SBML Model Report

Model name: "Goldbeter2007_Somitogenesis_Switch"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Lukas Endler[1] at November 17th 2010 at 8:39 a. m. and last time modified at April eighth 2016 at 4:19 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	5
events	0	constraints	0
reactions	9	function definitions	0
global parameters	24	unit definitions	7
rules	5	initial assignments	0

Model Notes

This is the simple model without diffusion described in th epublication
Sharp developmental thresholds defined through bistability by antagonistic gradients of retinoic acid and FGF signaling.
Goldbeter A, Gonze D, Pourqui O. Dev Dyn. 2007 Jun;236(6):1495-508. PMID: 17497689, doi:10.1016/j.jtbi.2008.01.006

[1] EMBL-EBI, lukas@ebi.ac.uk

Abstract:
The establishment of thresholds along morphogen gradients in the embryo is poorly understood. Using mathematical modeling, we show that mutually inhibitory gradients can generate and position sharp morphogen thresholds in the embryonic space. Taking vertebrate segmentation as a paradigm, we demonstrate that the antagonistic gradients of retinoic acid (RA) and Fibroblast Growth Factor (FGF) along the presomitic mesoderm (PSM) may lead to the coexistence of two stable steady states. Here, we propose that this bistability is associated with abrupt switches in the levels of FGF and RA signaling, which permit the synchronized activation of segmentation genes, such as mesp2, in successive cohorts of PSM cells in response to the segmentation clock, thereby defining the future segments. Bistability resulting from mutual inhibition of RA and FGF provides a molecular mechanism for the all-or-none transitions assumed in the ,,clock and wavefront,, somitogenesis model. Given that mutually antagonistic signaling gradients are common in development, such bistable switches could represent an important principle underlying embryonic patterning.

Originally created by libAntimony v1.4 (using libSBML 3.4.1)

2 Unit Definitions

This is an overview of nine unit definitions of which two are predefined by SBML and not mentioned in the model.

2.1 Unit `substance`

Name nmole

Definition nmol

2.2 Unit `time`

Name min

Definition 60 s

2.3 Unit `nM`

Name nM

Definition $\mathrm{nmol} \cdot \mathrm{l}^{-1}$

2.4 Unit nM_per_min

Name nM per min

Definition $\mathrm{nmol} \cdot \mathrm{l}^{-1} \cdot (60\ \mathrm{s})^{-1}$

2.5 Unit per_nM_per_min

Name per nM per min

Definition $\mathrm{nmol}^{-1} \cdot 1 \cdot (60\ \mathrm{s})^{-1}$

2.6 Unit per_min

Name per min

Definition $(60\ \mathrm{s})^{-1}$

2.7 Unit length

Name arbit. length

Definition dimensionless

2.8 Unit volume

Notes Litre is the predefined SBML unit for `volume`.

Definition l

2.9 Unit area

Notes Square metre is the predefined SBML unit for `area` since SBML Level 2 Version 1.

Definition m^2

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
PSM		0000290	3	1	litre	☑	

3.1 Compartment PSM

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

SBO:0000290 physical compartment

4 Species

This model contains five 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
RA		PSM	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
M_C	cyp26_mRNA	PSM	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
C	CYP26	PSM	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
F	FGF	PSM	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	⊟	⊟
M_F	FGF_mRNA	PSM	$\mathrm{nmol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 24 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
vs1		0000046	0.000	$\mathrm{nmol \cdot l^{-1} \cdot (60\ s)^{-1}}$	⊟
kd5		0000356	0.000	$\mathrm{(60\ s)^{-1}}$	☑
kd1		0000036	1.000	$\mathrm{nmol^{-1} \cdot 1 \cdot (60\ s)^{-1}}$	☑
V0		0000485	0.365	$\mathrm{nmol \cdot l^{-1} \cdot (60\ s)^{-1}}$	☑
Vsc		0000186	7.100	$\mathrm{nmol \cdot l^{-1} \cdot (60\ s)^{-1}}$	☑
n		0000190	2.000	dimensionless	☑
Ka		0000363	0.200	$\mathrm{nmol \cdot l^{-1}}$	☑
kd3		0000356	1.000	$\mathrm{(60\ s)^{-1}}$	☑
ks2		0000035	1.000	$\mathrm{(60\ s)^{-1}}$	☑
kd2		0000356	0.280	$\mathrm{(60\ s)^{-1}}$	☑
ks3		0000035	1.000	$\mathrm{(60\ s)^{-1}}$	☑
Ki		0000261	0.200	$\mathrm{nmol \cdot l^{-1}}$	☑
m		0000190	2.000	dimensionless	☑
kd4		0000356	1.000	$\mathrm{(60\ s)^{-1}}$	☑
ks1		0000035	1.000	$\mathrm{(60\ s)^{-1}}$	☑
RALDH2_0		0000505	7.100	$\mathrm{nmol \cdot l^{-1}}$	☑
x		0000466	15.000	dimensionless	☑
L		0000466	50.000	dimensionless	☑
M_0		0000196	5.000	$\mathrm{nmol \cdot l^{-1}}$	☑
rho		0000256	0.000	dimensionless	⊟
alpha2		0000256	0.000	dimensionless	⊟
alpha1		0000256	0.000	dimensionless	⊟
Kr1		0000282	1.000	$\mathrm{nmol \cdot l^{-1}}$	☑
Kr2		0000282	1.000	$\mathrm{nmol \cdot l^{-1}}$	☑

6 Rules

This is an overview of five rules.

6.1 Rule M_F

Rule M_F is an assignment rule for species M_F:

$$\mathrm{M\_F} = \mathrm{M\_0} \cdot \frac{\mathrm{x}}{\mathrm{L}} \tag{1}$$

Derived unit $\mathrm{nmol \cdot l^{-1}}$

6.2 Rule vs1

Rule vs1 is an assignment rule for parameter vs1:

$$\mathrm{vs1} = \mathrm{ks1} \cdot \mathrm{RALDH2\_0} \cdot \left(1 - \frac{\mathrm{x}}{\mathrm{L}}\right) \tag{2}$$

6.3 Rule rho

Rule rho is an assignment rule for parameter rho:

$$\mathrm{rho} = \frac{\mathrm{alpha2}}{\mathrm{alpha1}} \tag{3}$$

Derived unit dimensionless

6.4 Rule alpha2

Rule alpha2 is an assignment rule for parameter alpha2:

$$\mathrm{alpha2} = \frac{[\mathrm{F}]}{[\mathrm{F}] + \mathrm{Kr2}} \tag{4}$$

Derived unit dimensionless

6.5 Rule alpha1

Rule alpha1 is an assignment rule for parameter alpha1:

$$\mathrm{alpha1} = \frac{[\mathrm{RA}]}{[\mathrm{RA}] + \mathrm{Kr1}} \tag{5}$$

Derived unit dimensionless

7 Reactions

This model contains nine 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	RA_synthesis		$\emptyset \longrightarrow \mathrm{RA}$	0000205
2	RA_decay		$\mathrm{RA} \longrightarrow \emptyset$	0000179
3	RA_deg_by_Cyp26		$\mathrm{RA} \xrightarrow{\mathrm{C}} \emptyset$	0000179
4	M_C-_transcription		$\emptyset \xrightarrow{\mathrm{F}} \mathrm{M\_C}$	0000183
5	M_C_decay		$\mathrm{M\_C} \longrightarrow \emptyset$	0000179
6	C_translation		$\emptyset \xrightarrow{\mathrm{M\_C}} \mathrm{C}$	0000184
7	C_decay		$\mathrm{C} \longrightarrow \emptyset$	0000179
8	FGF_synthesis		$\emptyset \xrightarrow{\mathrm{RA,\ M\_F}} \mathrm{F}$	0000184
9	FGF_decay		$\mathrm{F} \longrightarrow \emptyset$	0000179

7.1 Reaction RA_synthesis

This is an irreversible reaction of no reactant forming one product.

SBO:0000205 composite biochemical process

Reaction equation

$$\emptyset \longrightarrow \mathrm{RA} \tag{6}$$

Product

Table 6: Properties of each product.

Id	Name	SBO
RA		

Kinetic Law

Derived unit $\mathrm{nmol} \cdot (60\ \mathrm{s})^{-1}$

$$v_1 = \mathrm{vol}(\mathrm{PSM}) \cdot \mathrm{vs1} \tag{7}$$

7.2 Reaction RA_decay

This is an irreversible reaction of one reactant forming no product.

SBO:0000179 degradation

Reaction equation

$$\mathrm{RA} \longrightarrow \emptyset \tag{8}$$

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
RA		

Kinetic Law

Derived unit $(60\ \mathrm{s})^{-1} \cdot \mathrm{nmol}$

$$v_2 = \mathrm{vol}\,(\mathrm{PSM}) \cdot \mathrm{kd5} \cdot [\mathrm{RA}] \tag{9}$$

7.3 Reaction RA_deg_by_Cyp26

This is an irreversible reaction of one reactant forming no product influenced by one modifier.

SBO:0000179 degradation

Reaction equation

$$\mathrm{RA} \xrightarrow{\mathrm{C}} \emptyset \tag{10}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
RA		

Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
C	CYP26	

Kinetic Law

Derived unit $(60\ \mathrm{s})^{-1} \cdot \mathrm{nmol}$

$$v_3 = \mathrm{vol}\,(\mathrm{PSM}) \cdot \mathrm{kd1} \cdot [\mathrm{RA}] \cdot [\mathrm{C}] \tag{11}$$

7.4 Reaction M_C_transcription

This is an irreversible reaction of no reactant forming one product influenced by one modifier.

SBO:0000183 transcription

Reaction equation

$$\emptyset \xrightarrow{\mathrm{F}} \mathrm{M\_C} \tag{12}$$

Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
F	FGF	

Product

Table 11: Properties of each product.

Id	Name	SBO
M_C	cyp26_mRNA	

Kinetic Law

Derived unit $\text{nmol} \cdot (60\ \text{s})^{-1}$

$$v_4 = \text{vol}(\text{PSM}) \cdot \left(\text{V0} + \frac{\text{Vsc} \cdot [\text{F}]^{\text{n}}}{\text{Ka}^{\text{n}} + [\text{F}]^{\text{n}}} \right) \tag{13}$$

7.5 Reaction M_C_decay

This is an irreversible reaction of one reactant forming no product.

SBO:0000179 degradation

Reaction equation

$$\text{M\_C} \longrightarrow \emptyset \tag{14}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
M_C	cyp26_mRNA	

Kinetic Law

Derived unit $(60\ \text{s})^{-1} \cdot \text{nmol}$

$$v_5 = \text{vol}(\text{PSM}) \cdot \text{kd3} \cdot [\text{M\_C}] \tag{15}$$

7.6 Reaction C_translation

This is an irreversible reaction of no reactant forming one product influenced by one modifier.

SBO:0000184 translation

Reaction equation

$$\emptyset \xrightarrow{\text{M\_C}} \text{C} \tag{16}$$

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
M_C	cyp26_mRNA	

Product

Table 14: Properties of each product.

Id	Name	SBO
C	CYP26	

Kinetic Law

Derived unit $(60\ \text{s})^{-1} \cdot \text{nmol}$

$$v_6 = \text{vol}\,(\text{PSM}) \cdot \text{ks2} \cdot [\text{M\_C}] \tag{17}$$

7.7 Reaction C_decay

This is an irreversible reaction of one reactant forming no product.

SBO:0000179 degradation

Reaction equation

$$\text{C} \longrightarrow \emptyset \tag{18}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
C	CYP26	

Kinetic Law

Derived unit $(60\ \mathrm{s})^{-1} \cdot \mathrm{nmol}$

$$v_7 = \mathrm{vol}(\mathrm{PSM}) \cdot \mathrm{kd2} \cdot [\mathrm{C}] \tag{19}$$

7.8 Reaction FGF_synthesis

This is an irreversible reaction of no reactant forming one product influenced by two modifiers.

SBO:0000184 translation

Reaction equation

$$\emptyset \xrightarrow{\mathrm{RA},\ \mathrm{M\_F}} \mathrm{F} \tag{20}$$

Modifiers

Table 16: Properties of each modifier.

Id	Name	SBO
RA		
M_F	FGF_mRNA	

Product

Table 17: Properties of each product.

Id	Name	SBO
F	FGF	

Kinetic Law

Derived unit $(60\ \mathrm{s})^{-1} \cdot \mathrm{nmol}$

$$v_8 = \mathrm{vol}(\mathrm{PSM}) \cdot \mathrm{ks3} \cdot [\mathrm{M\_F}] \cdot \frac{\mathrm{Ki}^{\mathrm{m}}}{\mathrm{Ki}^{\mathrm{m}} + [\mathrm{RA}]^{\mathrm{m}}} \tag{21}$$

7.9 Reaction FGF_decay

This is an irreversible reaction of one reactant forming no product.

SBO:0000179 degradation

Reaction equation

$$\mathrm{F} \longrightarrow \emptyset \tag{22}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
F	FGF	

Kinetic Law

Derived unit $(60\ \mathrm{s})^{-1} \cdot \mathrm{nmol}$

$$v_9 = \mathrm{vol}\,(\mathrm{PSM}) \cdot \mathrm{kd4} \cdot [\mathrm{F}] \tag{23}$$

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.

