SBML Model Report

Model name: "Barr2017 - Dynamics of p21 in hTert-RPE1 cells"

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 Emma Louise Fairbanks[2] at June nineth 2016 at 5:37 p. m. and last time modified at December sixth 2017 at 4:28 p. m. Table 1 gives 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	20
events	0	constraints	0
reactions	35	function definitions	14
global parameters	31	unit definitions	3
rules	3	initial assignments	0

Model Notes

Barr2017 - Dynamics of p21 in hTert-RPE1cellsThis deteministic model reveals that abistable switch created by Cdt2, promotes irreversible S-phaseentry by keeping p21 levels low, prevents premature S-phase exitupon DNA damage

[1]University of Oxford, stefan.heldt@bioch.ox.ac.uk
[2]EMBL-EBI, efairbanks@ebi.ac.uk

This model is described in the article:DNA damage during S-phase mediates the proliferation-quiescence decision in the subsequent G1 via p21 expression.Barr AR, Cooper S, Heldt FS, Butera F, Stoy H, Mansfeld J, Novk B, Bakal C.Nat Commun 2017 Mar; 8: 14728

Abstract:

Following DNA damage caused by exogenous sources, such as ionizing radiation, the tumour suppressor p53 mediates cell cycle arrest via expression of the CDK inhibitor, p21. However, the role of p21 in maintaining genomic stability in the absence of exogenous DNA-damaging agents is unclear. Here, using live single-cell measurements of p21 protein in proliferating cultures, we show that naturally occurring DNA damage incurred over S-phase causes p53-dependent accumulation of p21 during mother G2- and daughter G1-phases. High p21 levels mediate G1 arrest via CDK inhibition, yet lower levels have no impact on G1 progression, and the ubiquitin ligases CRL4Cdt2 and SCFSkp2 couple to degrade p21 prior to the G1/S transition. Mathematical modelling reveals that a bistable switch, created by CRL4Cdt2, promotes irreversible S-phase entry by keeping p21 levels low, preventing premature S-phase exit upon DNA damage. Thus, we characterize how p21 regulates the proliferation-quiescence decision to maintain genomic stability.

This model is hosted on BioModels Database and identified by: BIOMD0000000660.

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 20 species. The boundary condition of five 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
`MrnaP21`	MrnaP21	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`MrnaCy`	MrnaCy	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`MrnaP53`	MrnaP53	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`P21`	P21	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`Cy`	Cy	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`CyP21`	CyP21	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`aPcna`	aPcna	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`Rc`	Rc	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`pRc`	pRc	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`aRc`	aRc	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`iRc`	iRc	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`Dna`	Dna	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`Dam`	Dam	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`P53`	P53	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`Skp2`	Skp2	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
`Cdt2`	Cdt2	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☑	☑
`iPcna`	iPcna	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☐
`tP21`	tP21	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☑
`tCy`	tCy	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☑
`tPcna`	tPcna	`Cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☑

5 Parameters

This model contains 31 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kSyMrna	kSyMrna		0.020		☑
kSyMrnaP53	kSyMrnaP53		0.080		☑
kDeMrna	kDeMrna		0.020		☑
kSyP21	kSyP21		0.002		☑
kDeP21	kDeP21		0.003		☑
kDeP21Cy	kDeP21Cy		0.007		☑
kDeP21aRc	kDeP21aRc		1.000		☑
kSyCy	kSyCy		0.005		☑
kAsCyP21	kAsCyP21		1.000		☑
kDsCyP21	kDsCyP21		0.050		☑
kDeCy	kDeCy		0.002		☑
kDeCyCy	kDeCyCy		$2 \cdot 10^{-4}$		☑
kImPc	kImPc		0.003		☑
kExPc	kExPc		0.006		☑
kPhRc	kPhRc		0.100		☑
kDpRc	kDpRc		0.010		☑
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		0.007		☑
kSyP53	kSyP53		0.050		☑
kDeP53	kDeP53		0.050		☑
jP53	jP53		0.010		☑
kGeDam	kGeDam		0.001		☑
kGeDamArc	kGeDamArc		0.005		☑
kReDam	kReDam		0.001		☑
kReDamP53	kReDamP53		0.005		☑
jDam	jDam		0.500		☑

6 Function definitions

This is an overview of 14 function definitions.

6.1 Function definition `Constant_flux__irreversible`

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$v \tag{1}$$

6.2 Function definition `rDsRc`

Name Function for Dissassembly of RC

Arguments [Dna], [Rc]

Mathematical Expression

$$\begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{Rc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{Rc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{2}$$

6.3 Function definition `rDeP21_1`

Name Function for Degradation of p21

Arguments [Cdt2], [Cy], [P21], [Skp2], [aRc], kDeP21, kDeP21Cy, kDeP21aRc

Mathematical Expression

$$(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]) \cdot [\mathrm{P21}] \tag{3}$$

6.4 Function definition `rDeCy_1`

Name Function for Degradation of cyclins

Arguments [Cy], [Skp2], kDeCy, kDeCyCy

Mathematical Expression

$$(\mathrm{kDeCy} + \mathrm{kDeCyCy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}]) \cdot [\mathrm{Cy}] \tag{4}$$

6.5 Function definition `rDeCy_2`

Name Function for Degradation of cyclin in CDK2:Cyclin:p21 complexes

Arguments [Cy], [CyP21], [Skp2], kDeCy, kDeCyCy

Mathematical Expression

$$(\mathrm{kDeCy} + \mathrm{kDeCyCy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}]) \cdot [\mathrm{CyP21}] \tag{5}$$

6.6 Function definition rDeP21_2

Name Function for Degradation of p21 in CDK2:Cyclin:p21 complexes

Arguments [Cdt2], [Cy], [CyP21], [Skp2], [aRc], kDeP21, kDeP21Cy, kDeP21aRc

Mathematical Expression

$$(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]) \cdot [\mathrm{CyP21}] \tag{6}$$

6.7 Function definition rDeP21_3

Name Function for Degradation of p21 in PCNA:p21 complexes

Arguments [Cdt2], [Cy], [Skp2], [aRc], [iPcna], kDeP21, kDeP21Cy, kDeP21aRc

Mathematical Expression

$$(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]) \cdot [\mathrm{iPcna}] \tag{7}$$

6.8 Function definition rPhRc_1

Name Function for Phosphorylation/priming of replication complexes

Arguments [Cy], [Rc], jCy, kPhRc, n

Mathematical Expression

$$\frac{\mathrm{kPhRc} \cdot [\mathrm{Cy}]^{\mathrm{n}}}{\mathrm{jCy}^{\mathrm{n}} + [\mathrm{Cy}]^{\mathrm{n}}} \cdot [\mathrm{Rc}] \tag{8}$$

