SBML Model Report

Model name: "Ayati2010-_BoneRemodelingDynamics_WithTumour"

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 Chelliah[1] and Bruce P Ayati[2] at November 25th 2011 at 5:39 p. m. and last time modified at October nineth 2014 at 5:40 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	4
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 bone remodeling dynamics for normal bone cell populations and myeloma bone disease
Bruce P Ayati, Claire M Edwards, Glenn F Webb and John P Wikswo. Biology Direct2010 Apr

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Abstract:
BACKGROUND:Multiple myeloma is a hematologic malignancy associated with the development of a destructive osteolytic bone disease.RESULTS:Mathematical models are developed for normal bone remodeling and for the dysregulated bone remodeling that occurs in myeloma bone disease. The models examine the critical signaling between osteoclasts (bone resorption) and osteoblasts (bone formation). The interactions of osteoclasts and osteoblasts are modeled as a system of differential equations for these cell populations, which exhibit stable oscillations in the normal case and unstable oscillations in the myeloma case. In the case of untreated myeloma, osteoclasts increase and osteoblasts decrease, with net bone loss as the tumor grows. The therapeutic effects of targeting both myeloma cells and cells of the bone marrow microenvironment on these dynamics are examined.CONCLUSIONS:The current model accurately reflects myeloma bone disease and illustrates how treatment approaches may be investigated using such computational approaches.

Note:

The paper describes three models 1) Zero-dimensional Bone Model without Tumour, 2) Zero-dimensional Bone Model with Tumour and 3) Zero-dimensional Bone Model with Tumour and Drug Treatment. This model corresponds to the Zero-dimensional Bone Model with Tumour.

Typos in the publication:

Equation (4): The first term should be (1/1)^(g12/) and not (2/2)^(g12/)

Equation (14): The first term should be (1/1)^(((g12/(1+r12))/) and not (2/2)^(((g12/(1+r12))/)

Equation (13): The first term should be (1/1)^((1-g22+r22)/) and not (1/1)^((1-g22-r22)/)

All these corrections has been implemented in the model, with the authors agreement.

Beyond these, there are several mismatches between the equation numbers that are mentioned in for each equation and the reference that has been made to these equations in the figure legend.

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 four 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
`C`	Osteoclasts	`Compartment`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	$\boxminus$	$\boxminus$
`B`	Osteoblasts	`Compartment`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	$\boxminus$	$\boxminus$
`z`	BoneMass	`Compartment`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	$\boxminus$	$\boxminus$
`Tumour`	Tumour	`Compartment`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	$\boxminus$	$\boxminus$

5 Parameters

This model contains 21 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
y1	y1		0.000		☐
y2	y2		0.000		☐
C_bar	C_bar		0.000		☐
B_bar	B_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	0.075		☑
k2	k2	0000009	$6.395 \cdot 10^{-4}$		☑
g11	g11	0000009	1.100		☑
g21	g21	0000009	-0.500		☑
g12	g12	0000009	1.000		☑
g22	g22	0000009	0.000		☑
gamma	gamma	0000009	0.000		☐
gammaT	gammaT	0000009	0.005		☑
LT	LT	0000009	100.000		☑
r11	r11	0000009	0.005		☑
r21	r21	0000009	0.000		☑
r12	r12	0000009	0.000		☑
r22	r22	0000009	0.200		☑

6 Rules

This is an overview of nine rules.

6.1 Rule C

Rule C is a rate rule for species C:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C} = \mathrm{alpha1} \cdot [\mathrm{C}]^{\mathrm{g11} \cdot \left(1 + \frac{\mathrm{r11} \cdot [\mathrm{Tumour}]}{\mathrm{LT}}\right)} \cdot [\mathrm{B}]^{\mathrm{g21} \cdot \left(1 + \frac{\mathrm{r21} \cdot [\mathrm{Tumour}]}{\mathrm{LT}}\right)} - \mathrm{beta1} \cdot [\mathrm{C}] \tag{1}$$

6.2 Rule B

Rule B is a rate rule for species B:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{B} = \mathrm{alpha2} \cdot [\mathrm{C}]^{\frac{\mathrm{g12}}{1+\frac{\mathrm{r12}\cdot[\mathrm{Tumour}]}{\mathrm{LT}}}} \cdot [\mathrm{B}]^{\mathrm{g22}-\frac{\mathrm{r22}\cdot[\mathrm{Tumour}]}{\mathrm{LT}}} - \mathrm{beta2} \cdot [\mathrm{B}] \tag{2}$$

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:

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

6.5 Rule y2

Rule y2 is an assignment rule for parameter y2:

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

6.6 Rule C_bar

Rule C_bar is an assignment rule for parameter C_bar:

$$\mathrm{C\_bar} = \left(\frac{\mathrm{beta1}}{\mathrm{alpha1}}\right)^{\frac{1-\mathrm{g22}+\mathrm{r22}}{\mathrm{gamma}}} \cdot \left(\frac{\mathrm{beta2}}{\mathrm{alpha2}}\right)^{\frac{\mathrm{g21}\cdot(1+\mathrm{r21})}{\mathrm{gamma}}} \tag{6}$$

6.7 Rule B_bar

Rule B_bar is an assignment rule for parameter B_bar:

$$\mathrm{B\_bar} = \left(\frac{\mathrm{beta1}}{\mathrm{alpha1}}\right)^{\frac{\frac{\mathrm{g12}}{1+\mathrm{r12}}}{\mathrm{gamma}}} \cdot \left(\frac{\mathrm{beta2}}{\mathrm{alpha2}}\right)^{\frac{1-\mathrm{g11}\cdot(1+\mathrm{r11})}{\mathrm{gamma}}} \tag{7}$$

6.8 Rule gamma

Rule gamma is an assignment rule for parameter gamma:

$$\mathrm{gamma} = \frac{\mathrm{g12}}{1+\mathrm{r12}} \cdot \mathrm{g21} \cdot (1+\mathrm{r21}) - (1 - \mathrm{g11} \cdot (1+\mathrm{r11})) \cdot (1 - \mathrm{g22} + \mathrm{r22}) \tag{8}$$

6.9 Rule Tumour

Rule Tumour is a rate rule for species Tumour:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Tumour} = \mathrm{gammaT} \cdot [\mathrm{Tumour}] \cdot \left(\frac{\mathrm{LT}}{[\mathrm{Tumour}]}\right) \tag{9}$$

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 C

Name Osteoclasts

SBO:0000236 physical entity representation

Initial concentration $15\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule C

One rule which determines this species' quantity.

7.2 Species B

Name Osteoblasts

SBO:0000236 physical entity representation

Initial concentration $316\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule B

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.

7.4 Species `Tumour`

Name Tumour

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

Involved in rule `Tumour`

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: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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