

## SBML Model Report

# Model name: “Talemi2014 - Arsenic toxicity and detoxification mechanisms in yeast”



September 10, 2014

## 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following three authors: Vijayalakshmi Chelliah<sup>1</sup>, Soheil Rastgou Talemi<sup>2</sup> and Audald Lloret i Villas<sup>3</sup> at September fourth 2014 at 11:08 a. m. and last time modified at September tenth 2014 at 2:44 p. m. Table 1 shows an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	4
species types	0	species	12
events	0	constraints	0
reactions	14	function definitions	8
global parameters	52	unit definitions	1
rules	13	initial assignments	21

## Model Notes

Talemi2014 - Arsenic toxicity and detoxification mechanisms in yeastThe model implements arsenite (AsIII)transport regulation, its distribution within main cellular AsIIIpools and detoxification. The intracellular As pools considered arefree AsIII (AsIIIin), protein-bound AsIII

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(AsIIIprot), glutathioneconjugated AsIII (AsGS3) and vacuolar sequestered AsIII (vAsGS3).

This model is described in the article:[Mathematical modelling of arsenic transport, distribution and detoxification processes in yeast](#). Talemi SR, Jacobson T, Garla V, Navarrete C, Wagner A, Tams MJ, Schaber J. Mol. Microbiol. 2014 Jun; 92(6): 1343-1356

Abstract:

Arsenic has a dual role as causative and curative agent of human disease. Therefore, there is considerable interest in elucidating arsenic toxicity and detoxification mechanisms. By an ensemble modelling approach, we identified a best parsimonious mathematical model which recapitulates and predicts intracellular arsenic dynamics for different conditions and mutants, thereby providing novel insights into arsenic toxicity and detoxification mechanisms in yeast, which could partly be confirmed experimentally by dedicated experiments. Specifically, our analyses suggest that: (i) arsenic is mainly protein-bound during short-term (acute) exposure, whereas glutathione-conjugated arsenic dominates during long-term (chronic) exposure, (ii) arsenic is not stably retained, but can leave the vacuole via an export mechanism, and (iii) Fps1 is controlled by Hog1-dependent and Hog1-independent mechanisms during arsenite stress. Our results challenge glutathione depletion as a key mechanism for arsenic toxicity and instead suggest that (iv) increased glutathione biosynthesis protects the proteome against the damaging effects of arsenic and that (v) widespread protein inactivation contributes to the toxicity of this metalloid. Our work in yeast may prove useful to elucidate similar mechanisms in higher eukaryotes and have implications for the use of arsenic in medical therapy.

This model is hosted on [BioModels Database](#) and identified by: [BIOMD0000000547](#).

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## 2 Unit Definitions

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

### 2.1 Unit substance

**Name** substance

**Definition**  $\mu\text{mol}$

### 2.2 Unit volume

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

**Definition** 1

### 2.3 Unit area

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

**Definition**  $\text{m}^2$

### 2.4 Unit length

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

**Definition** m

### 2.5 Unit time

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

**Definition** s

## 3 Compartments

This model contains four compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial	Size	Unit	Constant	Outside
			Dimensions				
compartment_2	Medium		3	$5 \cdot 10^{-11}$	l	<input checked="" type="checkbox"/>	
compartment_3	Cell		3	$5 \cdot 10^{-14}$	l	<input checked="" type="checkbox"/>	
compartment_1	Vac		3	$2 \cdot 10^{-14}$	l	<input checked="" type="checkbox"/>	
compartment_4	Cell-vac		3	$3 \cdot 10^{-14}$	l	<input checked="" type="checkbox"/>	

#### 3.1 Compartment `compartment_2`

This is a three dimensional compartment with a constant size of  $5 \cdot 10^{-11}$  litre.

**Name** Medium

#### 3.2 Compartment `compartment_3`

This is a three dimensional compartment with a constant size of  $5 \cdot 10^{-14}$  litre.

**Name** Cell

#### 3.3 Compartment `compartment_1`

This is a three dimensional compartment with a constant size of  $2 \cdot 10^{-14}$  litre.

**Name** Vac

### **3.4 Compartment** compartment\_4

This is a three dimensional compartment with a constant size of  $3 \cdot 10^{-14}$  litre.

**Name** Cell-vac

## 4 Species

This model contains twelve species. The boundary condition of one of these species is set to `true` so that this species' amount cannot be changed by any reaction. Section 10 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 Condi- tion
species_6	AsIII <sub>ex</sub>	compartment_2	μmol	<input type="checkbox"/>	<input checked="" type="checkbox"/>
species_5	Ycf1	compartment_3	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_10	Hog1 <sup>PP</sup>	compartment_3	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_9	Hog1	compartment_3	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_15	Fps1 <sup>P</sup>	compartment_3	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_11	Fps1	compartment_3	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_14	Acr3	compartment_3	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_4	vAsGS3	compartment_1	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_3	AsGS3	compartment_4	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_1	AsIII <sub>in</sub>	compartment_4	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_2	AsIII <sub>Prot</sub>	compartment_4	μmol	<input type="checkbox"/>	<input type="checkbox"/>
species_7	GSH	compartment_4	μmol	<input type="checkbox"/>	<input type="checkbox"/>

## 5 Parameters

This model contains 52 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
parameter_5	AsIIIex_initial		100.000		<input checked="" type="checkbox"/>
parameter_6	AsIIIex_shock		1000.000		<input checked="" type="checkbox"/>
parameter_7	AsIIIex_t1		0.000		<input checked="" type="checkbox"/>
parameter_8	AsIIex_t2		3600.000		<input checked="" type="checkbox"/>
parameter_9	AsIIIex_tm		30.000		<input checked="" type="checkbox"/>
parameter_10	Asngpermil_tot		2.236		<input type="checkbox"/>
parameter_11	Asmolweight		74.922		<input checked="" type="checkbox"/>
parameter_13	Asngpermil_in		0.030		<input type="checkbox"/>
parameter_14	Asngpermil_pro		0.396		<input type="checkbox"/>
parameter_15	Asngpermil_GS3		1.562		<input type="checkbox"/>
parameter_16	Asngpermil_vac		0.248		<input type="checkbox"/>
parameter_17	Hog1PPfit		0.614		<input type="checkbox"/>
parameter_18	Fps1Pfit		94.485		<input type="checkbox"/>
parameter_1	Fps1PPmax		0.030		<input checked="" type="checkbox"/>
parameter_2	k18	$2.16561157822054 \cdot 10^{-17}$			<input type="checkbox"/>
parameter_3	k20		0.076		<input type="checkbox"/>
parameter_4	D_AsIIIin_initial		13.155		<input checked="" type="checkbox"/>
parameter_12	Hog1_SUM		0.167		<input type="checkbox"/>
parameter_19	GSH_wt		1600.000		<input checked="" type="checkbox"/>
parameter_20	GSH_Acr3Hog1D		5.999		<input checked="" type="checkbox"/>
parameter_21	GSH_Acr3		2.820		<input checked="" type="checkbox"/>
parameter_22	GSH_damping- _factor		1.000		<input type="checkbox"/>
parameter_23	ko-8		1.000		<input checked="" type="checkbox"/>
parameter_24	Ycf1_increase		20.000		<input checked="" type="checkbox"/>
parameter_25	v12_ko		1.000		<input checked="" type="checkbox"/>
parameter_26	v4_k		0.076		<input checked="" type="checkbox"/>
parameter_27	v5_k1		161.334		<input checked="" type="checkbox"/>
parameter_28	v4_ko		1.000		<input checked="" type="checkbox"/>
parameter_29	v6_k		$2.57134 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
parameter_30	v6_k1		1102.150		<input checked="" type="checkbox"/>
parameter_31	v6_kb		0.073		<input checked="" type="checkbox"/>
parameter_32	v7_k1		0.072		<input checked="" type="checkbox"/>
parameter_33	v1_k		0.002		<input checked="" type="checkbox"/>
parameter_34	v14_Vmax		1.000		<input checked="" type="checkbox"/>
parameter_35	v14_Km		$5.16159 \cdot 10^{-6}$		<input checked="" type="checkbox"/>
parameter_36	v10_k		$3.49703 \cdot 10^{-6}$		<input checked="" type="checkbox"/>

Id	Name	SBO	Value	Unit	Constant
parameter_37	v11.k		$1.92773 \cdot 10^{-7}$		<input checked="" type="checkbox"/>
parameter_38	v10.ko		1.000		<input checked="" type="checkbox"/>
parameter_39	v8.k		0.203		<input checked="" type="checkbox"/>
parameter_40	v9.k1		6.143		<input checked="" type="checkbox"/>
parameter_41	v2.k1		0.009		<input checked="" type="checkbox"/>
parameter_42	v3.k1		$6.56918 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
parameter_43	v13.k1		$9.01422 \cdot 10^{-13}$		<input checked="" type="checkbox"/>
Compartment- _3	Initial for Cell-vac		$3 \cdot 10^{-14}$		<input checked="" type="checkbox"/>
Metabolite_9	Initial for AsIIIin		13.155		<input checked="" type="checkbox"/>
Metabolite_6	Initial for Acr3		$3.16038478651879 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
Metabolite_5	Initial for Fps1		0.002		<input checked="" type="checkbox"/>
Metabolite_0	Initial for AsIIIex		100.000		<input checked="" type="checkbox"/>
Compartment- _2	Initial for Vac		$2 \cdot 10^{-14}$		<input checked="" type="checkbox"/>
ModelValue- _13	Initial for Fps1PPmax		0.030		<input checked="" type="checkbox"/>
ModelValue- _22	Initial for ko-8		1.000		<input checked="" type="checkbox"/>
Asngpermil- _ex	Asngpermil_ex		0.375		<input type="checkbox"/>

## 6 Initialassignments

This is an overview of 21 initialassignments.

### 6.1 Initialassignment [compartment\\_1](#)

**Derived unit** contains undeclared units

**Math**  $0.4 \cdot \text{vol}(\text{compartment}_3)$

### 6.2 Initialassignment [compartment\\_4](#)

**Derived unit** contains undeclared units

**Math**  $0.6 \cdot \text{vol}(\text{compartment}_3)$

### 6.3 Initialassignment [species\\_5](#)

**Derived unit** contains undeclared units

$$\text{Math} \begin{cases} 0.013151 & \text{if parameter\_25} > 0 \\ 0.013151 \cdot \text{parameter\_24} & \text{otherwise} \end{cases} \cdot \text{vol}(\text{compartment\_3})$$

#### 6.4 Initialassignment species\_10

**Derived unit** contains undeclared units

$$\text{Math} \begin{cases} \frac{\frac{\text{species\_9}}{\text{vol}(\text{compartment\_3})} \cdot \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} \cdot \text{parameter\_26}}{\text{parameter\_27}} & \text{if parameter\_28} > 0 \\ 0 & \text{otherwise} \end{cases} \cdot \text{vol}(\text{compartment\_3})$$

#### 6.5 Initialassignment species\_9

**Derived unit** contains undeclared units

$$\text{Math} \begin{cases} \frac{0.167 \cdot \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} \cdot \text{parameter\_26}}{\text{parameter\_27}} + 1 & \text{if parameter\_28} > 0 \\ 0.167 & \text{otherwise} \end{cases} \cdot \text{vol}(\text{compartment\_3})$$