6.9 Function definition rDeP21_4

Name Function for Degradation of p21 in inactive replication complexes

Arguments [Cdt2], [Cy], [Skp2], [aRc], [iRc], kDeP21, kDeP21Cy, kDeP21aRc

Mathematical Expression

$$(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]) \cdot [\mathrm{iRc}] \tag{9}$$

6.10 Function definition rDsRc_1

Name Function for Dissassembly of pRC

Arguments [Dna], [pRc]

Mathematical Expression

$$\begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{pRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{pRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{10}$$

6.11 Function definition rDsRc_2

Name Function for Dissassembly of aRC

Arguments [Dna], [aRc]

Mathematical Expression

$$\begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{aRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{aRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{11}$$

6.12 Function definition rDsRc_3

Name Function for Dissassembly of iRC

Arguments [Dna], [iRc]

Mathematical Expression

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

6.13 Function definition rDeP53_1

Name Function for Degradation of p53

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

Mathematical Expression

$$\frac{\mathrm{kDeP53}}{\mathrm{jP53} + [\mathrm{Dam}]} \cdot [\mathrm{P53}] \tag{13}$$

6.14 Function definition rReDam_1

Name Function for Repair of DNA damage

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

Mathematical Expression

$$\left(\mathrm{kReDam} + \frac{\mathrm{kReDamP53} \cdot [\mathrm{P53}]}{\mathrm{jDam} + [\mathrm{Dam}]}\right) \cdot [\mathrm{Dam}] \tag{14}$$

7 Rules

This is an overview of three rules.

7.1 Rule tP21

Rule tP21 is an assignment rule for species tP21:

$$\mathrm{tP21} = [\mathrm{P21}] + [\mathrm{CyP21}] + [\mathrm{iPcna}] + [\mathrm{iRc}] \quad (15)$$

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

7.2 Rule tCy

Rule tCy is an assignment rule for species tCy:

$$\mathrm{tCy} = [\mathrm{Cy}] + [\mathrm{CyP21}] \quad (16)$$

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

7.3 Rule tPcna

Rule tPcna is an assignment rule for species tPcna:

$$\mathrm{tPcna} = [\mathrm{aPcna}] + [\mathrm{iPcna}] + [\mathrm{aRc}] + [\mathrm{iRc}] \quad (17)$$

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

8 Reactions

This model contains 35 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	Synthesis_of_p21_mRNAs	Synthesis of p21 mRNAs	$\emptyset \longrightarrow \text{MrnaP21}$	
2	Synthesis_of_p21_mRNAs_by_p53	Synthesis of p21 mRNAs by p53	$\text{P53} \longrightarrow \text{MrnaP21} + \text{P53}$	
3	Synthesis_of_cyclin_mRNAs	Synthesis of cyclin mRNAs	$\emptyset \longrightarrow \text{MrnaCy}$	
4	Synthesis_of_p53_mRNAs	Synthesis of p53 mRNAs	$\emptyset \longrightarrow \text{MrnaP53}$	
5	Degradation_of_p21_mRNAs	Degradation of p21 mRNAs	$\text{MrnaP21} \longrightarrow \emptyset$	
6	Degradation_of_cyclin_mRNAs	Degradation of cyclin mRNAs	$\text{MrnaCy} \longrightarrow \emptyset$	
7	Degradation_of_p53_mRNAs	Degradation of p53 mRNAs	$\text{MrnaP53} \longrightarrow \emptyset$	
8	Synthesis_of_p21	Synthesis of p21	$\text{MrnaP21} \longrightarrow \text{MrnaP21} + \text{P21}$	
9	Degradation_of_p21	Degradation of p21	$\text{P21} \xrightarrow{\text{Skp2, Cy, Cdt2, aRc}} \emptyset$	
10	Synthesis_of_cyclins	Synthesis of cyclins	$\text{MrnaCy} \longrightarrow \text{MrnaCy} + \text{Cy}$	

№	Id	Name	Reaction Equation	SBO
11	Degradation_of-_cyclins	Degradation of cyclins	$\mathrm{Cy} \xrightarrow{\mathrm{Skp2,\ Cy}} \emptyset$	
12	Association-_and-_dissociation-_of_CDK2-_Cyclin_and_p21	Association and dissociation of CDK2:Cyclin and p21	$\mathrm{Cy} + \mathrm{P21} \rightleftharpoons \mathrm{CyP21}$	
13	Degradation-_of_cyclin_in-_CDK2_Cyclin-_p21_complexes	Degradation of cyclin in CDK2:Cyclin:p21 complexes	$\mathrm{CyP21} \xrightarrow{\mathrm{Skp2,\ Cy}} \mathrm{P21}$	
14	Degradation_of-_p21_in_CDK2-_Cyclin_p21-_complexes	Degradation of p21 in CDK2:Cyclin:p21 complexes	$\mathrm{CyP21} \xrightarrow{\mathrm{Skp2,\ Cy,\ Cdt2,\ aRc}} \mathrm{Cy}$	
15	Import_of-_active_PCNA	Import of active PCNA	$\emptyset \longrightarrow \mathrm{aPcna}$	
16	Export_of-_active_PCNA	Export of active PCNA	$\mathrm{aPcna} \longrightarrow \emptyset$	
17	Export_of-_inactive_PCNA	Export of inactive PCNA	$\mathrm{iPcna} \longrightarrow \mathrm{P21}$	
18	Association-_and-_dissociation-_of_PCNA_and_p21	Association and dissociation of PCNA and p21	$\mathrm{aPcna} + \mathrm{P21} \rightleftharpoons \mathrm{iPcna}$	

№	Id	Name	Reaction Equation	SBO
19	`Degradation_of_p21_in_PCNA_p21_complexes`	Degradation of p21 in PCNA:p21 complexes	$\mathrm{iPcna} \xrightarrow{\mathrm{Skp2,\ Cy,\ Cdt2,\ aRc}} \mathrm{aPcna}$	
20	`Phosphorylation_priming_of_replication_complexes`	Phosphorylation/priming of replication complexes	$\mathrm{Rc} \xrightarrow{\mathrm{Cy}} \mathrm{pRc}$	
21	`Dephosphorylation_of_replication_complexes`	Dephosphorylation of replication complexes	$\mathrm{pRc} \longrightarrow \mathrm{Rc}$	
22	`Association_and_dissociation_of_active_PCNA_and_replication_complexes`	Association and dissociation of active PCNA and replication complexes	$\mathrm{aPcna} + \mathrm{pRc} \rightleftharpoons \mathrm{aRc}$	
23	`Association_and_dissociation_of_inactive_PCNA_and_replication_complexes`	Association and dissociation of inactive PCNA and replication complexes	$\mathrm{iPcna} + \mathrm{pRc} \rightleftharpoons \mathrm{iRc}$	

