SBML Model Report

Model name: “Baker2013 - Cytokine Mediated Inflammation in Rheumatoid Arthritis - Age Dependant”

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Vincent Knight-Schrijver[1] at September 25th 2014 at 1:46 p. m. and last time modified at April eighth 2016 at 5:41 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	2
events	0	constraints	0
reactions	0	function definitions	0
global parameters	8	unit definitions	3
rules	3	initial assignments	0

Model Notes

Baker2013 - Cytokine Mediated Inflammation inRheumatoid Arthritis - Age DependantThis model by Baker M. 2013, describesthe interaction between pro and anti-inflammatory cytokinesignalling in rheumatoid arthritis.

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Using two ordinary differential equations, the first model [BIOMD0000000550]analyses bifurcation and describes different pathological states byaltering inflammatory regulation parameters. The second model [BIOMD0000000549]includes the effect that ageing has on pro-inflammatory signalling,allowing for time-dependant properties and disease progression tobe observed. The author also describes potential dosing forreversal of the disease state.

This model is described in the article:Mathematical modelling of cytokine-mediated inflammation in rheumatoid arthritis.Baker M, Denman-Johnson S, Brook BS, Gaywood I, Owen MR.Math Med Biol 2013 Dec; 30(4): 311-337

Abstract:

Rheumatoid arthritis (RA) is a chronic inflammatory disease preferentially affecting the joints and leading, if untreated, to progressive joint damage and disability. Cytokines, a group of small inducible proteins, which act as intercellular messengers, are key regulators of the inflammation that characterizes RA. They can be classified into pro-inflammatory and anti-inflammatory groups. Numerous cytokines have been implicated in the regulation of RA with complex up and down regulatory interactions. This paper considers a two-variable model for the interactions between pro-inflammatory and anti-inflammatory cytokines, and demonstrates that mathematical modelling may be used to investigate the involvement of cytokines in the disease process. The model displays a range of possible behaviours, such as bistability and oscillations, which are strongly reminiscent of the behaviour of RA e.g. genetic susceptibility and remitting-relapsing disease. We also show that the dose regimen as well as the dose level are important factors in RA treatments.

This model is hosted on BioModels Database and identified by: BIOMD0000000549.

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

2.1 Unit `volume`

Name volume

Definition dimensionless

2.2 Unit `time`

Name time

Definition dimensionless

2.3 Unit substance

Name substance

Definition dimensionless

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
compartment_1	Synovium		3	1	dimensionless	☑	

3.1 Compartment compartment_1

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

Name Synovium

Notes Compartment notes: {\textquotestraightdblbase}The synovium is modelled as a spatial

4 Species

This model contains two species. The boundary condition of two of these species is set to `true` so that these species' amount cannot be changed by any reaction. 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
`species_1`	a	`compartment_1`	dimensionless $\cdot$ dimensionless^{-1}	⊟	☑
`species_2`	p	`compartment_1`	dimensionless $\cdot$ dimensionless^{-1}	⊟	☑

5 Parameters

This model contains eight global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
parameter_1	alpha1		0.025		☑
parameter_2	alpha2		1.000		⊟
parameter_3	alpha3		0.500		☑
parameter_4	alpha4		7.000		☑
parameter_5	gamma		1.250		☑
parameter_6	alpha2T		15.000		☑
parameter_7	alpha2_min		1.000		☑
parameter_8	alpha2_max		50.000		☑

6 Rules

This is an overview of three rules.

6.1 Rule parameter_2

Rule parameter_2 is an assignment rule for parameter parameter_2:

$$\text{parameter\_2} = \text{parameter\_7} + \frac{(\text{parameter\_8} - \text{parameter\_7}) \cdot \text{time}^2}{\text{parameter\_6}^2 + \text{time}^2} \tag{1}$$

6.2 Rule species_1

Rule species_1 is a rate rule for species species_1:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_1} = [\text{species\_1}] + \text{parameter\_4} \cdot \frac{[\text{species\_2}]^2}{\text{parameter\_3}^2 + [\text{species\_2}]^2} \tag{2}$$

6.3 Rule species_2

Rule species_2 is a rate rule for species species_2:

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_2} = \text{parameter\_5} \cdot [\text{species\_2}] + \frac{1}{1 + [\text{species\_1}]^2} \\ \cdot \left(\text{parameter\_1} + \text{parameter\_2} \cdot \frac{[\text{species\_2}]^2}{1 + [\text{species\_2}]^2}\right)\end{aligned} \tag{3}$$

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 species_1

Name a

Notes Anti-inflammatory cytokine concentration (dimensionless)

Initial concentration $0.00577667577789773\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

Involved in rule species_1

One rule determines the species' quantity.

7.2 Species species_2

Name p

Notes Pro-inflammatory cytokine concentration (dimensionless)

Initial concentration $0.0203298264712407\ \text{dimensionless} \cdot \text{dimensionless}^{-1}$

Involved in rule species_2

One rule determines the 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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