SBML Model Report

Model name: “Proctor2008 - p53/Mdm2 circuit - p53 stabilisation by ATM”

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following three authors: Carole Proctor[1], Vijayalakshmi Chelliah[2] and Douglas A Gray[3] at September first 2008 at 11:45 a. m. and last time modified at April eighth 2016 at 3:43 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	20
events	2	constraints	0
reactions	20	function definitions	0
global parameters	21	unit definitions	5
rules	2	initial assignments	0

Model Notes

Proctor2008 - p53/Mdm2 circuit - p53 stabilisation by ATM

This model is described in the article:Explaining oscillations and variability in the p53-Mdm2 system.Proctor CJ, Gray DA.BMC Syst Biol 2008; 2: 75

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Abstract:

BACKGROUND: In individual living cells p53 has been found to be expressed in a series of discrete pulses after DNA damage. Its negative regulator Mdm2 also demonstrates oscillatory behaviour. Attempts have been made recently to explain this behaviour by mathematical models but these have not addressed explicit molecular mechanisms. We describe two stochastic mechanistic models of the p53/Mdm2 circuit and show that sustained oscillations result directly from the key biological features, without assuming complicated mathematical functions or requiring more than one feedback loop. Each model examines a different mechanism for providing a negative feedback loop which results in p53 activation after DNA damage. The first model (ARF model) looks at the mechanism of p14ARF which sequesters Mdm2 and leads to stabilisation of p53. The second model (ATM model) examines the mechanism of ATM activation which leads to phosphorylation of both p53 and Mdm2 and increased degradation of Mdm2, which again results in p53 stabilisation. The models can readily be modified as further information becomes available, and linked to other models of cellular ageing. RESULTS: The ARF model is robust to changes in its parameters and predicts undamped oscillations after DNA damage so long as the signal persists. It also predicts that if there is a gradual accumulation of DNA damage, such as may occur in ageing, oscillations break out once a threshold level of damage is acquired. The ATM model requires an additional step for p53 synthesis for sustained oscillations to develop. The ATM model shows much more variability in the oscillatory behaviour and this variability is observed over a wide range of parameter values. This may account for the large variability seen in the experimental data which so far has examined ARF negative cells. CONCLUSION: The models predict more regular oscillations if ARF is present and suggest the need for further experiments in ARF positive cells to test these predictions. Our work illustrates the importance of systems biology approaches to understanding the complex role of p53 in both ageing and cancer.

This model is hosted on BioModels Database and identified by: BIOMD0000000188.

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models.

2 Unit Definitions

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

2.1 Unit `molepsecpdGy`

Name molepsecpdGy

Definition $\mathrm{mol} \cdot \mathrm{s}^{-1} \cdot (10\ \mathrm{Gy})^{-1}$

2.2 Unit `decagray`

Name dGy

Definition 10 Gy

2.3 Unit `molepsec`

Name molpsec

Definition $\mathrm{mol} \cdot \mathrm{s}^{-1}$

2.4 Unit `pmolepsec`

Name pmolpsec

Definition $\mathrm{mol}^{-1} \cdot \mathrm{s}^{-1}$

2.5 Unit `psec`

Name psec

Definition s^{-1}

2.6 Unit `substance`

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

Definition mol

2.7 Unit `volume`

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

Definition l

2.8 Unit `area`

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

Definition m^2

2.9 Unit `length`

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

Definition m

2.10 Unit `time`

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

Definition s

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

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

3.1 Compartment `cell`

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

4 Species

This model contains 20 species. The boundary condition of two 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
Mdm2		cell	mol	☐	☐
p53		cell	mol	☐	☐
Mdm2_p53		cell	mol	☐	☐
Mdm2_mRNA		cell	mol	☐	☐
p53_mRNA		cell	mol	☐	☐
ATMA		cell	mol	☐	☐
ATMI		cell	mol	☐	☐
p53_P		cell	mol	☐	☐
Mdm2_P		cell	mol	☐	☐
damDNA		cell	mol	☐	☐
Sink		cell	mol	☑	☑
Source		cell	mol	☑	☑
p53deg		cell	mol	☐	☐
p53syn		cell	mol	☐	☐
mdm2deg		cell	mol	☐	☐
mdm2syn		cell	mol	☐	☐
Mdm2mRNAdeg		cell	mol	☐	☐
Mdm2mRNAsyn		cell	mol	☐	☐
totp53		cell	mol	☐	☐
totMdm2		cell	mol	☐	☐

