

## SBML Model Report

# Model name: “Kolodkin2013 - Nuclear receptor-mediated cortisol signalling network”



May 5, 2016

## 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Alastair Hume<sup>1</sup> and Nilgun Sahin<sup>2</sup> at July third 2015 at 11:56 a. m. and last time modified at September ninth 2015 at 11:03 a. m. Table 1 gives an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	2
species types	0	species	42
events	0	constraints	0
reactions	52	function definitions	3
global parameters	11	unit definitions	2
rules	2	initial assignments	0

## Model Notes

Kolodkin2013 - Nuclear receptor-mediatedcortisol signalling network

<sup>1</sup>The University of Edinburgh, [a.hume@ed.ac.uk](mailto:a.hume@ed.ac.uk)

<sup>2</sup>Molecular Cell Physiology, Netherlands Institute of Systems Biology, VU University Amsterdam, de Boelelaan 1085, NL-1081 HV Amsterdam, The Netherlands, [nilguenyilmaz@gmail.com](mailto:nilguenyilmaz@gmail.com)

This model is described in the article: [Optimization of stress response through the nuclear receptor-mediated cortisol signalling network](#). Kolodkin A, Sahin N, Phillips A, Hood SR, Bruggerman FJ, Westerhoff HV, Plant N. Nat Commun 2013; 4: 1792

Abstract:

It is an accepted paradigm that extended stress predisposes an individual to pathophysiology. However, the biological adaptations to minimize this risk are poorly understood. Using a computational model based upon realistic kinetic parameters we are able to reproduce the interaction of the stress hormone cortisol with its two nuclear receptors, the high-affinity glucocorticoid receptor and the low-affinity pregnane X-receptor. We demonstrate that regulatory signals between these two nuclear receptors are necessary to optimize the body's response to stress episodes, attenuating both the magnitude and duration of the biological response. In addition, we predict that the activation of pregnane X-receptor by multiple, low-affinity endobiotic ligands is necessary for the significant pregnane X-receptor-mediated transcriptional response observed following stress episodes. This integration allows responses mediated through both the high and low-affinity nuclear receptors, which we predict is an important strategy to minimize the risk of disease from chronic stress.

This model is hosted on [BioModels Database](#) and identified by: [BIOMD0000000576](#).

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

To the extent possible under law, all copyright and related or neighbouring rights to this encoded model have been dedicated to the public domain worldwide. Please refer to [CC0 Public Domain Dedication](#) for more information.

## 2 Unit Definitions

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

### 2.1 Unit time

**Name** time

**Definition** 60 s

### 2.2 Unit substance

**Name** substance

**Definition** nmol

### 2.3 Unit volume

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

**Definition** 1

## 2.4 Unit `area`

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

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

## 2.5 Unit `length`

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

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

# 3 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
<code>default</code>	<code>default</code>		3	1	litre	<input checked="" type="checkbox"/>	
<code>blood</code>	<code>blood</code>		3	5	l	<input checked="" type="checkbox"/>	

## 3.1 Compartment `default`

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

**Name** `default`

## 3.2 Compartment `blood`

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

**Name** `blood`

## 4 Species

This model contains 42 species. The boundary condition of eight 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
s28	S_RNA	default	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
s36	S_PROT	default	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
s46	PXR_GENE	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s32	PXR_RNA	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s42	PXR_PROT	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s30	P	default	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
s40	GR_GENE	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s33	GR_RNA	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s39	GR_PROT	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s114	Cort	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s155	CYP_GENE	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s172	CYP_PROT	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s173	CYP_RNA	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s185	TAT_RNA	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s84	GRgene_GRprot_Cort	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s165	CYPgene_PXRprot_Cort	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s109	PXRgene_GRprot_Cort	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s87	GRprot_Cort	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s119	PXRprot_Cort	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s183	TATgene_GRprot_Cort	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s178	TAT_GENE	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
s10	Cort_degr	default	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Cortisone	Cortisone	default	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
TAT_PROT	TAT_PROT	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
Ligand2	Ligand2	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
PXRprot_Ligand2	PXRprot_Ligand2	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
CYPgene_PXRprot-Ligand2	CYPgene_PXRprot_Ligand2	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
DEX	DEX	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
GRprot_DEX	GRprot_DEX	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
PXRprot_DEX	PXRprot_DEX	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
DEX_degr	DEX_degr	default	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
CYPgene_PXRprot-DEX	CYPgene_PXRprot_DEX	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
PXRgene_GRprot-DEX	PXRgene_GRprot_DEX	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
GRgene_GRprot_DEX	GRgene_GRprot_DEX	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
TATgene_GRprot-DEX	TATgene_GRprot_DEX	default	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
s2	CortOUT	blood	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
DEXout	DEXout	blood	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
CBG	CBG	blood	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
CBG_CortOUT	CBG_CortOUT	blood	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
Alb	Alb	blood	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
Alb_CortOUT	Alb_CortOUT	blood	$\text{nmol} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
CortAdded	CortAdded	blood	$\text{nmol} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

## 5 Parameters

This model contains eleven global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
GeneProteinBinding- _diff_limited	GeneProteinBinding- _diff_limited		60.000		<input checked="" type="checkbox"/>
cypGene- _PXRprotein	cypGene- _PXRprotein		1.000		<input checked="" type="checkbox"/>
cypMrna_synt	cypMrna_synt		0.050		<input checked="" type="checkbox"/>
PXRGene- _GRprotein	PXRGene- _GRprotein		200.000		<input checked="" type="checkbox"/>
TATGene- _GRprotein	TATGene- _GRprotein		300.000		<input checked="" type="checkbox"/>
GRGene- _GRprotein	GRGene- _GRprotein		60.000		<input checked="" type="checkbox"/>
grMrna_synt	grMrna_synt		$1.2 \cdot 10^{-6}$		<input checked="" type="checkbox"/>
tatMrna_synt	tatMrna_synt		0.005		<input checked="" type="checkbox"/>
pxrMrna_synt	pxrMrna_synt		$1.1 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
GRprotein	GRprotein		80.000		<input type="checkbox"/>
PXRprotein	PXRprotein		99.911		<input type="checkbox"/>

## 6 Function definitions

This is an overview of three function definitions.

### 6.1 Function definition `mRNA`

**Name** `mRNA`

**Arguments** `S_RNA`, `Activator`, `Ka`

**Mathematical Expression**

$$Ka \cdot S\_RNA \cdot Activator \quad (1)$$

### 6.2 Function definition `ptotein`

**Name** `ptotein`

**Arguments** `Ka`, `S_PROT`, `Activator`

**Mathematical Expression**

$$Ka \cdot S\_PROT \cdot Activator \quad (2)$$

### 6.3 Function definition `LigandDegrOld`

**Name** `LigandDegrOld`

**Arguments** `Act`, `Vm`, `S1`, `Kms1`, `S2`, `Kms2`, `S3`, `Kms3`

**Mathematical Expression**

$$\text{Act} \cdot \frac{\frac{Vm \cdot S1}{Kms1}}{1 + \frac{S1}{Kms1} + \frac{S2}{Kms2} + \frac{S3}{Kms3}} \quad (3)$$

## 7 Rules

This is an overview of two rules.

### 7.1 Rule `GRprotein`

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

$$\begin{aligned} \text{GRprotein} = & [\text{s39}] + [\text{s84}] + [\text{s109}] + [\text{s87}] + [\text{s183}] + [\text{GRprot\_DEX}] \\ & + [\text{PXRgene\_GRprot\_DEX}] + [\text{GRgene\_GRprot\_DEX}] + [\text{TATgene\_GRprot\_DEX}] \end{aligned} \quad (4)$$

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

### 7.2 Rule `PXRprotein`

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

$$\begin{aligned} \text{PXRprotein} = & [\text{s42}] + [\text{s165}] + [\text{s119}] + [\text{PXRprot\_Ligand2}] + [\text{CYPgene\_PXRprot\_Ligand2}] \\ & + [\text{PXRprot\_DEX}] + [\text{CYPgene\_PXRprot\_DEX}] \end{aligned} \quad (5)$$

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

## 8 Reactions

This model contains 52 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	re1	re1	$s_{28} \xrightarrow{s_{155}, s_{28}, s_{155}} s_{173}$	
2	re2	re2	$s_{173} \xrightarrow{s_{173}} s_{30}$	
3	re3	re3	$s_{36} \xrightarrow{s_{173}, s_{36}, s_{173}} s_{172}$	
4	re4	re4	$s_{172} \xrightarrow{s_{172}} s_{30}$	
5	re5	re5	$s_{28} \xrightarrow{s_{46}, s_{28}, s_{46}} s_{32}$	
6	re6	re6	$s_{32} \xrightarrow{s_{32}} s_{30}$	
7	re7	re7	$s_{36} \xrightarrow{s_{32}, s_{36}, s_{32}} s_{42}$	
8	re8	re8	$s_{42} \xrightarrow{s_{42}} s_{30}$	
9	re9	re9	$s_{28} \xrightarrow{s_{40}, s_{28}, s_{40}} s_{33}$	
10	re10	re10	$s_{33} \xrightarrow{s_{33}} s_{30}$	
11	re11	re11	$s_{36} \xrightarrow{s_{33}, s_{36}, s_{33}} s_{39}$	
12	re12	re12	$s_{39} \xrightarrow{s_{39}} s_{30}$	
13	re13	re13	$s_{28} \xrightarrow{s_{178}, s_{28}, s_{178}} s_{185}$	
14	re14	re14	$s_{185} \xrightarrow{s_{185}} s_{30}$	
15	re15	re15	$s_{114} + s_{39} \xrightleftharpoons{s_{114}, s_{39}, s_{87}} s_{87}$	
16	re16	re16	$s_{87} \xrightarrow{s_{87}} s_{114} + s_{30}$	



Nº	Id	Name	Reaction Equation	SBO
17	re17	re17	$s42 + s114 \xrightleftharpoons{s42, s114, s119} s119$	
18	re18	re18	$s119 \xrightarrow{s119} s114 + s30$	
19	re19	re19	$s114 \xrightarrow{s172, \text{Ligand2}, \text{DEX}, s172, s114, \text{Ligand2}, \text{DEX}} s10$	
20	re20	re20	$s155 + s119 \xrightleftharpoons{s155, s119, s165} s165$	
21	re21	re21	$s28 \xrightarrow{s165, s28, s165} s173$	
22	re22	re22	$s46 + s87 \xrightleftharpoons{s46, s87, s109} s109$	
23	re23	re23	$s28 \xrightarrow{s109, s28, s109} s32$	
24	re24	re24	$s40 + s87 \xrightleftharpoons{s40, s87, s84} s84$	
25	re25	re25	$s28 \xrightarrow{s84, s28, s84} s33$	
26	re26	re26	$s178 + s87 \xrightleftharpoons{s178, s87, s183} s183$	
27	re27	re27	$s28 \xrightarrow{s183, s28, s183} s185$	
28	re42	re42	$\text{Cortisone} \xrightleftharpoons{\text{Cortisone}, s114} s114$	
29	re44	re44	$\text{TAT\_PROT} \xrightarrow{\text{TAT\_PROT}} s30$	
30	re43	re43	$s36 \xrightarrow{s185, s36, s185} \text{TAT\_PROT}$	
31	cortisolTransportcortisolTransport		$s2 \xrightleftharpoons{s2, s114} s114$	
32	L2_PXR_binding	L2_PXR_binding	$s42 + \text{Ligand2} \xrightleftharpoons{s42, \text{Ligand2}, \text{PXRprot\_Ligand2}} \text{PXRprot\_Ligand2}$	
33	L2_PXR_deg	L2_PXR_deg	$\text{PXRprot\_Ligand2} \xrightarrow{\text{PXRprot\_Ligand2}} \text{Ligand2} + s30$	
34	CYPmRNA_synt- _PXR_L2	CYPmRNA_synt_PXR_L2	$s28 \xrightarrow{\text{CYPgene\_PXRprot\_Ligand2}, s28, \text{CYPgene\_PXRprot\_Ligand2}} s173$	

Nº	Id	Name	Reaction Equation	SBO
35	CYPmRNA_PXR_L2-binding	CYPmRNA_PXR_L2_binding	$s155 + \text{PXRprot\_Ligand2} \xrightleftharpoons{s155, \text{PXRprot\_Ligand2}, \text{CYPgene\_PXRprot\_Ligand2}} \text{CYPg}$	
36	re28	re28	$s39 + \text{DEX} \xrightleftharpoons{s39, \text{DEX}, \text{GRprot\_DEX}} \text{GRprot\_DEX}$	
37	re29	re29	$\text{GRprot\_DEX} \xrightarrow{\text{GRprot\_DEX}} s30 + \text{DEX}$	
38	re30	re30	$s42 + \text{DEX} \xrightleftharpoons{s42, \text{DEX}, \text{PXRprot\_DEX}} \text{PXRprot\_DEX}$	
39	re31	re31	$\text{PXRprot\_DEX} \xrightarrow{\text{PXRprot\_DEX}} \text{DEX} + s30$	
40	re32	re32	$\text{DEX} \xrightarrow{s172, \text{Ligand2}, s114, s172, \text{DEX}, \text{Ligand2}, s114} \text{DEX\_degr}$	
41	re33	re33	$s155 + \text{PXRprot\_DEX} \xrightleftharpoons{s155, \text{PXRprot\_DEX}, \text{CYPgene\_PXRprot\_DEX}} \text{CYPgene\_PXR}$	
42	re34	re34	$s28 \xrightarrow{\text{CYPgene\_PXRprot\_DEX}, s28, \text{CYPgene\_PXRprot\_DEX}} s173$	
43	re35	re35	$\text{GRprot\_DEX} + s46 \xrightleftharpoons{\text{GRprot\_DEX}, s46, \text{PXRgene\_GRprot\_DEX}} \text{PXRgene\_GRprot\_DE}$	
44	re36	re36	$s28 \xrightarrow{\text{PXRgene\_GRprot\_DEX}, s28, \text{PXRgene\_GRprot\_DEX}} s32$	
45	re37	re37	$\text{GRprot\_DEX} + s40 \xrightleftharpoons{\text{GRprot\_DEX}, s40, \text{GRgene\_GRprot\_DEX}} \text{GRgene\_GRprot\_DEX}$	
46	re38	re38	$s28 \xrightarrow{\text{GRgene\_GRprot\_DEX}, s28, \text{GRgene\_GRprot\_DEX}} s33$	
47	re39	re39	$\text{GRprot\_DEX} + s178 \xrightleftharpoons{\text{GRprot\_DEX}, s178, \text{TATgene\_GRprot\_DEX}} \text{TATgene\_GRprot\_D}$	
48	re40	re40	$s28 \xrightarrow{\text{TATgene\_GRprot\_DEX}, s28, \text{TATgene\_GRprot\_DEX}} s185$	
49	re41	re41	$\text{DEXout} \xrightleftharpoons{\text{DEXout}, \text{DEX}} \text{DEX}$	
50	Cortisol_CBG	Cortisol_CBG	$s2 + \text{CBG} \xrightleftharpoons{s2, \text{CBG}, \text{CBG\_CortOUT}} \text{CBG\_CortOUT}$	
51	Cort_Alb	Cort_Alb	$\text{Alb} + s2 \xrightleftharpoons{\text{Alb}, s2, \text{Alb\_CortOUT}} \text{Alb\_CortOUT}$	
52	cort-distribution	cort_distribution	$\text{CortAdded} \xrightarrow{\text{CortAdded}} s2$	

Nº	Id	Name	Reaction Equation	SBO
----	----	------	-------------------	-----

## 8.1 Reaction `re1`

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

**Name** `re1`

### Reaction equation



### Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
<code>s28</code>	<code>S_RNA</code>	

### Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
<code>s155</code>	<code>CYP_GENE</code>	
<code>s28</code>	<code>S_RNA</code>	
<code>s155</code>	<code>CYP_GENE</code>	

### Product

Table 8: Properties of each product.

Id	Name	SBO
<code>s173</code>	<code>CYP_RNA</code>	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_1 = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [s155], Ka) \quad (7)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, Ka) = Ka \cdot S\_RNA \cdot \text{Activator} \quad (8)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, Ka) = Ka \cdot S\_RNA \cdot \text{Activator} \quad (9)$$

Table 9: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Ka	Ka		0.003		<input checked="" type="checkbox"/>

## 8.2 Reaction re2

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

**Name** re2

### Reaction equation



### Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
s173	CYP_RNA	

### Modifier

Table 11: Properties of each modifier.

Id	Name	SBO
s173	CYP_RNA	

### Product

Table 12: Properties of each product.

Id	Name	SBO
s30	P	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_2 = \text{vol}(\text{default}) \cdot k_1 \cdot [s173] \quad (11)$$

Table 13: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.04		<input checked="" type="checkbox"/>

### 8.3 Reaction re3

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

**Name** re3

#### Reaction equation



#### Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
s36	S_PROT	

#### Modifiers

Table 15: Properties of each modifier.

Id	Name	SBO
s173	CYP_RNA	
s36	S_PROT	
s173	CYP_RNA	

#### Product

Table 16: Properties of each product.

Id	Name	SBO
s172	CYP_PROT	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_3 = \text{vol}(\text{default}) \cdot \text{ptotein}(\text{Ka}, [\text{s36}], [\text{s173}]) \quad (13)$$

$$\text{ptotein}(\text{Ka}, \text{S\_PROT}, \text{Activator}) = \text{Ka} \cdot \text{S\_PROT} \cdot \text{Activator} \quad (14)$$

$$\text{ptotein}(\text{Ka}, \text{S\_PROT}, \text{Activator}) = \text{Ka} \cdot \text{S\_PROT} \cdot \text{Activator} \quad (15)$$

Table 17: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Ka	Ka		2.5		<input checked="" type="checkbox"/>

## 8.4 Reaction re4

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

**Name** re4

### Reaction equation



### Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
s172	CYP_PROT	

### Modifier

Table 19: Properties of each modifier.

Id	Name	SBO
s172	CYP_PROT	

### Product

Table 20: Properties of each product.

Id	Name	SBO
s30	P	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_4 = \text{vol}(\text{default}) \cdot k1 \cdot [\text{s172}] \quad (17)$$

Table 21: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.002		<input checked="" type="checkbox"/>

## 8.5 Reaction re5

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

**Name** re5

### Reaction equation



### Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

### Modifiers

Table 23: Properties of each modifier.

Id	Name	SBO
s46	PXR_GENE	
s28	S_RNA	
s46	PXR_GENE	



Id	Name	SBO
----	------	-----

## Product

Table 24: Properties of each product.

Id	Name	SBO
s32	PXR_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_5 = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [s46], \text{Ka}) \quad (19)$$

$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (20)$$

$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (21)$$

Table 25: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Ka	Ka		$5.52 \cdot 10^{-5}$		<input checked="" type="checkbox"/>

## 8.6 Reaction re6

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

**Name** re6

### Reaction equation



## Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
s32	PXR_RNA	

## Modifier

Table 27: Properties of each modifier.

Id	Name	SBO
s32	PXR_RNA	

## Product

Table 28: Properties of each product.

Id	Name	SBO
s30	P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_6 = \text{vol}(\text{default}) \cdot k_1 \cdot [\text{s32}] \quad (23)$$

Table 29: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.006		<input checked="" type="checkbox"/>

## 8.7 Reaction re7

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

**Name** re7

### Reaction equation



## Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
s36	S_PROT	

Id	Name	SBO
----	------	-----

## Modifiers

Table 31: Properties of each modifier.

Id	Name	SBO
s32	PXR_RNA	
s36	S_PROT	
s32	PXR_RNA	

## Product

Table 32: Properties of each product.