№	Id	Name	Reaction Equation	SBO
24	`Association-_and-_dissociation-_of_p21_and-_replication-_complexes`	Association and dissociation of p21 and replication complexes	$\mathrm{aRc} + \mathrm{P21} \rightleftharpoons \mathrm{iRc}$	
25	`Degradation-_of_p21_in-_inactive-_replication-_complexes`	Degradation of p21 in inactive replication complexes	$\mathrm{iRc} \xrightarrow{\mathrm{Skp2,\ Cy,\ Cdt2,\ aRc}} \mathrm{aRc}$	
26	`Synthesis_of-_DNA`	Synthesis of DNA	$\mathrm{aRc} \longrightarrow \mathrm{aRc} + \mathrm{Dna}$	
27	`Dissassembly-_of_RC`	Dissassembly of RC	$\mathrm{Rc} \xrightarrow{\mathrm{Dna}} \emptyset$	
28	`Dissassembly-_of_pRC`	Dissassembly of pRC	$\mathrm{pRc} \xrightarrow{\mathrm{Dna}} \emptyset$	
29	`Dissassembly-_of_aRC`	Dissassembly of aRC	$\mathrm{aRc} \xrightarrow{\mathrm{Dna}} \mathrm{aPcna}$	
30	`Dissassembly-_of_iRC`	Dissassembly of iRC	$\mathrm{iRc} \xrightarrow{\mathrm{Dna}} \mathrm{iPcna}$	
31	`Synthesis_of-_p53`	Synthesis of p53	$\mathrm{MrnaP53} \longrightarrow \mathrm{MrnaP53} + \mathrm{P53}$	
32	`Degradation_of-_p53`	Degradation of p53	$\mathrm{P53} \xrightarrow{\mathrm{Dam}} \emptyset$	
33	`Induction_of-_DNA_damage`	Induction of DNA damage	$\emptyset \longrightarrow \mathrm{Dam}$	

№	Id	Name	Reaction Equation	SBO
34	`Induction_of_DNA_damage_by_replication`	Induction of DNA damage by replication	$\mathrm{aRc} \longrightarrow \mathrm{aRc} + \mathrm{Dam}$	
35	`Repair_of_DNA_damage`	Repair of DNA damage	$\mathrm{Dam} \xrightarrow{\mathrm{P53}} \emptyset$	

8.1 Reaction Synthesis_of_p21_mRNAs

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

Name Synthesis of p21 mRNAs

Reaction equation

$$\emptyset \longrightarrow \text{MrnaP21} \tag{18}$$

Product

Table 6: Properties of each product.

Id	Name	SBO
MrnaP21	MrnaP21	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{Cell}) \cdot \text{Constant\_flux\_\_irreversible}(\text{kSyMrna}) \tag{19}$$

$$\text{Constant\_flux\_\_irreversible}(\text{v}) = \text{v} \tag{20}$$

$$\text{Constant\_flux\_\_irreversible}(\text{v}) = \text{v} \tag{21}$$

8.2 Reaction Synthesis_of_p21_mRNAs_by_p53

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

Name Synthesis of p21 mRNAs by p53

Reaction equation

$$\text{P53} \longrightarrow \text{MrnaP21} + \text{P53} \tag{22}$$

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
P53	P53	

Products

Table 8: Properties of each product.

Id	Name	SBO
MrnaP21	MrnaP21	
P53	P53	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kSyMrnaP53} \cdot [\mathrm{P53}] \tag{23}$$

8.3 Reaction Synthesis_of_cyclin_mRNAs

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

Name Synthesis of cyclin mRNAs

Reaction equation

$$\emptyset \longrightarrow \mathrm{MrnaCy} \tag{24}$$

Product

Table 9: Properties of each product.

Id	Name	SBO
MrnaCy	MrnaCy	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{kSyMrna}\right) \tag{25}$$

$$\text{Constant\_flux\_\_irreversible}(\text{v}) = \text{v} \tag{26}$$

$$\text{Constant\_flux\_\_irreversible}(\text{v}) = \text{v} \tag{27}$$

8.4 Reaction `Synthesis_of_p53_mRNAs`

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

Name Synthesis of p53 mRNAs

Reaction equation

$$\emptyset \longrightarrow \text{MrnaP53} \tag{28}$$

Product

Table 10: Properties of each product.

Id	Name	SBO
`MrnaP53`	MrnaP53	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}(\text{Cell}) \cdot \text{Constant\_flux\_\_irreversible}(\text{kSyMrna}) \tag{29}$$

$$\text{Constant\_flux\_\_irreversible}(\text{v}) = \text{v} \tag{30}$$

$$\text{Constant\_flux\_\_irreversible}(\text{v}) = \text{v} \tag{31}$$

8.5 Reaction `Degradation_of_p21_mRNAs`

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

Name Degradation of p21 mRNAs

Reaction equation

$$\text{MrnaP21} \longrightarrow \emptyset \tag{32}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
MrnaP21	MrnaP21	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kDeMrna} \cdot [\mathrm{MrnaP21}] \tag{33}$$

8.6 Reaction Degradation_of_cyclin_mRNAs

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

Name Degradation of cyclin mRNAs

Reaction equation

$$\mathrm{MrnaCy} \longrightarrow \emptyset \tag{34}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
MrnaCy	MrnaCy	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kDeMrna} \cdot [\mathrm{MrnaCy}] \tag{35}$$

8.7 Reaction Degradation_of_p53_mRNAs

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

Name Degradation of p53 mRNAs

Reaction equation

$$\mathrm{MrnaP53} \longrightarrow \emptyset \tag{36}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
MrnaP53	MrnaP53	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kDeMrna} \cdot [\mathrm{MrnaP53}] \tag{37}$$

8.8 Reaction Synthesis_of_p21

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

Name Synthesis of p21

Reaction equation

$$\mathrm{MrnaP21} \longrightarrow \mathrm{MrnaP21} + \mathrm{P21} \tag{38}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
MrnaP21	MrnaP21	

Products

Table 15: Properties of each product.

Id	Name	SBO
MrnaP21	MrnaP21	
P21	P21	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{kSyP21} \cdot [\mathrm{MrnaP21}] \tag{39}$$

8.9 Reaction `Degradation_of_p21`

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

Name Degradation of p21

Reaction equation

$$\mathrm{P21} \xrightarrow{\mathrm{Skp2,\ Cy,\ Cdt2,\ aRc}} \emptyset \tag{40}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
`P21`	P21	

Modifiers

Table 17: Properties of each modifier.

Id	Name	SBO
`Skp2`	Skp2	
`Cy`	Cy	
`Cdt2`	Cdt2	
`aRc`	aRc	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{rDeP21\_1}\,([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{P21}], [\mathrm{Skp2}], [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}) \tag{41}$$

$$\begin{aligned}&\mathrm{rDeP21\_1}\,([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{P21}], [\mathrm{Skp2}], [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc})\\ &\quad = (\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]) \cdot [\mathrm{P21}]\end{aligned} \tag{42}$$

$$\begin{aligned}&\mathrm{rDeP21\_1}\left([\mathrm{Cdt2}],[\mathrm{Cy}],[\mathrm{P21}],[\mathrm{Skp2}],[\mathrm{aRc}],\mathrm{kDeP21},\mathrm{kDeP21Cy},\mathrm{kDeP21aRc}\right)\\&\quad=\left(\mathrm{kDeP21}+\mathrm{kDeP21Cy}\cdot[\mathrm{Skp2}]\cdot[\mathrm{Cy}]+\mathrm{kDeP21aRc}\cdot[\mathrm{Cdt2}]\cdot[\mathrm{aRc}]\right)\cdot[\mathrm{P21}]\end{aligned} \tag{43}$$

8.10 Reaction Synthesis_of_cyclins

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

Name Synthesis of cyclins

Reaction equation

$$\mathrm{MrnaCy} \longrightarrow \mathrm{MrnaCy} + \mathrm{Cy} \tag{44}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
MrnaCy	MrnaCy	

Products

Table 19: Properties of each product.

Id	Name	SBO
MrnaCy	MrnaCy	
Cy	Cy	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kSyCy} \cdot [\mathrm{MrnaCy}] \tag{45}$$

8.11 Reaction Degradation_of_cyclins

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

Name Degradation of cyclins

Reaction equation

$$\mathrm{Cy} \xrightarrow{\mathrm{Skp2},\ \mathrm{Cy}} \emptyset \tag{46}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
Cy	Cy	

Modifiers

Table 21: Properties of each modifier.

Id	Name	SBO
Skp2	Skp2	
Cy	Cy	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{rDeCy\_1}([\mathrm{Cy}], [\mathrm{Skp2}], \mathrm{kDeCy}, \mathrm{kDeCyCy}) \tag{47}$$

$$\mathrm{rDeCy\_1}([\mathrm{Cy}], [\mathrm{Skp2}], \mathrm{kDeCy}, \mathrm{kDeCyCy}) = (\mathrm{kDeCy} + \mathrm{kDeCyCy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}]) \cdot [\mathrm{Cy}] \tag{48}$$

$$\mathrm{rDeCy\_1}([\mathrm{Cy}], [\mathrm{Skp2}], \mathrm{kDeCy}, \mathrm{kDeCyCy}) = (\mathrm{kDeCy} + \mathrm{kDeCyCy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}]) \cdot [\mathrm{Cy}] \tag{49}$$

8.12 Reaction `Association_and_dissociation_of_CDK2_Cyclin_and_p21`

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

Name Association and dissociation of CDK2:Cyclin and p21

Reaction equation

$$\mathrm{Cy} + \mathrm{P21} \rightleftharpoons \mathrm{CyP21} \tag{50}$$

Reactants

Table 22: Properties of each reactant.

Id	Name	SBO
Cy	Cy	
P21	P21	

Product

Table 23: Properties of each product.

Id	Name	SBO
CyP21	CyP21	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \left(\mathrm{kAsCyP21} \cdot [\mathrm{Cy}] \cdot [\mathrm{P21}] - \mathrm{kDsCyP21} \cdot [\mathrm{CyP21}]\right) \tag{51}$$

8.13 Reaction Degradation_of_cyclin_in_CDK2_Cyclin_p21_complexes

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

Name Degradation of cyclin in CDK2:Cyclin:p21 complexes

Reaction equation

$$\mathrm{CyP21} \xrightarrow{\mathrm{Skp2,\ Cy}} \mathrm{P21} \tag{52}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
CyP21	CyP21	

Modifiers

Table 25: Properties of each modifier.

Id	Name	SBO
Skp2	Skp2	
Cy	Cy	

Product

Table 26: Properties of each product.

Id	Name	SBO
P21	P21	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{rDeCy\_2}\,([\mathrm{Cy}], [\mathrm{CyP21}], [\mathrm{Skp2}], \mathrm{kDeCy}, \mathrm{kDeCyCy}) \tag{53}$$

$$\begin{aligned} &\mathrm{rDeCy\_2}\,([\mathrm{Cy}], [\mathrm{CyP21}], [\mathrm{Skp2}], \mathrm{kDeCy}, \mathrm{kDeCyCy}) \\ &= (\mathrm{kDeCy} + \mathrm{kDeCyCy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}]) \cdot [\mathrm{CyP21}] \end{aligned} \tag{54}$$

$$\begin{aligned} &\mathrm{rDeCy\_2}\,([\mathrm{Cy}], [\mathrm{CyP21}], [\mathrm{Skp2}], \mathrm{kDeCy}, \mathrm{kDeCyCy}) \\ &= (\mathrm{kDeCy} + \mathrm{kDeCyCy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}]) \cdot [\mathrm{CyP21}] \end{aligned} \tag{55}$$

8.14 Reaction `Degradation_of_p21_in_CDK2_Cyclin_p21_complexes`

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

Name Degradation of p21 in CDK2:Cyclin:p21 complexes

Reaction equation

$$\mathrm{CyP21} \xrightarrow{\mathrm{Skp2},\ \mathrm{Cy},\ \mathrm{Cdt2},\ \mathrm{aRc}} \mathrm{Cy} \tag{56}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
CyP21	CyP21	

Modifiers

Table 28: Properties of each modifier.

Id	Name	SBO
Skp2	Skp2	
Cy	Cy	
Cdt2	Cdt2	
aRc	aRc	

Product

Table 29: Properties of each product.

Id	Name	SBO
Cy	Cy	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDeP21\_2}\left([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{CyP21}], [\mathrm{Skp2}], [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \tag{57}$$

$$\mathrm{rDeP21\_2}\left([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{CyP21}], [\mathrm{Skp2}], [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) = \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{CyP21}] \tag{58}$$

$$\mathrm{rDeP21\_2}\left([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{CyP21}], [\mathrm{Skp2}], [\mathrm{aRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) = \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{CyP21}] \tag{59}$$

8.15 Reaction `Import_of_active_PCNA`

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

Name Import of active PCNA

Reaction equation

$$\emptyset \longrightarrow \text{aPcna} \tag{60}$$

Product

Table 30: Properties of each product.

