SBML Model Report

Model name: "Brannmark2010-_InsulinSignalling_Mifamodel"

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 14th 2011 at 2:54 p. m. and last time modified at April eighth 2016 at 5:01 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	26
events	0	constraints	0
reactions	0	function definitions	0
global parameters	19	unit definitions	0
rules	25	initial assignments	0

Model Notes

This model is from the article:
Mass and information feedbacks through receptor endocytosis govern insulin signaling as revealed using a parameter-free modeling framework.
Brannmark C, Palmer R, Glad ST, Cedersund G, Stralfors P. J Biol Chem.2010 Jun 25;285(26):20171-9. 20421297,

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Abstract:
Insulin and other hormones control target cells through a network of signal-mediating molecules. Such networks are extremely complex due to multiple feedback loops in combination with redundancy, shared signal mediators, and cross-talk between signal pathways. We present a novel framework that integrates experimental work and mathematical modeling to quantitatively characterize the role and relation between co-existing submechanisms in complex signaling networks. The approach is independent of knowing or uniquely estimating model parameters because it only relies on (i) rejections and (ii) core predictions (uniquely identified properties in unidentifiable models). The power of our approach is demonstrated through numerous iterations between experiments, model-based data analyses, and theoretical predictions to characterize the relative role of co-existing feedbacks governing insulin signaling. We examined phosphorylation of the insulin receptor and insulin receptor substrate-1 and endocytosis of the receptor in response to various different experimental perturbations in primary human adipocytes. The analysis revealed that receptor endocytosis is necessary for two identified feedback mechanisms involving mass and information transfer, respectively. Experimental findings indicate that interfering with the feedback may substantially increase overall signaling strength, suggesting novel therapeutic targets for insulin resistance and type 2 diabetes. Because the central observations are present in other signaling networks, our results may indicate a general mechanism in hormonal control.

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
`compartment_0000001`	compartemnt 1		3	1	litre	☑	

3.1 Compartment `compartment_0000001`

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

Name compartemnt 1

4 Species

This model contains 26 species. The boundary condition of 25 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
IR	IR	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
IRins	IRins	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
IRp	IRp	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
IRip	IRip	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
IRi	IRi	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
IRS	IRS	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
IRSip	IRSip	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
X	X	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
Xp	Xp	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
V1a	V1a	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
V1b	V1b	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
V1c	V1c	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
V1d	V1d	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
V1e	V1e	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
V1g	V1g	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
V1r	v1r	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
V2	V2	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
Vm2	Vm2	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
V3	V3	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
Vm3	Vm3	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
simXP	simXp	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
intamount	intamount	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
measIRp	measIRp	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
measdoublestep	measdoublestep	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
measanna	measanna	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
measdosR	measdosR	compartment_0000001	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑

5 Parameters

This model contains 19 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1a	k1a	0000009	0.389		☑
k1abasic	k1abasic	0000009	0.012		☑
k1b	k1b	0000009	0.020		☑
k1e	k1e	0000009	$4.38334 \cdot 10^{-5}$		☑
k1f	k1f	0000009	20.073		☑
k1g	k1g	0000009	286.699		☑
k1r	k1r	0000009	3.633		☑
k21	k21	0000009	1.672		☑
k22	k22	0000009	0.036		☑
km2	km2	0000009	32.594		☑
k3	k3	0000009	1.629		☑
km3	km3	0000009	0.113		☑
ky1	ky1	0000009	152.963		☑
ky2	ky2	0000009	8936.220		☑
kyanna	kyanna	0000009	16760.120		☑
kyDosR	kyDosR	0000009	13740.432		☑
ins	ins	0000196	100.000		☑
k1c	k1c	0000009	0.364		☑
k1d	k1d	0000009	1580.678		☑

6 Rules

This is an overview of 25 rules.