Id	Name	SBO
s42	PXR_PROT	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_7 = \text{vol}(\text{default}) \cdot \text{ptotein}(\text{Ka}, [\text{s36}], [\text{s32}]) \quad (25)$$

$$\text{ptotein}(\text{Ka}, \text{S\_PROT}, \text{Activator}) = \text{Ka} \cdot \text{S\_PROT} \cdot \text{Activator} \quad (26)$$

$$\text{ptotein}(\text{Ka}, \text{S\_PROT}, \text{Activator}) = \text{Ka} \cdot \text{S\_PROT} \cdot \text{Activator} \quad (27)$$

Table 33: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Ka	Ka		10.0		✓

## 8.8 Reaction re8

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

**Name** re8

## Reaction equation



## Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
s42	PXR_PROT	

## Modifier

Table 35: Properties of each modifier.

Id	Name	SBO
s42	PXR_PROT	

## Product

Table 36: Properties of each product.

Id	Name	SBO
s30	P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_8 = \text{vol}(\text{default}) \cdot k1 \cdot [s42] \quad (29)$$

Table 37: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.003		<input checked="" type="checkbox"/>

## 8.9 Reaction re9

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

**Name** re9

### Reaction equation



### Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

### Modifiers

Table 39: Properties of each modifier.

Id	Name	SBO
s40	GR_GENE	
s28	S_RNA	
s40	GR_GENE	

### Product

Table 40: Properties of each product.

Id	Name	SBO
s33	GR_RNA	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_9 = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [s40], Ka) \quad (31)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, Ka) = Ka \cdot S\_RNA \cdot \text{Activator} \quad (32)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, Ka) = Ka \cdot S\_RNA \cdot \text{Activator} \quad (33)$$

Table 41: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Ka	Ka		$3.2 \cdot 10^{-6}$		<input checked="" type="checkbox"/>

### 8.10 Reaction `re10`

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

**Name** `re10`

#### Reaction equation



#### Reactant

Table 42: Properties of each reactant.

Id	Name	SBO
s33	GR_RNA	

#### Modifier

Table 43: Properties of each modifier.

Id	Name	SBO
s33	GR_RNA	

#### Product

Table 44: Properties of each product.

Id	Name	SBO
s30	P	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{10} = \text{vol}(\text{default}) \cdot k1 \cdot [s33] \quad (35)$$

Table 45: Properties of each parameter.

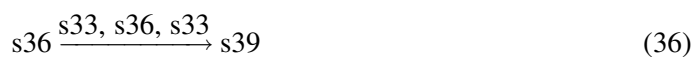
Id	Name	SBO	Value	Unit	Constant
k1	k1		0.003		<input checked="" type="checkbox"/>

### 8.11 Reaction `re11`

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

**Name** `re11`

#### Reaction equation



#### Reactant

Table 46: Properties of each reactant.

Id	Name	SBO
s36	S_PROT	

#### Modifiers

Table 47: Properties of each modifier.

Id	Name	SBO
s33	GR_RNA	
s36	S_PROT	
s33	GR_RNA	

#### Product

Table 48: Properties of each product.

Id	Name	SBO
s39	GR_PROT	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{11} = \text{vol}(\text{default}) \cdot \text{ptotein}(\text{Ka}, [\text{s36}], [\text{s33}]) \quad (37)$$

$$\text{ptotein}(\text{Ka}, \text{S\_PROT}, \text{Activator}) = \text{Ka} \cdot \text{S\_PROT} \cdot \text{Activator} \quad (38)$$

$$\text{ptotein}(\text{Ka}, \text{S\_PROT}, \text{Activator}) = \text{Ka} \cdot \text{S\_PROT} \cdot \text{Activator} \quad (39)$$

Table 49: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Ka	Ka		19.98		<input checked="" type="checkbox"/>

## 8.12 Reaction `re12`

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

**Name** `re12`

### Reaction equation



### Reactant

Table 50: Properties of each reactant.

Id	Name	SBO
s39	GR_PROT	

### Modifier

Table 51: Properties of each modifier.

Id	Name	SBO
s39	GR_PROT	

### Product



Table 52: Properties of each product.

Id	Name	SBO
s30	P	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{12} = \text{vol}(\text{default}) \cdot k1 \cdot [s39] \quad (41)$$

Table 53: Properties of each parameter.

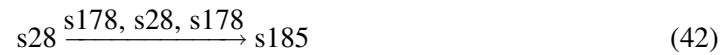
Id	Name	SBO	Value	Unit	Constant
k1	k1		0.001		<input checked="" type="checkbox"/>

### 8.13 Reaction re13

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

**Name** re13

### Reaction equation



### Reactant

Table 54: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

### Modifiers

Table 55: Properties of each modifier.

Id	Name	SBO
s178	TAT_GENE	
s28	S_RNA	
s178	TAT_GENE	

Id	Name	SBO
----	------	-----

## Product

Table 56: Properties of each product.

Id	Name	SBO
s185	TAT_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{13} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [s178], \text{Ka}) \quad (43)$$

$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (44)$$

$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (45)$$

Table 57: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Ka	Ka		$8.55 \cdot 10^{-4}$		<input checked="" type="checkbox"/>

## 8.14 Reaction re14

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

**Name** re14

## Reaction equation



## Reactant

Table 58: Properties of each reactant.

Id	Name	SBO
s185	TAT_RNA	

## Modifier

Table 59: Properties of each modifier.

Id	Name	SBO
s185	TAT_RNA	

## Product

Table 60: Properties of each product.

Id	Name	SBO
s30	P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{14} = \text{vol}(\text{default}) \cdot k1 \cdot [\text{s185}] \quad (47)$$

Table 61: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.064		<input checked="" type="checkbox"/>

### 8.15 Reaction `re15`

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** `re15`

#### Reaction equation



## Reactants

Table 62: Properties of each reactant.

Id	Name	SBO
s114	Cort	

Id	Name	SBO
s39	GR_PROT	

## Modifiers

Table 63: Properties of each modifier.

Id	Name	SBO
s114	Cort	
s39	GR_PROT	
s87	GRprot_Cort	

## Product

Table 64: Properties of each product.

Id	Name	SBO
s87	GRprot_Cort	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{15} = \text{vol}(\text{default}) \cdot (k1 \cdot [s114] \cdot [s39] - k2 \cdot [s87]) \quad (49)$$

Table 65: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		60.0		<input checked="" type="checkbox"/>
k2	k2		600.0		<input checked="" type="checkbox"/>

### 8.16 Reaction re16

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

**Name** re16

#### Reaction equation



## Reactant

Table 66: Properties of each reactant.

Id	Name	SBO
s87	GRprot_Cort	

## Modifier

Table 67: Properties of each modifier.

Id	Name	SBO
s87	GRprot_Cort	

## Products

Table 68: Properties of each product.

Id	Name	SBO
s114	Cort	
s30	P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{16} = \text{vol}(\text{default}) \cdot k_1 \cdot [\text{s87}] \quad (51)$$

Table 69: Properties of each parameter.

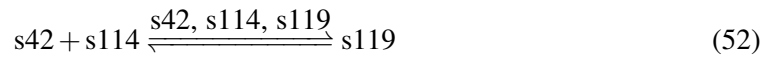
Id	Name	SBO	Value	Unit	Constant
k1	k1		0.001		✓

## 8.17 Reaction re17

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re17

## Reaction equation



## Reactants

Table 70: Properties of each reactant.

Id	Name	SBO
s42	PXR_PROT	
s114	Cort	

## Modifiers

Table 71: Properties of each modifier.

Id	Name	SBO
s42	PXR_PROT	
s114	Cort	
s119	PXRprot_Cort	

## Product

Table 72: Properties of each product.

Id	Name	SBO
s119	PXRprot_Cort	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{17} = \text{vol}(\text{default}) \cdot (k1 \cdot [s42] \cdot [s114] - k2 \cdot [s119]) \quad (53)$$

Table 73: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		60.0		<input checked="" type="checkbox"/>
k2	k2		600000.0		<input checked="" type="checkbox"/>

### 8.18 Reaction re18

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

**Name** re18

#### Reaction equation



#### Reactant

Table 74: Properties of each reactant.

Id	Name	SBO
s119	PXRprot_Cort	

#### Modifier

Table 75: Properties of each modifier.

Id	Name	SBO
s119	PXRprot_Cort	

#### Products

Table 76: Properties of each product.

Id	Name	SBO
s114	Cort	
s30	P	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{18} = \text{vol}(\text{default}) \cdot k1 \cdot [s119] \quad (55)$$

Table 77: Properties of each parameter.

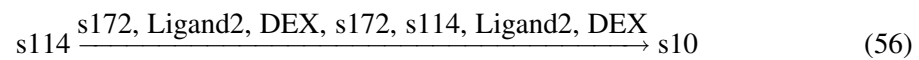
Id	Name	SBO	Value	Unit	Constant
k1	k1		0.002		<input checked="" type="checkbox"/>

### 8.19 Reaction `re19`

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

**Name** `re19`

#### Reaction equation



#### Reactant

Table 78: Properties of each reactant.

Id	Name	SBO
s114	Cort	

#### Modifiers

Table 79: Properties of each modifier.

Id	Name	SBO
s172	CYP.PROT	
Ligand2	Ligand2	
DEX	DEX	
s172	CYP.PROT	
s114	Cort	
Ligand2	Ligand2	
DEX	DEX	

#### Product



Table 80: Properties of each product.

Id	Name	SBO
s10	Cort_degr	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{19} = \text{vol}(\text{default}) \cdot \text{LigandDegrOld}([s172], Vm, [s114], Kms1, [\text{Ligand2}], Kms2, [\text{DEX}], Kms3) \quad (57)$$

$$\text{LigandDegrOld}(\text{Act}, Vm, S1, Kms1, S2, Kms2, S3, Kms3) = \text{Act} \cdot \frac{\frac{Vm \cdot S1}{Kms1}}{1 + \frac{S1}{Kms1} + \frac{S2}{Kms2} + \frac{S3}{Kms3}} \quad (58)$$

$$\text{LigandDegrOld}(\text{Act}, Vm, S1, Kms1, S2, Kms2, S3, Kms3) = \text{Act} \cdot \frac{\frac{Vm \cdot S1}{Kms1}}{1 + \frac{S1}{Kms1} + \frac{S2}{Kms2} + \frac{S3}{Kms3}} \quad (59)$$

Table 81: Properties of each parameter.

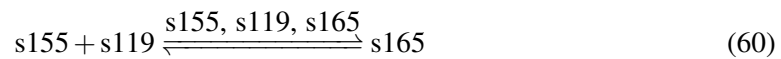
Id	Name	SBO	Value	Unit	Constant
Vm	Vm		0.083		<input checked="" type="checkbox"/>
Kms1	Kms1		15000.000		<input checked="" type="checkbox"/>
Kms2	Kms2		15000.000		<input checked="" type="checkbox"/>
Kms3	Kms3		23000.000		<input checked="" type="checkbox"/>

### 8.20 Reaction re20

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re20

#### Reaction equation



#### Reactants

Table 82: Properties of each reactant.

Id	Name	SBO
s155	CYP_GENE	
s119	PXRprot_Cort	

## Modifiers

Table 83: Properties of each modifier.

Id	Name	SBO
s155	CYP_GENE	
s119	PXRprot_Cort	
s165	CYPgene_PXRprot_Cort	

## Product

Table 84: Properties of each product.

Id	Name	SBO
s165	CYPgene_PXRprot_Cort	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{20} = \text{vol}(\text{default}) \cdot (\text{GeneProteinBinding\_diff\_limited} \cdot [s155] \cdot [s119] - \text{cypGene\_PXRprotein} \cdot [s165]) \quad (61)$$

### 8.21 Reaction re21

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

**Name** re21

### Reaction equation



## Reactant

Table 85: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

## Modifiers

Table 86: Properties of each modifier.

Id	Name	SBO
s165	CYPgene_PXRprot_Cort	
s28	S_RNA	
s165	CYPgene_PXRprot_Cort	

## Product

Table 87: Properties of each product.

Id	Name	SBO
s173	CYP_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{21} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [s165], \text{cypMrna\_synt}) \quad (63)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (64)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (65)$$

### 8.22 Reaction re22

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re22

#### Reaction equation



## Reactants

Table 88: Properties of each reactant.

Id	Name	SBO
s46	PXR_GENE	
s87	GRprot_Cort	

## Modifiers

Table 89: Properties of each modifier.

Id	Name	SBO
s46	PXR_GENE	
s87	GRprot_Cort	
s109	PXRgene_GRprot_Cort	

## Product

Table 90: Properties of each product.

Id	Name	SBO
s109	PXRgene_GRprot_Cort	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{22} = \text{vol}(\text{default}) \cdot (\text{GeneProteinBinding\_diff\_limited} \cdot [s46] \cdot [s87] - \text{PXRGene\_GRprotein} \cdot [s109]) \quad (67)$$

### 8.23 Reaction re23

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

**Name** re23

#### Reaction equation



## Reactant

Table 91: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

## Modifiers

Table 92: Properties of each modifier.

Id	Name	SBO
s109	PXRgene_GRprot_Cort	
s28	S_RNA	
s109	PXRgene_GRprot_Cort	

## Product

Table 93: Properties of each product.

Id	Name	SBO
s32	PXR_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{23} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [s109], \text{pxrMrna\_synt}) \quad (69)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (70)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (71)$$

### 8.24 Reaction re24

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re24

#### Reaction equation



## Reactants

Table 94: Properties of each reactant.

Id	Name	SBO
s40	GR_GENE	
s87	GRprot_Cort	

## Modifiers

Table 95: Properties of each modifier.

Id	Name	SBO
s40	GR_GENE	
s87	GRprot_Cort	
s84	GRgene_GRprot_Cort	

## Product

Table 96: Properties of each product.

Id	Name	SBO
s84	GRgene_GRprot_Cort	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{24} = \text{vol}(\text{default}) \cdot (\text{GeneProteinBinding\_diff\_limited} \cdot [s40] \cdot [s87] - \text{GRGene\_GRprotein} \cdot [s84]) \quad (73)$$

### 8.25 Reaction re25

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

**Name** re25

#### Reaction equation



## Reactant

Table 97: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

## Modifiers

Table 98: Properties of each modifier.

Id	Name	SBO
s84	GRgene_GRprot_Cort	
s28	S_RNA	
s84	GRgene_GRprot_Cort	

## Product

Table 99: Properties of each product.

Id	Name	SBO
s33	GR_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{25} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [s84], \text{grMrna\_synt}) \quad (75)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (76)$$

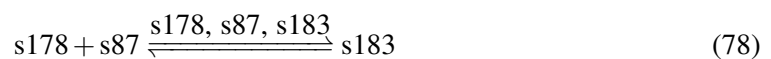
$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (77)$$

### 8.26 Reaction re26

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re26

#### Reaction equation



## Reactants

Table 100: Properties of each reactant.

Id	Name	SBO
s178	TAT_GENE	
s87	GRprot_Cort	

## Modifiers

Table 101: Properties of each modifier.

Id	Name	SBO
s178	TAT_GENE	
s87	GRprot_Cort	
s183	TATgene_GRprot_Cort	

## Product

Table 102: Properties of each product.

Id	Name	SBO
s183	TATgene_GRprot_Cort	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{26} = \text{vol}(\text{default}) \cdot (\text{GeneProteinBinding\_diff\_limited} \cdot [s178] \cdot [s87] - \text{TATGene\_GRprotein} \cdot [s183]) \quad (79)$$

### 8.27 Reaction re27

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

**Name** re27

#### Reaction equation



## Reactant



Table 103: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

## Modifiers

Table 104: Properties of each modifier.

Id	Name	SBO
s183	TATgene_GRprot_Cort	
s28	S_RNA	
s183	TATgene_GRprot_Cort	

## Product

Table 105: Properties of each product.

Id	Name	SBO
s185	TAT_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{27} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [s183], \text{tatMrna\_synt}) \quad (81)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (82)$$

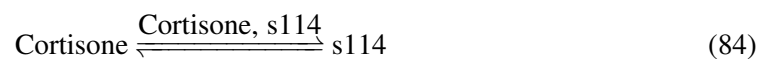
$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (83)$$

### 8.28 Reaction re42

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

**Name** re42

#### Reaction equation



## Reactant

Table 106: Properties of each reactant.

Id	Name	SBO
Cortisone	Cortisone	

## Modifiers

Table 107: Properties of each modifier.

Id	Name	SBO
Cortisone	Cortisone	
s114	Cort	

## Product

Table 108: Properties of each product.

Id	Name	SBO
s114	Cort	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{28} = \text{vol}(\text{default}) \cdot (k1 \cdot [\text{Cortisone}] - k2 \cdot [\text{s114}]) \quad (85)$$

Table 109: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.016		<input checked="" type="checkbox"/>
k2	k2		0.016		<input checked="" type="checkbox"/>

### 8.29 Reaction re44

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

**Name** re44

### Reaction equation



## Reactant

Table 110: Properties of each reactant.

Id	Name	SBO
TAT_PROT	TAT_PROT	

## Modifier

Table 111: Properties of each modifier.

Id	Name	SBO
TAT_PROT	TAT_PROT	

## Product

Table 112: Properties of each product.

Id	Name	SBO
s30	P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{29} = \text{vol}(\text{default}) \cdot k1 \cdot [\text{TAT\_PROT}] \quad (87)$$

Table 113: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.012		<input checked="" type="checkbox"/>

### 8.30 Reaction re43

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

**Name** re43

## Reaction equation



## Reactant

Table 114: Properties of each reactant.

Id	Name	SBO
s36	S_PROT	

## Modifiers

Table 115: Properties of each modifier.

Id	Name	SBO
s185	TAT_RNA	
s36	S_PROT	
s185	TAT_RNA	

## Product

Table 116: Properties of each product.

Id	Name	SBO
TAT_PROT	TAT_PROT	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{30} = \text{vol}(\text{default}) \cdot \text{ptotein}(\text{Ka}, [s36], [s185]) \quad (89)$$

$$\text{ptotein}(\text{Ka}, \text{S\_PROT}, \text{Activator}) = \text{Ka} \cdot \text{S\_PROT} \cdot \text{Activator} \quad (90)$$

$$\text{ptotein}(\text{Ka}, \text{S\_PROT}, \text{Activator}) = \text{Ka} \cdot \text{S\_PROT} \cdot \text{Activator} \quad (91)$$

Table 117: Properties of each parameter.

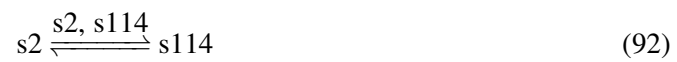
Id	Name	SBO	Value	Unit	Constant
Ka	Ka		0.5		<input checked="" type="checkbox"/>

### 8.31 Reaction cortisolTransport

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

**Name** cortisolTransport

#### Reaction equation



#### Reactant

Table 118: Properties of each reactant.

Id	Name	SBO
s2	CortOUT	

#### Modifiers

Table 119: Properties of each modifier.

Id	Name	SBO
s2	CortOUT	
s114	Cort	

#### Product

Table 120: Properties of each product.

Id	Name	SBO
s114	Cort	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{31} = k1 \cdot [s2] - k2 \cdot [s114] \quad (93)$$

Table 121: Properties of each parameter.

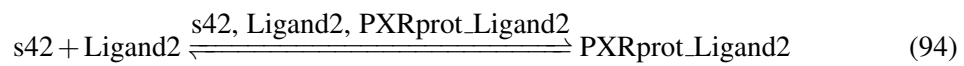
Id	Name	SBO	Value	Unit	Constant
k1	k1		1000.0		<input checked="" type="checkbox"/>
k2	k2		1000.0		<input checked="" type="checkbox"/>

### 8.32 Reaction L2\_PXR\_binding

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** L2\_PXR\_binding

#### Reaction equation



#### Reactants

Table 122: Properties of each reactant.