5 Parameters

This model contains 21 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
IR			0.000	10 Gy	☐
ksynMdm2			$4.95 \cdot 10^{-4}$	s^{-1}	☑
kdegMdm2			$4.33 \cdot 10^{-4}$	s^{-1}	☑
ksynp53			0.006	s^{-1}	☑
kdegp53			$8.25 \cdot 10^{-4}$	s^{-1}	☑
kbinMdm2p53			0.001	$mol^{-1} \cdot s^{-1}$	☑
krelMdm2p53			$1.155 \cdot 10^{-5}$	s^{-1}	☑
ksynMdm2mRNA			10^{-4}	s^{-1}	☑
kdegMdm2mRNA			10^{-4}	s^{-1}	☑
kactATM			10^{-4}	$mol^{-1} \cdot s^{-1}$	☑
kdegATMMdm2			$4 \cdot 10^{-4}$	s^{-1}	☑
kinactATM			$5 \cdot 10^{-4}$	s^{-1}	☑
kphosp53			$5 \cdot 10^{-4}$	$mol^{-1} \cdot s^{-1}$	☑
kdephosp53			0.500	s^{-1}	☑
kphosMdm2			2.000	$mol^{-1} \cdot s^{-1}$	☑
kdephosMdm2			0.500	s^{-1}	☑
kdam			0.080	$mol \cdot s^{-1} \cdot (10\,Gy)^{-1}$	☑
krepair			$2 \cdot 10^{-5}$	s^{-1}	☑
kproteff			1.000	dimensionless	☑
ksynp53mRNA			0.001	s^{-1}	☑
kdegp53mRNA			10^{-4}	s^{-1}	☑

6 Rules

This is an overview of two rules.

6.1 Rule totp53

Rule totp53 is an assignment rule for species totp53:

$$[\text{totp53}] = \text{p53} + \text{Mdm2\_p53} + \text{p53\_P} \tag{1}$$

Derived unit mol

6.2 Rule totMdm2

Rule totMdm2 is an assignment rule for species totMdm2:

$$[\text{totMdm2}] = \text{Mdm2} + \text{Mdm2\_p53} + \text{Mdm2\_P} \tag{2}$$

Derived unit mol

7 Events

This is an overview of two events. Each event is initiated whenever its trigger condition switches from false to true. A delay function postpones the effects of an event to a later time point. At the time of execution, an event can assign values to species, parameters or compartments if these are not set to constant.

7.1 Event stressCell

Trigger condition

$$t \geq 3600 \tag{3}$$

Assignment

$$\text{IR} = 25 \tag{4}$$

7.2 Event stopStress

Trigger condition

$$t \geq 3660 \tag{5}$$

Assignment

$$\text{IR} = 0 \tag{6}$$

8 Reactions

This model contains 20 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	p53mRNASynthesis		Source ⟶ p53_mRNA	
2	p53mRNADegradation		p53_mRNA ⟶ Sink	
3	Mdm2Synthesis		Mdm2_mRNA ⟶ Mdm2_mRNA + Mdm2 + mdm2syn	
4	Mdm2mRNASynthesis1		p53 ⟶ p53 + Mdm2_mRNA + Mdm2mRNAsyn	
5	Mdm2mRNASynthesis2		p53_P ⟶ p53_P + Mdm2_mRNA + Mdm2mRNAsyn	
6	Mdm2mRNADegradation		Mdm2_mRNA ⟶ Sink + Mdm2mRNAdeg	
7	Mdm2Degradation		Mdm2 ⟶ Sink + mdm2deg	
8	p53Synthesis		p53_mRNA ⟶ p53 + p53_mRNA + p53syn	
9	p53Degradation		Mdm2_p53 ⟶ Mdm2 + p53deg	
10	P53_Mdm2Binding		p53 + Mdm2 ⟶ Mdm2_p53	
11	P53_Mdm2Release		Mdm2_p53 ⟶ p53 + Mdm2	
12	DNAdamage		∅ ⟶ damDNA	
13	DNArepair		damDNA ⟶ Sink	
14	ATMactivation		damDNA + ATMI ⟶ damDNA + ATMA	
15	p53phoshorylation		p53 + ATMA ⟶ p53_P + ATMA	
16	p53dephosorylation		p53_P ⟶ p53	
17	Mdm2phoshorylation		Mdm2 + ATMA ⟶ Mdm2_P + ATMA	
18	Mdm2dephosorylation		Mdm2_P ⟶ Mdm2	
19	Mdm2Pdegradation		Mdm2_P ⟶ Sink + mdm2deg	
20	ATMInactivation		ATMA ⟶ ATMI	

