# **SBML Model Report**

# Model name: "Fribourg2014 - Dynamics of viral antagonism and innate immune response (H1N1 influenza A virus - Cal/09)"



May 6, 2016

# 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah<sup>1</sup> and Miguel Fribourg<sup>2</sup> at April third 2014 at 1:51 p.m. and last time modified at February 24<sup>th</sup> 2015 at 8:30 p.m. Table 1 provides an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	3
species types	2	species	13
events	0	constraints	0
reactions	12	function definitions	0
global parameters	49	unit definitions	5
rules	5	initial assignments	0

#### **Model Notes**

Fribourg2014 - Dynamics of viral antagonism and innate immune response (H1N1 influenza A virus - Cal/09)

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The dynamics of the interplay between the viral antagonism and the innate immune response has been studied using modelling approaches. The responses of human monocytederived dendritic cells infected by two influenza A H1N1 strains (the pandemic swine-origin A/California/4/2009 (Cal/09) and the seasonal A/New Caledonia/20/1999 (NC/99)) that have different clinical outcomes have been modelled. From the time course gene expression measurements of a set of selected genes, the dynamic features of viral antagonism and innate immune response are extracted. It is found that the strength and the time scale of action of viral antagonism is significantly different between the two viruses. This model describes the viral infection by seasonal Cal/09.

This model is described in the article:Model of influenza A virus infection: Dynamics of viral antagonism and innate immune response. Fribourg M, Hartmann B, Schmolke M, Marjanovic N, Albrecht RA, Garca-Sastre A, Sealfon SC, Jayaprakash C, Hayot F.J Theor Biol. 2014 Mar 2;351C:47-57.

#### Abstract:

Viral antagonism of host responses is an essential component of virus pathogenicity. The study of the interplay between immune response and viral antagonism is challenging due to the involvement of many processes acting at multiple time scales. Here we develop an ordinary differential equation model to investigate the early, experimentally measured, responses of human monocyte-derived dendritic cells to infection by two H1N1 influenza A viruses of different clinical outcomes: pandemic A/California/4/2009 and seasonal A/New Caledonia/20/1999. Our results reveal how the strength of virus antagonism, and the time scale over which it acts to thwart the innate immune response, differs significantly between the two viruses, as is made clear by their impact on the temporal behavior of a number of measured genes. The model thus sheds light on the mechanisms that underlie the variability of innate immune responses to different H1N1 viruses.

This model is hosted on BioModels Database and identified by: MODEL1403310002.

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

To the extent possible under law, all copyright and related orneighbouring rights to this encoded model have been dedicated to the publicdomain worldwide. Please refer to CCO Public DomainDedication for more information.

#### 2 Unit Definitions

This is an overview of five unit definitions.

#### 2.1 Unit substance

Name substance

**Definition**  $10^{-6}$  mol

#### 2.2 Unit volume

Name volume

**Definition** 1

#### 2.3 Unit area

Name area

**Definition** m<sup>2</sup>

# 2.4 Unit length

Name length

**Definition** m

#### 2.5 Unit time

Name time

**Definition** 3600 s

# 3 Compartments

This model contains three compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
default		0000290	3	1	litre	<b></b>	
c2	Environment	0000290	3	1	litre	$\overline{\mathbf{Z}}$	default
compartment	Cell	0000290	3	1	litre	$   \overline{\mathbf{Z}} $	default

# 3.1 Compartment default

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

SBO:0000290 physical compartment

# 3.2 Compartment c2

This is a three dimensional compartment with a constant size of one litre, which is surrounded by default.

Name Environment

SBO:0000290 physical compartment

# 3.3 Compartment compartment

This is a three dimensional compartment with a constant size of one litre, which is surrounded by default.

Name Cell

SBO:0000290 physical compartment

# 4 Species types

This is an overview of two species types.

# 4.1 Species type mRNA

Name mRNA

This model does not contain any species of this type.

# **4.2 Species type** Protein

Name Protein

This model does not contain any species of this type.

