# **SBML Model Report**

# Model name: "Sedaghat2002-InsulinSignalling\_noFeedback"



May 6, 2016

#### 1 General Overview

This is a document in SBML Level 2 Version 1 format. This model was created by Harish Dharuri<sup>1</sup> at August sixth 2007 at 3:09 p.m. and last time modified at October tenth 2014 at 10:25 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	2
species types	0	species	21
events	3	constraints	0
reactions	20	function definitions	0
global parameters	40	unit definitions	2
rules	6	initial assignments	0

#### **Model Notes**

Model reproduces the various plots in Figure 6 and 7 of the paper. It was successfully tested on MathSBML.

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

#### 2.1 Unit substance

Name femtomole

**Definition** fmol

#### 2.2 Unit time

Name minute

**Definition** 60 s

#### 2.3 Unit volume

**Notes** Litre is the predefined SBML unit for volume.

**Definition** 1

#### 2.4 Unit area

**Notes** Square metre is the predefined SBML unit for area since SBML Level 2 Version 1.

**Definition** m<sup>2</sup>

#### 2.5 Unit length

**Notes** Metre is the predefined SBML unit for length since SBML Level 2 Version 1.

**Definition** m

# 3 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
CellSurface			3	1	litre	Ø	
Intracellular			3	1	litre		CellSurface

# 3.1 Compartment CellSurface

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

# 3.2 Compartment Intracellular

This is a three dimensional compartment with a constant size of one litre, which is surrounded by CellSurface.

# 4 Species

This model contains 21 species. Section 9 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
x1	Insulin	CellSurface	$fmol \cdot l^{-1}$		
x2	Unbound Insulin Receptor	CellSurface	$\mathrm{fmol}\cdot\mathrm{l}^{-1}$		
x3	Unphosphorylated once bound receptor	CellSurface	$fmol \cdot l^{-1}$		$\Box$
x5	Phosphorylated once bound receptor	CellSurface	$fmol \cdot l^{-1}$		$\Box$
x4	Phosphorylated twice bound receptor	CellSurface	$fmol \cdot l^{-1}$		$\Box$
x6	Unbound unphosphorylated intracellular receptor	Intracellular	$fmol \cdot l^{-1}$		
x7	Phosphorylated twice bound intracellular receptor	Intracellular	$\operatorname{fmol} \cdot l^{-1}$		
x8	Phosphorylated once bound intracellular receptor	Intracellular	$\operatorname{fmol} \cdot l^{-1}$		
x9	Unphosphorylated IRS1	Intracellular	$fmol \cdot l^{-1}$		
x10	Phosphorylated IRS1	Intracellular	$fmol \cdot l^{-1}$		$\Box$
x11	PI3 Kinase	Intracellular	$fmol \cdot l^{-1}$		$\Box$
x12	IRS1- PI3 Kinase Complex	Intracellular	$fmol \cdot l^{-1}$		$\Box$
x13	PI3,4,5P3	Intracellular	$\mathrm{fmol}\cdot\mathrm{l}^{-1}$		$\Box$
x14	PI4,5P2	Intracellular	$fmol \cdot l^{-1}$		$\Box$
x15	PI3,4P2	Intracellular	$fmol \cdot l^{-1}$		$\Box$
x16	Unactivated Akt	Intracellular	$fmol \cdot l^{-1}$		$\Box$
x17	Activated Akt	Intracellular	$fmol \cdot l^{-1}$		
x18	Unactivated PKC	Intracellular	$\mathrm{fmol}\cdot\mathrm{l}^{-1}$		
x19	Activated PKC	Intracellular	$\mathrm{fmol}\cdot\mathrm{l}^{-1}$		

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Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
x20	Intracellular GLUT4	Intracellular	$fmol \cdot l^{-1}$		
x21	Cell surface GLUT4	CellSurface	$fmol \cdot l^{-1}$	$\Box$	

# **5 Parameters**

This model contains 40 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1			6 · 10	-8	Ø
kminus1			0.200		<b>Z</b>
k2			6 · 10	-8	<b>Z</b>
kminus2			20.000		$\overline{\mathbf{Z}}$
k3			2500.000		$\overline{\mathbf{Z}}$
kminus3			0.200		$\overline{\mathbf{Z}}$
k4		3	3.3333334 · 10	-4	
kminus4			0.003		
k4prime			0.002		
kminus4prime	:		$2.1 \cdot 10^{-1}$	-4	$\checkmark$
k5			0.000		
kminus5			$1.67 \cdot 10^{-1}$	18	$\square$
k6			0.461		
k7			4.160		$\square$
kminus7			1.396		$\square$
k8			$7.06 \cdot 10^{-1}$	-4	$\checkmark$
kminus8			10.000		$\checkmark$
k9			0.000		$\Box$
k9-			1.390		$\checkmark$
$\_\mathtt{stimulated}$					
k9_basal			0.131		$\square$
kminus9			42.150		$\square$
k10			2.961		$\square$
kminus10			2.770		$\square$
k11			0.000		
kminus11			6.932		<b>☑</b> ⊟
k12			0.000		
kminus12			6.932		$\mathbf{Z}_{\underline{\cdot}}$
k13			0.007		$\mathbf{Z}_{\underline{i}}$
kminus13			0.167		
k13prime			0.000		
k14			0.111		Z
kminus14			0.001		<b>⊉</b> ⊟
Effect			0.000		
IRp			897.000		$\mathbf{Z}$
SHIP			1.000		$\overline{\mathbf{Z}}$
PTEN			1.000		

Id	Name	SBO	Value	Unit	Constant
PTP			1.000		
APequil			9.091		
PI3K			5.000		
x4x5			0.000		

# 6 Rules

This is an overview of six rules.

### **6.1 Rule** k9

Rule k9 is an assignment rule for parameter k9:

$$k9 = (k9\_stimulated + k9\_basal) \cdot \frac{[x12]}{PI3K} + k9\_basal$$
 (1)

#### **6.2 Rule k11**

Rule k11 is an assignment rule for parameter k11:

$$k11 = \frac{0.1 \cdot kminus11 \cdot ([x13] - 0.31)}{3.1 - 0.31}$$
 (2)

## **6.3 Rule** k12

Rule k12 is an assignment rule for parameter k12:

$$k12 = \frac{0.1 \cdot \text{kminus} 12 \cdot ([x13] - 0.31)}{3.1 - 0.31}$$
(3)

#### 6.4 Rule Effect

Rule Effect is an assignment rule for parameter Effect:

$$Effect = \frac{0.2 \cdot [x17] + 0.8 \cdot [x19]}{APequil}$$
(4)

# 6.5 Rule k13prime

Rule k13prime is an assignment rule for parameter k13prime:

$$k13prime = \left(\frac{40}{60} - \frac{4}{96}\right) \cdot kminus13 \cdot Effect \tag{5}$$

## **6.6 Rule** x4x5

Rule x4x5 is an assignment rule for parameter x4x5:

$$x4x5 = [x4] + [x5] \tag{6}$$

**Derived unit**  $fmol \cdot l^{-1}$ 

## 7 Events

This is an overview of three events. Each event is initiated whenever its trigger condition switches from false to true. A delay function postpones the effects of an event to a later time point. At the time of execution, an event can assign values to species, parameters or compartments if these are not set to constant.

#### **7.1 Event** event\_0000001

**Notes** When time is greater than or equal to 15 minutes Insulin input is set to zero

$$t \ge 15 \tag{7}$$

$$x1 = 0 \tag{8}$$

#### **7.2 Event** event\_0000002

**Notes** This is the condition to assign values to k5 as given in the appendix

## **Trigger condition**

$$[x6] + [x7] + [x8] > 100 (9)$$

**Assignment** 

$$k5 = 0.0167$$
 (10)

#### **7.3 Event** event\_0000003

#### **Trigger condition**

$$[x6] + [x7] + [x8] \le 100 \tag{11}$$

**Assignment** 

$$k5 = 0.1002$$
 (12)

10

# 8 Reactions

This model contains 20 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

N⁰	Id	Name	Reaction Equation	SBO
1	R1	Insulin binding	$x2 \stackrel{x1}{\rightleftharpoons} x3$	
2	R2	Receptor Autophosphorylation	$x3 \longrightarrow x5$	
3	R3	Insulin Binding	$x5 \rightleftharpoons x4$	
4	R4	Receptor dephosphorylation	$x5 \longrightarrow x2$	
5	R5	Receptor endocytosis	x2 <u>←</u> x6	
6	R6	Receptor transport	x4 <u>←</u> x7	
7	R7	Receptor transport	x5 <u></u>	
8	R8	Receptor synthesis	$\emptyset \longrightarrow x6$	
9	R9	Receptor degradation	$x6 \longrightarrow \emptyset$	
10	R10	Intracellular receptor dephosphorylation	$x7 \longrightarrow x6$	
11	R11	Intracellular receptor dephosphorylation	$x8 \longrightarrow x6$	
12	R12	IRS1 activation	$x9 \stackrel{x4, x5}{\rightleftharpoons} x10$	
13	R13	IRS1-PI3K complex formation	$x11 + x10 \Longrightarrow x12$	
14	R14	PI 3,4,5 P3 generation	x14 <u></u>	
15	R15	PI 3,4,5P3 generation	x15 <del>←</del> x13	
16	R16	Akt activation	x16 <del>←</del> x17	
17	R17	PKC activation	x18 <del>←</del> x19	
18	R18	GLUT4 synthesis	Ø → x20	
19	R19	GLUT4 degradation	$x20 \longrightarrow \emptyset$	
20	R20	GLUT4 translocation	x20 <u>←</u> x21	

#### 8.1 Reaction R1

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Name Insulin binding

## **Reaction equation**

$$x2 \stackrel{x1}{\rightleftharpoons} x3$$
 (13)

#### Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
x2	Unbound Insulin Receptor	

#### **Modifier**

Table 7: Properties of each modifier.

Id	Name	SBO
x1	Insulin	

#### **Product**

Table 8: Properties of each product.

Id	Name	SBO
х3	Unphosphorylated once bound receptor	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_1 = \text{vol}\left(\text{CellSurface}\right) \cdot \left(\text{k1} \cdot [\text{x1}] \cdot [\text{x2}] - \text{kminus1} \cdot [\text{x3}]\right) \tag{14}$$

#### 8.2 Reaction R2

This is an irreversible reaction of one reactant forming one product.

Name Receptor Autophosphorylation

## **Reaction equation**

$$x3 \longrightarrow x5$$
 (15)

#### Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
х3	Unphosphorylated once bound receptor	

#### **Product**

Table 10: Properties of each product.

Id	Name	SBO
х5	Phosphorylated once bound receptor	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_2 = \text{vol}\left(\text{CellSurface}\right) \cdot \text{k3} \cdot [\text{x3}]$$
 (16)

## 8.3 Reaction R3

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Name Insulin Binding

#### **Reaction equation**

$$x5 \stackrel{x1}{\rightleftharpoons} x4$$
 (17)

## Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
х5	Phosphorylated once bound receptor	

#### **Modifier**

Table 12: Properties of each modifier.

Id	Name	SBO
x1	Insulin	

#### **Product**

Table 13: Properties of each product.

Id	Name	SBO
x4	Phosphorylated twice bound receptor	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_3 = \text{vol}\left(\text{CellSurface}\right) \cdot \text{k2} \cdot [\text{x1}] \cdot [\text{x5}] - \text{kminus2} \cdot [\text{x4}]$$
 (18)

## 8.4 Reaction R4

This is an irreversible reaction of one reactant forming one product.

Name Receptor dephosphorylation

## **Reaction equation**

$$x5 \longrightarrow x2$$
 (19)

#### Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
х5	Phosphorylated once bound receptor	

#### **Product**

Table 15: Properties of each product

	Name	SBO
x2	Unbound Insulin Receptor	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_4 = \text{vol}\left(\text{CellSurface}\right) \cdot \text{kminus} \cdot \text{PTP} \cdot [\text{x5}]$$
 (20)

#### 8.5 Reaction R5

This is a reversible reaction of one reactant forming one product.

Name Receptor endocytosis

## **Reaction equation**

$$x2 \rightleftharpoons x6$$
 (21)

#### Reactant

Table 16: Properties of each reactant.

rable 10. 110perties of each reactant.		
Id	Name	SBO
x2	Unbound Insulin Receptor	

#### **Product**

Table 17: Properties of each product.

Id	Name	SBO
х6	Unbound unphosphorylated intracellular receptor	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_5 = \text{vol}\left(\text{CellSurface}\right) \cdot \left(\text{k4} \cdot [\text{x2}] - \text{kminus4} \cdot [\text{x6}]\right)$$
 (22)

#### 8.6 Reaction R6

This is a reversible reaction of one reactant forming one product.

Name Receptor transport

## **Reaction equation**

$$x4 \rightleftharpoons x7$$
 (23)

#### Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
x4	Phosphorylated twice bound receptor	

#### **Product**

Table 19: Properties of each product.

Id	Name	SBO
x7	Phosphorylated twice bound intracellular receptor	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_6 = \text{vol}\left(\text{CellSurface}\right) \cdot \left(\text{k4prime} \cdot [\text{x4}] - \text{kminus4prime} \cdot [\text{x7}]\right)$$
 (24)

## 8.7 Reaction R7

This is a reversible reaction of one reactant forming one product.

Name Receptor transport

## **Reaction equation**

$$x5 \rightleftharpoons x8$$
 (25)

#### Reactant

Table 20: Properties of each reactant.

	Tueste Zer Freperines er euem reuemann	
Id	Name	SBO
x5	Phosphorylated once bound receptor	

#### **Product**

Table 21: Properties of each product.

Id	Name	SBO
x8	Phosphorylated once bound intracellular receptor	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_7 = \text{vol}\left(\text{CellSurface}\right) \cdot \left(\text{k4prime} \cdot [\text{x5}] - \text{kminus4prime} \cdot [\text{x8}]\right)$$
 (26)

#### 8.8 Reaction R8

This is an irreversible reaction of no reactant forming one product.

Name Receptor synthesis

#### **Reaction equation**

$$\emptyset \longrightarrow x6$$
 (27)

#### **Product**

Table 22: Properties of each product.

	* *	
Id	Name	SBO
х6	Unbound unphosphorylated intracellular recept	or

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_8 = \text{vol}\left(\text{Intracellular}\right) \cdot \text{k5}$$
 (28)

#### 8.9 Reaction R9

This is an irreversible reaction of one reactant forming no product.

Name Receptor degradation

## **Reaction equation**

$$x6 \longrightarrow \emptyset$$
 (29)

#### Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
х6	Unbound unphosphorylated intracellular receptor	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_9 = \text{vol}\left(\text{Intracellular}\right) \cdot \text{kminus5} \cdot [\text{x6}]$$
 (30)

## 8.10 Reaction R10

This is an irreversible reaction of one reactant forming one product.

Name Intracellular receptor dephosphorylation

## **Reaction equation**

$$x7 \longrightarrow x6$$
 (31)

#### Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
x7	Phosphorylated twice bound intracellular receptor	

#### **Product**

Table 25: Properties of each product.

Id	Name	SBO
х6	Unbound unphosphorylated intracellular receptor	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{10} = \text{vol}\left(\text{Intracellular}\right) \cdot \text{k6} \cdot \text{PTP} \cdot [\text{x7}]$$
 (32)

#### 8.11 Reaction R11

This is an irreversible reaction of one reactant forming one product.

Name Intracellular receptor dephosphorylation

## **Reaction equation**

$$x8 \longrightarrow x6$$
 (33)

#### Reactant

Table 26: Properties of each reactant.

Table 20. Hopefules of each reactant.			
Id	Name	SBO	
x8	Phosphorylated once bound intracellular receptor		

#### **Product**

Table 27: Properties of each product.

