SBML Model Report

Model name: “Raia2010_IL13_Signalling_MedB1”

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: Lukas Endler[1] and Marcel Schilling[2] at February 14th 2011 at 3:36 a. m. and last time modified at October nineth 2014 at 5:36 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	16
events	0	constraints	0
reactions	16	function definitions	0
global parameters	18	unit definitions	4
rules	1	initial assignments	0

Model Notes

This is the model of IL13 induced signalling in MedB-1 cell described in the article:
Dynamic Mathematical Modeling of IL13-Induced Signaling in Hodgkin and Primary Mediastinal B-Cell Lymphoma Allows Prediction of Therapeutic Targets.
Raia V, Schilling M, Bhm M, Hahn B, Kowarsch A, Raue A, Sticht C, Bohl S, Saile M, Mller P,

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

[2] German Cancer Research Center, `m.schilling@dkfz.de`

Gretz N, Timmer J, Theis F, Lehmann WD, Lichter P and Klingmller U. Cancer Res. 2011 Feb 1;71(3):693-704. PubmedID:21127196; DOI:10.1158/0008-5472.CAN-10-2987

Abstract:
Primary mediastinal B-cell lymphoma (PMBL) and classical Hodgkin lymphoma (cHL) share a frequent constitutive activation of JAK (Janus kinase)/STAT signaling pathway. Because of complex, nonlinear relations within the pathway, key dynamic properties remained to be identified to predict possible strategies for intervention. We report the development of dynamic pathway models based on quantitative data collected on signaling components of JAK/STAT pathway in two lymphoma-derived cell lines, MedB-1 and L1236, representative of PMBL and cHL, respectively. We show that the amounts of STAT5 and STAT6 are higher whereas those of SHP1 are lower in the two lymphoma cell lines than in normal B cells. Distinctively, L1236 cells harbor more JAK2 and less SHP1 molecules per cell than MedB-1 or control cells. In both lymphoma cell lines, we observe interleukin-13 (IL13)-induced activation of IL4 receptor , JAK2, and STAT5, but not of STAT6. Genome-wide, 11 early and 16 sustained genes are upregulated by IL13 in both lymphoma cell lines. Specifically, the known STAT-inducible negative regulators CISH and SOCS3 are upregulated within 2 hours in MedB-1 but not in L1236 cells. On the basis of this detailed quantitative information, we established two mathematical models, MedB-1 and L1236 model, able to describe the respective experimental data. Most of the model parameters are identifiable and therefore the models are predictive. Sensitivity analysis of the model identifies six possible therapeutic targets able to reduce gene expression levels in L1236 cells and three in MedB-1. We experimentally confirm reduction in target gene expression in response to inhibition of STAT5 phosphorylation, thereby validating one of the predicted targets.

All concentrations in the model, apart from IL13, are in molecules/cell. IL13 is given in ng/ml. As the cell volume is not explicitely given in the article, it is just approximately derived from the MW of IL13 () and the conversion factor 2.265 molecules IL13/cell = 1 ng/ml to be around 60 fl.

SBML model exported from PottersWheel on 2010-08-10 12:14:57.
Inline follows the original matlab code:

```
% PottersWheel model definition file

function m = Raia2010_IL13_MedB1()

m             = pwGetEmptyModel();

%% Meta information

m.ID          = 'Raia2010_IL13_MedB1';
m.name        = 'Raia2010_IL13_MedB1';
m.description = '';
m.authors     = {'Raia et al'};
m.dates       = {'2010'};
m.type        = 'PW-2-0-47';
```

```
%% X: Dynamic variables
% m = pwAddX(m, ID, startValue, type, minValue, maxValue, unit, compartment, name, descri

m = pwAddX(m, ’Rec’         ,              1.3, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’Rec_i’       , 113.193916718733, ’global’,  0.001, 10000, ’molecules/cell
m = pwAddX(m, ’IL13_Rec’    ,                0, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’p_IL13_Rec’  ,                0, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’p_IL13_Rec_i’,                0, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’JAK2’        ,              2.8, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’pJAK2’       ,                0, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’SHP1’        ,               91, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’STAT5’       ,              165, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’pSTAT5’      ,                0, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’SOCS3mRNA’   ,                0, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’DecoyR’      ,             0.34, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’IL13_DecoyR’ ,                0, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’SOCS3’       ,                0, ’fix’   , 1e-006, 10000, ’molecules/cell
m = pwAddX(m, ’CD274mRNA’   ,                0, ’fix’   , 1e-006, 10000, ’molecules/cell


%% R: Reactions
% m = pwAddR(m, reactants, products, modifiers, type, options, rateSignature, parameters

m = pwAddR(m, {’Rec’         }, {’IL13_Rec’    }, {’IL13stimulation’   }, ’C’ , [] , ’k1
m = pwAddR(m, {’Rec’         }, {’Rec_i’       }, {                    }, ’MA’, [] , []
m = pwAddR(m, {’Rec_i’       }, {’Rec’         }, {                    }, ’MA’, [] , []
m = pwAddR(m, {’IL13_Rec’    }, {’p_IL13_Rec’  }, {’pJAK2’             }, ’E’ , [] , []
m = pwAddR(m, {’JAK2’        }, {’pJAK2’       }, {’IL13_Rec’,’SOCS3’  }, ’C’ , [] , ’k1
m = pwAddR(m, {’JAK2’        }, {’pJAK2’       }, {’p_IL13_Rec’,’SOCS3’}, ’C’ , [] , ’k1
m = pwAddR(m, {’p_IL13_Rec’  }, {’p_IL13_Rec_i’}, {                    }, ’MA’, [] , []
m = pwAddR(m, {’p_IL13_Rec_i’}, {              }, {                    }, ’MA’, [] , []
m = pwAddR(m, {’pJAK2’       }, {’JAK2’        }, {’SHP1’              }, ’E’ , [] , []
m = pwAddR(m, {’STAT5’       }, {’pSTAT5’      }, {’pJAK2’             }, ’E’ , [] , []
m = pwAddR(m, {’pSTAT5’      }, {’STAT5’       }, {’SHP1’              }, ’E’ , [] , []
m = pwAddR(m, {’DecoyR’      }, {’IL13_DecoyR’ }, {’IL13stimulation’   }, ’C’ , [] , ’k1
m = pwAddR(m, {              }, {’SOCS3mRNA’   }, {’pSTAT5’            }, ’C’ , [] , ’m1
m = pwAddR(m, {              }, {’SOCS3’       }, {’SOCS3mRNA’         }, ’C’ , [] , ’m1
m = pwAddR(m, {’SOCS3’       }, {              }, {                    }, ’MA’, [] , []
m = pwAddR(m, {              }, {’CD274mRNA’   }, {’pSTAT5’            }, ’C’ , [] , ’m1
```

```
%% C: Compartments
% m = pwAddC(m, ID, size,  outside, spatialDimensions, name, unit, constant)

m = pwAddC(m, 'cell', 1);


%% K: Dynamical parameters
% m = pwAddK(m, ID, value, type, minValue, maxValue, unit, name, description)

m = pwAddK(m, 'Kon_IL13Rec'               , 0.00341992477561527  , 'global', 1e-009, 1000)
m = pwAddK(m, 'Rec_phosphorylation'       , 999.630699390459     , 'global', 1e-009, 1000)
m = pwAddK(m, 'pRec_intern'               , 0.152540135862128    , 'global', 1e-009, 1000)
m = pwAddK(m, 'pRec_degradation'          , 0.17292753960894     , 'global', 1e-009, 1000)
m = pwAddK(m, 'Rec_intern'                , 0.103345784175639    , 'global', 1e-009, 1000)
m = pwAddK(m, 'Rec_recycle'               , 0.00135598001330518  , 'global', 1e-009, 1000)
m = pwAddK(m, 'JAK2_phosphorylation'      , 0.157057142470047    , 'global', 1e-009, 1000)
m = pwAddK(m, 'pJAK2_dephosphorylation'   , 0.000621906059346898 , 'global', 1e-009, 1000)
m = pwAddK(m, 'STAT5_phosphorylation'     , 0.0382596267705733   , 'global', 1e-009, 1000)
m = pwAddK(m, 'pSTAT5_dephosphorylation', 0.000343391620492938 , 'global', 1e-009, 1000)
m = pwAddK(m, 'SOCS3mRNA_production'      , 0.00215826062955433  , 'global', 1e-009, 1000)
m = pwAddK(m, 'DecoyR_binding'            , 0.000124391087466499 , 'global', 1e-009, 1000)
m = pwAddK(m, 'JAK2_p_inhibition'         , 0.0168267797836881   , 'global', 1e-009, 1000)
m = pwAddK(m, 'SOCS3_translation'         , 11.9086462945188     , 'global', 1e-009, 1000)
m = pwAddK(m, 'SOCS3_accumulation'        , 3.70803336415341     , 'global', 1     , 1000)
m = pwAddK(m, 'SOCS3_degradation'         , 0.0429185935645562   , 'global', 1e-009, 1000)
m = pwAddK(m, 'CD274mRNA_production'      , 8.21752278733562e-005, 'global', 1e-009, 1000)


%% U: Driving input
% m = pwAddU(m, ID, uType, uTimes, uValues, compartment, name, description, u2Values, alt

m = pwAddU(m, 'IL13stimulation', 'steps', [-100 0]  , [0 1]  , [], [], [], [], {}, [], 'p


%% Default sampling time points
m.t = 0:1:120;


%% Y: Observables
% m = pwAddY(m, rhs, ID, scalingParameter, errorModel, noiseType, unit, name, descriptio

m = pwAddY(m, 'Rec + IL13_Rec + p_IL13_Rec'                        , 'RecSurf_obs'  , 'sca
m = pwAddY(m, 'IL13_Rec + p_IL13_Rec + p_IL13_Rec_i + IL13_DecoyR', 'IL13-cell_obs', 'sca
```

```
m = pwAddY(m, 'p_IL13_Rec + p_IL13_Rec_i'                         , 'pIL4Ra_obs'   , 'sca
m = pwAddY(m, 'pJAK2'                                             , 'pJAK2_obs'    , 'sca
m = pwAddY(m, 'SOCS3mRNA'                                         , 'SOCS3mRNA_obs', 'sca
m = pwAddY(m, 'CD274mRNA'                                         , 'CD274mRNA_obs', 'sca
m = pwAddY(m, 'SOCS3'                                             , 'SOCS3_obs'    , 'sca
m = pwAddY(m, 'pSTAT5'                                            , 'pSTAT5_obs'   , 'sca


%% S: Scaling parameters
% m = pwAddS(m, ID, value, type, minValue, maxValue, unit, name, description)

m = pwAddS(m, 'scale_pJAK2'    , 1.39039557075997, 'global', 0.001, 10000);
m = pwAddS(m, 'scale_pIL4Ra'   , 1.88700484471494, 'global', 0.001, 10000);
m = pwAddS(m, 'scale_RecSurf'  ,                1,    'fix', 0.001, 10000);
m = pwAddS(m, 'scale_IL13-cell', 5.56750251420935, 'global', 0.001, 10000);
m = pwAddS(m, 'scale_SOCS3mRNA', 17.6699101927908, 'global', 0.001, 10000);
m = pwAddS(m, 'scale_CD274mRNA', 2.48547378765387, 'global', 0.001, 10000);
m = pwAddS(m, 'scale_pSTAT5'   ,                1,    'fix', 0.001, 10000);
m = pwAddS(m, 'scale_SOCS3'    ,                1,    'fix', 0.001, 10000);


%% Designer properties (do not modify)
m.designerPropsM = [1 1 1 0 0 0 400 250 600 400 1 1 1 0 0 0 0];
```

2 Unit Definitions

This is an overview of six unit definitions of which two are predefined by SBML and not mentioned in the model.

2.1 Unit `substance`

Name molecules

Definition item

2.2 Unit `time`

Name minutes

Definition 60 s

2.3 Unit `volume`

Name cell_volumes

Definition 60 fl

2.4 Unit `ng_per_ml`

Name ng_per_ml

Definition ng · ml

2.5 Unit `area`

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

Definition m^2

2.6 Unit `length`

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

Definition m

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`cell`	cell	0000290	3	1	litre	☑	

3.1 Compartment `cell`

This is a three dimensional compartment with a constant size of one 60 fl.

Name cell

SBO:0000290 physical compartment

4 Species

This model contains 16 species. The boundary condition of one of these species is set to `true` so that this species' amount cannot be changed by any reaction. 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
`Rec`	Rec	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`Rec_i`	Rec_i	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`IL13_Rec`	IL13_Rec	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`p_IL13_Rec`	p_IL13_Rec	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`p_IL13_Rec_i`	p_IL13_Rec_i	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`JAK2`	JAK2	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`pJAK2`	pJAK2	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`SHP1`	SHP1	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`STAT5`	STAT5	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`pSTAT5`	pSTAT5	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`SOCS3mRNA`	SOCS3mRNA	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`DecoyR`	DecoyR	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`IL13_DecoyR`	IL13_DecoyR	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`SOCS3`	SOCS3	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`CD274mRNA`	CD274mRNA	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	⊟
`IL13`	IL13	`cell`	$\mathrm{item} \cdot (60\ \mathrm{fl})^{-1}$	⊟	☑

5 Parameters

This model contains 18 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`IL13stimulation`	IL13stimulation	0000228	1.000	$\mathrm{ng} \cdot \mathrm{ml}$	☑
`Kon_IL13Rec`		0000339	0.003		☑
`Rec_phosphorylation`		0000036	999.631		☑
`pRec_intern`		0000035	0.153		☑
`pRec_degradation`		0000356	0.173		☑
`Rec_intern`		0000035	0.103		☑
`Rec_recycle`		0000035	0.001		☑
`JAK2_phosphorylation`		0000036	0.157		☑
`pJAK2_dephosphorylation`		0000036	$6.21906 \cdot 10^{-4}$		☑
`STAT5_phosphorylation`		0000036	0.038		☑
`pSTAT5_dephosphorylation`		0000036	$3.43392 \cdot 10^{-4}$		☑
`SOCS3mRNA_production`		0000035	0.002		☑
`DecoyR_binding`		0000339	$1.24391 \cdot 10^{-4}$		☑
`JAK2_p_inhibition`		0000308	0.017		☑
`SOCS3_translation`		0000324	11.909		☑
`SOCS3_accumulation`		0000027	3.708		☑
`SOCS3_degradation`		0000356	0.043		☑
`CD274mRNA_production`		0000035	$8.21752 \cdot 10^{-5}$		☑

6 Rule

This is an overview of one rule.

6.1 Rule `IL13`

Rule `IL13` is an assignment rule for species `IL13`:

$$\mathrm{IL13} = 2.265 \cdot \mathrm{IL13stimulation} \tag{1}$$

7 Reactions

This model contains 16 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	`reaction_1`		$\text{Rec} \xrightarrow{\text{IL13}} \text{IL13\_Rec}$	0000177
2	`reaction_2`		$\text{Rec} \longrightarrow \text{Rec\_i}$	0000185
3	`reaction_3`		$\text{Rec\_i} \longrightarrow \text{Rec}$	0000185
4	`reaction_4`		$\text{IL13\_Rec} \xrightarrow{\text{pJAK2}} \text{p\_IL13\_Rec}$	0000216
5	`reaction_5`		$\text{JAK2} \xrightarrow{\text{IL13\_Rec, SOCS3}} \text{pJAK2}$	0000216
6	`reaction_6`		$\text{JAK2} \xrightarrow{\text{p\_IL13\_Rec, SOCS3}} \text{pJAK2}$	0000216
7	`reaction_7`		$\text{p\_IL13\_Rec} \longrightarrow \text{p\_IL13\_Rec\_i}$	0000185
8	`reaction_8`		$\text{p\_IL13\_Rec\_i} \longrightarrow \emptyset$	0000179
9	`reaction_9`		$\text{pJAK2} \xrightarrow{\text{SHP1}} \text{JAK2}$	0000330
10	`reaction_10`		$\text{STAT5} \xrightarrow{\text{pJAK2}} \text{pSTAT5}$	0000216
11	`reaction_11`		$\text{pSTAT5} \xrightarrow{\text{SHP1}} \text{STAT5}$	0000330
12	`reaction_12`		$\text{DecoyR} \xrightarrow{\text{IL13}} \text{IL13\_DecoyR}$	0000177
13	`reaction_13`		$\emptyset \xrightarrow{\text{pSTAT5}} \text{SOCS3mRNA}$	0000183
14	`reaction_14`		$\emptyset \xrightarrow{\text{SOCS3mRNA}} \text{SOCS3}$	0000181
15	`reaction_15`		$\text{SOCS3} \longrightarrow \emptyset$	0000179
16	`reaction_16`		$\emptyset \xrightarrow{\text{pSTAT5}} \text{CD274mRNA}$	0000183

7.1 Reaction `reaction_1`

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

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{Rec} \xrightarrow{\mathrm{IL13}} \mathrm{IL13\_Rec} \tag{2}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
`Rec`	Rec	

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
`IL13`	IL13	0000461

Product

Table 8: Properties of each product.

Id	Name	SBO
`IL13_Rec`	IL13_Rec	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \mathrm{Kon\_IL13Rec} \cdot [\mathrm{IL13}] \cdot [\mathrm{Rec}] \cdot \mathrm{vol}\,(\mathrm{cell}) \tag{3}$$

7.2 Reaction `reaction_2`

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

SBO:0000185 transport reaction

Reaction equation

$$\text{Rec} \longrightarrow \text{Rec\_i} \tag{4}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
`Rec`	Rec	

Product

Table 10: Properties of each product.

Id	Name	SBO
`Rec_i`	Rec_i	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{Rec\_intern} \cdot [\text{Rec}] \cdot \text{vol}\,(\text{cell}) \tag{5}$$

7.3 Reaction `reaction_3`

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

SBO:0000185 transport reaction

Reaction equation

$$\text{Rec\_i} \longrightarrow \text{Rec} \tag{6}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
`Rec_i`	Rec_i	

Product

Table 12: Properties of each product.

Id	Name	SBO
`Rec`	Rec	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{Rec\_recycle} \cdot [\text{Rec\_i}] \cdot \text{vol}\left(\text{cell}\right) \tag{7}$$

7.4 Reaction `reaction_4`

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

SBO:0000216 phosphorylation

Reaction equation

$$\text{IL13\_Rec} \xrightarrow{\text{pJAK2}} \text{p\_IL13\_Rec} \tag{8}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
`IL13_Rec`	IL13_Rec	

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
`pJAK2`	pJAK2	

Product

Table 15: Properties of each product.

Id	Name	SBO
`p_IL13_Rec`	p_IL13_Rec	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{Rec\_phosphorylation} \cdot [\mathrm{IL13\_Rec}] \cdot [\mathrm{pJAK2}] \cdot \mathrm{vol}\left(\mathrm{cell}\right) \tag{9}$$

7.5 Reaction `reaction_5`

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

SBO:0000216 phosphorylation

Reaction equation

$$\mathrm{JAK2} \xrightarrow{\mathrm{IL13\_Rec},\ \mathrm{SOCS3}} \mathrm{pJAK2} \tag{10}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
`JAK2`	JAK2	

Modifiers

Table 17: Properties of each modifier.

Id	Name	SBO
`IL13_Rec`	IL13_Rec	
`SOCS3`	SOCS3	

Product

Table 18: Properties of each product.

Id	Name	SBO
`pJAK2`	pJAK2	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \frac{\mathrm{JAK2\_phosphorylation} \cdot [\mathrm{IL13\_Rec}] \cdot [\mathrm{JAK2}]}{1 + \mathrm{JAK2\_p\_inhibition} \cdot [\mathrm{SOCS3}]} \cdot \mathrm{vol}\left(\mathrm{cell}\right) \tag{11}$$

7.6 Reaction `reaction_6`

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

SBO:0000216 phosphorylation

Reaction equation

$$\mathrm{JAK2} \xrightarrow{\mathrm{p\_IL13\_Rec},\ \mathrm{SOCS3}} \mathrm{pJAK2} \tag{12}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
`JAK2`	JAK2	

Modifiers

Table 20: Properties of each modifier.

Id	Name	SBO
`p_IL13_Rec`	p_IL13_Rec	
`SOCS3`	SOCS3	

Product

Table 21: Properties of each product.

Id	Name	SBO
`pJAK2`	pJAK2	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \frac{\mathrm{JAK2\_phosphorylation} \cdot [\mathrm{p\_IL13\_Rec}] \cdot [\mathrm{JAK2}]}{1 + \mathrm{JAK2\_p\_inhibition} \cdot [\mathrm{SOCS3}]} \cdot \mathrm{vol}\,(\mathrm{cell}) \tag{13}$$

7.7 Reaction `reaction_7`

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

SBO:0000185 transport reaction

Reaction equation

$$\mathrm{p\_IL13\_Rec} \longrightarrow \mathrm{p\_IL13\_Rec\_i} \tag{14}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
`p_IL13_Rec`	p_IL13_Rec	

Product

Table 23: Properties of each product.

Id	Name	SBO
`p_IL13_Rec_i`	p_IL13_Rec_i	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{pRec\_intern} \cdot [\mathrm{p\_IL13\_Rec}] \cdot \mathrm{vol}\,(\mathrm{cell}) \tag{15}$$

7.8 Reaction `reaction_8`

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

SBO:0000179 degradation

Reaction equation

$$\mathrm{p\_IL13\_Rec\_i} \longrightarrow \emptyset \tag{16}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
`p_IL13_Rec_i`	p_IL13_Rec_i	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{pRec\_degradation} \cdot [\mathrm{p\_IL13\_Rec\_i}] \cdot \mathrm{vol}\,(\mathrm{cell}) \tag{17}$$

7.9 Reaction `reaction_9`

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

SBO:0000330 dephosphorylation

Reaction equation

$$\mathrm{pJAK2} \xrightarrow{\mathrm{SHP1}} \mathrm{JAK2} \tag{18}$$

Reactant

Table 25: Properties of each reactant.

Id	Name	SBO
`pJAK2`	pJAK2	

Modifier

Table 26: Properties of each modifier.

Id	Name	SBO
`SHP1`	SHP1	

Product

Table 27: Properties of each product.

Id	Name	SBO
`JAK2`	JAK2	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{pJAK2\_dephosphorylation} \cdot [\mathrm{pJAK2}] \cdot [\mathrm{SHP1}] \cdot \mathrm{vol}(\mathrm{cell}) \tag{19}$$

7.10 Reaction `reaction_10`

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

SBO:0000216 phosphorylation

Reaction equation

$$\mathrm{STAT5} \xrightarrow{\mathrm{pJAK2}} \mathrm{pSTAT5} \tag{20}$$

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
`STAT5`	STAT5	

Modifier

Table 29: Properties of each modifier.

Id	Name	SBO
`pJAK2`	pJAK2	

Product

Table 30: Properties of each product.

Id	Name	SBO
`pSTAT5`	pSTAT5	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{STAT5\_phosphorylation} \cdot [\mathrm{STAT5}] \cdot [\mathrm{pJAK2}] \cdot \mathrm{vol}\left(\mathrm{cell}\right) \tag{21}$$

7.11 Reaction `reaction_11`

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

SBO:0000330 dephosphorylation

Reaction equation

$$\mathrm{pSTAT5} \xrightarrow{\mathrm{SHP1}} \mathrm{STAT5} \tag{22}$$

Reactant

Table 31: Properties of each reactant.

Id	Name	SBO
`pSTAT5`	pSTAT5	

Modifier

Table 32: Properties of each modifier.

Id	Name	SBO
`SHP1`	SHP1	

Product

Table 33: Properties of each product.

Id	Name	SBO
`STAT5`	STAT5	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{pSTAT5\_dephosphorylation} \cdot [\mathrm{pSTAT5}] \cdot [\mathrm{SHP1}] \cdot \mathrm{vol}\left(\mathrm{cell}\right) \qquad (23)$$

7.12 Reaction `reaction_12`

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

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{DecoyR} \xrightarrow{\mathrm{IL13}} \mathrm{IL13\_DecoyR} \qquad (24)$$

Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
`DecoyR`	DecoyR	

Modifier

Table 35: Properties of each modifier.

Id	Name	SBO
`IL13`	IL13	

Product

Table 36: Properties of each product.

Id	Name	SBO
`IL13_DecoyR`	IL13_DecoyR	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{DecoyR\_binding} \cdot [\text{IL13}] \cdot [\text{DecoyR}] \cdot \text{vol}\,(\text{cell}) \tag{25}$$

7.13 Reaction `reaction_13`

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

SBO:0000183 transcription

Reaction equation

$$\emptyset \xrightarrow{\text{pSTAT5}} \text{SOCS3mRNA} \tag{26}$$

Modifier

Table 37: Properties of each modifier.

Id	Name	SBO
`pSTAT5`	pSTAT5	

Product

Table 38: Properties of each product.

Id	Name	SBO
`SOCS3mRNA`	SOCS3mRNA	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = [\text{pSTAT5}] \cdot \text{SOCS3mRNA\_production} \cdot \text{vol}\,(\text{cell}) \tag{27}$$

7.14 Reaction `reaction_14`

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

SBO:0000181 conformational transition

Reaction equation

$$\emptyset \xrightarrow{\text{SOCS3mRNA}} \text{SOCS3} \tag{28}$$

Modifier

Table 39: Properties of each modifier.

Id	Name	SBO
`SOCS3mRNA`	SOCS3mRNA	

Product

Table 40: Properties of each product.

Id	Name	SBO
`SOCS3`	SOCS3	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \frac{[\text{SOCS3mRNA}] \cdot \text{SOCS3\_translation}}{\text{SOCS3\_accumulation} + [\text{SOCS3mRNA}]} \cdot \text{vol}\left(\text{cell}\right) \tag{29}$$

7.15 Reaction `reaction_15`

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

SBO:0000179 degradation

Reaction equation

$$\text{SOCS3} \longrightarrow \emptyset \tag{30}$$

Reactant

Table 41: Properties of each reactant.

Id	Name	SBO
`SOCS3`	SOCS3	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \text{SOCS3\_degradation} \cdot [\text{SOCS3}] \cdot \text{vol}(\text{cell}) \tag{31}$$

7.16 Reaction `reaction_16`

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

SBO:0000183 transcription

Reaction equation

$$\emptyset \xrightarrow{\text{pSTAT5}} \text{CD274mRNA} \tag{32}$$

Modifier

Table 42: Properties of each modifier.

Id	Name	SBO
`pSTAT5`	pSTAT5	

Product

Table 43: Properties of each product.

Id	Name	SBO
`CD274mRNA`	CD274mRNA	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = [\text{pSTAT5}] \cdot \text{CD274mRNA\_production} \cdot \text{vol}(\text{cell}) \tag{33}$$

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 `Rec`

Name Rec

SBO:0000297 protein complex

Initial concentration $1.3 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in three reactions (as a reactant in `reaction_1`, `reaction_2` and as a product in `reaction_3`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Rec} = v_3 - v_1 - v_2 \tag{34}$$

8.2 Species `Rec_i`

Name Rec_i

SBO:0000297 protein complex

Initial concentration $113.194 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in two reactions (as a reactant in `reaction_3` and as a product in `reaction_2`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Rec\_i} = v_2 - v_3 \tag{35}$$

8.3 Species `IL13_Rec`

Name IL13_Rec

SBO:0000297 protein complex

Initial concentration $0 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in three reactions (as a reactant in `reaction_4` and as a product in `reaction_1` and as a modifier in `reaction_5`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{IL13\_Rec} = v_1 - v_4 \tag{36}$$

8.4 Species `p_IL13_Rec`

Name p_IL13_Rec

SBO:0000297 protein complex

Initial concentration $0 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in three reactions (as a reactant in `reaction_7` and as a product in `reaction_4` and as a modifier in `reaction_6`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{p\_IL13\_Rec} = v_4 - v_7 \tag{37}$$

8.5 Species `p_IL13_Rec_i`

Name p_IL13_Rec_i

SBO:0000297 protein complex

Initial concentration $0 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in two reactions (as a reactant in `reaction_8` and as a product in `reaction_7`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{p\_IL13\_Rec\_i} = v_7 - v_8 \tag{38}$$

8.6 Species `JAK2`

Name JAK2

SBO:0000252 polypeptide chain

Initial concentration $2.8 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in three reactions (as a reactant in `reaction_5`, `reaction_6` and as a product in `reaction_9`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{JAK2} = v_9 - v_5 - v_6 \tag{39}$$

8.7 Species `pJAK2`

Name pJAK2

SBO:0000252 polypeptide chain

Initial concentration $0 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in five reactions (as a reactant in `reaction_9` and as a product in `reaction_5`, `reaction_6` and as a modifier in `reaction_4`, `reaction_10`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{pJAK2} = v_5 + v_6 - v_9 \tag{40}$$

8.8 Species `SHP1`

Name SHP1

SBO:0000252 polypeptide chain

Initial concentration $91 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in two reactions (as a modifier in `reaction_9`, `reaction_11`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{SHP1} = 0 \tag{41}$$

8.9 Species `STAT5`

Name STAT5

SBO:0000252 polypeptide chain

Initial concentration $165 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in two reactions (as a reactant in `reaction_10` and as a product in `reaction_11`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{STAT5} = v_{11} - v_{10} \tag{42}$$

8.10 Species `pSTAT5`

Name pSTAT5

SBO:0000252 polypeptide chain

Initial concentration $0 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in four reactions (as a reactant in `reaction_11` and as a product in `reaction_10` and as a modifier in `reaction_13`, `reaction_16`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{pSTAT5} = v_{10} - v_{11} \tag{43}$$

8.11 Species `SOCS3mRNA`

Name SOCS3mRNA

SBO:0000250 ribonucleic acid

Initial concentration $0 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in two reactions (as a product in `reaction_13` and as a modifier in `reaction_14`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{SOCS3mRNA} = v_{13} \tag{44}$$

8.12 Species `DecoyR`

Name DecoyR

SBO:0000297 protein complex

Initial concentration $0.34 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in one reaction (as a reactant in `reaction_12`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{DecoyR} = -\,v_{12} \tag{45}$$

8.13 Species `IL13_DecoyR`

Name IL13_DecoyR

SBO:0000297 protein complex

Initial concentration $0 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in one reaction (as a product in `reaction_12`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{IL13\_DecoyR} = v_{12} \tag{46}$$

8.14 Species `SOCS3`

Name SOCS3

SBO:0000252 polypeptide chain

Initial concentration $0 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in four reactions (as a reactant in `reaction_15` and as a product in `reaction_14` and as a modifier in `reaction_5`, `reaction_6`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{SOCS3} = v_{14} - v_{15} \tag{47}$$

8.15 Species `CD274mRNA`

Name CD274mRNA

SBO:0000250 ribonucleic acid

Initial concentration $0 \text{ item} \cdot (60 \text{ fl})^{-1}$

This species takes part in one reaction (as a product in `reaction_16`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{CD274mRNA} = v_{16} \tag{48}$$

8.16 Species `IL13`

Name IL13

SBO:0000252 polypeptide chain

Involved in rule `IL13`

This species takes part in two reactions (as a modifier in `reaction_1`, `reaction_12`). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

A Glossary of Systems Biology Ontology Terms

SBO:0000027 Michaelis constant: Substrate concentration at which the velocity of reaction is half its maximum. Michaelis constant is an experimental parameter. According to the underlying molecular mechanism it can be interpreted differently in terms of microscopic constants

SBO:0000035 forward unimolecular rate constant, continuous case: Numerical parameter that quantifies the forward velocity of a chemical reaction involving only one reactant. This parameter encompasses all the contributions to the velocity except the quantity of the reactant. It is to be used in a reaction modelled using a continuous framework

SBO:0000036 forward bimolecular rate constant, continuous case: Numerical parameter that quantifies the forward velocity of a chemical reaction involving two reactants. This parameter encompasses all the contributions to the velocity except the quantity of the reactants. It is to be used in a reaction modelled using a continuous framework

SBO:0000177 non-covalent binding: Interaction between several biochemical entities that results in the formation of a non-covalent comple

SBO:0000179 degradation: Complete disappearance of a physical entity

SBO:0000181 conformational transition: Biochemical reaction that does not result in the modification of covalent bonds of reactants, but rather modifies the conformation of some reactants, that is the relative position of their atoms in space

SBO:0000183 transcription: Process through which a DNA sequence is copied to produce a complementary RNA

SBO:0000185 transport reaction: Movement of a physical entity without modification of the structure of the entity

SBO:0000216 phosphorylation: Addition of a phosphate group (-H2PO4) to a chemical entity

SBO:0000228 volume density of an entity: Mass of an entity per unit volume

SBO:0000250 ribonucleic acid: Macromolecule formed by a repetition of ribonucleosides linked by phosphodiester bonds. CHEBI:3369

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:0000297 protein complex: Macromolecular complex containing one or more polypeptide chains possibly associated with simple chemicals. CHEBI:3608

SBO:0000308 equilibrium or steady-state characteristic: Quantitative parameter that characterises a biochemical equilibrium.

SBO:0000324 forward maximal velocity: Limiting maximal velocity of the forward reaction of a reversible enzyme, reached when the substrate is in large excess and all the enzyme is complexed.

SBO:0000330 dephosphorylation: Removal of a phosphate group (-H2PO4) from a chemical entity.

SBO:0000339 bimolecular association rate constant: Rate with which two components associate into a complex

SBO:0000356 decay constant: Kinetic constant characterising a mono-exponential decay. It is the inverse of the mean lifetime of the continuant being decayed. Its unit is“per tim”.

SBO:0000461 essential activator: A substance that is absolutely required for occurrence and stimulation of a reaction

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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[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