# 5 Species

This model contains 13 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 9 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

		Two to controportions of twent species.			
Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
W	W	compartment	$10^{-6} \text{ mol} \cdot 1^{-1}$		
${\tt IFNb\_mRNA}$	IFNb_mRNA	compartment	$10^{-6}  \text{mol} \cdot 1^{-1}$		
${\tt IFNb\_env}$	IFNb_env	c2	$10^{-6}  \text{mol} \cdot 1^{-1}$		$\Box$
STATP2n	STATP2n	compartment	$10^{-6}  \text{mol} \cdot 1^{-1}$		$\Box$
SOCS1m	SOCS1m	compartment	$10^{-6}  \text{mol} \cdot 1^{-1}$		
IRF7m	IRF7m	compartment	$10^{-6} \mathrm{mol}\cdot\mathrm{l}^{-1}$		
IRF7Pn	IRF7Pn	compartment	$10^{-6} \mathrm{mol}\cdot\mathrm{l}^{-1}$		
${\tt IFNa\_mRNA}$	IFNa_mRNA	compartment	$10^{-6} \mathrm{mol}\cdot\mathrm{l}^{-1}$	$\Box$	
${\tt IFNa\_env}$	IFNa_env	c2	$10^{-6}  \text{mol} \cdot 1^{-1}$		$\Box$
TNFam	TNFam	compartment	$10^{-6} \mathrm{mol}\cdot\mathrm{l}^{-1}$		
TNFenv	TNFenv	c2	$10^{-6} \mathrm{mol}\cdot\mathrm{l}^{-1}$		
STATm	STATm	compartment	$10^{-6} \mathrm{mol}\cdot\mathrm{l}^{-1}$		
STAT	STAT	compartment	$10^{-6} \operatorname{mol} \cdot 1^{-1}$		

# **6 Parameters**

This model contains 49 global parameters.

Table 4: Properties of each parameter.

NS r5	Id	Name	SBO	Value	Unit	Constant
n3       5.000       10 <sup>-6</sup> mol       ✓         bm       6.000       10 <sup>-6</sup> mol       ✓         IC1       0.000       □       □         sp       0.300       10 <sup>-6</sup> mol       ✓         n1       1.000       10 <sup>-6</sup> mol       ✓         n1       1.000       10 <sup>-6</sup> mol       ✓         sv       0.100       10 <sup>-6</sup> mol       ✓         delta2       0.400       10 <sup>-6</sup> mol       ✓         sv       0.100       10 <sup>-6</sup> mol       ✓         delta2       0.400       10 <sup>-6</sup> mol       ✓         r2       5.000       10 <sup>-6</sup> mol       ✓         r3       0.000       □       □         r4       10 <sup>-6</sup> mol       ✓         r5       0.004       10 <sup>-6</sup> mol       ✓         r0       0.001       10 <sup>-6</sup> mol       ✓         r0       0.001<	NS			0.000		
bm         6.000         10−6 mol         ☑           IC1         0.000         □         □           sp         0.300         10−6 mol         ☑           delta1         0.100         10−6 mol         ☑           n1         1.000         10−6 mol         ☑           IC2         0.000         □         □           sv         0.100         10−6 mol         ☑           delta2         0.400         10−6 mol         ☑           n2         5.000         10−6 mol         ☑           IC2ifa         0.000         □         □           TJ         0.000         □         □           TJ         0.000         □         □           K3         0.004         10−6 mol         ☑           K9         780.000         10−6 mol         ☑           K9         780.000         10−6 mol         ☑           k15         3.6·10−8         10−6 mol         ☑           k15         3.6·10−8         10−6 mol         ☑           tao1         2.500         10−6 mol         ☑           wmax2         72000.000         10−6 mol         ☑	r5			1.000	dimensionless	$\square$
bm         6.000         10-6 mol         ☑           IC1         0.0000         □         □           sp         0.300         10-6 mol         ☑           delta1         0.100         10-6 mol         ☑           n1         1.000         10-6 mol         ☑           sv         0.100         10-6 mol         ☑           delta2         0.400         10-6 mol         ☑           n2         5.000         10-6 mol         ☑           IC2ifa         0.000         □         □           TJ         0.000         □         □           K3         0.004         10-6 mol         ☑           K3         0.004         10-6 mol         ☑           K9         780.000         10-6 mol         ☑           K9         780.000         10-6 mol         ☑           k15         3.6·10-8         10-6 mol         ☑           k15         3.6·10-8         10-6 mol         ☑           k2         50000.000         10-6 mol         ☑           K2         0.002         10-6 mol         ☑           K3         0.010         10-6 mol         ☑	n3			5.000	$10^{-6}  \text{mol}$	
IC1	bm			6.000	$10^{-6}$ mol	_
delta1       0.100       10 <sup>-6</sup> mol       ✓         n1       1.000       10 <sup>-6</sup> mol       ✓         IC2       0.000       □       □         sv       0.100       10 <sup>-6</sup> mol       ✓         delta2       0.400       10 <sup>-6</sup> mol       ✓         n2       5.000       10 <sup>-6</sup> mol       ✓         IC2ifa       0.000       □       □         TJ       0.000       □       □         K3       0.004       10 <sup>-6</sup> mol       ✓         K3       0.004       10 <sup>-6</sup> mol       ✓         K9       780.000       10 <sup>-6</sup> mol       ✓         k6       780.000       10 <sup>-6</sup> mol       ✓         k15       3.6·10 <sup>-8</sup> 10 <sup>-6</sup> mol       ✓         k15       3.6·10 <sup>-8</sup> 10 <sup>-6</sup> mol       ✓         tao1       2.500       10 <sup>-6</sup> mol       ✓         tao2       72000.000       10 <sup>-6</sup> mol       ✓         wmx2       72000.000       10 <sup>-6</sup> mol       ✓         K5       0.010       10 <sup>-6</sup> mol       ✓         tao3       0.560       10 <sup>-6</sup> mol       ✓         k8       0.040       10 <sup>-6</sup> mol       ✓         k8 <td>IC1</td> <td></td> <td></td> <td>0.000</td> <td></td> <td></td>	IC1			0.000		
delta1       0.100       10 <sup>-6</sup> mol       ✓         n1       1.000       10 <sup>-6</sup> mol       ✓         sv       0.100       10 <sup>-6</sup> mol       ✓         delta2       0.400       10 <sup>-6</sup> mol       ✓         n2       5.000       10 <sup>-6</sup> mol       ✓         IC2ifa       0.000       □       □         TJ       0.000       □       □         K3       0.004       10 <sup>-6</sup> mol       ✓         K9       780.000       10 <sup>-6</sup> mol       ✓         k9       780.000       10 <sup>-6</sup> mol       ✓         r0       0.001       10 <sup>-6</sup> mol       ✓         k15       3.6·10 <sup>-8</sup> 10 <sup>-6</sup> mol       ✓         tao1       2.500       10 <sup>-6</sup> mol       ✓         tao1       2.500       10 <sup>-6</sup> mol       ✓         vmax2       72000.000       10 <sup>-6</sup> mol       ✓         K2       0.002       10 <sup>-6</sup> mol       ✓         K5       0.010       10 <sup>-6</sup> mol       ✓         tao3       0.560       10 <sup>-6</sup> mol       ✓         tao3       0.560       10 <sup>-6</sup> mol       ✓         k8       0.046       10 <sup>-6</sup> mol       ✓	sp			0.300	$10^{-6}$ mol	
n1       1.000       10 <sup>-6</sup> mol       ☑         sv       0.000       □       □         delta2       0.400       10 <sup>-6</sup> mol       ☑         n2       5.000       10 <sup>-6</sup> mol       ☑         IC2ifa       0.000       □       □         TJ       0.000       □       □         K3       0.004       10 <sup>-6</sup> mol       ☑         K9       780.000       10 <sup>-6</sup> mol       ☑         k9       780.000       10 <sup>-6</sup> mol       ☑         r0       0.001       10 <sup>-6</sup> mol       ☑         k15       3.6·10 <sup>-8</sup> 10 <sup>-6</sup> mol       ☑         tao1       2.500       10 <sup>-6</sup> mol       ☑         vmax2       72000.000       10 <sup>-6</sup> mol       ☑         K2       0.002       10 <sup>-6</sup> mol       ☑         K5       0.010       10 <sup>-6</sup> mol       ☑         K8       0.560       10 <sup>-6</sup> mol       ☑         tao3       0.560       10 <sup>-6</sup> mol       ☑         k8       0.004       10 <sup>-6</sup> mol       ☑         k8       0.004       10 <sup>-6</sup> mol       ☑         k8       0.006       10 <sup>-6</sup> mol       ☑         k11 <td>delta1</td> <td></td> <td></td> <td>0.100</td> <td><math>10^{-6}  \text{mol}</math></td> <td>_</td>	delta1			0.100	$10^{-6}  \text{mol}$	_
IC2	n1			1.000	$10^{-6}$ mol	_
sv       0.100       10⁻⁶ mol       ☑         delta2       0.400       10⁻⁶ mol       ☑         n2       5.000       10⁻⁶ mol       ☑         IC2ifa       0.000       □       □         TJ       0.000       □       □         K3       0.004       10⁻⁶ mol       ☑         K9       780.000       10⁻⁶ mol       ☑         k9       780.000       10⁻⁶ mol       ☑         k0elta       3⋅10⁻⁶ mol       ☑       ☑         k9       780.000       10⁻⁶ mol       ☑         k9       780.000       10⁻⁶ mol       ☑         k9       780.000       10⁻⁶ mol       ☑         k15       3.6⋅10⁻⁶ mol       ☑         k15       3.6⋅10⁻⁶ mol       ☑         tao1       2.500       10⁻⁶ mol       ☑         vmax2       72000.000       10⁻⁶ mol       ☑         k2       0.002       10⁻⁶ mol       ☑         k5       0.010       10⁻⁶ mol       ☑         k8       0.046       10⁻⁶ mol       ☑         k8       0.040       10⁻⁶ mol       ☑         k11       3.6⋅10⁻弮       10⁻₆ mol	IC2			0.000		
delta2       0.400       10 <sup>-6</sup> mol       ✓         n2       5.000       10 <sup>-6</sup> mol       ✓         IC2ifa       0.000       □       □         TJ       0.000       □       □         TJtot       10 <sup>-4</sup> 10 <sup>-6</sup> mol       ✓         K3       0.004 10 <sup>-6</sup> mol       ✓         K9       780.000 10 <sup>-6</sup> mol       ✓         K9       780.000 10 <sup>-6</sup> mol       ✓         k0       780.000 10 <sup>-6</sup> mol       ✓         k15       3.6·10 <sup>-8</sup> 10 <sup>-6</sup> mol       ✓         k15       3.6·10 <sup>-8</sup> 10 <sup>-6</sup> mol       ✓         tao1       2.500 10 <sup>-6</sup> mol       ✓         tao2       500000.000 10 <sup>-6</sup> mol       ✓         vmax2       72000.000 10 <sup>-6</sup> mol       ✓         vm       6.023·10 <sup>23</sup> 10 <sup>-6</sup> mol       ✓         K5       0.010 10 <sup>-6</sup> mol       ✓         tao3       0.560 10 <sup>-6</sup> mol       ✓         r3       10 <sup>-7</sup> 10 <sup>-6</sup> mol       ✓         k8       0.040 10 <sup>-6</sup> mol       ✓         k11       3.6·10 <sup>-4</sup> 10 <sup>-6</sup> mol       ✓         k14       3.204·10 <sup>-7</sup> 10 <sup>-6</sup> mol       ✓         k12       360.000 10 <sup>-6</sup> mol       ✓         k16 <td>sv</td> <td></td> <td></td> <td>0.100</td> <td><math>10^{-6}</math> mol</td> <td></td>	sv			0.100	$10^{-6}$ mol	
Decision   Decision	delta2			0.400	$10^{-6}$ mol	
TJ	n2			5.000	$10^{-6} \text{ mol}$	_
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	IC2ifa			0.000		
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r0 $0.001$ $10^{-6}$ mol         k15 $3.6 \cdot 10^{-8}$ $10^{-6}$ mol         tao1 $2.500$ $10^{-6}$ mol $2.500$ C $500000.000$ $10^{-6}$ mol $2.500$ Vmax2 $72000.000$ $10^{-6}$ mol $2.500$ NA $6.023 \cdot 10^{23}$ $10^{-6}$ mol $2.500$ K2 $0.002$ $10^{-6}$ mol $2.500$ K5 $0.010$ $10^{-6}$ mol $2.500$ tao3 $0.560$ $10^{-6}$ mol $2.500$ k8 $0.004$ $10^{-6}$ mol $2.500$ k8 $0.004$ $10^{-6}$ mol $2.5000$ k11 $3.6 \cdot 10^{-4}$ $10^{-6}$ mol $2.5000$ k12 $3.60.000$ $10^{-6}$ mol $2.5000$ k16 $0.360$ $10^{-6}$ mol $2.5000$ tao8 $2.000$ $10^{-6}$ mol $2.5000$	delta			$3 \cdot 10^{-4}$	$10^{-6}$ mol	
k15 $3.6 \cdot 10^{-8}$ $10^{-6}$ mol         tao1 $2.500$ $10^{-6}$ mol         C $500000.000$ $10^{-6}$ mol         vmax2 $72000.000$ $10^{-6}$ mol         NA $6.023 \cdot 10^{23}$ $10^{-6}$ mol         K2 $0.002$ $10^{-6}$ mol         K5 $0.010$ $10^{-6}$ mol         tao3 $0.560$ $10^{-6}$ mol         r3 $10^{-7}$ $10^{-6}$ mol         k8 $0.004$ $10^{-6}$ mol         tao4 $0.460$ $10^{-6}$ mol         k11 $3.6 \cdot 10^{-4}$ $10^{-6}$ mol         k14 $3.204 \cdot 10^{-7}$ $10^{-6}$ mol         tao6 $1.000$ $2.000$ k12 $360.000$ $10^{-6}$ mol         k16 $0.360$ $10^{-6}$ mol         tao8 $2.000$ $10^{-6}$ mol	r0			0.001	$10^{-6}$ mol	_
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C $500000.000$ $10^{-6}$ mol         vmax2 $72000.000$ $10^{-6}$ mol         NA $6.023 \cdot 10^{23}$ $10^{-6}$ mol         K2 $0.002$ $10^{-6}$ mol         K5 $0.010$ $10^{-6}$ mol         tao3 $0.560$ $10^{-6}$ mol         r3 $10^{-7}$ $10^{-6}$ mol         k8 $0.004$ $10^{-6}$ mol         tao4 $0.460$ $10^{-6}$ mol         k11 $3.6 \cdot 10^{-4}$ $10^{-6}$ mol         k14 $3.204 \cdot 10^{-7}$ $10^{-6}$ mol         tao6 $1.000$ k12 $360.000$ $10^{-6}$ mol         k16 $0.360$ $10^{-6}$ mol         tao8 $2.000$ $10^{-6}$ mol	tao1			2.500	$10^{-6}  \text{mol}$	_
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NA $6.023 \cdot 10^{23}$ $10^{-6}$ mol         K2 $0.002$ $10^{-6}$ mol         K5 $0.010$ $10^{-6}$ mol         tao3 $0.560$ $10^{-6}$ mol         r3 $10^{-7}$ $10^{-6}$ mol         k8 $0.004$ $10^{-6}$ mol         tao4 $0.460$ $10^{-6}$ mol         k11 $3.6 \cdot 10^{-4}$ $10^{-6}$ mol         k14 $3.204 \cdot 10^{-7}$ $10^{-6}$ mol         tao6 $1.000$ $\checkmark$ k12 $360.000$ $10^{-6}$ mol         k16 $0.360$ $10^{-6}$ mol         tao8 $2.000$ $10^{-6}$ mol	vmax2			72000.000	$10^{-6}  \text{mol}$	
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k11 $3.6 \cdot 10^{-4}$ $10^{-6}$ mol         k14 $3.204 \cdot 10^{-7}$ $10^{-6}$ mol         tao6 $1.000$ \mathbb{Z}          k12 $360.000$ $10^{-6}$ mol          \mathbb{Z}          k16 $0.360$ $10^{-6}$ mol          \mathbb{Z}          tao8 $2.000$ $10^{-6}$ mol          \mathbb{Z}	k8			0.004	$10^{-6}  \text{mol}$	
k11 $3.6 \cdot 10^{-4}$ $10^{-6}$ mol         k14 $3.204 \cdot 10^{-7}$ $10^{-6}$ mol         tao6 $1.000$ \bigsize          k12 $360.000$ $10^{-6}$ mol         k16 $0.360$ $10^{-6}$ mol         tao8 $2.000$ $10^{-6}$ mol	tao4			0.460		_
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k16 $0.360   10^{-6}   mol$ tao8 $2.000   10^{-6}   mol$	k12			360.000		
tao8 $2.000   10^{-6}   mol$	k16			0.360		
	tao8			2.000		
	vmax17			72000.000	$10^{-6}  \text{mol}$	

Id	Name	SBO	Value	Unit	Constant
K17			0.002	$10^{-6}  \mathrm{mol}$	$\overline{\hspace{1cm}}$
r1			$10^{-4}$	$10^{-6}  \mathrm{mol}$	$ \overline{\mathbf{Z}} $
rmax20			0.001	$10^{-6}  \mathrm{mol}$	
K20			$6 \cdot 10^{-4}$	$10^{-6}  \mathrm{mol}$	$ \overline{\mathbf{Z}} $
tao9			2.000	$10^{-6}  \text{mol}$	
vmax19			154800.000	$10^{-6}  \text{mol}$	
K19			0.004	$10^{-6}$ mol	
r4			$10^{-5}$	$10^{-6}$ mol	
k26			0.360	$10^{-6}$ mol	
tao12			1.000	$10^{-6}  \text{mol}$	
k28			360.000	$10^{-6}  \mathrm{mol}$	
tao13			15.000	$10^{-6}$ mol	$\square$

# 7 Rules

This is an overview of five rules.

#### **7.1 Rule NS**

Rule NS is an assignment rule for parameter NS:

$$NS = \frac{r5 \cdot time^{n3}}{bm^{n3} + time^{n3}} \tag{1}$$

 $\textbf{Derived unit} \ \left(3600 \ s\right)^5 \cdot \left(10^{-6} \ mol\right)^{-5}$ 

# **7.2 Rule IC1**

Rule IC1 is an assignment rule for parameter IC1:

$$IC1 = \frac{1 + sp \cdot \left(\frac{NS}{delta1}\right)^{n1}}{1 + \left(\frac{NS}{delta1}\right)^{n1}}$$
(2)

## **7.3 Rule IC2**

Rule IC2 is an assignment rule for parameter IC2:

$$IC2 = 1 (3)$$

# 7.4 Rule IC2ifa

Rule IC2ifa is an assignment rule for parameter IC2ifa:

$$IC2ifa = 1 (4)$$

# **7.5 Rule** TJ

Rule TJ is an assignment rule for parameter TJ:

$$TJ = \frac{\frac{TJtot \cdot ([IFNb\_env] + [IFNa\_env])}{K3 + [IFNb\_env] + [IFNa\_env]} \cdot 1}{1 + \frac{K9 \cdot [SOCS1m]}{delta}}$$
(5)

# 8 Reactions

This model contains twelve 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

N⁰	Id	Name	Reaction Equation	SBO
1	J1	J1	$w \xrightarrow{IRF7Pn} IFNb\_mRNA$	
2	J2	J2	$w \xrightarrow{IFNb\_mRNA} IFNb\_env$	
3	Ј3	J3	$w \xrightarrow{STAT} STATP2n$	
4	J4	J4	$w \xrightarrow{STATP2n} SOCS1m$	
5	J5	J5	w $\xrightarrow{\text{STATP2n, IRF7Pn}}$ IRF7m	
6	J6	J6	$w \xrightarrow{IRF7m} IRF7Pn$	
7	J7	J7	$w \xrightarrow{IRF7Pn} IFNa\_mRNA$	
8	Ј8	18	$w \xrightarrow{IFNa\_mRNA} IFNa\_env$	
9	J9	J9	$w \xrightarrow{TNFenv} TNFam$	
10	J10	J10	$w \xrightarrow{TNFam} TNFenv$	
11	J11	J11	$w \xrightarrow{STATP2n} STATm$	
12	J12	J12	$w \xrightarrow{STATm} STAT$	

#### 8.1 Reaction J1

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

#### Name J1

# **Reaction equation**

$$w \xrightarrow{IRF7Pn} IFNb\_mRNA$$
 (6)

#### Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 7: Properties of each modifier.

Id	Name	SBO
IRF7Pn	IRF7Pn	

#### **Product**

Table 8: Properties of each product.

Id	Name	SBO
IFNb_mRNA	IFNb_mRNA	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_1 = (r0 \cdot IC1 + k15 \cdot [IRF7Pn]) \cdot IC2 - \frac{[IFNb\_mRNA] \cdot ln2}{tao1}$$
 (7)

#### 8.2 Reaction J2

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

#### Name J2

# **Reaction equation**

$$w \xrightarrow{IFNb\_mRNA} IFNb\_env$$
 (8)

#### Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 10: Properties of each modifier.

Id	Name	SBO
IFNb_mRNA	IFNb_mRNA	

#### **Product**

Table 11: Properties of each product.

Id	Name	SBO
IFNb_env	IFNb_env	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{2} = \frac{\frac{1000000000 \cdot \text{C} \cdot \text{vmax2}}{\text{NA}} \cdot [\text{IFNb\_mRNA}]}{\text{K2} + [\text{IFNb\_mRNA}]}$$
(9)

# 8.3 Reaction J3

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

# Name J3

# **Reaction equation**

$$w \xrightarrow{STAT} STATP2n \tag{10}$$

#### Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 13: Properties of each modifier.

Id	Name	SBO
STAT	STAT	

#### **Product**

Table 14: Properties of each product.

