SBML Model Report

Model name: "Mears1997_CRAC_PancreaticBetaCells"

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: Ishan Ajmera[1] and Catherine Lloyd[2] at September 29th 2011 at 10:10 p. m. and last time modified at April eighth 2016 at 5:07 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	0	function definitions	0
global parameters	61	unit definitions	0
rules	31	initial assignments	0

Model Notes

This a model from the article:
Evidence that calcium release-activated current mediates the biphasic electricalactivity of mouse pancreatic beta-cells.
Mears D, Sheppard NF Jr, Atwater I, Rojas E, Bertram R, Sherman A. J Membr Biol1997 Jan

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1;155(1):47-59 9002424,

Abstract:
The electrical response of pancreatic beta-cells to step increases in glucoseconcentration is biphasic, consisting of a prolonged depolarization with actionpotentials (Phase 1) followed by membrane potential oscillations known asbursts. We have proposed that the Phase 1 response results from the combineddepolarizing influences of potassium channel closure and an inward, nonselectivecation current (ICRAN) that activates as intracellular calcium stores emptyduring exposure to basal glucose (Bertram et al., 1995). The stores refillduring Phase 1, deactivating ICRAN and allowing steady-state bursting tocommence. We support this hypothesis with additional simulations andexperimental results indicating that Phase 1 duration is sensitive to thefilling state of intracellular calcium stores. First, the duration of the Phase1 transient increases with duration of prior exposure to basal (2.8 mM) glucose,reflecting the increased time required to fill calcium stores that have beenemptying for longer periods. Second, Phase 1 duration is reduced when islets areexposed to elevated K+ to refill calcium stores in the presence of basalglucose. Third, when extracellular calcium is removed during the basal glucoseexposure to reduce calcium influx into the stores, Phase 1 duration increases.Finally, no Phase 1 is observed following hyperpolarization of the beta-cellmembrane with diazoxide in the continued presence of 11 mm glucose, a conditionin which intracellular calcium stores remain full. Application of carbachol toempty calcium stores during basal glucose exposure did not increase Phase 1duration as the model predicts. Despite this discrepancy, the good agreementbetween most of the experimental results and the model predictions providesevidence that a calcium release-activated current mediates the Phase 1electrical response of the pancreatic beta-cell.

This model was taken from the CellML repository and automatically converted to SBML.
The original model was:**Mears D, Sheppard NF Jr, Atwater I, Rojas E, Bertram R, Sherman A. (1997) - version=1.0**
The original CellML model was created by:
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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 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

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

3.1 Compartment `COMpartment`

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

Name COMpartment

4 Species

This model contains five 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
V_membrane	V_membrane	COMpartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
n	n	COMpartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
jm	jm	COMpartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Ca_er_Ca_equations	Ca_er_Ca_equations	COMpartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Ca_i	Ca_i	COMpartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 61 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Cm	Cm	0000258	6158.000		☑
i_K	i_K		17.550		☐
V_K	V_K	0000009	-70.000		☑
g_K	g_K	0000009	3900.000		☑
n_infinity	n_infinity		$4.67956725632935 \cdot 10^{-4}$		☐
tau_n	tau_n		9.086		☐
Vn	Vn	0000009	-15.000		☑
Sn	Sn	0000009	6.000		☑
lambda_n	lambda_n	0000009	1.850		☑
i_K_ATP	i_K_ATP		1350.000		☐
g_K_ATP	g_K_ATP		150.000		☐
i_Ca_f	i_Ca_f		-548.702		☐
V_Ca	V_Ca	0000009	100.000		☑
g_Ca_f	g_Ca_f	0000009	810.000		☑
m_f_infinity	m_f_infinity		0.004		☐
Vm_f	Vm_f	0000009	-20.000		☑
Sm_f	Sm_f	0000009	7.500		☑
i_Ca_s	i_Ca_s		-793.881		☐
g_Ca_s	g_Ca_s	0000009	510.000		☑
m_s_infinity	m_s_infinity		0.011		☐
Vm_s	Vm_s	0000009	-16.000		☑
Sm_s	Sm_s	0000009	10.000		☑
jm_infinity	jm_infinity		0.018		☐
Vj	Vj	0000009	-53.000		☑
tau_j	tau_j		8145.056		☐
Sj	Sj	0000009	2.000		☑
i_Ca	i_Ca		-1342.583		☐
i_K_Ca	i_K_Ca		3.455		☐
g_K_Ca	g_K_Ca	0000009	1200.000		☑
kdkca	kdkca	0000009	0.550		☑
i_CRAC	i_CRAC		-5.815		☐
g_CRAC	g_CRAC	0000009	75.000		☑
V_CRAC	V_CRAC	0000009	0.000		☑
r_infinity	r_infinity		0.001		☐
Ca_er_bar	Ca_er_bar	0000009	40.000		☑
sloper	sloper	0000009	3.000		☑
i_leak	i_leak		0.000		☐

Id	Name	SBO	Value	Unit	Constant
g_leak	g_leak	0000009	0.000		☑
J_er_p	J_er_p		0.144		☐
IP3	IP3	0000196	0.000		☑
kerp	kerp	0000009	0.090		☑
verp	verp	0000009	0.240		☑
dact	dact	0000009	0.350		☑
dinh	dinh	0000009	0.400		☑
dip3	dip3	0000009	0.200		☑
a_infinity	a_infinity		0.239		☐
b_infinity	b_infinity		0.000		☐
h_infinity	h_infinity		0.784		☐
O	O		0.000		☐
J_er_tot	J_er_tot		0.036		☐
J_er_IP3	J_er_IP3		0.000		☐
J_er_leak	J_er_leak		0.180		☐
perl	perl	0000009	0.003		☑
lambda_er	lambda_er	0000009	250.000		☑
sigma_er	sigma_er	0000009	1.000		☑
kmp	kmp	0000009	0.350		☑
vmp	vmp	0000009	0.080		☑
gamma	gamma	0000009	$3.607 \cdot 10^{-6}$		☑
J_mem_tot	J_mem_tot		$-2.34898089778648 \cdot 10^{-5}$		☐
Jmp	Jmp		0.007		☐
f	f	0000009	0.010		☑

6 Rules

This is an overview of 31 rules.

6.1 Rule tau_n

Rule tau_n is an assignment rule for parameter tau_n:

$$\text{tau\_n} = \frac{9.09}{1 + \exp\left(\frac{[\text{V\_membrane}]+15}{6}\right)} \tag{1}$$

6.2 Rule i_K

Rule i_K is an assignment rule for parameter i_K:

$$\text{i\_K} = \text{g\_K} \cdot [\text{n}] \cdot ([\text{V\_membrane}] - \text{V\_K}) \tag{2}$$

6.3 Rule n_infinity

Rule n_infinity is an assignment rule for parameter n_infinity:

$$\text{n\_infinity} = \frac{1}{1 + \exp\left(\frac{15 - [\text{V\_membrane}]}{6}\right)} \tag{3}$$

6.4 Rule g_K_ATP

Rule g_K_ATP is an assignment rule for parameter g_K_ATP:

$$\text{g\_K\_ATP} = \begin{cases} 2000 & \text{if } (\text{time} > 60000) \wedge (\text{time} < 660000) \\ 150 & \text{otherwise} \end{cases} \tag{4}$$

6.5 Rule i_K_ATP

Rule i_K_ATP is an assignment rule for parameter i_K_ATP:

$$\text{i\_K\_ATP} = \text{g\_K\_ATP} \cdot ([\text{V\_membrane}] - \text{V\_K}) \tag{5}$$

6.6 Rule m_f_infinity

Rule m_f_infinity is an assignment rule for parameter m_f_infinity:

$$\text{m\_f\_infinity} = \frac{1}{1 + \exp\left(\frac{20 - [\text{V\_membrane}]}{7.5}\right)} \tag{6}$$

6.7 Rule i_Ca_f

Rule i_Ca_f is an assignment rule for parameter i_Ca_f:

$$\text{i\_Ca\_f} = \text{g\_Ca\_f} \cdot \text{m\_f\_infinity} \cdot ([\text{V\_membrane}] - \text{V\_Ca}) \tag{7}$$

6.8 Rule m_s_infinity

Rule m_s_infinity is an assignment rule for parameter m_s_infinity:

$$\text{m\_s\_infinity} = \frac{1}{1 + \exp\left(\frac{16 - [\text{V\_membrane}]}{10}\right)} \tag{8}$$

6.9 Rule i_Ca_s

Rule i_Ca_s is an assignment rule for parameter i_Ca_s:

$$\text{i\_Ca\_s} = \text{g\_Ca\_s} \cdot \text{m\_s\_infinity} \cdot (1 - [\text{jm}]) \cdot ([\text{V\_membrane}] - \text{V\_Ca}) \tag{9}$$

6.10 Rule jm_infinity

Rule jm_infinity is an assignment rule for parameter jm_infinity:

$$\text{jm\_infinity} = 1 - \frac{1}{1 + \exp\left(\frac{[\text{V\_membrane}]+53}{2}\right)} \tag{10}$$

6.11 Rule tau_j

Rule tau_j is an assignment rule for parameter tau_j:

$$\text{tau\_j} = \frac{50000}{\exp\left(\frac{[\text{V\_membrane}]+53}{4}\right) + \exp\left(\frac{53-[\text{V\_membrane}]}{4}\right)} + 1500 \tag{11}$$

6.12 Rule i_Ca

Rule i_Ca is an assignment rule for parameter i_Ca:

$$\text{i\_Ca} = \text{i\_Ca\_f} + \text{i\_Ca\_s} \tag{12}$$

6.13 Rule i_K_Ca

Rule i_K_Ca is an assignment rule for parameter i_K_Ca:

$$\text{i\_K\_Ca} = \frac{\text{g\_K\_Ca} \cdot [\text{Ca\_i}]^5}{[\text{Ca\_i}]^5 + \text{kdkca}^5} \cdot ([\text{V\_membrane}] - \text{V\_K}) \tag{13}$$

6.14 Rule r_infinity

Rule r_infinity is an assignment rule for parameter r_infinity:

$$\text{r\_infinity} = \frac{1}{1 + \exp\left(\frac{[\text{Ca\_er\_Ca\_equations}]-\text{Ca\_er\_bar}}{\text{sloper}}\right)} \tag{14}$$

6.15 Rule i_CRAC

Rule i_CRAC is an assignment rule for parameter i_CRAC:

$$\text{i\_CRAC} = \text{g\_CRAC} \cdot \text{r\_infinity} \cdot ([\text{V\_membrane}] - \text{V\_CRAC}) \tag{15}$$

6.16 Rule i_leak

Rule i_leak is an assignment rule for parameter i_leak:

$$\text{i\_leak} = \text{g\_leak} \cdot ([\text{V\_membrane}] - \text{V\_CRAC}) \tag{16}$$

6.17 Rule J_er_p

Rule J_er_p is an assignment rule for parameter J_er_p:

$$\mathrm{J\_er\_p} = \frac{\mathrm{verp} \cdot [\mathrm{Ca\_i}]^2}{[\mathrm{Ca\_i}]^2 + \mathrm{kerp}^2} \tag{17}$$

6.18 Rule a_infinity

Rule a_infinity is an assignment rule for parameter a_infinity:

$$\mathrm{a\_infinity} = \frac{1}{1 + \frac{\mathrm{dact}}{[\mathrm{Ca\_i}]}} \tag{18}$$

6.19 Rule b_infinity

Rule b_infinity is an assignment rule for parameter b_infinity:

$$\mathrm{b\_infinity} = \frac{\mathrm{IP3}}{\mathrm{IP3} + \mathrm{dip3}} \tag{19}$$

6.20 Rule h_infinity

Rule h_infinity is an assignment rule for parameter h_infinity:

$$\mathrm{h\_infinity} = \frac{1}{1 + \frac{[\mathrm{Ca\_i}]}{\mathrm{dinh}}} \tag{20}$$

6.21 Rule O

Rule O is an assignment rule for parameter O:

$$\mathrm{O} = \mathrm{a\_infinity}^3 \cdot \mathrm{b\_infinity}^3 \cdot \mathrm{h\_infinity}^3 \cdot 1 \tag{21}$$

6.22 Rule J_er_IP3

Rule J_er_IP3 is an assignment rule for parameter J_er_IP3:

$$\mathrm{J\_er\_IP3} = \mathrm{O} \cdot ([\mathrm{Ca\_er\_Ca\_equations}] - [\mathrm{Ca\_i}]) \tag{22}$$

6.23 Rule J_er_leak

Rule J_er_leak is an assignment rule for parameter J_er_leak:

$$\mathrm{J\_er\_leak} = \mathrm{perl} \cdot ([\mathrm{Ca\_er\_Ca\_equations}] - [\mathrm{Ca\_i}]) \tag{23}$$

6.24 Rule J_er_tot

Rule J_er_tot is an assignment rule for parameter J_er_tot:

$$\mathrm{J\_er\_tot} = \mathrm{J\_er\_leak} + \mathrm{J\_er\_IP3} - \mathrm{J\_er\_p} \tag{24}$$

6.25 Rule Jmp

Rule Jmp is an assignment rule for parameter Jmp:

$$\mathrm{Jmp} = \frac{\mathrm{vmp} \cdot [\mathrm{Ca\_i}]^2}{[\mathrm{Ca\_i}]^2 + \mathrm{kmp}^2} \tag{25}$$

6.26 Rule J_mem_tot

Rule J_mem_tot is an assignment rule for parameter J_mem_tot:

$$\mathrm{J\_mem\_tot} = \mathrm{f} \cdot (\mathrm{gamma} \cdot \mathrm{i\_Ca} + \mathrm{Jmp}) \tag{26}$$

6.27 Rule V_membrane

Rule V_membrane is a rate rule for species V_membrane:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{V\_membrane} = \frac{(\mathrm{i\_Ca} + \mathrm{i\_K} + \mathrm{i\_K\_ATP} + \mathrm{i\_K\_Ca} + \mathrm{i\_CRAC} + \mathrm{i\_leak})}{\mathrm{Cm}} \tag{27}$$

6.28 Rule n

Rule n is a rate rule for species n:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{n} = \frac{\mathrm{lambda\_n} \cdot (\mathrm{n\_infinity} - [\mathrm{n}])}{\mathrm{tau\_n}} \tag{28}$$

6.29 Rule jm

Rule jm is a rate rule for species jm:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{jm} = \frac{\mathrm{jm\_infinity} - [\mathrm{jm}]}{\mathrm{tau\_j}} \tag{29}$$

6.30 Rule Ca_er_Ca_equations

Rule Ca_er_Ca_equations is a rate rule for species Ca_er_Ca_equations:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ca\_er\_Ca\_equations} = \frac{\mathrm{J\_er\_tot}}{\mathrm{lambda\_er} \cdot \mathrm{sigma\_er}} \tag{30}$$

6.31 Rule Ca_i

Rule Ca_i is a rate rule for species Ca_i:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ca\_i} = \frac{\mathrm{J\_er\_tot}}{\mathrm{lambda\_er}} + \mathrm{J\_mem\_tot} \tag{31}$$

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.

7.1 Species V_membrane

Name V_membrane

SBO:0000259 voltage

Initial amount -61 mol

Involved in rule V_membrane

One rule which determines this species' quantity.

7.2 Species n

Name n

Initial amount $5 \cdot 10^{-4}$ mol

Involved in rule n

One rule which determines this species' quantity.

7.3 Species jm

Name jm

SBO:0000412 biological activity

Initial amount 0.12 mol

Involved in rule jm

One rule which determines this species' quantity.

7.4 Species Ca_er_Ca_equations

Name Ca_er_Ca_equations

Initial amount 60 mol

Involved in rule Ca_er_Ca_equations

One rule which determines this species' quantity.

7.5 Species Ca_i

Name Ca_i

Initial amount 0.11 mol

Involved in rule Ca_i

One rule which determines this species' quantity.

A Glossary of Systems Biology Ontology Terms

SBO:0000009 kinetic constant: Numerical parameter that quantifies the velocity of a chemical reaction

SBO:0000196 concentration of an entity pool: The amount of an entity per unit of volume.

SBO:0000258 capacitance: Measure of the amount of electric charge stored (or separated) for a given electric potential. The unit of capacitance id the Farad

SBO:0000259 voltage: Difference of electrical potential between two points of an electrical network, expressed in volts

SBO:0000412 biological activity: The potential action that a biological entity has on other entities. Example are enzymatic activity, binding activity etc

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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