**SBML Model Report**

# Model name: “HIVHPVcoinfection”

December 1, 2016

## 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following eight authors: Andrew Leber[1], Raquel Hontecillas[2], Stanca Ciupe[3], Stefan Hoops[4], Meghna Verma[5], Samantha Erwin[6], Vida Abedi[7] and Josep Bassaganya-Riera[8] at December 16th 2015 at 1:33 p. m. and last time modified at December 16th 2015 at 1:33 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 | 1 |
| species types | 0 | species | 7 |
| events | 0 | constraints | 0 |
| reactions | 18 | function definitions | 11 |
| global parameters | 10 | unit definitions | 3 |
| rules | 0 | initial assignments | 3 |

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### Model Notes

This is a COPASI version of the HIV/HPV coinfection model submitted to PLoS One.

Title: Modeling the mechanisms by which HIV-associated immunosuppression influences HPV p

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## 2 Unit Definitions

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

### 2.1 Unit volume

**Name** volume

**Definition** ml

### 2.2 Unit time

**Name** time

**Definition** 86400 s

### 2.3 Unit substance

**Name** substance

**Definition** item

### 2.4 Unit area

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

**Definition** $m^2$

### 2.5 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 |
|---|---|---|---|---|---|---|---|
| `default` | default | | 3 | 1 | litre | ☑ | |

## 3.1 Compartment `default`

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

**Name** default

## 4 Species

This model contains seven species. 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 |
|---|---|---|---|---|---|
| s2 | V | default | $\mathrm{item} \cdot \mathrm{ml}^{-1}$ | ⊟ | ⊟ |
| s3 | I | default | $\mathrm{item} \cdot \mathrm{ml}^{-1}$ | ⊟ | ⊟ |
| s4 | T | default | $\mathrm{item} \cdot \mathrm{ml}^{-1}$ | ⊟ | ⊟ |
| s14 | W | default | $\mathrm{item} \cdot \mathrm{ml}^{-1}$ | ⊟ | ⊟ |
| s16 | E | default | $\mathrm{item} \cdot \mathrm{ml}^{-1}$ | ⊟ | ⊟ |
| s13 | Y2 | default | $\mathrm{item} \cdot \mathrm{ml}^{-1}$ | ⊟ | ⊟ |
| s12 | Y1 | default | $\mathrm{item} \cdot \mathrm{ml}^{-1}$ | ⊟ | ⊟ |

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# 5 Parameters

This model contains ten global parameters.

Table 4: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| e_rt | e_rt | | 0.000 | | ☑ |
| e_pi | e_pi | | 0.000 | | ☑ |
| epi | epi | | 0.500 | | ☑ |
| omega | omega | | 0.001 | | ☑ |
| mu | mu | | 0.048 | | ☑ |
| beta | beta | | $1.53907922912206 \cdot 10^{-7}$ | | ☑ |
| c1 | c1 | | 23.000 | | ☑ |
| N1 | N1 | | 467.000 | | ☑ |
| s | s | | 5564.026 | | ☑ |
| d | d | | 0.010 | | ☑ |

# 6 Initialassignments

This is an overview of three initialassignments.

## 6.1 Initialassignment s3

**Derived unit** contains undeclared units

**Math** $\text{beta} \cdot [\text{s4}] \cdot [\text{s2}]$

## 6.2 Initialassignment beta

**Derived unit** contains undeclared units

**Math** $\frac{\text{c1}}{\text{N1} \cdot [\text{s4}]}$

## 6.3 Initialassignment s

**Derived unit** contains undeclared units

**Math** $\text{d} \cdot [\text{s4}] + \text{beta} \cdot [\text{s4}] \cdot [\text{s2}]$

# 7 Function definitions

This is an overview of eleven function definitions.

