathrm{Ca}], [\mathrm{Ce}], \mathrm{kDeCe}, \mathrm{kDeCeCa}\right) \tag{73}$$

$$\mathrm{rDeCe\_1}\left([\mathrm{Ca}], [\mathrm{Ce}], \mathrm{kDeCe}, \mathrm{kDeCeCa}\right) = \left(\mathrm{kDeCe} + \mathrm{kDeCeCa} \cdot [\mathrm{Ca}]\right) \cdot [\mathrm{Ce}] \tag{74}$$

$$\mathrm{rDeCe\_1}\left([\mathrm{Ca}], [\mathrm{Ce}], \mathrm{kDeCe}, \mathrm{kDeCeCa}\right) = \left(\mathrm{kDeCe} + \mathrm{kDeCeCa} \cdot [\mathrm{Ca}]\right) \cdot [\mathrm{Ce}] \tag{75}$$

8.16 Reaction Degradation_of_CycE_in_CycE_Cdk2_p21_complexes

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

Name Degradation of CycE in CycE:Cdk2:p21 complexes

Reaction equation

$$\mathrm{CeP21} \xrightarrow{\mathrm{Ca}} \mathrm{P21} \tag{76}$$

Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
CeP21	CyclinE_Cdk2_P21_complex_inactive	

Modifier

Table 40: Properties of each modifier.

Id	Name	SBO
Ca	CyclinA_Cdk2	

Product

Table 41: Properties of each product.

Id	Name	SBO
P21	P21	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{rDeCe\_2}([\mathrm{Ca}], [\mathrm{CeP21}], \mathrm{kDeCe}, \mathrm{kDeCeCa}) \tag{77}$$

$$\mathrm{rDeCe\_2}([\mathrm{Ca}], [\mathrm{CeP21}], \mathrm{kDeCe}, \mathrm{kDeCeCa}) = (\mathrm{kDeCe} + \mathrm{kDeCeCa} \cdot [\mathrm{Ca}]) \cdot [\mathrm{CeP21}] \tag{78}$$

$$\mathrm{rDeCe\_2}([\mathrm{Ca}], [\mathrm{CeP21}], \mathrm{kDeCe}, \mathrm{kDeCeCa}) = (\mathrm{kDeCe} + \mathrm{kDeCeCa} \cdot [\mathrm{Ca}]) \cdot [\mathrm{CeP21}] \tag{79}$$

8.17 Reaction Degradation_of_CycA_in_CycA_Cdk2_complexes

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

Name Degradation of CycA in CycA:Cdk2 complexes

Reaction equation

$$\mathrm{Ca} \xrightarrow{\mathrm{C1}} \emptyset \tag{80}$$

Reactant

Table 42: Properties of each reactant.

Id	Name	SBO
Ca	CyclinA_Cdk2	

Modifier

Table 43: Properties of each modifier.

Id	Name	SBO
C1	Cdh1_C_APC_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDeCa\_1}\left([\mathrm{C1}], [\mathrm{Ca}], \mathrm{kDeCa}, \mathrm{kDeCaC1}\right) \tag{81}$$

$$\mathrm{rDeCa\_1}\left([\mathrm{C1}], [\mathrm{Ca}], \mathrm{kDeCa}, \mathrm{kDeCaC1}\right) = \left(\mathrm{kDeCa} + \mathrm{kDeCaC1} \cdot [\mathrm{C1}]\right) \cdot [\mathrm{Ca}] \tag{82}$$

$$\mathrm{rDeCa\_1}\left([\mathrm{C1}], [\mathrm{Ca}], \mathrm{kDeCa}, \mathrm{kDeCaC1}\right) = \left(\mathrm{kDeCa} + \mathrm{kDeCaC1} \cdot [\mathrm{C1}]\right) \cdot [\mathrm{Ca}] \tag{83}$$

8.18 Reaction Degradation_of_CycA_in_CycA_Cdk2_p21_complexes

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

Name Degradation of CycA in CycA:Cdk2:p21 complexes

Reaction equation

$$\mathrm{CaP21} \xrightarrow{\mathrm{C1}} \mathrm{P21} \tag{84}$$

Reactant

Table 44: Properties of each reactant.

Id	Name	SBO
CaP21	CyclinA_Cdk2_P21_complex_inactive	

Modifier

Table 45: Properties of each modifier.

Id	Name	SBO
C1	Cdh1_C_APC_active	

Product

Table 46: Properties of each product.

Id	Name	SBO
P21	P21	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{rDeCa\_2}([\mathrm{C1}], [\mathrm{CaP21}], \mathrm{kDeCa}, \mathrm{kDeCaC1}) \tag{85}$$

$$\mathrm{rDeCa\_2}([\mathrm{C1}], [\mathrm{CaP21}], \mathrm{kDeCa}, \mathrm{kDeCaC1}) = (\mathrm{kDeCa} + \mathrm{kDeCaC1} \cdot [\mathrm{C1}]) \cdot [\mathrm{CaP21}] \tag{86}$$

$$\mathrm{rDeCa\_2}([\mathrm{C1}], [\mathrm{CaP21}], \mathrm{kDeCa}, \mathrm{kDeCaC1}) = (\mathrm{kDeCa} + \mathrm{kDeCaC1} \cdot [\mathrm{C1}]) \cdot [\mathrm{CaP21}] \tag{87}$$

8.19 Reaction Degradation_of_free_p21

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

Name Degradation of free p21

Reaction equation

$$\mathrm{P21} \xrightarrow{\mathrm{Ce,\ Ca,\ aRc}} \emptyset \tag{88}$$

Reactant

Table 47: Properties of each reactant.

Id	Name	SBO
P21	P21	

Modifiers

Table 48: Properties of each modifier.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	
Ca	CyclinA_Cdk2	
aRc	Pre_Replication_complex_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDeP21\_3}\left([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], [\mathrm{P21}], \mathrm{Skp2}, [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \tag{89}$$

$$\begin{aligned}&\mathrm{rDeP21\_3}\left([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], [\mathrm{P21}], \mathrm{Skp2}, [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right)\\ &= \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot \left([\mathrm{Ce}] + [\mathrm{Ca}]\right) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{P21}]\end{aligned} \tag{90}$$

$$\begin{aligned}&\mathrm{rDeP21\_3}\left([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], [\mathrm{P21}], \mathrm{Skp2}, [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right)\\ &= \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot \left([\mathrm{Ce}] + [\mathrm{Ca}]\right) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{P21}]\end{aligned} \tag{91}$$

8.20 Reaction Synthesis_of_Emi1

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

Name Synthesis of Emi1

Reaction equation

$$\mathrm{E2f} \longrightarrow \mathrm{E2f} + \mathrm{E1} \tag{92}$$

Reactant

Table 49: Properties of each reactant.

Id	Name	SBO
E2f	E2f_active	

Products

Table 50: Properties of each product.

Id	Name	SBO
E2f	E2f_active	
E1	Emi1	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{kSyE1} \cdot [\mathrm{E2f}] \tag{93}$$

8.21 Reaction Degradation_of_Emi1

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

Name Degradation of Emi1

Reaction equation

$$\mathrm{E1} \longrightarrow \emptyset \tag{94}$$

Reactant

Table 51: Properties of each reactant.

Id	Name	SBO
E1	Emi1	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{kDeE1} \cdot [\mathrm{E1}] \tag{95}$$

8.22 Reaction `Association_dissociation_of_Emi1_APC_C_Cdh1_complexes`

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

Name Association/dissociation of Emi1:APC/CĈdh1 complexes

Reaction equation

$$\mathrm{E1} + \mathrm{C1} \rightleftharpoons \mathrm{E1C1} \tag{96}$$

Reactants

Table 52: Properties of each reactant.

Id	Name	SBO
E1	Emi1	
C1	Cdh1_C_APC_active	

Product

Table 53: Properties of each product.

Id	Name	SBO
E1C1	Emi1_C_Cdh1_complex_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \left(\mathrm{kAsE1C1} \cdot [\mathrm{E1}] \cdot [\mathrm{C1}] - \mathrm{kDsE1C1} \cdot [\mathrm{E1C1}]\right) \tag{97}$$

8.23 Reaction `Degradation_of_Emi1_in_Emi1_APC_C_Cdh1_complexes`

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

Name Degradation of Emi1 in Emi1:APC/CĈdh1 complexes

Reaction equation

$$\mathrm{E1C1} \longrightarrow \mathrm{C1} \tag{98}$$

Reactant

Table 54: Properties of each reactant.

Id	Name	SBO
E1C1	Emi1_C_Cdh1_complex_inactive	

Product

Table 55: Properties of each product.

Id	Name	SBO
C1	Cdh1_C_APC_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kDeE1C1} \cdot [\mathrm{E1C1}] \tag{99}$$

8.24 Reaction Phosphorylation_of_free_APC_C_Cdh1

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

Name Phosphorylation of free APC/CĈdh1

Reaction equation

$$\mathrm{C1} \xrightarrow{\mathrm{Ce},\ \mathrm{Ca}} \mathrm{pC1} \tag{100}$$

Reactant

Table 56: Properties of each reactant.

Id	Name	SBO
C1	Cdh1_C_APC_active	

Modifiers

Table 57: Properties of each modifier.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	
Ca	CyclinA_Cdk2	

Product

Table 58: Properties of each product.

Id	Name	SBO
pC1	C_Cdh1_APC_phosphorylated_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{rPhC1\_1}\,([\mathrm{C1}], [\mathrm{Ca}], [\mathrm{Ce}], \mathrm{kPhC1}, \mathrm{kPhC1Ca}, \mathrm{kPhC1Ce}) \tag{101}$$

$$\begin{aligned} &\mathrm{rPhC1\_1}\,([\mathrm{C1}], [\mathrm{Ca}], [\mathrm{Ce}], \mathrm{kPhC1}, \mathrm{kPhC1Ca}, \mathrm{kPhC1Ce}) \\ &\quad = (\mathrm{kPhC1} + \mathrm{kPhC1Ce} \cdot [\mathrm{Ce}] + \mathrm{kPhC1Ca} \cdot [\mathrm{Ca}]) \cdot [\mathrm{C1}] \end{aligned} \tag{102}$$

$$\begin{aligned} &\mathrm{rPhC1\_1}\,([\mathrm{C1}], [\mathrm{Ca}], [\mathrm{Ce}], \mathrm{kPhC1}, \mathrm{kPhC1Ca}, \mathrm{kPhC1Ce}) \\ &\quad = (\mathrm{kPhC1} + \mathrm{kPhC1Ce} \cdot [\mathrm{Ce}] + \mathrm{kPhC1Ca} \cdot [\mathrm{Ca}]) \cdot [\mathrm{C1}] \end{aligned} \tag{103}$$

8.25 Reaction `Phosphorylation_of_APC_C_Cdh1_in_Emi1_APC_C_Cdh1_complexes`

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

Name Phosphorylation of APC/CĈdh1 in Emi1:APC/CĈdh1 complexes

Reaction equation

$$\mathrm{E1C1} \xrightarrow{\mathrm{Ce,\ Ca}} \mathrm{E1} + \mathrm{pC1} \tag{104}$$

Reactant

Table 59: Properties of each reactant.

Id	Name	SBO
E1C1	Emi1_C_Cdh1_complex_inactive	

Modifiers

Table 60: Properties of each modifier.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	
Ca	CyclinA_Cdk2	

Products

Table 61: Properties of each product.

Id	Name	SBO
E1	Emi1	
pC1	C_Cdh1_APC_phosphorylated_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rPhC1\_2}\left([\mathrm{Ca}], [\mathrm{Ce}], [\mathrm{E1C1}], \mathrm{kPhC1}, \mathrm{kPhC1Ca}, \mathrm{kPhC1Ce}\right) \tag{105}$$

$$\begin{aligned} &\mathrm{rPhC1\_2}\left([\mathrm{Ca}], [\mathrm{Ce}], [\mathrm{E1C1}], \mathrm{kPhC1}, \mathrm{kPhC1Ca}, \mathrm{kPhC1Ce}\right) \\ &\quad = \left(\mathrm{kPhC1} + \mathrm{kPhC1Ce} \cdot [\mathrm{Ce}] + \mathrm{kPhC1Ca} \cdot [\mathrm{Ca}]\right) \cdot [\mathrm{E1C1}] \end{aligned} \tag{106}$$

$$\begin{aligned} &\mathrm{rPhC1\_2}\left([\mathrm{Ca}], [\mathrm{Ce}], [\mathrm{E1C1}], \mathrm{kPhC1}, \mathrm{kPhC1Ca}, \mathrm{kPhC1Ce}\right) \\ &\quad = \left(\mathrm{kPhC1} + \mathrm{kPhC1Ce} \cdot [\mathrm{Ce}] + \mathrm{kPhC1Ca} \cdot [\mathrm{Ca}]\right) \cdot [\mathrm{E1C1}] \end{aligned} \tag{107}$$

8.26 Reaction `Dephosphorylation_of_APC_C_Cdh1`

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

Name Dephosphorylation of APC/CĈdh1

Reaction equation

$$\mathrm{pC1} \longrightarrow \mathrm{C1} \tag{108}$$

Reactant

Table 62: Properties of each reactant.

