

SBML Model Report

Model name:
“Alexander2010_Tcell_Regulation_Sys2”



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: Nick Juty¹ and Lukas Endler² at December 22nd 2010 at 2:02 a. m. and last time modified at March eleventh 2014 at 1:52 p. m. Table 1 shows 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	5
events	0	constraints	0
reactions	12	function definitions	0
global parameters	16	unit definitions	5
rules	3	initial assignments	0

Model Notes

This is system 2, the model with Michelis Menten type antigen uptake by pAPCs, described in the article:

Self-tolerance and Autoimmunity in a Regulatory T Cell Model.

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Alexander HK, Wahl LM. Bull Math Biol. 2010 Mar 2. PMID: [20195912](#) , doi: [10.1007/s11538-010-9519-2](#) ;

Abstract:

The class of immunosuppressive lymphocytes known as regulatory T cells (Tregs) has been identified as a key component in preventing autoimmune diseases. Although Tregs have been incorporated previously in mathematical models of autoimmunity, we take a novel approach which emphasizes the importance of professional antigen presenting cells (pAPCs). We examine three possible mechanisms of Treg action (each in isolation) through ordinary differential equation (ODE) models. The immune response against a particular autoantigen is suppressed both by Tregs specific for that antigen and by Tregs of arbitrary specificities, through their action on either maturing or already mature pAPCs or on autoreactive effector T cells. In this deterministic approach, we find that qualitative long-term behaviour is predicted by the basic reproductive ratio $R(0)$ for each system. When $R(0) < 1$, only the trivial equilibrium exists and is stable; when $R(0) > 1$, this equilibrium loses its stability and a stable non-trivial equilibrium appears. We interpret the absence of self-damaging populations at the trivial equilibrium to imply a state of self-tolerance, and their presence at the non-trivial equilibrium to imply a state of chronic autoimmunity. Irrespective of mechanism, our model predicts that Tregs specific for the autoantigen in question play no role in the system's qualitative long-term behaviour, but have quantitative effects that could potentially reduce an autoimmune response to sub-clinical levels. Our results also suggest an important role for Tregs of arbitrary specificities in modulating the qualitative outcome. A stochastic treatment of the same model demonstrates that the probability of developing a chronic autoimmune response increases with the initial exposure to self antigen or autoreactive effector T cells. The three different mechanisms we consider, while leading to a number of similar predictions, also exhibit key differences in both transient dynamics (ODE approach) and the probability of chronic autoimmunity (stochastic approach).

Originally created by libAntimony v1.4 (using libSBML 3.4.1)

2 Unit Definitions

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

2.1 Unit substance

Name number

Definition item

2.2 Unit time

Name days

Definition 86400 s

2.3 Unit per_day

Name per_day

Definition $(86400\text{ s})^{-1}$

2.4 Unit per_day_per_item

Name per_day_per_item

Definition $(86400\text{ s})^{-1} \cdot \text{item}^{-1}$

2.5 Unit items_per_day

Name items_per_day

Definition $(86400\text{ s})^{-1} \cdot \text{item}$

2.6 Unit volume

Notes Litre is the predefined SBML unit for volume.

Definition l

2.7 Unit area

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

Definition m²

2.8 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
body			3	1	litre	<input checked="" type="checkbox"/>	

3.1 Compartment body

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

4 Species

This model contains five 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 Condi- tion
A		body	item	<input type="checkbox"/>	<input type="checkbox"/>
R		body	item	<input type="checkbox"/>	<input type="checkbox"/>
E		body	item	<input type="checkbox"/>	<input type="checkbox"/>
G		body	item	<input type="checkbox"/>	<input type="checkbox"/>
A_im		body	item	<input type="checkbox"/>	<input checked="" type="checkbox"/>

