SBML Model Report

Model name: "Rateitschak2012 - Interferon-gamma (IFN) induced STAT1 signalling (PC_IFNg100)"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by the following three authors: Felix Winter[1], Katja Rateitschak[2] and Vijayalakshmi Chelliah[3] at March 14th 2015 at 8:22 a. m. and last time modified at February 16th 2016 at 12:13 a. 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	28
events	0	constraints	0
reactions	0	function definitions	0
global parameters	22	unit definitions	0
rules	28	initial assignments	0

Model Notes

Rateitschak2012 - Interferon-gamma (IFN) induced STAT1 signalling (PC_IFNg100)

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This model is described in the article:Parameter identifiability and sensitivity analysis predict targets for enhancement of STAT1 activity in pancreatic cancer and stellate cells. Rateitschak K, Winter F, Lange F, Jaster R, Wolkenhauer O. PLoS Comput. Biol. 2012; 8(12): e1002815

Abstract:

The present work exemplifies how parameter identifiability analysis can be used to gain insights into differences in experimental systems and how uncertainty in parameter estimates can be handled. The case study, presented here, investigates interferon-gamma (IFN) induced STAT1 signalling in two cell types that play a key role in pancreatic cancer development: pancreatic stellate and cancer cells. IFN inhibits the growth for both types of cells and may be prototypic of agents that simultaneously hit cancer and stroma cells. We combined time-course experiments with mathematical modelling to focus on the common situation in which variations between profiles of experimental time series, from different cell types, are observed. To understand how biochemical reactions are causing the observed variations, we performed a parameter identifiability analysis. We successfully identified reactions that differ in pancreatic stellate cells and cancer cells, by comparing confidence intervals of parameter value estimates and the variability of model trajectories. Our analysis shows that useful information can also be obtained from nonidentifiable parameters. For the prediction of potential therapeutic targets we studied the consequences of uncertainty in the values of identifiable and nonidentifiable parameters. Interestingly, the sensitivity of model variables is robust against parameter variations and against differences between IFN induced STAT1 signalling in pancreatic stellate and cancer cells. This provides the basis for a prediction of therapeutic targets that are valid for both cell types.

This model is hosted on BioModels Database and identified by: BIOMD0000000585.

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models.

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 28 species. The boundary condition of 28 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
Ifng	Ifng	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
II	II	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
d1	d1	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
d2	d2	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
d3	d3	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
d4	d4	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
Stat1Pd	STAT1D	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
Stat1Pdn	STAT1Dn	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
i1	i1	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
i2	i2	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
i3	i3	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
i4	i4	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
j1	j1	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
j2	j2	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
j3	j3	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
j4	j4	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
Ir	Ir	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
Stat1U	STAT1Uc	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
Stat1Un	STAT1Un	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
mRNA	SOCS1	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
Stat1ex	STAT1 (observed)	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
`Stat1cex`	STAT1c (observed)	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
`Stat1nex`	STAT1n (observed)	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
`Stat1Pex`	STAT1D (observed)	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
`Stat1Pcex`	STAT1Dc (observed)	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
`Stat1Pnex`	STAT1Dn (observed)	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
`Socs1ex`	SOCS1 (observed)	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
`RSNCex`	RSNC (observed)	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑

5 Parameters

This model contains 22 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$9.4915 \cdot 10^{-4}$		☑
k3	k3		0.096		☑
k4	k4		0.100		☑
k5	k5		298.763		☑
k6	k6		0.067		☑
k9	k7		4179.560		☑
k10	k8		0.058		☑
k11	k9		8.902		☑
k12	k10		12.268		☑
k13	k11		0.009		☑
k14	k12		0.748		☑
taud	tau_1		277.363		☑
tau	tau_2		79.335		☑
tauj	tau_3		451.937		☑
scale-_Stat1ex	WB_STAT1		1.000		☑
scale-_Stat1cex	WB_STAT1c		0.748		☑
scale-_Stat1nex	WB_STAT1n		1.219		☑
scale-_Stat1Pex	WB_STAT1D		34.401		☑
scale-_Stat1Pcex	WB_STAT1Dc		19.057		☑
scale-_Stat1Pnex	WB_STAT1Dn		91677.700		☑
scale-_Socs1ex	PCR_SOCS1		1.000		☑
scale_RSNCex	scale_RSNCex		1.000		☑

6 Rules

This is an overview of 28 rules.

6.1 Rule `Stat1cex`

Rule `Stat1cex` is an assignment rule for species `Stat1cex`:

$$\mathrm{Stat1cex} = ([\mathrm{Stat1U}] + [\mathrm{Stat1Pd}]) \cdot \mathrm{scale\_Stat1cex} \tag{1}$$

6.2 Rule `Stat1ex`

Rule `Stat1ex` is an assignment rule for species `Stat1ex`:

$$\mathrm{Stat1ex} = \frac{[\mathrm{Stat1U}] + [\mathrm{Stat1Pd}] + [\mathrm{Stat1Un}] + [\mathrm{Stat1Pdn}]}{2} \tag{2}$$

6.3 Rule `RSNCex`

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

$$\mathrm{RSNCex} = \frac{[\mathrm{Stat1Un}] + [\mathrm{Stat1Pdn}]}{[\mathrm{Stat1U}] + [\mathrm{Stat1Pd}]} \tag{3}$$

Derived unit dimensionless

6.4 Rule `Socs1ex`

Rule `Socs1ex` is an assignment rule for species `Socs1ex`:

$$\mathrm{Socs1ex} = [\mathrm{mRNA}] \tag{4}$$

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

6.5 Rule `Stat1Pnex`

Rule `Stat1Pnex` is an assignment rule for species `Stat1Pnex`:

$$\mathrm{Stat1Pnex} = [\mathrm{Stat1Pdn}] \cdot \mathrm{scale\_Stat1Pnex} \tag{5}$$

6.6 Rule `Stat1Pcex`

Rule `Stat1Pcex` is an assignment rule for species `Stat1Pcex`:

$$\mathrm{Stat1Pcex} = [\mathrm{Stat1Pd}] \cdot \mathrm{scale\_Stat1Pcex} \tag{6}$$

6.7 Rule `Stat1Pex`

Rule `Stat1Pex` is an assignment rule for species `Stat1Pex`:

$$\mathrm{Stat1Pex} = \frac{[\mathrm{Stat1Pd}] + [\mathrm{Stat1Pdn}]}{2} \cdot \mathrm{scale\_Stat1Pex} \tag{7}$$

6.8 Rule Stat1nex

Rule Stat1nex is an assignment rule for species Stat1nex:

$$\text{Stat1nex} = ([\text{Stat1Un}] + [\text{Stat1Pdn}]) \cdot \text{scale\_Stat1nex} \tag{8}$$

6.9 Rule Ifng

Rule Ifng is a rate rule for species Ifng:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Ifng} = (\text{k1} \cdot [\text{Ifng}] \cdot [\text{Ir}]) \tag{9}$$

Derived unit $\text{mol}^2 \cdot \text{l}^{-2}$

6.10 Rule II

Rule II is a rate rule for species II:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{II} = \text{k1} \cdot [\text{Ifng}] \cdot [\text{Ir}] \tag{10}$$

6.11 Rule d1

Rule d1 is a rate rule for species d1:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{d1} = \frac{4 \cdot ([\text{II}] - [\text{d1}])}{\text{taud}} \tag{11}$$

6.12 Rule d2

Rule d2 is a rate rule for species d2:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{d2} = \frac{4 \cdot ([\text{d1}] - [\text{d2}])}{\text{taud}} \tag{12}$$

6.13 Rule d3

Rule d3 is a rate rule for species d3:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{d3} = \frac{4 \cdot ([\text{d2}] - [\text{d3}])}{\text{taud}} \tag{13}$$

6.14 Rule d4

Rule d4 is a rate rule for species d4:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{d4} = \frac{4 \cdot ([\text{d3}] - [\text{d4}])}{\text{taud}} \tag{14}$$

6.15 Rule Stat1Pd

Rule Stat1Pd is a rate rule for species Stat1Pd:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Stat1Pd} = \frac{\mathrm{k4} \cdot [\mathrm{II}] \cdot [\mathrm{Stat1U}]}{1 + \mathrm{k14} \cdot [\mathrm{j4}]} - \mathrm{k6} \cdot [\mathrm{Stat1Pd}] \tag{15}$$

6.16 Rule Stat1Pdn

Rule Stat1Pdn is a rate rule for species Stat1Pdn:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Stat1Pdn} = \mathrm{k6} \cdot [\mathrm{Stat1Pd}] - \mathrm{k5} \cdot [\mathrm{Stat1Pdn}] \tag{16}$$

6.17 Rule i1

Rule i1 is a rate rule for species i1:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{i1} = \frac{4 \cdot ([\mathrm{Stat1Pdn}] - [\mathrm{i1}])}{\mathrm{tau}} \tag{17}$$

6.18 Rule i2

Rule i2 is a rate rule for species i2:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{i2} = \frac{4 \cdot ([\mathrm{i1}] - [\mathrm{i2}])}{\mathrm{tau}} \tag{18}$$

6.19 Rule i3

Rule i3 is a rate rule for species i3:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{i3} = \frac{4 \cdot ([\mathrm{i2}] - [\mathrm{i3}])}{\mathrm{tau}} \tag{19}$$

6.20 Rule i4

Rule i4 is a rate rule for species i4:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{i4} = \frac{4 \cdot ([\mathrm{i3}] - [\mathrm{i4}])}{\mathrm{tau}} \tag{20}$$

6.21 Rule j1

Rule j1 is a rate rule for species j1:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{j1} = \frac{4 \cdot ([\mathrm{mRNA}] - [\mathrm{j1}])}{\mathrm{tauj}} \tag{21}$$

6.22 Rule j2

Rule j2 is a rate rule for species j2:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{j2} = \frac{4 \cdot ([\mathrm{j1}] - [\mathrm{j2}])}{\mathrm{tauj}} \tag{22}$$

6.23 Rule j3

Rule j3 is a rate rule for species j3:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{j3} = \frac{4 \cdot ([\mathrm{j2}] - [\mathrm{j3}])}{\mathrm{tauj}} \tag{23}$$

6.24 Rule j4

Rule j4 is a rate rule for species j4:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{j4} = \frac{4 \cdot ([\mathrm{j3}] - [\mathrm{j4}])}{\mathrm{tauj}} \tag{24}$$

6.25 Rule Ir

Rule Ir is a rate rule for species Ir:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ir} = (\mathrm{k1} \cdot [\mathrm{Ifng}] \cdot [\mathrm{Ir}]) \tag{25}$$

Derived unit $\mathrm{mol}^{2} \cdot \mathrm{l}^{-2}$

6.26 Rule Stat1U

Rule Stat1U is a rate rule for species Stat1U:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Stat1U} = \mathrm{k3} \cdot [\mathrm{d4}] + \mathrm{k12} \cdot [\mathrm{Stat1Un}] - \mathrm{k11} \cdot [\mathrm{Stat1U}] - \frac{\mathrm{k4} \cdot [\mathrm{II}] \cdot [\mathrm{Stat1U}]}{1 + \mathrm{k14} \cdot [\mathrm{j4}]} \tag{26}$$

6.27 Rule Stat1Un

Rule Stat1Un is a rate rule for species Stat1Un:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Stat1Un} = \mathrm{k11} \cdot [\mathrm{Stat1U}] - \mathrm{k12} \cdot [\mathrm{Stat1Un}] + \mathrm{k5} \cdot [\mathrm{Stat1Pdn}] \tag{27}$$

6.28 Rule mRNA

Rule mRNA is a rate rule for species mRNA:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mRNA} = \mathrm{k13} + \mathrm{k9} \cdot [\mathrm{i4}] - \mathrm{k10} \cdot [\mathrm{mRNA}] \tag{28}$$

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 Ifng

Name Ifng

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

Involved in rule Ifng

One rule determines the species' quantity.

7.2 Species II

Name II

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

Involved in rule II

One rule determines the species' quantity.

7.3 Species d1

Name d1

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

Involved in rule d1

One rule determines the species' quantity.

7.4 Species d2

Name d2

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

Involved in rule d2

One rule determines the species' quantity.

7.5 Species d3

Name d3

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

Involved in rule d3

One rule determines the species' quantity.

7.6 Species d4

Name d4

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

Involved in rule d4

One rule determines the species' quantity.

7.7 Species Stat1Pd

Name STAT1D

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

Involved in rule Stat1Pd

One rule determines the species' quantity.

7.8 Species Stat1Pdn

Name STAT1Dn

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

Involved in rule Stat1Pdn

One rule determines the species' quantity.

7.9 Species i1

Name i1

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

Involved in rule i1

One rule determines the species' quantity.

7.10 Species i2

Name i2

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

Involved in rule i2

One rule determines the species' quantity.

7.11 Species i3

Name i3

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

Involved in rule i3

One rule determines the species' quantity.

7.12 Species i4

Name i4

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

Involved in rule i4

One rule determines the species' quantity.

7.13 Species j1

Name j1

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

Involved in rule j1

One rule determines the species' quantity.

7.14 Species j2

Name j2

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

Involved in rule j2

One rule determines the species' quantity.

7.15 Species j3

Name j3

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

Involved in rule j3

One rule determines the species' quantity.

7.16 Species j4

Name j4

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

Involved in rule j4

One rule determines the species' quantity.

7.17 Species Ir

Name Ir

Initial concentration $0.05721\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule Ir

One rule determines the species' quantity.

7.18 Species Stat1U

Name STAT1Uc

Initial concentration $0.950418\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule Stat1U

One rule determines the species' quantity.

7.19 Species Stat1Un

Name STAT1Un

Initial concentration $0.661213\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule Stat1Un

One rule determines the species' quantity.

7.20 Species mRNA

Name SOCS1

Initial concentration $0.108325 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule mRNA

One rule determines the species' quantity.

7.21 Species Stat1ex

Name STAT1 (observed)

Initial concentration $0.8058155 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule Stat1ex

One rule determines the species' quantity.

7.22 Species Stat1cex

Name STAT1c (observed)

Initial concentration $0.710624687346 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule Stat1cex

One rule determines the species' quantity.

7.23 Species Stat1nex

Name STAT1n (observed)

Initial concentration $0.80569465263 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule Stat1nex

One rule determines the species' quantity.

7.24 Species Stat1Pex

Name STAT1D (observed)

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

Involved in rule Stat1Pex

One rule determines the species' quantity.

7.25 Species Stat1Pcex

Name STAT1Dc (observed)

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

Involved in rule Stat1Pcex

One rule determines the species' quantity.

7.26 Species Stat1Pnex

Name STAT1Dn (observed)

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

Involved in rule Stat1Pnex

One rule determines the species' quantity.

7.27 Species Socs1ex

Name SOCS1 (observed)

Initial concentration $0.108325\ \text{mol} \cdot \text{l}^{-1}$

Involved in rule Socs1ex

One rule determines the species' quantity.

7.28 Species RSNCex

Name RSNC (observed)

Initial concentration $0.69570757287846\ \text{mol} \cdot \text{l}^{-1}$

Involved in rule RSNCex

One rule determines the species' quantity.

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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