Id	Name	SBO
pC1	C_Cdh1_APC_phosphorylated_inactive	

Product

Table 63: Properties of each product.

Id	Name	SBO
C1	Cdh1_C_APC_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kDpC1} \cdot [\mathrm{pC1}] \tag{109}$$

8.27 Reaction Nuclear_import_of_active_PCNA

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

Name Nuclear import of active PCNA

Reaction equation

$$\emptyset \longrightarrow \mathrm{aPcna} \tag{110}$$

Product

Table 64: Properties of each product.

Id	Name	SBO
aPcna	Pcna_nuclear_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{Constant\_flux\_\_irreversible}\,(\mathrm{kImPc}) \tag{111}$$

$$\mathrm{Constant\_flux\_\_irreversible}\,(\mathrm{v}) = \mathrm{v} \tag{112}$$

$$\mathrm{Constant\_flux\_\_irreversible}\,(\mathrm{v}) = \mathrm{v} \tag{113}$$

8.28 Reaction `Nuclear_export_of_active_PCNA`

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

Name Nuclear export of active PCNA

Reaction equation

$$\mathrm{aPcna} \longrightarrow \emptyset \tag{114}$$

Reactant

Table 65: Properties of each reactant.

Id	Name	SBO
`aPcna`	Pcna_nuclear_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{kExPc} \cdot [\mathrm{aPcna}] \tag{115}$$

8.29 Reaction `Nuclear_export_of_inactive_PCNA`

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

Name Nuclear export of inactive PCNA

Reaction equation

$$\mathrm{iPcna} \longrightarrow \mathrm{P21} \tag{116}$$

Reactant

Table 66: Properties of each reactant.

Id	Name	SBO
iPcna	PCNA_Nuclear_inactive	

Product

Table 67: Properties of each product.

Id	Name	SBO
P21	P21	

Kinetic Law

Derived unit contains undeclared units

$$v_{29} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{kExPc} \cdot [\mathrm{iPcna}] \tag{117}$$

8.30 Reaction Association_dissociation_of_PCNA_and_p21

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

Name Association/dissociation of PCNA and p21

Reaction equation

$$\mathrm{aPcna} + \mathrm{P21} \rightleftharpoons \mathrm{iPcna} \tag{118}$$

Reactants

Table 68: Properties of each reactant.

Id	Name	SBO
aPcna	Pcna_nuclear_active	
P21	P21	

Product

Table 69: Properties of each product.

Id	Name	SBO
iPcna	PCNA_Nuclear_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{30} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \left(\mathrm{kAsPcP21} \cdot [\mathrm{aPcna}] \cdot [\mathrm{P21}] - \mathrm{kDsPcP21} \cdot [\mathrm{iPcna}]\right) \tag{119}$$

8.31 Reaction Degradation_of_p21_in_PCNA_p21_complexes

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

Name Degradation of p21 in PCNA:p21 complexes

Reaction equation

$$\mathrm{iPcna} \xrightarrow{\mathrm{Ce,\ Ca,\ aRc}} \mathrm{aPcna} \tag{120}$$

Reactant

Table 70: Properties of each reactant.

Id	Name	SBO
iPcna	PCNA_Nuclear_inactive	

Modifiers

Table 71: Properties of each modifier.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	
Ca	CyclinA_Cdk2	
aRc	Pre_Replication_complex_active	

Product

Table 72: Properties of each product.

Id	Name	SBO
aPcna	Pcna_nuclear_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{31} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDeP21\_4}\left([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], \mathrm{Skp2}, [\mathrm{aRc}], [\mathrm{iPcna}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \quad (121)$$

$$\begin{aligned}&\mathrm{rDeP21\_4}\left([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], \mathrm{Skp2}, [\mathrm{aRc}], [\mathrm{iPcna}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right)\\ &= \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot \left([\mathrm{Ce}] + [\mathrm{Ca}]\right) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{iPcna}]\end{aligned} \quad (122)$$

$$\begin{aligned}&\mathrm{rDeP21\_4}\left([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], \mathrm{Skp2}, [\mathrm{aRc}], [\mathrm{iPcna}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right)\\ &= \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot \left([\mathrm{Ce}] + [\mathrm{Ca}]\right) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{iPcna}]\end{aligned} \quad (123)$$

8.32 Reaction Association_dissociation_of_active_PCNA_and_replication_complexes

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

Name Association/dissociation of active PCNA and replication complexes

Reaction equation

$$\mathrm{aPcna} + \mathrm{pRc} \rightleftharpoons \mathrm{aRc} \quad (124)$$

Reactants

Table 73: Properties of each reactant.

Id	Name	SBO
aPcna	Pcna_nuclear_active	
pRc	Pre_Replication_complex_primed	

Product

Table 74: Properties of each product.

Id	Name	SBO
aRc	Pre_Replication_complex_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{32} = \mathrm{vol}(\mathrm{Cell}) \cdot (\mathrm{kAsRcPc} \cdot [\mathrm{aPcna}] \cdot [\mathrm{pRc}] - \mathrm{kDsRcPc} \cdot [\mathrm{aRc}]) \quad (125)$$

8.33 Reaction Association_dissociation_of_inactive_PCNA_and_replication_complexes

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

Name Association/dissociation of inactive PCNA and replication complexes

Reaction equation

$$\mathrm{iPcna} + \mathrm{pRc} \rightleftharpoons \mathrm{iRc} \quad (126)$$

Reactants

Table 75: Properties of each reactant.

Id	Name	SBO
iPcna	PCNA_Nuclear_inactive	
pRc	Pre_Replication_complex_primed	

Product

Table 76: Properties of each product.

Id	Name	SBO
iRc	Pre_Replication_complex_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{33} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \left(\mathrm{kAsRcPc} \cdot [\mathrm{iPcna}] \cdot [\mathrm{pRc}] - \mathrm{kDsRcPc} \cdot [\mathrm{iRc}]\right) \quad (127)$$

8.34 Reaction Phosphorylation_priming_of_replication_complexes

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

Name Phosphorylation/priming of replication complexes

Reaction equation

$$\mathrm{Rc} \xrightarrow{\mathrm{Ce,\ Ca}} \mathrm{pRc} \quad (128)$$

Reactant

Table 77: Properties of each reactant.

Id	Name	SBO
Rc	Pre_Replication_complex	

Modifiers

Table 78: Properties of each modifier.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	
Ca	CyclinA_Cdk2	

Product

Table 79: Properties of each product.

Id	Name	SBO
pRc	Pre_Replication_complex_primed	

Kinetic Law

Derived unit contains undeclared units

$$v_{34} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rPhRc\_1}\left([\mathrm{Ca}], [\mathrm{Ce}], [\mathrm{Rc}], \mathrm{jCy}, \mathrm{kPhRc}, \mathrm{n}\right) \quad (129)$$

$$\mathrm{rPhRc\_1}\left([\mathrm{Ca}],[\mathrm{Ce}],[\mathrm{Rc}],\mathrm{jCy},\mathrm{kPhRc},\mathrm{n}\right)=\frac{\mathrm{kPhRc}\cdot\left([\mathrm{Ce}]+[\mathrm{Ca}]\right)^{\mathrm{n}}}{\mathrm{jCy}^{\mathrm{n}}+\left([\mathrm{Ce}]+[\mathrm{Ca}]\right)^{\mathrm{n}}}\cdot[\mathrm{Rc}] \tag{130}$$

$$\mathrm{rPhRc\_1}\left([\mathrm{Ca}],[\mathrm{Ce}],[\mathrm{Rc}],\mathrm{jCy},\mathrm{kPhRc},\mathrm{n}\right)=\frac{\mathrm{kPhRc}\cdot\left([\mathrm{Ce}]+[\mathrm{Ca}]\right)^{\mathrm{n}}}{\mathrm{jCy}^{\mathrm{n}}+\left([\mathrm{Ce}]+[\mathrm{Ca}]\right)^{\mathrm{n}}}\cdot[\mathrm{Rc}] \tag{131}$$

8.35 Reaction `Dephosphorylation_of_replication_complexes`

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

Name Dephosphorylation of replication complexes

Reaction equation

$$\mathrm{pRc}\longrightarrow\mathrm{Rc} \tag{132}$$

Reactant

Table 80: Properties of each reactant.

Id	Name	SBO
pRc	Pre_Replication_complex_primed	

Product

Table 81: Properties of each product.

Id	Name	SBO
Rc	Pre_Replication_complex	

Kinetic Law

Derived unit contains undeclared units

$$v_{35}=\mathrm{vol}\left(\mathrm{Cell}\right)\cdot\mathrm{kDpRc}\cdot[\mathrm{pRc}] \tag{133}$$

8.36 Reaction `Association_dissociation_of_p21_and_replication_complexes`

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

Name Association/dissociation of p21 and replication complexes

Reaction equation

$$aRc + P21 \rightleftharpoons iRc \tag{134}$$

Reactants

Table 82: Properties of each reactant.

Id	Name	SBO
aRc	Pre_Replication_complex_active	
P21	P21	

Product

Table 83: Properties of each product.

Id	Name	SBO
iRc	Pre_Replication_complex_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{36} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \left(\mathrm{kAsPcP21} \cdot [\mathrm{aRc}] \cdot [\mathrm{P21}] - \mathrm{kDsPcP21} \cdot [\mathrm{iRc}]\right) \tag{135}$$

8.37 Reaction Degradation_of_p21_in_inactive_replication_complexes

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

Name Degradation of p21 in inactive replication complexes

Reaction equation

$$iRc \xrightarrow{Ce,\ Ca,\ aRc} aRc \tag{136}$$

Reactant

Table 84: Properties of each reactant.

Id	Name	SBO
iRc	Pre_Replication_complex_inactive	

Modifiers

Table 85: Properties of each modifier.

Id	Name	SBO
Ce	CyclinE_Cdk2_active	
Ca	CyclinA_Cdk2	
aRc	Pre_Replication_complex_active	

Product

Table 86: Properties of each product.

Id	Name	SBO
aRc	Pre_Replication_complex_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{37} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDeP21\_5}\left([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], \mathrm{Skp2}, [\mathrm{aRc}], [\mathrm{iRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \tag{137}$$

$$\begin{aligned} &\mathrm{rDeP21\_5}\left([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], \mathrm{Skp2}, [\mathrm{aRc}], [\mathrm{iRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \\ &\quad = \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot \left([\mathrm{Ce}] + [\mathrm{Ca}]\right) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{iRc}] \end{aligned} \tag{138}$$

$$\begin{aligned} &\mathrm{rDeP21\_5}\left([\mathrm{Ca}], \mathrm{Cdt2}, [\mathrm{Ce}], \mathrm{Skp2}, [\mathrm{aRc}], [\mathrm{iRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \\ &\quad = \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot \mathrm{Skp2} \cdot \left([\mathrm{Ce}] + [\mathrm{Ca}]\right) + \mathrm{kDeP21aRc} \cdot \mathrm{Cdt2} \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{iRc}] \end{aligned} \tag{139}$$

8.38 Reaction `Dissassembly_of_RC`

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

Name Dissassembly of RC

Reaction equation

$$\mathrm{Rc} \xrightarrow{\mathrm{Dna}} \emptyset \tag{140}$$

Reactant

Table 87: Properties of each reactant.

Id	Name	SBO
Rc	Pre_Replication_complex	

Modifier

Table 88: Properties of each modifier.

Id	Name	SBO
Dna	Dna	

Kinetic Law

Derived unit contains undeclared units

$$v_{38} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDsRc\_1}\left([\mathrm{Dna}], [\mathrm{Rc}]\right) \tag{141}$$

$$\mathrm{rDsRc\_1}\left([\mathrm{Dna}], [\mathrm{Rc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{Rc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{Rc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{142}$$

$$\mathrm{rDsRc\_1}\left([\mathrm{Dna}], [\mathrm{Rc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{Rc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{Rc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{143}$$

8.39 Reaction Dissassembly_of_pRC

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

Name Dissassembly of pRC

Reaction equation

$$\mathrm{pRc} \xrightarrow{\mathrm{Dna}} \emptyset \tag{144}$$

Reactant

Table 89: Properties of each reactant.

Id	Name	SBO
pRc	Pre_Replication_complex_primed	

Modifier

Table 90: Properties of each modifier.

Id	Name	SBO
Dna	Dna	

Kinetic Law

Derived unit contains undeclared units

$$v_{39} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDsRc\_2}\left([\mathrm{Dna}], [\mathrm{pRc}]\right) \tag{145}$$

$$\mathrm{rDsRc\_2}\left([\mathrm{Dna}], [\mathrm{pRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{pRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{pRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{146}$$

$$\mathrm{rDsRc\_2}\left([\mathrm{Dna}], [\mathrm{pRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{pRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{pRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{147}$$

8.40 Reaction Dissassembly_of_aRC

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

Name Dissassembly of aRC

Reaction equation

$$\mathrm{aRc} \xrightarrow{\mathrm{Dna}} \mathrm{aPcna} \tag{148}$$

Reactant

Table 91: Properties of each reactant.

Id	Name	SBO
aRc	Pre_Replication_complex_active	

Modifier

Table 92: Properties of each modifier.

Id	Name	SBO
Dna	Dna	

Product

Table 93: Properties of each product.

Id	Name	SBO
aPcna	Pcna_nuclear_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{40} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDsRc\_3}\left([\mathrm{Dna}], [\mathrm{aRc}]\right) \tag{149}$$

$$\mathrm{rDsRc\_3}\left([\mathrm{Dna}], [\mathrm{aRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{aRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{aRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{150}$$

$$\mathrm{rDsRc\_3}\left([\mathrm{Dna}], [\mathrm{aRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{aRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{aRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{151}$$

8.41 Reaction Dissassembly_of_iRC

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

Name Dissassembly of iRC

Reaction equation

$$\mathrm{iRc} \xrightarrow{\mathrm{Dna}} \mathrm{iPcna} \tag{152}$$

Reactant

Table 94: Properties of each reactant.

Id	Name	SBO
iRc	Pre_Replication_complex_inactive	

Modifier

Table 95: Properties of each modifier.

Id	Name	SBO
Dna	Dna	

Product

Table 96: Properties of each product.

Id	Name	SBO
iPcna	PCNA_Nuclear_inactive	

Kinetic Law

Derived unit contains undeclared units

$$v_{41} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDsRc\_4}\left([\mathrm{Dna}], [\mathrm{iRc}]\right) \tag{153}$$

$$\mathrm{rDsRc\_4}\left([\mathrm{Dna}], [\mathrm{iRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{iRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{iRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{154}$$

$$\mathrm{rDsRc\_4}\left([\mathrm{Dna}], [\mathrm{iRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{iRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{iRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{155}$$

8.42 Reaction `Synthesis_of_DNA`

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

Name Synthesis of DNA

Reaction equation

$$\mathrm{aRc} \longrightarrow \mathrm{aRc} + \mathrm{Dna} \tag{156}$$

Reactant

Table 97: Properties of each reactant.

Id	Name	SBO
`aRc`	Pre_Replication_complex_active	

Products

Table 98: Properties of each product.

Id	Name	SBO
`aRc`	Pre_Replication_complex_active	
`Dna`	Dna	

Kinetic Law

Derived unit contains undeclared units

$$v_{42} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kSyDna} \cdot [\mathrm{aRc}] \tag{157}$$

8.43 Reaction `Synthesis_of_p53`

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

Name Synthesis of p53

Reaction equation

$$\emptyset \longrightarrow \mathrm{P53} \tag{158}$$

Product

Table 99: Properties of each product.

Id	Name	SBO
P53	P53	

Kinetic Law

Derived unit contains undeclared units

$$v_{43} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{kSyP53}\right) \tag{159}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{160}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{161}$$

8.44 Reaction Degradation_of_p53

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

Name Degradation of p53

Reaction equation

$$\mathrm{P53} \xrightarrow{\mathrm{Dam}} \emptyset \tag{162}$$

Reactant

Table 100: Properties of each reactant.

Id	Name	SBO
P53	P53	

Modifier

Table 101: Properties of each modifier.

Id	Name	SBO
Dam	Dna_damage	

Kinetic Law

Derived unit contains undeclared units

$$v_{44} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{rDeP53\_1}([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jP53}, \mathrm{kDeP53}) \tag{163}$$

$$\mathrm{rDeP53\_1}([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jP53}, \mathrm{kDeP53}) = \frac{\mathrm{kDeP53}}{\mathrm{jP53} + [\mathrm{Dam}]} \cdot [\mathrm{P53}] \tag{164}$$

$$\mathrm{rDeP53\_1}([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jP53}, \mathrm{kDeP53}) = \frac{\mathrm{kDeP53}}{\mathrm{jP53} + [\mathrm{Dam}]} \cdot [\mathrm{P53}] \tag{165}$$

8.45 Reaction `Induction_of_DNA_damage`

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

Name Induction of DNA damage

Reaction equation

$$\emptyset \longrightarrow \mathrm{Dam} \tag{166}$$

Product

Table 102: Properties of each product.

Id	Name	SBO
Dam	Dna_damage	

Kinetic Law

Derived unit contains undeclared units

$$v_{45} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{Constant\_flux\_\_irreversible}(\mathrm{kGeDam}) \tag{167}$$

$$\mathrm{Constant\_flux\_\_irreversible}(\mathrm{v}) = \mathrm{v} \tag{168}$$

$$\text{Constant\_flux\_\_irreversible}\,(v) = v \tag{169}$$

8.46 Reaction Induction_of_DNA_damage_by_replication

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

Name Induction of DNA damage by replication

Reaction equation

$$\text{aRc} \longrightarrow \text{aRc} + \text{Dam} \tag{170}$$

Reactant

Table 103: Properties of each reactant.

Id	Name	SBO
aRc	Pre_Replication_complex_active	

Products

Table 104: Properties of each product.

Id	Name	SBO
aRc	Pre_Replication_complex_active	
Dam	Dna_damage	

Kinetic Law

Derived unit contains undeclared units

$$v_{46} = \text{vol}\,(\text{Cell}) \cdot \text{kGeDamArc} \cdot [\text{aRc}] \tag{171}$$

8.47 Reaction Synthesis_of_APC_C_Cdh1_activity_probe

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

Name Synthesis of APC/CĈdh1 activity probe

Reaction equation

$$\emptyset \longrightarrow \text{Pr} \tag{172}$$

Product

Table 105: Properties of each product.

Id	Name	SBO
Pr	Activity_probe_of_APC_C_Cdh1	

Kinetic Law

Derived unit contains undeclared units

$$v_{47} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{kSyPr}\right) \tag{173}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{174}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{175}$$

8.48 Reaction Degradation_of_APC_C_Cdh1_activity_probe

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

Name Degradation of APC/CĈdh1 activity probe

Reaction equation

$$\mathrm{Pr} \xrightarrow{\mathrm{C1}} \emptyset \tag{176}$$

Reactant

Table 106: Properties of each reactant.

Id	Name	SBO
Pr	Activity_probe_of_APC_C_Cdh1	

Modifier

Table 107: Properties of each modifier.

Id	Name	SBO
C1	Cdh1_C_APC_active	

Kinetic Law

Derived unit contains undeclared units

$$v_{48} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{rDePr\_1}([\mathrm{C1}], [\mathrm{Pr}], \mathrm{kDeCaC1}, \mathrm{kDePr}) \tag{177}$$

$$\mathrm{rDePr\_1}([\mathrm{C1}], [\mathrm{Pr}], \mathrm{kDeCaC1}, \mathrm{kDePr}) = (\mathrm{kDePr} + \mathrm{kDeCaC1} \cdot [\mathrm{C1}]) \cdot [\mathrm{Pr}] \tag{178}$$

$$\mathrm{rDePr\_1}([\mathrm{C1}], [\mathrm{Pr}], \mathrm{kDeCaC1}, \mathrm{kDePr}) = (\mathrm{kDePr} + \mathrm{kDeCaC1} \cdot [\mathrm{C1}]) \cdot [\mathrm{Pr}] \tag{179}$$

8.49 Reaction Repair_of_DNA_damage

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

Name Repair of DNA damage

Reaction equation

$$\mathrm{Dam} \xrightarrow{\mathrm{P53}} \emptyset \tag{180}$$

Reactant

Table 108: Properties of each reactant.

Id	Name	SBO
Dam	Dna_damage	

Modifier

Table 109: Properties of each modifier.

Id	Name	SBO
P53	P53	

Kinetic Law

Derived unit contains undeclared units

$$v_{49} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{rReDam\_1}([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jDam}, \mathrm{kReDam}, \mathrm{kReDamP53}) \tag{181}$$

$$\begin{aligned}&\mathrm{rReDam\_1}([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jDam}, \mathrm{kReDam}, \mathrm{kReDamP53})\\ &= \left(\mathrm{kReDam} + \frac{\mathrm{kReDamP53} \cdot [\mathrm{P53}]}{\mathrm{jDam} + [\mathrm{Dam}]}\right) \cdot [\mathrm{Dam}]\end{aligned} \tag{182}$$

$$\begin{aligned}&\mathrm{rReDam\_1}([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jDam}, \mathrm{kReDam}, \mathrm{kReDamP53})\\ &= \left(\mathrm{kReDam} + \frac{\mathrm{kReDamP53} \cdot [\mathrm{P53}]}{\mathrm{jDam} + [\mathrm{Dam}]}\right) \cdot [\mathrm{Dam}]\end{aligned} \tag{183}$$

9 Derived Rate Equations

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

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.

9.1 Species `Rb`

Name Retinoblastoma_protein

Notes `(AU) hypo-phosphorylated Rb`

Initial concentration $0 \ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in `Phosphorylation_of_Rb`, `Association_dissociation_of_Rb_and_E2F` and as a product in `Dephosphorylation_of_Rb`, `Degradation_of_E2F_in_Rb_E2F_complexes`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Rb} = v_3 + v_6 - v_1 - v_7 \tag{184}$$

9.2 Species pRb

Name Retinoblastoma_protein_hyperphosphorylated

Notes (AU) hyper-phosphorylated Rb

Initial concentration $5 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in three reactions (as a reactant in Dephosphorylation_of_Rb and as a product in Phosphorylation_of_Rb, Phosphorylation_Rb_in_Rb_E2F_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pRb} = v_1 + v_2 - v_3 \tag{185}$$

9.3 Species E2f

Name E2f_active

Notes (AU) free, active E2F

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in eleven reactions (as a reactant in Degradation_of_E2F, Association_dissociation_of_Rb_and_E2F, Synthesis_of_CycE, Synthesis_of_CycA, Synthesis_of_Emi1 and as a product in Phosphorylation_Rb_in_Rb_E2F_complexes, Synthesis_of_E2F, Synthesis_of_CycE, Synthesis_of_CycA, Synthesis_of_Emi1 and as a modifier in Synthesis_of_E2F).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E2f} = v_2 + v_4 + v_9 + v_{10} + v_{20} - v_5 - v_7 - v_9 - v_{10} - v_{20} \tag{186}$$

9.4 Species RbE2f

Name Retinoblastoma_protein_E2f_complex_inactive

Notes (AU) Rb:E2F complexes (inactive)

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in three reactions (as a reactant in Phosphorylation_Rb_in_Rb_E2F_complexes, Degradation_of_E2F_in_Rb_E2F_complexes and as a product in Association_dissociation_of_Rb_and_E2F).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{RbE2f} = v_7 - v_2 - v_6 \tag{187}$$

9.5 Species E1

Name Emi1

Notes `(AU) free Emi1`

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in four reactions (as a reactant in Degradation_of_Emi1, Association_dissociation_of_Emi1_APC_C_Cdh1_complexes and as a product in Synthesis_of_Emi1, Phosphorylation_of_APC_C_Cdh1_in_Emi1_APC_C_Cdh1_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E1} = v_{20} + v_{25} - v_{21} - v_{22} \tag{188}$$

