SBML Model Report

Model name: "Komarova2005_PTHaction-_OsteoclastOsteoblastCoupling"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following three authors: Catherine Lloyd[1], Vijayalakshmi Chelliah[2] and Svetlana V Komarova[3] at November 23rd 2010 at 10:56 a. m. and last time modified at October nineth 2014 at 4:33 p. 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	1
species types	0	species	3
events	0	constraints	0
reactions	0	function definitions	0
global parameters	15	unit definitions	0
rules	8	initial assignments	0

Model Notes

This a model from the article:
Mathematical model of paracrine interactions between osteoclasts and osteoblasts predicts anabolic action of parathyroid hormone on bone.

[1]University of Auckland, c.lloyd@auckland.ac.nz
[2]EMBL-EBI, viji@ebi.ac.uk
[3]McGill University, Montreal, Canada H3A 2B2., svetlana.komarova@mcgill.ca

Komarova SV. Endocrinology.2005 Aug;146(8):3589-95. 15860557,
Abstract:
To restore falling plasma calcium levels, PTH promotes calcium liberation from bone. PTH targets bone-forming cells, osteoblasts, to increase expression of the cytokine receptor activator of nuclear factor kappaB ligand (RANKL), which then stimulates osteoclastic bone resorption. Intriguingly, whereas continuous administration of PTH decreases bone mass, intermittent PTH has an anabolic effect on bone, which was proposed to arise from direct effects of PTH on osteoblastic bone formation. However, antiresorptive therapies impair the ability of PTH to increase bone mass, indicating a complex role for osteoclasts in the process. We developed a mathematical model that describes the actions of PTH at a single site of bone remodeling, where osteoclasts and osteoblasts are regulated by local autocrine and paracrine factors. It was assumed that PTH acts only to increase the production of RANKL by osteoblasts. As a result, PTH stimulated osteoclasts upon application, followed by compensatory osteoblast activation due to the coupling of osteoblasts to osteoclasts through local paracrine factors. Continuous PTH administration resulted in net bone loss, because bone resorption preceded bone formation at all times. In contrast, over a wide range of model parameters, short application of PTH resulted in a net increase in bone mass, because osteoclasts were rapidly removed upon PTH withdrawal, enabling osteoblasts to rebuild the bone. In excellent agreement with experimental findings, increase in the rate of osteoclast death abolished the anabolic effect of PTH on bone. This study presents an original concept for the regulation of bone remodeling by PTH, currently the only approved anabolic treatment for osteoporosis.

The model reproduces Figures 1B and 2A of the reference publication. To obtain the figures 1B, the parameter g21 needs changes. To obtain the figures 1A, the parameters g21, g12 and k2 need to changed. For details look at the curation tab.

The initial concentration of Osteoclasts (x1) is corrected to 1.06066 from 10.06066.

This model was taken from the CellML repository and automatically converted to SBML.
The original model was: **CellMLdetails**
The original CellML model was created by:
Lloyd, Catherine, May
c.lloyd@auckland.ac.nz
The University of Auckland
The Bioengineering Institute

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`		0000290	3	1	litre	☑	

3.1 Compartment `Compartment`

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

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 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
x1	Osteoclasts	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
x2	Osteoblasts	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
z	BoneMass	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 15 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
y1	y1		0.000		☐
y2	y2		0.000		☐
x1_bar	x1_bar		0.000		☐
x2_bar	x2_bar		0.000		☐
alpha1	alpha1	0000009	3.000		☑
beta1	beta1	0000009	0.200		☑
alpha2	alpha2	0000009	4.000		☑
beta2	beta2	0000009	0.020		☑
k1	k1	0000009	0.240		☑
k2	k2	0000009	0.002		☑
g11	g11	0000009	0.500		☑
g21	g21	0000009	−0.500		☑
g12	g12	0000009	1.000		☑
g22	g22	0000009	0.000		☑
gamma	gamma	0000009	0.000		☐

6 Rules

This is an overview of eight rules.

6.1 Rule x1

Rule x1 is a rate rule for species x1:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{x1} = \mathrm{alpha1} \cdot [\mathrm{x1}]^{\mathrm{g11}} \cdot [\mathrm{x2}]^{\mathrm{g21}} - \mathrm{beta1} \cdot [\mathrm{x1}] \tag{1}$$

6.2 Rule x2

Rule x2 is a rate rule for species x2:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{x2} = \mathrm{alpha2} \cdot [\mathrm{x1}]^{\mathrm{g12}} \cdot [\mathrm{x2}]^{\mathrm{g22}} - \mathrm{beta2} \cdot [\mathrm{x2}] \tag{2}$$

6.3 Rule z

Rule z is a rate rule for species z:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{z} = \mathrm{k2} \cdot \mathrm{y2} - \mathrm{k1} \cdot \mathrm{y1} \tag{3}$$

6.4 Rule y1

Rule y1 is an assignment rule for parameter y1:

$$\mathrm{y1} = \begin{cases} [\mathrm{x1}] - \mathrm{x1\_bar} & \text{if } [\mathrm{x1}] > \mathrm{x1\_bar} \\ 0 & \text{otherwise} \end{cases} \tag{4}$$

6.5 Rule y2

Rule y2 is an assignment rule for parameter y2:

$$\mathrm{y2} = \begin{cases} [\mathrm{x2}] - \mathrm{x2\_bar} & \text{if } [\mathrm{x2}] > \mathrm{x2\_bar} \\ 0 & \text{otherwise} \end{cases} \tag{5}$$

6.6 Rule x1_bar

Rule x1_bar is an assignment rule for parameter x1_bar:

$$\mathrm{x1\_bar} = \left(\frac{\mathrm{beta1}}{\mathrm{alpha1}}\right)^{\frac{1-\mathrm{g22}}{\mathrm{gamma}}} \cdot \left(\frac{\mathrm{beta2}}{\mathrm{alpha2}}\right)^{\frac{\mathrm{g21}}{\mathrm{gamma}}} \tag{6}$$

6.7 Rule x2_bar

Rule x2_bar is an assignment rule for parameter x2_bar:

$$\mathrm{x2\_bar} = \left(\frac{\mathrm{beta1}}{\mathrm{alpha1}}\right)^{\frac{\mathrm{g12}}{\mathrm{gamma}}} \cdot \left(\frac{\mathrm{beta2}}{\mathrm{alpha2}}\right)^{\frac{1-\mathrm{g11}}{\mathrm{gamma}}} \tag{7}$$

6.8 Rule gamma

Rule gamma is an assignment rule for parameter gamma:

$$\mathrm{gamma} = \mathrm{g12} \cdot \mathrm{g21} - (1 - \mathrm{g11}) \cdot (1 - \mathrm{g22}) \tag{8}$$

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 Osteoclasts

Initial concentration $1.06066\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule x1

One rule which determines this species' quantity.

7.2 Species x2

Name Osteoblasts

Initial concentration $212.132\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Involved in rule x2

One rule which determines this species' quantity.

7.3 Species z

Name BoneMass

Initial concentration $100\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

Involved in rule z

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: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.

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany