

SBML Model Report

Model name: “Dunster2014 - WBC Interactions (Model1)”



March 14, 2017

1 General Overview

This is a document in SBML Level 3 Version 1 format. This model was created by Thawfeek Varusai¹ at August 16th 2016 at 3:36 p.m. and last time modified at August 17th 2016 at 1:39 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	4
events	0	constraints	0
reactions	10	function definitions	10
global parameters	8	unit definitions	5
rules	0	initial assignments	0

Model Notes

Dunster2014 - WBC Interactions (Model1)

This is a sub-model of a three step modelling study of the inflammatory response. The model includes distinct populations of

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white blood cells namely, macrophages and active and apoptotic neutrophil populations. Neutrophil apoptosis rate is predicted to be crucial for the qualitative nature of the system.

This model is described in the article: [The resolution of inflammation: a mathematical model of neutrophil and macrophage interactions](#). Dunster JL, Byrne HM, King JR. Bull. Math. Biol. 2014 Aug; 76(8): 1953-1980

Abstract:

There is growing interest in inflammation due to its involvement in many diverse medical conditions, including Alzheimer's disease, cancer, arthritis and asthma. The traditional view that resolution of inflammation is a passive process is now being superseded by an alternative hypothesis whereby its resolution is an active, anti-inflammatory process that can be manipulated therapeutically. This shift in mindset has stimulated a resurgence of interest in the biological mechanisms by which inflammation resolves. The anti-inflammatory processes central to the resolution of inflammation revolve around macrophages and are closely related to pro-inflammatory processes mediated by neutrophils and their ability to damage healthy tissue. We develop a spatially averaged model of inflammation centring on its resolution, accounting for populations of neutrophils and macrophages and incorporating both pro- and anti-inflammatory processes. Our ordinary differential equation model exhibits two outcomes that we relate to healthy and unhealthy states. We use bifurcation analysis to investigate how variation in the system parameters affects its outcome. We find that therapeutic manipulation of the rate of macrophage phagocytosis can aid in resolving inflammation but success is critically dependent on the rate of neutrophil apoptosis. Indeed our model predicts that an effective treatment protocol would take a dual approach, targeting macrophage phagocytosis alongside neutrophil apoptosis.

This model is hosted on [BioModels Database](#) and identified by: [BIOMD0000000616](#).

To cite BioModels Database, please use: [BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models](#).

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2 Unit Definitions

This is an overview of five unit definitions.

2.1 Unit length

Name length

Definition m

2.2 Unit area

Name area

Definition m^2

2.3 Unit volume

Name volume

Definition 1

2.4 Unit time

Name time

Definition s

2.5 Unit substance

Name substance

Definition mol

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
default_compartment	Soft_Tissue	0000410	3	1		<input checked="" type="checkbox"/>	

3.1 Compartment default_compartment

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

Name Soft_Tissue

SBO:0000410 implicit compartment

4 Species

This model contains four species. Section 8 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 Condi- tion
n	n	default_compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
c	c	default_compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
a	a	default_compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
m	m	default_compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square

5 Parameters

This model contains eight global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
vt	vt		0.100		<input checked="" type="checkbox"/>
Gat	Gat		1.000		<input checked="" type="checkbox"/>
Tt	Tt		0.001		<input checked="" type="checkbox"/>
Gmt	Gmt		0.010		<input checked="" type="checkbox"/>
alt	alt		0.050		<input checked="" type="checkbox"/>
Bat	Bat		0.100		<input checked="" type="checkbox"/>
A	A		1.000		<input checked="" type="checkbox"/>
t1	t1		10.000		<input checked="" type="checkbox"/>

6 Function definitions

This is an overview of ten function definitions.

6.1 Function definition `Function_for_R2`

Name Function for R2

Arguments `ModelValue_4`, `vol (default_compartment)`, `[n]`

Mathematical Expression

$$\frac{\text{ModelValue_4} \cdot [\text{n}]}{\text{vol}(\text{default_compartment})} \quad (1)$$

6.2 Function definition `Function_for_R1`

Name Function for R1

Arguments `[c]`, `vol (default_compartment)`

Mathematical Expression

$$\frac{[\text{c}]}{\text{vol}(\text{default_compartment})} \quad (2)$$

6.3 Function definition [Function_for_R6](#)

Name Function for R6

Arguments $[c]$, $\text{vol}(\text{default_compartment})$

Mathematical Expression

$$\frac{[c]}{\text{vol}(\text{default_compartment})} \quad (3)$$

6.4 Function definition [Function_for_R8](#)

Name Function for R8

Arguments $\text{Dunster2014_Model1_WBC_Interactions}$, ModelValue_10 , ModelValue_11 , ModelValue_8 ,
 $\text{vol}(\text{default_compartment})$

Mathematical Expression

$$\frac{\text{ModelValue_8} \cdot \begin{cases} (\sin \text{Dunster2014_Model1_WBC_Interactions})^2 & \text{if } \text{Dunster2014_Model1_WBC_Interactions} < 1 \\ 0 & \text{otherwise} \end{cases}}{\text{vol}(\text{default_compartment})} \quad (4)$$

6.5 Function definition [Function_for_R5](#)

Name Function for R5

Arguments ModelValue_6 , $[a]$, $\text{vol}(\text{default_compartment})$, $[m]$

Mathematical Expression

$$\frac{\text{ModelValue_6} \cdot [m] \cdot [a]}{\text{vol}(\text{default_compartment})} \quad (5)$$

6.6 Function definition [Function_for_R10](#)

Name Function for R10

Arguments $[c]$, $\text{vol}(\text{default_compartment})$

Mathematical Expression

$$\frac{[c]}{\text{vol}(\text{default_compartment})} \quad (6)$$

6.7 Function definition [Function_for_R3](#)

Name Function for R3

Arguments ModelValue_4, vol (default_compartment), [n]

Mathematical Expression

$$\frac{\text{ModelValue_4} \cdot [\text{n}]}{\text{vol}(\text{default_compartment})} \quad (7)$$

6.8 Function definition [Function_for_R4](#)

Name Function for R4

Arguments ModelValue_5, [a], vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue_5} \cdot [\text{a}]}{\text{vol}(\text{default_compartment})} \quad (8)$$

6.9 Function definition [Function_for_R9](#)

Name Function for R9

Arguments ModelValue_5, ModelValue_9, [a], vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue_5} \cdot \frac{[\text{a}]^2}{\text{ModelValue_9}^2 + [\text{a}]^2}}{\text{vol}(\text{default_compartment})} \quad (9)$$

6.10 Function definition [Function_for_R7](#)

Name Function for R7

Arguments ModelValue_7, vol (default_compartment), [m]

Mathematical Expression

$$\frac{\text{ModelValue_7} \cdot [\text{m}]}{\text{vol}(\text{default_compartment})} \quad (10)$$

7 Reactions

This model contains ten 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

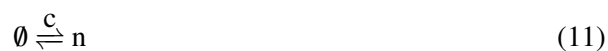
Nº	Id	Name	Reaction Equation	SBO
1	R1	R1	$\emptyset \xrightarrow{c} n$	
2	R2	R2	$n \rightleftharpoons \emptyset$	
3	R3	R3	$\emptyset \xrightarrow{n} a$	
4	R4	R4	$a \rightleftharpoons \emptyset$	
5	R5	R5	$a \xrightarrow{m} \emptyset$	
6	R6	R6	$\emptyset \xrightarrow{c} m$	
7	R7	R7	$m \rightleftharpoons \emptyset$	
8	R8	R8	$\emptyset \rightleftharpoons c$	
9	R9	R9	$\emptyset \xrightarrow{a} c$	
10	R10	R10	$c \rightleftharpoons \emptyset$	

7.1 Reaction R1

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name R1

Reaction equation



Modifier

Table 6: Properties of each modifier.

Id	Name	SBO
c	c	

Product

Table 7: Properties of each product.

Id	Name	SBO
n	n	

Kinetic Law

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

$$v_1 = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R1}([c], \text{vol}(\text{default_compartment})) \quad (12)$$

$$\text{Function_for_R1}([c], \text{vol}(\text{default_compartment})) = \frac{[c]}{\text{vol}(\text{default_compartment})} \quad (13)$$

$$\text{Function_for_R1}([c], \text{vol}(\text{default_compartment})) = \frac{[c]}{\text{vol}(\text{default_compartment})} \quad (14)$$

7.2 Reaction R2

This is a reversible reaction of one reactant forming no product.

Name R2

Reaction equation



Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
n	n	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R2}(\text{vt}, \text{vol}(\text{default_compartment}), [n]) \quad (16)$$

$$\text{Function_for_R2}(\text{ModelValue_4}, \text{vol}(\text{default_compartment}), [n]) = \frac{\text{ModelValue_4} \cdot [n]}{\text{vol}(\text{default_compartment})} \quad (17)$$

$$\text{Function_for_R2}(\text{ModelValue_4}, \text{vol}(\text{default_compartment}), [n]) = \frac{\text{ModelValue_4} \cdot [n]}{\text{vol}(\text{default_compartment})} \quad (18)$$

7.3 Reaction R3

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name R3

Reaction equation



Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
n	n	

Product

Table 10: Properties of each product.