9.6 Species C1

Name Cdh1_C_APC_active

Notes `(AU) free, active APC/C^Cdh1`

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in seven reactions (as a reactant in Association_dissociation_of_Emi1_APC_C_Cdh1_complexes, Phosphorylation_of_free_APC_C_Cdh1 and as a product in Degradation_of_Emi1_in_Emi1_APC_C_Cdh1_complexes, Dephosphorylation_of_APC_C_Cdh1 and as a modifier in Degradation_of_CycA_in_CycA_Cdk2_complexes, Degradation_of_CycA_in_CycA_Cdk2_p21_complexes, Degradation_of_APC_C_Cdh1_activity_probe).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C1} = v_{23} + v_{26} - v_{22} - v_{24} \tag{189}$$

9.7 Species pC1

Name C_Cdh1_APC_phosphorylated_inactive

Notes `(AU) phosphorylated APC/C^Cdh1 (inactive)`

Initial concentration $1 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in three reactions (as a reactant in Dephosphorylation_of_APC_C_Cdh1 and as a product in Phosphorylation_of_free_APC_C_Cdh1, Phosphorylation_of_APC_C_Cdh1_in_Emi1_APC_C_Cdh1_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pC1} = v_{24} + v_{25} - v_{26} \tag{190}$$

9.8 Species E1C1

Name Emi1_C_Cdh1_complex_inactive

Notes (AU) Emi1:APC/C^Cdh1 complexes (inactive) ; Emi1 is an APC_C_Cdh1 inhibitator

Initial concentration $0\ \mathrm{mmol\cdot ml^{-1}}$

This species takes part in three reactions (as a reactant in Degradation_of_Emi1_in_Emi1_APC_C_Cdh1_complexes, Phosphorylation_of_APC_C_Cdh1_in_Emi1_APC_C_Cdh1_complexes and as a product in Association_dissociation_of_Emi1_APC_C_Cdh1_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E1C1} = v_{22} - v_{23} - v_{25} \tag{191}$$

9.9 Species P21

Name P21

Notes (AU) free p21

Initial concentration $0.6\ \mathrm{mmol\cdot ml^{-1}}$

This species takes part in nine reactions (as a reactant in Association_dissociation_of_CycE_Cdk2_and_p21, Association_dissociation_of_CycA_Cdk2_and_p21, Degradation_of_free_p21, Association_dissociation_of_PCNA_and_p21, Association_dissociation_of_p21_and_replication_complexes and as a product in Synthesis_of_p21, Degradation_of_CycE_in_CycE_Cdk2_p21_complexes, Degradation_of_CycA_in_CycA_Cdk2_p21_complexes, Nuclear_export_of_inactive_PCNA).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P21} = v_{8} + v_{16} + v_{18} + v_{29} - v_{11} - v_{12} - v_{19} - v_{30} - v_{36} \tag{192}$$

9.10 Species Ce

Name CyclinE_Cdk2_active

Notes (AU) free, active CycE:Cdk2

Initial concentration $0.5\ \mathrm{mmol\cdot ml^{-1}}$

This species takes part in 14 reactions (as a reactant in Association_dissociation_of_CycE_Cdk2_and_p21, Degradation_of_CycE_in_CycE_Cdk2_complexes and as a product in Synthesis_of_CycE, Degradation_of_p21_in_CycE_Cdk2_p21_complexes and as a modifier in Phosphorylation_of_Rb, Phosphorylation_Rb_in_Rb_E2F_complexes, Degradation_of_p21_in_CycE_Cdk2_p21_complexes, Degradation_of_p21_in_CycA_Cdk2_p21_complexes, Degradation_of_free_p21, Phosphorylation_of_free_APC_C_Cdh1, Phosphorylation_of_APC_C_Cdh1_in_Emi1_APC_C_Cdh1_complexes, Degradation_of_p21_in_PCNA_p21_complexes, Phosphorylation_priming_of_replication_complexes, Degradation_of_p21_in_inactive_replication_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ce} = v_9 + v_{13} - v_{11} - v_{15} \tag{193}$$

9.11 Species Ca

Name CyclinA_Cdk2

Notes `(AU) free, active CycA:Cdk2`

Initial concentration $1.2 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in 16 reactions (as a reactant in Association_dissociation_of_CycA_Cdk2_and_p21, Degradation_of_CycA_in_CycA_Cdk2_complexes and as a product in Synthesis_of_CycA, Degradation_of_p21_in_CycA_Cdk2_p21_complexes and as a modifier in Phosphorylation_of_Rb, Phosphorylation_Rb_in_Rb_E2F_complexes, Degradation_of_p21_in_CycE_Cdk2_p21_complexes, Degradation_of_p21_in_CycA_Cdk2_p21_complexes, Degradation_of_CycE_in_CycE_Cdk2_complexes, Degradation_of_CycE_in_CycE_Cdk2_p21_complexes, Degradation_of_free_p21, Phosphorylation_of_free_APC_C_Cdh1, Phosphorylation_of_APC_C_Cdh1_in_Emi1_APC_C_Cdh1_complexes, Degradation_of_p21_in_PCNA_p21_complexes, Phosphorylation_priming_of_replication_complexes, Degradation_of_p21_in_inactive_replication_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ca} = v_{10} + v_{14} - v_{12} - v_{17} \tag{194}$$

9.12 Species CeP21

Name CyclinE_Cdk2_P21_complex_inactive

Notes `(AU) CycE:Cdk2:p21 complexes (inactive)`

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in three reactions (as a reactant in Degradation_of_p21_in_CycE_Cdk2_p21_complexes, Degradation_of_CycE_in_CycE_Cdk2_p21_complexes and as a product in Association_dissociation_of_CycE_Cdk2_and_p21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CeP21} = v_{11} - v_{13} - v_{16} \tag{195}$$

9.13 Species CaP21

Name CyclinA_Cdk2_P21_complex_inactive

Notes `(AU) CycA:Cdk2:p21 complexes (inactive)`

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in Degradation_of_p21_in_CycA_Cdk2_p21_complexes, Degradation_of_CycA_in_CycA_Cdk2_p21_complexes and as a product in Association_dissociation_of_CycA_Cdk2_and_p21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CaP21} = v_{12} - v_{14} - v_{18} \tag{196}$$