## 7.1 Function definition Constant_flux__irreversible

**Name** Constant flux (irreversible)

**Argument** v

**Mathematical Expression**

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

## 7.2 Function definition Death_of_HPV_self_proliferating_cells_due_to_effector_cells

**Name** Death of HPV self-proliferating cells due to effector cells

**Arguments** a, [s13], [s16]

**Mathematical Expression**

$$\mathrm{a} \cdot [\mathrm{s16}] \cdot [\mathrm{s13}] \tag{2}$$

## 7.3 Function definition Rate_Law_for_Production_of_HPV_due_to_HPVinfected_1

**Name** Rate Law for Production of HPV due to HPVinfected_1

**Arguments** k1, mu, [s12]

**Mathematical Expression**

$$\mathrm{mu} \cdot \mathrm{k1} \cdot [\mathrm{s12}] \tag{3}$$

## 7.4 Function definition Logistic_term_for_Effector_cells_1

**Name** Logistic term for Effector cells_1

**Arguments** b, omega, [s13], [s16], [s4]

**Mathematical Expression**

$$\frac{\mathrm{omega} \cdot [\mathrm{s13}] \cdot [\mathrm{s16}] \cdot [\mathrm{s16}]}{\mathrm{b} \cdot [\mathrm{s4}]} \tag{4}$$

## 7.5 Function definition Productionof_HPV_infected_cells

**Name** Productionof HPV infected cells

**Arguments** N2, p, phi, psi, [s12], [s14], [s2]

**Mathematical Expression**

$$\mathrm{psi} \cdot [\mathrm{s14}] \cdot \frac{(1 + \mathrm{p} \cdot [\mathrm{s2}]) \cdot \mathrm{N2} - [\mathrm{s12}]}{\mathrm{phi} + (1 + \mathrm{p} \cdot [\mathrm{s2}]) \cdot \mathrm{N2} - [\mathrm{s12}]} \tag{5}$$

### 7.6 Function definition Rate_Law_for_production_of_HIV_infected_cells_1

**Name** Rate Law for production of HIV infected cells_1

**Arguments** beta, e_rt, [s2], [s4]

**Mathematical Expression**

$$(1 - \text{e\_rt}) \cdot \text{beta} \cdot [\text{s4}] \cdot [\text{s2}] \tag{6}$$

### 7.7 Function definition Production_of_HPV_due_to_HPV_self_proliferating_1

**Name** Production of HPV due to HPV self-proliferating_1

**Arguments** k2, mu, [s13]

**Mathematical Expression**

$$\text{mu} \cdot \text{k2} \cdot [\text{s13}] \tag{7}$$

### 7.8 Function definition Rate_Law_for_Production_of_HIV_virion_1

**Name** Rate Law for Production of HIV virion_1

**Arguments** N1, delta, e_pi, [s3]

**Mathematical Expression**

$$(1 - \text{e\_pi}) \cdot \text{N1} \cdot \text{delta} \cdot [\text{s3}] \tag{8}$$

### 7.9 Function definition Rate_Law_for_Production_of_Effector_cell_1_1

**Name** Rate Law for Production of Effector cell_1_1

**Arguments** omega, [s13], [s16]

**Mathematical Expression**

$$\text{omega} \cdot [\text{s13}] \cdot [\text{s16}] \tag{9}$$

### 7.10 Function definition Proliferation_of_HPV_self_proliferating

**Name** Proliferation of HPV self-proliferating

**Arguments** epi, r, [s13]

**Mathematical Expression**

$$\text{r} \cdot \text{epi} \cdot [\text{s13}] \tag{10}$$

## 7.11 Function definition

Death_of_HPV_self_proliferating_due_to_Effector_cells

**Name** Death of HPV self-proliferating due to Effector cells

**Arguments** a, [s12], [s16]

**Mathematical Expression**

$$a \cdot [s12] \cdot [s16] \tag{11}$$

## 8 Reactions

This model contains 18 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 | re1 | Production of HIV virion | $\emptyset \xrightarrow{s3} s2$ | |
| 2 | re3 | Death of HIV | $s2 \longrightarrow \emptyset$ | |
| 3 | re4 | Production of HIV infected cells | $s4 \xrightarrow{s2} s3$ | |
| 4 | re5 | Production of T cells | $\emptyset \longrightarrow s4$ | |
| 5 | re7 | Decay of T cells | $s4 \longrightarrow \emptyset$ | |
| 6 | re8 | Decay of HIV-infected | $s3 \longrightarrow \emptyset$ | |
| 7 | re9 | Production of HPV-self-proliferating cells by HPV infected | $s12 \longrightarrow s13$ | |
| 8 | re11 | Production of HPV due to HPVinfected | $\emptyset \xrightarrow{s12} s14$ | |
| 9 | re12 | Death of HPV infected due to Effector cells | $s12 \xrightarrow{s16} \emptyset$ | |
| 10 | re14 | Decay of HPV self-proliferating | $s13 \longrightarrow \emptyset$ | |
| 11 | re15 | Logistic term for Effector cells | $s16 \xrightarrow{s13,\ s4} \emptyset$ | |
| 12 | re17 | Death of HPV self-proliferating cells due to effector cells | $s13 \xrightarrow{s16} \emptyset$ | |
| 13 | re18 | Decay of HPV-infected cells | $s12 \longrightarrow \emptyset$ | |
| 14 | re20 | Decay of HPV | $s14 \longrightarrow \emptyset$ | |
| 15 | re24 | Proliferation of HPV self-proliferating cells | $s13 \xrightarrow{s13} 2\,s13$ | |
| 16 | re25 | Productionof HPV infected cells | $s12 \xrightarrow{s14,\ s2} 2\,s12$ | |
| 17 | re26 | Production of Effector cell | $s16 \xrightarrow{s13} 2\,s16$ | |

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| № | Id | Name | Reaction Equation | SBO |
|---|---|---|---|---|
| 18 | Production_of_HPV_due_to_HPV_self_proliferating | Production of HPV due to HPV self proliferating | $\emptyset \xrightarrow{s13} s14$ | |

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## 8.1 Reaction re1

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

**Name** Production of HIV virion

**Notes** N1 - Ciupe MS, Bivort BL, Bortz DM, Nelson PW. Estimating kinetic parameters from

delta - Klatt NR, Shudo E, Ortiz AM, Engram JC, Paiardini M, Lawson B, et al. CD8+ l

### Reaction equation

$$\emptyset \xrightarrow{\text{s3}} \text{s2} \tag{12}$$

### Modifier

Table 6: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| s3 | I | |

### Product

Table 7: Properties of each product.

| Id | Name | SBO |
|---|---|---|
| s2 | V | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_1 = \text{vol}\,(\text{default}) \cdot \text{Rate\_Law\_for\_Production\_of\_HIV\_virion\_1}\,(\text{N1}, \text{delta}, \text{e\_pi}, [\text{s3}]) \tag{13}$$

$$\text{Rate\_Law\_for\_Production\_of\_HIV\_virion\_1}\,(\text{N1}, \text{delta}, \text{e\_pi}, [\text{s3}]) = (1 - \text{e\_pi}) \cdot \text{N1} \cdot \text{delta} \cdot [\text{s3}] \tag{14}$$

$$\text{Rate\_Law\_for\_Production\_of\_HIV\_virion\_1}\,(\text{N1}, \text{delta}, \text{e\_pi}, [\text{s3}]) = (1 - \text{e\_pi}) \cdot \text{N1} \cdot \text{delta} \cdot [\text{s3}] \tag{15}$$

Table 8: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| delta | delta | | 1.0 | | ☑ |

## 8.2 Reaction re3

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

**Name** Death of HIV

**Notes** Ramratnam B, Bonhoeffer S, Binley J, Hurley A, Zhang L, Mittler JE, et al. Rapid p

### Reaction equation

$$\mathrm{s2} \longrightarrow \emptyset \tag{16}$$

### Reactant

Table 9: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s2 | V | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{c1} \cdot [\mathrm{s2}] \tag{17}$$

## 8.3 Reaction re4

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

**Name** Production of HIV infected cells

### Reaction equation

$$\mathrm{s4} \xrightarrow{\mathrm{s2}} \mathrm{s3} \tag{18}$$

### Reactant

Table 10: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s4 | T | |

### Modifier

Table 11: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| s2 | V | |

### Product

Table 12: Properties of each product.

| Id | Name | SBO |
|---|---|---|
| s3 | I | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_3 = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{Rate\_Law\_for\_production\_of\_HIV\_infected\_cells\_1}\,(\mathrm{beta}, \mathrm{e\_rt}, [\mathrm{s2}], [\mathrm{s4}]) \quad (19)$$

$$\begin{aligned} &\mathrm{Rate\_Law\_for\_production\_of\_HIV\_infected\_cells\_1}\,(\mathrm{beta}, \mathrm{e\_rt}, [\mathrm{s2}], [\mathrm{s4}]) \\ &\quad = (1 - \mathrm{e\_rt}) \cdot \mathrm{beta} \cdot [\mathrm{s4}] \cdot [\mathrm{s2}] \end{aligned} \quad (20)$$

$$\begin{aligned} &\mathrm{Rate\_Law\_for\_production\_of\_HIV\_infected\_cells\_1}\,(\mathrm{beta}, \mathrm{e\_rt}, [\mathrm{s2}], [\mathrm{s4}]) \\ &\quad = (1 - \mathrm{e\_rt}) \cdot \mathrm{beta} \cdot [\mathrm{s4}] \cdot [\mathrm{s2}] \end{aligned} \quad (21)$$

## 8.4 Reaction re5

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

**Name** Production of T cells

### Reaction equation

$$\emptyset \longrightarrow \mathrm{s4} \quad (22)$$

### Product

Table 13: Properties of each product.

| Id | Name | SBO |
|---|---|---|
| s4 | T | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_4 = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{Constant\_flux\_\_irreversible}\,(\mathrm{s}) \tag{23}$$

$$\mathrm{Constant\_flux\_\_irreversible}\,(\mathrm{v}) = \mathrm{v} \tag{24}$$

$$\mathrm{Constant\_flux\_\_irreversible}\,(\mathrm{v}) = \mathrm{v} \tag{25}$$

## 8.5 Reaction re7

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

**Name** Decay of T cells

**Notes** Mohri H, Perelson AS, Tung K, Ribeiro RM, Ramratnam B, Markowitz M, et al. Increase

### Reaction equation

$$\mathrm{s4} \longrightarrow \emptyset \tag{26}$$

### Reactant

Table 14: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s4 | T | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_5 = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{d} \cdot [\mathrm{s4}] \tag{27}$$

## 8.6 Reaction re8

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

**Name** Decay of HIV-infected

**Notes** `Klatt NR, Shudo E, Ortiz AM, Engram JC, Paiardini M, Lawson B, et al. CD8+ lymphocy`

### Reaction equation

$$\mathrm{s3} \longrightarrow \emptyset \tag{28}$$

### Reactant

Table 15: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s3 | I | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{k1} \cdot [\mathrm{s3}] \tag{29}$$

Table 16: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| k1 | k1 | | 1.0 | | ☑ |

## 8.7 Reaction re9

This is an irreversible reaction of one reactant forming one product.

**Name** Production of HPV-self-proliferating cells by HPV infected

**Notes** `Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence`

### Reaction equation

$$\mathrm{s12} \longrightarrow \mathrm{s13} \tag{30}$$

### Reactant

Table 17: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s12 | Y1 | |

### Product

Table 18: Properties of each product.

| Id | Name | SBO |
|---|---|---|
| s13 | Y2 | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_7 = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{epi} \cdot [\mathrm{s12}] \tag{31}$$

## 8.8 Reaction re11

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

**Name** Production of HPV due to HPVinfected

**Notes** Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence

### Reaction equation

$$\emptyset \xrightarrow{\mathrm{s12}} \mathrm{s14} \tag{32}$$

### Modifier

Table 19: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| s12 | Y1 | |

### Product

Table 20: Properties of each product.

| Id | Name | SBO |
|---|---|---|
| s14 | W | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_8 = \text{vol}\,(\text{default}) \cdot \text{Rate\_Law\_for\_Production\_of\_HPV\_due\_to\_HPVinfected\_1}\,(\text{k1}, \text{mu}, [\text{s12}]) \tag{33}$$

$$\text{Rate\_Law\_for\_Production\_of\_HPV\_due\_to\_HPVinfected\_1}\,(\text{k1}, \text{mu}, [\text{s12}]) = \text{mu} \cdot \text{k1} \cdot [\text{s12}] \tag{34}$$

$$\text{Rate\_Law\_for\_Production\_of\_HPV\_due\_to\_HPVinfected\_1}\,(\text{k1}, \text{mu}, [\text{s12}]) = \text{mu} \cdot \text{k1} \cdot [\text{s12}] \tag{35}$$

Table 21: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| k1 | k1 | | 1000.0 | | ☑ |

## 8.9 Reaction re12

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

**Name** Death of HPV infected due to Effector cells

**Notes** Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence

### Reaction equation

$$\text{s12} \xrightarrow{\text{s16}} \emptyset \tag{36}$$

### Reactant

Table 22: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s12 | Y1 | |

### Modifier

Table 23: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| s16 | E | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_9 = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{Death\_of\_HPV\_self\_proliferating\_due\_to\_Effector\_cells}\,(\mathrm{a}, [\mathrm{s12}], [\mathrm{s16}]) \quad (37)$$

$$\mathrm{Death\_of\_HPV\_self\_proliferating\_due\_to\_Effector\_cells}\,(\mathrm{a}, [\mathrm{s12}], [\mathrm{s16}]) = \mathrm{a} \cdot [\mathrm{s12}] \cdot [\mathrm{s16}] \quad (38)$$

$$\mathrm{Death\_of\_HPV\_self\_proliferating\_due\_to\_Effector\_cells}\,(\mathrm{a}, [\mathrm{s12}], [\mathrm{s16}]) = \mathrm{a} \cdot [\mathrm{s12}] \cdot [\mathrm{s16}] \quad (39)$$

Table 24: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| a | a | | 0.01 | | ☑ |

## 8.10 Reaction re14

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

**Name** Decay of HPV self-proliferating

**Notes** Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence

### Reaction equation

$$\mathrm{s13} \longrightarrow \emptyset \quad (40)$$

### Reactant

Table 25: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s13 | Y2 | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{10} = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{k1} \cdot [\mathrm{s13}] \tag{41}$$

Table 26: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| k1 | k1 | | 0.048 | | ☑ |

## 8.11 Reaction re15

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

**Name** Logistic term for Effector cells

### Reaction equation

$$\mathrm{s16} \xrightarrow{\mathrm{s13,\ s4}} \emptyset \tag{42}$$

### Reactant

Table 27: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s16 | E | |

### Modifiers

Table 28: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| s13 | Y2 | |
| s4 | T | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{11} = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{Logistic\_term\_for\_Effector\_cells\_1}\,(\mathrm{b}, \mathrm{omega}, [\mathrm{s13}], [\mathrm{s16}], [\mathrm{s4}]) \tag{43}$$

$$\text{Logistic\_term\_for\_Effector\_cells\_1}\left(\text{b}, \text{omega}, [\text{s13}], [\text{s16}], [\text{s4}]\right) = \frac{\text{omega} \cdot [\text{s13}] \cdot [\text{s16}] \cdot [\text{s16}]}{\text{b} \cdot [\text{s4}]} \tag{44}$$

$$\text{Logistic\_term\_for\_Effector\_cells\_1}\left(\text{b}, \text{omega}, [\text{s13}], [\text{s16}], [\text{s4}]\right) = \frac{\text{omega} \cdot [\text{s13}] \cdot [\text{s16}] \cdot [\text{s16}]}{\text{b} \cdot [\text{s4}]} \tag{45}$$