Id	Name	SBO
х6	Unbound unphosphorylated intracellular receptor	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{11} = \text{vol}\left(\text{Intracellular}\right) \cdot \text{k6} \cdot \text{PTP} \cdot [\text{x8}]$$
 (34)

#### 8.12 Reaction R12

This is a fast reversible reaction of one reactant forming one product influenced by two modifiers.

Name IRS1 activation

## **Reaction equation**

$$x9 \stackrel{x4, x5}{\rightleftharpoons} x10 \tag{35}$$

#### Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
x9	Unphosphorylated IRS1	

#### **Modifiers**

Table 29: Properties of each modifier.

Id	Name	SBO
x4	Phosphorylated twice bound receptor	
x5	Phosphorylated once bound receptor	

## **Product**

Table 30: Properties of each product.

	1 1	
Id	Name	SBO
x10	Phosphorylated IRS1	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{12} = vol\left(Intracellular\right) \cdot \left(\frac{k7 \cdot [x9] \cdot ([x4] + [x5])}{IRp} - kminus7 \cdot PTP \cdot [x10]\right) \tag{36}$$

#### 8.13 Reaction R13

This is a reversible reaction of two reactants forming one product.

## Name IRS1-PI3K complex formation

## **Reaction equation**

$$x11 + x10 \Longrightarrow x12 \tag{37}$$

#### **Reactants**

Table 31: Properties of each reactant.

Id	Name	SBO
x11	PI3 Kinase	
x10	Phosphorylated IRS1	

#### **Product**

Table 32: Properties of each product.

Id	Name	SBO
x12	IRS1- PI3 Kinase Complex	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{13} = \text{vol}\left(\text{Intracellular}\right) \cdot \left(\text{k8} \cdot [\text{x}10] \cdot [\text{x}11] - \text{kminus8} \cdot [\text{x}12]\right) \tag{38}$$

## 8.14 Reaction R14

This is a reversible reaction of one reactant forming one product.

Name PI 3,4,5 P3 generation

## **Reaction equation**

$$x14 \rightleftharpoons x13$$
 (39)

#### Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
x14	PI4,5P2	

### **Product**

Table 34: Properties of each product.

Id	Name	SBO
x13	PI3,4,5P3	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{14} = \text{vol}\left(\text{Intracellular}\right) \cdot \left(\text{k9} \cdot [\text{x}14] - \text{kminus}9 \cdot \text{PTEN} \cdot [\text{x}13]\right)$$
 (40)

#### 8.15 Reaction R15

This is a reversible reaction of one reactant forming one product.

Name PI 3,4,5P3 generation

#### **Reaction equation**

$$x15 \rightleftharpoons x13$$
 (41)

#### Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
x15	PI3,4P2	

## **Product**

Table 36: Properties of each product.

Id	Name	SBO
x13	PI3,4,5P3	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{15} = \text{vol}\left(\text{Intracellular}\right) \cdot \left(\text{k10} \cdot \left[\text{x15}\right] - \text{kminus10} \cdot \text{SHIP} \cdot \left[\text{x13}\right]\right)$$
 (42)

#### 8.16 Reaction R16

This is a reversible reaction of one reactant forming one product.

Name Akt activation

## **Reaction equation**

$$x16 \rightleftharpoons x17$$
 (43)

#### Reactant

Table 37: Properties of each reactant.

Id	Name	SBO
x16	Unactivated Akt	

#### **Product**

Table 38: Properties of each product.

Id	Name	SBO
x17	Activated Akt	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{16} = \text{vol}\left(\text{Intracellular}\right) \cdot \left(\text{k11} \cdot [\text{x16}] - \text{kminus11} \cdot [\text{x17}]\right) \tag{44}$$

## **8.17 Reaction R17**

This is a reversible reaction of one reactant forming one product.

Name PKC activation

## **Reaction equation**

$$x18 \rightleftharpoons x19$$
 (45)

#### Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
x18	Unactivated PKC	

#### **Product**

Table 40: Properties of each product.

Id	Name	SBO
x19	Activated PKC	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{17} = \text{vol}\left(\text{Intracellular}\right) \cdot \left(\text{k12} \cdot [\text{x18}] - \text{kminus12} \cdot [\text{x19}]\right) \tag{46}$$

#### 8.18 Reaction R18

This is an irreversible reaction of no reactant forming one product.

Name GLUT4 synthesis

## **Reaction equation**

$$\emptyset \longrightarrow x20$$
 (47)

#### **Product**

Table 41: Properties of each product.

Id	Name	SBO
x20	Intracellular GLUT4	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{18} = \text{vol}\left(\text{Intracellular}\right) \cdot \text{k14}$$
 (48)

#### 8.19 Reaction R19

This is an irreversible reaction of one reactant forming no product.

Name GLUT4 degradation

## **Reaction equation**

$$x20 \longrightarrow \emptyset \tag{49}$$

#### Reactant

Table 42: Properties of each reactant.

Id	Name	SBO
x20	Intracellular GLUT4	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{19} = \text{vol}\left(\text{Intracellular}\right) \cdot \text{kminus} 14 \cdot [\text{x}20]$$
 (50)

#### 8.20 Reaction R20

This is a reversible reaction of one reactant forming one product.

Name GLUT4 translocation

## **Reaction equation**

$$x20 \rightleftharpoons x21$$
 (51)

#### Reactant

Table 43: Properties of each reactant.

Id	Name	SBO
x20	Intracellular GLUT4	

#### **Product**

Table 44: Properties of each product.

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Id	Name	SBO
x21	Cell surface GLUT4	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{20} = \text{vol}\left(\text{Intracellular}\right) \cdot \left(\left(\text{k13} + \text{k13prime}\right) \cdot \left[\text{x20}\right] - \text{kminus13} \cdot \left[\text{x21}\right]\right) \tag{52}$$

## 9 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.

#### 9.1 Species x1

Name Insulin

Initial concentration  $10^8 \, \text{fmol} \cdot l^{-1}$ 

Involved in event event\_0000001

This species takes part in two reactions (as a modifier in R1, R3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathbf{x}\mathbf{1} = 0\tag{53}$$

Furthermore, one event influences this species' rate of change.

#### 9.2 Species x2

Name Unbound Insulin Receptor

Initial concentration  $900 \text{ fmol} \cdot l^{-1}$ 

This species takes part in three reactions (as a reactant in R1, R5 and as a product in R4).

$$\frac{\mathrm{d}}{\mathrm{d}t}x2 = |v_4| - |v_1| - |v_5| \tag{54}$$

#### 9.3 Species x3

Name Unphosphorylated once bound receptor

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

This species takes part in two reactions (as a reactant in R2 and as a product in R1).

$$\frac{\mathrm{d}}{\mathrm{d}t}x3 = |v_1| - |v_2| \tag{55}$$

## 9.4 Species x5

Name Phosphorylated once bound receptor

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

This species takes part in five reactions (as a reactant in R3, R4, R7 and as a product in R2 and as a modifier in R12).

$$\frac{d}{dt}x5 = |v_2| - |v_3| - |v_4| - |v_7| \tag{56}$$

#### 9.5 Species x4

Name Phosphorylated twice bound receptor

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

This species takes part in three reactions (as a reactant in R6 and as a product in R3 and as a modifier in R12).

$$\frac{\mathrm{d}}{\mathrm{d}t}x4 = v_3 - v_6 \tag{57}$$

## 9.6 Species x6

Name Unbound unphosphorylated intracellular receptor

Initial concentration  $100 \, \text{fmol} \cdot l^{-1}$ 

This species takes part in five reactions (as a reactant in R9 and as a product in R5, R8, R10, R11).

$$\frac{\mathrm{d}}{\mathrm{d}t}x6 = |v_5| + |v_8| + |v_{10}| + |v_{11}| - |v_9| \tag{58}$$

#### 9.7 Species x7

Name Phosphorylated twice bound intracellular receptor

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

This species takes part in two reactions (as a reactant in R10 and as a product in R6).

$$\frac{d}{dt}x7 = |v_6| - |v_{10}| \tag{59}$$

## 9.8 Species x8

Name Phosphorylated once bound intracellular receptor

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

This species takes part in two reactions (as a reactant in R11 and as a product in R7).

$$\frac{\mathrm{d}}{\mathrm{d}t}x8 = v_7 - v_{11} \tag{60}$$

## 9.9 Species x9

Name Unphosphorylated IRS1

Initial concentration  $1000 \, \mathrm{fmol} \cdot l^{-1}$ 

This species takes part in one reaction (as a reactant in R12).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathbf{x}9 = -v_{12} \tag{61}$$

### **9.10 Species** x10

Name Phosphorylated IRS1

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

This species takes part in two reactions (as a reactant in R13 and as a product in R12).

$$\frac{d}{dt}x10 = |v_{12}| - |v_{13}| \tag{62}$$

## **9.11 Species** x11

Name PI3 Kinase

Initial concentration  $100 \text{ fmol} \cdot l^{-1}$ 

This species takes part in one reaction (as a reactant in R13).

$$\frac{d}{dt}x11 = -v_{13} \tag{63}$$

## **9.12 Species** x12

Name IRS1- PI3 Kinase Complex

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

This species takes part in one reaction (as a product in R13).

$$\frac{\mathrm{d}}{\mathrm{d}t}x12 = v_{13} \tag{64}$$

## **9.13 Species** x13

Name PI3,4,5P3

Initial concentration  $0.31 \; \mathrm{fmol} \cdot l^{-1}$ 

This species takes part in two reactions (as a product in R14, R15).

$$\frac{\mathrm{d}}{\mathrm{d}t}x13 = |v_{14}| + |v_{15}| \tag{65}$$

## **9.14 Species** x14

Name PI4,5P2

Initial concentration  $99.4 \text{ fmol} \cdot l^{-1}$ 

This species takes part in one reaction (as a reactant in R14).

$$\frac{\mathrm{d}}{\mathrm{d}t}x14 = -v_{14} \tag{66}$$

### **9.15 Species** x15

Name PI3,4P2

Initial concentration  $0.29 \text{ fmol} \cdot l^{-1}$ 

This species takes part in one reaction (as a reactant in R15).

$$\frac{\mathrm{d}}{\mathrm{d}t}x15 = -v_{15} \tag{67}$$

## **9.16 Species** x16

Name Unactivated Akt

Initial concentration  $100 \text{ fmol} \cdot l^{-1}$ 

This species takes part in one reaction (as a reactant in R16).

$$\frac{d}{dt}x16 = -v_{16} \tag{68}$$

#### **9.17 Species** x17

Name Activated Akt

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

This species takes part in one reaction (as a product in R16).

$$\frac{\mathrm{d}}{\mathrm{d}t}x17 = v_{16} \tag{69}$$

## **9.18 Species** x18

Name Unactivated PKC

Initial concentration  $100 \text{ fmol} \cdot l^{-1}$ 

This species takes part in one reaction (as a reactant in R17).

$$\frac{\mathrm{d}}{\mathrm{d}t}x18 = -v_{17} \tag{70}$$

## **9.19 Species** x19

Name Activated PKC

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

This species takes part in one reaction (as a product in R17).

$$\frac{\mathrm{d}}{\mathrm{d}t}x19 = v_{17} \tag{71}$$

## **9.20 Species** x20

Name Intracellular GLUT4

Initial concentration  $96 \text{ fmol} \cdot l^{-1}$ 

This species takes part in three reactions (as a reactant in R19, R20 and as a product in R18).

$$\frac{\mathrm{d}}{\mathrm{d}t}x20 = |v_{18}| - |v_{19}| - |v_{20}| \tag{72}$$

## **9.21 Species** x21

Name Cell surface GLUT4

Initial concentration  $4 \text{ fmol} \cdot 1^{-1}$ 

This species takes part in one reaction (as a product in R20).

$$\frac{\mathrm{d}}{\mathrm{d}t}x21 = v_{20} \tag{73}$$

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