#### 6.6 Initialassignment species\_15

**Derived unit** contains undeclared units

$$\text{Math} \frac{\frac{\text{species\_11}}{\text{vol}(\text{compartment\_3})} \cdot \left( \text{parameter\_29} \cdot \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} + \text{parameter\_30} \cdot \frac{\text{species\_10}}{\text{vol}(\text{compartment\_3})} + \text{parameter\_31} \right)}{\text{parameter\_32}} \cdot \text{vol}(\text{compartment\_3})$$

#### 6.7 Initialassignment species\_11

**Derived unit** contains undeclared units

$$\text{Math} \frac{0.03 \cdot \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} + \text{parameter\_30} \cdot \frac{\text{species\_10}}{\text{vol}(\text{compartment\_3})} + \text{parameter\_31}}{\text{parameter\_29} \cdot \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} + \text{parameter\_30} \cdot \frac{\text{species\_10}}{\text{vol}(\text{compartment\_3})} + \text{parameter\_31}} \cdot \text{vol}(\text{compartment\_3}) + 1$$

#### 6.8 Initialassignment species\_14

**Derived unit** contains undeclared units

$$\text{Math} \begin{cases} \frac{\frac{\text{species\_11}}{\text{vol}(\text{compartment\_3})} \cdot \text{parameter\_33} \cdot \left( \frac{\text{species\_6}}{\text{vol}(\text{compartment\_2})} - \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} \right)}{\frac{\text{parameter\_34} \cdot \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})}}{\text{parameter\_35} + \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})}}} & \text{if parameter\_25} > 0 \\ 0 & \text{otherwise} \end{cases} \cdot \text{vol}(\text{compartment\_3})$$



### 6.9 Initialassignment species\_4

**Derived unit** contains undeclared units

$$\text{Math} \begin{cases} \frac{\text{parameter\_36} \cdot \frac{\text{species\_5}}{\text{vol}(\text{compartment\_3})} \cdot \frac{\text{species\_3}}{\text{vol}(\text{compartment\_4})}}{\text{parameter\_37}} & \text{if } \text{parameter\_38} > 0 \\ 0 & \text{otherwise} \end{cases} \cdot \text{vol}(\text{compartment\_1})$$

### 6.10 Initialassignment species\_3

**Derived unit** contains undeclared units

$$\text{Math} \frac{\text{parameter\_39} \cdot \text{parameter\_22} \cdot \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} \cdot \frac{\text{species\_7}}{\text{vol}(\text{compartment\_4})}}{\text{parameter\_40}} \cdot \text{vol}(\text{compartment\_4})$$

### 6.11 Initialassignment species\_1

**Derived unit** contains undeclared units

$$\text{Math} \begin{cases} \text{parameter\_4} & \text{if } \text{parameter\_25} > 0 \\ 100 & \text{otherwise} \end{cases} \cdot \text{vol}(\text{compartment\_4})$$

### 6.12 Initialassignment species\_2

**Derived unit** contains undeclared units

$$\text{Math} \frac{\text{parameter\_41} \cdot \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})}}{\text{parameter\_42}} \cdot \text{vol}(\text{compartment\_4})$$

### 6.13 Initialassignment species\_7

**Derived unit** contains undeclared units

$$\text{Math} \begin{cases} \text{parameter\_19} \cdot \text{parameter\_22} & \text{if } \text{parameter\_25} > 0 \\ \begin{cases} \text{parameter\_19} \cdot \text{parameter\_21} & \text{if } \text{parameter\_28} > 0 \\ \text{parameter\_19} \cdot \text{parameter\_20} & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \cdot \text{vol}(\text{compartment\_4})$$

### 6.14 Initialassignment Compartment\_3

**Derived unit** 1

$$\text{Math} \text{vol}(\text{compartment\_4})$$

### 6.15 Initialassignment Metabolite\_9

**Derived unit**  $\mu\text{mol}$

$$\text{Math} \text{species\_1}$$

### 6.16 Initialassignment Metabolite\_6

**Derived unit**  $\mu\text{mol}$

**Math** species\_14

### 6.17 Initialassignment Metabolite\_5

**Derived unit**  $\mu\text{mol}$

**Math** species\_11

### 6.18 Initialassignment Metabolite\_0

**Derived unit**  $\mu\text{mol}$

**Math** species\_6

### 6.19 Initialassignment Compartment\_2

**Derived unit** 1

**Math**  $\text{vol}(\text{compartment}_1)$

### 6.20 Initialassignment ModelValue\_13

**Derived unit** contains undeclared units

**Math** parameter\_1

### 6.21 Initialassignment ModelValue\_22

**Derived unit** contains undeclared units

**Math** parameter\_23

## 7 Function definitions

This is an overview of eight function definitions.

### 7.1 Function definition function\_3

**Name** 2p modified mass action (irrev)

**Arguments** S, M, k, ko

**Mathematical Expression**

$$k \cdot ko \cdot M \cdot S \quad (1)$$

## 7.2 Function definition [function\\_7](#)

**Name** 2p modified constant flux (irrev)

**Arguments** M, k, ko

**Mathematical Expression**

$$k \cdot ko \cdot M \quad (2)$$

## 7.3 Function definition [function\\_6](#)

**Name** Mixed Hill

**Arguments** Substrate, k, Mod1, Mod, k1, kb

**Mathematical Expression**

$$\text{Substrate} \cdot (k \cdot \text{Mod1} + k1 \cdot \text{Mod} + kb) \quad (3)$$

## 7.4 Function definition [function\\_2](#)

**Name** 2p 2sub

**Arguments** k, ko, sub, sub2

**Mathematical Expression**

$$k \cdot ko \cdot \text{sub} \cdot \text{sub2} \quad (4)$$

## 7.5 Function definition [function\\_1](#)

**Name** corrected modified diffusion

**Arguments** V, Mod, k, Ex, In

**Mathematical Expression**

$$(36 \cdot \pi)^{\frac{1}{3}} \cdot V^{\frac{2}{3}} \cdot \text{Mod} \cdot k \cdot (\text{Ex} - \text{In}) \quad (5)$$