6.1 Rule measanna

Rule measanna is an assignment rule for species measanna:

$$\text{measanna} = \text{kyanna} \cdot [\text{IRSip}] \tag{1}$$

6.2 Rule measdosR

Rule measdosR is an assignment rule for species measdosR:

$$\text{measdosR} = \text{kyDosR} \cdot [\text{IRSip}] \tag{2}$$

6.3 Rule `measdoublestep`

Rule `measdoublestep` is an assignment rule for species `measdoublestep`:

$$\mathrm{measdoublestep} = \mathrm{ky2} \cdot [\mathrm{IRSip}] \tag{3}$$

6.4 Rule `V1a`

Rule `V1a` is an assignment rule for species `V1a`:

$$\mathrm{V1a} = \mathrm{k1a} \cdot \mathrm{ins} \cdot [\mathrm{IR}] + \mathrm{k1abasic} \cdot [\mathrm{IR}] \tag{4}$$

6.5 Rule `V1b`

Rule `V1b` is an assignment rule for species `V1b`:

$$\mathrm{V1b} = \mathrm{k1b} \cdot [\mathrm{IRins}] \tag{5}$$

6.6 Rule `V1c`

Rule `V1c` is an assignment rule for species `V1c`:

$$\mathrm{V1c} = \mathrm{k1c} \cdot [\mathrm{IRins}] \tag{6}$$

6.7 Rule `V1d`

Rule `V1d` is an assignment rule for species `V1d`:

$$\mathrm{V1d} = \mathrm{k1d} \cdot [\mathrm{IRp}] \tag{7}$$

6.8 Rule `V1e`

Rule `V1e` is an assignment rule for species `V1e`:

$$\mathrm{V1e} = [\mathrm{IRip}] \cdot \left(\mathrm{k1e} + \frac{\mathrm{k1f} \cdot [\mathrm{Xp}]}{1 + [\mathrm{Xp}]}\right) \tag{8}$$

6.9 Rule `V1g`

Rule `V1g` is an assignment rule for species `V1g`:

$$\mathrm{V1g} = \mathrm{k1g} \cdot [\mathrm{IRp}] \tag{9}$$

6.10 Rule `V1r`

Rule `V1r` is an assignment rule for species `V1r`:

$$\mathrm{V1r} = \mathrm{k1r} \cdot [\mathrm{IRi}] \tag{10}$$

6.11 Rule V2

Rule V2 is an assignment rule for species V2:

$$V2 = k21 \cdot ([IRp] + k22 \cdot [IRip]) \cdot [IRS] \tag{11}$$

6.12 Rule Vm2

Rule Vm2 is an assignment rule for species Vm2:

$$Vm2 = km2 \cdot [IRSip] \tag{12}$$

6.13 Rule V3

Rule V3 is an assignment rule for species V3:

$$V3 = k3 \cdot [X] \cdot [IRSip] \tag{13}$$

6.14 Rule Vm3

Rule Vm3 is an assignment rule for species Vm3:

$$Vm3 = km3 \cdot [Xp] \tag{14}$$

6.15 Rule simXP

Rule simXP is an assignment rule for species simXP:

$$simXP = [Xp] \tag{15}$$

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

6.16 Rule intamount

Rule intamount is an assignment rule for species intamount:

$$intamount = \frac{[IRi] + [IRip]}{10} \tag{16}$$

6.17 Rule IR

Rule IR is a rate rule for species IR:

$$\frac{\mathrm{d}}{\mathrm{d}t} IR = [V1a] + [V1b] + [V1r] + [V1g] \tag{17}$$

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

6.18 Rule IRins

Rule IRins is a rate rule for species IRins:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRins} = [\mathrm{V1a}] - [\mathrm{V1b}] - [\mathrm{V1c}] \tag{18}$$

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

6.19 Rule IRp

Rule IRp is a rate rule for species IRp:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRp} = [\mathrm{V1c}] - [\mathrm{V1d}] - [\mathrm{V1g}] \tag{19}$$

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

6.20 Rule IRip

Rule IRip is a rate rule for species IRip:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRip} = [\mathrm{V1d}] - [\mathrm{V1e}] \tag{20}$$

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

6.21 Rule IRi

Rule IRi is a rate rule for species IRi:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRi} = [\mathrm{V1e}] - [\mathrm{V1r}] \tag{21}$$

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

6.22 Rule IRS

Rule IRS is a rate rule for species IRS:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRS} = [\mathrm{V2}] + [\mathrm{Vm2}] \tag{22}$$

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

6.23 Rule IRSip

Rule IRSip is a rate rule for species IRSip:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IRSip} = [\mathrm{V2}] - [\mathrm{Vm2}] \tag{23}$$

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

6.24 Rule X

Rule X is a rate rule for species X:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{X} = [\mathrm{V3}] + [\mathrm{Vm3}] \tag{24}$$

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

6.25 Rule Xp

Rule Xp is a rate rule for species Xp:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Xp} = [\mathrm{V3}] - [\mathrm{Vm3}] \tag{25}$$

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

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 IR

Name IR

SBO:0000244 receptor

Initial amount 10 mol

Involved in rule IR

One rule determines the species' quantity.

