SBML Model Report

Model name: “Ribba2012 - Low-grade gliomas, tumour growth inhibition model”

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Vijayalakshmi Chelliah[1] at March first 2014 at 4:41 p. m. and last time modified at October nineth 2014 at 5:37 p. 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	2
species types	0	species	4
events	0	constraints	0
reactions	0	function definitions	0
global parameters	10	unit definitions	0
rules	5	initial assignments	0

Model Notes

Ribba2012 - Low-grade gliomas, tumour growth inhibition model

Using longitudinal mean tumour diameter (MTD) data, this model describe the size evolution of low-grade glioma (LGG) in patients treated with chemotherapy or radiotherapy.

This model is described in the article:A tumour growth inhibition model for low-grade glioma treated with chemotherapy or radiotherapyRibba B, Kaloshi G, Peyre M, Ricard D, Calvez V,

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Tod M, Cajavec-Bernard B, Idbaih A, Psimaras D, Dainese L, Pallud J, Cartalat-Carel S, Delattre JY, Honnorat J, Grenier E, Ducray F.Clin. Cancer Res. 2012 Sep; 18(18): 5071-5080

Abstract:

PURPOSE: To develop a tumor growth inhibition model for adult diffuse low-grade gliomas (LGG) able to describe tumor size evolution in patients treated with chemotherapy or radiotherapy.

EXPERIMENTAL DESIGN: Using longitudinal mean tumor diameter (MTD) data from 21 patients treated with first-line procarbazine, 1-(2-chloroethyl)-3-cyclohexyl-l-nitrosourea, and vincristine (PCV) chemotherapy, we formulated a model consisting of a system of differential equations, incorporating tumor-specific and treatment-related parameters that reflect the response of proliferative and quiescent tumor tissue to treatment. The model was then applied to the analysis of longitudinal tumor size data in 24 patients treated with first-line temozolomide (TMZ) chemotherapy and in 25 patients treated with first-line radiotherapy.

RESULTS: The model successfully described the MTD dynamics of LGG before, during, and after PCV chemotherapy. Using the same model structure, we were also able to successfully describe the MTD dynamics in LGG patients treated with TMZ chemotherapy or radiotherapy. Tumor-specific parameters were found to be consistent across the three treatment modalities. The model is robust to sensitivity analysis, and preliminary results suggest that it can predict treatment response on the basis of pretreatment tumor size data.

CONCLUSIONS: Using MTD data, we propose a tumor growth inhibition model able to describe LGG tumor size evolution in patients treated with chemotherapy or radiotherapy. In the future, this model might be used to predict treatment efficacy in LGG patients and could constitute a rational tool to conceive more effective chemotherapy schedules.

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 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

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

3.1 Compartment `plama`

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

Name plasma

3.2 Compartment `tissue`

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

Name tissue

4 Species

This model contains four 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
C	PCV_plasma	plama	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
P	Proliferative tissue	tissue	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Q	nonproliferative quiescent tissue	tissue	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Qp	damaged quiescent cells	tissue	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains ten global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Pstar	Pstar		0.000		☐
P0	P0		7.130		☑
Q0	Q0		41.200		☑
lambda_P	lambda_P		0.121		☑
k_PQ	k_PQ		0.003		☑
k_Qp_P	k_Qp_P		0.003		☑
delta_QP	delta_QP		0.009		☑
gamma	gamma		0.729		☑
KDE	KDE		0.240		☑
K	K		100.000		☑

6 Rules

This is an overview of five rules.

6.1 Rule Pstar

Rule Pstar is an assignment rule for parameter Pstar:

$$\text{Pstar} = [\text{P}] + [\text{Q}] + [\text{Qp}] \tag{1}$$

Derived unit $\text{mol} \cdot \text{l}^{-1}$

6.2 Rule C

Rule C is a rate rule for species C:

$$\frac{\text{d}}{\text{d}t}\text{C} = \text{KDE} \cdot [\text{C}] \tag{2}$$

Derived unit $\text{mol} \cdot \text{l}^{-1}$

6.3 Rule P

Rule P is a rate rule for species P:

$$\frac{\text{d}}{\text{d}t}\text{P} = \text{lambda\_P} \cdot [\text{P}] \cdot \left(1 - \frac{\text{Pstar}}{\text{K}}\right) + \text{k\_Qp\_P} \cdot [\text{Qp}] - \text{k\_PQ} \cdot [\text{P}] - \text{gamma} \cdot [\text{C}] \cdot \text{KDE} \cdot [\text{P}] \tag{3}$$

6.4 Rule Q

Rule Q is a rate rule for species Q:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Q} = \mathrm{k\_PQ} - \mathrm{gamma} \cdot [\mathrm{C}] \cdot \mathrm{KDE} \cdot [\mathrm{Q}] \tag{4}$$

6.5 Rule Qp

Rule Qp is a rate rule for species Qp:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Qp} = \mathrm{gamma} \cdot [\mathrm{C}] \cdot \mathrm{KDE} \cdot [\mathrm{Q}] - \mathrm{k\_Qp\_P} \cdot [\mathrm{Qp}] - \mathrm{delta\_QP} \cdot [\mathrm{Qp}] \tag{5}$$

7 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.

7.1 Species C

Name PCV_plasma

Initial concentration $1\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule C

One rule which determines this species' quantity.

7.2 Species P

Name Proliferative tissue

Initial concentration $7.13\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule P

One rule which determines this species' quantity.

7.3 Species Q

Name nonproliferative quiescent tissue

Initial concentration $41.2\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule Q

One rule which determines this species' quantity.

7.4 Species Qp

Name damaged quiescent cells

Initial concentration $0\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule Qp

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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