8.1 Reaction p53mRNASynthesis

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

Reaction equation

$$\text{Source} \longrightarrow \text{p53\_mRNA} \tag{7}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
Source		

Product

Table 7: Properties of each product.

Id	Name	SBO
p53_mRNA		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_1 = \text{ksynp53mRNA} \cdot \text{Source} \tag{8}$$

8.2 Reaction p53mRNADegradation

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

Reaction equation

$$\text{p53\_mRNA} \longrightarrow \text{Sink} \tag{9}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
p53_mRNA		

Product

Table 9: Properties of each product.

Id	Name	SBO
Sink		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_2 = \mathrm{kdegp53mRNA} \cdot \mathrm{p53\_mRNA} \tag{10}$$

8.3 Reaction Mdm2Synthesis

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

Reaction equation

$$\mathrm{Mdm2\_mRNA} \longrightarrow \mathrm{Mdm2\_mRNA} + \mathrm{Mdm2} + \mathrm{mdm2syn} \tag{11}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
Mdm2_mRNA		

Products

Table 11: Properties of each product.

Id	Name	SBO
Mdm2_mRNA		
Mdm2		
mdm2syn		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_3 = \mathrm{ksynMdm2} \cdot \mathrm{Mdm2\_mRNA} \tag{12}$$

8.4 Reaction Mdm2mRNASynthesis1

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

Reaction equation

$$\text{p53} \longrightarrow \text{p53} + \text{Mdm2\_mRNA} + \text{Mdm2mRNAsyn} \tag{13}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
p53		

Products

Table 13: Properties of each product.

Id	Name	SBO
p53		
Mdm2_mRNA		
Mdm2mRNAsyn		

Kinetic Law

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

$$v_4 = \text{ksynMdm2mRNA} \cdot \text{p53} \tag{14}$$

8.5 Reaction Mdm2mRNASynthesis2

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

Reaction equation

$$\text{p53\_P} \longrightarrow \text{p53\_P} + \text{Mdm2\_mRNA} + \text{Mdm2mRNAsyn} \tag{15}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
p53_P		

Products

Table 15: Properties of each product.

Id	Name	SBO
p53_P		
Mdm2_mRNA		
Mdm2mRNAsyn		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_5 = \mathrm{ksynMdm2mRNA} \cdot \mathrm{p53\_P} \tag{16}$$

8.6 Reaction Mdm2mRNADegradation

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

Reaction equation

$$\mathrm{Mdm2\_mRNA} \longrightarrow \mathrm{Sink} + \mathrm{Mdm2mRNAdeg} \tag{17}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
Mdm2_mRNA		

Products

Table 17: Properties of each product.

Id	Name	SBO
Sink		

Id	Name	SBO
Mdm2mRNAdeg		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_6 = \mathrm{kdegMdm2mRNA} \cdot \mathrm{Mdm2\_mRNA} \tag{18}$$

8.7 Reaction Mdm2Degradation

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

Reaction equation

$$\mathrm{Mdm2} \longrightarrow \mathrm{Sink} + \mathrm{mdm2deg} \tag{19}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
Mdm2		

Products

Table 19: Properties of each product.

Id	Name	SBO
Sink		
mdm2deg		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_7 = \mathrm{kdegMdm2} \cdot \mathrm{Mdm2} \cdot \mathrm{kproteff} \tag{20}$$

8.8 Reaction p53Synthesis

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

Reaction equation

$$\text{p53\_mRNA} \longrightarrow \text{p53} + \text{p53\_mRNA} + \text{p53syn} \tag{21}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
p53_mRNA		

Products

Table 21: Properties of each product.

