SBML Model Report

Model name: “Schittler2010 - Cell fate of progenitor cells, osteoblasts or chondrocytes”

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1 General Overview

This is a document in SBML Level 3 Version 1 format. This model was created by the following two authors: Vijayalakshmi Chelliah[1] and Steffen Waldherr[2] at November 19th 2013 at 3:43 p. m. and last time modified at October nineth 2014 at 4:40 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	3
events	2	constraints	0
reactions	6	function definitions	0
global parameters	23	unit definitions	0
rules	0	initial assignments	0

Model Notes

Schittler2010 - Cell fate of progenitor cells, osteoblasts or chondrocytes

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Mathematical model describing the mechanism of differentiation of mesenchymal stem cells to bone (osteoblasts) or cartilage (chondrocytes) cells.

This model is described in the article:Cell differentiation modeled via a coupled two-switch regulatory network.Schittler D, Hasenauer J, Allgwer F, Waldherr S.Chaos 2010 Dec; 20(4): 045121

Abstract:

Mesenchymal stem cells can give rise to bone and other tissue cells, but their differentiation still escapes full control. In this paper we address this issue by mathematical modeling. We present a model for a genetic switch determining the cell fate of progenitor cells which can differentiate into osteoblasts (bone cells) or chondrocytes (cartilage cells). The model consists of two switch mechanisms and reproduces the experimentally observed three stable equilibrium states: a progenitor, an osteogenic, and a chondrogenic state. Conventionally, the loss of an intermediate (progenitor) state and the entailed attraction to one of two opposite (differentiated) states is modeled as a result of changing parameters. In our model in contrast, we achieve this by distributing the differentiation process to two functional switch parts acting in concert: one triggering differentiation and the other determining cell fate. Via stability and bifurcation analysis, we investigate the effects of biochemical stimuli associated with different system inputs. We employ our model to generate differentiation scenarios on the single cell as well as on the cell population level. The single cell scenarios allow to reconstruct the switching upon extrinsic signals, whereas the cell population scenarios provide a framework to identify the impact of intrinsic properties and the limiting factors for successful differentiation.

This model is hosted on BioModels Database and identifiedby: BIOMD0000000493 .

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resourcefor published quantitative kinetic models .

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
default_compartment		0000410	3	1	litre	☑	

3.1 Compartment default_compartment

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

SBO:0000410 implicit compartment

4 Species

This model contains three species. Section 8 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
P		default_compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
O		default_compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
C		default_compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 23 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
aP			0.2		☑
n			2.0		☑
bP			0.5		☑
mP			10.0		☑
zD			0.0		☐
cPP			0.1		☑
kP			0.1		☑
aO			0.1		☑
bO			1.0		☑
zO			0.0		☐
mO			1.0		☑
cOC			0.1		☑
cOP			0.5		☑
cOO			0.1		☑
kO			0.1		☑
aC			0.1		☑
bC			1.0		☑
zC			0.0		☑
mC			1.0		☑
cCO			0.1		☑
cCP			0.5		☑
cCC			0.1		☑
kC			0.1		☑

6 Events

This is an overview of two events. Each event is initiated whenever its trigger condition switches from `false` to `true`. A delay function postpones the effects of an event to a later time point. At the time of execution, an event can assign values to species, parameters or compartments if these are not set to constant.

6.1 Event _E0

Trigger condition

$$[\mathrm{P}] > 12.03 \tag{1}$$

Delay

$$100 \tag{2}$$

Assignments

$$\mathrm{zO} = 1 \tag{3}$$
$$\mathrm{zD} = 0.8 \tag{4}$$

6.2 Event _E1

Trigger condition

$$[\mathrm{P}] > 12.03 \tag{5}$$

Delay

$$800 \tag{6}$$

Assignments

$$\mathrm{zO} = 0 \tag{7}$$
$$\mathrm{zD} = 0 \tag{8}$$

7 Reactions

This model contains six reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	a1		$\emptyset \rightleftharpoons P$	
2	a2		$P \rightleftharpoons \emptyset$	
3	a3		$\emptyset \overset{P,\ C}{\rightleftharpoons} O$	
4	a4		$O \rightleftharpoons \emptyset$	
5	a5		$\emptyset \overset{P,\ O}{\rightleftharpoons} C$	
6	a6		$C \rightleftharpoons \emptyset$	

7.1 Reaction a1

This is a reversible reaction of no reactant forming one product.

Reaction equation

$$\emptyset \rightleftharpoons \mathrm{P} \tag{9}$$

Product

Table 6: Properties of each product.

Id	Name	SBO
P		

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{\mathrm{aP} \cdot [\mathrm{P}]^{\mathrm{n}} + \mathrm{bP}}{\mathrm{mP} + \mathrm{zD} + \mathrm{cPP} \cdot [\mathrm{P}]^{\mathrm{n}}} \tag{10}$$

7.2 Reaction a2

This is a reversible reaction of one reactant forming no product.

Reaction equation

$$\mathrm{P} \rightleftharpoons \emptyset \tag{11}$$

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
P		

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{kP} \cdot [\mathrm{P}] \tag{12}$$

7.3 Reaction a3

This is a reversible reaction of no reactant forming one product influenced by two modifiers.

Reaction equation

$$\emptyset \underset{}{\overset{\text{P, C}}{\rightleftharpoons}} \text{O} \tag{13}$$

Modifiers

Table 8: Properties of each modifier.

Id	Name	SBO
P		
C		

Product

Table 9: Properties of each product.

Id	Name	SBO
O		

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \frac{\text{aO} \cdot [\text{O}]^{\text{n}} + \text{bO} + \text{zO}}{\text{mO} + \text{cOC} \cdot [\text{C}]^{\text{n}} + \text{cOP} \cdot [\text{P}]^{\text{n}} + \text{cOO} \cdot [\text{O}]^{\text{n}}} \tag{14}$$

7.4 Reaction a4

This is a reversible reaction of one reactant forming no product.

Reaction equation

$$\text{O} \rightleftharpoons \emptyset \tag{15}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
O		

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{kO} \cdot [\mathrm{O}] \tag{16}$$

7.5 Reaction a5

This is a reversible reaction of no reactant forming one product influenced by two modifiers.

Reaction equation

$$\emptyset \underset{}{\overset{\mathrm{P,\ O}}{\rightleftharpoons}} \mathrm{C} \tag{17}$$

Modifiers

Table 11: Properties of each modifier.

Id	Name	SBO
P		
O		

Product

Table 12: Properties of each product.

Id	Name	SBO
C		

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \frac{\mathrm{aC} \cdot [\mathrm{C}]^{\mathrm{n}} + \mathrm{bC} + \mathrm{zC}}{\mathrm{mC} + \mathrm{cCO} \cdot [\mathrm{O}]^{\mathrm{n}} + \mathrm{cCP} \cdot [\mathrm{P}]^{\mathrm{n}} + \mathrm{cCC} \cdot [\mathrm{C}]^{\mathrm{n}}} \tag{18}$$

7.6 Reaction a6

This is a reversible reaction of one reactant forming no product.

Reaction equation

$$\mathrm{C} \rightleftharpoons \emptyset \tag{19}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
C		

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{kC} \cdot [\mathrm{C}] \tag{20}$$

8 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.

Identifiers for kinetic laws highlighted in gray cannot be verified to evaluate to units of SBML `substance` per `time`. As a result, some SBML interpreters may not be able to verify the consistency of the units on quantities in the model. Please check if

- parameters without an unit definition are involved or
- volume correction is necessary because the `hasOnlySubstanceUnits` flag may be set to `false` and `spacialDimensions`> 0 for certain species.

8.1 Species P

Initial concentration $12.03\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in a2 and as a product in a1 and as a modifier in a3, a5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P} = v_1 - v_2 \tag{21}$$

8.2 Species O

Initial concentration $0.14\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in a4 and as a product in a3 and as a modifier in a5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{O} = v_3 - v_4 \tag{22}$$

8.3 Species C

Initial concentration $0.14\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in a6 and as a product in a5 and as a modifier in a3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C} = v_5 - v_6 \tag{23}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000410 implicit compartment: A compartment whose existence is inferred due to the presence of known material entities which must be bounded, allowing the creation of material entity pools

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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