7.2 Species IRins

Name IRins

SBO:0000240 material entity

Initial amount 0 mol

Involved in rule IRins

One rule determines the species' quantity.

7.3 Species IRp

Name IRp

SBO:0000240 material entity

Initial amount 0 mol

Involved in rule IRp

One rule determines the species' quantity.

7.4 Species IRip

Name IRip

SBO:0000240 material entity

Initial amount 0 mol

Involved in rule IRip

One rule determines the species' quantity.

7.5 Species IRi

Name IRi

SBO:0000240 material entity

Initial amount 0 mol

Involved in rule IRi

One rule determines the species' quantity.

7.6 Species IRS

Name IRS

SBO:0000240 material entity

Initial concentration $10 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule IRS

One rule determines the species' quantity.

7.7 Species IRSip

Name IRSip

SBO:0000240 material entity

Initial amount 0 mol

Involved in rule IRSip

One rule determines the species' quantity.

7.8 Species X

Name X

SBO:0000240 material entity

Initial amount 10 mol

Involved in rule X

One rule determines the species' quantity.

7.9 Species Xp

Name Xp

SBO:0000240 material entity

Initial amount 0 mol

Involved in rule Xp

One rule determines the species' quantity.

7.10 Species V1a

Name V1a

Initial concentration $389.41271264 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule V1a

One rule determines the species' quantity.

7.11 Species `V1b`

Name V1b

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

Involved in rule `V1b`

One rule determines the species' quantity.

7.12 Species `V1c`

Name V1c

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

Involved in rule `V1c`

One rule determines the species' quantity.

7.13 Species `V1d`

Name V1d

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

Involved in rule `V1d`

One rule determines the species' quantity.

7.14 Species `V1e`

Name V1e

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

Involved in rule `V1e`

One rule determines the species' quantity.

7.15 Species `V1g`

Name V1g

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

Involved in rule `V1g`

One rule determines the species' quantity.

7.16 Species `V1r`

Name v1r

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

Involved in rule `V1r`

One rule determines the species' quantity.

7.17 Species `V2`

Name V2

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

Involved in rule `V2`

One rule determines the species' quantity.

7.18 Species `Vm2`

Name Vm2

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

Involved in rule `Vm2`

One rule determines the species' quantity.

7.19 Species `V3`

Name V3

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

Involved in rule `V3`

One rule determines the species' quantity.

7.20 Species `Vm3`

Name Vm3

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

Involved in rule `Vm3`

One rule determines the species' quantity.

7.21 Species `simXP`

Name simXp

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

Involved in rule `simXP`

One rule determines the species' quantity.

7.22 Species `intamount`

Name intamount

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

Involved in rule `intamount`

One rule determines the species' quantity.

7.23 Species `measIRp`

Name measIRp

SBO:0000196 concentration of an entity pool

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

This species does not take part in any reactions. Its quantity does hence not change over time:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{measIRp} = 0 \tag{26}$$

7.24 Species `measdoublestep`

Name measdoublestep

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

Involved in rule `measdoublestep`

One rule determines the species' quantity.

7.25 Species `measanna`

Name measanna

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

Involved in rule `measanna`

One rule determines the species' quantity.

7.26 Species `measdosR`

Name measdosR

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

Involved in rule `measdosR`

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:0000196 concentration of an entity pool: The amount of an entity per unit of volume.

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

SBO:0000244 receptor: Participating entity that binds to a specific physical entity and initiates the response to that physical entity.The original concept of the receptor was introduced independently at the end of the 19th century by John Newport Langley (1852-1925) and Paul Ehrlich (1854-1915). Langley JN.On the reaction of cells and of nerve-endings to certain poisons, chiefly as regards the reaction of striated muscle to nicotine and to curari. J Physiol. 1905 Dec 30;33(4-5):374-413

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