Id	Name	SBO
a	a	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R3}(\text{vt}, \text{vol}(\text{default_compartment}), [n]) \quad (20)$$

$$\text{Function_for_R3}(\text{ModelValue_4}, \text{vol}(\text{default_compartment}), [n]) = \frac{\text{ModelValue_4} \cdot [n]}{\text{vol}(\text{default_compartment})} \quad (21)$$

$$\text{Function_for_R3}(\text{ModelValue_4}, \text{vol}(\text{default_compartment}), [n]) = \frac{\text{ModelValue_4} \cdot [n]}{\text{vol}(\text{default_compartment})} \quad (22)$$

7.4 Reaction R4

This is a reversible reaction of one reactant forming no product.

Name R4

Reaction equation



Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
a	a	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R4}(\text{Gat}, [a], \text{vol}(\text{default_compartment})) \quad (24)$$

$$\text{Function_for_R4}(\text{ModelValue_5}, [a], \text{vol}(\text{default_compartment})) = \frac{\text{ModelValue_5} \cdot [a]}{\text{vol}(\text{default_compartment})} \quad (25)$$

$$\text{Function_for_R4}(\text{ModelValue_5}, [a], \text{vol}(\text{default_compartment})) = \frac{\text{ModelValue_5} \cdot [a]}{\text{vol}(\text{default_compartment})} \quad (26)$$

7.5 Reaction R5

This is a reversible reaction of one reactant forming no product influenced by one modifier.

Name R5

Reaction equation



Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
a	a	

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
m	m	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R5}(\text{Tt}, [a], \text{vol}(\text{default_compartment}), [m]) \quad (28)$$

$$\begin{aligned} &\text{Function_for_R5}(\text{ModelValue_6}, [a], \text{vol}(\text{default_compartment}), [m]) \\ &= \frac{\text{ModelValue_6} \cdot [m] \cdot [a]}{\text{vol}(\text{default_compartment})} \end{aligned} \quad (29)$$

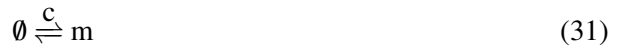
$$\begin{aligned} & \text{Function_for_R5}(\text{ModelValue_6}, [a], \text{vol}(\text{default_compartment}), [m]) \\ &= \frac{\text{ModelValue_6} \cdot [m] \cdot [a]}{\text{vol}(\text{default_compartment})} \end{aligned} \quad (30)$$

7.6 Reaction R6

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name R6

Reaction equation



Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
c	c	

Product

Table 15: Properties of each product.

Id	Name	SBO
m	m	

Kinetic Law

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

$$v_6 = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R6}([c], \text{vol}(\text{default_compartment})) \quad (32)$$

$$\text{Function_for_R6}([c], \text{vol}(\text{default_compartment})) = \frac{[c]}{\text{vol}(\text{default_compartment})} \quad (33)$$

$$\text{Function_for_R6}([c], \text{vol}(\text{default_compartment})) = \frac{[c]}{\text{vol}(\text{default_compartment})} \quad (34)$$

7.7 Reaction R7

This is a reversible reaction of one reactant forming no product.

Name R7

Reaction equation



Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
m	m	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R7}(\text{Gmt}, \text{vol}(\text{default_compartment}), [m]) \quad (36)$$

$$\text{Function_for_R7}(\text{ModelValue_7}, \text{vol}(\text{default_compartment}), [m]) = \frac{\text{ModelValue_7} \cdot [m]}{\text{vol}(\text{default_compartment})} \quad (37)$$

$$\text{Function_for_R7}(\text{ModelValue_7}, \text{vol}(\text{default_compartment}), [m]) = \frac{\text{ModelValue_7} \cdot [m]}{\text{vol}(\text{default_compartment})} \quad (38)$$

7.8 Reaction R8

This is a reversible reaction of no reactant forming one product.

Name R8

Reaction equation



Product

Table 17: Properties of each product.

