SBML Model Report

Model name: "Leloup1999_CircadianRhythms_Drosophila"

August 10, 2016

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by the following two authors: Catherine Lloyd[1] and Vijayalakshmi Chelliah[2] at April 28th 2009 at 3:31 p. m. and last time modified at February 25th 2015 at 1:41 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	10
events	0	constraints	0
reactions	0	function definitions	0
global parameters	39	unit definitions	0
rules	11	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 1a-1j (Drosophila).

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 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`Compartment`			3	1	litre	☑	

3.1 Compartment `Compartment`

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

4 Species

This model contains ten 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
MP	MP	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
CN	CN	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
C	C	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
T2	T2	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
T1	T1	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
T0	T0	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
MT	MT	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
P0	P0	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
P1	P1	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
P2	P2	Compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 39 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
vsP	vsP	0000186	1.10		☑
vmP	vmP	0000186	1.00		☑
KmP	KmP	0000027	0.20		☑
KIP	KIP	0000009	1.00		☑
Pt	Pt	0000360	0.00		☐
ksP	ksP	0000022	0.90		☑
vdP	vdP	0000186	2.20		☑
KdP	KdP	0000027	0.20		☑
vsT	vsT	0000186	1.00		☑
vmT	vmT	0000186	0.70		☑
KmT	KmT	0000027	0.20		☑
KIT	KIT	0000009	1.00		☑
ksT	ksT	0000022	0.90		☑
vdT	vdT	0000186	3.00		☑
KdT	KdT	0000027	0.20		☑
kdC	kdC	0000356	0.01		☑
kdN	kdN	0000356	0.01		☑
k1	k1	0000022	0.80		☑
k2	k2	0000022	0.20		☑
k3	k3	0000153	1.20		☑
k4	k4	0000156	0.60		☑
kd	kd	0000356	0.01		☑
V1P	V1P	0000186	8.00		☑
V1T	V1T	0000186	8.00		☑
V2P	V2P	0000186	1.00		☑
V2T	V2T	0000186	1.00		☑
V3P	V3P	0000186	8.00		☑
V3T	V3T	0000186	8.00		☑
V4P	V4P	0000186	1.00		☑
V4T	V4T	0000186	1.00		☑
K1P	K1P	0000027	2.00		☑
K1T	K1T	0000027	2.00		☑
K2P	K2P	0000027	2.00		☑
K2T	K2T	0000027	2.00		☑
K3P	K3P	0000027	2.00		☑
K3T	K3T	0000027	2.00		☑
K4P	K4P	0000027	2.00		☑

Id	Name	SBO	Value	Unit	Constant
K4T	K4T	0000027	2.00		☑
n	n	0000190	4.00		☑

6 Rules

This is an overview of eleven rules.

6.1 Rule MP

Rule MP is a rate rule for species MP:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MP} = \mathrm{vsP} \cdot \frac{\mathrm{KIP}^{\mathrm{n}}}{\mathrm{KIP}^{\mathrm{n}} + [\mathrm{CN}]^{\mathrm{n}}} - \left(\mathrm{vmP} \cdot \frac{[\mathrm{MP}]}{\mathrm{KmP} + [\mathrm{MP}]} + \mathrm{kd} \cdot [\mathrm{MP}]\right) \tag{1}$$

6.2 Rule P0

Rule P0 is a rate rule for species P0:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P0} = \mathrm{ksP} \cdot [\mathrm{MP}] + \mathrm{V2P} \cdot \frac{[\mathrm{P1}]}{\mathrm{K2P} + [\mathrm{P1}]} - \left(\mathrm{V1P} \cdot \frac{[\mathrm{P0}]}{\mathrm{K1P} + [\mathrm{P0}]} + \mathrm{kd} \cdot [\mathrm{P0}]\right) \tag{2}$$

6.3 Rule P1

Rule P1 is a rate rule for species P1:

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P1} = {} & \mathrm{V1P} \cdot \frac{[\mathrm{P0}]}{\mathrm{K1P} + [\mathrm{P0}]} + \mathrm{V4P} \cdot \frac{[\mathrm{P2}]}{\mathrm{K4P} + [\mathrm{P2}]} \\ & - \left(\mathrm{V2P} \cdot \frac{[\mathrm{P1}]}{\mathrm{K2P} + [\mathrm{P1}]} + \mathrm{V3P} \cdot \frac{[\mathrm{P1}]}{\mathrm{K3P} + [\mathrm{P1}]} + \mathrm{kd} \cdot [\mathrm{P1}]\right)\end{aligned} \tag{3}$$

6.4 Rule P2

Rule P2 is a rate rule for species P2:

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P2} = {} & \mathrm{V3P} \cdot \frac{[\mathrm{P1}]}{\mathrm{K3P} + [\mathrm{P1}]} + \mathrm{k4} \cdot [\mathrm{C}] \\ & - \left(\mathrm{V4P} \cdot \frac{[\mathrm{P2}]}{\mathrm{K4P} + [\mathrm{P2}]} + \mathrm{k3} \cdot [\mathrm{P2}] \cdot [\mathrm{T2}] + \mathrm{vdP} \cdot \frac{[\mathrm{P2}]}{\mathrm{KdP} + [\mathrm{P2}]} + \mathrm{kd} \cdot [\mathrm{P2}]\right)\end{aligned} \tag{4}$$

6.5 Rule MT

Rule MT is a rate rule for species MT:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MT} = \mathrm{vsT} \cdot \frac{\mathrm{KIT}^{\mathrm{n}}}{\mathrm{KIT}^{\mathrm{n}} + [\mathrm{CN}]^{\mathrm{n}}} - \left(\mathrm{vmT} \cdot \frac{[\mathrm{MT}]}{\mathrm{KmT} + [\mathrm{MT}]} + \mathrm{kd} \cdot [\mathrm{MT}]\right) \tag{5}$$

6.6 Rule T0

Rule T0 is a rate rule for species T0:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{T0} = \mathrm{ksT} \cdot [\mathrm{MT}] + \mathrm{V2T} \cdot \frac{[\mathrm{T1}]}{\mathrm{K2T} + [\mathrm{T1}]} - \left(\mathrm{V1T} \cdot \frac{[\mathrm{T0}]}{\mathrm{K1T} + [\mathrm{T0}]} + \mathrm{kd} \cdot [\mathrm{T0}]\right) \tag{6}$$

6.7 Rule T1

Rule T1 is a rate rule for species T1:

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{T1} = \mathrm{V1T} \cdot \frac{[\mathrm{T0}]}{\mathrm{K1T} + [\mathrm{T0}]} + \mathrm{V4T} \cdot \frac{[\mathrm{T2}]}{\mathrm{K4T} + [\mathrm{T2}]} \\ - \left(\mathrm{V2T} \cdot \frac{[\mathrm{T1}]}{\mathrm{K2T} + [\mathrm{T1}]} + \mathrm{V3T} \cdot \frac{[\mathrm{T1}]}{\mathrm{K3T} + [\mathrm{T1}]} + \mathrm{kd} \cdot [\mathrm{T1}]\right)\end{aligned} \tag{7}$$

6.8 Rule T2

Rule T2 is a rate rule for species T2:

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{T2} = \mathrm{V3T} \cdot \frac{[\mathrm{T1}]}{\mathrm{K3T} + [\mathrm{T1}]} + \mathrm{k4} \cdot [\mathrm{C}] \\ - \left(\mathrm{V4T} \cdot \frac{[\mathrm{T2}]}{\mathrm{K4T} + [\mathrm{T2}]} + \mathrm{k3} \cdot [\mathrm{P2}] \cdot [\mathrm{T2}] + \mathrm{vdT} \cdot \frac{[\mathrm{T2}]}{\mathrm{KdT} + [\mathrm{T2}]} + \mathrm{kd} \cdot [\mathrm{T2}]\right)\end{aligned} \tag{8}$$

6.9 Rule C

Rule C is a rate rule for species C:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C} = \mathrm{k3} \cdot [\mathrm{P2}] \cdot [\mathrm{T2}] + \mathrm{k2} \cdot [\mathrm{CN}] - (\mathrm{k4} \cdot [\mathrm{C}] + \mathrm{k1} \cdot [\mathrm{C}] + \mathrm{kdC} \cdot [\mathrm{C}]) \tag{9}$$

6.10 Rule CN

Rule CN is a rate rule for species CN:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{CN} = \mathrm{k1} \cdot [\mathrm{C}] - (\mathrm{k2} \cdot [\mathrm{CN}] + \mathrm{kdN} \cdot [\mathrm{CN}]) \tag{10}$$

6.11 Rule Pt

Rule Pt is an assignment rule for parameter Pt:

$$\mathrm{Pt} = [\mathrm{P0}] + [\mathrm{P1}] + [\mathrm{P2}] + [\mathrm{C}] + [\mathrm{CN}] \tag{11}$$

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 MP

Name MP

SBO:0000278 messenger RNA

Initial concentration $0.0614368\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule MP

One rule which determines this species' quantity.

7.2 Species CN

Name CN

SBO:0000296 macromolecular complex

Initial concentration $1.34728\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule CN

One rule which determines this species' quantity.

7.3 Species C

Name C

SBO:0000296 macromolecular complex

Initial concentration $0.207614\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule C

One rule which determines this species' quantity.

7.4 Species T2

Name T2

SBO:0000245 macromolecule

Initial concentration $0.0145428\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule T2

One rule which determines this species' quantity.

7.5 Species T1

Name T1

SBO:0000245 macromolecule

Initial concentration $0.0213384\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule T1

One rule which determines this species' quantity.

7.6 Species T0

Name T0

SBO:0000245 macromolecule

Initial concentration $0.0217261\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule T0

One rule which determines this species' quantity.

7.7 Species MT

Name MT

SBO:0000278 messenger RNA

Initial concentration $0.0860342\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule MT

One rule which determines this species' quantity.

7.8 Species P0

Name P0

SBO:0000245 macromolecule

Initial concentration $0.0169928\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

Involved in rule P0

One rule which determines this species' quantity.

7.9 Species P1

Name P1

SBO:0000245 macromolecule

Initial concentration $0.0141356 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule P1

One rule which determines this species' quantity.

7.10 Species P2

Name P2

SBO:0000245 macromolecule

Initial concentration $0.0614368 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule P2

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:0000156 reverse 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:0000296 macromolecular complex: Non-covalent complex of one or more macromolecules and zero or more simple chemicals

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: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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