Id	Name	SBO
s42	PXR_PROT	
Ligand2	Ligand2	

#### Modifiers

Table 123: Properties of each modifier.

Id	Name	SBO
s42	PXR_PROT	
Ligand2	Ligand2	
PXRprot_Ligand2	PXRprot_Ligand2	

#### Product

Table 124: Properties of each product.

Id	Name	SBO
PXRprot_Ligand2	PXRprot_Ligand2	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{32} = \text{vol}(\text{default}) \cdot (k1 \cdot [s42] \cdot [\text{Ligand2}] - k2 \cdot [\text{PXRprot\_Ligand2}]) \quad (95)$$

Table 125: Properties of each parameter.

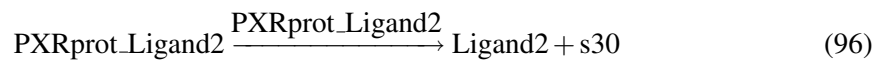
Id	Name	SBO	Value	Unit	Constant
k1	k1		60.0		<input checked="" type="checkbox"/>
k2	k2		600000.0		<input checked="" type="checkbox"/>

### 8.33 Reaction L2\_PXR\_deg

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

**Name** L2\_PXR\_deg

#### Reaction equation



#### Reactant

Table 126: Properties of each reactant.

Id	Name	SBO
PXRprot_Ligand2	PXRprot_Ligand2	

#### Modifier

Table 127: Properties of each modifier.

Id	Name	SBO
PXRprot_Ligand2	PXRprot_Ligand2	

## Products

Table 128: Properties of each product.

Id	Name	SBO
Ligand2	Ligand2	
s30	P	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{33} = \text{vol}(\text{default}) \cdot k1 \cdot [\text{PXRprot.Ligand2}] \quad (97)$$

Table 129: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.002		<input checked="" type="checkbox"/>

### 8.34 Reaction CYPmRNA\_synt\_PXR\_L2

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

**Name** CYPmRNA\_synt\_PXR\_L2

#### Reaction equation



## Reactant

Table 130: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

## Modifiers



Table 131: Properties of each modifier.

Id	Name	SBO
CYPgene_PXRprot_Ligand2	CYPgene_PXRprot_Ligand2	
s28	S_RNA	
CYPgene_PXRprot_Ligand2	CYPgene_PXRprot_Ligand2	

## Product

Table 132: Properties of each product.

Id	Name	SBO
s173	CYP_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{34} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [\text{CYPgene\_PXRprot\_Ligand2}], \text{cypMrna\_synt}) \quad (99)$$

$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, K_a) = K_a \cdot \text{S\_RNA} \cdot \text{Activator} \quad (100)$$

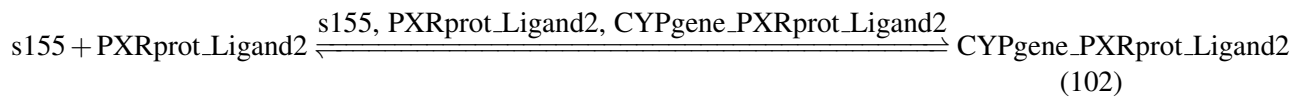
$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, K_a) = K_a \cdot \text{S\_RNA} \cdot \text{Activator} \quad (101)$$

### 8.35 Reaction CYPmRNA\_PXR\_L2\_binding

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** CYPmRNA\_PXR\_L2\_binding

#### Reaction equation



## Reactants

Table 133: Properties of each reactant.

Id	Name	SBO
s155	CYP_GENE	
PXRprot_Ligand2	PXRprot_Ligand2	

## Modifiers

Table 134: Properties of each modifier.

Id	Name	SBO
s155	CYP_GENE	
PXRprot_Ligand2	PXRprot_Ligand2	
CYPgene_PXRprot_Ligand2	CYPgene_PXRprot_Ligand2	

## Product

Table 135: Properties of each product.

Id	Name	SBO
CYPgene_PXRprot_Ligand2	CYPgene_PXRprot_Ligand2	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{35} = \text{vol}(\text{default}) \cdot (\text{GeneProteinBinding\_diff\_limited} \cdot [\text{s155}] \cdot [\text{PXRprot\_Ligand2}] - \text{cypGene\_PXRprotein} \cdot [\text{CYPgene\_PXRprot\_Ligand2}]) \quad (103)$$

### 8.36 Reaction re28

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re28

#### Reaction equation



## Reactants

Table 136: Properties of each reactant.

Id	Name	SBO
s39	GR_PROT	
DEX	DEX	

## Modifiers

Table 137: Properties of each modifier.

Id	Name	SBO
s39	GR_PROT	
DEX	DEX	
GRprot_DEX	GRprot_DEX	

## Product

Table 138: Properties of each product.

Id	Name	SBO
GRprot_DEX	GRprot_DEX	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{36} = \text{vol}(\text{default}) \cdot (k1 \cdot [s39] \cdot [\text{DEX}] - k2 \cdot [\text{GRprot\_DEX}]) \quad (105)$$

Table 139: Properties of each parameter.

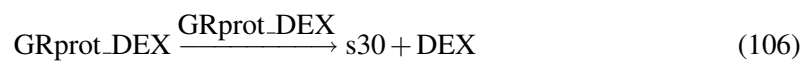
Id	Name	SBO	Value	Unit	Constant
k1	k1		60.0		<input checked="" type="checkbox"/>
k2	k2		60.0		<input checked="" type="checkbox"/>

### 8.37 Reaction re29

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

**Name** re29

#### Reaction equation



## Reactant

Table 140: Properties of each reactant.

Id	Name	SBO
GRprot_DEX	GRprot_DEX	

## Modifier

Table 141: Properties of each modifier.

Id	Name	SBO
GRprot_DEX	GRprot_DEX	

## Products

Table 142: Properties of each product.

Id	Name	SBO
s30	P	
DEX	DEX	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{37} = \text{vol}(\text{default}) \cdot k1 \cdot [\text{GRprot\_DEX}] \quad (107)$$

Table 143: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.001		<input checked="" type="checkbox"/>

### 8.38 Reaction re30

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re30

#### Reaction equation



## Reactants

Table 144: Properties of each reactant.

Id	Name	SBO
s42	PXR_PROT	
DEX	DEX	

## Modifiers

Table 145: Properties of each modifier.

Id	Name	SBO
s42	PXR_PROT	
DEX	DEX	
PXRprot_DEX	PXRprot_DEX	

## Product

Table 146: Properties of each product.

Id	Name	SBO
PXRprot_DEX	PXRprot_DEX	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{38} = \text{vol}(\text{default}) \cdot (k1 \cdot [s42] \cdot [\text{DEX}] - k2 \cdot [\text{PXRprot\_DEX}]) \quad (109)$$

Table 147: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		60.0		✓
k2	k2		60000.0		✓

### 8.39 Reaction re31

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

**Name** re31

### Reaction equation



### Reactant

Table 148: Properties of each reactant.

Id	Name	SBO
PXRprot_DEX	PXRprot_DEX	

### Modifier

Table 149: Properties of each modifier.

Id	Name	SBO
PXRprot_DEX	PXRprot_DEX	

### Products

Table 150: Properties of each product.

Id	Name	SBO
DEX	DEX	
s30	P	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{39} = \text{vol}(\text{default}) \cdot k1 \cdot [\text{PXRprot\_DEX}] \quad (111)$$

Table 151: Properties of each parameter.

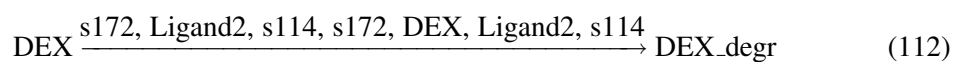
Id	Name	SBO	Value	Unit	Constant
k1	k1		0.002		<input checked="" type="checkbox"/>

## 8.40 Reaction re32

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

**Name** re32

### Reaction equation



### Reactant

Table 152: Properties of each reactant.

Id	Name	SBO
DEX	DEX	

### Modifiers

Table 153: Properties of each modifier.

Id	Name	SBO
s172	CYP_PROT	
Ligand2	Ligand2	
s114	Cort	
s172	CYP_PROT	
DEX	DEX	
Ligand2	Ligand2	
s114	Cort	

### Product

Table 154: Properties of each product.

Id	Name	SBO
DEX_degr	DEX_degr	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{40} = \text{vol}(\text{default}) \cdot \text{LigandDegrOld}([s172], Vm, [DEX], Kms1, [Ligand2], Kms2, [s114], Kms3) \quad (113)$$

$$\text{LigandDegrOld}(\text{Act}, Vm, S1, Kms1, S2, Kms2, S3, Kms3) = \text{Act} \cdot \frac{\frac{Vm \cdot S1}{Kms1}}{1 + \frac{S1}{Kms1} + \frac{S2}{Kms2} + \frac{S3}{Kms3}} \quad (114)$$

$$\text{LigandDegrOld}(\text{Act}, Vm, S1, Kms1, S2, Kms2, S3, Kms3) = \text{Act} \cdot \frac{\frac{Vm \cdot S1}{Kms1}}{1 + \frac{S1}{Kms1} + \frac{S2}{Kms2} + \frac{S3}{Kms3}} \quad (115)$$

Table 155: Properties of each parameter.

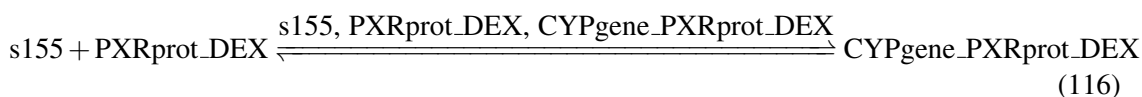
Id	Name	SBO	Value	Unit	Constant
Vm	Vm		0.004		<input checked="" type="checkbox"/>
Kms1	Kms1		23000.000		<input checked="" type="checkbox"/>
Kms2	Kms2		15000.000		<input checked="" type="checkbox"/>
Kms3	Kms3		15000.000		<input checked="" type="checkbox"/>

#### 8.41 Reaction re33

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re33

##### Reaction equation



##### Reactants

Table 156: Properties of each reactant.