Id	Name	SBO
c	c	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R8}(\text{time}, A, t1, \text{alt}, \text{vol}(\text{default_compartment})) \tag{40}$$

$$\text{Function_for_R8}(\text{Dunster2014_Model1_WBC_Interactions}, \text{ModelValue_10}, \text{ModelValue_11}, \text{ModelValue_8}, \text{vol}(\text{default_compartment})) \tag{41}$$

$$= \frac{\text{ModelValue_8} \cdot \begin{cases} (\sin \text{Dunster2014_Model1_WBC_Interactions})^2 & \text{if Dunster2014_Model1_WBC_Interactions} < 0 \\ 0 & \text{otherwise} \end{cases}}{\text{vol}(\text{default_compartment})}$$

$$\text{Function_for_R8}(\text{Dunster2014_Model1_WBC_Interactions}, \text{ModelValue_10}, \text{ModelValue_11}, \text{ModelValue_8}, \text{vol}(\text{default_compartment})) \tag{42}$$

$$= \frac{\text{ModelValue_8} \cdot \begin{cases} (\sin \text{Dunster2014_Model1_WBC_Interactions})^2 & \text{if Dunster2014_Model1_WBC_Interactions} < 0 \\ 0 & \text{otherwise} \end{cases}}{\text{vol}(\text{default_compartment})}$$

7.9 Reaction R9

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name R9

Reaction equation



Modifier

Table 18: Properties of each modifier.

Id	Name	SBO
a	a	

Product

Table 19: Properties of each product.

Id	Name	SBO
c	c	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R9}(\text{Gat}, \text{Bat}, [a], \text{vol}(\text{default_compartment})) \quad (44)$$

$$\begin{aligned} & \text{Function_for_R9}(\text{ModelValue_5}, \text{ModelValue_9}, [a], \text{vol}(\text{default_compartment})) \\ &= \frac{\text{ModelValue_5} \cdot \frac{[a]^2}{\text{ModelValue_9}^2 + [a]^2}}{\text{vol}(\text{default_compartment})} \end{aligned} \quad (45)$$

$$\begin{aligned} & \text{Function_for_R9}(\text{ModelValue_5}, \text{ModelValue_9}, [a], \text{vol}(\text{default_compartment})) \\ &= \frac{\text{ModelValue_5} \cdot \frac{[a]^2}{\text{ModelValue_9}^2 + [a]^2}}{\text{vol}(\text{default_compartment})} \end{aligned} \quad (46)$$

7.10 Reaction R10

This is a reversible reaction of one reactant forming no product.

Name R10

Reaction equation



Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
c	c	

Kinetic Law

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

$$v_{10} = \text{vol}(\text{default_compartment}) \cdot \text{Function_for_R10}([c], \text{vol}(\text{default_compartment})) \quad (48)$$

$$\text{Function_for_R10}([c], \text{vol}(\text{default_compartment})) = \frac{[c]}{\text{vol}(\text{default_compartment})} \quad (49)$$

$$\text{Function_for_R10}([c], \text{vol}(\text{default_compartment})) = \frac{[c]}{\text{vol}(\text{default_compartment})} \quad (50)$$

8 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.

8.1 Species `n`

Name `n`

SBO:0000410 implicit compartment

Notes Active neutrophils

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

This species takes part in three reactions (as a reactant in [R2](#) and as a product in [R1](#) and as a modifier in [R3](#)).

$$\frac{d}{dt}n = v_1 - v_2 \quad (51)$$

8.2 Species c

Name c

SBO:0000410 implicit compartment

Notes Pro-inflammatory mediators

Initial concentration 0 mol · l⁻¹

This species takes part in five reactions (as a reactant in [R10](#) and as a product in [R8](#), [R9](#) and as a modifier in [R1](#), [R6](#)).

$$\frac{d}{dt}c = v_8 + v_9 - v_{10} \quad (52)$$

8.3 Species a

Name a

SBO:0000410 implicit compartment

Notes Apoptotic neutrophils

Initial concentration 0 mol · l⁻¹

This species takes part in four reactions (as a reactant in [R4](#), [R5](#) and as a product in [R3](#) and as a modifier in [R9](#)).

$$\frac{d}{dt}a = v_3 - v_4 - v_5 \quad (53)$$

8.4 Species m

Name m

SBO:0000410 implicit compartment

Notes Macrophages

Initial concentration 0 mol · l⁻¹

This species takes part in three reactions (as a reactant in [R7](#) and as a product in [R6](#) and as a modifier in [R5](#)).

$$\frac{d}{dt}m = v_6 - v_7 \quad (54)$$

A Glossary of Systems Biology Ontology Terms

SBO:0000410 implicit compartment: A compartment whose existence is inferred due to the presence of known material entities which must be bounded, allowing the creation of material entity pools

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