Id	Name	SBO
p53		
p53_mRNA		
p53syn		

Kinetic Law

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

$$v_8 = \text{ksynp53} \cdot \text{p53\_mRNA} \tag{22}$$

8.9 Reaction p53Degradation

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

Reaction equation

$$\text{Mdm2\_p53} \longrightarrow \text{Mdm2} + \text{p53deg} \tag{23}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
Mdm2_p53		

Products

Table 23: Properties of each product.

Id	Name	SBO
Mdm2		
p53deg		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_9 = \mathrm{kdegp53} \cdot \mathrm{Mdm2\_p53} \cdot \mathrm{kproteff} \tag{24}$$

8.10 Reaction P53_Mdm2Binding

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

Reaction equation

$$\mathrm{p53} + \mathrm{Mdm2} \longrightarrow \mathrm{Mdm2\_p53} \tag{25}$$

Reactants

Table 24: Properties of each reactant.

Id	Name	SBO
p53		
Mdm2		

Product

Table 25: Properties of each product.

Id	Name	SBO
Mdm2_p53		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{10} = \mathrm{kbinMdm2p53} \cdot \mathrm{p53} \cdot \mathrm{Mdm2} \tag{26}$$

8.11 Reaction P53_Mdm2Release

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

Reaction equation

$$\text{Mdm2\_p53} \longrightarrow \text{p53} + \text{Mdm2} \tag{27}$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
Mdm2_p53		

Products

Table 27: Properties of each product.

Id	Name	SBO
p53		
Mdm2		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{11} = \text{krelMdm2p53} \cdot \text{Mdm2\_p53} \tag{28}$$

8.12 Reaction DNAdamage

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

Reaction equation

$$\emptyset \longrightarrow \text{damDNA} \tag{29}$$

Product

Table 28: Properties of each product.

Id	Name	SBO
damDNA		

Kinetic Law

Derived unit $\mathrm{mol} \cdot \mathrm{s}^{-1}$

$$v_{12} = \mathrm{kdam} \cdot \mathrm{IR} \tag{30}$$

8.13 Reaction `DNArepair`

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

Reaction equation

$$\mathrm{damDNA} \longrightarrow \mathrm{Sink} \tag{31}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
`damDNA`		

Product

Table 30: Properties of each product.

Id	Name	SBO
`Sink`		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{13} = \mathrm{krepair} \cdot \mathrm{damDNA} \tag{32}$$

8.14 Reaction `ATMactivation`

This is an irreversible reaction of two reactants forming two products.

Reaction equation

$$\mathrm{damDNA} + \mathrm{ATMI} \longrightarrow \mathrm{damDNA} + \mathrm{ATMA} \tag{33}$$

Reactants

Table 31: Properties of each reactant.

Id	Name	SBO
damDNA		
ATMI		

Products

Table 32: Properties of each product.

Id	Name	SBO
damDNA		
ATMA		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{14} = \mathrm{kactATM} \cdot \mathrm{damDNA} \cdot \mathrm{ATMI} \tag{34}$$

8.15 Reaction p53phoshorylation

This is an irreversible reaction of two reactants forming two products.

Reaction equation

$$\mathrm{p53} + \mathrm{ATMA} \longrightarrow \mathrm{p53\_P} + \mathrm{ATMA} \tag{35}$$

Reactants

Table 33: Properties of each reactant.

Id	Name	SBO
p53		
ATMA		

Products

Table 34: Properties of each product.

Id	Name	SBO
p53_P		

Id	Name	SBO
ATMA		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{15} = \mathrm{kphosp53} \cdot \mathrm{p53} \cdot \mathrm{ATMA} \tag{36}$$

8.16 Reaction p53dephosorylation

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

Reaction equation

$$\mathrm{p53\_P} \longrightarrow \mathrm{p53} \tag{37}$$

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
p53_P		

Product

Table 36: Properties of each product.

