SBML Model Report

Model name: "Kim2011_Oscillator_SimpleIII"

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 Jongmin Kim[2] at December eighth 2010 at 4:54 p. m. and last time modified at April 20$^{\text{th}}$ 2012 at 9:58 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	6	function definitions	2
global parameters	3	unit definitions	3
rules	0	initial assignments	0

Model Notes

This a model from the article:
Synthetic in vitro transcriptional oscillators.
Kim J, Winfree E <u>Mol. Syst. Biol.</u> 2011 Feb 1;7:465. 21283141 ,
Abstract:
The construction of synthetic biochemical circuits from simple components illuminates how

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complex behaviors can arise in chemistry and builds a foundation for future biological technologies. A simplified analog of genetic regulatory networks, in vitro transcriptional circuits, provides a modular platform for the systematic construction of arbitrary circuits and requires only two essential enzymes, bacteriophage T7 RNA polymerase and Escherichia coli ribonuclease H, to produce and degrade RNA signals. In this study, we design and experimentally demonstrate three transcriptional oscillators in vitro. First, a negative feedback oscillator comprising two switches, regulated by excitatory and inhibitory RNA signals, showed up to five complete cycles. To demonstrate modularity and to explore the design space further, a positive-feedback loop was added that modulates and extends the oscillatory regime. Finally, a three-switch ring oscillator was constructed and analyzed. Mathematical modeling guided the design process, identified experimental conditions likely to yield oscillations, and explained the system's robust response to interference by short degradation products. Synthetic transcriptional oscillators could prove valuable for systematic exploration of biochemical circuit design principles and for controlling nanoscale devices and orchestrating processes within artificial cells.

Notes:

The paper describes 7 models (MODEL1012090000-6) and all these are submitted by the authors. This model (MODEL1012090001) corresponds to the Simple model of the three-switch ring oscillator (Design III). The model reproduces figure 6 (central figures) of the reference publication. The time is rescaled by s=v_d/K_I*t where K_I=0.333 and v_d=1 (for alpha = 1) and v_d=0.5 (for alpha = 0.5). i.e. For alpha = 1, s = 0.003 * t (roughly 10 unitless time = 1hr; the time-course should be run for 60 timeunits (6hrs) to get figure 6a). For alpha = 2, s= 0.0015 * t (roughly 5 unitless time = 1hr; the time-course shoue be run for 100 timesunits (20hrs) to get figure 6b).

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To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler L, Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novre N, Laibe C (2010) BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

2 Unit Definitions

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

2.1 Unit `volume`

Definition dimensionless

2.2 Unit `time`

Definition dimensionless

2.3 Unit `substance`

Definition dimensionless

2.4 Unit `area`

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

Definition m^2

2.5 Unit `length`

Notes Metre is the predefined SBML unit for `length` since SBML Level 2 Version 1.

Definition m

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
compartment_1	compartment	0000290	3	1	dimensionless	☑	

3.1 Compartment `compartment_1`

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

Name compartment

SBO:0000290 physical 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
species_1	x1	compartment_1	dimensionless $\cdot$ dimensionless^{-1}	⊟	⊟
species_2	x2	compartment_1	dimensionless $\cdot$ dimensionless^{-1}	⊟	⊟
species_3	x3	compartment_1	dimensionless $\cdot$ dimensionless^{-1}	⊟	⊟

5 Parameters

This model contains three global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
parameter_1	alpha	0000009	1.0		☑
parameter_2	beta	0000009	0.3		☑
parameter_3	n	0000190	5.0		☑

6 Function definitions

This is an overview of two function definitions.

6.1 Function definition `function_1`

Name Hill inhibition

Arguments V, Shalve, h, substrate

Mathematical Expression

$$\frac{V}{Shalve^h + substrate^h} \tag{1}$$

6.2 Function definition `function_3`

Name Simple inhibition

Arguments x, beta

Mathematical Expression

$$\frac{\frac{x}{beta}}{1 + \frac{x}{beta}} \tag{2}$$

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	reaction_1	reaction1	$species\_1 \longrightarrow species\_1 + species\_3$	
2	reaction_2	reaction2	$species\_2 \longrightarrow species\_2 + species\_1$	
3	reaction_3	reaction3	$species\_3 \longrightarrow species\_3 + species\_2$	
4	reaction_4	reaction4	$species\_1 \longrightarrow \emptyset$	
5	reaction_5	reaction5	$species\_2 \longrightarrow \emptyset$	
6	reaction_6	reaction6	$species\_3 \longrightarrow \emptyset$	

7.1 Reaction `reaction_1`

This is an irreversible reaction of one reactant forming two products.

Name reaction1

Reaction equation

$$\text{species\_1} \longrightarrow \text{species\_1} + \text{species\_3} \tag{3}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
species_1	x1	

Products

Table 7: Properties of each product.

Id	Name	SBO
species_1	x1	
species_3	x3	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}\,(\text{compartment\_1}) \cdot \text{function\_1}\,(\text{parameter\_1}, \text{Shalve}, \text{parameter\_3}, [\text{species\_1}]) \tag{4}$$

$$\text{function\_1}\,(V, \text{Shalve}, h, \text{substrate}) = \frac{V}{\text{Shalve}^h + \text{substrate}^h} \tag{5}$$

$$\text{function\_1}\,(V, \text{Shalve}, h, \text{substrate}) = \frac{V}{\text{Shalve}^h + \text{substrate}^h} \tag{6}$$
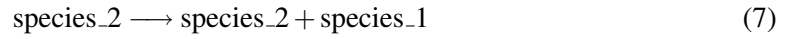
Table 8: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Shalve	Shalve	0000009	1.0		✓

7.2 Reaction `reaction_2`

This is an irreversible reaction of one reactant forming two products.

Name reaction2

Reaction equation

$$species\_2 \longrightarrow species\_2 + species\_1 \tag{7}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
species_2	x2	

Products

Table 10: Properties of each product.

Id	Name	SBO
species_2	x2	
species_1	x1	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}\,(\text{compartment\_1}) \cdot \text{function\_1}\,(\text{parameter\_1}, \text{Shalve}, \text{parameter\_3}, [\text{species\_2}]) \tag{8}$$

$$\text{function\_1}\,(V, \text{Shalve}, h, \text{substrate}) = \frac{V}{\text{Shalve}^h + \text{substrate}^h} \tag{9}$$

$$\text{function\_1}\,(V, \text{Shalve}, h, \text{substrate}) = \frac{V}{\text{Shalve}^h + \text{substrate}^h} \tag{10}$$

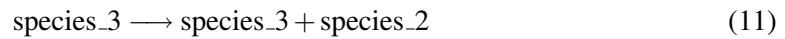Table 11: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Shalve	Shalve	0000009	1.0		☑

7.3 Reaction `reaction_3`

This is an irreversible reaction of one reactant forming two products.

Name reaction3

Reaction equation

$$\text{species\_3} \longrightarrow \text{species\_3} + \text{species\_2} \tag{11}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
species_3	x3	

Products

Table 13: Properties of each product.

Id	Name	SBO
species_3	x3	
species_2	x2	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{vol}\left(\text{compartment\_1}\right) \cdot \text{function\_1}\left(\text{parameter\_1}, \text{Shalve}, \text{parameter\_3}, [\text{species\_3}]\right) \tag{12}$$

$$\text{function\_1}\left(\text{V}, \text{Shalve}, \text{h}, \text{substrate}\right) = \frac{\text{V}}{\text{Shalve}^{\text{h}} + \text{substrate}^{\text{h}}} \tag{13}$$

$$\text{function\_1}\left(\text{V}, \text{Shalve}, \text{h}, \text{substrate}\right) = \frac{\text{V}}{\text{Shalve}^{\text{h}} + \text{substrate}^{\text{h}}} \tag{14}$$

Table 14: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Shalve	Shalve	0000009	1.0		☑

7.4 Reaction `reaction_4`

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

Name reaction4

Reaction equation

$$\text{species\_1} \longrightarrow \emptyset \tag{15}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
species_1	x1	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}\,(\text{compartment\_1}) \cdot \text{function\_3}\,([\text{species\_1}], \text{parameter\_2}) \tag{16}$$

$$\text{function\_3}\,(\text{x}, \text{beta}) = \frac{\frac{\text{x}}{\text{beta}}}{1 + \frac{\text{x}}{\text{beta}}} \tag{17}$$

$$\text{function\_3}\,(\text{x}, \text{beta}) = \frac{\frac{\text{x}}{\text{beta}}}{1 + \frac{\text{x}}{\text{beta}}} \tag{18}$$

7.5 Reaction `reaction_5`

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

Name reaction5

Reaction equation

$$\text{species\_2} \longrightarrow \emptyset \tag{19}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
species_2	x2	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}\left(\text{compartment\_1}\right) \cdot \text{function\_3}\left([\text{species\_2}], \text{parameter\_2}\right) \tag{20}$$

$$\text{function\_3}\left(x, \text{beta}\right) = \frac{\frac{x}{\text{beta}}}{1 + \frac{x}{\text{beta}}} \tag{21}$$

$$\text{function\_3}\left(x, \text{beta}\right) = \frac{\frac{x}{\text{beta}}}{1 + \frac{x}{\text{beta}}} \tag{22}$$

7.6 Reaction reaction_6

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

Name reaction6

Reaction equation

$$\text{species\_3} \longrightarrow \emptyset \tag{23}$$

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
species_3	x3	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{vol}\left(\text{compartment\_1}\right) \cdot \text{function\_3}\left([\text{species\_3}], \text{parameter\_2}\right) \tag{24}$$

$$\text{function\_3}\left(x, \text{beta}\right) = \frac{\frac{x}{\text{beta}}}{1 + \frac{x}{\text{beta}}} \tag{25}$$

$$\text{function\_3}(x, \text{beta}) = \frac{\frac{x}{\text{beta}}}{1 + \frac{x}{\text{beta}}} \tag{26}$$

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 `species_1`

Name x1

SBO:0000020 inhibitor

Initial concentration $0\,\text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in four reactions (as a reactant in `reaction_1`, `reaction_4` and as a product in `reaction_1`, `reaction_2`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_1} = v_1 + v_2 - v_1 - v_4 \tag{27}$$

8.2 Species `species_2`

Name x2

SBO:0000020 inhibitor

Initial concentration $0\,\text{dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in four reactions (as a reactant in `reaction_2`, `reaction_5` and as a product in `reaction_2`, `reaction_3`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_2} = v_2 + v_3 - v_2 - v_5 \tag{28}$$

8.3 Species `species_3`

Name x3

SBO:0000020 inhibitor

Initial concentration $0.33\,\mathrm{dimensionless \cdot dimensionless^{-1}}$

This species takes part in four reactions (as a reactant in `reaction_3`, `reaction_6` and as a product in `reaction_1`, `reaction_3`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_3} = v_1 + v_3 - v_3 - v_6 \tag{29}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000009 kinetic constant: Numerical parameter that quantifies the velocity of a chemical reaction

SBO:0000020 inhibitor: Substance that decreases the probability of a chemical reaction without itself being consumed or transformed by the reaction

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