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[1], Soheil Rastgou Talemi[2] and Audald Lloret i Villas[3] 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 anddetoxification 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.

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

2.1 Unit `substance`

Name substance

Definition µmol

2.2 Unit `volume`

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

Definition l

2.3 Unit area

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

Definition 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 Dimensions	Size	Unit	Constant	Outside
compartment_2	Medium		3	$5 \cdot 10^{-11}$	l	☑	
compartment_3	Cell		3	$5 \cdot 10^{-14}$	l	☑	
compartment_1	Vac		3	$2 \cdot 10^{-14}$	l	☑	
compartment_4	Cell-vac		3	$3 \cdot 10^{-14}$	l	☑	

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 Condition
species_6	AsIIIex	compartment_2	µmol	⊟	☑
species_5	Ycf1	compartment_3	µmol	⊟	⊟
species_10	Hog1PP	compartment_3	µmol	⊟	⊟
species_9	Hog1	compartment_3	µmol	⊟	⊟
species_15	Fps1P	compartment_3	µmol	⊟	⊟
species_11	Fps1	compartment_3	µmol	⊟	⊟
species_14	Acr3	compartment_3	µmol	⊟	⊟
species_4	vAsGS3	compartment_1	µmol	⊟	⊟
species_3	AsGS3	compartment_4	µmol	⊟	⊟
species_1	AsIIIin	compartment_4	µmol	⊟	⊟
species_2	AsIIIProt	compartment_4	µmol	⊟	⊟
species_7	GSH	compartment_4	µmol	⊟	⊟

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

Id	Name	SBO	Value	Unit	Constant
parameter_37	v11_k		$1.92773 \cdot 10^{-7}$		☑
parameter_38	v10_ko		1.000		☑
parameter_39	v8_k		0.203		☑
parameter_40	v9_k1		6.143		☑
parameter_41	v2_k1		0.009		☑
parameter_42	v3_k1		$6.56918 \cdot 10^{-4}$		☑
parameter_43	v13_k1		$9.01422 \cdot 10^{-13}$		☑
Compartment_3	Initial for Cell-vac		$3 \cdot 10^{-14}$		☑
Metabolite_9	Initial for AsIIIin		13.155		☑
Metabolite_6	Initial for Acr3		$3.16038478651879 \cdot 10^{-4}$		☑
Metabolite_5	Initial for Fps1		0.002		☑
Metabolite_0	Initial for AsIIIex		100.000		☑
Compartment_2	Initial for Vac		$2 \cdot 10^{-14}$		☑
ModelValue_13	Initial for Fps1PPmax		0.030		☑
ModelValue_22	Initial for ko-8		1.000		☑
Asngpermil_ex	Asngpermil_ex		0.375		⊟

6 Initialassignments

This is an overview of 21 initialassignments.

6.1 Initialassignment compartment_1

Derived unit contains undeclared units

Math $0.4 \cdot \mathrm{vol}\,(\mathrm{compartment\_3})$

6.2 Initialassignment compartment_4

Derived unit contains undeclared units

Math $0.6 \cdot \mathrm{vol}\,(\mathrm{compartment\_3})$

6.3 Initialassignment species_5

Derived unit contains undeclared units

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

6.4 Initialassignment species_10

Derived unit contains undeclared units

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

6.5 Initialassignment species_9

Derived unit contains undeclared units

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

6.6 Initialassignment species_15

Derived unit contains undeclared units

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

6.7 Initialassignment species_11

Derived unit contains undeclared units

Math $\frac{0.03}{\frac{\text{parameter\_29} \cdot \frac{\text{species\_1}}{\text{vol}(\text{compartment\_4})} + \text{parameter\_30} \cdot \frac{\text{species\_10}}{\text{vol}(\text{compartment\_3})} + \text{parameter\_31}}{\text{parameter\_32}} + 1} \cdot \text{vol}\left(\text{compartment\_3}\right)$