5 Parameters

This model contains 16 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
v_max			125000.000	$(86400 \text{ s})^{-1} \cdot \text{item}$	<input checked="" type="checkbox"/>
k			$5 \cdot 10^7$	item	<input checked="" type="checkbox"/>
f			10^{-4}	dimensionless	<input checked="" type="checkbox"/>
gamma			2000.000	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
beta			200.000	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
pi1			0.016	$(86400 \text{ s})^{-1}$ item ⁻¹	<input checked="" type="checkbox"/>
lambdaE			1000.000	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
muA			0.250	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
muR			0.250	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
muE			0.250	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
muG			5.000	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
b1			0.250	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
sigma1			$3 \cdot 10^{-6}$	$(86400 \text{ s})^{-1}$ item ⁻¹	<input checked="" type="checkbox"/>
mA			0.000	$(86400 \text{ s})^{-1}$	<input type="checkbox"/>
mG			0.000	$(86400 \text{ s})^{-1}$	<input type="checkbox"/>
RO			0.000	dimensionless	<input type="checkbox"/>

6 Rules

This is an overview of three rules.

6.1 Rule mA

Rule mA is an assignment rule for parameter mA:

$$mA = b1 + muA \quad (1)$$

Derived unit $(86400 \text{ s})^{-1}$

6.2 Rule mG

Rule mG is an assignment rule for parameter mG:

$$mG = muG + \frac{v_max}{k} \quad (2)$$

Derived unit $(86400\text{ s})^{-1}$

6.3 Rule R_0

Rule R_0 is an assignment rule for parameter R_0 :

$$R_0 = \frac{f \cdot \frac{v_{\max}}{k} \cdot \lambda E \cdot \gamma}{mG \cdot mA \cdot \mu E} \quad (3)$$

Derived unit dimensionless

7 Reactions

This model contains twelve 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

Nº	Id	Name	Reaction Equation	SBO
1	r1a	r1a: self-antigen uptake	$G \longrightarrow \emptyset$	0000185
2	r1b	r1b: pAPC maturation	$A \xrightarrow{G} A$	0000182
3	r2	r2: self-antigen release triggered by E	$\emptyset \xrightarrow{E} G$	0000185
4	r3	r3: R activation by A	$\emptyset \xrightarrow{A} R$	0000170
5	r4	r4: R activation by A and E	$\emptyset \xrightarrow{A, E} R$	0000170
6	r5	r5: E generation by A	$\emptyset \xrightarrow{A} E$	0000393
7	r6	r6: A death	$A \longrightarrow \emptyset$	0000394
8	r7	r7: R death	$R \longrightarrow \emptyset$	0000394
9	r8	r8: E death	$E \longrightarrow \emptyset$	0000394
10	r9	r9: G clearance	$G \longrightarrow \emptyset$	0000394
11	r10	r10: A suppression by Tregs of other specificity	$A \longrightarrow \emptyset$	0000169
12	r11	r11: A suppression by R	$A \xrightarrow{R} \emptyset$	0000169

7.1 Reaction r1a

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

Name r1a: self-antigen uptake

SBO:0000185 transport reaction

Reaction equation



Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
G		

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_1 = \frac{v_{\max}}{k + G} \cdot G \quad (5)$$

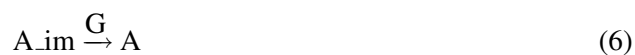
7.2 Reaction r1b

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

Name r1b: pAPC maturation

SBO:0000182 conversion

Reaction equation



Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
A_im		

Modifier

Table 8: Properties of each modifier.

Id	Name	SBO
G		

Product

Table 9: Properties of each product.

Id	Name	SBO
A		

Kinetic Law

Derived unit $(86400\text{ s})^{-1} \cdot \text{item}$

$$v_2 = f \cdot \frac{v_{\max}}{k + G} \cdot G \quad (7)$$

7.3 Reaction r_2

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

Name r_2 : self-antigen release triggered by E

SBO:0000185 transport reaction

Reaction equation



Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
E		

Product

Table 11: Properties of each product.

Id	Name	SBO
G		

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_3 = \text{gamma} \cdot E \quad (9)$$

7.4 Reaction r3

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

Name r3: R activation by A

SBO:0000170 stimulation

Reaction equation



Modifier

Table 12: Properties of each modifier.

Id	Name	SBO
A		

Product

Table 13: Properties of each product.

Id	Name	SBO
R		

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_4 = \text{beta} \cdot A \quad (11)$$

7.5 Reaction r4

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

Name r4: R activation by A and E

SBO:0000170 stimulation

Reaction equation



Modifiers

Table 14: Properties of each modifier.

Id	Name	SBO
A		
E		

Product

Table 15: Properties of each product.

Id	Name	SBO
R		

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_5 = \text{pi1} \cdot E \cdot A \quad (13)$$

7.6 Reaction r5

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

Name r5: E generation by A

SBO:0000393 production

Reaction equation



Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
A		

Product

Table 17: Properties of each product.

Id	Name	SBO
E		

Kinetic Law

Derived unit $(86400\text{ s})^{-1} \cdot \text{item}$

$$v_6 = \text{lambdaE} \cdot A \tag{15}$$

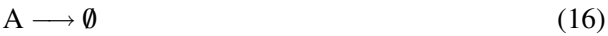
7.7 Reaction r6

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

Name r6: A death

SBO:0000394 consumption

Reaction equation



Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
A		

Kinetic Law

Derived unit $(86400\text{ s})^{-1} \cdot \text{item}$

$$v_7 = \mu A \cdot A \quad (17)$$

7.8 Reaction r_7

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

Name r_7 : R death

SBO:0000394 consumption

Reaction equation



Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
R		

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_8 = \mu R \cdot R \quad (19)$$

7.9 Reaction r_8

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

Name r_8 : E death

SBO:0000394 consumption

Reaction equation



Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
E		

Kinetic Law

Derived unit $(86400\text{ s})^{-1} \cdot \text{item}$

$$v_9 = \mu_E \cdot E \quad (21)$$

7.10 Reaction r9

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

Name r9: G clearance

SBO:0000394 consumption

Reaction equation



Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
G		

Kinetic Law

Derived unit $(86400\text{ s})^{-1} \cdot \text{item}$

$$v_{10} = \mu_G \cdot G \quad (23)$$

7.11 Reaction r10

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

Name r10: A suppression by Tregs of other specificity

SBO:0000169 inhibition

Reaction equation



Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
A		

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_{11} = b1 \cdot A \quad (25)$$

7.12 Reaction r11

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

Name r11: A suppression by R

SBO:0000169 inhibition

Reaction equation



Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
A		

Modifier

Table 24: Properties of each modifier.

Id	Name	SBO
R		

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_{12} = \text{sigma1} \cdot A \cdot R \quad (27)$$

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.

8.1 Species A

Initial amount 1 item

This species takes part in seven reactions (as a reactant in [r6](#), [r10](#), [r11](#) and as a product in [r1b](#) and as a modifier in [r3](#), [r4](#), [r5](#)).

$$\frac{d}{dt}A = v_2 - v_7 - v_{11} - v_{12} \quad (28)$$

8.2 Species R

Initial amount 0 item

This species takes part in four reactions (as a reactant in [r7](#) and as a product in [r3](#), [r4](#) and as a modifier in [r11](#)).

$$\frac{d}{dt}R = v_4 + v_5 - v_8 \quad (29)$$

8.3 Species E

Initial amount 0 item

This species takes part in four reactions (as a reactant in [r8](#) and as a product in [r5](#) and as a modifier in [r2](#), [r4](#)).

$$\frac{d}{dt}E = v_6 - v_9 \quad (30)$$

8.4 Species G

Initial amount 10^8 item

This species takes part in four reactions (as a reactant in [r1a](#), [r9](#) and as a product in [r2](#) and as a modifier in [r1b](#)).

$$\frac{d}{dt}G = v_3 - v_1 - v_{10} \quad (31)$$

8.5 Species A_{im}

Initial amount 0 item

This species takes part in one reaction (as a reactant in [r1b](#)), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{d}{dt}A_{im} = 0 \quad (32)$$

A Glossary of Systems Biology Ontology Terms

SBO:0000169 inhibition: Negative modulation of the execution of a process

SBO:0000170 stimulation: Positive modulation of the execution of a process

SBO:0000182 conversion: Biochemical reaction that results in the modification of some covalent bonds

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

SBO:0000393 production: Generation of a material or conceptual entity.

SBO:0000394 consumption: Decrease in amount of a material or conceptual entity.

SBML²TeX 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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