## 7.6 Function definition [function\\_8](#)

**Name** corrected mass action

**Arguments** V, k, Sub

**Mathematical Expression**

$$(36 \cdot \pi)^{\frac{1}{3}} \cdot V^{\frac{2}{3}} \cdot k \cdot \text{Sub} \quad (6)$$

## 7.7 Function definition `function_4`

**Name** corrected 2p modified mass action

**Arguments** ko, Mod, k, V, Sub

**Mathematical Expression**

$$ko \cdot Mod \cdot k \cdot (36 \cdot \pi)^{\frac{1}{3}} \cdot V^{\frac{2}{3}} \cdot Sub \quad (7)$$

## 7.8 Function definition `function_5`

**Name** Rate Law for v20

**Arguments** V, Mod, Vmax, Sub, Km

**Mathematical Expression**

$$\frac{(36 \cdot \pi)^{\frac{1}{3}} \cdot V^{\frac{2}{3}} \cdot Mod \cdot Vmax \cdot Sub}{Km + Sub} \quad (8)$$

# 8 Rules

This is an overview of 13 rules.

## 8.1 Rule `parameter_10`

Rule `parameter_10` is an assignment rule for parameter `parameter_10`:

$$\begin{aligned} \text{parameter\_10} = & \left( \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} + \frac{\text{species\_2}}{\text{vol}(\text{compartment\_4})} + \frac{\text{species\_3}}{\text{vol}(\text{compartment\_4})} \right) \\ & \cdot \text{Compartment\_3} \cdot \text{parameter\_11} \cdot 10^9 + \frac{\text{species\_4}}{\text{vol}(\text{compartment\_1})} \\ & \cdot \text{Compartment\_2} \cdot \text{parameter\_11} \cdot 10^9 \end{aligned} \quad (9)$$

## 8.2 Rule `parameter_13`

Rule `parameter_13` is an assignment rule for parameter `parameter_13`:

$$\text{parameter\_13} = \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} \cdot \text{Compartment\_3} \cdot \text{parameter\_11} \cdot 10^9 \quad (10)$$

## 8.3 Rule `parameter_14`

Rule `parameter_14` is an assignment rule for parameter `parameter_14`:

$$\text{parameter\_14} = \frac{\text{species\_2}}{\text{vol}(\text{compartment\_4})} \cdot \text{Compartment\_3} \cdot \text{parameter\_11} \cdot 10^9 \quad (11)$$

#### 8.4 Rule parameter\_15

Rule parameter\_15 is an assignment rule for parameter parameter\_15:

$$\text{parameter\_15} = \frac{\text{species\_3}}{\text{vol}(\text{compartment\_4})} \cdot \text{Compartment\_3} \cdot \text{parameter\_11} \cdot 10^9 \quad (12)$$

#### 8.5 Rule species\_6

Rule species\_6 is an assignment rule for species species\_6:

$$\begin{aligned} & [\text{species\_6}] \quad (13) \\ & = \begin{cases} \text{parameter\_5} & \text{if time} < \text{parameter\_8} \\ \left\{ \begin{array}{ll} (\text{parameter\_5} + \text{parameter\_6}) \cdot \exp\left(\frac{\text{parameter\_8} - \text{time}}{\text{parameter\_9}}\right) & \text{if time} > \text{parameter\_8} \\ \text{parameter\_5} + \text{parameter\_6} \cdot \left(1 - \exp\left(\frac{\text{parameter\_7} - \text{time}}{\text{parameter\_9}}\right)\right) & \text{otherwise} \end{array} \right\} & \text{otherwise} \end{cases} \\ & \cdot \text{vol}(\text{compartment\_2}) \end{aligned}$$

#### 8.6 Rule parameter\_16

Rule parameter\_16 is an assignment rule for parameter parameter\_16:

$$\text{parameter\_16} = \frac{\text{species\_4}}{\text{vol}(\text{compartment\_1})} \cdot \text{Compartment\_2} \cdot \text{parameter\_11} \cdot 10^9 \quad (14)$$

#### 8.7 Rule parameter\_18

Rule parameter\_18 is an assignment rule for parameter parameter\_18:

$$\text{parameter\_18} = \frac{100 \cdot \frac{\text{species\_15}}{\text{vol}(\text{compartment\_3})}}{\text{ModelValue\_13}} \quad (15)$$

#### 8.8 Rule parameter\_2

Rule parameter\_2 is an assignment rule for parameter parameter\_2:

$$\text{parameter\_2} = \frac{\text{parameter\_43} \cdot \text{Metabolite\_6}}{\text{Metabolite\_9}} \quad (16)$$

#### 8.9 Rule parameter\_3

Rule parameter\_3 is an assignment rule for parameter parameter\_3:

$$\begin{aligned} & \text{parameter\_3} \\ & = \begin{cases} \frac{\text{parameter\_33} \cdot \text{Metabolite\_5} \cdot (\text{Metabolite\_0} - \text{Metabolite\_9})}{\text{Metabolite\_6} \cdot \text{Metabolite\_9}} & \text{if parameter\_25} > 0 \\ 0 & \text{otherwise} \end{cases} \quad (17) \end{aligned}$$

### 8.10 Rule `parameter_12`

Rule `parameter_12` is an assignment rule for parameter `parameter_12`:

$$\text{parameter\_12} = \frac{\text{species\_9}}{\text{vol}(\text{compartment\_3})} + \frac{\text{species\_10}}{\text{vol}(\text{compartment\_3})} \quad (18)$$

