SBML Model Report

Model name: “Rosas2015 - Caffeine-induced luminal SR calcium changes”

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following eleven authors: Nick Juty[1], Vijayalakshmi Chelliah[2], Ryan Gutenkunst[3], Daniel Macias[4], Emmet Andrews[5], Ryan Mammana[6], Sara Carey[7], Emily Merritt[8], Julie McGrath[9], Joshua Kochanowsky[10] and Norma Citlalcue Perez-Rosas[11] at April 18th 2016 at 1:46 p. m. and last time modified at April 18th 2016 at 2:54 p. m. Table 1 gives an overview of the quantities of all components of this model.

Model Notes

hyperref

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This SBML model reproduced the calcium release from SR by application of 20 mM or 2mM ca

* Ca_i_Total and Ca_SR_Total respectively represent the total calcium concentration in th
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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	5
events	2	constraints	0
reactions	3	function definitions	0
global parameters	18	unit definitions	0
rules	6	initial assignments	0

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* Ca_i  and Ca_SR respectively represent the free calcium concentration in the sarcoplasm
* J1 is the calcium  flux due to all mechanisms (except SERCA pumps) that remove the exce
* J2 is the calcium flux from the reticulum to the sarcoplasm via the ryanodine receptors
* J3 is the calcium flux from the sarcoplasm to the reticulum by the SERCA pumps located
*The parameters are a,  b, B c, Ca_i_basal, Ca_SR_basal, caff, csq,  gamma, KC, kf, KR, P
* The value of KC for the model were calculated for J2=J3, after substituting Ca_i=Ca_i_b
* Po represents the RyR open probability based on CICR.
* Caffeine (caff)** increases the calcium affinity of smooth muscle's RyR so they open ev
** Due to caffeine-induced calcium release, a 5 seconds  pulse of caffeine (20 mM) was ap
* PE denotes the concentration of calcium binding sites.
* Xi=Ca_SR_Total+PE+KR
*In order to reproduce the dynamics of calcium following the application of 2 mM of caffe
*The unit of the calcium concentration is mol/L.
* The unit of time is second.
*The original SBML code was exported from COPASI 4.12 (Build 81).
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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	C
mw0dac359a_a4cd_40bf_97a0_45006cef2a7c	SR		3	0.052	l	☑	
mw44539b83_caa2_4da5_bae0_a8dcf7439431	cytoplasm		3	1	litre	☑	

3.1 Compartment mw0dac359a_a4cd_40bf_97a0_45006cef2a7c

This is a three dimensional compartment with a constant size of 0.052 litre.

Name SR

3.2 Compartment mw44539b83_caa2_4da5_bae0_a8dcf7439431

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

Name cytoplasm

4 Species

This model contains five 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 9 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
mwd805cc43-_4a96_472f_a894-_c119a6aa895f	Ca_SR_Total	mw0dac359a_a4cd_40bf-_97a0_45006cef2a7c	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
mw447078ee-_8bc8_4358_abcd-_ade10dba93b0	Ca_SR	mw0dac359a_a4cd_40bf-_97a0_45006cef2a7c	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
mw40a96ef6-_32da_46d1_9712-_4f53f60bad43	Ca_i_Total	mw44539b83_caa2_4da5-_bae0_a8dcf7439431	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
mwe1a0a651-_d2d5_4f75_8d45-_9336c60eb9a6	Ca_i	mw44539b83_caa2_4da5-_bae0_a8dcf7439431	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑
mw168e0d8a-_b9f7_4d4c_b437-_a81206c5d381	caff	mw44539b83_caa2_4da5-_bae0_a8dcf7439431	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 18 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
parameter_1	a		35.000		☑
parameter_2	b		65.000		☑
parameter_3	c		$1.125 \cdot 10^{-5}$		☑
parameter_4	Ca_i_basal		$7.5 \cdot 10^{-6}$		☑
parameter_5	gamma		0.052		☑
parameter_6	nv		1.700		☑
parameter_7	Ks		$3 \cdot 10^{-7}$		☑
parameter_8	ns		2.000		☑
parameter_9	B		100.000		☑
parameter_10	nf		1.800		☑
parameter_11	kf		4000.000		☑
parameter_14	KR		$1.515 \cdot 10^{-4}$		☑
parameter_15	csq		10.000		☑
parameter_22	KC		$9.45128810336575 \cdot 10^{-7}$		⊟
parameter_23	Po		0.010		⊟
parameter_24	PE		$1.50000000000001 \cdot 10^{-5}$		⊟
parameter_25	Ca_SR_basal		$1.5 \cdot 10^{-4}$		☑
parameter_26	Xi		0.002		⊟

6 Rules

This is an overview of six rules.

6.1 Rule parameter_24

Rule parameter_24 is an assignment rule for parameter parameter_24:

$$\text{parameter\_24} = \text{parameter\_15} \cdot (\text{parameter\_14} - \text{parameter\_25}) \tag{1}$$

6.2 Rule parameter_26

Rule parameter_26 is an assignment rule for parameter parameter_26:

$$\text{parameter\_26} = [\text{mwd805cc43\_4a96\_472f\_a894\_c119a6aa895f}] + \text{parameter\_24} + \text{parameter\_14} \tag{2}$$

6.3 Rule mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6

Rule mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6 is an assignment rule for species mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6:

$$\begin{aligned}&\text{mwe1a0a651\_d2d5\_4f75\_8d45\_9336c60eb9a6}\\&= \frac{[\text{mw40a96ef6\_32da\_46d1\_9712\_4f53f60bad43}]}{\text{parameter\_9}}\end{aligned} \tag{3}$$

6.4 Rule mw447078ee_8bc8_4358_abcd_ade10dba93b0

Rule mw447078ee_8bc8_4358_abcd_ade10dba93b0 is an assignment rule for species mw447078ee_8bc8_4358_abcd_ade10dba93b0:

$$\begin{aligned}&\text{mw447078ee\_8bc8\_4358\_abcd\_ade10dba93b0}\\&= \frac{\text{parameter\_26} - \left(\text{parameter\_26}^2 - 4 \cdot [\text{mwd805cc43\_4a96\_472f\_a894\_c119a6aa895f}] \cdot \text{parameter\_14}\right)^{\frac{1}{2}}}{2}\end{aligned} \tag{4}$$

6.5 Rule parameter_22

Rule parameter_22 is an assignment rule for parameter parameter_22:

$$\begin{aligned}\text{parameter\_22} = \Bigg(&\text{parameter\_2} \cdot \text{parameter\_5}^{\text{parameter\_6}} \cdot \left(\frac{\text{parameter\_4}}{\text{parameter\_9}}\right)^{\text{parameter\_10}}\\&\cdot \left(\text{parameter\_25} - \frac{\text{parameter\_4}}{\text{parameter\_9}}\right)\\&\cdot \frac{\left(\frac{\text{parameter\_4}}{\text{parameter\_9}}\right)^{\text{parameter\_8}} + \text{parameter\_7}^{\text{parameter\_8}}}{\text{parameter\_3} \cdot \left(\frac{\text{parameter\_4}}{\text{parameter\_9}}\right)^{\text{parameter\_8}}}\\&- \left(\frac{\text{parameter\_4}}{\text{parameter\_9}}\right)^{\text{parameter\_10}}\Bigg)^{\frac{1}{\text{parameter\_10}}}\end{aligned} \tag{5}$$

6.6 Rule parameter_23

Rule parameter_23 is an assignment rule for parameter parameter_23:

$$\begin{aligned}&\text{parameter\_23}\\&= \frac{([\text{mwe1a0a651\_d2d5\_4f75\_8d45\_9336c60eb9a6}] \cdot (1 + \text{parameter\_11} \cdot [\text{mw168e0d8a\_b9f7\_4d4c\_b43}}{\text{parameter\_22}^{\text{parameter\_10}} + ([\text{mwe1a0a651\_d2d5\_4f75\_8d45\_9336c60eb9a6}] \cdot (1 + \text{parameter\_11} \cdot [\text{mw168e0d8a\_b}}\end{aligned} \tag{6}$$

7 Events

This is an overview of two events. Each event is initiated whenever its trigger condition switches from `false` to `true`. A delay function postpones the effects of an event to a later time point. At the time of execution, an event can assign values to species, parameters or compartments if these are not set to constant.

7.1 Event `Caff_ON`

Name Caff_ON

Trigger condition

$$\text{time} > 10 \tag{7}$$

Assignment

$$\text{mw168e0d8a\_b9f7\_4d4c\_b437\_a81206c5d381} = 0.02 \tag{8}$$

7.2 Event `Caff_OFF`

Name Caff_OFF

Trigger condition

$$\text{time} > 15 \tag{9}$$

Assignment

$$\text{mw168e0d8a\_b9f7\_4d4c\_b437\_a81206c5d381} = 0 \tag{10}$$

8 Reactions

This model contains three 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	mw97ca2b6b-_8c30-_48ef_80cb-_5ce4ebaa420f	J3	mw40a96ef6_32da_46d1_9712_4f53f60bad43 + mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6 ⟶ mwd805cc43_4a96_472f_a894_c119 mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6	
2	mw18c30692-_65ff-_4c7a_b820-_079f8ddd9b33	J2	mwd805cc43_4a96_472f_a894_c119a6aa895f + mw447078ee_8bc8_4358_abcd_ade10dba93b0 + mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6 ⟶ mw40a96ef6_32da_46d1_9712_4f53 mw447078ee_8bc8_4358_abcd_ade10dba93b0 + mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6	
3	mwf3ceaa7c-_ebe4-_4e1b_842a-_b4446b0aa527	J1	mw40a96ef6_32da_46d1_9712_4f53f60bad43 + mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6 ⟶ mwe1a0a651_d2d5_4f75_8d45_9336	

8.1 Reaction mw97ca2b6b_8c30_48ef_80cb_5ce4ebaa420f

This is an irreversible reaction of two reactants forming two products.

Name J3

Reaction equation

$$\text{mw40a96ef6\_32da\_46d1\_9712\_4f53f60bad43} + \text{mwe1a0a651\_d2d5\_4f75\_8d45\_9336c60eb9a6} \longrightarrow \text{mwd805cc43\_4a} \tag{11}$$

Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
mw40a96ef6_32da_46d1_9712_4f53f60bad43	Ca_i_Total	
mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6	Ca_i	

Products

Table 7: Properties of each product.

Id	Name	SBO
mwd805cc43_4a96_472f_a894_c119a6aa895f	Ca_SR_Total	
mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6	Ca_i	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{\text{parameter\_3} \cdot [\text{mwe1a0a651\_d2d5\_4f75\_8d45\_9336c60eb9a6}]^{\text{parameter\_8}}}{\text{parameter\_7}^{\text{parameter\_8}} + [\text{mwe1a0a651\_d2d5\_4f75\_8d45\_9336c60eb9a6}]^{\text{parameter\_8}}} \tag{12}$$

8.2 Reaction mw18c30692_65ff_4c7a_b820_079f8ddd9b33

This is an irreversible reaction of three reactants forming three products.

Name J2

Reaction equation

$$\text{mwd805cc43\_4a96\_472f\_a894\_c119a6aa895f} + \text{mw447078ee\_8bc8\_4358\_abcd\_ade10dba93b0} + \text{mwe1a0a651\_d2d5} \tag{13}$$

Reactants

Table 8: Properties of each reactant.

Id	Name	SBO
mwd805cc43_4a96_472f_a894_c119a6aa895f	Ca_SR_Total	
mw447078ee_8bc8_4358_abcd_ade10dba93b0	Ca_SR	
mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6	Ca_i	

Products

Table 9: Properties of each product.

Id	Name	SBO
mw40a96ef6_32da_46d1_9712_4f53f60bad43	Ca_i_Total	
mw447078ee_8bc8_4358_abcd_ade10dba93b0	Ca_SR	
mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6	Ca_i	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{parameter\_2} \cdot \text{parameter\_5}^{\text{parameter\_6}} \cdot \text{parameter\_23} \cdot ([\text{mw447078ee\_8bc8\_4358\_abcd\_ade10dba93b0}] - [\text{mwe1a0a651\_d2d5\_4f75\_8d45\_9336c60eb9a6}]) \quad (14)$$

8.3 Reaction mwf3ceaa7c_ebe4_4e1b_842a_b4446b0aa527

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

Name J1

Reaction equation

$$\text{mw40a96ef6\_32da\_46d1\_9712\_4f53f60bad43} + \text{mwe1a0a651\_d2d5\_4f75\_8d45\_9336c60eb9a6} \longrightarrow \text{mwe1a0a651\_d2} \quad (15)$$

Reactants

Table 10: Properties of each reactant.

Id	Name	SBO
mw40a96ef6_32da_46d1_9712_4f53f60bad43	Ca_i_Total	
mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6	Ca_i	

Product

Table 11: Properties of each product.

Id	Name	SBO
mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6	Ca_i	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{mw44539b83\_caa2\_4da5\_bae0\_a8dcf7439431}\right) \cdot \frac{\mathrm{parameter\_1} \cdot \left(\left[\mathrm{mwe1a0a651\_d2d5\_4f75\_8d45\_9336c60eb9a6}\right] - \frac{\mathrm{parameter\_4}}{\mathrm{parameter\_9}}\right)}{\mathrm{vol}\left(\mathrm{mw44539b83\_caa2\_4da5\_bae0\_a8dcf7439431}\right)} \quad (16)$$

9 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.

9.1 Species mwd805cc43_4a96_472f_a894_c119a6aa895f

Name Ca_SR_Total

Initial amount 0.00165 mol

This species takes part in two reactions (as a reactant in mw18c30692_65ff_4c7a_b820_079f8ddd9b33 and as a product in mw97ca2b6b_8c30_48ef_80cb_5ce4ebaa420f).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mwd805cc43\_4a96\_472f\_a894\_c119a6aa895f} = v_1 - v_2 \quad (17)$$

9.2 Species mw447078ee_8bc8_4358_abcd_ade10dba93b0

Name Ca_SR

Initial amount $7.8 \cdot 10^{-6}$ mol

Involved in rule mw447078ee_8bc8_4358_abcd_ade10dba93b0

This species takes part in two reactions (as a reactant in mw18c30692_65ff_4c7a_b820_079f8ddd9b33 and as a product in mw18c30692_65ff_4c7a_b820_079f8ddd9b33). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

9.3 Species mw40a96ef6_32da_46d1_9712_4f53f60bad43

Name Ca_i_Total

Initial amount $7.5 \cdot 10^{-6}$ mol

This species takes part in three reactions (as a reactant in mw97ca2b6b_8c30_48ef_80cb_5ce4ebaa420f, mwf3ceaa7c_ebe4_4e1b_842a_b4446b0aa527 and as a product in mw18c30692_65ff_4c7a_b820_079f8ddd9b33).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mw40a96ef6\_32da\_46d1\_9712\_4f53f60bad43} = v_2 - v_1 - v_3 \tag{18}$$

9.4 Species mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6

Name Ca_i

Initial amount $7.5 \cdot 10^{-8}$ mol

Involved in rule mwe1a0a651_d2d5_4f75_8d45_9336c60eb9a6

This species takes part in six reactions (as a reactant in mw97ca2b6b_8c30_48ef_80cb_5ce4ebaa420f, mw18c30692_65ff_4c7a_b820_079f8ddd9b33, mwf3ceaa7c_ebe4_4e1b_842a_b4446b0aa527 and as a product in mw97ca2b6b_8c30_48ef_80cb_5ce4ebaa420f, mw18c30692_65ff_4c7a_b820_079f8ddd9b33, mwf3ceaa7c_ebe4_4e1b_842a_b4446b0aa527). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

9.5 Species mw168e0d8a_b9f7_4d4c_b437_a81206c5d381

Name caff

Initial amount 0 mol

Involved in events Caff_ON, Caff_OFF

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mw168e0d8a\_b9f7\_4d4c\_b437\_a81206c5d381} = 0 \tag{19}$$

Furthermore, two events influence this species' rate of change.

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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