SBML Model Report

Model name: "Topp2000_BetaCellMass_Diabetes"

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 July seventh 2011 at 3:51 p. m. and last time modified at October tenth 2014 at 10:28 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	3
events	0	constraints	0
reactions	0	function definitions	0
global parameters	9	unit definitions	0
rules	3	initial assignments	0

Model Notes

This model is from the article:
A model of beta-cell mass, insulin, and glucose kinetics: pathways to diabetes.
Topp B, Promislow K, deVries G, Miura RM, Finegood DT. J Theor Biol.2000 Oct 21;206(4):605-19. 11013117,
Abstract:

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Diabetes is a disease of the glucose regulatory system that is associated with increased morbidity and early mortality. The primary variables of this system are beta-cell mass, plasma insulin concentrations, and plasma glucose concentrations. Existing mathematical models of glucose regulation incorporate only glucose and/or insulin dynamics. Here we develop a novel model of beta -cell mass, insulin, and glucose dynamics, which consists of a system of three nonlinear ordinary differential equations, where glucose and insulin dynamics are fast relative to beta-cell mass dynamics. For normal parameter values, the model has two stable fixed points (representing physiological and pathological steady states), separated on a slow manifold by a saddle point. Mild hyperglycemia leads to the growth of the beta -cell mass (negative feedback) while extreme hyperglycemia leads to the reduction of the beta-cell mass (positive feedback). The model predicts that there are three pathways in prolonged hyperglycemia: (1) the physiological fixed point can be shifted to a hyperglycemic level (regulated hyperglycemia), (2) the physiological and saddle points can be eliminated (bifurcation), and (3) progressive defects in glucose and/or insulin dynamics can drive glucose levels up at a rate faster than the adaptation of the beta -cell mass which can drive glucose levels down (dynamical hyperglycemia).

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 three species. The boundary condition of three 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
`G`	glucose	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
`I`	insulin	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
`B`	Mass	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑

5 Parameters

This model contains nine global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
si	si	0000009	0.720		☑
Eg0	Eg0	0000009	1.440		☑
R0	R0	0000393	864.000		☑
sigma	sigma	0000009	43.200		☑
alpha	alpha	0000009	20000.000		☑
k	k	0000009	432.000		☑
d0	d0	0000179	0.060		☑
r1	r1	0000009	$8.4 \cdot 10^{-4}$		☑
r2	r2	0000009	$2.4 \cdot 10^{-6}$		☑

6 Rules

This is an overview of three rules.

6.1 Rule G

Rule G is a rate rule for species G:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{G} = \mathrm{R0} - (\mathrm{Eg0} + \mathrm{si} \cdot [\mathrm{I}]) \cdot [\mathrm{G}] \tag{1}$$

6.2 Rule I

Rule I is a rate rule for species I:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{I} = \frac{[\mathrm{B}] \cdot \mathrm{sigma} \cdot [\mathrm{G}]^2}{\mathrm{alpha} + [\mathrm{G}]^2} - \mathrm{k} \cdot [\mathrm{I}] \tag{2}$$

6.3 Rule B

Rule B is a rate rule for species B:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{B} = \left(\mathrm{d0} + \mathrm{r1} \cdot [\mathrm{G}] - \mathrm{r2} \cdot [\mathrm{G}]^2\right) \cdot [\mathrm{B}] \tag{3}$$

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 G

Name glucose

SBO:0000247 simple chemical

Initial concentration $250\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule G

One rule determines the species' quantity.

7.2 Species I

Name insulin

SBO:0000252 polypeptide chain

Initial concentration $2.8\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule I

One rule determines the species' quantity.

7.3 Species B

Name Mass

SBO:0000240 material entity

Initial concentration $37\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule B

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:0000179 **degradation:** Complete disappearance of a physical entity

SBO:0000240 **material entity:** A real thing that is defined by its physico-chemical structure.

SBO:0000247 **simple chemical:** Simple, non-repetitive chemical entity

SBO:0000252 **polypeptide chain:** Naturally occurring macromolecule formed by the repetition of amino-acid residues linked by peptidic bonds. A polypeptide chain is synthesized by the ribosome. CHEBI:1654

SBO:0000393 **production:** Generation of a material or conceptual entity.

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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