SBML Model Report

Model name: “Goldbeter1991 - Min Mit Oscil, Expl Inact”

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Bruce Shapiro[1] at February eighth 2005 at 5:34 p. m. and last time modified at December eleventh 2012 at 3:30 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	5
events	0	constraints	0
reactions	7	function definitions	0
global parameters	5	unit definitions	0
rules	2	initial assignments	0

Model Notes

Goldbeter1991 - Min Mit Oscil, Expl Inact

This model represents the inactive forms of CDC-2 Kinase and Cyclin Protease as separate species, unlike the ODEs in the published paper, in which the equations for the inactive forms are substituted into the equations for the active forms using a mass conservation rule

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M+MI=1,X+XI=1. Mass is still conserved in this model through the explicit reactions M<->MI and X<->XI. The terms in the kinetic laws are identical to the corresponding terms in the kinetic laws in the published paper.

This model has been generated by MathSBML 2.4.6 (14-January-2005) 14-January-2005 18:37:35.503857.

This model is described in the article:A minimal cascade model for the mitotic oscillator involving cyclin and cdc2 kinase.Goldbeter A.Proc. Natl. Acad. Sci. USA 1991 Oct; 88(20):9107-11

Abstract:

A minimal model for the mitotic oscillator is presented. The model, built on recent experimental advances, is based on the cascade of post-translational modification that modulates the activity of cdc2 kinase during the cell cycle. The model pertains to the situation encountered in early amphibian embryos, where the accumulation of cyclin suffices to trigger the onset of mitosis. In the first cycle ofthe bicyclic cascade model, cyclin promotes the activation of cdc2 kinase through reversible dephosphorylation, and in the second cycle, cdc2 kinase activates a cyclin protease by reversible phosphorylation. That cyclin activates cdc2 kinase while the kinase triggers the degradation of cyclin has suggested that oscillations may originate from such a negative feedback loop [Flix, M. A., Labb, J. C., Dore, M., Hunt, T. & Karsenti, E. (1990) Nature (London) 346, 379-382]. Thisconjecture is corroborated by the model, which indicates that sustained oscillations of the limit cycle type can arise in the cascade, provided that a threshold exists in the activation of cdc2 kinase by cyclin and in the activation of cyclinproteolysis by cdc2 kinase. The analysis shows how miototic oscillations may readily arise from time lags associated with these thresholds and from the delayed negative feedback provided by cdc2-induced cyclin degradation. A mechanism for theorigin of the thresholds is proposed in terms of the phenomenon of zero-order ultrasensitivity previously described for biochemical systems regulated by covalent modification.

This model is hosted on BioModels Database and identified by: BIOMD0000000004 .

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models .

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
cell	cell		3	1	litre	☑	

3.1 Compartment cell

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

Name cell

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
C	Cyclin	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
M	Active CDC-2 Kinase	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
X	Active Cyclin Protease	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
MI	Inactive CDC-2 Kinase	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
XI	Inactive Cyclin Protease	cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains five global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
V1	V1		0.0		☐
V3	V3		0.0		☐
VM1	VM1		3.0		☑
VM3	VM3		1.0		☑
Kc	Kc		0.5		☑

6 Rules

This is an overview of two rules.

6.1 Rule V1

Rule V1 is an assignment rule for parameter V1:

$$\mathrm{V1} = [\mathrm{C}] \cdot \mathrm{VM1} \cdot ([\mathrm{C}] + \mathrm{Kc})^{-1} \tag{1}$$

6.2 Rule V3

Rule V3 is an assignment rule for parameter V3:

$$\mathrm{V3} = [\mathrm{M}] \cdot \mathrm{VM3} \tag{2}$$

7 Reactions

This model contains seven 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	`reaction1`	creation of cyclin	$\emptyset \longrightarrow C$	
2	`reaction2`	default degradation of cyclin	$C \longrightarrow \emptyset$	
3	`reaction3`	cdc2 kinase triggered degration of cyclin	$C \xrightarrow{X} \emptyset$	
4	`reaction4`	activation of cdc2 kinase	$MI \longrightarrow M$	
5	`reaction5`	deactivation of cdc2 kinase	$M \longrightarrow MI$	
6	`reaction6`	activation of cyclin protease	$XI \longrightarrow X$	
7	`reaction7`	deactivation of cyclin protease	$X \longrightarrow XI$	

7.1 Reaction `reaction1`

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

Name creation of cyclin

Reaction equation

$$\emptyset \longrightarrow \mathrm{C} \tag{3}$$

Product

Table 6: Properties of each product.

