SBML Model Report

Model name: "Miao2010 - Innate and adaptive immune responses to primary Influenza A Virus infection"

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[1] and Alain Leblanc[2] at September fourth 2014 at 4:07 p. m. and last time modified at October tenth 2014 at eleven o' clock in the morning. 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	1
species types	3	species	7
events	0	constraints	0
reactions	5	function definitions	0
global parameters	5	unit definitions	5
rules	0	initial assignments	3

Model Notes

Miao2010 - Innate and adaptive immuneresponses to primary Influenza A Virus infection

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This model is described in the article:Quantifying the early immune response and adaptive immune response kinetics in mice infected with influenza A virus.Miao H, Hollenbaugh JA, Zand MS, Holden-Wiltse J, Mosmann TR, Perelson AS, Wu H, Topham DJ.J. Virol. 2010 Jul; 84(13): 6687-6698

Abstract:

Seasonal and pandemic influenza A virus (IAV) continues to be a public health threat. However, we lack a detailed and quantitative understanding of the immune response kinetics to IAV infection and which biological parameters most strongly influence infection outcomes. To address these issues, we use modeling approaches combined with experimental data to quantitatively investigate the innate and adaptive immune responses to primary IAV infection. Mathematical models were developed to describe the dynamic interactions between target (epithelial) cells, influenza virus, cytotoxic T lymphocytes (CTLs), and virus-specific IgG and IgM. IAV and immune kinetic parameters were estimated by fitting models to a large data set obtained from primary H3N2 IAV infection of 340 mice. Prior to a detectable virus-specific immune response (before day 5), the estimated half-life of infected epithelial cells is approximately 1.2 days, and the half-life of free infectious IAV is approximately 4 h. During the adaptive immune response (after day 5), the average half-life of infected epithelial cells is approximately 0.5 days, and the average half-life of free infectious virus is approximately 1.8 min. During the adaptive phase, model fitting confirms that CD8(+) CTLs are crucial for limiting infected cells, while virus-specific IgM regulates free IAV levels. This may imply that CD4 T cells and class-switched IgG antibodies are more relevant for generating IAV-specific memory and preventing future infection via a more rapid secondary immune response. Also, simulation studies were performed to understand the relative contributions of biological parameters to IAV clearance. This study provides a basis to better understand and predict influenza virus immunity.

This model is hosted on BioModels Database and identified by: BIOMD0000000546.

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.

2.1 Unit `substance`

Name substance

Definition mol

2.2 Unit `volume`

Name volume

Definition l

2.3 Unit `area`

Name area

Definition m^2

2.4 Unit `length`

Name length

Definition m

2.5 Unit `time`

Name 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
`default`			3	1	litre	☑	

3.1 Compartment `default`

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

4 Species types

This is an overview of three species types.

4.1 Species type `Virus`

Name Virus

This model does not contain any species of this type.

4.2 Species type `Infected_Cell`

Name Infected Cell

This model does not contain any species of this type.

4.3 Species type `Uninfected_Cell`

Name Uninfected Cell

This model does not contain any species of this type.

5 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
s1	Ep	default	mol	⊟	⊟
s2	Eps	default	mol	⊟	⊟
s3	V	default	mol	⊟	⊟
s4	s4	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s5	s5	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s6	s6	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
s7	s7	default	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

6 Parameters

This model contains five global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
rho_E	rho_E		$6.2 \cdot 10^{-8}$	mol	☑
beta_a	beta_a		$2.4 \cdot 10^{-6}$	mol	☑
delta_Es	delta_Es		0.600	mol	☑
pi_a	pi_a		100.000	mol	☑
c_V	c_V		4.200	mol	☑

7 Initialassignments

This is an overview of three initialassignments.

7.1 Initialassignment s1

Derived unit contains undeclared units

Math 580000.0

7.2 Initialassignment s2

Derived unit contains undeclared units

Math 0

7.3 Initialassignment s3

Derived unit contains undeclared units

Math 1473.0

8 Reactions

This model contains five 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		$s1 \xrightarrow{s3,\ s1,\ s3,\ s1,\ s3} s2$	
2	re3		$s4 \xrightarrow{s1,\ s1} s1$	
3	re5		$s2 \xrightarrow{s2,\ s2} s5$	
4	re6		$s3 \xrightarrow{s3,\ s3} s6$	
5	re7		$s7 \xrightarrow{s2,\ s2,\ s2} s3$	

8.1 Reaction re1

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

Reaction equation

$$\mathrm{s1} \xrightarrow{\mathrm{s3,\ s1,\ s3,\ s1,\ s3}} \mathrm{s2} \tag{1}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
s1	Ep	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
s3	V	
s1	Ep	
s3	V	
s1	Ep	
s3	V	

Product

Table 8: Properties of each product.

Id	Name	SBO
s2	Eps	

Kinetic Law

Derived unit mol^3

$$v_1 = \mathrm{beta\_a} \cdot \mathrm{s1} \cdot \mathrm{s3} \tag{2}$$

8.2 Reaction re3

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

Reaction equation

$$\mathrm{s4} \xrightarrow{\mathrm{s1},\ \mathrm{s1}} \mathrm{s1} \tag{3}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
s4	s4	

Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
s1	Ep	
s1	Ep	

Product

Table 11: Properties of each product.

Id	Name	SBO
s1	Ep	

Kinetic Law

Derived unit mol^2

$$v_2 = \mathrm{rho\_E} \cdot \mathrm{s1} \tag{4}$$

8.3 Reaction re5

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

Reaction equation

$$\mathrm{s2} \xrightarrow{\mathrm{s2},\ \mathrm{s2}} \mathrm{s5} \tag{5}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
s2	Eps	

Modifiers

Table 13: Properties of each modifier.

Id	Name	SBO
s2	Eps	
s2	Eps	

Product

Table 14: Properties of each product.

Id	Name	SBO
s5	s5	

Kinetic Law

Derived unit mol^2

$$v_3 = \text{delta\_Es} \cdot \text{s2} \tag{6}$$

8.4 Reaction re6

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

Reaction equation

$$\text{s3} \xrightarrow{\text{s3, s3}} \text{s6} \tag{7}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
s3	V	

Modifiers

Table 16: Properties of each modifier.

Id	Name	SBO
s3	V	
s3	V	

Product

Table 17: Properties of each product.

Id	Name	SBO
s6	s6	

Kinetic Law

Derived unit mol^2

$$v_4 = \mathrm{c\_V} \cdot \mathrm{s3} \tag{8}$$

8.5 Reaction re7

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

Reaction equation

$$\mathrm{s7} \xrightarrow{\mathrm{s2},\ \mathrm{s2},\ \mathrm{s2}} \mathrm{s3} \tag{9}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
s7	s7	

Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
s2	Eps	
s2	Eps	
s2	Eps	

Product

Table 20: Properties of each product.

Id	Name	SBO
s3	V	

Kinetic Law

Derived unit mol^2

$$v_5 = \text{pi\_a} \cdot \text{s2} \tag{10}$$

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 `s1`

Name Ep

Notes Initial no. of uninfected and infectible epithelial cells per lung

Initial amount 580000 mol

Charge 0

Initial assignment `s1`

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s1} = v_2 - v_1 \tag{11}$$

9.2 Species s2

Name Eps

Notes This entity is refered as Ep* in the paper. Infected epithelial cells per lung.

Initial amount 0 mol

Charge 0

Initial assignment s2

This species takes part in seven reactions (as a reactant in re5 and as a product in re1 and as a modifier in re5, re5, re7, re7, re7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s2} = v_1 - v_3 \tag{12}$$

9.3 Species s3

Name V

Notes Infective viral titer (EID50/ml)

Initial amount 1473 mol

Charge 0

Initial assignment s3

This species takes part in seven reactions (as a reactant in re6 and as a product in re7 and as a modifier in re1, re1, re1, re6, re6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s3} = v_5 - v_4 \tag{13}$$

9.4 Species s4

Name s4

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in one reaction (as a reactant in re3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s4} = -v_2 \tag{14}$$

9.5 Species s5

Name s5

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in one reaction (as a product in re5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s5} = v_3 \tag{15}$$

9.6 Species s6

Name s6

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in one reaction (as a product in re6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s6} = v_4 \tag{16}$$

9.7 Species s7

Name s7

SBO:0000291 empty set

Initial amount 0 mol

This species takes part in one reaction (as a reactant in re7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{s7} = -v_5 \tag{17}$$

A Glossary of Systems Biology Ontology Terms

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[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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