SBML Model Report

Model name: “Lemaire2004 - Role of RANK/RANKL/OPG pathway in bone remodelling process”

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: Vijayalakshmi Chelliah[1], Vincent Lemaire[2] and Frank L Tobin[3] at November 18th 2010 at 11:20 a. m. and last time modified at October nineth 2014 at 4:31 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	30	unit definitions	0
rules	10	initial assignments	0

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Model Notes

This a model from the article:
Modeling the interactions between osteoblast and osteoclast activities in bone remodeling.
Lemaire V, Tobin FL, Greller LD, Cho CR, Suva LJ. J Theor Biol.2004 Aug 7;229(3):293-309. 15234198,
Abstract:
We propose a mathematical model explaining the interactions between osteoblasts and osteoclasts, two cell types specialized in the maintenance of the bone integrity. Bone is a dynamic, living tissue whose structure and shape continuously evolves during life. It has the ability to change architecture by removal of old bone and replacement with newly formed bone in a localized process called remodeling. The model described here is based on the idea that the relative proportions of immature and mature osteoblasts control the degree of osteoclastic activity. In addition, osteoclasts control osteoblasts differentially depending on their stage of differentiation. Despite the tremendous complexity of the bone regulatory system and its fragmentary understanding, we obtain surprisingly good correlations between the model simulations and the experimental observations extracted from the literature. The model results corroborate all behaviors of the bone remodeling system that we have simulated, including the tight coupling between osteoblasts and osteoclasts, the catabolic effect induced by continuous administration of PTH, the catabolic action of RANKL, as well as its reversal by soluble antagonist OPG. The model is also able to simulate metabolic bone diseases such as estrogen deficiency, vitamin D deficiency, senescence and glucocorticoid excess. Conversely, possible routes for therapeutic interventions are tested and evaluated. Our model confirms that anti-resorptive therapies are unable to partially restore bone loss, whereas bone formation therapies yield better results. The model enables us to determine and evaluate potential therapies based on their efficacy. In particular, the model predicts that combinations of anti-resorptive and anabolic therapies provide significant benefits compared with monotherapy, especially for certain type of skeletal disease. Finally, the model clearly indicates that increasing the size of the pool of preosteoblasts is an essential ingredient for the therapeutic manipulation of bone formation. This model was conceived as the first step in a bone turnover modeling platform. These initial modeling results are extremely encouraging and lead us to proceed with additional explorations into bone turnover and skeletal remodeling.

This model corresponds to the core model published in the paper. There is no corresponding plot to reproduce for this model.To obtain each of the 9 plots in the Figure 2 of the reference publication, there are some changes to be made to the core model.The curation figure reproduces figure 2 of the reference publication. There is a corresponding SBML and Copasi files for each of the plot. See curation tab for more details.

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	0000290	3	1	litre	☑	

3.1 Compartment `Compartment`

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

Name Compartment

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
R	Responding_Osteoblasts	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
B	Active_Osteoblasts	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
C	Active_Osteoclasts	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 30 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
C_s	C_s	0000188	0.005		☑
D_A	D_A	0000009	0.700		☑
d_B	d_B	0000009	0.700		☑
D_C	D_C	0000009	0.002		☑
D_R	D_R	0000009	$7 \cdot 10^{-4}$		☑
f0	f0	0000009	0.050		☑
I_L	I_L	0000188	0.000		☑
I_O	I_O	0000188	0.000		☑
I_P	I_P	0000188	0.000		☑
K	K	0000188	10.000		☑
k1	k1	0000009	0.010		☑
k2	k2	0000009	10.000		☑
k3	k3	0000009	$5.8 \cdot 10^{-4}$		☑
k4	k4	0000009	0.017		☑
k5	k5	0000009	0.020		☑
k6	k6	0000009	3.000		☑
k_B	k_B	0000009	0.189		☑
K_L_P	K_L_P	0000188	3000000.000		☑
kO	kO	0000009	0.350		☑
K_O_P	K_O_P	0000188	200000.000		☑
k_P	k_P	0000009	86.000		☑
r_L	r_L	0000009	1000.000		☑
S_P	S_P	0000009	250.000		☑
Phi_C	Phi_C		0.000		⊟
D_B	D_B		0.000		⊟
Phi_L	Phi_L		0.000		⊟
Phi_P	Phi_P		0.000		⊟
Pbar	Pbar		0.000		⊟
P_O	P_O		0.000		⊟
P_S	P_S		0.000		⊟

6 Rules

This is an overview of ten rules.

6.1 Rule D_B

Rule D_B is an assignment rule for parameter D_B:

$$\mathrm{D\_B} = \mathrm{f0} \cdot \mathrm{d\_B} \tag{1}$$

6.2 Rule Phi_C

Rule Phi_C is an assignment rule for parameter Phi_C:

$$\mathrm{Phi\_C} = \frac{[\mathrm{C}] + \mathrm{f0} \cdot \mathrm{C\_s}}{[\mathrm{C}] + \mathrm{C\_s}} \tag{2}$$

6.3 Rule Phi_L

Rule Phi_L is an assignment rule for parameter Phi_L:

$$\mathrm{Phi\_L} = \frac{\frac{\mathrm{k3}}{\mathrm{k4}} \cdot \mathrm{K\_L\_P} \cdot \mathrm{Phi\_P} \cdot [\mathrm{B}]}{1 + \frac{\mathrm{k3} \cdot \mathrm{K}}{\mathrm{k4}} + \frac{\mathrm{k1}}{\mathrm{k2} \cdot \mathrm{kO}} \cdot \left(\mathrm{I\_O} + \frac{\mathrm{K\_O\_P} \cdot [\mathrm{R}]}{\mathrm{Phi\_P}}\right)} \cdot \left(1 + \frac{\mathrm{I\_L}}{\mathrm{r\_L}}\right) \tag{3}$$

6.4 Rule Phi_P

Rule Phi_P is an assignment rule for parameter Phi_P:

$$\mathrm{Phi\_P} = \frac{\mathrm{Pbar} + \mathrm{P\_O}}{\mathrm{Pbar} + \mathrm{P\_S}} \tag{4}$$

6.5 Rule Pbar

Rule Pbar is an assignment rule for parameter Pbar:

$$\mathrm{Pbar} = \frac{\mathrm{I\_P}}{\mathrm{k\_P}} \tag{5}$$

6.6 Rule P_O

Rule P_O is an assignment rule for parameter P_O:

$$\mathrm{P\_O} = \frac{\mathrm{S\_P}}{\mathrm{k\_P}} \tag{6}$$

6.7 Rule P_S

Rule P_S is an assignment rule for parameter P_S:

$$\mathrm{P\_S} = \frac{\mathrm{k6}}{\mathrm{k5}} \tag{7}$$

6.8 Rule R

Rule R is a rate rule for species R:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{R} = \mathrm{D\_R} \cdot \mathrm{Phi\_C} - \frac{\mathrm{D\_B} \cdot [\mathrm{R}]}{\mathrm{Phi\_C}} \tag{8}$$

6.9 Rule B

Rule B is a rate rule for species B:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{B} = \frac{\mathrm{D\_B} \cdot [\mathrm{R}]}{\mathrm{Phi\_C}} - \mathrm{k\_B} \cdot [\mathrm{B}] \tag{9}$$

6.10 Rule C

Rule C is a rate rule for species C:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C} = \mathrm{D\_C} \cdot \mathrm{Phi\_L} - \mathrm{D\_A} \cdot \mathrm{Phi\_C} \cdot [\mathrm{C}] \tag{10}$$

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 R

Name Responding_Osteoblasts

SBO:0000236 physical entity representation

Initial concentration $7.734 \cdot 10^{-4}$ mol $\cdot$ l^{-1}

Involved in rule R

One rule which determines this species' quantity.

7.2 Species B

Name Active_Osteoblasts

SBO:0000236 physical entity representation

Initial concentration $7.282 \cdot 10^{-4}$ mol $\cdot$ l^{-1}

Involved in rule B

One rule which determines this species' quantity.

7.3 Species C

Name Active_Osteoclasts

SBO:0000236 physical entity representation

Initial concentration $9.127 \cdot 10^{-4}$ mol $\cdot 1^{-1}$

Involved in rule C

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:0000188 number of biochemical items: A number of objects of the same type, identical or different, involved in a biochemical event

SBO:0000236 physical entity representation: Representation of an entity that may participate in an interaction, a process or relationship of significance.

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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