Id	Name	SBO
C	Cyclin	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{vi} \tag{4}$$

Table 7: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
vi			0.025		☑

7.2 Reaction `reaction2`

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

Name default degradation of cyclin

Reaction equation

$$\mathrm{C} \longrightarrow \emptyset \tag{5}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
C	Cyclin	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = [\mathrm{C}] \cdot \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{kd} \tag{6}$$

Table 9: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kd			0.01		☑

7.3 Reaction reaction3

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

Name cdc2 kinase triggered degration of cyclin

Reaction equation

$$\mathrm{C} \xrightarrow{\mathrm{X}} \emptyset \tag{7}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
C	Cyclin	

Modifier

Table 11: Properties of each modifier.

Id	Name	SBO
X	Active Cyclin Protease	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = [\mathrm{C}] \cdot \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{vd} \cdot [\mathrm{X}] \cdot ([\mathrm{C}] + \mathrm{Kd})^{-1} \tag{8}$$

Table 12: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
vd			0.25		☑
Kd			0.02		☑

7.4 Reaction reaction4

This is an irreversible reaction of one reactant forming one product.

Name activation of cdc2 kinase

Reaction equation

$$\mathrm{MI} \longrightarrow \mathrm{M} \tag{9}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
MI	Inactive CDC-2 Kinase	

Product

Table 14: Properties of each product.

Id	Name	SBO
M	Active CDC-2 Kinase	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{MI}] \cdot \mathrm{V1} \cdot (\mathrm{K1} + [\mathrm{MI}])^{-1} \tag{10}$$

Table 15: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K1			0.005		☑

7.5 Reaction reaction5

This is an irreversible reaction of one reactant forming one product.

Name deactivation of cdc2 kinase

Reaction equation

$$\mathrm{M} \longrightarrow \mathrm{MI} \tag{11}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
M	Active CDC-2 Kinase	

Product

Table 17: Properties of each product.

Id	Name	SBO
MI	Inactive CDC-2 Kinase	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{M}] \cdot \mathrm{V2} \cdot (\mathrm{K2} + [\mathrm{M}])^{-1} \tag{12}$$

Table 18: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
V2			1.500		☑
K2			0.005		☑

7.6 Reaction reaction6

This is an irreversible reaction of one reactant forming one product.

Name activation of cyclin protease

Reaction equation

$$\mathrm{XI} \longrightarrow \mathrm{X} \tag{13}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
XI	Inactive Cyclin Protease	

Product

Table 20: Properties of each product.

Id	Name	SBO
X	Active Cyclin Protease	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{V3} \cdot [\mathrm{XI}] \cdot (\mathrm{K3} + [\mathrm{XI}])^{-1} \tag{14}$$

Table 21: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K3			0.005		☑

7.7 Reaction reaction7

This is an irreversible reaction of one reactant forming one product.

Name deactivation of cyclin protease

Reaction equation

$$\mathrm{X} \longrightarrow \mathrm{XI} \tag{15}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
X	Active Cyclin Protease	

Product

Table 23: Properties of each product.

Id	Name	SBO
XI	Inactive Cyclin Protease	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{V4} \cdot [\mathrm{X}] \cdot (\mathrm{K4} + [\mathrm{X}])^{-1} \tag{16}$$

Table 24: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K4			0.005		☑
V4			0.500		☑

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 `C`

Name Cyclin

Initial concentration $0.01\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in `reaction2`, `reaction3` and as a product in `reaction1`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C} = v_1 - v_2 - v_3 \tag{17}$$

8.2 Species `M`

Name Active CDC-2 Kinase

Initial concentration $0.01\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in `reaction5` and as a product in `reaction4`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{M} = v_4 - v_5 \tag{18}$$

8.3 Species `X`

Name Active Cyclin Protease

Initial concentration $0.01\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in `reaction7` and as a product in `reaction6` and as a modifier in `reaction3`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{X} = v_6 - v_7 \tag{19}$$

8.4 Species `MI`

Name Inactive CDC-2 Kinase

Initial concentration $0.99\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in `reaction4` and as a product in `reaction5`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{MI} = v_5 - v_4 \tag{20}$$

8.5 Species XI

Name Inactive Cyclin Protease

Initial concentration $0.99\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in reaction6 and as a product in reaction7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{XI} = v_7 - v_6 \tag{21}$$

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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