Id	Name	SBO
STATP2n	STATP2n	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_3 = \frac{\frac{\text{K5-TJ-[STAT]}}{2}}{\text{K5} + [\text{STAT}]} - \frac{[\text{STATP2n}] \cdot \ln 2}{\tan 3}$$
 (11)

# 8.4 Reaction J4

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

# Name J4

# **Reaction equation**

$$w \xrightarrow{STATP2n} SOCS1m \tag{12}$$

# Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 16: Properties of each modifier.

Id	Name	SBO
STATP2n	STATP2n	

#### **Product**

Table 17: Properties of each product.

Id	Name	SBO
SOCS1m	SOCS1m	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_4 = (r3 \cdot IC1 + k8 \cdot [STATP2n]) \cdot IC2 - \frac{[SOCS1m] \cdot ln \cdot 2}{tao4}$$
 (13)

#### 8.5 Reaction J5

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

#### Name J5

# **Reaction equation**

$$w \xrightarrow{STATP2n, IRF7Pn} IRF7m$$
 (14)

#### Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifiers**

Table 19: Properties of each modifier.

Id	Name	SBO
STATP2n	STATP2n	
IRF7Pn	IRF7Pn	

#### **Product**

Table 20: Properties of each product.

Id	Name	SBO
IRF7m	IRF7m	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_5 = (k11 \cdot [STATP2n] + k14 \cdot [IRF7Pn]) \cdot IC2 - \frac{[IRF7m] \cdot ln2}{tao6}$$
 (15)

#### 8.6 Reaction J6

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

#### Name J6

# **Reaction equation**

$$w \xrightarrow{IRF7m} IRF7Pn \tag{16}$$

#### Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
W	W	

## **Modifier**

Table 22: Properties of each modifier.

Id	Name	SBO
IRF7m	IRF7m	

#### **Product**

Table 23: Properties of each product.

Id	Name	SBO
IRF7Pn	IRF7Pn	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_6 = k12 \cdot IC1 \cdot [IRF7m] \tag{17}$$

#### **8.7 Reaction** J7

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

#### Name J7

# **Reaction equation**

$$w \xrightarrow{IRF7Pn} IFNa\_mRNA$$
 (18)

#### Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 25: Properties of each modifier.

Id	Name	SBO
IRF7Pn	IRF7Pn	

## **Product**

Table 26: Properties of each product.

Tuble 20: I Toperties of each product:			
Id	Name	SBO	
IFNa_mRNA	IFNa_mRNA		

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_7 = k16 \cdot [IRF7Pn] \cdot IC2ifa - \frac{[IFNa\_mRNA] \cdot ln2}{tao8}$$
 (19)

#### 8.8 Reaction J8

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

#### Name J8

# **Reaction equation**

$$w \xrightarrow{IFNa\_mRNA} IFNa\_env$$
 (20)

## Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 28: Properties of each modifier.

Id	Name	SBO
IFNa_mRNA	IFNa_mRNA	

Table 29: Properties of each product.

Id	Name	SBO
IFNa_env	IFNa_env	

**Derived unit** contains undeclared units

$$v_8 = \frac{\frac{1000000000 \cdot \text{C} \cdot \text{vmax} 17}{\text{NA}} \cdot [\text{IFNa\_mRNA}]}{\text{K17} + [\text{IFNa\_mRNA}]}$$
(21)

#### 8.9 Reaction J9

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

#### Name J9

# **Reaction equation**

$$w \xrightarrow{TNFenv} TNFam \tag{22}$$

#### Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 31: Properties of each modifier.

Id	Name	SBO
TNFenv	TNFenv	

Table 32: Properties of each product.

Id	Name	SBO
TNFam	TNFam	

**Derived unit** contains undeclared units

$$v_9 = \left(r1 \cdot IC1 + \frac{rmax20 \cdot [TNFenv]}{K20 + [TNFenv]}\right) \cdot IC2 - \frac{[TNFam] \cdot ln 2}{tao9}$$
 (23)

#### 8.10 Reaction J10

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

#### Name J<sub>10</sub>

#### **Reaction equation**

$$w \xrightarrow{\text{TNFam}} \text{TNFenv} \tag{24}$$

#### Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 34: Properties of each modifier.

Id	Name	SBO
TNFam	TNFam	

Table 35: Properties of each product.

Id	Name	SBO
TNFenv	TNFenv	

**Derived unit** contains undeclared units

$$v_{10} = \frac{\frac{1000000000 \cdot \text{C} \cdot \text{vmax} 19}{\text{NA}} \cdot [\text{TNFam}]}{\text{K}19 + [\text{TNFam}]}$$
(25)

# **8.11 Reaction** J11

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

#### Name J11

# **Reaction equation**

$$w \xrightarrow{STATP2n} STATm$$
 (26)

#### Reactant

Table 36: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 37: Properties of each modifier.

Id	Name	SBO
STATP2n	STATP2n	

Table 38: Properties of each product.

Id	Name	SBO
STATm	STATm	

**Derived unit** contains undeclared units

$$v_{11} = (r4 \cdot IC1 + k26 \cdot [STATP2n]) \cdot IC2 - \frac{[STATm] \cdot ln2}{tao12}$$
(27)

# 8.12 Reaction J12

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

#### Name J12

# **Reaction equation**

$$w \xrightarrow{STATm} STAT \tag{28}$$

#### Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
W	W	

#### **Modifier**

Table 40: Properties of each modifier.

Id	Name	SBO
STATm	STATm	

Table 41: Properties of each product.

Id	Name	SBO
STAT	STAT	

Id	Name	SBO

**Derived unit**  $(10^{-6} \text{ mol})^2 \cdot 1^{-1}$ 

$$v_{12} = k28 \cdot [STATm] - \frac{[STAT] \cdot \ln 2}{\tan 13}$$
 (29)

# 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 w

Name w

**SBO:0000291** empty set

Initial concentration  $0.10^{-6} \, \mathrm{mol} \cdot l^{-1}$ 

This species takes part in twelve reactions (as a reactant in J1, J2, J3, J4, J5, J6, J7, J8, J9, J10, J11, J12), which do not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathbf{w} = 0\tag{30}$$

## 9.2 Species IFNb\_mRNA

Name IFNb\_mRNA

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in two reactions (as a product in J1 and as a modifier in J2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IFNb\_mRNA} = v_1 \tag{31}$$

# 9.3 Species IFNb\_env

Name IFNb\_env

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in one reaction (as a product in J2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IFNb\_env} = v_2 \tag{32}$$

## 9.4 Species STATP2n

Name STATP2n

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in four reactions (as a product in J3 and as a modifier in J4, J5, J11).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{STATP2n} = v_3 \tag{33}$$

# 9.5 Species SOCS1m

Name SOCS1m

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in one reaction (as a product in J4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{SOCS1m} = v_4 \tag{34}$$

## 9.6 Species IRF7m

Name IRF7m

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in two reactions (as a product in J5 and as a modifier in J6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRF7m} = v_5 \tag{35}$$

#### 9.7 Species IRF7Pn

Name IRF7Pn

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in four reactions (as a product in J6 and as a modifier in J1, J5, J7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRF7Pn} = v_6 \tag{36}$$

#### 9.8 Species IFNa\_mRNA

Name IFNa\_mRNA

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in two reactions (as a product in J7 and as a modifier in J8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IFNa\_mRNA} = v_7 \tag{37}$$

## 9.9 Species IFNa\_env

Name IFNa\_env

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in one reaction (as a product in J8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IFNa\_env} = v_8 \tag{38}$$

## 9.10 Species TNFam

Name TNFam

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in two reactions (as a product in J9 and as a modifier in J10).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{TNFam} = v_9 \tag{39}$$

## 9.11 Species TNFenv

Name TNFenv

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in two reactions (as a product in J10 and as a modifier in J9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{TNFenv} = v_{10} \tag{40}$$

# 9.12 Species STATm

Name STATm

Initial concentration  $0.10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in two reactions (as a product in J11 and as a modifier in J12).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{STATm} = v_{11} \tag{41}$$

#### 9.13 Species STAT

Name STAT

Initial concentration  $0.1 \ 10^{-6} \ \text{mol} \cdot l^{-1}$ 

This species takes part in two reactions (as a product in J12 and as a modifier in J3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{STAT} = |v_{12}| \tag{42}$$

# A Glossary of Systems Biology Ontology Terms

**SBO:0000290 physical compartment:** Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions

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

SBML2LATEX was developed by Andreas Dräger<sup>a</sup>, Hannes Planatscher<sup>a</sup>, Dieudonné M Wouamba<sup>a</sup>, Adrian Schröder<sup>a</sup>, Michael Hucka<sup>b</sup>, Lukas Endler<sup>c</sup>, Martin Golebiewski<sup>d</sup> and Andreas Zell<sup>a</sup>. Please see http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX for more information.

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