Id	Name	SBO
s155	CYP_GENE	
PXRprot_DEX	PXRprot_DEX	

##### Modifiers



Table 157: Properties of each modifier.

Id	Name	SBO
s155	CYP_GENE	
PXRprot_DEX	PXRprot_DEX	
CYPgene_PXRprot_DEX	CYPgene_PXRprot_DEX	

## Product

Table 158: Properties of each product.

Id	Name	SBO
CYPgene_PXRprot_DEX	CYPgene_PXRprot_DEX	

## Kinetic Law

**Derived unit** contains undeclared units

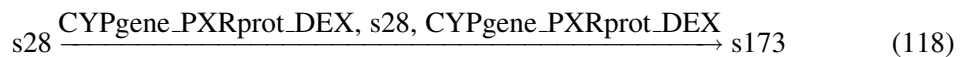
$$v_{41} = \text{vol}(\text{default}) \cdot (\text{GeneProteinBinding\_diff\_limited} \cdot [\text{s155}] \cdot [\text{PXRprot\_DEX}] - \text{cypGene\_PXRprotein} \cdot [\text{CYPgene\_PXRprot\_DEX}]) \quad (117)$$

## 8.42 Reaction re34

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

**Name** re34

## Reaction equation



## Reactant

Table 159: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

## Modifiers

Table 160: Properties of each modifier.

Id	Name	SBO
CYPgene_PXRprot_DEX	CYPgene_PXRprot_DEX	
s28	S_RNA	
CYPgene_PXRprot_DEX	CYPgene_PXRprot_DEX	

## Product

Table 161: Properties of each product.

Id	Name	SBO
s173	CYP_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{42} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [\text{CYPgene\_PXRprot\_DEX}], \text{cypMrna\_synt}) \quad (119)$$

$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (120)$$

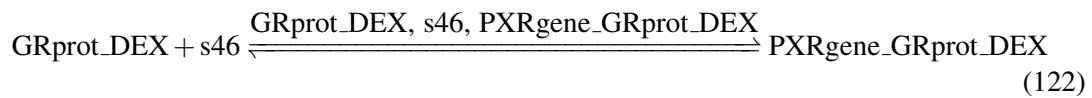
$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (121)$$

## 8.43 Reaction re35

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re35

## Reaction equation



## Reactants

Table 162: Properties of each reactant.

Id	Name	SBO
GRprot_DEX	GRprot_DEX	
s46	PXR_GENE	

## Modifiers

Table 163: Properties of each modifier.

Id	Name	SBO
GRprot_DEX	GRprot_DEX	
s46	PXR_GENE	
PXRgene_GRprot_DEX	PXRgene_GRprot_DEX	

## Product

Table 164: Properties of each product.

Id	Name	SBO
PXRgene_GRprot_DEX	PXRgene_GRprot_DEX	

## Kinetic Law

**Derived unit** contains undeclared units

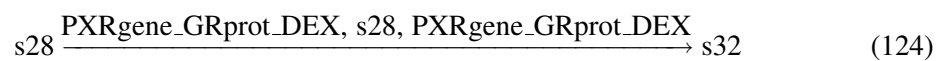
$$v_{43} = \text{vol}(\text{default}) \cdot (\text{GeneProteinBinding\_diff\_limited} \cdot [\text{GRprot\_DEX}] \cdot [\text{s46}] - \text{PXRGene\_GRprotein} \cdot [\text{PXRgene\_GRprot\_DEX}]) \quad (123)$$

### 8.44 Reaction re36

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

**Name** re36

#### Reaction equation



## Reactant

Table 165: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

## Modifiers

Table 166: Properties of each modifier.

Id	Name	SBO
PXRgene_GRprot_DEX	PXRgene_GRprot_DEX	
s28	S_RNA	
PXRgene_GRprot_DEX	PXRgene_GRprot_DEX	

## Product

Table 167: Properties of each product.

Id	Name	SBO
s32	PXR_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{44} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [\text{PXRgene\_GRprot\_DEX}], \text{pxrMrna\_synt}) \quad (125)$$

$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (126)$$

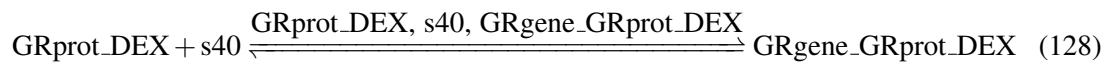
$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (127)$$

### 8.45 Reaction re37

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re37

#### Reaction equation



## Reactants

Table 168: Properties of each reactant.

Id	Name	SBO
GRprot_DEX	GRprot_DEX	
s40	GR_GENE	

## Modifiers

Table 169: Properties of each modifier.

Id	Name	SBO
GRprot_DEX	GRprot_DEX	
s40	GR_GENE	
GRgene_GRprot_DEX	GRgene_GRprot_DEX	

## Product

Table 170: Properties of each product.

Id	Name	SBO
GRgene_GRprot_DEX	GRgene_GRprot_DEX	

## Kinetic Law

**Derived unit** contains undeclared units

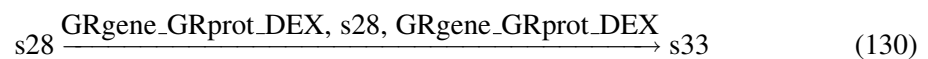
$$v_{45} = \text{vol}(\text{default}) \cdot (\text{GeneProteinBinding\_diff\_limited} \cdot [\text{GRprot\_DEX}] \cdot [\text{s40}] - \text{GRGene\_GRprotein} \cdot [\text{GRgene\_GRprot\_DEX}]) \quad (129)$$

### 8.46 Reaction re38

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

**Name** re38

#### Reaction equation



## Reactant

Table 171: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

## Modifiers

Table 172: Properties of each modifier.

Id	Name	SBO
GRgene_GRprot_DEX	GRgene_GRprot_DEX	
s28	S_RNA	
GRgene_GRprot_DEX	GRgene_GRprot_DEX	

## Product

Table 173: Properties of each product.

Id	Name	SBO
s33	GR_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{46} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [\text{GRgene\_GRprot\_DEX}], \text{grMrna\_synt}) \quad (131)$$

$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (132)$$

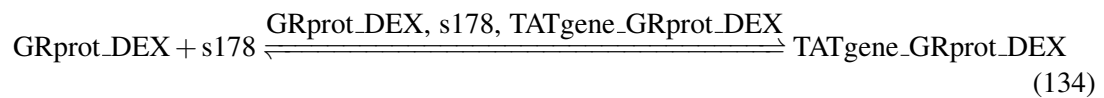
$$\text{mRNA}(\text{S\_RNA}, \text{Activator}, \text{Ka}) = \text{Ka} \cdot \text{S\_RNA} \cdot \text{Activator} \quad (133)$$

### 8.47 Reaction re39

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** re39

#### Reaction equation



## Reactants

Table 174: Properties of each reactant.

Id	Name	SBO
GRprot_DEX	GRprot_DEX	
s178	TAT_GENE	

## Modifiers

Table 175: Properties of each modifier.

Id	Name	SBO
GRprot_DEX	GRprot_DEX	
s178	TAT_GENE	
TATgene_GRprot_DEX	TATgene_GRprot_DEX	

## Product

Table 176: Properties of each product.

Id	Name	SBO
TATgene_GRprot_DEX	TATgene_GRprot_DEX	

## Kinetic Law

**Derived unit** contains undeclared units

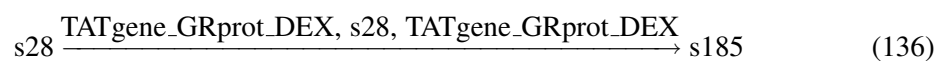
$$v_{47} = \text{vol}(\text{default}) \cdot (\text{GeneProteinBinding\_diff\_limited} \cdot [\text{GRprot\_DEX}] \cdot [\text{s178}] - \text{TATGene\_GRprotein} \cdot [\text{TATgene\_GRprot\_DEX}]) \quad (135)$$

### 8.48 Reaction re40

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

**Name** re40

#### Reaction equation



## Reactant

Table 177: Properties of each reactant.

Id	Name	SBO
s28	S_RNA	

## Modifiers

Table 178: Properties of each modifier.

Id	Name	SBO
TATgene_GRprot_DEX	TATgene_GRprot_DEX	
s28	S_RNA	
TATgene_GRprot_DEX	TATgene_GRprot_DEX	

## Product

Table 179: Properties of each product.

Id	Name	SBO
s185	TAT_RNA	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{48} = \text{vol}(\text{default}) \cdot \text{mRNA}([s28], [TATgene\_GRprot\_DEX], \text{tatMrna\_synt}) \quad (137)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (138)$$

$$\text{mRNA}(S\_RNA, \text{Activator}, K_a) = K_a \cdot S\_RNA \cdot \text{Activator} \quad (139)$$

### 8.49 Reaction re41

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

**Name** re41

#### Reaction equation



## Reactant



Table 180: Properties of each reactant.

Id	Name	SBO
DEXout	DEXout	

## Modifiers

Table 181: Properties of each modifier.

Id	Name	SBO
DEXout	DEXout	
DEX	DEX	

## Product

Table 182: Properties of each product.

Id	Name	SBO
DEX	DEX	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{49} = k1 \cdot [\text{DEXout}] - k2 \cdot [\text{DEX}] \quad (141)$$

Table 183: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		100.0		<input checked="" type="checkbox"/>
k2	k2		100.0		<input checked="" type="checkbox"/>

### 8.50 Reaction Cortisol\_CBG

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** Cortisol\_CBG

#### Reaction equation



## Reactants

Table 184: Properties of each reactant.

Id	Name	SBO
s2	CortOUT	
CBG	CBG	

## Modifiers

Table 185: Properties of each modifier.

Id	Name	SBO
s2	CortOUT	
CBG	CBG	
CBG_CortOUT	CBG_CortOUT	

## Product

Table 186: Properties of each product.

Id	Name	SBO
CBG_CortOUT	CBG_CortOUT	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{50} = \text{vol}(\text{blood}) \cdot (k1 \cdot [s2] \cdot [\text{CBG}] - k2 \cdot [\text{CBG\_CortOUT}]) \quad (143)$$

Table 187: Properties of each parameter.

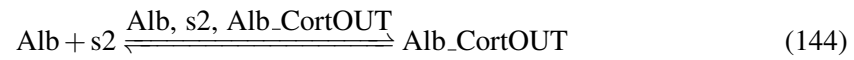
Id	Name	SBO	Value	Unit	Constant
k1	k1		60.0		<input checked="" type="checkbox"/>
k2	k2		270.0		<input checked="" type="checkbox"/>

### 8.51 Reaction Cort\_Alb

This is a reversible reaction of two reactants forming one product influenced by three modifiers.

**Name** Cort\_Alb

### Reaction equation



### Reactants

Table 188: Properties of each reactant.

Id	Name	SBO
Alb	Alb	
s2	CortOUT	

### Modifiers

Table 189: Properties of each modifier.

Id	Name	SBO
Alb	Alb	
s2	CortOUT	
Alb_CortOUT	Alb_CortOUT	

### Product

Table 190: Properties of each product.

Id	Name	SBO
Alb_CortOUT	Alb_CortOUT	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{51} = \text{vol}(\text{blood}) \cdot (k1 \cdot [\text{Alb}] \cdot [\text{s2}] - k2 \cdot [\text{Alb\_CortOUT}]) \quad (145)$$

Table 191: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		60.0		✓
k2	k2		900000.0		✓

## 8.52 Reaction cort\_distribution

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

**Name** cort\_distribution

### Reaction equation



### Reactant

Table 192: Properties of each reactant.

Id	Name	SBO
CortAdded	CortAdded	

### Modifier

Table 193: Properties of each modifier.

Id	Name	SBO
CortAdded	CortAdded	

### Product

Table 194: Properties of each product.

Id	Name	SBO
s2	CortOUT	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{52} = \text{vol}(\text{blood}) \cdot k1 \cdot [\text{CortAdded}] \quad (147)$$

Table 195: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1000.0		<input checked="" type="checkbox"/>

## 9 Derived Rate Equations

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

Identifiers for kinetic laws highlighted in gray cannot be verified to evaluate to units of SBML substance per time. As a result, some SBML interpreters may not be able to verify the consistency of the units on quantities in the model. Please check if

- parameters without an unit definition are involved or
- volume correction is necessary because the `hasOnlySubstanceUnits` flag may be set to `false` and `spacialDimensions`  $> 0$  for certain species.

### 9.1 Species `s28`

**Name** S\_RNA

**Initial concentration**  $1.00000029723653 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in 26 reactions (as a reactant in [re1](#), [re5](#), [re9](#), [re13](#), [re21](#), [re23](#), [re25](#), [re27](#), [CYPmRNA\\_synt\\_PXR\\_L2](#), [re34](#), [re36](#), [re38](#), [re40](#) and as a modifier in [re1](#), [re5](#), [re9](#), [re13](#), [re21](#), [re23](#), [re25](#), [re27](#), [CYPmRNA\\_synt\\_PXR\\_L2](#), [re34](#), [re36](#), [re38](#), [re40](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}s_{28} = 0 \quad (148)$$

### 9.2 Species `s36`

**Name** S\_PROT

**Initial concentration**  $1.00000029723653 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in eight reactions (as a reactant in [re3](#), [re7](#), [re11](#), [re43](#) and as a modifier in [re3](#), [re7](#), [re11](#), [re43](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}s_{36} = 0 \quad (149)$$

### 9.3 Species `s46`

**Name** PXR\_GENE

**Initial concentration**  $0.780000231844494 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in six reactions (as a reactant in [re22](#), [re35](#) and as a modifier in [re5](#), [re5](#), [re22](#), [re35](#)).

$$\frac{d}{dt}s_{46} = -v_{22} - v_{43} \quad (150)$$

## 9.4 Species s32

**Name** PXR\_RNA

**Initial concentration** 0.00700000208065571 nmol · l<sup>-1</sup>

This species takes part in seven reactions (as a reactant in [re6](#) and as a product in [re5](#), [re23](#), [re36](#) and as a modifier in [re6](#), [re7](#), [re7](#)).

$$\frac{d}{dt}s_{32} = v_5 + v_{23} + v_{44} - v_6 \quad (151)$$

## 9.5 Species s42

**Name** PXR\_PROT

**Initial concentration** 99.9000296939294 nmol · l<sup>-1</sup>

This species takes part in nine reactions (as a reactant in [re8](#), [re17](#), [L2\\_PXR\\_binding](#), [re30](#) and as a product in [re7](#) and as a modifier in [re8](#), [re17](#), [L2\\_PXR\\_binding](#), [re30](#)).

$$\frac{d}{dt}s_{42} = v_7 - v_8 - v_{17} - v_{32} - v_{38} \quad (152)$$

## 9.6 Species s30

**Name** P

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in 13 reactions (as a product in [re2](#), [re4](#), [re6](#), [re8](#), [re10](#), [re12](#), [re14](#), [re16](#), [re18](#), [re44](#), [L2\\_PXR\\_deg](#), [re29](#), [re31](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}s_{30} = 0 \quad (153)$$

## 9.7 Species s40

**Name** GR\_GENE

**Initial concentration** 0.500000148618265 nmol · l<sup>-1</sup>

This species takes part in six reactions (as a reactant in [re24](#), [re37](#) and as a modifier in [re9](#), [re9](#), [re24](#), [re37](#)).

$$\frac{d}{dt}s_{40} = -v_{24} - v_{45} \quad (154)$$

## 9.8 Species s33

**Name** GR\_RNA

**Initial concentration**  $8.00000237789224 \cdot 10^{-4} \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in seven reactions (as a reactant in [re10](#) and as a product in [re9](#), [re25](#), [re38](#) and as a modifier in [re10](#), [re11](#), [re11](#)).

$$\frac{d}{dt}s33 = v_9 + v_{25} + v_{46} - v_{10} \quad (155)$$

## 9.9 Species s39

**Name** GR\_PROT

**Initial concentration**  $47.2400140414537 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in seven reactions (as a reactant in [re12](#), [re15](#), [re28](#) and as a product in [re11](#) and as a modifier in [re12](#), [re15](#), [re28](#)).

$$\frac{d}{dt}s39 = v_{11} - v_{12} - v_{15} - v_{36} \quad (156)$$

## 9.10 Species s114

**Name** Cort

**Initial concentration**  $1.14000033884965 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in 14 reactions (as a reactant in [re15](#), [re17](#), [re19](#) and as a product in [re16](#), [re18](#), [re42](#), [cortisolTransport](#) and as a modifier in [re15](#), [re17](#), [re19](#), [re42](#), [cortisolTransport](#), [re32](#), [re32](#)).

$$\frac{d}{dt}s114 = v_{16} + v_{18} + v_{28} + v_{31} - v_{15} - v_{17} - v_{19} \quad (157)$$

## 9.11 Species s155

**Name** CYP\_GENE

**Initial concentration**  $0.829760246634984 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in eight reactions (as a reactant in [re20](#), [CYPmRNA\\_PXR.L2.binding](#), [re33](#) and as a modifier in [re1](#), [re1](#), [re20](#), [CYPmRNA\\_PXR.L2.binding](#), [re33](#)).

$$\frac{d}{dt}s155 = -v_{20} - v_{35} - v_{41} \quad (158)$$

### 9.12 Species s172

**Name** CYP\_PROT

**Initial concentration** 104.000030912599 nmol · l<sup>-1</sup>

This species takes part in seven reactions (as a reactant in [re4](#) and as a product in [re3](#) and as a modifier in [re4](#), [re19](#), [re19](#), [re32](#), [re32](#)).

$$\frac{d}{dt}s172 = v_3 - v_4 \quad (159)$$

### 9.13 Species s173

**Name** CYP\_RNA

**Initial concentration** 0.0750000222927398 nmol · l<sup>-1</sup>

This species takes part in eight reactions (as a reactant in [re2](#) and as a product in [re1](#), [re21](#), [CYPmRNA\\_synt\\_PXR\\_L2](#), [re34](#) and as a modifier in [re2](#), [re3](#), [re3](#)).

$$\frac{d}{dt}s173 = v_1 + v_{21} + v_{34} + v_{42} - v_2 \quad (160)$$

### 9.14 Species s185

**Name** TAT\_RNA

**Initial concentration** 0.100000029723653 nmol · l<sup>-1</sup>

This species takes part in seven reactions (as a reactant in [re14](#) and as a product in [re13](#), [re27](#), [re40](#) and as a modifier in [re14](#), [re43](#), [re43](#)).

$$\frac{d}{dt}s185 = v_{13} + v_{27} + v_{48} - v_{14} \quad (161)$$

### 9.15 Species s84

**Name** GRgene\_GRprot\_Cort

**Initial concentration** 0.330000098088055 nmol · l<sup>-1</sup>

This species takes part in four reactions (as a product in [re24](#) and as a modifier in [re24](#), [re25](#), [re25](#)).

$$\frac{d}{dt}s84 = v_{24} \quad (162)$$



### 9.16 Species s165

**Name** CYPgene\_PXRprot\_Cort

**Initial concentration**  $2.40000071336767 \cdot 10^{-4} \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in four reactions (as a product in [re20](#) and as a modifier in [re20](#), [re21](#), [re21](#)).

$$\frac{d}{dt}s165 = v_{20} \quad (163)$$

### 9.17 Species s109

**Name** PXRgene\_GRprot\_Cort

**Initial concentration**  $0.0500000148618265 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in four reactions (as a product in [re22](#) and as a modifier in [re22](#), [re23](#), [re23](#)).

$$\frac{d}{dt}s109 = v_{22} \quad (164)$$

### 9.18 Species s87

**Name** GRprot\_Cort

**Initial concentration**  $32.3600096185741 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in ten reactions (as a reactant in [re16](#), [re22](#), [re24](#), [re26](#) and as a product in [re15](#) and as a modifier in [re15](#), [re16](#), [re22](#), [re24](#), [re26](#)).

$$\frac{d}{dt}s87 = v_{15} - v_{16} - v_{22} - v_{24} - v_{26} \quad (165)$$

### 9.19 Species s119

**Name** PXRprot\_Cort

**Initial concentration**  $0.0100000029723653 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in six reactions (as a reactant in [re18](#), [re20](#) and as a product in [re17](#) and as a modifier in [re17](#), [re18](#), [re20](#)).

$$\frac{d}{dt}s119 = v_{17} - v_{18} - v_{20} \quad (166)$$

## 9.20 Species s183

**Name** TATgene\_GRprot\_Cort

**Initial concentration** 0.0200000059447306 nmol · l<sup>-1</sup>

This species takes part in four reactions (as a product in [re26](#) and as a modifier in [re26](#), [re27](#), [re27](#)).

$$\frac{d}{dt}s183 = v_{26} \quad (167)$$

## 9.21 Species s178

**Name** TAT\_GENE

**Initial concentration** 0.81000024076159 nmol · l<sup>-1</sup>

This species takes part in six reactions (as a reactant in [re26](#), [re39](#) and as a modifier in [re13](#), [re13](#), [re26](#), [re39](#)).

$$\frac{d}{dt}s178 = -v_{26} - v_{47} \quad (168)$$

## 9.22 Species s10

**Name** Cort\_degr

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in one reaction (as a product in [re19](#)), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}s10 = 0 \quad (169)$$

## 9.23 Species Cortisone

**Name** Cortisone

**Initial concentration** 24.0000071336767 nmol · l<sup>-1</sup>

This species takes part in two reactions (as a reactant in [re42](#) and as a modifier in [re42](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{Cortisone} = 0 \quad (170)$$

## 9.24 Species TAT\_PROT

**Name** TAT\_PROT

**Initial concentration** 0.46202810387596 nmol · l<sup>-1</sup>

This species takes part in three reactions (as a reactant in [re44](#) and as a product in [re43](#) and as a modifier in [re44](#)).

$$\frac{d}{dt} \text{TAT\_PROT} = v_{30} - v_{29} \quad (171)$$

## 9.25 Species Ligand2

**Name** Ligand2

**Initial concentration** 100.000029723653 nmol · l<sup>-1</sup>

This species takes part in seven reactions (as a reactant in [L2\\_PXR\\_binding](#) and as a product in [L2\\_PXR\\_deg](#) and as a modifier in [re19](#), [re19](#), [L2\\_PXR\\_binding](#), [re32](#), [re32](#)).

$$\frac{d}{dt} \text{Ligand2} = v_{33} - v_{32} \quad (172)$$

## 9.26 Species PXRprot\_Ligand2

**Name** PXRprot\_Ligand2

**Initial concentration** 0.00100000029723653 nmol · l<sup>-1</sup>

This species takes part in six reactions (as a reactant in [L2\\_PXR\\_deg](#), [CYPmRNA\\_PXR\\_L2\\_binding](#) and as a product in [L2\\_PXR\\_binding](#) and as a modifier in [L2\\_PXR\\_binding](#), [L2\\_PXR\\_deg](#), [CYPmRNA\\_PXR\\_L2\\_binding](#)).

$$\frac{d}{dt} \text{PXRprot\_Ligand2} = v_{32} - v_{33} - v_{35} \quad (173)$$

## 9.27 Species CYPgene\_PXRprot\_Ligand2

**Name** CYPgene\_PXRprot\_Ligand2

**Initial concentration** 2.40000071336767 · 10<sup>-5</sup> nmol · l<sup>-1</sup>

This species takes part in four reactions (as a product in [CYPmRNA\\_PXR\\_L2\\_binding](#) and as a modifier in [CYPmRNA\\_synt\\_PXR\\_L2](#), [CYPmRNA\\_synt\\_PXR\\_L2](#), [CYPmRNA\\_PXR\\_L2\\_binding](#)).

$$\frac{d}{dt} \text{CYPgene\_PXRprot\_Ligand2} = v_{35} \quad (174)$$

### 9.28 Species DEX

**Name** DEX

**Initial concentration**  $0 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in twelve reactions (as a reactant in [re28](#), [re30](#), [re32](#) and as a product in [re29](#), [re31](#), [re41](#) and as a modifier in [re19](#), [re19](#), [re28](#), [re30](#), [re32](#), [re41](#)).

$$\frac{d}{dt}\text{DEX} = v_{37} + v_{39} + v_{49} - v_{36} - v_{38} - v_{40} \quad (175)$$

### 9.29 Species GRprot\_DEX

**Name** GRprot\_DEX

**Initial concentration**  $0 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in ten reactions (as a reactant in [re29](#), [re35](#), [re37](#), [re39](#) and as a product in [re28](#) and as a modifier in [re28](#), [re29](#), [re35](#), [re37](#), [re39](#)).

$$\frac{d}{dt}\text{GRprot\_DEX} = v_{36} - v_{37} - v_{43} - v_{45} - v_{47} \quad (176)$$

### 9.30 Species PXRprot\_DEX

**Name** PXRprot\_DEX

**Initial concentration**  $0 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in six reactions (as a reactant in [re31](#), [re33](#) and as a product in [re30](#) and as a modifier in [re30](#), [re31](#), [re33](#)).

$$\frac{d}{dt}\text{PXRprot\_DEX} = v_{38} - v_{39} - v_{41} \quad (177)$$

### 9.31 Species DEX\_degr

**Name** DEX\_degr

**Initial concentration**  $0 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in one reaction (as a product in [re32](#)), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{DEX\_degr} = 0 \quad (178)$$

### 9.32 Species CYPgene\_PXRprot\_DEX

**Name** CYPgene\_PXRprot\_DEX

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in four reactions (as a product in [re33](#) and as a modifier in [re33](#), [re34](#), [re34](#)).

$$\frac{d}{dt} \text{CYPgene\_PXRprot\_DEX} = v_{41} \quad (179)$$

### 9.33 Species PXRgene\_GRprot\_DEX

**Name** PXRgene\_GRprot\_DEX

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in four reactions (as a product in [re35](#) and as a modifier in [re35](#), [re36](#), [re36](#)).

$$\frac{d}{dt} \text{PXRgene\_GRprot\_DEX} = v_{43} \quad (180)$$

### 9.34 Species GRgene\_GRprot\_DEX

**Name** GRgene\_GRprot\_DEX

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in four reactions (as a product in [re37](#) and as a modifier in [re37](#), [re38](#), [re38](#)).

$$\frac{d}{dt} \text{GRgene\_GRprot\_DEX} = v_{45} \quad (181)$$

### 9.35 Species TATgene\_GRprot\_DEX

**Name** TATgene\_GRprot\_DEX

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in four reactions (as a product in [re39](#) and as a modifier in [re39](#), [re40](#), [re40](#)).

$$\frac{d}{dt} \text{TATgene\_GRprot\_DEX} = v_{47} \quad (182)$$

### 9.36 Species s2

**Name** CortOUT

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in seven reactions (as a reactant in [cortisolTransport](#), [Cortisol\\_CBG](#), [Cort\\_Alb](#) and as a product in [cort\\_distribution](#) and as a modifier in [cortisolTransport](#), [Cortisol\\_CBG](#), [Cort\\_Alb](#)).

$$\frac{d}{dt}s2 = v_{52} - v_{31} - v_{50} - v_{51} \quad (183)$$

### 9.37 Species DEXout

**Name** DEXout

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in two reactions (as a reactant in [re41](#) and as a modifier in [re41](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}DEXout = 0 \quad (184)$$

### 9.38 Species CBG

**Name** CBG

**Initial concentration** 550.000163480092 nmol · l<sup>-1</sup>

This species takes part in two reactions (as a reactant in [Cortisol\\_CBG](#) and as a modifier in [Cortisol\\_CBG](#)).

$$\frac{d}{dt}CBG = -v_{50} \quad (185)$$

### 9.39 Species CBG\_CortOUT

**Name** CBG\_CortOUT

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in two reactions (as a product in [Cortisol\\_CBG](#) and as a modifier in [Cortisol\\_CBG](#)).

$$\frac{d}{dt}CBG\_CortOUT = v_{50} \quad (186)$$

## 9.40 Species Alb

**Name** Alb

**Initial concentration** 60000.0178341918 nmol · l<sup>-1</sup>

This species takes part in two reactions (as a reactant in [Cort\\_Alb](#) and as a modifier in [Cort\\_Alb](#)).

$$\frac{d}{dt}\text{Alb} = -v_{51} \quad (187)$$

## 9.41 Species Alb\_CortOUT

**Name** Alb\_CortOUT

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in two reactions (as a product in [Cort\\_Alb](#) and as a modifier in [Cort\\_Alb](#)).

$$\frac{d}{dt}\text{Alb\_CortOUT} = v_{51} \quad (188)$$

## 9.42 Species CortAdded

**Name** CortAdded

**Initial concentration** 0 nmol · l<sup>-1</sup>

This species takes part in two reactions (as a reactant in [cort\\_distribution](#) and as a modifier in [cort\\_distribution](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{CortAdded} = 0 \quad (189)$$

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.

<sup>a</sup>Center for Bioinformatics Tübingen (ZBIT), Germany

<sup>b</sup>California Institute of Technology, Beckman Institute BNMC, Pasadena, United States

<sup>c</sup>European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom

<sup>d</sup>EML Research gGmbH, Heidelberg, Germany