9.14 Species aPcna

Name Pcna_nuclear_active

Notes `(AU) active, nuclear PCNA`

Initial concentration $0.5\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in six reactions (as a reactant in Nuclear_export_of_active_PCNA, Association_dissociation_of_PCNA_and_p21, Association_dissociation_of_active_PCNA_and_replication_complexes and as a product in Nuclear_import_of_active_PCNA, Degradation_of_p21_in_PCNA_p21_complexes, Dissassembly_of_aRC).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{aPcna} = v_{27} + v_{31} + v_{40} - v_{28} - v_{30} - v_{32} \tag{197}$$

9.15 Species iPcna

Name PCNA_Nuclear_inactive

Notes `(AU) inactive, nuclear PCNA`

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in five reactions (as a reactant in Nuclear_export_of_inactive_PCNA, Degradation_of_p21_in_PCNA_p21_complexes, Association_dissociation_of_inactive_PCNA_and_replication_complexes and as a product in Association_dissociation_of_PCNA_and_p21, Dissassembly_of_iRC).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{iPcna} = v_{30} + v_{41} - v_{29} - v_{31} - v_{33} \tag{198}$$

9.16 Species Rc

Name Pre_Replication_complex

Notes (AU) pre-replication complexes

Initial concentration $1 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in three reactions (as a reactant in Phosphorylation_priming_of_replication_complexes, Dissassembly_of_RC and as a product in Dephosphorylation_of_replication_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Rc} = v_{35} - v_{34} - v_{38} \tag{199}$$

9.17 Species pRc

Name Pre_Replication_complex_primed

Notes (AU) primed replication complexes

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in five reactions (as a reactant in Association_dissociation_of_active_PCNA_and_replication_complexes, Association_dissociation_of_inactive_PCNA_and_replication_complexes, Dephosphorylation_of_replication_complexes, Dissassembly_of_pRC and as a product in Phosphorylation_priming_of_replication_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pRc} = v_{34} - v_{32} - v_{33} - v_{35} - v_{39} \tag{200}$$

9.18 Species aRc

Name Pre_Replication_complex_active

Notes (AU) active replication complexes

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in 13 reactions (as a reactant in Association_dissociation_of_p21_and_replication_complexes, Dissassembly_of_aRC, Synthesis_of_DNA, Induction_of_DNA_damage_by_replication and as a product in Association_dissociation_of_active_PCNA_and_replication_complexes, Degradation_of_p21_in_inactive_replication_complexes, Synthesis_of_DNA, Induction_of_DNA_damage_by_replication and as a modifier in Degradation_of_p21_in_CycE_Cdk2_p21_complexes, Degradation_of_p21_in_CycA_Cdk2_p21_complexes, Degradation_of_free_p21, Degradation_of_p21_in_PCNA_p21_complexes, Degradation_of_p21_in_inactive_replication_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{aRc} = v_{32} + v_{37} + v_{42} + v_{46} - v_{36} - v_{40} - v_{42} - v_{46} \tag{201}$$

9.19 Species iRc

Name Pre_Replication_complex_inactive

Notes `(AU) inactive replication complexes`

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in four reactions (as a reactant in Degradation_of_p21_in_inactive_replication_complexes, Dissassembly_of_iRC and as a product in Association_dissociation_of_inactive_PCNA_and_replication_complexes, Association_dissociation_of_p21_and_replication_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{iRc} = v_{33} + v_{36} - v_{37} - v_{41} \tag{202}$$

9.20 Species Dna

Name Dna

Notes `(AU) DNA`

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in five reactions (as a product in Synthesis_of_DNA and as a modifier in Dissassembly_of_RC, Dissassembly_of_pRC, Dissassembly_of_aRC, Dissassembly_of_iRC).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Dna} = v_{42} \tag{203}$$

9.21 Species P53

Name P53

Notes `(AU) p53 transcription factor`

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in four reactions (as a reactant in Degradation_of_p53 and as a product in Synthesis_of_p53 and as a modifier in Synthesis_of_p21, Repair_of_DNA_damage).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P53} = v_{43} - v_{44} \tag{204}$$

9.22 Species Dam

Name Dna_damage

Notes (AU) DNA damage

Initial concentration $0\ \text{mmol} \cdot \text{ml}^{-1}$

This species takes part in four reactions (as a reactant in Repair_of_DNA_damage and as a product in Induction_of_DNA_damage, Induction_of_DNA_damage_by_replication and as a modifier in Degradation_of_p53).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Dam} = v_{45} + v_{46} - v_{49} \tag{205}$$

9.23 Species Pr

Name Activity_probe_of_APC_C_Cdh1

Notes (AU) APC/C^Cdh1 activity probe

Initial concentration $0.5\ \text{mmol} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a reactant in Degradation_of_APC_C_Cdh1_activity-_probe and as a product in Synthesis_of_APC_C_Cdh1_activity_probe).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Pr} = v_{47} - v_{48} \tag{206}$$

9.24 Species tRb

Name Retinoblastoma_protein_total

Notes (AU) total Rb protein

Initial concentration $5\ \text{mmol} \cdot \text{ml}^{-1}$

Involved in rule tRb

One rule determines the species' quantity.

9.25 Species tE2f

Name E2f_total

Notes (AU) total E2F protein

Initial concentration $0\ \text{mmol} \cdot \text{ml}^{-1}$

Involved in rule tE2f

One rule determines the species' quantity.

9.26 Species tE1

Name Emi1_total

Notes (AU) total Emi1 protein

Initial concentration $0 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule tE1

One rule determines the species' quantity.

9.27 Species tC1

Name C_Cdh1_APC_total

Notes (AU) total APC/C^Cdh1 protein ; APC/C^Cdh1 protein ubiquitin E3 ligase that is act

Initial concentration $1 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule tC1

One rule determines the species' quantity.

9.28 Species tCe

Name CyclinE_Cdk2_total

Notes (AU) total CycE:Cdk2

Initial concentration $0.5 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule tCe

One rule determines the species' quantity.

9.29 Species tCa

Name CyclinA_Cdk2_total

Notes (AU) total CycA:Cdk2

Initial concentration $1.2 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule tCa

One rule determines the species' quantity.

9.30 Species tP21

Name P21_total

Notes (AU) total p21 protein

Initial concentration $0.6\,\mathrm{mmol}\cdot\mathrm{ml}^{-1}$

Involved in rule tP21

One rule determines the species' quantity.