SBML Model Report

Model name: “Kaiser2014 - Salmonella persistence after ciprofloxacin treatment”

May 6, 2016

1 General Overview

This is a document in SBML Level 3 Version 1 format. This model was created by the following two authors: Vijayalakshmi Chelliah[1] and Roland Regoes[2] at March 25th 2014 at 4:03 p. m. and last time modified at October tenth 2014 at 10:48 a. 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	1
events	0	constraints	0
reactions	0	function definitions	0
global parameters	16	unit definitions	2
rules	1	initial assignments	0

Model Notes

Kaiser2014 - Salmonella persistence after ciprofloxacin treatment

The model describes the bacterial tolerance to antibiotics. Using a mouse model for Salmonella diarrhea, the authors have found that bacterial persistence occurs in the presence of the antibiotic

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ciprofloxacin because Salmonella can exist in two different states. One, the fast-growing population that spreads in the host's tissues and the other, slow-growing „persister„ population that hide out inside dendritic cells of the host's immune system and cannot be attacked by the antibiotics. However, this can be killed by adding agents that directly stimulate the host's immune defense.

This model is described in the article:Cecum lymph node dendritic cells harbor slow-growing bacteria phenotypically tolerant to antibiotic treatment.Kaiser P, Regoes RR, Dolowschiak T, Wotzka SY, Lengefeld J, Slack E, Grant AJ, Ackermann M, Hardt WD.PLoS Biol. 2014 Feb 18;12(2):e1001793.

Abstract:

In vivo, antibiotics are often much less efficient than ex vivo and relapses can occur. The reasons for poor in vivo activity are still not completely understood. We have studied the fluoroquinolone antibiotic ciprofloxacin in an animal model for complicated Salmonellosis. High-dose ciprofloxacin treatment efficiently reduced pathogen loads in feces and most organs. However, the cecum draining lymph node (cLN), the gut tissue, and the spleen retained surviving bacteria. In cLN, approximately 10%-20% of the bacteria remained viable. These phenotypically tolerant bacteria lodged mostly within CD103CXCR1CD11c dendritic cells, remained genetically susceptible to ciprofloxacin, were sufficient to reinitiate infection after the end of the therapy, and displayed an extremely slow growth rate, as shown by mathematical analysis of infections with mixed inocula and segregative plasmid experiments. The slow growth was sufficient to explain recalcitrance to antibiotics treatment. Therefore, slow-growing antibiotic-tolerant bacteria lodged within dendritic cells can explain poor in vivo antibiotic activity and relapse. Administration of LPS or CpG, known elicitors of innate immune defense, reduced the loads of tolerant bacteria. Thus, manipulating innate immunity may augment the in vivo activity of antibiotics.

This model is hosted on BioModels Database and identifiedby: MODEL1312170001.

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

2 Unit Definitions

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

2.1 Unit `day`

Name day

Definition 86400 das

2.2 Unit per_day

Name per_day

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

2.3 Unit substance

Notes Mole is the predefined SBML unit for `substance`.

Definition mol

2.4 Unit volume

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

Definition l

2.5 Unit area

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

Definition m^2

2.6 Unit length

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

Definition m

2.7 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
LN	Lymph node		3	1		☑	

3.1 Compartment LN

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

Name Lymph node

4 Species

This model contains one 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
L	L	LN	dimensionless	⊟	⊟

5 Parameters

This model contains 16 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
mu1	mu1		297.790	$(86400\ \mathrm{das})^{-1}$	☑
r1	r1		2.820	$(86400\ \mathrm{das})^{-1}$	☑
c1	c1		0.000	$(86400\ \mathrm{das})^{-1}$	☑
t1	t1		1.000	86400 das	☑
mu3	mu3		0.000	$(86400\ \mathrm{das})^{-1}$	☑
r3	r3		4.587	$(86400\ \mathrm{das})^{-1}$	☑
c3	c3		5.043	$(86400\ \mathrm{das})^{-1}$	☑
t3	t3		3.000	86400 das	☑
mu5	mu5		0.000	$(86400\ \mathrm{das})^{-1}$	☑
r5	r5		1.881	$(86400\ \mathrm{das})^{-1}$	☑
c5	c5		2.498	$(86400\ \mathrm{das})^{-1}$	☑
t5	t5		5.000	86400 das	☑
mu10	mu10		0.000	$(86400\ \mathrm{das})^{-1}$	☑
r10	r10		0.376	$(86400\ \mathrm{das})^{-1}$	☑
c10	c10		$2.43 \cdot 10^{-7}$	$(86400\ \mathrm{das})^{-1}$	☑
t10	t10		10.000	86400 das	☑

6 Rule

This is an overview of one rule.

6.1 Rule L

Rule L is a rate rule for species L:

$$\frac{\mathrm{d}}{\mathrm{d}t}[\mathrm{L}] = \begin{cases} \mathrm{mu1} + (\mathrm{r1} - \mathrm{c1}) \cdot \mathrm{L} & \text{if } (\mathrm{time} \geq 0) \wedge (\mathrm{time} \leq \mathrm{t1}) \\ \mathrm{mu3} + (\mathrm{r3} - \mathrm{c3}) \cdot \mathrm{L} & \text{if } (\mathrm{time} > \mathrm{t1}) \wedge (\mathrm{time} \leq \mathrm{t3}) \\ \mathrm{mu5} + (\mathrm{r5} - \mathrm{c5}) \cdot \mathrm{L} & \text{if } (\mathrm{time} > \mathrm{t3}) \wedge (\mathrm{time} \leq \mathrm{t5}) \\ \mathrm{mu10} + (\mathrm{r10} - \mathrm{c10}) \cdot \mathrm{L} & \text{if } (\mathrm{time} > \mathrm{t5}) \wedge (\mathrm{time} \leq \mathrm{t10}) \end{cases} \tag{1}$$

Derived unit $(86400\ \mathrm{das})^{-1}$

7 Derived Rate Equation

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rate of change of the following species.

7.1 Species L

Name L

Initial amount 0 dimensionless

Involved in rule L

One rule which determines this species' quantity.

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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