**Derived unit**  $\mu\text{mol} \cdot \text{l}^{-1}$

### 8.11 Rule `parameter_17`

Rule `parameter_17` is an assignment rule for parameter `parameter_17`:

$$\text{parameter\_17} = \frac{100 \cdot \frac{\text{species\_10}}{\text{vol}(\text{compartment\_3})}}{\text{parameter\_12}} \quad (19)$$

### 8.12 Rule `parameter_22`

Rule `parameter_22` is an assignment rule for parameter `parameter_22`:

$$\text{parameter\_22} = \begin{cases} 1 & \text{if ModelValue\_22} > 0 \\ 0.2175 & \text{otherwise} \end{cases} \quad (20)$$

### 8.13 Rule `Asngpermil_ex`

Rule `Asngpermil_ex` is an assignment rule for parameter `Asngpermil_ex`:

$$\text{Asngpermil\_ex} = \frac{\text{species\_6}}{\text{vol}(\text{compartment\_2})} \cdot \text{vol}(\text{compartment\_3}) \cdot \text{parameter\_11} \cdot 10^9 \quad (21)$$

## 9 Reactions

This model contains 14 reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

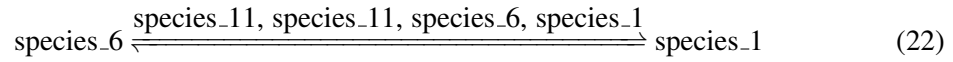
Nº	Id	Name	Reaction Equation	SBO
1	reaction_1	v1	$\text{species}_6 \xrightarrow{\text{species}_{11}, \text{species}_{11}, \text{species}_6, \text{species}_1} \text{species}_1$	
2	reaction_4	v4	$\text{species}_9 \xrightarrow{\text{species}_1, \text{species}_9, \text{species}_1} \text{species}_{10}$	
3	reaction_5	v5	$\text{species}_{10} \xrightarrow{\text{species}_{10}} \text{species}_9$	
4	reaction_6	v7	$\text{species}_{15} \xrightarrow{\text{species}_{15}} \text{species}_{11}$	
5	reaction_7	v2	$\text{species}_1 \xrightarrow{\text{species}_1} \text{species}_2$	
6	reaction_8	v3	$\text{species}_2 \xrightarrow{\text{species}_2} \text{species}_1$	
7	reaction_9	v8	$\text{species}_1 + \text{species}_7 \xrightarrow{\text{species}_1, \text{species}_7} \text{species}_3$	
8	reaction_10	v10	$\text{species}_3 \xrightarrow{\text{species}_5, \text{species}_5, \text{species}_3} \text{species}_4$	
9	reaction_13	v12	$\emptyset \xrightarrow{\text{species}_1, \text{species}_1} \text{species}_{14}$	
10	reaction_14	v13	$\text{species}_{14} \xrightarrow{\text{species}_{14}} \emptyset$	
11	reaction_15	v14	$\text{species}_1 \xrightarrow{\text{species}_{14}, \text{species}_{14}, \text{species}_1} \text{species}_6$	
12	reaction_16	v6	$\text{species}_{11} \xrightarrow{\text{species}_1, \text{species}_{10}, \text{species}_{11}, \text{species}_1, \text{species}_{10}} \text{species}_{15}$	
13	reaction_17	v9	$\text{species}_3 \xrightarrow{\text{species}_3} \text{species}_1 + \text{species}_7$	
14	reaction_18	v11	$\text{species}_4 \xrightarrow{\text{species}_4} \text{species}_3$	

## 9.1 Reaction `reaction_1`

This is a reversible reaction of one reactant forming one product influenced by four modifiers.

**Name** `v1`

### Reaction equation



### Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
<code>species_6</code>	AsIIIex	

### Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
<code>species_11</code>	Fps1	
<code>species_11</code>	Fps1	
<code>species_6</code>	AsIIIex	
<code>species_1</code>	AsIIIin	

### Product

Table 8: Properties of each product.

Id	Name	SBO
<code>species_1</code>	AsIIIin	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_1 = \text{function\_1} \left( \text{vol}(\text{compartment\_3}), \frac{\text{species\_11}}{\text{vol}(\text{compartment\_3})}, \text{parameter\_33}, \frac{\text{species\_6}}{\text{vol}(\text{compartment\_2})}, \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} \right) \quad (23)$$



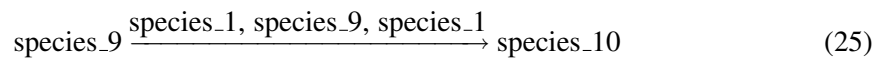
$$\text{function\_1}(V, \text{Mod}, k, \text{Ex}, \text{In}) = (36 \cdot \pi)^{\frac{1}{3}} \cdot V^{\frac{2}{3}} \cdot \text{Mod} \cdot k \cdot (\text{Ex} - \text{In}) \quad (24)$$

## 9.2 Reaction `reaction_4`

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

**Name** `v4`

### Reaction equation



### Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
<code>species_9</code>	Hog1	

### Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
<code>species_1</code>	AsIIIin	
<code>species_9</code>	Hog1	
<code>species_1</code>	AsIIIin	

### Product

Table 11: Properties of each product.

Id	Name	SBO
<code>species_10</code>	Hog1PP	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_2 = \text{vol}(\text{compartment\_3}) \cdot \text{function\_3} \left( \frac{\text{species\_9}}{\text{vol}(\text{compartment\_3})}, \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})}, \text{parameter\_26}, \text{parameter\_28} \right) \quad (26)$$

$$\text{function\_3}(S, M, k, k_o) = k \cdot k_o \cdot M \cdot S \quad (27)$$

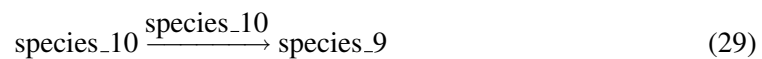
$$\text{function\_3}(S, M, k, k_o) = k \cdot k_o \cdot M \cdot S \quad (28)$$

### 9.3 Reaction `reaction_5`

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

**Name** `v5`

#### Reaction equation



#### Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
<code>species_10</code>	Hog1PP	

#### Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
<code>species_10</code>	Hog1PP	

#### Product

Table 14: Properties of each product.

