**SBML Model Report**

# Model name: "Maree2006_DuCa_Type1DiabetesModel"

May 6, 2016

## 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Ishan Ajmera[1] at October seventh 2011 at 3:36 p. m. and last time modified at October tenth 2014 at 10:36 a. m. Table 1 gives 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 | 5 |
| events | 0 | constraints | 0 |
| reactions | 0 | function definitions | 0 |
| global parameters | 17 | unit definitions | 0 |
| rules | 7 | initial assignments | 0 |

### Model Notes

This a model from the article:
**Modelling the onset of Type 1 diabetes: can impaired macrophage phagocytosis make the difference between health and disease?**
Maree AF, Kublik R, Finegood DT, Edelstein-Keshet L.Philos Transact A Math Phys Eng Sci.2006 May 15;364(1842):1267-82. 16608707,

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**Abstract:**
A wave of apoptosis (programmed cell death) occurs normally in pancreatic beta-cells of newborn mice. We previously showed that macrophages from non-obese diabetic (NOD) mice become activated more slowly and engulf apoptotic cells at a lower rate than macrophages from control (Balb/c) mice. It has been hypothesized that this low clearance could result in secondary necrosis, escalating inflammation and self-antigen presentation that later triggers autoimmune, Type 1 diabetes (T1D). We here investigate whether this hypothesis could offer a reasonable and parsimonious explanation for onset of T1D in NOD mice. We quantify variants of the Copenhagen model (Freiesleben De Blasio et al. 1999 Diabetes 48, 1677), based on parameters from NOD and Balb/c experimental data. We show that the original Copenhagen model fails to explain observed phenomena within a reasonable range of parameter values, predicting an unrealistic all-or-none disease occurrence for both strains. However, if we take into account that, in general, activated macrophages produce harmful cytokines only when engulfing necrotic (but not apoptotic) cells, then the revised model becomes qualitatively and quantitatively reasonable. Further, we show that known differences between NOD and Balb/c mouse macrophage kinetics are large enough to account for the fact that an apoptotic wave can trigger escalating inflammatory response in NOD, but not Balb/c mice. In Balb/c mice, macrophages clear the apoptotic wave so efficiently, that chronic inflammation is prevented.

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To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler L, Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novre N, Laibe C (2010) BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

## 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 |
|---|---|---|---|---|---|---|---|
| compartment1 | compartment1 | | 3 | 1 | litre | ☑ | |

### 3.1 Compartment compartment1

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

**Name** compartment1

## 4 Species

This model contains five species. The boundary condition of five 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 |
|---|---|---|---|---|---|
| `M` | M | `compartment1` | $\mathrm{mol} \cdot \mathrm{l}^{-1}$ | ⊟ | ☑ |
| `Ma` | Ma | `compartment1` | $\mathrm{mol} \cdot \mathrm{l}^{-1}$ | ⊟ | ☑ |
| `Bn` | Bn | `compartment1` | $\mathrm{mol} \cdot \mathrm{l}^{-1}$ | ⊟ | ☑ |
| `Ba` | Ba | `compartment1` | $\mathrm{mol} \cdot \mathrm{l}^{-1}$ | ⊟ | ☑ |
| `Cy` | Cy | `compartment1` | $\mathrm{mol} \cdot \mathrm{l}^{-1}$ | ⊟ | ☑ |

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# 5 Parameters

This model contains 17 global parameters.

Table 4: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| J | J | 0000185 | 50000.000 | | ☑ |
| c | c | 0000009 | 0.100 | | ☑ |
| b | b | 0000009 | 0.090 | | ☑ |
| d | d | 0000009 | 0.500 | | ☑ |
| k | k | 0000009 | 0.400 | | ☑ |
| e1 | e1 | 0000009 | $10^{-8}$ | | ☑ |
| e2 | e2 | 0000009 | $10^{-8}$ | | ☑ |
| Amax | Amax | 0000009 | $2 \cdot 10^{7}$ | | ☑ |
| kc | kc | 0000009 | 1.000 | | ☑ |
| alpha | alpha | 0000009 | $5 \cdot 10^{-9}$ | | ☑ |
| delta | delta | 0000009 | 25.000 | | ☑ |
| g | g | 0000009 | $10^{-5}$ | | ☑ |
| f1 | f1 | 0000009 | $10^{-5}$ | | ☑ |
| f2 | f2 | 0000009 | $10^{-5}$ | | ☑ |
| Wmax | Wmax | 0000009 | $4 \cdot 10^{7}$ | | ☑ |
| W | W | 0000009 | 4936.392 | | ⊟ |
| parameter_1 | x | 0000009 | 9.000 | | ⊟ |

# 6 Rules

This is an overview of seven rules.

## 6.1 Rule parameter_1

Rule parameter_1 is an assignment rule for parameter parameter_1:

$$\text{parameter\_1} = \left(\frac{\text{time} - 9}{3}\right)^2 \tag{1}$$

## 6.2 Rule W

Rule W is an assignment rule for parameter W:

$$\text{W} = \text{Wmax} \cdot \exp\left(\text{parameter\_1}\right) \tag{2}$$

### 6.3 Rule M

Rule M is a rate rule for species M:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{M} = \mathrm{J} + (\mathrm{k} + \mathrm{b}) \cdot [\mathrm{Ma}] - \mathrm{c} \cdot [\mathrm{M}] - \mathrm{f1} \cdot [\mathrm{M}] \cdot [\mathrm{Ba}] - \mathrm{e1} \cdot [\mathrm{M}] \cdot ([\mathrm{M}] + [\mathrm{Ma}]) \tag{3}$$

### 6.4 Rule Ma

Rule Ma is a rate rule for species Ma:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ma} = \mathrm{f1} \cdot [\mathrm{M}] \cdot [\mathrm{Ba}] - \mathrm{k} \cdot [\mathrm{Ma}] - \mathrm{e2} \cdot [\mathrm{Ma}] \cdot ([\mathrm{M}] + [\mathrm{Ma}]) \tag{4}$$

### 6.5 Rule Bn

Rule Bn is a rate rule for species Bn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Bn} = \mathrm{d} \cdot [\mathrm{Ba}] - (\mathrm{f1} \cdot [\mathrm{M}] + \mathrm{f2} \cdot [\mathrm{Ma}]) \cdot [\mathrm{Bn}] \tag{5}$$

### 6.6 Rule Ba

Rule Ba is a rate rule for species Ba:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ba} = \mathrm{W} + \frac{\mathrm{Amax} \cdot [\mathrm{Cy}]}{\mathrm{kc} + [\mathrm{Cy}]} - (\mathrm{f1} \cdot [\mathrm{M}] + \mathrm{f2} \cdot [\mathrm{Ma}] + \mathrm{d}) \cdot [\mathrm{Ba}] \tag{6}$$

### 6.7 Rule Cy

Rule Cy is a rate rule for species Cy:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Cy} = \mathrm{alpha} \cdot [\mathrm{Bn}] \cdot [\mathrm{Ma}] - \mathrm{delta} \cdot [\mathrm{Cy}] \tag{7}$$

## 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 M

**Name** M

**Initial concentration** $477000\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

**Involved in rule** M

One rule determines the species' quantity.

### 7.2 Species Ma

**Name** Ma

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

**Involved in rule** Ma

One rule determines the species' quantity.

### 7.3 Species Bn

**Name** Bn

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

**Involved in rule** Bn

One rule determines the species' quantity.

### 7.4 Species Ba

**Name** Ba

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

**Involved in rule** Ba

One rule determines the species' quantity.

### 7.5 Species Cy

**Name** Cy

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

**Involved in rule** Cy

One rule determines the species' quantity.

## A Glossary of Systems Biology Ontology Terms

**SBO:0000009 kinetic constant:** Numerical parameter that quantifies the velocity of a chemical reaction

**SBO:0000185 transport reaction:** Movement of a physical entity without modification of the structure of the entity

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