Id	Name	SBO
p53		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{16} = \mathrm{kdephosp53} \cdot \mathrm{p53\_P} \tag{38}$$

8.17 Reaction Mdm2phoshorylation

This is an irreversible reaction of two reactants forming two products.

Reaction equation

$$\mathrm{Mdm2} + \mathrm{ATMA} \longrightarrow \mathrm{Mdm2\_P} + \mathrm{ATMA} \tag{39}$$

Reactants

Table 37: Properties of each reactant.

Id	Name	SBO
Mdm2		
ATMA		

Products

Table 38: Properties of each product.

Id	Name	SBO
Mdm2_P		
ATMA		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{17} = \mathrm{kphosMdm2} \cdot \mathrm{Mdm2} \cdot \mathrm{ATMA} \tag{40}$$

8.18 Reaction Mdm2dephosorylation

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

Reaction equation

$$\mathrm{Mdm2\_P} \longrightarrow \mathrm{Mdm2} \tag{41}$$

Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
Mdm2_P		

Product

Table 40: Properties of each product.

Id	Name	SBO
Mdm2		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{18} = \mathrm{kdephosMdm2} \cdot \mathrm{Mdm2\_P} \tag{42}$$

8.19 Reaction Mdm2Pdegradation

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

Reaction equation

$$\mathrm{Mdm2\_P} \longrightarrow \mathrm{Sink} + \mathrm{mdm2deg} \tag{43}$$

Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
Mdm2_P		

Products

Table 42: Properties of each product.

Id	Name	SBO
Sink		
mdm2deg		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{19} = \mathrm{kdegATMMdm2} \cdot \mathrm{Mdm2\_P} \tag{44}$$

8.20 Reaction ATMInactivation

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

Reaction equation

$$\text{ATMA} \longrightarrow \text{ATMI} \tag{45}$$

Reactant

Table 43: Properties of each reactant.

Id	Name	SBO
ATMA		

Product

Table 44: Properties of each product.

Id	Name	SBO
ATMI		

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{20} = \text{kinactATM} \cdot \text{ATMA} \tag{46}$$

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.

9.1 Species Mdm2

SBO:0000252 polypeptide chain

Initial amount 5 mol

This species takes part in seven reactions (as a reactant in Mdm2Degradation, P53_Mdm2Binding, Mdm2phoshorylation and as a product in Mdm2Synthesis, p53Degradation, P53_Mdm2Release, Mdm2dephosorylation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Mdm2} = v_3 + v_9 + v_{11} + v_{18} - v_7 - v_{10} - v_{17} \tag{47}$$

9.2 Species p53

SBO:0000252 polypeptide chain

Initial amount 5 mol

This species takes part in seven reactions (as a reactant in Mdm2mRNASynthesis1, P53_Mdm2Binding, p53phoshorylation and as a product in Mdm2mRNASynthesis1, p53Synthesis, P53_Mdm2Release, p53dephosorylation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{p53} = v_4 + v_8 + v_{11} + v_{16} - v_4 - v_{10} - v_{15} \tag{48}$$

9.3 Species Mdm2_p53

SBO:0000297 protein complex

Initial amount 95 mol

This species takes part in three reactions (as a reactant in p53Degradation, P53_Mdm2Release and as a product in P53_Mdm2Binding).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mdm2\_p53} = v_{10} - v_9 - v_{11} \tag{49}$$

9.4 Species Mdm2_mRNA

SBO:0000250 ribonucleic acid

Initial amount 10 mol

This species takes part in five reactions (as a reactant in Mdm2Synthesis, Mdm2mRNADegradation and as a product in Mdm2Synthesis, Mdm2mRNASynthesis1, Mdm2mRNASynthesis2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mdm2\_mRNA} = v_3 + v_4 + v_5 - v_3 - v_6 \tag{50}$$

9.5 Species p53_mRNA

SBO:0000250 ribonucleic acid

Initial amount 10 mol

This species takes part in four reactions (as a reactant in p53mRNADegradation, p53Synthesis and as a product in p53mRNASynthesis, p53Synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{p53\_mRNA} = v_1 + v_8 - v_2 - v_8 \tag{51}$$