Table 29: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| b | b | | $3.5 \cdot 10^{-5}$ | | ☑ |

## 8.12 Reaction re17

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

**Name** Death of HPV self-proliferating cells due to effector cells

**Notes** Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence

### Reaction equation

$$\text{s13} \xrightarrow{\text{s16}} \emptyset \tag{46}$$

### Reactant

Table 30: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s13 | Y2 | |

### Modifier

Table 31: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| s16 | E | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{12} = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{Death\_of\_HPV\_self\_proliferating\_cells\_due\_to\_effector\_cells}\,(\mathrm{a}, [\mathrm{s13}], [\mathrm{s16}]) \tag{47}$$

$$\mathrm{Death\_of\_HPV\_self\_proliferating\_cells\_due\_to\_effector\_cells}\,(\mathrm{a}, [\mathrm{s13}], [\mathrm{s16}]) = \mathrm{a} \cdot [\mathrm{s16}] \cdot [\mathrm{s13}] \tag{48}$$

$$\mathrm{Death\_of\_HPV\_self\_proliferating\_cells\_due\_to\_effector\_cells}\,(\mathrm{a}, [\mathrm{s13}], [\mathrm{s16}]) = \mathrm{a} \cdot [\mathrm{s16}] \cdot [\mathrm{s13}] \tag{49}$$

Table 32: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| a | a | | 0.01 | | ☑ |

## 8.13 Reaction re18

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

**Name** Decay of HPV-infected cells

**Notes** Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence

### Reaction equation

$$\mathrm{s12} \longrightarrow \emptyset \tag{50}$$

### Reactant

Table 33: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s12 | Y1 | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{13} = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{mu} \cdot [\mathrm{s12}] \tag{51}$$

## 8.14 Reaction re20

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

**Name** Decay of HPV

**Notes** Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence

### Reaction equation

$$\mathrm{s14} \longrightarrow \emptyset \tag{52}$$

### Reactant

Table 34: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s14 | W | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{14} = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{k1} \cdot [\mathrm{s14}] \tag{53}$$

Table 35: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| k1 | k1 | | 0.05 | | ☑ |

## 8.15 Reaction re24

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

**Name** Proliferation of HPV self-proliferating cells

**Notes** Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence

### Reaction equation

$$\mathrm{s13} \xrightarrow{\mathrm{s13}} 2\,\mathrm{s13} \tag{54}$$

### Reactant

Table 36: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s13 | Y2 | |

### Modifier

Table 37: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| s13 | Y2 | |

### Product

Table 38: Properties of each product.

| Id | Name | SBO |
|---|---|---|
| s13 | Y2 | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{15} = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{Proliferation\_of\_HPV\_self\_proliferating}\,(\mathrm{epi}, \mathrm{r}, [\mathrm{s13}]) \tag{55}$$

$$\mathrm{Proliferation\_of\_HPV\_self\_proliferating}\,(\mathrm{epi}, \mathrm{r}, [\mathrm{s13}]) = \mathrm{r} \cdot \mathrm{epi} \cdot [\mathrm{s13}] \tag{56}$$

$$\mathrm{Proliferation\_of\_HPV\_self\_proliferating}\,(\mathrm{epi}, \mathrm{r}, [\mathrm{s13}]) = \mathrm{r} \cdot \mathrm{epi} \cdot [\mathrm{s13}] \tag{57}$$

Table 39: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| r | r | | 0.1 | | ☑ |

## 8.16 Reaction re25

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

**Name** Productionof HPV infected cells

**Notes** Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence

### Reaction equation

$$\mathrm{s12} \xrightarrow{\mathrm{s14,\ s2}} 2\,\mathrm{s12} \tag{58}$$

### Reactant

Table 40: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s12 | Y1 | |

### Modifiers

Table 41: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| s14 | W | |
| s2 | V | |

### Product

Table 42: Properties of each product.

| Id | Name | SBO |
|---|---|---|
| s12 | Y1 | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{16} = \mathrm{vol}\,(\mathrm{default}) \cdot \mathrm{Productionof\_HPV\_infected\_cells}\,(\mathrm{N2}, \mathrm{p}, \mathrm{phi}, \mathrm{psi}, [\mathrm{s12}], [\mathrm{s14}], [\mathrm{s2}]) \tag{59}$$

$$\begin{aligned}&\mathrm{Productionof\_HPV\_infected\_cells}\,(\mathrm{N2}, \mathrm{p}, \mathrm{phi}, \mathrm{psi}, [\mathrm{s12}], [\mathrm{s14}], [\mathrm{s2}])\\ &= \mathrm{psi} \cdot [\mathrm{s14}] \cdot \frac{(1 + \mathrm{p} \cdot [\mathrm{s2}]) \cdot \mathrm{N2} - [\mathrm{s12}]}{\mathrm{phi} + (1 + \mathrm{p} \cdot [\mathrm{s2}]) \cdot \mathrm{N2} - [\mathrm{s12}]}\end{aligned} \tag{60}$$

$$\begin{aligned}&\mathrm{Productionof\_HPV\_infected\_cells}\,(\mathrm{N2}, \mathrm{p}, \mathrm{phi}, \mathrm{psi}, [\mathrm{s12}], [\mathrm{s14}], [\mathrm{s2}])\\ &= \mathrm{psi} \cdot [\mathrm{s14}] \cdot \frac{(1 + \mathrm{p} \cdot [\mathrm{s2}]) \cdot \mathrm{N2} - [\mathrm{s12}]}{\mathrm{phi} + (1 + \mathrm{p} \cdot [\mathrm{s2}]) \cdot \mathrm{N2} - [\mathrm{s12}]}\end{aligned} \tag{61}$$

Table 43: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| N2 | N2 | | 10000.000 | | ☑ |
| p | p | | $2.0833 \cdot 10^{-5}$ | | ☑ |
| phi | phi | | 1000000.000 | | ☑ |
| psi | psi | | 0.007 | | ☑ |

## 8.17 Reaction re26

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

**Name** Production of Effector cell

**Notes** Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence

### Reaction equation

$$\mathrm{s16} \xrightarrow{\mathrm{s13}} 2\,\mathrm{s16} \tag{62}$$

### Reactant

Table 44: Properties of each reactant.

| Id | Name | SBO |
|---|---|---|
| s16 | E | |

### Modifier

Table 45: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| s13 | Y2 | |

### Product

Table 46: Properties of each product.

| Id | Name | SBO |
|---|---|---|
| s16 | E | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{17} = \text{vol}\,(\text{default}) \cdot \text{Rate\_Law\_for\_Production\_of\_Effector\_cell\_1\_1}\,(\text{omega}, [\text{s13}], [\text{s16}]) \quad (63)$$

$$\text{Rate\_Law\_for\_Production\_of\_Effector\_cell\_1\_1}\,(\text{omega}, [\text{s13}], [\text{s16}]) = \text{omega} \cdot [\text{s13}] \cdot [\text{s16}] \quad (64)$$

$$\text{Rate\_Law\_for\_Production\_of\_Effector\_cell\_1\_1}\,(\text{omega}, [\text{s13}], [\text{s16}]) = \text{omega} \cdot [\text{s13}] \cdot [\text{s16}] \quad (65)$$

## 8.18 Reaction `Production_of_HPV_due_to_HPV_self_proliferating`

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

**Name** Production of HPV due to HPV self proliferating

**Notes** `Murall CL, Bauch CT, Day T. Could the human papillomavirus vaccines drive virulence`

### Reaction equation

$$\emptyset \xrightarrow{\text{s13}} \text{s14} \quad (66)$$

### Modifier

Table 47: Properties of each modifier.

| Id | Name | SBO |
|---|---|---|
| `s13` | Y2 | |

### Product

Table 48: Properties of each product.

| Id | Name | SBO |
|---|---|---|
| `s14` | W | |

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{18} = \text{vol}\,(\text{default}) \cdot \text{Production\_of\_HPV\_due\_to\_HPV\_self\_proliferating\_1}\,(\text{k2}, \text{mu}, [\text{s13}]) \quad (67)$$

$$\text{Production\_of\_HPV\_due\_to\_HPV\_self\_proliferating\_1}\,(\text{k2}, \text{mu}, [\text{s13}]) = \text{mu} \cdot \text{k2} \cdot [\text{s13}] \quad (68)$$

$$\text{Production\_of\_HPV\_due\_to\_HPV\_self\_proliferating\_1}\,(\text{k2}, \text{mu}, [\text{s13}]) = \text{mu} \cdot \text{k2} \cdot [\text{s13}] \quad (69)$$

Table 49: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| k2 | k2 | | 1000.0 | | ☑ |

# 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 s2

**Name** V

**Notes** HIV

**Initial concentration** 48000 item $\cdot$ ml$^{-1}$

This species takes part in four reactions (as a reactant in re3 and as a product in re1 and as a modifier in re4, re25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{s2} = v_1 - v_2 \quad (70)$$

## 9.2 Species s3

**Name** I

**Notes** HIV infected cells

**Initial concentration** 2364.02569593148 item $\cdot$ ml$^{-1}$

**Initial assignment** s3

This species takes part in three reactions (as a reactant in re8 and as a product in re4 and as a modifier in re1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{s3} = v_3 - v_6 \quad (71)$$

## 9.3 Species s4

**Name** T

**Notes** CD4+ T cells

**Initial concentration** $320000\ \text{item} \cdot \text{ml}^{-1}$

This species takes part in four reactions (as a reactant in re4, re7 and as a product in re5 and as a modifier in re15).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s4} = v_4 - v_3 - v_5 \tag{72}$$

## 9.4 Species s14

**Name** W

**Notes** HPV

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

This species takes part in four reactions (as a reactant in re20 and as a product in re11, Production_of_HPV_due_to_HPV_self_proliferating and as a modifier in re25).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s14} = v_8 + v_{18} - v_{14} \tag{73}$$

## 9.5 Species s16

**Name** E

**Notes** HPV specific CTL

**Initial concentration** $0.01\ \text{item} \cdot \text{ml}^{-1}$

This species takes part in five reactions (as a reactant in re15, re26 and as a product in re26 and as a modifier in re12, re17).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s16} = 2\,v_{17} - v_{11} - v_{17} \tag{74}$$

## 9.6 Species s13

**Name** Y2

**Notes** HPV self-proliferating cells

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

This species takes part in nine reactions (as a reactant in re14, re17, re24 and as a product in re9, re24 and as a modifier in re15, re24, re26, Production_of_HPV_due_to_HPV_self-_proliferating).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s13} = v_7 + 2\,v_{15} - v_{10} - v_{12} - v_{15} \tag{75}$$

## 9.7 Species s12

**Name** Y1

**Notes** HPV infected cells

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

This species takes part in six reactions (as a reactant in re9, re12, re18, re25 and as a product in re25 and as a modifier in re11).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s12} = 2\,v_{16} - v_7 - v_9 - v_{13} - v_{16} \tag{76}$$

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

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