8.1 Species RA

SBO:0000247 simple chemical

Initial concentration $0.1\ \mathrm{nmol} \cdot \mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in RA_decay, RA_deg_by_Cyp26 and as a product in RA_synthesis and as a modifier in FGF_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{RA} = v_1 - v_2 - v_3 \tag{24}$$

8.2 Species M_C

Name cyp26_mRNA

SBO:0000250 ribonucleic acid

Initial concentration $0.1\ \mathrm{nmol} \cdot \mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in M_C_decay and as a product in M_C_transcription and as a modifier in C_translation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{M\_C} = v_4 - v_5 \tag{25}$$

8.3 Species C

Name CYP26

SBO:0000252 polypeptide chain

Initial concentration $0.1\ \mathrm{nmol} \cdot \mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in C_decay and as a product in C_translation and as a modifier in RA_deg_by_Cyp26).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C} = v_6 - v_7 \tag{26}$$

8.4 Species F

Name FGF

SBO:0000252 polypeptide chain

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

This species takes part in three reactions (as a reactant in FGF_decay and as a product in FGF_synthesis and as a modifier in M_C_transcription).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{F} = v_8 - v_9 \tag{27}$$

8.5 Species M_F

Name FGF_mRNA

SBO:0000250 ribonucleic acid

Involved in rule M_F

This species takes part in one reaction (as a modifier in FGF_synthesis) and is also involved in one rule which determines this species' quantity.

A Glossary of Systems Biology Ontology Terms

SBO:0000035 forward unimolecular rate constant, continuous case: Numerical parameter that quantifies the forward velocity of a chemical reaction involving only one reactant. This parameter encompasses all the contributions to the velocity except the quantity of the reactant. It is to be used in a reaction modelled using a continuous framework

SBO:0000036 forward bimolecular rate constant, continuous case: Numerical parameter that quantifies the forward velocity of a chemical reaction involving two reactants. This parameter encompasses all the contributions to the velocity except the quantity of the reactants. It is to be used in a reaction modelled using a continuous framework

SBO:0000046 zeroth order rate constant: Numerical parameter that quantifies the velocity of a chemical reaction independant of the reactant quantities. This parameter encompasses all the contributions to the velocity

SBO:0000179 degradation: Complete disappearance of a physical entity

SBO:0000183 transcription: Process through which a DNA sequence is copied to produce a complementary RNA

SBO:0000184 translation: Process in which a polypeptide chain is produced from a messenger RNA

SBO:0000186 maximal velocity: Limiting maximal velocity of an enzymatic reaction, reached when the substrate is in large excess and all the enzyme is complexed.

SBO:0000190 Hill coefficient: Empirical parameter created by Archibald Vivian Hill to describe the cooperative binding of oxygen on hemoglobine (Hill (1910). The possible effects of the aggregation of the molecules of haemoglobin on its dissociation curves. J Physiol 40: iv-vii)

SBO:0000196 concentration of an entity pool: The amount of an entity per unit of volume.

SBO:0000205 composite biochemical process: Process that involves the participation of chemical or biological entities and is composed of several elementary steps or reactions.

SBO:0000247 simple chemical: Simple, non-repetitive chemical entity

SBO:0000250 ribonucleic acid: Macromolecule formed by a repetition of ribonucleosides linked by phosphodiester bonds. CHEBI:3369

SBO:0000252 polypeptide chain: Naturally occurring macromolecule formed by the repetition of amino-acid residues linked by peptidic bonds. A polypeptide chain is synthesized by the ribosome. CHEBI:1654

SBO:0000256 biochemical parameter: Parameter that depends on the biochemical properties of a system

SBO:0000261 inhibitory constant: Dissociation constant of a compound from a target of which it inhibits the function.

SBO:0000282 dissociation constant: Equilibrium constant that measures the propensity of a larger object to separate (dissociate) reversibly into smaller components, as when a complex falls apart into its component molecules, or when a salt splits up into its component ions. The dissociation constant is usually denoted Kd and is the inverse of the affinity constant.

SBO:0000290 physical compartment: Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions

SBO:0000356 decay constant: Kinetic constant characterising a mono-exponential decay. It is the inverse of the mean lifetime of the continuant being decayed. Its unit is"per tim".

SBO:0000363 activation constant: Dissociation constant of a potentiator (activator) from a target (e.g. an enzyme) of which it activates the function

SBO:0000466 length: The length of an object is the longest measurable distance between its extremities.

SBO:0000485 basal rate constant: The minimal velocity observed under defined conditions, which may or may not include the presence of an effector. For example in an inhibitory system, this would be the residual velocity observed under full inhibition. In non-essential activation, this would be the velocity in the absence of any activator

SBO:0000505 concentration of enzyme: Amount of enzyme present per unit of volume. The participant role 'enzymatic catalyst' is defined in SBO:0000460

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