9.6 Species ATMA

SBO:0000252 polypeptide chain

Initial amount 0 mol

This species takes part in six reactions (as a reactant in p53phoshorylation, Mdm2phoshorylation, ATMInactivation and as a product in ATMactivation, p53phoshorylation, Mdm2phoshorylation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ATMA} = v_{14} + v_{15} + v_{17} - v_{15} - v_{17} - v_{20} \tag{52}$$

9.7 Species ATMI

SBO:0000252 polypeptide chain

Initial amount 200 mol

This species takes part in two reactions (as a reactant in ATMactivation and as a product in ATMInactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ATMI} = v_{20} - v_{14} \tag{53}$$

9.8 Species p53_P

SBO:0000252 polypeptide chain

Initial amount 0 mol

This species takes part in four reactions (as a reactant in Mdm2mRNASynthesis2, p53dephosorylation and as a product in Mdm2mRNASynthesis2, p53phoshorylation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{p53\_P} = v_5 + v_{15} - v_5 - v_{16} \tag{54}$$

9.9 Species Mdm2_P

SBO:0000252 polypeptide chain

Initial amount 0 mol

This species takes part in three reactions (as a reactant in Mdm2dephosorylation, Mdm2Pdegradation and as a product in Mdm2phoshorylation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mdm2\_P} = v_{17} - v_{18} - v_{19} \tag{55}$$

9.10 Species damDNA

SBO:0000405 perturbing agent

Initial amount 0 mol

This species takes part in four reactions (as a reactant in DNArepair, ATMactivation and as a product in DNAdamage, ATMactivation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{damDNA} = v_{12} + v_{14} - v_{13} - v_{14} \tag{56}$$

9.11 Species Sink

SBO:0000291 empty set

Initial amount 1 mol

This species takes part in five reactions (as a product in p53mRNADegradation, Mdm2mRNADegradation, Mdm2Degradation, DNArepair, Mdm2Pdegradation), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Sink} = 0 \tag{57}$$

9.12 Species Source

SBO:0000291 empty set

Initial amount 1 mol

This species takes part in one reaction (as a reactant in p53mRNASynthesis), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Source} = 0 \tag{58}$$

9.13 Species p53deg

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in one reaction (as a product in p53Degradation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{p53deg} = v_9 \tag{59}$$

9.14 Species p53syn

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in one reaction (as a product in p53Synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{p53syn} = v_8 \tag{60}$$

9.15 Species mdm2deg

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in two reactions (as a product in Mdm2Degradation, Mdm2Pdegradation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mdm2deg} = v_7 + v_{19} \tag{61}$$

9.16 Species mdm2syn

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in one reaction (as a product in Mdm2Synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mdm2syn} = v_3 \tag{62}$$

9.17 Species Mdm2mRNAdeg

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in one reaction (as a product in Mdm2mRNADegradation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mdm2mRNAdeg} = v_6 \tag{63}$$

9.18 Species Mdm2mRNAsyn

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in two reactions (as a product in Mdm2mRNASynthesis1, Mdm2mRNASynthesis2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Mdm2mRNAsyn} = v_4 + v_5 \tag{64}$$

9.19 Species totp53

SBO:0000252 polypeptide chain

Initial amount 0 mol

Involved in rule totp53

One rule which determines this species' quantity.

9.20 Species totMdm2

SBO:0000252 polypeptide chain

Initial amount 0 mol

Involved in rule totMdm2

One rule which determines this species' quantity.

A Glossary of Systems Biology Ontology Terms

SBO:0000250 ribonucleic acid: Macromolecule formed by a repetition of ribonucleosides linked by phosphodiester bonds. CHEBI:3369

SBO:0000252 polypeptide chain: Naturally occurring macromolecule formed by the repetition of amino-acid residues linked by peptidic bonds. A polypeptide chain is synthesized by the ribosome. CHEBI:1654

SBO:0000291 empty set: Entity defined by the absence of any actual object. An empty set is often used to represent the source of a creation process or the result of a degradation process.

SBO:0000297 protein complex: Macromolecular complex containing one or more polypeptide chains possibly associated with simple chemicals. CHEBI:3608

SBO:0000405 perturbing agent: A material entity that is responsible for a perturbing effec

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