6.8 Initialassignment species_14

Derived unit contains undeclared units

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

6.9 Initialassignment species_4

Derived unit contains undeclared units

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

6.10 Initialassignment species_3

Derived unit contains undeclared units

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

6.11 Initialassignment species_1

Derived unit contains undeclared units

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

6.12 Initialassignment species_2

Derived unit contains undeclared units

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

6.13 Initialassignment species_7

Derived unit contains undeclared units

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

6.14 Initialassignment Compartment_3

Derived unit l

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

6.15 Initialassignment Metabolite_9

Derived unit µmol

Math species_1

6.16 Initialassignment Metabolite_6

Derived unit µmol

Math species_14

6.17 Initialassignment Metabolite_5

Derived unit µmol

Math species_11

6.18 Initialassignment Metabolite_0

Derived unit µmol

Math species_6

6.19 Initialassignment Compartment_2

Derived unit l

Math vol (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

$$k \cdot ko \cdot M \cdot S \tag{1}$$

7.2 Function definition function_7

Name 2p modified constant flux (irrev)

Arguments M, k, ko

Mathematical Expression

$$\mathrm{k} \cdot \mathrm{ko} \cdot \mathrm{M} \tag{2}$$

7.3 Function definition function_6

Name Mixed Hill

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

Mathematical Expression

$$\mathrm{Substrate} \cdot (\mathrm{k} \cdot \mathrm{Mod1} + \mathrm{k1} \cdot \mathrm{Mod} + \mathrm{kb}) \tag{3}$$

7.4 Function definition function_2

Name 2p 2sub

Arguments k, ko, sub, sub2

Mathematical Expression

$$\mathrm{k} \cdot \mathrm{ko} \cdot \mathrm{sub} \cdot \mathrm{sub2} \tag{4}$$

7.5 Function definition function_1

Name corrected modified diffusion

Arguments V, Mod, k, Ex, In

Mathematical Expression

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

7.6 Function definition function_8

Name corrected mass action

Arguments V, k, Sub

Mathematical Expression

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

7.7 Function definition function_4

Name corrected 2p modified mass action

Arguments ko, Mod, k, V, Sub

Mathematical Expression

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

7.8 Function definition function_5

Name Rate Law for v20

Arguments V, Mod, Vmax, Sub, Km

Mathematical Expression

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

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:

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

8.2 Rule parameter_13

Rule parameter_13 is an assignment rule for parameter parameter_13:

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

8.3 Rule parameter_14

Rule parameter_14 is an assignment rule for parameter parameter_14:

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

8.4 Rule parameter_15

Rule parameter_15 is an assignment rule for parameter parameter_15:

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

8.5 Rule species_6

Rule species_6 is an assignment rule for species species_6:

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

8.6 Rule parameter_16

Rule parameter_16 is an assignment rule for parameter parameter_16:

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

8.7 Rule parameter_18

Rule parameter_18 is an assignment rule for parameter parameter_18:

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

8.8 Rule parameter_2

Rule parameter_2 is an assignment rule for parameter parameter_2:

$$\text{parameter\_2} = \frac{\text{parameter\_43} \cdot \text{Metabolite\_6}}{\text{Metabolite\_9}} \tag{16}$$

8.9 Rule parameter_3

Rule parameter_3 is an assignment rule for parameter parameter_3:

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

8.10 Rule parameter_12

Rule parameter_12 is an assignment rule for parameter parameter_12:

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

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:

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

8.12 Rule parameter_22

Rule parameter_22 is an assignment rule for parameter parameter_22:

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

8.13 Rule Asngpermil_ex

Rule Asngpermil_ex is an assignment rule for parameter Asngpermil_ex:

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

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

№	Id	Name	Reaction Equation	SBO
1	reaction_1	v1	$\text{species\_6} \xrightleftharpoons{\text{species\_11, species\_11, species\_6, species\_1}} \text{species\_1}$	
2	reaction_4	v4	$\text{species\_9} \xrightarrow{\text{species\_1, species\_9, species\_1}} \text{species\_10}$	
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	$\text{species\_1} + \text{species\_7} \xrightarrow{\text{species\_1, species\_7}} \text{species\_3}$	
8	reaction_10	v10	$\text{species\_3} \xrightarrow{\text{species\_5, species\_5, species\_3}} \text{species\_4}$	
9	reaction_13	v12	$\emptyset \xrightarrow{\text{species\_1, species\_1}} \text{species\_14}$	
10	reaction_14	v13	$\text{species\_14} \xrightarrow{\text{species\_14}} \emptyset$	
11	reaction_15	v14	$\text{species\_1} \xrightarrow{\text{species\_14, species\_14, species\_1}} \text{species\_6}$	
12	reaction_16	v6	$\text{species\_11} \xrightarrow{\text{species\_1, species\_10, species\_11, species\_1, species\_10}} \text{species\_15}$	
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

$$\text{species\_6} \xrightleftharpoons{\text{species\_11, species\_11, species\_6, species\_1}} \text{species\_1} \tag{22}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
species_6	AsIIIex	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
species_11	Fps1	
species_11	Fps1	
species_6	AsIIIex	
species_1	AsIIIin	

Product

Table 8: Properties of each product.

Id	Name	SBO
species_1	AsIIIin	

Kinetic Law

Derived unit contains undeclared units

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

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

9.2 Reaction `reaction_4`

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

Name v4

Reaction equation

$$\text{species\_9} \xrightarrow{\text{species\_1, species\_9, species\_1}} \text{species\_10} \tag{25}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
`species_9`	Hog1	

Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
`species_1`	AsIIIin	
`species_9`	Hog1	
`species_1`	AsIIIin	

Product

Table 11: Properties of each product.

Id	Name	SBO
`species_10`	Hog1PP	

Kinetic Law

Derived unit contains undeclared units

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

$$\mathrm{function\_3}\left(\mathrm{S}, \mathrm{M}, \mathrm{k}, \mathrm{ko}\right) = \mathrm{k} \cdot \mathrm{ko} \cdot \mathrm{M} \cdot \mathrm{S} \tag{27}$$

$$\mathrm{function\_3}\left(\mathrm{S}, \mathrm{M}, \mathrm{k}, \mathrm{ko}\right) = \mathrm{k} \cdot \mathrm{ko} \cdot \mathrm{M} \cdot \mathrm{S} \tag{28}$$

9.3 Reaction `reaction_5`

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

Name v5

Reaction equation

$$\mathrm{species\_10} \xrightarrow{\mathrm{species\_10}} \mathrm{species\_9} \tag{29}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
`species_10`	Hog1PP	

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
`species_10`	Hog1PP	

Product

Table 14: Properties of each product.

Id	Name	SBO
`species_9`	Hog1	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{parameter\_27} \cdot \text{species\_10} \tag{30}$$

9.4 Reaction `reaction_6`

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

Name v7

Reaction equation

$$\text{species\_15} \xrightarrow{\text{species\_15}} \text{species\_11} \tag{31}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
`species_15`	Fps1P	

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
`species_15`	Fps1P	

Product

Table 17: Properties of each product.

Id	Name	SBO
`species_11`	Fps1	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{parameter\_32} \cdot \text{species\_15} \tag{32}$$

9.5 Reaction reaction_7

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

Name v2

Reaction equation

$$\text{species\_1} \xrightarrow{\text{species\_1}} \text{species\_2} \tag{33}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
species_1	AsIIIin	

Modifier

Table 19: Properties of each modifier.

Id	Name	SBO
species_1	AsIIIin	

Product

Table 20: Properties of each product.

Id	Name	SBO
species_2	AsIIIProt	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{parameter\_41} \cdot \text{species\_1} \tag{34}$$

9.6 Reaction reaction_8

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

Name v3

Reaction equation

$$\text{species\_2} \xrightarrow{\text{species\_2}} \text{species\_1} \tag{35}$$

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

$$v_6 = \text{parameter\_42} \cdot \text{species\_2} \tag{36}$$

9.7 Reaction reaction_9

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

Name v8

Reaction equation

$$\text{species\_1} + \text{species\_7} \xrightarrow{\text{species\_1, species\_7}} \text{species\_3} \tag{37}$$

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

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

$$\mathrm{function\_2}\left(\mathrm{k}, \mathrm{ko}, \mathrm{sub}, \mathrm{sub2}\right) = \mathrm{k} \cdot \mathrm{ko} \cdot \mathrm{sub} \cdot \mathrm{sub2} \tag{39}$$

$$\mathrm{function\_2}\left(\mathrm{k}, \mathrm{ko}, \mathrm{sub}, \mathrm{sub2}\right) = \mathrm{k} \cdot \mathrm{ko} \cdot \mathrm{sub} \cdot \mathrm{sub2} \tag{40}$$

9.8 Reaction reaction_10

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

Name v10

Reaction equation

$$\text{species\_3} \xrightarrow{\text{species\_5, species\_5, species\_3}} \text{species\_4} \tag{41}$$

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	Ycf1	
species_5	Ycf1	
species_3	AsGS3	

Product

Table 29: Properties of each product.

Id	Name	SBO
species_4	vAsGS3	

Kinetic Law

Derived unit contains undeclared units

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

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

9.9 Reaction reaction_13

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

Name v12

Reaction equation

$$\emptyset \xrightarrow{\text{species\_1, species\_1}} \text{species\_14} \tag{44}$$

Modifiers

Table 30: Properties of each modifier.

Id	Name	SBO
species_1	AsIIIin	
species_1	AsIIIin	

Product

Table 31: Properties of each product.

Id	Name	SBO
species_14	Acr3	

Kinetic Law

Derived unit contains undeclared units

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

$$\text{function\_7}\left(\text{M}, \text{k}, \text{ko}\right) = \text{k} \cdot \text{ko} \cdot \text{M} \tag{46}$$

$$\text{function\_7}\left(\text{M}, \text{k}, \text{ko}\right) = \text{k} \cdot \text{ko} \cdot \text{M} \tag{47}$$

9.10 Reaction reaction_14

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

Name v13

Reaction equation

$$\text{species\_14} \xrightarrow{\text{species\_14}} \emptyset \tag{48}$$

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

$$v_{10} = \text{parameter\_43} \cdot \text{species\_14} \tag{49}$$

9.11 Reaction reaction_15

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

Name v14

Reaction equation

$$\text{species\_1} \xrightarrow{\text{species\_14, species\_14, species\_1}} \text{species\_6} \tag{50}$$

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

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

$$\text{function\_5}\left(\text{V}, \text{Mod}, \text{Vmax}, \text{Sub}, \text{Km}\right) = \frac{\left(36 \cdot \pi\right)^{\frac{1}{3}} \cdot \text{V}^{\frac{2}{3}} \cdot \text{Mod} \cdot \text{Vmax} \cdot \text{Sub}}{\text{Km} + \text{Sub}} \tag{52}$$

9.12 Reaction reaction_16

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

Name v6

Reaction equation

$$\text{species\_11} \xrightarrow{\text{species\_1, species\_10, species\_11, species\_1, species\_10}} \text{species\_15} \tag{53}$$

Reactant

Table 37: Properties of each reactant.

Id	Name	SBO
species_11	Fps1	

Modifiers

Table 38: Properties of each modifier.