Id	Name	SBO
aPcna	aPcna	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \text{vol}(\text{Cell}) \cdot \text{Constant\_flux\_\_irreversible}(\text{kImPc}) \tag{61}$$

$$\text{Constant\_flux\_\_irreversible}(\text{v}) = \text{v} \tag{62}$$

$$\text{Constant\_flux\_\_irreversible}(\text{v}) = \text{v} \tag{63}$$

8.16 Reaction Export_of_active_PCNA

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

Name Export of active PCNA

Reaction equation

$$\text{aPcna} \longrightarrow \emptyset \tag{64}$$

Reactant

Table 31: Properties of each reactant.

Id	Name	SBO
aPcna	aPcna	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{kExPc} \cdot [\mathrm{aPcna}] \tag{65}$$

8.17 Reaction Export_of_inactive_PCNA

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

Name Export of inactive PCNA

Reaction equation

$$\mathrm{iPcna} \longrightarrow \mathrm{P21} \tag{66}$$

Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
iPcna	iPcna	

Product

Table 33: Properties of each product.

Id	Name	SBO
P21	P21	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{kExPc} \cdot [\mathrm{iPcna}] \tag{67}$$

8.18 Reaction Association_and_dissociation_of_PCNA_and_p21

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

Name Association and dissociation of PCNA and p21

Reaction equation

$$\mathrm{aPcna} + \mathrm{P21} \rightleftharpoons \mathrm{iPcna} \tag{68}$$

Reactants

Table 34: Properties of each reactant.

Id	Name	SBO
aPcna	aPcna	
P21	P21	

Product

Table 35: Properties of each product.

Id	Name	SBO
iPcna	iPcna	

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \left(\mathrm{kAsPcP21} \cdot [\mathrm{aPcna}] \cdot [\mathrm{P21}] - \mathrm{kDsPcP21} \cdot [\mathrm{iPcna}]\right) \tag{69}$$

8.19 Reaction Degradation_of_p21_in_PCNA_p21_complexes

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

Name Degradation of p21 in PCNA:p21 complexes

Reaction equation

$$\mathrm{iPcna} \xrightarrow{\mathrm{Skp2,\ Cy,\ Cdt2,\ aRc}} \mathrm{aPcna} \tag{70}$$

Reactant

Table 36: Properties of each reactant.

Id	Name	SBO
iPcna	iPcna	

Modifiers

Table 37: Properties of each modifier.

Id	Name	SBO
Skp2	Skp2	
Cy	Cy	
Cdt2	Cdt2	
aRc	aRc	

Product

Table 38: Properties of each product.

Id	Name	SBO
aPcna	aPcna	

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDeP21\_3}\left([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{Skp2}], [\mathrm{aRc}], [\mathrm{iPcna}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \tag{71}$$

$$\begin{aligned} &\mathrm{rDeP21\_3}\left([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{Skp2}], [\mathrm{aRc}], [\mathrm{iPcna}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \\ &\quad = (\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]) \cdot [\mathrm{iPcna}] \end{aligned} \tag{72}$$

$$\begin{aligned} &\mathrm{rDeP21\_3}\left([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{Skp2}], [\mathrm{aRc}], [\mathrm{iPcna}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \\ &\quad = (\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]) \cdot [\mathrm{iPcna}] \end{aligned} \tag{73}$$

8.20 Reaction Phosphorylation_priming_of_replication_complexes

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

Name Phosphorylation/priming of replication complexes

Reaction equation

$$\mathrm{Rc} \xrightarrow{\mathrm{Cy}} \mathrm{pRc} \tag{74}$$

Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
`Rc`	Rc	

Modifier

Table 40: Properties of each modifier.

Id	Name	SBO
`Cy`	Cy	

Product

Table 41: Properties of each product.

Id	Name	SBO
`pRc`	pRc	

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rPhRc\_1}\left([\mathrm{Cy}], [\mathrm{Rc}], \mathrm{jCy}, \mathrm{kPhRc}, \mathrm{n}\right) \tag{75}$$

$$\mathrm{rPhRc\_1}\left([\mathrm{Cy}], [\mathrm{Rc}], \mathrm{jCy}, \mathrm{kPhRc}, \mathrm{n}\right) = \frac{\mathrm{kPhRc} \cdot [\mathrm{Cy}]^{\mathrm{n}}}{\mathrm{jCy}^{\mathrm{n}} + [\mathrm{Cy}]^{\mathrm{n}}} \cdot [\mathrm{Rc}] \tag{76}$$

$$\mathrm{rPhRc\_1}\left([\mathrm{Cy}], [\mathrm{Rc}], \mathrm{jCy}, \mathrm{kPhRc}, \mathrm{n}\right) = \frac{\mathrm{kPhRc} \cdot [\mathrm{Cy}]^{\mathrm{n}}}{\mathrm{jCy}^{\mathrm{n}} + [\mathrm{Cy}]^{\mathrm{n}}} \cdot [\mathrm{Rc}] \tag{77}$$

8.21 Reaction `Dephosphorylation_of_replication_complexes`

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

Name Dephosphorylation of replication complexes

Reaction equation

$$\mathrm{pRc} \longrightarrow \mathrm{Rc} \tag{78}$$

Reactant

Table 42: Properties of each reactant.

Id	Name	SBO
pRc	pRc	

Product

Table 43: Properties of each product.

Id	Name	SBO
Rc	Rc	

Kinetic Law

Derived unit contains undeclared units

$$v_{21} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kDpRc} \cdot [\mathrm{pRc}] \tag{79}$$

8.22 Reaction Association_and_dissociation_of_active_PCNA_and_replication_complexes

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

Name Association and dissociation of active PCNA and replication complexes

Reaction equation

$$\mathrm{aPcna} + \mathrm{pRc} \rightleftharpoons \mathrm{aRc} \tag{80}$$

Reactants

Table 44: Properties of each reactant.

Id	Name	SBO
aPcna	aPcna	
pRc	pRc	

Product

Table 45: Properties of each product.

Id	Name	SBO
aRc	aRc	

Kinetic Law

Derived unit contains undeclared units

$$v_{22} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \left(\mathrm{kAsRcPc} \cdot [\mathrm{aPcna}] \cdot [\mathrm{pRc}] - \mathrm{kDsRcPc} \cdot [\mathrm{aRc}]\right) \tag{81}$$

8.23 Reaction Association_and_dissociation_of_inactive_PCNA_and_replication_complexes

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

Name Association and dissociation of inactive PCNA and replication complexes

Reaction equation

$$\mathrm{iPcna} + \mathrm{pRc} \rightleftharpoons \mathrm{iRc} \tag{82}$$

Reactants

Table 46: Properties of each reactant.

Id	Name	SBO
iPcna	iPcna	
pRc	pRc	

Product

Table 47: Properties of each product.

Id	Name	SBO
iRc	iRc	

Kinetic Law

Derived unit contains undeclared units

$$v_{23} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \left(\mathrm{kAsRcPc} \cdot [\mathrm{iPcna}] \cdot [\mathrm{pRc}] - \mathrm{kDsRcPc} \cdot [\mathrm{iRc}]\right) \tag{83}$$

8.24 Reaction `Association_and_dissociation_of_p21_and_replication_complexes`

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

Name Association and dissociation of p21 and replication complexes

Reaction equation

$$\mathrm{aRc} + \mathrm{P21} \rightleftharpoons \mathrm{iRc} \tag{84}$$

Reactants

Table 48: Properties of each reactant.

Id	Name	SBO
`aRc`	aRc	
`P21`	P21	

Product

Table 49: Properties of each product.

Id	Name	SBO
`iRc`	iRc	

Kinetic Law

Derived unit contains undeclared units

$$v_{24} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \left(\mathrm{kAsPcP21} \cdot [\mathrm{aRc}] \cdot [\mathrm{P21}] - \mathrm{kDsPcP21} \cdot [\mathrm{iRc}]\right) \tag{85}$$

8.25 Reaction `Degradation_of_p21_in_inactive_replication_complexes`

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

Name Degradation of p21 in inactive replication complexes

Reaction equation

$$\mathrm{iRc} \xrightarrow{\mathrm{Skp2,\ Cy,\ Cdt2,\ aRc}} \mathrm{aRc} \tag{86}$$

Reactant

Table 50: Properties of each reactant.

Id	Name	SBO
iRc	iRc	

Modifiers

Table 51: Properties of each modifier.

Id	Name	SBO
Skp2	Skp2	
Cy	Cy	
Cdt2	Cdt2	
aRc	aRc	

Product

Table 52: Properties of each product.

Id	Name	SBO
aRc	aRc	

Kinetic Law

Derived unit contains undeclared units

$$v_{25} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDeP21\_4}\left([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{Skp2}], [\mathrm{aRc}], [\mathrm{iRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \tag{87}$$

$$\begin{aligned} &\mathrm{rDeP21\_4}\left([\mathrm{Cdt2}], [\mathrm{Cy}], [\mathrm{Skp2}], [\mathrm{aRc}], [\mathrm{iRc}], \mathrm{kDeP21}, \mathrm{kDeP21Cy}, \mathrm{kDeP21aRc}\right) \\ &\quad = \left(\mathrm{kDeP21} + \mathrm{kDeP21Cy} \cdot [\mathrm{Skp2}] \cdot [\mathrm{Cy}] + \mathrm{kDeP21aRc} \cdot [\mathrm{Cdt2}] \cdot [\mathrm{aRc}]\right) \cdot [\mathrm{iRc}] \end{aligned} \tag{88}$$

$$
\begin{aligned}
&\text{rDeP21\_4}\left([\text{Cdt2}], [\text{Cy}], [\text{Skp2}], [\text{aRc}], [\text{iRc}], \text{kDeP21}, \text{kDeP21Cy}, \text{kDeP21aRc}\right) \\
&\quad = (\text{kDeP21} + \text{kDeP21Cy} \cdot [\text{Skp2}] \cdot [\text{Cy}] + \text{kDeP21aRc} \cdot [\text{Cdt2}] \cdot [\text{aRc}]) \cdot [\text{iRc}]
\end{aligned}
\tag{89}
$$

8.26 Reaction Synthesis_of_DNA

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

Name Synthesis of DNA

Reaction equation

$$\text{aRc} \longrightarrow \text{aRc} + \text{Dna} \tag{90}$$

Reactant

Table 53: Properties of each reactant.

Id	Name	SBO
aRc	aRc	

Products

Table 54: Properties of each product.

Id	Name	SBO
aRc	aRc	
Dna	Dna	

Kinetic Law

Derived unit contains undeclared units

$$v_{26} = \text{vol}\left(\text{Cell}\right) \cdot \text{kSyDna} \cdot [\text{aRc}] \tag{91}$$

8.27 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

$$\mathrm{Rc} \xrightarrow{\mathrm{Dna}} \emptyset \tag{92}$$

Reactant

Table 55: Properties of each reactant.

Id	Name	SBO
Rc	Rc	

Modifier

Table 56: Properties of each modifier.

Id	Name	SBO
Dna	Dna	

Kinetic Law

Derived unit contains undeclared units

$$v_{27} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDsRc}\left([\mathrm{Dna}], [\mathrm{Rc}]\right) \tag{93}$$

$$\mathrm{rDsRc}\left([\mathrm{Dna}], [\mathrm{Rc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{Rc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{Rc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{94}$$

$$\mathrm{rDsRc}\left([\mathrm{Dna}], [\mathrm{Rc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{Rc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{Rc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{95}$$

8.28 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

$$\mathrm{pRc} \xrightarrow{\mathrm{Dna}} \emptyset \tag{96}$$

Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
pRc	pRc	

Modifier

Table 58: Properties of each modifier.

Id	Name	SBO
Dna	Dna	

Kinetic Law

Derived unit contains undeclared units

$$v_{28} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDsRc\_1}\left([\mathrm{Dna}], [\mathrm{pRc}]\right) \tag{97}$$

$$\mathrm{rDsRc\_1}\left([\mathrm{Dna}], [\mathrm{pRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{pRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{pRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{98}$$

$$\mathrm{rDsRc\_1}\left([\mathrm{Dna}], [\mathrm{pRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{pRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{pRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{99}$$

8.29 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

$$\mathrm{aRc} \xrightarrow{\mathrm{Dna}} \mathrm{aPcna} \tag{100}$$

Reactant

Table 59: Properties of each reactant.

Id	Name	SBO
aRc	aRc	

Modifier

Table 60: Properties of each modifier.

Id	Name	SBO
Dna	Dna	

Product

Table 61: Properties of each product.

