SBML Model Report

Model name: "Aguilera 2014 - HIV latency. Interaction between HIV proteins and immune response"

SBML2LaTeX

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: Audald Lloret i Villas[1] and Luis Ubaldo Aguilera de Lira[2] at March 30th 2015 at 1:07 p. m. and last time modified at April eighth 2016 at 5:53 p. m. Table 1 shows an overview of the quantities of all components of this model.

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

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	2
events	0	constraints	0
reactions	7	function definitions	2
global parameters	0	unit definitions	1
rules	0	initial assignments	0

Model Notes

Aguilera 2014 - HIV latency. Interactionbetween HIV proteins and immune response

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This model is described in the article:Studying HIV latency by modeling the interaction between HIV proteins and the innate immune response.Aguilera LU, Rodrguez-Gonzlez J.J. Theor. Biol. 2014 Nov; 360: 67-77

Abstract:

HIV infection leads to two cell fates, the viral productive state or viral latency (a reversible non-productive state). HIV latency is relevant because infected active CD4+ T-lymphocytes can reach a resting memory state in which the provirus remains silent for long periods of time. Despite experimental and theoretical efforts, the causal molecular mechanisms responsible for HIV latency are only partially understood. Studies have determined that HIV latency is influenced by the innate immune response carried out by cell restriction factors that inhibit the postintegration steps in the virus replication cycle. In this study, we present a mathematical study that combines deterministic and stochastic approaches to analyze the interactions between HIV proteins and the innate immune response. Using wide ranges of parameter values, we observed the following: (1) a phenomenological description of the viral productive and latent cell phenotypes is obtained by bistable and bimodal dynamics, (2) biochemical noise reduces the probability that an infected cell adopts the latent state, (3) the effects of the innate immune response enhance the HIV latency state, (4) the conditions of the cell before infection affect the latent phenotype, i.e., the existing expression of cell restriction factors propitiates HIV latency, and existing expression of HIV proteins reduces HIV latency.

This model is hosted on BioModels Database and identified by: BIOMD0000000573.

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

2 Unit Definitions

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

2.1 Unit `substance`

Name substance

Definition item

2.2 Unit `volume`

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

Definition l

2.3 Unit `area`

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

Definition m^2

2.4 Unit `length`

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

Definition m

2.5 Unit `time`

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

Definition s

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

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

3.1 Compartment `compartment`

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

Name cell

4 Species

This model contains two species. Section 7 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
`V`	V	`compartment`	$\text{item} \cdot \text{l}^{-1}$	⊟	⊟
`C`	C	`compartment`	$\text{item} \cdot \text{l}^{-1}$	⊟	⊟

5 Function definitions

This is an overview of two function definitions.

5.1 Function definition `Constant_flux__irreversible`

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$\mathrm{v} \tag{1}$$

5.2 Function definition `Michaellis_Menten`

Name Michaellis Menten

Arguments substrate, Km, Vmax

Mathematical Expression

$$\frac{\mathrm{Vmax} \cdot \mathrm{substrate}}{\mathrm{Km} + \mathrm{substrate}} \tag{2}$$

6 Reactions

This model contains seven 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 4: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	`Kb`	Kb	$\emptyset \longrightarrow \mathrm{V}$	
2	`Kv`	Kv	$\mathrm{V} \xrightarrow{\mathrm{V}} 2\,\mathrm{V}$	
3	`Kcv`	Kvc	$\mathrm{V} + \mathrm{C} \xrightarrow{\mathrm{V},\,\mathrm{C}} \mathrm{C}$	
4	`Kdv`	Kdv	$\mathrm{V} \xrightarrow{\mathrm{V}} \emptyset$	
5	`Kc`	Kc	$\emptyset \longrightarrow \mathrm{C}$	
6	`Kvc`	Kcv	$\mathrm{V} + \mathrm{C} \xrightarrow{\mathrm{V},\,\mathrm{C}} \mathrm{V}$	
7	`Kdc`	Kdc	$\mathrm{C} \xrightarrow{\mathrm{C}} \emptyset$	

6.1 Reaction Kb

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

Name Kb

Reaction equation

$$\emptyset \longrightarrow \mathrm{V} \tag{3}$$

Product

Table 5: Properties of each product.

Id	Name	SBO
V	V	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \mathrm{vol}\left(\mathrm{compartment}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) \tag{4}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{5}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{6}$$

Table 6: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
v	v		0.001		☑

6.2 Reaction Kv

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

Name Kv

Reaction equation

$$\mathrm{V} \xrightarrow{\mathrm{V}} 2\,\mathrm{V} \tag{7}$$

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
V	V	

Modifier

Table 8: Properties of each modifier.

Id	Name	SBO
V	V	

Product

Table 9: Properties of each product.

Id	Name	SBO
V	V	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\left(\mathrm{compartment}\right) \cdot \mathrm{Michaellis\_Menten}\left([\mathrm{V}], \mathrm{Km}, \mathrm{Vmax}\right) \tag{8}$$

$$\mathrm{Michaellis\_Menten}\left(\mathrm{substrate}, \mathrm{Km}, \mathrm{Vmax}\right) = \frac{\mathrm{Vmax} \cdot \mathrm{substrate}}{\mathrm{Km} + \mathrm{substrate}} \tag{9}$$

$$\mathrm{Michaellis\_Menten}\left(\mathrm{substrate}, \mathrm{Km}, \mathrm{Vmax}\right) = \frac{\mathrm{Vmax} \cdot \mathrm{substrate}}{\mathrm{Km} + \mathrm{substrate}} \tag{10}$$

Table 10: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Km	Km		380.000		☑
Vmax	Vmax		0.134		☑

6.3 Reaction `Kcv`

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

Name Kvc

Reaction equation

$$V + C \xrightarrow{V,\, C} C \tag{11}$$

Reactants

Table 11: Properties of each reactant.

Id	Name	SBO
`V`	V	
`C`	C	

Modifiers

Table 12: Properties of each modifier.

Id	Name	SBO
`V`	V	
`C`	C	

Product

Table 13: Properties of each product.

Id	Name	SBO
`C`	C	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{compartment}\right) \cdot \mathrm{k1} \cdot [\mathrm{V}] \cdot [\mathrm{C}] \tag{12}$$

Table 14: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.030		☑

6.4 Reaction Kdv

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

Name Kdv

Reaction equation

$$\mathrm{V} \xrightarrow{\mathrm{V}} \emptyset \tag{13}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
V	V	

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
V	V	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\left(\mathrm{compartment}\right) \cdot \mathrm{k1} \cdot [\mathrm{V}] \tag{14}$$

Table 17: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$6.85 \cdot 10^{-5}$		☑

6.5 Reaction `Kc`

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

Name Kc

Reaction equation

$$\emptyset \longrightarrow \mathrm{C} \tag{15}$$

Product

Table 18: Properties of each product.

Id	Name	SBO
`C`	C	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\left(\mathrm{compartment}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) \tag{16}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{17}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{18}$$

Table 19: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`v`	v		0.07		☑

6.6 Reaction `Kvc`

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

Name Kcv

Reaction equation

$$\mathrm{V} + \mathrm{C} \xrightarrow{\mathrm{V},\,\mathrm{C}} \mathrm{V} \tag{19}$$

Reactants

Table 20: Properties of each reactant.

Id	Name	SBO
V	V	
C	C	

Modifiers

Table 21: Properties of each modifier.

Id	Name	SBO
V	V	
C	C	

Product

Table 22: Properties of each product.

Id	Name	SBO
V	V	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\left(\mathrm{compartment}\right) \cdot \mathrm{k1} \cdot [\mathrm{V}] \cdot [\mathrm{C}] \tag{20}$$

Table 23: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.927		☑

6.7 Reaction Kdc

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

Name Kdc

Reaction equation

$$\mathrm{C} \xrightarrow{\mathrm{C}} \emptyset \tag{21}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
C	C	

Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
C	C	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{compartment}\right) \cdot \mathrm{k1} \cdot [\mathrm{C}] \tag{22}$$

Table 26: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$5.01 \cdot 10^{-5}$		☑

7 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.

7.1 Species V

Name V

Initial concentration $1 \text{ item} \cdot \text{l}^{-1}$

This species takes part in eleven reactions (as a reactant in Kv, Kcv, Kdv, Kvc and as a product in Kb, Kv, Kvc and as a modifier in Kv, Kcv, Kdv, Kvc).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{V} = v_1 + 2\, v_2 + v_6 - v_2 - v_3 - v_4 - v_6 \tag{23}$$

7.2 Species C

Name C

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

This species takes part in eight reactions (as a reactant in Kcv, Kvc, Kdc and as a product in Kcv, Kc and as a modifier in Kcv, Kvc, Kdc).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C} = v_3 + v_5 - v_3 - v_6 - v_7 \tag{24}$$