Id	Name	SBO
<code>species_9</code>	Hog1	

## Kinetic Law

**Derived unit** contains undeclared units

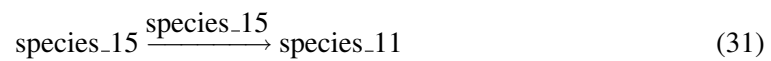
$$v_3 = \text{parameter\_27} \cdot \text{species\_10} \quad (30)$$

## 9.4 Reaction `reaction_6`

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

**Name** `v7`

### Reaction equation



### Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
<code>species_15</code>	<code>Fps1P</code>	

### Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
<code>species_15</code>	<code>Fps1P</code>	

### Product

Table 17: Properties of each product.

Id	Name	SBO
<code>species_11</code>	<code>Fps1</code>	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_4 = \text{parameter\_32} \cdot \text{species\_15} \quad (32)$$

## 9.5 Reaction `reaction_7`

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

**Name** `v2`

### Reaction equation



### Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
<code>species_1</code>	AsIIIin	

### Modifier

Table 19: Properties of each modifier.

Id	Name	SBO
<code>species_1</code>	AsIIIin	

### Product

Table 20: Properties of each product.

Id	Name	SBO
<code>species_2</code>	AsIIIProt	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_5 = \text{parameter\_41} \cdot \text{species\_1} \quad (34)$$

## 9.6 Reaction `reaction_8`

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

**Name** `v3`

### Reaction equation



### Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
species_2	AsIIIProt	

### Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
species_2	AsIIIProt	

### Product

Table 23: Properties of each product.

Id	Name	SBO
species_1	AsIIIin	

### Kinetic Law

**Derived unit** contains undeclared units

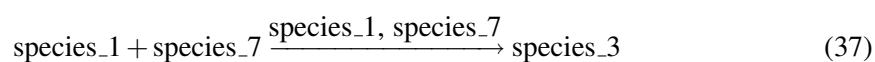
$$v_6 = \text{parameter\_42} \cdot \text{species\_2} \quad (36)$$

## 9.7 Reaction reaction\_9

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

**Name** v8

### Reaction equation



### Reactants

Table 24: Properties of each reactant.

Id	Name	SBO
species_1	AsIIIin	
species_7	GSH	

## Modifiers

Table 25: Properties of each modifier.

Id	Name	SBO
species_1	AsIIIin	
species_7	GSH	

## Product

Table 26: Properties of each product.

Id	Name	SBO
species_3	AsGS3	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_7 = \text{vol}(\text{compartment}_4) \cdot \text{function\_2} \left( \text{parameter\_39}, \text{parameter\_22}, \frac{\text{species\_1}}{\text{vol}(\text{compartment}_4)}, \frac{\text{species\_7}}{\text{vol}(\text{compartment}_4)} \right) \quad (38)$$

$$\text{function\_2}(k, ko, \text{sub}, \text{sub2}) = k \cdot ko \cdot \text{sub} \cdot \text{sub2} \quad (39)$$

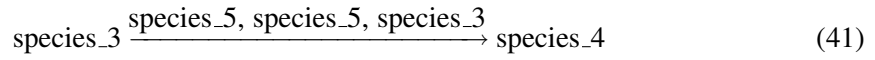
$$\text{function\_2}(k, ko, \text{sub}, \text{sub2}) = k \cdot ko \cdot \text{sub} \cdot \text{sub2} \quad (40)$$

## 9.8 Reaction `reaction_10`

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

**Name** v10

## Reaction equation



## Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
species_3	AsGS3	

## Modifiers

Table 28: Properties of each modifier.

Id	Name	SBO
species_5	Ycfl	
species_5	Ycfl	
species_3	AsGS3	

## Product

Table 29: Properties of each product.

Id	Name	SBO
species_4	vAsGS3	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_8 = \text{function\_4} \left( \text{parameter\_38}, \frac{\text{species\_5}}{\text{vol}(\text{compartment\_3})}, \text{parameter\_36}, \text{vol}(\text{compartment\_1}), \frac{\text{species\_3}}{\text{vol}(\text{compartment\_4})} \right) \quad (42)$$

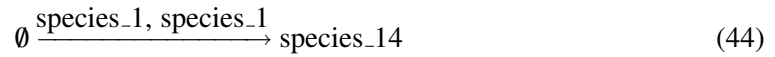
$$\text{function\_4}(\text{ko}, \text{Mod}, \text{k}, \text{V}, \text{Sub}) = \text{ko} \cdot \text{Mod} \cdot \text{k} \cdot (36 \cdot \pi)^{\frac{1}{3}} \cdot \text{V}^{\frac{2}{3}} \cdot \text{Sub} \quad (43)$$

## 9.9 Reaction `reaction_13`

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

**Name** `v12`

### Reaction equation



### Modifiers

Table 30: Properties of each modifier.

Id	Name	SBO
<code>species_1</code>	AsIIIin	
<code>species_1</code>	AsIIIin	

### Product

Table 31: Properties of each product.

Id	Name	SBO
<code>species_14</code>	Acr3	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_9 = \text{vol}(\text{compartment\_3}) \cdot \text{function\_7} \left( \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})}, \text{parameter\_2}, \text{parameter\_25} \right) \quad (45)$$

$$\text{function\_7}(M, k, k_0) = k \cdot k_0 \cdot M \quad (46)$$

$$\text{function\_7}(M, k, k_0) = k \cdot k_0 \cdot M \quad (47)$$

## 9.10 Reaction `reaction_14`

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

**Name** `v13`



### Reaction equation



### Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
species_14	Acr3	

### Modifier

Table 33: Properties of each modifier.

Id	Name	SBO
species_14	Acr3	

### Kinetic Law

**Derived unit** contains undeclared units

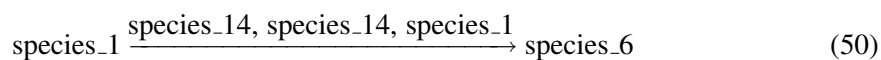
$$v_{10} = \text{parameter\_43} \cdot \text{species\_14} \quad (49)$$

## 9.11 Reaction `reaction_15`

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

**Name** `v14`

### Reaction equation



### Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
species_1	AsIIIin	

## Modifiers

Table 35: Properties of each modifier.

Id	Name	SBO
species_14	Acr3	
species_14	Acr3	
species_1	AsIIIin	

## Product

Table 36: Properties of each product.

Id	Name	SBO
species_6	AsIIIex	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{11} = \text{function\_5} \left( \text{vol}(\text{compartment\_3}), \frac{\text{species\_14}}{\text{vol}(\text{compartment\_3})}, \text{parameter\_34}, \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})}, \text{parameter\_35} \right) \quad (51)$$

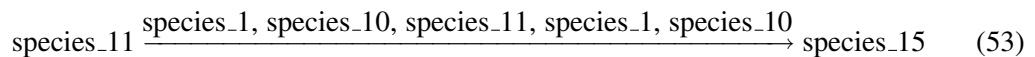
$$\text{function\_5}(V, \text{Mod}, V_{\max}, \text{Sub}, K_m) = \frac{(36 \cdot \pi)^{\frac{1}{3}} \cdot V^{\frac{2}{3}} \cdot \text{Mod} \cdot V_{\max} \cdot \text{Sub}}{K_m + \text{Sub}} \quad (52)$$

### 9.12 Reaction [reaction\\_16](#)

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

**Name** v6

#### Reaction equation



## Reactant

Table 37: Properties of each reactant.

Id	Name	SBO
species_11	Fpsl	

## Modifiers

Table 38: Properties of each modifier.

Id	Name	SBO
species_1	AsIIIin	
species_10	Hog1PP	
species_11	Fpsl	
species_1	AsIIIin	
species_10	Hog1PP	

## Product

Table 39: Properties of each product.

Id	Name	SBO
species_15	Fps1P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{12} = \text{vol}(\text{compartment}_3) \cdot \text{function}_6 \left( \frac{\text{species}_{11}}{\text{vol}(\text{compartment}_3)}, \text{parameter}_{29}, \frac{\text{species}_1}{\text{vol}(\text{compartment}_4)}, \frac{\text{species}_{10}}{\text{vol}(\text{compartment}_3)}, \text{parameter}_{30}, \text{parameter}_{31} \right) \quad (54)$$

$$\text{function}_6(\text{Substrate}, k, \text{Mod1}, \text{Mod}, k1, kb) = \text{Substrate} \cdot (k \cdot \text{Mod1} + k1 \cdot \text{Mod} + kb) \quad (55)$$

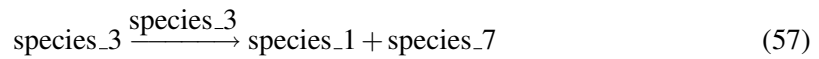
$$\text{function}_6(\text{Substrate}, k, \text{Mod1}, \text{Mod}, k1, kb) = \text{Substrate} \cdot (k \cdot \text{Mod1} + k1 \cdot \text{Mod} + kb) \quad (56)$$

### 9.13 Reaction `reaction_17`

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

**Name** v9

## Reaction equation



## Reactant

Table 40: Properties of each reactant.

Id	Name	SBO
species_3	AsGS3	

## Modifier

Table 41: Properties of each modifier.

Id	Name	SBO
species_3	AsGS3	

## Products

Table 42: Properties of each product.

Id	Name	SBO
species_1	AsIIIin	
species_7	GSH	

## Kinetic Law

**Derived unit** contains undeclared units

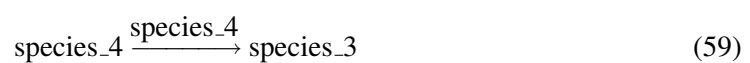
$$v_{13} = \text{parameter\_40} \cdot \text{species\_3} \quad (58)$$

### 9.14 Reaction `reaction_18`

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

**Name** `v11`

## Reaction equation



## Reactant

Table 43: Properties of each reactant.

Id	Name	SBO
species_4	vAsGS3	

## Modifier

Table 44: Properties of each modifier.

Id	Name	SBO
species_4	vAsGS3	

## Product

Table 45: Properties of each product.

Id	Name	SBO
species_3	AsGS3	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{14} = \text{function\_8} \left( \text{vol}(\text{compartment\_1}), \text{parameter\_37}, \frac{\text{species\_4}}{\text{vol}(\text{compartment\_1})} \right) \quad (60)$$

$$\text{function\_8}(V, k, \text{Sub}) = (36 \cdot \pi)^{\frac{1}{3}} \cdot V^{\frac{2}{3}} \cdot k \cdot \text{Sub} \quad (61)$$

## 10 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.

### 10.1 Species `species_6`

**Name** AsIIIex

**Initial amount**  $5 \cdot 10^{-9} \mu\text{mol}$

**Involved in rule** `species_6`

This species takes part in three reactions (as a reactant in `reaction_1` and as a product in `reaction_15` and as a modifier in `reaction_1`). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

### 10.2 Species `species_5`

**Name** Ycfl

**Initial amount**  $6.5755 \cdot 10^{-16} \mu\text{mol}$

**Initial assignment** `species_5`

This species takes part in two reactions (as a modifier in `reaction_10`, `reaction_10`).