Id	Name	SBO
aPcna	aPcna	

Kinetic Law

Derived unit contains undeclared units

$$v_{29} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDsRc\_2}\left([\mathrm{Dna}], [\mathrm{aRc}]\right) \tag{101}$$

$$\mathrm{rDsRc\_2}\left([\mathrm{Dna}], [\mathrm{aRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{aRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{aRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{102}$$

$$\mathrm{rDsRc\_2}\left([\mathrm{Dna}], [\mathrm{aRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{aRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{aRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{103}$$

8.30 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

$$\mathrm{iRc} \xrightarrow{\mathrm{Dna}} \mathrm{iPcna} \tag{104}$$

Reactant

Table 62: Properties of each reactant.

Id	Name	SBO
iRc	iRc	

Modifier

Table 63: Properties of each modifier.

Id	Name	SBO
Dna	Dna	

Product

Table 64: Properties of each product.

Id	Name	SBO
iPcna	iPcna	

Kinetic Law

Derived unit contains undeclared units

$$v_{30} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{rDsRc\_3}\left([\mathrm{Dna}], [\mathrm{iRc}]\right) \tag{105}$$

$$\mathrm{rDsRc\_3}\left([\mathrm{Dna}], [\mathrm{iRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{iRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{iRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{106}$$

$$\mathrm{rDsRc\_3}\left([\mathrm{Dna}], [\mathrm{iRc}]\right) = \begin{cases} 0 & \text{if } [\mathrm{Dna}] < 1 \\ \begin{cases} 1 \cdot [\mathrm{iRc}] & \text{if } [\mathrm{Dna}] > 1 \\ 0.5 \cdot [\mathrm{iRc}] & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{107}$$

8.31 Reaction `Synthesis_of_p53`

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

Name Synthesis of p53

Reaction equation

$$\mathrm{MrnaP53} \longrightarrow \mathrm{MrnaP53} + \mathrm{P53} \tag{108}$$

Reactant

Table 65: Properties of each reactant.

Id	Name	SBO
`MrnaP53`	MrnaP53	

Products

Table 66: Properties of each product.

Id	Name	SBO
`MrnaP53`	MrnaP53	
`P53`	P53	

Kinetic Law

Derived unit contains undeclared units

$$v_{31} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{kSyP53} \cdot [\mathrm{MrnaP53}] \tag{109}$$

8.32 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

$$\mathrm{P53} \xrightarrow{\mathrm{Dam}} \emptyset \tag{110}$$

Reactant

Table 67: Properties of each reactant.

Id	Name	SBO
P53	P53	

Modifier

Table 68: Properties of each modifier.

Id	Name	SBO
Dam	Dam	

Kinetic Law

Derived unit contains undeclared units

$$v_{32} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{rDeP53\_1}\,([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jP53}, \mathrm{kDeP53}) \tag{111}$$

$$\mathrm{rDeP53\_1}\,([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jP53}, \mathrm{kDeP53}) = \frac{\mathrm{kDeP53}}{\mathrm{jP53} + [\mathrm{Dam}]} \cdot [\mathrm{P53}] \tag{112}$$

$$\mathrm{rDeP53\_1}\,([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jP53}, \mathrm{kDeP53}) = \frac{\mathrm{kDeP53}}{\mathrm{jP53} + [\mathrm{Dam}]} \cdot [\mathrm{P53}] \tag{113}$$

8.33 Reaction `Induction_of_DNA_damage`

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

Name Induction of DNA damage

Reaction equation

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

Product

Table 69: Properties of each product.

Id	Name	SBO
Dam	Dam	

Kinetic Law

Derived unit contains undeclared units

$$v_{33} = \mathrm{vol}\left(\mathrm{Cell}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{kGeDam}\right) \tag{115}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{116}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{117}$$

8.34 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

$$\mathrm{aRc} \longrightarrow \mathrm{aRc} + \mathrm{Dam} \tag{118}$$

Reactant

Table 70: Properties of each reactant.

Id	Name	SBO
aRc	aRc	

Products

Table 71: Properties of each product.

Id	Name	SBO
aRc	aRc	
Dam	Dam	

Kinetic Law

Derived unit contains undeclared units

$$v_{34} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{kGeDamArc} \cdot [\mathrm{aRc}] \tag{119}$$

8.35 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

$$\mathrm{Dam} \xrightarrow{\mathrm{P53}} \emptyset \tag{120}$$

Reactant

Table 72: Properties of each reactant.

Id	Name	SBO
`Dam`	Dam	

Modifier

Table 73: Properties of each modifier.

Id	Name	SBO
`P53`	P53	

Kinetic Law

Derived unit contains undeclared units

$$v_{35} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{rReDam\_1}\,([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jDam}, \mathrm{kReDam}, \mathrm{kReDamP53}) \tag{121}$$

$$\begin{aligned} &\mathrm{rReDam\_1}\,([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jDam}, \mathrm{kReDam}, \mathrm{kReDamP53}) \\ &= \left(\mathrm{kReDam} + \frac{\mathrm{kReDamP53} \cdot [\mathrm{P53}]}{\mathrm{jDam} + [\mathrm{Dam}]}\right) \cdot [\mathrm{Dam}] \end{aligned} \tag{122}$$

$$\begin{aligned} &\mathrm{rReDam\_1}\left([\mathrm{Dam}], [\mathrm{P53}], \mathrm{jDam}, \mathrm{kReDam}, \mathrm{kReDamP53}\right) \\ &= \left(\mathrm{kReDam} + \frac{\mathrm{kReDamP53} \cdot [\mathrm{P53}]}{\mathrm{jDam} + [\mathrm{Dam}]}\right) \cdot [\mathrm{Dam}] \end{aligned} \tag{123}$$

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 `MrnaP21`

Name MrnaP21

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

This species takes part in five reactions (as a reactant in `Degradation_of_p21_mRNAs`, `Synthesis_of_p21` and as a product in `Synthesis_of_p21_mRNAs`, `Synthesis_of_p21_mRNAs_by_p53`, `Synthesis_of_p21`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MrnaP21} = v_1 + v_2 + v_8 - v_5 - v_8 \tag{124}$$

9.2 Species `MrnaCy`

Name MrnaCy

Notes `mRNAs encoding for both CyclinA:Cdk2 and CyclinE:Cdk2 complexes`

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

This species takes part in four reactions (as a reactant in `Degradation_of_cyclin_mRNAs`, `Synthesis_of_cyclins` and as a product in `Synthesis_of_cyclin_mRNAs`, `Synthesis_of_cyclins`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MrnaCy} = v_3 + v_{10} - v_6 - v_{10} \tag{125}$$

9.3 Species MrnaP53

Name MrnaP53

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

This species takes part in four reactions (as a reactant in Degradation_of_p53_mRNAs, Synthesis_of_p53 and as a product in Synthesis_of_p53_mRNAs, Synthesis_of_p53).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MrnaP53} = v_4 + v_{31} - v_7 - v_{31} \tag{126}$$

9.4 Species P21

Name P21

Initial concentration $0.72 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in seven reactions (as a reactant in Degradation_of_p21, Association_and_dissociation_of_CDK2_Cyclin_and_p21, Association_and_dissociation_of_PCNA_and_p21, Association_and_dissociation_of_p21_and_replication_complexes and as a product in Synthesis_of_p21, Degradation_of_cyclin_in_CDK2_Cyclin_p21_complexes, Export_of_inactive_PCNA).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P21} = v_8 + v_{13} + v_{17} - v_9 - v_{12} - v_{18} - v_{24} \tag{127}$$

9.5 Species Cy

Name Cy

Notes `Both CyclinA:Cdk2 and CyclinE:Cdk2 complexes`

Initial concentration $0.4 \text{ mmol} \cdot \text{ml}^{-1}$

This species takes part in eleven reactions (as a reactant in Degradation_of_cyclins, Association_and_dissociation_of_CDK2_Cyclin_and_p21 and as a product in Synthesis_of_cyclins, Degradation_of_p21_in_CDK2_Cyclin_p21_complexes and as a modifier in Degradation_of_p21, Degradation_of_cyclins, Degradation_of_cyclin_in_CDK2_Cyclin_p21_complexes, Degradation_of_p21_in_CDK2_Cyclin_p21_complexes, Degradation_of_p21_in_PCNA_p21_complexes, Phosphorylation_priming_of_replication_complexes, Degradation_of_p21_in_inactive_replication_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Cy} = v_{10} + v_{14} - v_{11} - v_{12} \tag{128}$$

9.6 Species CyP21

Name CyP21

Notes Both CyclinA:Cdk2:p21 and CyclinE:Cdk2:p21 complexes

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

This species takes part in three reactions (as a reactant in Degradation_of_cyclin_in_CDK2_Cyclin_p21_complexes, Degradation_of_p21_in_CDK2_Cyclin_p21_complexes and as a product in Association_and_dissociation_of_CDK2_Cyclin_and_p21).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CyP21} = v_{12} - v_{13} - v_{14} \tag{129}$$

9.7 Species aPcna

Name aPcna

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

This species takes part in six reactions (as a reactant in Export_of_active_PCNA, Association_and_dissociation_of_PCNA_and_p21, Association_and_dissociation_of_active_PCNA_and_replication_complexes and as a product in Import_of_active_PCNA, Degradation_of_p21_in_PCNA_p21_complexes, Dissassembly_of_aRC).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{aPcna} = v_{15} + v_{19} + v_{29} - v_{16} - v_{18} - v_{22} \tag{130}$$

9.8 Species Rc

Name Rc

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Rc} = v_{21} - v_{20} - v_{27} \tag{131}$$

9.9 Species pRc

Name pRc

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pRc} = v_{20} - v_{21} - v_{22} - v_{23} - v_{28} \tag{132}$$

9.10 Species aRc

Name aRc

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

This species takes part in twelve reactions (as a reactant in Association_and_dissociation_of_p21_and_replication_complexes, Synthesis_of_DNA, Dissassembly_of_aRC, Induction_of_DNA_damage_by_replication and as a product in Association_and_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, Degradation_of_p21_in_CDK2_Cyclin_p21_complexes, Degradation_of_p21_in_PCNA_p21_complexes, Degradation_of_p21_in_inactive_replication_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{aRc} = v_{22} + v_{25} + v_{26} + v_{34} - v_{24} - v_{26} - v_{29} - v_{34} \tag{133}$$

9.11 Species iRc

Name iRc

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

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_and_dissociation_of_inactive_PCNA_and_replication_complexes, Association_and_dissociation_of_p21_and_replication_complexes).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{iRc} = v_{23} + v_{24} - v_{25} - v_{30} \tag{134}$$

9.12 Species Dna

Name Dna

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

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Dna} = v_{26} \tag{135}$$

9.13 Species Dam

Name Dam

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Dam} = v_{33} + v_{34} - v_{35} \tag{136}$$

9.14 Species P53

Name P53

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

This species takes part in five reactions (as a reactant in Synthesis_of_p21_mRNAs_by_p53, Degradation_of_p53 and as a product in Synthesis_of_p21_mRNAs_by_p53, Synthesis_of_p53 and as a modifier in Repair_of_DNA_damage).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P53} = v_{2} + v_{31} - v_{2} - v_{32} \tag{137}$$

9.15 Species Skp2

Name Skp2

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

This species takes part in six reactions (as a modifier in Degradation_of_p21, Degradation_of_cyclins, Degradation_of_cyclin_in_CDK2_Cyclin_p21_complexes, Degradation_of_p21_in_CDK2_Cyclin_p21_complexes, Degradation_of_p21_in_PCNA_p21_complexes, Degradation_of_p21_in_inactive_replication_complexes), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Skp2} = 0 \tag{138}$$

9.16 Species Cdt2

Name Cdt2

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

This species takes part in four reactions (as a modifier in Degradation_of_p21, Degradation_of_p21_in_CDK2_Cyclin_p21_complexes, Degradation_of_p21_in_PCNA_p21_complexes, Degradation_of_p21_in_inactive_replication_complexes), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{Cdt2} = 0 \tag{139}$$

9.17 Species iPcna

Name iPcna

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

This species takes part in five reactions (as a reactant in Export_of_inactive_PCNA, Degradation_of_p21_in_PCNA_p21_complexes, Association_and_dissociation_of_inactive_PCNA_and_replication_complexes and as a product in Association_and_dissociation_of_PCNA_and_p21, Dissassembly_of_iRC).

$$\frac{d}{dt}\text{iPcna} = v_{18} + v_{30} - v_{17} - v_{19} - v_{23} \tag{140}$$

9.18 Species tP21

Name tP21

Initial concentration $0.72 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule tP21

One rule determines the species' quantity.

9.19 Species tCy

Name tCy

Notes `Total level of both CyclinA:Cdk2 and CyclinE:Cdk2 complexes`

Initial concentration $0.4 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule tCy

One rule determines the species' quantity.

9.20 Species tPcna

Name tPcna

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

Involved in rule tPcna

One rule determines the species' quantity.

SBML2LaTeX was developed by Andreas Dräger[a], Hannes Planatscher[a], Dieudonné M Wouamba[a], Adrian Schröder[a], Michael Hucka[b], Lukas Endler[c], Martin Golebiewski[d] and Andreas Zell[a]. Please see http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX for more information.

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany