

SBML Model Report

Model name: “Shrestha2010_HypoCalcemia-PTHresponse”



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 Chelliah¹ and Rajiv P Shrestha² at November 15th 2010 at 2:42 p. m. and last time modified at October ninth 2014 at 4:15 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	2
species types	0	species	3
events	0	constraints	0
reactions	0	function definitions	0
global parameters	21	unit definitions	0
rules	9	initial assignments	0

Model Notes

This a model from the article:

A mathematical model of parathyroid hormone response to acute changes in plasma ionized calcium concentration in humans.

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Shrestha RP, Hollot CV, Chipkin SR, Schmitt CP, Chait Y. Math Biosci.2010 Jul;226(1):46-57. [20406649](#),

Abstract:

A complex bio-mechanism, commonly referred to as calcium homeostasis, regulates plasma ionized calcium ($\text{Ca}(2+)$) concentration in the human body within a narrow range which is crucial for maintaining normal physiology and metabolism. Taking a step towards creating a complete mathematical model of calcium homeostasis, we focus on the short-term dynamics of calcium homeostasis and consider the response of the parathyroid glands to acute changes in plasma $\text{Ca}(2+)$ concentration. We review available models, discuss their limitations, then present a two-pool, linear, time-varying model to describe the dynamics of this calcium homeostasis subsystem, the Ca-PTH axis. We propose that plasma PTH concentration and plasma $\text{Ca}(2+)$ concentration bear an asymmetric reverse sigmoid relation. The parameters of our model are successfully estimated based on clinical data corresponding to three healthy subjects that have undergone induced hypocalcemic clamp tests. In the first validation of this kind, with parameters estimated separately for each subject we test the model's ability to predict the same subject's induced hypercalcemic clamp test responses. Our results demonstrate that a two-pool, linear, time-varying model with an asymmetric reverse sigmoid relation characterizes the short-term dynamics of the Ca-PTH axis.

The model corresponds to hypocalcemic clamp test explained in the paper and parameter values used in the model are that of „subject 1,. In order to obtain the plots corresponding to „subject 2,, and „subject 3,, the following parameters to be changed: λ_1 , λ_2 , m_1 , m_2 , R , β , x_{1_n} , x_{2_n} , $x_{2_{\min}}$, $x_{2_{\max}}$, Ca_0 , Ca_1 , t_0 and α .

parameter	Subject 1	Subject 2	Subject 3
λ_1	0.0125	0.0122	0.0269
λ_2	0.5595	0.4642	0.4935
m_1	112.5200	150.0000	90.8570
m_2	15.0000	15.0000	15.0000
R	1.2162	1.1627	1.1889
β	$10\text{e}+06$	$10\text{e}+06$	$10\text{e}+06$
x_{1_n}	490.7800	452.8200	298.8200
x_{2_n}	6.6290	9.5894	5.4600
$x_{2_{\min}}$	0.6697	1.4813	0.8287
$x_{2_{\max}}$	14.0430	17.8710	15.1990
Ca_0	1.2550	1.2369	1.2475
Ca_1	0.1817	0.2211	0.1985
t_0	575	577	575
α	0.0442	0.0488	0.0472

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To cite BioModels Database, please use: [Li C](#), [Donizelli M](#), [Rodriguez N](#), [Dharuri H](#), [Endler L](#),

Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novre N, Laibe C (2010) BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

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 m²

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 3: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
PTG_pool	PTG_pool	0000290	3	1	litre	<input checked="" type="checkbox"/>	
Plasma_pool	Plasma_pool	0000290	3	1	litre	<input checked="" type="checkbox"/>	

3.1 Compartment [PTG_pool](#)

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

Name PTG_pool

SBO:0000290 physical compartment

3.2 Compartment [Plasma_pool](#)

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

Name Plasma_pool

SBO:0000290 physical compartment

4 Species

This model contains three species. Section 7 provides further details and the derived rates of change of each species.

Table 4: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
x1	PTH_in_PTG	PTG_pool	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
x2	PTH_in_Plasma	Plasma_pool	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
Ca	Ca_in_Plasma	Plasma_pool	$\text{mol} \cdot \text{l}^{-1}$	\square	\square

5 Parameters

This model contains 21 global parameters.

Table 5: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k	k	0000002	9.844		<input type="checkbox"/>
lambda_Ca	lambda_Ca		170.000		<input type="checkbox"/>
m_Ca	m_Ca		170.000		<input type="checkbox"/>
m1	m1	0000002	112.520		<input checked="" type="checkbox"/>
m2	m2	0000002	15.000		<input checked="" type="checkbox"/>
beta	beta	0000002	1000000.000		<input checked="" type="checkbox"/>
R	R	0000002	1.216		<input checked="" type="checkbox"/>
lambda_1	lambda_1	0000002	0.013		<input checked="" type="checkbox"/>
lambda_2	lambda_2	0000002	0.560		<input checked="" type="checkbox"/>
A	A		0.049		<input type="checkbox"/>
B	B		$4.9 \cdot 10^{-4}$		<input type="checkbox"/>
S	S		1.216		<input type="checkbox"/>
Ca0	Ca0		1.255		<input checked="" type="checkbox"/>
Ca1	Ca1		0.182		<input checked="" type="checkbox"/>
t0	t0		575.000		<input checked="" type="checkbox"/>
alpha	alpha		0.044		<input checked="" type="checkbox"/>
x1_n	x1_n		490.780		<input checked="" type="checkbox"/>
x2_n	x2_n		6.629		<input checked="" type="checkbox"/>
x2_min	x2_min		0.670		<input checked="" type="checkbox"/>
x2_max	x2_max		14.043		<input checked="" type="checkbox"/>
Ca0_baseline	Ca0_baseline		1.255		<input checked="" type="checkbox"/>

6 Rules

This is an overview of nine rules.

6.1 Rule lambda_Ca

Rule lambda_Ca is an assignment rule for parameter lambda_Ca:

$$\text{lambda_Ca} = \frac{A - B}{1 + \left(\frac{[\text{Ca}]}{S}\right)^{m_Ca}} + B \quad (1)$$

6.2 Rule m_Ca

Rule m_Ca is an assignment rule for parameter m_Ca :

$$m_Ca = \frac{m1}{1 + \exp(\beta \cdot (R - [Ca]))} + m2 \quad (2)$$

6.3 Rule Ca

Rule Ca is an assignment rule for species Ca :

$$Ca = \begin{cases} Ca0 & \text{if time} < t0 \\ Ca0 - Ca1 \cdot (1 - \exp(\alpha \cdot (\text{time} - t0))) & \text{otherwise} \end{cases} \quad (3)$$

6.4 Rule $x1$

Rule $x1$ is a rate rule for species $x1$:

$$\frac{d}{dt}x1 = k - \lambda_{Ca} \cdot [x1] - \lambda_{x1} \cdot [x1] \quad (4)$$

6.5 Rule $x2$

Rule $x2$ is a rate rule for species $x2$:

$$\frac{d}{dt}x2 = \lambda_{Ca} \cdot [x1] - \lambda_{x2} \cdot [x2] \quad (5)$$

6.6 Rule S

Rule S is an assignment rule for parameter S :

$$S = Ca0_baseline \cdot \left(\frac{(x1_n \cdot B - \lambda_{x2} \cdot x2_n)}{x1_n \cdot A - \lambda_{x2} \cdot x2_n} \right)^{\frac{1}{m_Ca}} \quad (6)$$

6.7 Rule k

Rule k is an assignment rule for parameter k :

$$k = \lambda_{x2} \cdot x2_n + \lambda_{x1} \cdot x1_n \quad (7)$$

6.8 Rule A

Rule A is an assignment rule for parameter A :

$$A = \frac{\lambda_{x1} \cdot \lambda_{x2} \cdot x2_max}{k - \lambda_{x2} \cdot x2_max} \quad (8)$$

6.9 Rule B

Rule B is an assignment rule for parameter B:

$$B = \frac{\text{lambda}_1 \cdot \text{lambda}_2 \cdot x2_min}{k - \text{lambda}_2 \cdot x2_min} \quad (9)$$

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 [x1](#)

Name PTH_in_PTG

SBO:0000245 macromolecule

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule [x1](#)

One rule which determines this species' quantity.

7.2 Species [x2](#)

Name PTH_in_Plasma

SBO:0000245 macromolecule

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule [x2](#)

One rule which determines this species' quantity.

7.3 Species [Ca](#)

Name Ca_in_Plasma

SBO:0000247 simple chemical

Initial concentration $1.22 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule [Ca](#)

One rule which determines this species' quantity.

A Glossary of Systems Biology Ontology Terms

SBO:0000002 quantitative systems description parameter: A numerical value that defines certain characteristics of systems or system functions. It may be part of a calculation, but its value is not determined by the form of the equation itself, and may be arbitrarily assigned

SBO:0000245 macromolecule: Molecular entity mainly built-up by the repetition of pseudo-identical units. CHEBI:3383

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

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