SBML Model Report

Model name: "Tan2012 - Antibiotic Treatment, Inoculum Effect"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 1 format. This model was created by the following two authors: Vijayalakshmi Chelliah[1] and Cheemeng Tan[2] at November first 2012 at 3:23 p. m. and last time modified at October tenth 2014 at 10:47 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	4	function definitions	0
global parameters	0	unit definitions	0
rules	0	initial assignments	0

Model Notes

Tan2012 - Antibiotic Treatment, Inoculum Effect

The efficacy of many antibiotics decreases with increasing bacterial density, a phenomenon called the inoculum effect (IE). This study reveals that, for ribosome-targeting antibiotics, IE

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is due to bistable inhibition of bacterial growth, which reduces the efficacy of certain treatment frequencies.

This model is described in the article:The inoculum effect and band-pass bacterial response to periodic antibiotic treatment.Tan C, Phillip Smith R, Srimani JK, Riccione KA, Prasada S, Kuehn M, You L.Mol Syst Biol. 2012 Oct 9; 8:617

Abstract:

The inoculum effect (IE) refers to the decreasing efficacy of an antibiotic with increasing bacterial density. It represents a unique strategy of antibiotic tolerance and it can complicate design of effective antibiotic treatment of bacterial infections. To gain insight into this phenomenon, we have analyzed responses of a lab strain of Escherichia coli to antibiotics that target the ribosome. We show that the IE can be explained by bistable inhibition of bacterial growth. A critical requirement for this bistability is sufficiently fast degradation of ribosomes, which can result from antibiotic-induced heat-shock response. Furthermore, antibiotics that elicit the IE can lead to 'band-pass' response of bacterial growth to periodic antibiotic treatment: the treatment efficacy drastically diminishes at intermediate frequencies of treatment. Our proposed mechanism for the IE may be generally applicable to other bacterial species treated with antibiotics targeting the ribosomes.

This model is hosted on BioModels Database and identified by: MODEL1208300000 .

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 which are all predefined by SBML and not mentioned in the model.

2.1 Unit `substance`

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

Definition mol

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
`cell`	cell		3	1	litre	☑	

3.1 Compartment `cell`

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

Name cell

4 Species

This model contains one species. Section 6 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
c	ribosome concentration	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Reactions

This model contains four 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	`reaction_1`	reaction_1	$\emptyset \longrightarrow c$	
2	`reaction_3`	reaction_3	$c \xrightarrow{c} \emptyset$	
3	`reaction_2`	reaction_2	$\emptyset \xrightarrow{c} c$	
4	`reaction_4`	reaction_4	$c \xrightarrow{c} \emptyset$	

5.1 Reaction reaction_1

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

Name reaction_1

Reaction equation

$$\emptyset \longrightarrow \mathrm{c} \tag{1}$$

Product

Table 5: Properties of each product.

Id	Name	SBO
c	ribosome concentration	

Kinetic Law

Derived unit not available

$$v_1 = \mathrm{alpha} \tag{2}$$

Table 6: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
alpha	alpha		0.001		☑

5.2 Reaction reaction_3

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

Name reaction_3

Reaction equation

$$\mathrm{c} \xrightarrow{\mathrm{c}} \emptyset \tag{3}$$

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
c	ribosome concentration	

Modifier

Table 8: Properties of each modifier.

Id	Name	SBO
c	ribosome concentration	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{kd} \cdot [\mathrm{c}] \tag{4}$$

Table 9: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kd	kd		1.0		☑

5.3 Reaction reaction_2

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

Name reaction_2

Reaction equation

$$\emptyset \xrightarrow{\mathrm{c}} \mathrm{c} \tag{5}$$

Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
c	ribosome concentration	

Product

Table 11: Properties of each product.

Id	Name	SBO
c	ribosome concentration	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \frac{[\mathrm{c}]}{\mathrm{kappa} + [\mathrm{c}]} \tag{6}$$

Table 12: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kappa	kappa		0.5		☑

5.4 Reaction reaction_4

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

Name reaction_4

Reaction equation

$$\mathrm{c} \xrightarrow{\mathrm{c}} \emptyset \tag{7}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
c	ribosome concentration	

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
c	ribosome concentration	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \frac{\text{phi} \cdot [\text{c}]}{\text{delta} + \text{gamma} \cdot [\text{c}]} \tag{8}$$

Table 15: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
phi	phi		$5 \cdot 10^{-6}$		☑
delta	delta		10^{-5}		☑
gamma	gamma		10^{-5}		☑

6 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.

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.

6.1 Species c

Name ribosome concentration

Notes c represents concentration of ribosomes C

Initial amount 1 mol

This species takes part in seven reactions (as a reactant in reaction_3, reaction_4 and as a product in reaction_1, reaction_2 and as a modifier in reaction_3, reaction_2, reaction_4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{c} = v_1 + v_3 - v_2 - v_4 \tag{9}$$

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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