SBML Model Report

Model name: "Tomida2003 - Calcium Oscillatory-induced translocation of nuclear factor of activated T cells"

May 17, 2018

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Matthew Grant Roberts[1] at February 22nd 2018 at 3:25 p. m. and last time modified at March 14th 2018 at 9:35 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	4
events	0	constraints	0
reactions	4	function definitions	2
global parameters	11	unit definitions	2
rules	5	initial assignments	2

Model Notes

Tomida2003 - NFAT functions CalciumOscillation

This model is described in the article:NFAT functions as a working memory of Ca2+ signals in decoding Ca2+ oscillation.Tomida T, Hirose K, Takizawa A, Shibasaki F, Iino M.EMBO J. 2003 Aug; 22(15): 3825-3832

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Abstract:

Transcription by the nuclear factor of activated T cells (NFAT) is regulated by the frequency of Ca(2+) oscillation. However, why and how Ca(2+) oscillation regulates NFAT activity remain elusive. NFAT is dephosphorylated by Ca(2+)-dependent phosphatase calcineurin and translocates from the cytoplasm to the nucleus to initiate transcription. We analyzed the kinetics of dephosphorylation and translocation of NFAT. We show that Ca(2+)-dependent dephosphorylation proceeds rapidly, while the rephosphorylation and nuclear transport of NFAT proceed slowly. Therefore, after brief Ca(2+) stimulation, dephosphorylated NFAT has a lifetime of several minutes in the cytoplasm. Thus, Ca(2+) oscillation induces a build-up of dephosphorylated NFAT in the cytoplasm, allowing effective nuclear translocation, provided that the oscillation interval is shorter than the lifetime of dephosphorylated NFAT. We also show that Ca(2+) oscillation is more cost-effective in inducing the translocation of NFAT than continuous Ca(2+) signaling. Thus, the lifetime of dephosphorylated NFAT functions as a working memory of Ca(2+) signals and enables the control of NFAT nuclear translocation by the frequency of Ca(2+) oscillation at a reduced cost of Ca(2+) signaling.

This model is hosted on BioModels Database and identified by: BIOMD0000000678.

To cite BioModels Database, please use: Chelliah V et al. BioModels: ten-year anniversary. Nucl. Acids Res. 2015, 43(Database issue):D542-8.

2 Unit Definitions

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

2.1 Unit `volume`

Name volume

Definition ml

2.2 Unit `substance`

Name substance

Definition mmol

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
`Jurkat_cell`	Jurkat cell		3	1	litre	☑	

3.1 Compartment `Jurkat_cell`

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

Name Jurkat cell

4 Species

This model contains four species. The boundary condition of two of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 10 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
`NFAT_phosphorylated`	NFAT_phosphorylated	`Jurkat_cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
`NFAT_dephosphorylated`	NFAT_dephosphorylated	`Jurkat_cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	⊟
`NFAT_transported`	NFAT_transported	`Jurkat_cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	☑
`stimulus`	stimulus	`Jurkat_cell`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	⊟	☑

5 Parameters

This model contains eleven global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.359		☑
k2	k2		0.147		☑
k3	k3		0.060		☑
k4	k4		0.035		☑
stim-_frequency	stim_frequency		3.000		☑
dNFAT	dNFAT%		0.000		☐
pNFAT	pNFAT%		100.000		☐
tNFAT	tNFAT%		0.000		☐
stim-_duration	stim_duration		1.000		☑
ModelValue-_17	Initial for stim-_duration		1.000		☑
ModelValue-_13	Initial for stim-_frequency		3.000		☑

6 Initialassignments

This is an overview of two initialassignments.

6.1 Initialassignment ModelValue_17

Derived unit contains undeclared units

Math stim_duration

6.2 Initialassignment ModelValue_13

Derived unit contains undeclared units

Math stim_frequency

7 Function definitions

This is an overview of two function definitions.

7.1 Function definition function_for_modified_reaction_1

Name function for modified reaction_1

Arguments [NFAT_phosphorylated], k1, [stimulus]

Mathematical Expression

$$\mathrm{k1} \cdot [\mathrm{stimulus}] \cdot [\mathrm{NFAT\_phosphorylated}] \tag{1}$$

7.2 Function definition function_for_modified_reaction_0

Name function for modified reaction

Arguments k1, [stimulus], substrate

Mathematical Expression

$$\mathrm{k1} \cdot [\mathrm{stimulus}] \cdot \mathrm{substrate} \tag{2}$$

8 Rules

This is an overview of five rules.

8.1 Rule NFAT_transported

Rule NFAT_transported is an assignment rule for species NFAT_transported:

$$\mathrm{NFAT\_transported} = 1 - [\mathrm{NFAT\_phosphorylated}] - [\mathrm{NFAT\_dephosphorylated}] \tag{3}$$

8.2 Rule pNFAT

Rule pNFAT is an assignment rule for parameter pNFAT:

$$\mathrm{pNFAT} = 100 \cdot [\mathrm{NFAT\_phosphorylated}] \tag{4}$$

8.3 Rule tNFAT

Rule tNFAT is an assignment rule for parameter tNFAT:

$$\mathrm{tNFAT} = 100 \cdot [\mathrm{NFAT\_transported}] \tag{5}$$

8.4 Rule dNFAT

Rule dNFAT is an assignment rule for parameter dNFAT:

$$\mathrm{dNFAT} = 100 \cdot [\mathrm{NFAT\_dephosphorylated}] \tag{6}$$

8.5 Rule `stimulus`

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

$$\text{stimulus} = \begin{cases} 1 & \text{if time} - \left\lfloor \frac{\text{time}}{\text{ModelValue\_13}} \right\rfloor \cdot \text{ModelValue\_13} < \text{ModelValue\_17} \\ 0 & \text{otherwise} \end{cases} \tag{7}$$

9 Reactions

This model contains four 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	`Dephosphorylation`	Dephosphorylation	NFAT_phosphorylated $\xrightarrow{\text{stimulus}}$ NFAT_dephosphorylated	
2	`Phosphorylation`	Phosphorylation	NFAT_dephosphorylated $\longrightarrow$ NFAT_phosphorylated	
3	`Translocation`	Translocation	NFAT_dephosphorylated $\longrightarrow$ NFAT_transported	
4	`Nuclear_export`	Nuclear_export	NFAT_transported $\longrightarrow$ NFAT_phosphorylated	

9.1 Reaction Dephosphorylation

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

Name Dephosphorylation

Reaction equation

$$\text{NFAT\_phosphorylated} \xrightarrow{\text{stimulus}} \text{NFAT\_dephosphorylated} \tag{8}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
NFAT_phosphorylated	NFAT_phosphorylated	

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
stimulus	stimulus	

Product

Table 8: Properties of each product.

Id	Name	SBO
NFAT_dephosphorylated	NFAT_dephosphorylated	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}\,(\text{Jurkat\_cell}) \cdot \text{function\_for\_modified\_reaction\_1}\,([\text{NFAT\_phosphorylated}], \text{k1}, [\text{stimulus}]) \tag{9}$$

$$\begin{aligned}&\text{function\_for\_modified\_reaction\_1}\,([\text{NFAT\_phosphorylated}], \text{k1}, [\text{stimulus}]) \\ &\quad = \text{k1} \cdot [\text{stimulus}] \cdot [\text{NFAT\_phosphorylated}]\end{aligned} \tag{10}$$

$$\text{function\_for\_modified\_reaction\_1}\left([\text{NFAT\_phosphorylated}], \text{k1}, [\text{stimulus}]\right) = \text{k1} \cdot [\text{stimulus}] \cdot [\text{NFAT\_phosphorylated}] \tag{11}$$

9.2 Reaction `Phosphorylation`

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

Name Phosphorylation

Reaction equation

$$\text{NFAT\_dephosphorylated} \longrightarrow \text{NFAT\_phosphorylated} \tag{12}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
`NFAT_dephosphorylated`	NFAT_dephosphorylated	

Product

Table 10: Properties of each product.

Id	Name	SBO
`NFAT_phosphorylated`	NFAT_phosphorylated	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}\left(\text{Jurkat\_cell}\right) \cdot \text{k2} \cdot [\text{NFAT\_dephosphorylated}] \tag{13}$$

9.3 Reaction `Translocation`

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

Name Translocation

Reaction equation

$$\text{NFAT\_dephosphorylated} \longrightarrow \text{NFAT\_transported} \tag{14}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
NFAT_dephosphorylated	NFAT_dephosphorylated	

Product

Table 12: Properties of each product.

Id	Name	SBO
NFAT_transported	NFAT_transported	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{Jurkat\_cell}\right) \cdot \mathrm{k3} \cdot [\mathrm{NFAT\_dephosphorylated}] \tag{15}$$

9.4 Reaction Nuclear_export

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

Name Nuclear_export

Reaction equation

$$\mathrm{NFAT\_transported} \longrightarrow \mathrm{NFAT\_phosphorylated} \tag{16}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
NFAT_transported	NFAT_transported	

Product

Table 14: Properties of each product.

Id	Name	SBO
NFAT_phosphorylated	NFAT_phosphorylated	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\left(\mathrm{Jurkat\_cell}\right) \cdot \mathrm{k4} \cdot [\mathrm{NFAT\_transported}] \tag{17}$$

10 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.

10.1 Species `NFAT_phosphorylated`

Name NFAT_phosphorylated

Initial concentration $1\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in `Dephosphorylation` and as a product in `Phosphorylation`, `Nuclear_export`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NFAT\_phosphorylated} = v_2 + v_4 - v_1 \tag{18}$$

10.2 Species `NFAT_dephosphorylated`

Name NFAT_dephosphorylated

Initial concentration $0\ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in `Phosphorylation`, `Translocation` and as a product in `Dephosphorylation`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NFAT\_dephosphorylated} = v_1 - v_2 - v_3 \tag{19}$$

10.3 Species NFAT_transported

Name NFAT_transported

Initial concentration $0 \, \text{mmol} \cdot \text{ml}^{-1}$

Involved in rule NFAT_transported

This species takes part in two reactions (as a reactant in Nuclear_export and as a product in Translocation). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

10.4 Species stimulus

Name stimulus

Initial concentration $1 \, \text{mmol} \cdot \text{ml}^{-1}$

Involved in rule stimulus

This species takes part in one reaction (as a modifier in Dephosphorylation). Not this but one rule determines the species' quantity because this species is on the boundary of the reaction system.

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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