SBML Model Report

Model name: "Abell2011_CalciumSignaling-_WithoutAdaptation"

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: Vijayalakshmi Chelliah[1] and Mary N Teruel[2] at August 17th 2011 at 3:56 p. m. and last time modified at September eighth 2011 at 12:16 a. 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	4
species types	0	species	6
events	0	constraints	0
reactions	11	function definitions	0
global parameters	20	unit definitions	0
rules	0	initial assignments	0

Model Notes

This model is from the article:
Parallel adaptive feedback enhances reliability of the Ca2+ signaling system.
Abell E, Ahrends R, Bandara S, Park BO, Teruel MN. Proc Natl Acad Sci U S A. 2011 Aug 15.

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Abstract:
Despite large cell-to-cell variations in the concentrations of individual signaling proteins, cells transmit signals correctly. This phenomenon raises the question of what signaling systems do to prevent a predicted high failure rate. Here we combine quantitative modeling, RNA interference, and targeted selective reaction monitoring (SRM) mass spectrometry, and we show for the ubiquitous and fundamental calcium signaling system that cells monitor cytosolic and endoplasmic reticulum (ER) Ca(2+) levels and adjust in parallel the concentrations of the store-operated Ca(2+) influx mediator stromal interaction molecule (STIM), the plasma membrane Ca(2+) pump plasma membrane Ca-ATPase (PMCA), and the ER Ca(2+) pump sarco/ER Ca(2+)-ATPase (SERCA). Model calculations show that this combined parallel regulation in protein expression levels effectively stabilizes basal cytosolic and ER Ca(2+) levels and preserves receptor signaling. Our results demonstrate that, rather than directly controlling the relative level of signaling proteins in a forward regulation strategy, cells prevent transmission failure by sensing the state of the signaling pathway and using multiple parallel adaptive feedbacks.

Note:

There are two models described in the paper to simulate basal and receptor stimulated Ca $^{2+}$ signaling. 1) No adaptive feedback (this model: MODEL1108050000) and 2) with three slow adaptive feedback loops (MODEL1108050001).

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 four compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
cytosol	cytosol	0000290	3	1	litre	☐	
outside	Outside	0000290	3	1	litre	☑	
ER_store	ER_store	0000290	3	1	litre	☐	cytosol
mitochondria	mito	0000290	3	1	litre	☑	cytosol

3.1 Compartment cytosol

This is a three dimensional compartment with a not constant size of one litre.

Name cytosol

SBO:0000290 physical compartment

3.2 Compartment outside

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

Name Outside

SBO:0000290 physical compartment

3.3 Compartment ER_store

This is a three dimensional compartment with a not constant size of one litre, which is surrounded by cytosol (cytosol).

Name ER_store

SBO:0000290 physical compartment

3.4 Compartment `mitochondria`

This is a three dimensional compartment with a constant size of one litre, which is surrounded by `cytosol` (cytosol).

Name mito

SBO:0000290 physical compartment

4 Species

This model contains six species. 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
CaI	CaI	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
IP3	IP3	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
g	g	cytosol	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
CaO	CaO	outside	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
CaS	CaS	ER_store	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
CaM	CaM	mitochondria	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 20 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
A	IP3R		3.000		☑
B	SERCA		0.266		☑
D	IP3degradation		2.000		☑
E	IP3Rinhibition		5.000		☑
F	IP3Rrecovery		0.018		☑
k2	kSERCA		0.175		☑
L	ERleak		0.010		☑
R	R		1.000		☑
kIP3R	kIP3R		0.175		☑
PMleak	PMleak		0.035		☑
kSTIM	kSTIM		1.000		☑
mw004dcb62-_da5f-_41c7_a7bd-_033574894f48	STIM		0.020		☑
mw78dd80b8-_e003-_4c62_81d1-_547d001767af	kIP3Rca		0.130		☑
mw3a93c3a6-_623a-_44fe_84e9-_a47823defd1f	kPMCA		0.200		☑
mwd21d3f76-_d133-_4053_8e44-_02a538657e0a	PMCA		0.013		☑
mwf998b218-_be11-_4aa4_81ae-_41141861fb42	kG		1.000		☑
mwc714c217-_c8fd-_4024_912c-_681cd6931f59	DirTransf		0.030		☑

Id	Name	SBO	Value	Unit	Constant
mwd90ce3ea-_f8d5-_4f0a_8093-_e39a2d3dbf33	MitNaCaEx		0.005		☑
mw886be93a-_22c7-_4966_a1fa-_113afd832ae3	UniPort		0.030		☑
mwc8d6bdb5-_59d4-_43fa_b96d-_7426f4857e0d	kUniP		0.600		☑

6 Reactions

This model contains eleven 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	kPLC	PLC: Receptor and Ca2+ regulated IP3 production	$\emptyset \xrightarrow{\text{CaI}} \text{IP3}$	
2	JPump	SERCA: Pumps Ca2+ into ER Ca2+ stores	$\text{CaI} \longrightarrow \text{CaS}$	
3	JChannel	IP3R: IP3 and Ca2+ regulated Ca2+ channel, plus leak	$\text{CaS} \xrightarrow{\text{g, IP3}} \text{CaI}$	
4	kPhosphatase	IP3 phosphatase: Degradation of IP3	$\text{IP3} \longrightarrow \emptyset$	
5	inhibition_parameter1	Inhibition of IP3R (mechanism not well understood)	$\emptyset \xrightarrow{\text{CaI}} \text{g}$	
6	inhibition_parameter2	Recovery of IP3R from Ca2+ iinhibition when Ca2+ drops	$\text{g} \longrightarrow \emptyset$	
7	mwbdcd6a40_1ae7_4c86_a99f_1fba0b8beaf7	Regulation of Orai by STIM, plus leak	$\emptyset \xrightarrow{\text{CaS}} \text{CaI}$	
8	mw530793e3_76b2_4483_be11_e94364306712	PMCA: Pumps Ca2+ across PM out of cell	$\text{CaI} \longrightarrow \emptyset$	

№	Id	Name	Reaction Equation	SBO
9	mwfaf5e05a-_b642-_4ee2_a069-_3c2fc783fba4	UniporterFromCytosol	CaI $\longrightarrow$ CaM	
10	mw69f19152-_7258-_45b0_bf9e-_b196f19d7e03	MitoToCytosol	CaM $\longrightarrow$ CaI	
11	ERtoMito	ERtoMito	CaS $\xrightarrow{\text{CaI, g, IP3}}$ CaM	

6.1 Reaction kPLC

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

Name PLC: Receptor and Ca2+ regulated IP3 production

Reaction equation

$$\emptyset \xrightarrow{\text{CaI}} \text{IP3} \tag{1}$$

Modifier

Table 6: Properties of each modifier.

Id	Name	SBO
CaI	CaI	

Product

Table 7: Properties of each product.

Id	Name	SBO
IP3	IP3	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{R} \cdot [\text{CaI}] \tag{2}$$

6.2 Reaction JPump

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

Name SERCA: Pumps Ca2+ into ER Ca2+ stores

Reaction equation

$$\text{CaI} \longrightarrow \text{CaS} \tag{3}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
CaI	CaI	

Product

Table 9: Properties of each product.

Id	Name	SBO
CaS	CaS	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \frac{\mathrm{B} \cdot [\mathrm{CaI}]^2}{[\mathrm{CaI}]^2 + \mathrm{k2}^2} \tag{4}$$

6.3 Reaction JChannel

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

Name IP3R: IP3 and Ca2+ regulated Ca2+ channel, plus leak

Reaction equation

$$\mathrm{CaS} \xrightarrow{\mathrm{g,\ IP3}} \mathrm{CaI} \tag{5}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
CaS	CaS	

Modifiers

Table 11: Properties of each modifier.

Id	Name	SBO
g	g	
IP3	IP3	

Product

Table 12: Properties of each product.

Id	Name	SBO
CaI	CaI	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = (1 - \text{mwc714c217\_c8fd\_4024\_912c\_681cd6931f59}) \cdot \left(\text{L} + \frac{\frac{(1-[\text{g}])\cdot \text{A}\cdot[\text{IP3}]^2}{[\text{IP3}]^2+\text{kIP3R}^2} \cdot [\text{CaI}]^2}{[\text{CaI}]^2 + \text{mw78dd80b8\_e003\_4c62\_81d1\_547d001767af}^2} \right) \cdot [\text{CaS}] \tag{6}$$

6.4 Reaction kPhosphatase

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

Name IP3 phosphatase: Degradation of IP3

Reaction equation

$$\text{IP3} \longrightarrow \emptyset \tag{7}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
IP3	IP3	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{D} \cdot [\mathrm{IP3}] \tag{8}$$

6.5 Reaction `inhibition_parameter1`

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

Name Inhibition of IP3R (mechanism not well understood)

Reaction equation

$$\emptyset \xrightarrow{\mathrm{CaI}} \mathrm{g} \tag{9}$$

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
`CaI`	CaI	

Product

Table 15: Properties of each product.

Id	Name	SBO
g	g	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \frac{\mathrm{E} \cdot [\mathrm{CaI}]^4}{[\mathrm{CaI}]^4 + \mathrm{mwf998b218\_be11\_4aa4\_81ae\_41141861fb42}^4} \cdot (1 - [\mathrm{g}]) \tag{10}$$

6.6 Reaction `inhibition_parameter2`

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

Name Recovery of IP3R from Ca2+ iinhibition when Ca2+ drops

Reaction equation

$$\mathrm{g} \longrightarrow \emptyset \tag{11}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
g	g	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{F} \cdot [\mathrm{g}] \tag{12}$$

6.7 Reaction mwbdcd6a40_1ae7_4c86_a99f_1fba0b8beaf7

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

Name Regulation of Orai by STIM, plus leak

Reaction equation

$$\emptyset \xrightarrow{\mathrm{CaS}} \mathrm{CaI} \tag{13}$$

Modifier

Table 17: Properties of each modifier.

Id	Name	SBO
CaS	CaS	

Product

Table 18: Properties of each product.

Id	Name	SBO
CaI	CaI	

Kinetic Law

Derived unit not available

$$v_7 = \mathrm{mw004dcb62\_da5f\_41c7\_a7bd\_033574894f48} \cdot \left(\mathrm{PMleak} + \frac{\mathrm{kSTIM}^8}{[\mathrm{CaS}]^8 + \mathrm{kSTIM}^8} \right) \tag{14}$$

6.8 Reaction mw530793e3_76b2_4483_be11_e94364306712

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

Name PMCA: Pumps Ca2+ across PM out of cell

Reaction equation

$$\mathrm{CaI} \longrightarrow \emptyset \tag{15}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
CaI	CaI	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \frac{\text{mwd21d3f76\_d133\_4053\_8e44\_02a538657e0a} \cdot [\mathrm{CaI}]^2}{[\mathrm{CaI}]^2 + \text{mw3a93c3a6\_623a\_44fe\_84e9\_a47823defd1f}^2} \tag{16}$$

6.9 Reaction mwfaf5e05a_b642_4ee2_a069_3c2fc783fba4

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

Name UniporterFromCytosol

Reaction equation

$$\mathrm{CaI} \longrightarrow \mathrm{CaM} \tag{17}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
CaI	CaI	

Product

Table 21: Properties of each product.

Id	Name	SBO
CaM	CaM	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \frac{\text{mw886be93a\_22c7\_4966\_a1fa\_113afd832ae3} \cdot [\text{CaI}]^4}{[\text{CaI}]^4 + \text{mwc8d6bdb5\_59d4\_43fa\_b96d\_7426f4857e0d}^4} \tag{18}$$

6.10 Reaction mw69f19152_7258_45b0_bf9e_b196f19d7e03

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

Name MitoToCytosol

Reaction equation

$$\text{CaM} \longrightarrow \text{CaI} \tag{19}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
CaM	CaM	

Product

Table 23: Properties of each product.

Id	Name	SBO
CaI	CaI	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \frac{\text{mwd90ce3ea\_f8d5\_4f0a\_8093\_e39a2d3dbf33} \cdot [\text{CaM}]}{[\text{CaM}] + 0.01} \tag{20}$$

6.11 Reaction ERtoMito

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

Name ERtoMito

Reaction equation

$$\mathrm{CaS} \xrightarrow{\mathrm{CaI,\ g,\ IP3}} \mathrm{CaM} \tag{21}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
CaS	CaS	

Modifiers

Table 25: Properties of each modifier.

Id	Name	SBO
CaI	CaI	
g	g	
IP3	IP3	

Product

Table 26: Properties of each product.

Id	Name	SBO
CaM	CaM	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{mwc714c217\_c8fd\_4024\_912c\_681cd6931f59} \cdot \left(\mathrm{L} + \frac{\frac{(1-[\mathrm{g}])\cdot \mathrm{A}\cdot[\mathrm{IP3}]^2}{[\mathrm{IP3}]^2+\mathrm{kIP3R}^2}\cdot[\mathrm{CaI}]^2}{[\mathrm{CaI}]^2 + \mathrm{mw78dd80b8\_e003\_4c62\_81d1\_547d001767af}^2} \right) \cdot [\mathrm{CaS}] \tag{22}$$

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.

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.

7.1 Species `CaI`

Name CaI

SBO:0000247 simple chemical

Initial amount 0.05 mol

This species takes part in nine reactions (as a reactant in `JPump`, `mw530793e3_76b2_4483-_be11_e94364306712`, `mwfaf5e05a_b642_4ee2_a069_3c2fc783fba4` and as a product in `JChannel`, `mwbdcd6a40_1ae7_4c86_a99f_1fba0b8beaf7`, `mw69f19152_7258_45b0_bf9e_b196f19d7e03` and as a modifier in `kPLC`, `inhibition_parameter1`, `ERtoMito`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CaI} = v_3 + v_7 + v_{10} - v_2 - v_8 - v_9 \tag{23}$$

7.2 Species `IP3`

Name IP3

SBO:0000247 simple chemical

Initial amount 0 mol

This species takes part in four reactions (as a reactant in `kPhosphatase` and as a product in `kPLC` and as a modifier in `JChannel`, `ERtoMito`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IP3} = v_1 - v_4 \tag{24}$$

7.3 Species g

Name g

Initial amount 0.0020 mol

This species takes part in four reactions (as a reactant in inhibition_parameter2 and as a product in inhibition_parameter1 and as a modifier in JChannel, ERtoMito).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{g} = v_5 - v_6 \tag{25}$$

7.4 Species CaO

Name CaO

SBO:0000247 simple chemical

Initial amount 1000 mol

This species does not take part in any reactions. Its quantity does hence not change over time:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CaO} = 0 \tag{26}$$

7.5 Species CaS

Name CaS

SBO:0000247 simple chemical

Initial amount 2 mol

This species takes part in four reactions (as a reactant in JChannel, ERtoMito and as a product in JPump and as a modifier in mwbdcd6a40_1ae7_4c86_a99f_1fba0b8beaf7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CaS} = v_2 - v_3 - v_{11} \tag{27}$$

7.6 Species CaM

Name CaM

SBO:0000247 simple chemical

Initial amount 0 mol

This species takes part in three reactions (as a reactant in mw69f19152_7258_45b0_bf9e-_b196f19d7e03 and as a product in mwfaf5e05a_b642_4ee2_a069_3c2fc783fba4, ERtoMito).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CaM} = v_9 + v_{11} - v_{10} \tag{28}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000247 simple chemical: Simple, non-repetitive chemical entity

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

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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