$$\frac{d}{dt}\text{species}_5 = 0 \quad (62)$$

### 10.3 Species `species_10`

**Name** Hog1PP

**Initial amount**  $5.12422021489774 \cdot 10^{-17} \mu\text{mol}$

**Initial assignment** `species_10`

This species takes part in five reactions (as a reactant in `reaction_5` and as a product in `reaction_4` and as a modifier in `reaction_5`, `reaction_16`, `reaction_16`).

$$\frac{d}{dt}\text{species}_{10} = v_2 - v_3 \quad (63)$$

### 10.4 Species `species_9`

**Name** Hog1

**Initial amount**  $8.29875779785102 \cdot 10^{-15} \mu\text{mol}$

**Initial assignment** `species_9`

This species takes part in three reactions (as a reactant in `reaction_4` and as a product in `reaction_5` and as a modifier in `reaction_4`).

$$\frac{d}{dt}\text{species}_9 = v_3 - v_2 \quad (64)$$

### 10.5 Species `species_15`

**Name** Fps1P

**Initial amount**  $1.41558600877709 \cdot 10^{-15}$   $\mu\text{mol}$

**Initial assignment** `species_15`

This species takes part in three reactions (as a reactant in [reaction\\_6](#) and as a product in [reaction\\_16](#) and as a modifier in [reaction\\_6](#)).

$$\frac{d}{dt}\text{species\_15} = v_{12} - v_4 \quad (65)$$

### 10.6 Species `species_11`

**Name** Fps1

**Initial amount**  $8.44139912229068 \cdot 10^{-17}$   $\mu\text{mol}$

**Initial assignment** `species_11`

This species takes part in five reactions (as a reactant in [reaction\\_16](#) and as a product in [reaction\\_6](#) and as a modifier in [reaction\\_1](#), [reaction\\_1](#), [reaction\\_16](#)).

$$\frac{d}{dt}\text{species\_11} = v_4 - v_{12} \quad (66)$$

### 10.7 Species `species_14`

**Name** Acr3

**Initial amount**  $1.5801923932594 \cdot 10^{-17}$   $\mu\text{mol}$

**Initial assignment** `species_14`

This species takes part in five reactions (as a reactant in [reaction\\_14](#) and as a product in [reaction\\_13](#) and as a modifier in [reaction\\_14](#), [reaction\\_15](#), [reaction\\_15](#)).

$$\frac{d}{dt}\text{species\_14} = v_9 - v_{10} \quad (67)$$

### 10.8 Species `species_4`

**Name** vAsGS3

**Initial amount**  $3.31525035810391 \cdot 10^{-12}$   $\mu\text{mol}$

**Initial assignment** `species_4`

This species takes part in three reactions (as a reactant in [reaction\\_18](#) and as a product in [reaction\\_10](#) and as a modifier in [reaction\\_18](#)).

$$\frac{d}{dt}\text{species\_4} = v_8 - v_{14} \quad (68)$$

## 10.9 Species `species_3`

**Name** AsGS3

**Initial amount**  $2.08447005232452 \cdot 10^{-11}$   $\mu\text{mol}$

**Initial assignment** `species_3`

This species takes part in six reactions (as a reactant in [reaction\\_10](#), [reaction\\_17](#) and as a product in [reaction\\_9](#), [reaction\\_18](#) and as a modifier in [reaction\\_10](#), [reaction\\_17](#)).

$$\frac{d}{dt}\text{species\_3} = v_7 + v_{14} - v_8 - v_{13} \quad (69)$$

## 10.10 Species `species_1`

**Name** AsIIIin

**Initial amount**  $3.94647 \cdot 10^{-13}$   $\mu\text{mol}$

**Initial assignment** `species_1`

This species takes part in 16 reactions (as a reactant in [reaction\\_7](#), [reaction\\_9](#), [reaction\\_15](#) and as a product in [reaction\\_1](#), [reaction\\_8](#), [reaction\\_17](#) and as a modifier in [reaction\\_1](#), [reaction\\_4](#), [reaction\\_4](#), [reaction\\_7](#), [reaction\\_9](#), [reaction\\_13](#), [reaction\\_13](#), [reaction\\_15](#), [reaction\\_16](#), [reaction\\_16](#)).

$$\frac{d}{dt}\text{species\_1} = v_1 + v_6 + v_{13} - v_5 - v_7 - v_{11} \quad (70)$$

## 10.11 Species `species_2`

**Name** AsIIIProt

**Initial amount**  $5.29105658389632 \cdot 10^{-12}$   $\mu\text{mol}$

**Initial assignment** `species_2`

This species takes part in three reactions (as a reactant in [reaction\\_8](#) and as a product in [reaction\\_7](#) and as a modifier in [reaction\\_8](#)).

$$\frac{d}{dt}\text{species\_2} = v_5 - v_6 \quad (71)$$



## 10.12 Species `species_7`

**Name** GSH

**Initial amount**  $4.8 \cdot 10^{-11} \mu\text{mol}$

**Initial assignment** `species_7`

This species takes part in three reactions (as a reactant in [reaction\\_9](#) and as a product in [reaction\\_17](#) and as a modifier in [reaction\\_9](#)).

$$\frac{d}{dt}\text{species\_7} = v_{13} - v_7 \quad (72)$$

SBML2<sup>LaTeX</sup> was developed by Andreas Dräger<sup>a</sup>, Hannes Planatscher<sup>a</sup>, Dieudonné M Wouamba<sup>a</sup>, Adrian Schröder<sup>a</sup>, Michael Hucka<sup>b</sup>, Lukas Endler<sup>c</sup>, Martin Golebiewski<sup>d</sup> and Andreas Zell<sup>a</sup>. Please see <http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX> for more information.

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