Id	Name	SBO
species_1	AsIIIin	
species_10	Hog1PP	
species_11	Fps1	
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

$$v_{12} = \mathrm{vol}\left(\mathrm{compartment\_3}\right) \cdot \mathrm{function\_6}\left(\frac{\mathrm{species\_11}}{\mathrm{vol}\left(\mathrm{compartment\_3}\right)}, \mathrm{parameter\_29}, \frac{\mathrm{species\_1}}{\mathrm{vol}\left(\mathrm{compartment\_4}\right)}, \frac{\mathrm{species\_10}}{\mathrm{vol}\left(\mathrm{compartment\_3}\right)}, \mathrm{parameter\_30}, \mathrm{parameter\_31}\right) \tag{54}$$

$$\mathrm{function\_6}\left(\mathrm{Substrate}, \mathrm{k}, \mathrm{Mod1}, \mathrm{Mod}, \mathrm{k1}, \mathrm{kb}\right) = \mathrm{Substrate} \cdot \left(\mathrm{k} \cdot \mathrm{Mod1} + \mathrm{k1} \cdot \mathrm{Mod} + \mathrm{kb}\right) \tag{55}$$

$$\mathrm{function\_6}\left(\mathrm{Substrate}, \mathrm{k}, \mathrm{Mod1}, \mathrm{Mod}, \mathrm{k1}, \mathrm{kb}\right) = \mathrm{Substrate} \cdot \left(\mathrm{k} \cdot \mathrm{Mod1} + \mathrm{k1} \cdot \mathrm{Mod} + \mathrm{kb}\right) \tag{56}$$

9.13 Reaction reaction_17

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

Name v9

Reaction equation

$$\text{species\_3} \xrightarrow{\text{species\_3}} \text{species\_1} + \text{species\_7} \tag{57}$$

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

$$v_{13} = \text{parameter\_40} \cdot \text{species\_3} \tag{58}$$

9.14 Reaction reaction_18

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

Name v11

Reaction equation

$$\text{species\_4} \xrightarrow{\text{species\_4}} \text{species\_3} \tag{59}$$

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

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

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

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 $5 \cdot 10^{-9}$ µmol

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 Ycf1

Initial amount $6.5755 \cdot 10^{-16}$ µmol

Initial assignment species_5

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_5} = 0 \tag{62}$$

10.3 Species species_10

Name Hog1PP

Initial amount $5.12422021489774 \cdot 10^{-17}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_10} = v_2 - v_3 \tag{63}$$

10.4 Species species_9

Name Hog1

Initial amount $8.29875779785102 \cdot 10^{-15}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_9} = v_3 - v_2 \tag{64}$$

10.5 Species species_15

Name Fps1P

Initial amount $1.41558600877709 \cdot 10^{-15}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_15} = v_{12} - v_4 \tag{65}$$

10.6 Species species_11

Name Fps1

Initial amount $8.44139912229068 \cdot 10^{-17}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_11} = v_4 - v_{12} \tag{66}$$

10.7 Species species_14

Name Acr3

Initial amount $1.5801923932594 \cdot 10^{-17}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_14} = v_9 - v_{10} \tag{67}$$

10.8 Species species_4

Name vAsGS3

Initial amount $3.31525035810391 \cdot 10^{-12}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_4} = v_8 - v_{14} \tag{68}$$

10.9 Species species_3

Name AsGS3

Initial amount $2.08447005232452 \cdot 10^{-11}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_3} = v_7 + v_{14} - v_8 - v_{13} \tag{69}$$

10.10 Species species_1

Name AsIIIin

Initial amount $3.94647 \cdot 10^{-13}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_1} = v_1 + v_6 + v_{13} - v_5 - v_7 - v_{11} \tag{70}$$

10.11 Species species_2

Name AsIIIProt

Initial amount $5.29105658389632 \cdot 10^{-12}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_2} = v_5 - v_6 \tag{71}$$

10.12 Species species_7

Name GSH

Initial amount $4.8 \cdot 10^{-11}$ µmol

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).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_7} = v_{13} - v_7 \tag{72}$$

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