SBML Model Report

Model name: "Leloup1999-_CircadianRhythms_Neurospora"

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Catherine Lloyd[1] and Vijayalakshmi Chelliah[2] at January 14th 2011 at 2:22 p. m. and last time modified at February 25th 2015 at 1:49 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	2
species types	0	species	3
events	0	constraints	0
reactions	0	function definitions	0
global parameters	11	unit definitions	0
rules	4	initial assignments	0

Model Notes

This a model from the article:
Limit cycle models for circadian rhythms based on transcriptional regulation in Drosophila and Neurospora.
Leloup JC, Gonze D, Goldbeter A. J Biol Rhythms. 1999 Dec;14(6):433-48. 10643740 ,

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Abstract:
We examine theoretical models for circadian oscillations based on transcriptional regulation in Drosophila and Neurospora. For Drosophila, the molecular model is based on the negative feedback exerted on the expression of the per and tim genes by the complex formed between the PER and TIM proteins. For Neurospora, similarly, the model relies on the feedback exerted on the expression of the frq gene by its protein product FRQ. In both models, sustained rhythmic variations in protein and mRNA levels occur in continuous darkness, in the form of limit cycle oscillations. The effect of light on circadian rhythms is taken into account in the models by considering that it triggers degradation of the TIM protein in Drosophila, and frq transcription in Neurospora. When incorporating the control exerted by light at the molecular level, we show that the models can account for the entrainment of circadian rhythms by light-dark cycles and for the damping of the oscillations in constant light, though such damping occurs more readily in the Drosophila model. The models account for the phase shifts induced by light pulses and allow the construction of phase response curves. These compare well with experimental results obtained in Drosophila. The model for Drosophila shows that when applied at the appropriate phase, light pulses of appropriate duration and magnitude can permanently or transiently suppress circadian rhythmicity. We investigate the effects of the magnitude of light-induced changes on oscillatory behavior. Finally, we discuss the common and distinctive features of circadian oscillations in the two organisms.

This particular version of the model has been translated from equations 4a-4c (Neurospora).

This model was taken from the CellML repository and automatically converted to SBML.
The original model was: **Leloup JC, Gonze D, Goldbeter A. (1999) - version02**
The original CellML model was created by:
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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 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

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

3.1 Compartment Cytoplasm

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

SBO:0000290 physical compartment

3.2 Compartment `Nucleus`

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

SBO:0000290 physical compartment

4 Species

This model contains three 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
M	M	Nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
FC	FC	Cytoplasm	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
FN	FN	Nucleus	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains eleven global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
vs	vs	0000153	1.600		☑
vm	vm	0000186	0.505		☑
Km	Km	0000027	0.500		☑
KI	KI	0000009	1.000		☑
n	n	0000190	4.000		☑
Ft	Ft	0000360	0.000		☐
ks	ks	0000022	0.500		☑
vd	vd	0000186	1.400		☑
Kd	Kd	0000027	0.130		☑
k1	k1	0000022	0.500		☑
k2	k2	0000022	0.600		☑

6 Rules

This is an overview of four rules.

6.1 Rule M

Rule M is a rate rule for species M:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{M} = \mathrm{vs} \cdot \frac{\mathrm{KI}^{\mathrm{n}}}{\mathrm{KI}^{\mathrm{n}} + [\mathrm{FN}]^{\mathrm{n}}} - \mathrm{vm} \cdot \frac{[\mathrm{M}]}{\mathrm{Km} + [\mathrm{M}]} \tag{1}$$

6.2 Rule FC

Rule FC is a rate rule for species FC:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{FC} = \mathrm{ks} \cdot [\mathrm{M}] + \mathrm{k2} \cdot [\mathrm{FN}] - \left(\mathrm{vd} \cdot \frac{[\mathrm{FC}]}{\mathrm{Kd} + [\mathrm{FC}]} + \mathrm{k1} \cdot [\mathrm{FC}]\right) \tag{2}$$

6.3 Rule FN

Rule FN is a rate rule for species FN:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{FN} = \mathrm{k1} \cdot [\mathrm{FC}] - \mathrm{k2} \cdot [\mathrm{FN}] \tag{3}$$

6.4 Rule Ft

Rule Ft is an assignment rule for parameter Ft:

$$\mathrm{Ft} = [\mathrm{FC}] + [\mathrm{FN}] \tag{4}$$

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

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 M

Name M

SBO:0000278 messenger RNA

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

Involved in rule M

One rule which determines this species' quantity.

7.2 Species FC

Name FC

SBO:0000245 macromolecule

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

Involved in rule FC

One rule which determines this species' quantity.

7.3 Species FN

Name FN

SBO:0000245 macromolecule

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

Involved in rule FN

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:0000022 forward unimolecular rate constant: 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

SBO:0000027 Michaelis constant: Substrate concentration at which the velocity of reaction is half its maximum. Michaelis constant is an experimental parameter. According to the underlying molecular mechanism it can be interpreted differently in terms of microscopic constants

SBO:0000153 forward rate constant: Numerical parameter that quantifies the forward velocity of a chemical reaction. This parameter encompasses all the contributions to the velocity except the quantity of the reactants

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:0000245 macromolecule: Molecular entity mainly built-up by the repetition of pseudo-identical units. CHEBI:3383

SBO:0000278 messenger RNA: A messenger RNA is a ribonucleic acid synthesized during the transcription of a gene, and that carries the information to encode one or several proteins

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:0000360 quantity of an entity pool: The enumeration of co-localised, identical biochemical entities of a specific state, which constitute a pool. The form of enumeration may be purely numerical, or may be given in relation to another dimension such as length or volume

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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