SBML Model Report

Model name: "Sturis1991-_InsulinGlucoseModel_UltradianOscillation"

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 18th 2011 at 10:36 a. m. and last time modified at April eighth 2016 at 5:10 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	1
species types	0	species	6
events	0	constraints	0
reactions	0	function definitions	0
global parameters	13	unit definitions	0
rules	11	initial assignments	0

Model Notes

This a model from the article:
Computer model for mechanisms underlying ultradian oscillations of insulin and glucose.
Sturis J, Polonsky KS, Mosekilde E, Van Cauter E. Am J Physiol.1991 May;260(5 Pt 1):E801-9. 2035636,
Abstract:
Oscillations in human insulin secretion have been observed in two distinct period ranges, 10-15

[1]EMBL-EBI, ajmera@ebi.ac.uk

min (i.e. rapid) and 100-150 min (i.e., ultradian). The cause of the ultradian oscillations remains to be elucidated. To determine whether the oscillations could result from the feedback loops between insulin and glucose, a parsimonious mathematical model including the major mechanisms involved in glucose regulation was developed. This model comprises two major negative feedback loops describing the effects of insulin on glucose utilization and glucose production, respectively, and both loops include the stimulatory effect of glucose on insulin secretion. Model formulations and parameters are representative of results from published clinical investigations. The occurrence of sustained insulin and glucose oscillations was found to be dependent on two essential features: 1) a time delay of 30-45 min for the effect of insulin on glucose production and 2) a sluggish effect of insulin on glucose utilization, because insulin acts from a compartment remote from plasma. When these characteristics were incorporated in the model, numerical simulations mimicked all experimental findings so far observed for these ultradian oscillations, including 1) self-sustained oscillations during constant glucose infusion at various rates; 2) damped oscillations after meal or oral glucose ingestion; 3) increased amplitude of oscillation after increased stimulation of insulin secretion, without change in frequency; and 4) slight advance of the glucose oscillation compared with the insulin oscillation.(ABSTRACT TRUNCATED AT 250 WORDS)

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 six 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
x	x	compartment1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
y	y	compartment1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
z	z	compartment1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
h1	h1	compartment1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
h2	h2	compartment1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
h3	h3	compartment1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 13 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
f1	f1	0000375	0.00		☐
f2	f2	0000375	0.00		☐
f3	f3	0000375	0.00		☐
f4	f4	0000375	0.00		☐
f5	f5	0000393	0.00		☐
v1	v1	0000468	3.00		☑
v2	v2	0000468	11.00		☑
v3	v3	0000468	10.00		☑
t1	t1	0000225	6.00		☑
t2	t2	0000225	100.00		☑
t3	t3	0000225	36.00		☑
I	I	0000009	216.00		☑
E	E	0000009	0.21		☑

6 Rules

This is an overview of eleven rules.

6.1 Rule x

Rule x is a rate rule for species x:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{x} = \mathrm{f1} - \mathrm{E} \cdot \left(\frac{[\mathrm{x}]}{\mathrm{v1}} - \frac{[\mathrm{y}]}{\mathrm{v2}}\right) - \frac{[\mathrm{x}]}{\mathrm{t1}} \tag{1}$$

6.2 Rule y

Rule y is a rate rule for species y:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{y} = \mathrm{E} \cdot \left(\frac{[\mathrm{x}]}{\mathrm{v1}} - \frac{[\mathrm{y}]}{\mathrm{v2}}\right) - \frac{[\mathrm{y}]}{\mathrm{t2}} \tag{2}$$

6.3 Rule z

Rule z is a rate rule for species z:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{z} = \mathrm{f5} + \mathrm{I} - \mathrm{f2} - \mathrm{f3} \cdot \mathrm{f4} \tag{3}$$

6.4 Rule `h1`

Rule `h1` is a rate rule for species `h1`:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{h1} = \frac{3 \cdot ([\mathrm{x}] - [\mathrm{h1}])}{\mathrm{t3}} \tag{4}$$

6.5 Rule `h2`

Rule `h2` is a rate rule for species `h2`:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{h2} = \frac{3 \cdot ([\mathrm{h1}] - [\mathrm{h2}])}{\mathrm{t3}} \tag{5}$$

6.6 Rule `h3`

Rule `h3` is a rate rule for species `h3`:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{h3} = \frac{3 \cdot ([\mathrm{h2}] - [\mathrm{h3}])}{\mathrm{t3}} \tag{6}$$

6.7 Rule `f1`

Rule `f1` is an assignment rule for parameter `f1`:

$$\mathrm{f1} = \frac{209}{1 + \exp\left(\frac{[\mathrm{z}]}{300 \cdot \mathrm{v3}} + 6.6\right)} \tag{7}$$

6.8 Rule `f2`

Rule `f2` is an assignment rule for parameter `f2`:

$$\mathrm{f2} = 72 \cdot \left(1 - \exp\left(\frac{[\mathrm{z}]}{144} \cdot \mathrm{v3}\right)\right) \tag{8}$$

6.9 Rule `f3`

Rule `f3` is an assignment rule for parameter `f3`:

$$\mathrm{f3} = \frac{0.01 \cdot [\mathrm{z}]}{\mathrm{v3}} \tag{9}$$

6.10 Rule `f5`

Rule `f5` is an assignment rule for parameter `f5`:

$$\mathrm{f5} = \frac{180}{1 + \exp\left(\frac{0.29 \cdot [\mathrm{h3}]}{\mathrm{v1}} - 7.5\right)} \tag{10}$$

6.11 Rule `f4`

Rule `f4` is an assignment rule for parameter `f4`:

$$f4 = \frac{90}{1 + \exp\left(-1.772 \cdot \left([y] \cdot \left(\frac{1}{v2} + \frac{1}{E \cdot t2}\right)\right) + 7.76\right)} + 4 \tag{11}$$

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 `x`

Name x

Initial amount 90 mol

Involved in rule `x`

One rule which determines this species' quantity.

7.2 Species `y`

Name y

Initial amount 180 mol

Involved in rule `y`

One rule which determines this species' quantity.

7.3 Species `z`

Name z

Initial amount 13000 mol

Involved in rule `z`

One rule which determines this species' quantity.

7.4 Species `h1`

Name h1

SBO:0000225 delay

Initial amount 70 mol

Involved in rule `h1`

One rule which determines this species' quantity.

7.5 Species `h2`

Name h2

SBO:0000225 delay

Initial amount 70 mol

Involved in rule `h2`

One rule which determines this species' quantity.

7.6 Species `h3`

Name h3

SBO:0000225 delay

Initial amount 70 mol

Involved in rule `h3`

One rule which determines this species' quantity.

A Glossary of Systems Biology Ontology Terms

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

SBO:0000225 **delay:** Time during which some action is awaited

SBO:0000375 **process:** A sequential series of actions, motions, or occurrences, such as chemical reactions, that affect one or more entities in a phenomenologically characteristic manner

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

SBO:0000468 **volume:** A quantity representing the three-dimensional space occupied by all or part of an object

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.

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany