SBML Model Report

Model name: “Boehm2014 - isoform-specific dimerization of pSTAT5A and pSTAT5B”

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Lorenz Adlung[1] and Thawfeek Varusai[2] at February eleventh 2016 at 10:59 a. m. and last time modified at February 25th 2016 at 1:19 p. 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	8
events	0	constraints	0
reactions	9	function definitions	0
global parameters	7	unit definitions	0
rules	0	initial assignments	2

Model Notes

Boehm2014 - isoform-specific dimerization of pSTAT5A and pSTAT5BTo study STAT5 activation, the authors build a dynamic model of pSTAT5 isoform dimerization. Combinatorial binding of pSTAT5A and pSTAT5B is analysed using model hypotheses and concurrent experiments. Model parameters are derived from the experiments on Ba/F3 cells. Results show that

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pSTAT5 heterodimerization hypothesis for STAT5 activation favours experimental results.

This model is described in the article:Identification of isoform-specific dynamics in phosphorylation-dependent STAT5 dimerization by quantitative mass spectrometry and mathematical modelingBoehm ME, Adlung L, Schilling M, Roth S, Klingmller U, Lehmann WDJ Proteome Res. 2014 Dec 5;13(12):5685-94

Abstract:

STAT5A and STAT5B are important transcription factors that dimerize and transduce activation signals of cytokine receptors directly to the nucleus. A typical cytokine that mediates STAT5 activation is erythropoietin (Epo). Differential functions of STAT5A and STAT5B have been reported. However, the extent to which phosphorylated STAT5A and STAT5B (pSTAT5A, pSTAT5B) form homo- or heterodimers is not understood, nor is how this might influence the signal transmission to the nucleus. To study this, we designed a concept to investigate the isoform-specific dimerization behavior of pSTAT5A and pSTAT5B that comprises isoform-specific immunoprecipitation (IP), measurement of the degree of phosphorylation, and isoform ratio determination between STAT5A and STAT5B. For the main analytical method, we employed quantitative label-free and -based mass spectrometry. For the cellular model system, we used Epo receptor (EpoR)-expressing BaF3 cells (BaF3-EpoR) stimulated with Epo. Three hypotheses of dimer formation between pSTAT5A and pSTAT5B were used to explain the analytical results by a static mathematical model: formation of (i) homodimers only, (ii) heterodimers only, and (iii) random formation of homo- and heterodimers. The best agreement between experimental data and model simulations was found for the last case. Dynamics of cytoplasmic STAT5 dimerization could be explained by distinct nuclear import rates and individual nuclear retention for homo- and heterodimers of phosphorylated STAT5.

This model is hosted on BioModels Database and identified by: BIOMD0000000591.

To cite BioModels Database, please use: BioModels: Content, Features, Functionality, and Use..

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 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
cyt		0000290	3	1.4	l	☑	
nuc		0000290	3	0.45	l	☑	

3.1 Compartment cyt

This is a three dimensional compartment with a constant size of 1.4 litre.

SBO:0000290 physical compartment

3.2 Compartment nuc

This is a three dimensional compartment with a constant size of 0.45 litre.

SBO:0000290 physical compartment

4 Species

This model contains eight species. Section 8 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
STAT5A		cyt	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
STAT5B		cyt	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pApB		cyt	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pApA		cyt	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pBpB		cyt	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
nucpApA		nuc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
nucpApB		nuc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
nucpBpB		nuc	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains seven global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Epo-_degradation-_BaF3			0.027		☑
k_exp_hetero			$1.00097114635938 \cdot 10^{-5}$		☑
k_exp_homo			0.006		☑
k_imp_hetero			0.016		☑
k_imp_homo			96807.682		☑
k_phos			15767.647		☑
ratio			0.693		☑

6 Initialassignments

This is an overview of two initialassignments.

6.1 Initialassignment STAT5A

Derived unit contains undeclared units

Math $207.6 \cdot \mathrm{ratio}$

6.2 Initialassignment STAT5B

Derived unit contains undeclared units

Math $207.6 - 207.6 \cdot \mathrm{ratio}$

7 Reactions

This model contains nine 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

№	Id	Name	Reaction Equation	SBO
1	reaction1		$2\,\mathrm{STAT5A} \xrightarrow{\mathrm{STAT5A}} \mathrm{pApA}$	
2	reaction2		$\mathrm{STAT5A} + \mathrm{STAT5B} \xrightarrow{\mathrm{STAT5A,\ STAT5B}} \mathrm{pApB}$	
3	reaction3		$2\,\mathrm{STAT5B} \xrightarrow{\mathrm{STAT5B}} \mathrm{pBpB}$	
4	reaction4		$\mathrm{pApA} \xrightarrow{\mathrm{pApA}} \mathrm{nucpApA}$	
5	reaction5		$\mathrm{pApB} \xrightarrow{\mathrm{pApB}} \mathrm{nucpApB}$	
6	reaction6		$\mathrm{pBpB} \xrightarrow{\mathrm{pBpB}} \mathrm{nucpBpB}$	
7	reaction7		$\mathrm{nucpApA} \xrightarrow{\mathrm{nucpApA}} 2\,\mathrm{STAT5A}$	
8	reaction8		$\mathrm{nucpApB} \xrightarrow{\mathrm{nucpApB}} \mathrm{STAT5A} + \mathrm{STAT5B}$	
9	reaction9		$\mathrm{nucpBpB} \xrightarrow{\mathrm{nucpBpB}} 2\,\mathrm{STAT5B}$	

7.1 Reaction reaction1

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Reaction equation

$$2\,\mathrm{STAT5A} \xrightarrow{\mathrm{STAT5A}} \mathrm{pApA} \tag{1}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
STAT5A		

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
STAT5A		

Product

Table 8: Properties of each product.

Id	Name	SBO
pApA		

Kinetic Law

Derived unit contains undeclared units

$$v_1 = 1.25E-7 \cdot [\mathrm{STAT5A}]^2 \cdot \mathrm{k\_phos} \cdot \exp\left(\mathrm{Epo\_degradation\_BaF3} \cdot \mathrm{time}\right) \tag{2}$$

7.2 Reaction reaction2

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Reaction equation

$$\mathrm{STAT5A} + \mathrm{STAT5B} \xrightarrow{\mathrm{STAT5A,\ STAT5B}} \mathrm{pApB} \tag{3}$$

Reactants

Table 9: Properties of each reactant.

Id	Name	SBO
STAT5A		
STAT5B		

Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
STAT5A		
STAT5B		

Product

Table 11: Properties of each product.

Id	Name	SBO
pApB		

Kinetic Law

Derived unit contains undeclared units

$$v_2 = 1.25E-7 \cdot [\text{STAT5A}] \cdot [\text{STAT5B}] \cdot \text{k\_phos} \cdot \exp\left(\text{Epo\_degradation\_BaF3} \cdot \text{time}\right) \quad (4)$$

7.3 Reaction `reaction3`

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Reaction equation

$$2\,\text{STAT5B} \xrightarrow{\text{STAT5B}} \text{pBpB} \quad (5)$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
STAT5B		

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
STAT5B		

Product

Table 14: Properties of each product.

Id	Name	SBO
pBpB		

Kinetic Law

Derived unit contains undeclared units

$$v_3 = 1.25E-7 \cdot [\text{STAT5B}]^2 \cdot \text{k\_phos} \cdot \exp\left(\text{Epo\_degradation\_BaF3} \cdot \text{time}\right) \tag{6}$$

7.4 Reaction `reaction4`

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Reaction equation

$$\text{pApA} \xrightarrow{\text{pApA}} \text{nucpApA} \tag{7}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
pApA		

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
pApA		

Product

Table 17: Properties of each product.

Id	Name	SBO
nucpApA		

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{k\_imp\_homo} \cdot [\text{pApA}] \tag{8}$$

7.5 Reaction `reaction5`

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Reaction equation

$$\text{pApB} \xrightarrow{\text{pApB}} \text{nucpApB} \tag{9}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
pApB		

Modifier

Table 19: Properties of each modifier.

Id	Name	SBO
pApB		

Id	Name	SBO

Product

Table 20: Properties of each product.

Id	Name	SBO
nucpApB		

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{k\_imp\_hetero} \cdot [\text{pApB}] \tag{10}$$

7.6 Reaction reaction6

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Reaction equation

$$\text{pBpB} \xrightarrow{\text{pBpB}} \text{nucpBpB} \tag{11}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
pBpB		

Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
pBpB		

Product

Table 23: Properties of each product.

Id	Name	SBO
nucpBpB		

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{k\_imp\_homo} \cdot [\text{pBpB}] \tag{12}$$

7.7 Reaction reaction7

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Reaction equation

$$\text{nucpApA} \xrightarrow{\text{nucpApA}} 2\,\text{STAT5A} \tag{13}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
nucpApA		

Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
nucpApA		

Product

Table 26: Properties of each product.

Id	Name	SBO
STAT5A		

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{k\_exp\_homo} \cdot [\text{nucpApA}] \tag{14}$$

7.8 Reaction `reaction8`

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Reaction equation

$$\text{nucpApB} \xrightarrow{\text{nucpApB}} \text{STAT5A} + \text{STAT5B} \tag{15}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
`nucpApB`		

Modifier

Table 28: Properties of each modifier.

Id	Name	SBO
`nucpApB`		

Products

Table 29: Properties of each product.

Id	Name	SBO
`STAT5A`		
`STAT5B`		

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{k\_exp\_hetero} \cdot [\text{nucpApB}] \tag{16}$$

7.9 Reaction `reaction9`

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Reaction equation

$$\text{nucpBpB} \xrightarrow{\text{nucpBpB}} 2\,\text{STAT5B} \tag{17}$$

Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
`nucpBpB`		

Modifier

Table 31: Properties of each modifier.

Id	Name	SBO
`nucpBpB`		

Product

Table 32: Properties of each product.

Id	Name	SBO
`STAT5B`		

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{k\_exp\_homo} \cdot [\text{nucpBpB}] \tag{18}$$

8 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.

8.1 Species `STAT5A`

SBO:0000252 polypeptide chain

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

Initial assignment `STAT5A`

This species takes part in six reactions (as a reactant in `reaction1`, `reaction2` and as a product in `reaction7`, `reaction8` and as a modifier in `reaction1`, `reaction2`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{STAT5A} = 2\,v_7 + v_8 - 2\,v_1 - v_2 \tag{19}$$

8.2 Species `STAT5B`

SBO:0000252 polypeptide chain

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

Initial assignment `STAT5B`

This species takes part in six reactions (as a reactant in `reaction2`, `reaction3` and as a product in `reaction8`, `reaction9` and as a modifier in `reaction2`, `reaction3`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{STAT5B} = v_8 + 2\,v_9 - v_2 - 2\,v_3 \tag{20}$$

8.3 Species `pApB`

SBO:0000609 heterodimer

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

This species takes part in three reactions (as a reactant in `reaction5` and as a product in `reaction2` and as a modifier in `reaction5`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pApB} = v_2 - v_5 \tag{21}$$

8.4 Species pApA

SBO:0000608 homodimer

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

This species takes part in three reactions (as a reactant in reaction4 and as a product in reaction1 and as a modifier in reaction4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pApA} = v_1 - v_4 \tag{22}$$

8.5 Species pBpB

SBO:0000608 homodimer

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

This species takes part in three reactions (as a reactant in reaction6 and as a product in reaction3 and as a modifier in reaction6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pBpB} = v_3 - v_6 \tag{23}$$

8.6 Species nucpApA

SBO:0000608 homodimer

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

This species takes part in three reactions (as a reactant in reaction7 and as a product in reaction4 and as a modifier in reaction7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{nucpApA} = v_4 - v_7 \tag{24}$$

8.7 Species nucpApB

SBO:0000609 heterodimer

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

This species takes part in three reactions (as a reactant in reaction8 and as a product in reaction5 and as a modifier in reaction8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{nucpApB} = v_5 - v_8 \tag{25}$$

8.8 Species nucpBpB

SBO:0000608 homodimer

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

This species takes part in three reactions (as a reactant in reaction9 and as a product in reaction6 and as a modifier in reaction9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{nucpBpB} = v_6 - v_9 \tag{26}$$

A Glossary of Systems Biology Ontology Terms

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:0000290 physical compartment: Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions

SBO:0000608 homodimer: A macromolecular complex composed of precisely two identical monomeric units, which are usually non-covalently bound

SBO:0000609 heterodimer: A macromolecular complex composed of precisely two non-identical monomeric units, which are usually non-covalently bound

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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