SBML Model Report

Model name: “Kim2011_Oscillator_SimpleI”

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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 3:19 p. m. and last time modified at June seventh 2013 at 3:14 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	9	function definitions	2
global parameters	6	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 Mol. Syst. Biol. 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 simplifiedanalog of genetic regulatory networks, in vitro transcriptional circuits, provides a modular platformfor 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.

Note:

The paper describes 7 models (MODEL1012090000-6) and all these are submitted by the authors. Thismodel (MODEL1012090000) corresponds to the Simple model for both mode I and II (Design I and II). The model reproduces timecourse figure plotted in the supplementary material (page 10 of Supplementary material) of the reference publication.

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 four 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	x	compartment_1	dimensionless $\cdot$ dimensionless^{-1}	⊟	⊟
species_2	y	compartment_1	dimensionless $\cdot$ dimensionless^{-1}	⊟	⊟
species_3	u	compartment_1	dimensionless $\cdot$ dimensionless^{-1}	⊟	⊟
species_4	v	compartment_1	dimensionless $\cdot$ dimensionless^{-1}	⊟	⊟

5 Parameters

This model contains six global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
parameter_1	alpha	0000009	0.57		☑
parameter_2	beta	0000009	2.50		☑
parameter_3	gamma	0000009	1.00		☑
parameter_4	n	0000190	6.50		☑
parameter_5	m	0000190	6.50		☑
parameter_6	delta	0000009	1.50		☑

6 Function definitions

This is an overview of two function definitions.

6.1 Function definition `function_2`

Name Hill Cooperativity

Arguments substrate, Shalve, V, h

Mathematical Expression

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

6.2 Function definition `function_1`

Name Hill inhibition

Arguments V, Shalve, h, substrate

Mathematical Expression

$$\frac{\mathrm{V}}{\mathrm{Shalve}^{\mathrm{h}} + \mathrm{substrate}^{\mathrm{h}}} \tag{2}$$

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	reaction_1	reaction1	species_1 $\longrightarrow \emptyset$	
2	reaction_2	reaction2	species_2 $\longrightarrow \emptyset$	
3	reaction_3	reaction3	species_3 $\longrightarrow \emptyset$	
4	reaction_4	reaction4	species_4 $\longrightarrow \emptyset$	
5	reaction_5	reaction5	species_3 $\longrightarrow$ species_3 + species_1	
6	reaction_6	reaction6	species_4 $\longrightarrow$ species_4 + species_2	
7	reaction_7	reaction7	species_2 $\longrightarrow$ species_2 + species_3	
8	reaction_8	reaction8	species_1 $\longrightarrow$ species_1 + species_4	
9	reaction_9	reaction9	species_4 $\longrightarrow$ species_4 + species_1	

7.1 Reaction `reaction_1`

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

Name reaction1

Reaction equation

$$\text{species\_1} \longrightarrow \emptyset \tag{3}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
`species_1`	x	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}\left(\text{compartment\_1}\right) \cdot \text{k1} \cdot [\text{species\_1}] \tag{4}$$

Table 7: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`k1`	k1	0000009	1.0		☑

7.2 Reaction `reaction_2`

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

Name reaction2

Reaction equation

$$\text{species\_2} \longrightarrow \emptyset \tag{5}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
species_2	y	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{k1} \cdot [\mathrm{species\_2}] \tag{6}$$

Table 9: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1	0000009	1.0		☑

7.3 Reaction reaction_3

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

Name reaction3

Reaction equation

$$\mathrm{species\_3} \longrightarrow \emptyset \tag{7}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
species_3	u	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{k1} \cdot [\mathrm{species\_3}] \tag{8}$$

Table 11: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`k1`	k1	0000009	1.0		☑

7.4 Reaction `reaction_4`

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

Name reaction4

Reaction equation

$$\text{species\_4} \longrightarrow \emptyset \tag{9}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
`species_4`	v	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}\left(\text{compartment\_1}\right) \cdot \text{k1} \cdot [\text{species\_4}] \tag{10}$$

Table 13: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`k1`	k1	0000009	1.0		☑

7.5 Reaction `reaction_5`

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

Name reaction5

Reaction equation

$$\text{species\_3} \longrightarrow \text{species\_3} + \text{species\_1} \tag{11}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
species_3	u	

Products

Table 15: Properties of each product.

Id	Name	SBO
species_3	u	
species_1	x	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{parameter\_1} \cdot [\mathrm{species\_3}] \tag{12}$$

7.6 Reaction `reaction_6`

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

Name reaction6

Reaction equation

$$\mathrm{species\_4} \longrightarrow \mathrm{species\_4} + \mathrm{species\_2} \tag{13}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
species_4	v	

Products

Table 17: Properties of each product.

Id	Name	SBO
species_4	v	
species_2	y	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{parameter\_2} \cdot [\mathrm{species\_4}] \tag{14}$$

7.7 Reaction `reaction_7`

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

Name reaction7

Reaction equation

$$\mathrm{species\_2} \longrightarrow \mathrm{species\_2} + \mathrm{species\_3} \tag{15}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
species_2	y	

Products

Table 19: Properties of each product.

Id	Name	SBO
species_2	y	
species_3	u	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{function\_1}\left(\mathrm{V}, \mathrm{Shalve}, \mathrm{parameter\_4}, [\mathrm{species\_2}]\right) \tag{16}$$

$$\mathrm{function\_1}(\mathrm{V},\mathrm{Shalve},\mathrm{h},\mathrm{substrate}) = \frac{\mathrm{V}}{\mathrm{Shalve}^{\mathrm{h}} + \mathrm{substrate}^{\mathrm{h}}} \tag{17}$$

$$\mathrm{function\_1}(\mathrm{V},\mathrm{Shalve},\mathrm{h},\mathrm{substrate}) = \frac{\mathrm{V}}{\mathrm{Shalve}^{\mathrm{h}} + \mathrm{substrate}^{\mathrm{h}}} \tag{18}$$

Table 20: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
V	V	0000009	1.0		☑
Shalve	Shalve	0000009	1.0		☑

7.8 Reaction reaction_8

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

Name reaction8

Reaction equation

$$\mathrm{species\_1} \longrightarrow \mathrm{species\_1} + \mathrm{species\_4} \tag{19}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
species_1	x	

Products

Table 22: Properties of each product.

Id	Name	SBO
species_1	x	
species_4	v	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}(\mathrm{compartment\_1}) \cdot \mathrm{function\_2}([\mathrm{species\_1}], \mathrm{Shalve}, \mathrm{V}, \mathrm{parameter\_5}) \tag{20}$$

$$\text{function\_2}\left(\text{substrate},\text{Shalve},\text{V},\text{h}\right)=\frac{\text{V}\cdot\text{substrate}^{\text{h}}}{\text{Shalve}^{\text{h}}+\text{substrate}^{\text{h}}} \tag{21}$$

$$\text{function\_2}\left(\text{substrate},\text{Shalve},\text{V},\text{h}\right)=\frac{\text{V}\cdot\text{substrate}^{\text{h}}}{\text{Shalve}^{\text{h}}+\text{substrate}^{\text{h}}} \tag{22}$$

Table 23: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Shalve	Shalve	0000009	1.0		☑
V	V	0000009	1.0		☑

7.9 Reaction reaction_9

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

Name reaction9

Reaction equation

$$\text{species\_4}\longrightarrow\text{species\_4}+\text{species\_1} \tag{23}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
species_4	v	

Products

Table 25: Properties of each product.

Id	Name	SBO
species_4	v	
species_1	x	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\left(\mathrm{compartment\_1}\right) \cdot \mathrm{parameter\_6} \cdot [\mathrm{species\_4}] \tag{24}$$

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 x

SBO:0000459 stimulator

Initial concentration 0.1 dimensionless $\cdot$ dimensionless^{-1}

This species takes part in five reactions (as a reactant in `reaction_1`, `reaction_8` and as a product in `reaction_5`, `reaction_8`, `reaction_9`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_1} = v_5 + v_8 + v_9 - v_1 - v_8 \tag{25}$$

8.2 Species `species_2`

Name y

SBO:0000020 inhibitor

Initial concentration 0.1 dimensionless $\cdot$ dimensionless^{-1}

This species takes part in four reactions (as a reactant in `reaction_2`, `reaction_7` and as a product in `reaction_6`, `reaction_7`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species\_2} = v_6 + v_7 - v_2 - v_7 \tag{26}$$

8.3 Species species_3

Name u

SBO:0000540 fraction of an entity pool

Initial concentration $0.1 \text{ dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in four reactions (as a reactant in reaction_3, reaction_5 and as a product in reaction_5, reaction_7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_3} = v_5 + v_7 - v_3 - v_5 \tag{27}$$

8.4 Species species_4

Name v

SBO:0000540 fraction of an entity pool

Initial concentration $0.1 \text{ dimensionless} \cdot \text{dimensionless}^{-1}$

This species takes part in six reactions (as a reactant in reaction_4, reaction_6, reaction_9 and as a product in reaction_6, reaction_8, reaction_9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{species\_4} = v_6 + v_8 + v_9 - v_4 - v_6 - v_9 \tag{28}$$

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

SBO:0000459 stimulator: Substance that accelerates the velocity of a chemical reaction without itself being consumed or transformed.

SBO:0000540 fraction of an entity pool: A ratio that represents the quantity of a defined constituent entity over the total number of all constituent entities present.

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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