

SBML Model Report

Model name: “Ayati2010_BoneRemodelingDynamics- _WithTumour+DrugTreatment”



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 Bruce P Ayati² at November 25th 2011 at 5:39 p. m. and last time modified at April fourth 2014 at 5:29 p. m. Table 1 provides 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 | 25 | unit definitions | 0 |
| rules | 11 | initial assignments | 0 |

Model Notes

This a model from the article:

A mathematical model of bone remodeling dynamics for normal bone cell populations and

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myeloma bone disease

Bruce P Ayati, Claire M Edwards, Glenn F Webb and John P Wikswo. *Biology Direct* 2010 Apr 20;5(28). 20406449,

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 and Drug Treatment.

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 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 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 | <input checked="" type="checkbox"/> | |

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 | $\text{mol} \cdot \text{l}^{-1}$ | \square | \square |
| B | Osteoblasts | Compartment | $\text{mol} \cdot \text{l}^{-1}$ | \square | \square |
| z | BoneMass | Compartment | $\text{mol} \cdot \text{l}^{-1}$ | \square | \square |
| Tumour | Tumour | Compartment | $\text{mol} \cdot \text{l}^{-1}$ | \square | \square |

5 Parameters

This model contains 25 global parameters.

Table 4: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|--------|--------|---------|-----------------------|------|-------------------------------------|
| y1 | y1 | | 0.000 | | <input type="checkbox"/> |
| y2 | y2 | | 0.000 | | <input type="checkbox"/> |
| C_bar | C_bar | | 0.000 | | <input type="checkbox"/> |
| B_bar | B_bar | | 0.000 | | <input type="checkbox"/> |
| alpha1 | alpha1 | 0000009 | 3.000 | | <input checked="" type="checkbox"/> |
| beta1 | beta1 | 0000009 | 0.200 | | <input checked="" type="checkbox"/> |
| alpha2 | alpha2 | 0000009 | 4.000 | | <input checked="" type="checkbox"/> |
| beta2 | beta2 | 0000009 | 0.020 | | <input checked="" type="checkbox"/> |
| k1 | k1 | 0000009 | 0.075 | | <input checked="" type="checkbox"/> |
| k2 | k2 | 0000009 | $6.395 \cdot 10^{-4}$ | | <input checked="" type="checkbox"/> |
| g11 | g11 | 0000009 | 1.100 | | <input checked="" type="checkbox"/> |
| g21 | g21 | 0000009 | -0.500 | | <input checked="" type="checkbox"/> |
| g12 | g12 | 0000009 | 1.000 | | <input checked="" type="checkbox"/> |
| g22 | g22 | 0000009 | 0.000 | | <input checked="" type="checkbox"/> |
| gamma | gamma | 0000009 | 0.000 | | <input type="checkbox"/> |
| gammaT | gammaT | 0000009 | 0.005 | | <input checked="" type="checkbox"/> |
| LT | LT | 0000009 | 100.000 | | <input checked="" type="checkbox"/> |
| r11 | r11 | 0000009 | 0.005 | | <input checked="" type="checkbox"/> |
| r21 | r21 | 0000009 | 0.000 | | <input checked="" type="checkbox"/> |
| r12 | r12 | 0000009 | 0.000 | | <input checked="" type="checkbox"/> |
| r22 | r22 | 0000009 | 0.200 | | <input checked="" type="checkbox"/> |
| V1 | V1 | 0000009 | 0.000 | | <input type="checkbox"/> |
| V2 | V2 | 0000009 | 0.000 | | <input type="checkbox"/> |
| v1 | v1 | 0000009 | 0.001 | | <input checked="" type="checkbox"/> |
| v2 | v2 | 0000009 | 0.008 | | <input checked="" type="checkbox"/> |

6 Rules

This is an overview of eleven rules.

6.1 Rule C

Rule C is a rate rule for species C:

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

6.2 Rule B

Rule B is a rate rule for species B:

$$\frac{d}{dt}B = \alpha_2 \cdot [C]^{\frac{g_{12}}{1+r_{12} \cdot \frac{[Tumour]}{LT}}} \cdot [B]^{g_{22} - \frac{r_{22} \cdot [Tumour]}{LT}} - (\beta_2 - V_1) \cdot [B] \quad (2)$$

6.3 Rule z

Rule z is a rate rule for species z:

$$\frac{d}{dt}z = k_2 \cdot y_2 - k_1 \cdot y_1 \quad (3)$$

6.4 Rule y1

Rule y1 is an assignment rule for parameter y1:

$$y_1 = \begin{cases} [C] - C_{\text{bar}} & \text{if } [C] > C_{\text{bar}} \\ 0 & \text{otherwise} \end{cases} \quad (4)$$

6.5 Rule y2

Rule y2 is an assignment rule for parameter y2:

$$y_2 = \begin{cases} [B] - B_{\text{bar}} & \text{if } [B] > B_{\text{bar}} \\ 0 & \text{otherwise} \end{cases} \quad (5)$$

6.6 Rule C_bar

Rule C_bar is an assignment rule for parameter C_bar:

$$C_{\text{bar}} = \left(\frac{\beta_1}{\alpha_1} \right)^{\frac{1-g_{22}+r_{22}}{\gamma}} \cdot \left(\frac{\beta_2}{\alpha_2} \right)^{\frac{g_{21} \cdot (1+r_{21})}{\gamma}} \quad (6)$$

6.7 Rule B_bar

Rule B_bar is an assignment rule for parameter B_bar:

$$B_{\text{bar}} = \left(\frac{\beta_1}{\alpha_1} \right)^{\frac{\frac{g_{12}}{1+r_{12}}}{\gamma}} \cdot \left(\frac{\beta_2}{\alpha_2} \right)^{\frac{1-g_{11} \cdot (1+r_{11})}{\gamma}} \quad (7)$$

6.8 Rule gamma

Rule gamma is an assignment rule for parameter gamma:

$$\gamma = \frac{g_{12}}{1+r_{12}} \cdot g_{21} \cdot (1+r_{21}) - (1-g_{11} \cdot (1+r_{11})) \cdot (1-g_{22}+r_{22}) \quad (8)$$

6.9 Rule Tumour

Rule Tumour is a rate rule for species Tumour:

$$\frac{d}{dt}\text{Tumour} = (\text{gammaT} - V2) \cdot [\text{Tumour}] \cdot \left(\frac{LT}{[\text{Tumour}]} \right) \quad (9)$$

6.10 Rule V1

Rule V1 is an assignment rule for parameter V1:

$$V1 = \begin{cases} v1 & \text{if time} \geq 600 \\ 0 & \text{otherwise} \end{cases} \quad (10)$$

6.11 Rule V2

Rule V2 is an assignment rule for parameter V2:

$$V2 = \begin{cases} v2 & \text{if time} \geq 600 \\ 0 & \text{otherwise} \end{cases} \quad (11)$$

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 13 mol · 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 300 mol · l⁻¹

Involved in rule B

One rule which determines this species' quantity.

7.3 Species *z*

Name BoneMass

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

Involved in rule *z*

One rule which determines this species' quantity.

7.4 Species *Tumour*

Name Tumour

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

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

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