SBML Model Report

Model name: “Nelson2000_HIV-1_general_model”

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1 General Overview

This is a document in SBML Level 2 Version 4 format. 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	4
events	0	constraints	0
reactions	8	function definitions	0
global parameters	8	unit definitions	8
rules	1	initial assignments	0

Model Notes

This is the general model without delay described by the equation system (1) in: **A model of HIV-1 pathogenesis that includes an intracellular delay.**
Nelson PW, Murray JD, Perelson AS; Math Biosci. 2000 Feb;163(2):201-15. PMID: 10701304 ; doi: 10.1016/S0025-5564(99)00055-3
Abstract:
Mathematical modeling combined with experimental measurements have yielded important insights into HIV-1 pathogenesis. For example, data from experiments in which HIV-infected patients are given potent antiretroviral drugs that perturb the infection process have been used

to estimate kinetic parameters underlying HIV infection. Many of the models used to analyze data have assumed drug treatments to be completely efficacious and that upon infection a cell instantly begins producing virus. We consider a model that allows for less then perfect drug effects and which includes a delay in the initiation of virus production. We present detailed analysis of this delay differential equation model and compare the results to a model without delay. Our analysis shows that when drug efficacy is less than 100%, as may be the case in vivo, the predicted rate of decline in plasma virus concentration depends on three factors: the death rate of virus producing cells, the efficacy of therapy, and the length of the delay. Thus, previous estimates of infected cell loss rates can be improved upon by considering more realistic models of viral infection.
Author Keywords: HIV; Delay; Viral life cycle; T-cells

As there are no results given for this model in the article it cannot be checked for MIRIAM compliance. The SBML file should be equivalent to the described ODE file though.

2 Unit Definitions

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

2.1 Unit `time`

Name day

Definition 86400 s

2.2 Unit `substance`

Name items

Definition item

2.3 Unit `perday`

Name per day

Definition $(86400\ \mathrm{s})^{-1}$

2.4 Unit `volume`

Name ml

Definition ml

2.5 Unit `items_per_ml`

Name items per ml

Definition $\mathrm{item} \cdot \mathrm{ml}^{-1}$

2.6 Unit `ml_per_item_day`

Name ml per (item*day)

Definition $\mathrm{ml} \cdot (86400\ \mathrm{s})^{-1} \cdot \mathrm{item}^{-1}$

2.7 Unit `virions_per_cell`

Name virions_per_cell

Definition dimensionless

2.8 Unit `items_perml_d`

Name items per (ml*day)

Definition $\mathrm{item} \cdot \mathrm{ml}^{-1} \cdot (86400\ \mathrm{s})^{-1}$

2.9 Unit `area`

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

Definition m^2

2.10 Unit `length`

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

Definition m

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

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

3.1 Compartment `plasma`

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

Name plasma

4 Species

This model contains four species. Section 8 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
T	T	plasma	$\mathrm{item} \cdot \mathrm{ml}^{-1}$	⊟	⊟
T_i	T*	plasma	$\mathrm{item} \cdot \mathrm{ml}^{-1}$	⊟	⊟
V_I	V_I	plasma	$\mathrm{item} \cdot \mathrm{ml}^{-1}$	⊟	⊟
V_NI	V_NI	plasma	$\mathrm{item} \cdot \mathrm{ml}^{-1}$	⊟	⊟

5 Parameters

This model contains eight global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k	k		$3.43 \cdot 10^{-8}$	$\text{ml} \cdot (86400\ \text{s})^{-1} \cdot \text{item}^{-1}$	☑
delta	delta		0.500	$(86400\ \text{s})^{-1}$	☑
N	N		480.000	dimensionless	☑
c	c		3.000	$(86400\ \text{s})^{-1}$	☑
np	np		0.100	dimensionless	☑
HIV	HIV		0.000	$\text{item} \cdot \text{ml}^{-1}$	☐
lambda			10.000	$\text{item} \cdot \text{ml}^{-1} \cdot (86400\ \text{s})^{-1}$	☑
delta1			0.030	$(86400\ \text{s})^{-1}$	☑

6 Rule

This is an overview of one rule.

6.1 Rule HIV

Rule HIV is an assignment rule for parameter HIV:

$$\text{HIV} = [\text{V\_I}] + [\text{V\_NI}] \tag{1}$$

Derived unit $\text{item} \cdot \text{ml}^{-1}$

7 Reactions

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

Table 5: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	`T_cell_source`	creation of T-cells	$\emptyset \longrightarrow \text{T}$	
2	`T_cell_loss`	loss of uninfected T-cell	$\text{T} \longrightarrow \emptyset$	
3	`infection`	T-cell infection	$\text{T} \xrightarrow{\text{V\_I}} \text{T\_i}$	
4	`T_i_lysis`	infected T-cell lysis	$\text{T\_i} \longrightarrow \emptyset$	
5	`T_lysis_infect`	release of infectious virions on lysis	$\emptyset \xrightarrow{\text{T\_i}} \text{V\_I}$	
6	`T_lysis_noninf`	release of non infectious virions on lysis	$\emptyset \xrightarrow{\text{T\_i}} \text{V\_NI}$	
7	`V_I_clearance`	clearance of infectious virions	$\text{V\_I} \rightleftharpoons \emptyset$	
8	`V_NI_clearance`	non-infect. virion clearance	$\text{V\_NI} \longrightarrow \emptyset$	

7.1 Reaction `T_cell_source`

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

Name creation of T-cells

Reaction equation

$$\emptyset \longrightarrow \mathrm{T} \tag{2}$$

Product

Table 6: Properties of each product.

Id	Name	SBO
T	T	

Kinetic Law

Derived unit item $\cdot$ $(86400\ \mathrm{s})^{-1}$

$$v_1 = \mathrm{lambda} \cdot \mathrm{vol}\left(\mathrm{plasma}\right) \tag{3}$$

7.2 Reaction `T_cell_loss`

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

Name loss of uninfected T-cell

Reaction equation

$$\mathrm{T} \longrightarrow \emptyset \tag{4}$$

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
T	T	

Kinetic Law

Derived unit $(86400\ \mathrm{s})^{-1}$ $\cdot$ item

$$v_2 = \mathrm{delta1} \cdot [\mathrm{T}] \cdot \mathrm{vol}\left(\mathrm{plasma}\right) \tag{5}$$

7.3 Reaction `infection`

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

Name T-cell infection

Reaction equation

$$\mathrm{T} \xrightarrow{\mathrm{V\_I}} \mathrm{T\_i} \tag{6}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
`T`	T	

Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
`V_I`	V_I	

Product

Table 10: Properties of each product.

Id	Name	SBO
`T_i`	T*	

Kinetic Law

Derived unit $(86400\ \mathrm{s})^{-1} \cdot \mathrm{item}$

$$v_3 = \mathrm{k} \cdot [\mathrm{V\_I}] \cdot [\mathrm{T}] \cdot \mathrm{vol}\left(\mathrm{plasma}\right) \tag{7}$$

7.4 Reaction `T_i_lysis`

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

Name infected T-cell lysis

Reaction equation

$$\mathrm{T\_i} \longrightarrow \emptyset \tag{8}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
T_i	T*	

Kinetic Law

Derived unit $(86400\ \mathrm{s})^{-1} \cdot \mathrm{item}$

$$v_4 = \mathrm{delta} \cdot [\mathrm{T\_i}] \cdot \mathrm{vol}\,(\mathrm{plasma}) \tag{9}$$

7.5 Reaction T_lysis_infect

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

Name release of infectious virions on lysis

Reaction equation

$$\emptyset \xrightarrow{\mathrm{T\_i}} \mathrm{V\_I} \tag{10}$$

Modifier

Table 12: Properties of each modifier.

Id	Name	SBO
T_i	T*	

Product

Table 13: Properties of each product.

Id	Name	SBO
V_I	V_I	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = (1 - \mathrm{np}) \cdot \mathrm{N} \cdot \mathrm{delta} \cdot [\mathrm{T\_i}] \cdot \mathrm{vol}(\mathrm{plasma}) \tag{11}$$

7.6 Reaction `T_lysis_noninf`

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

Name release of non infectious virions on lysis

Reaction equation

$$\emptyset \xrightarrow{\mathrm{T\_i}} \mathrm{V\_NI} \tag{12}$$

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
`T_i`	T*	

Product

Table 15: Properties of each product.

Id	Name	SBO
`V_NI`	V_NI	

Kinetic Law

Derived unit $(86400\ \mathrm{s})^{-1} \cdot \mathrm{item}$

$$v_6 = \mathrm{np} \cdot \mathrm{N} \cdot \mathrm{delta} \cdot [\mathrm{T\_i}] \cdot \mathrm{vol}(\mathrm{plasma}) \tag{13}$$

7.7 Reaction `V_I_clearance`

This is a reversible reaction of one reactant forming no product.

Name clearance of infectious virions

Reaction equation

$$\mathrm{V\_I} \rightleftharpoons \emptyset \tag{14}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
V_I	V_I	

Kinetic Law

Derived unit $(86400\ \mathrm{s})^{-1} \cdot \mathrm{item}$

$$v_7 = \mathrm{c} \cdot [\mathrm{V\_I}] \cdot \mathrm{vol}\left(\mathrm{plasma}\right) \tag{15}$$

7.8 Reaction V_NI_clearance

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

Name non-infect. virion clearance

Reaction equation

$$\mathrm{V\_NI} \longrightarrow \emptyset \tag{16}$$

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
V_NI	V_NI	

Kinetic Law

Derived unit $(86400\ \mathrm{s})^{-1} \cdot \mathrm{item}$

$$v_8 = \mathrm{c} \cdot [\mathrm{V\_NI}] \cdot \mathrm{vol}\left(\mathrm{plasma}\right) \tag{17}$$

8 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.

8.1 Species T

Name T

Notes uninfected T-cells

Initial concentration $180000\ \mathrm{item} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in T_cell_loss, infection and as a product in T_cell_source).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{T} = v_1 - v_2 - v_3 \tag{18}$$

8.2 Species T_i

Name T*

Notes infected T-cells

Initial concentration $1675\ \mathrm{item} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in T_i_lysis and as a product in infection and as a modifier in T_lysis_infect, T_lysis_noninf).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{T\_i} = v_3 - v_4 \tag{19}$$

8.3 Species V_I

Name V_I

Notes infectious virius (V_I)

Initial concentration $134000\ \mathrm{item} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in V_I_clearance and as a product in T_lysis_infect and as a modifier in infection).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{V\_I} = v_5 - v_7 \tag{20}$$

8.4 Species V_NI

Name V_NI

Notes non-infectious virus (V_{NI})

Initial concentration $0\ \mathrm{item} \cdot \mathrm{ml}^{-1}$

This species takes part in two reactions (as a reactant in V_NI_clearance and as a product in T_lysis_noninf).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{V\_NI} = v_6 - v_8 \tag{21}$$

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