SBML Model Report

Model name: “Ortega2006 - bistability from double phosphorylation in signal transduction”

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: Vijayalakshmi Chelliah[1] and Marta Cascante[2] at July 29th 2010 at 10:50 a. m. and last time modified at May 22nd 2015 at 1:15 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	3
events	0	constraints	0
reactions	4	function definitions	0
global parameters	9	unit definitions	0
rules	0	initial assignments	0

Model Notes

Ortega2006 - bistability from doublephosphorylation in signal transduction

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This model is described in the article:Bistability from double phosphorylation in signal transduction. Kinetic and structural requirements.Ortega F, Garcs JL, Mas F, Kholodenko BN, Cascante M.FEBS J. 2006 Sep; 273(17): 3915-3926

Abstract:

Previous studies have suggested that positive feedback loops and ultrasensitivity are prerequisites for bistability in covalent modification cascades. However, it was recently shown that bistability and hysteresis can also arise solely from multisite phosphorylation. Here we analytically demonstrate that double phosphorylation of a protein (or other covalent modification) generates bistability only if: (a) the two phosphorylation (or the two dephosphorylation) reactions are catalyzed by the same enzyme; (b) the kinetics operate at least partly in the zero-order region; and (c) the ratio of the catalytic constants of the phosphorylation and dephosphorylation steps in the first modification cycle is less than this ratio in the second cycle. We also show that multisite phosphorylation enlarges the region of kinetic parameter values in which bistability appears, but does not generate multistability. In addition, we conclude that a cascade of phosphorylation/dephosphorylation cycles generates multiple steady states in the absence of feedback or feedforward loops. Our results show that bistable behavior in covalent modification cascades relies not only on the structure and regulatory pattern of feedback/feedforward loops, but also on the kinetic characteristics of their component proteins.

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 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
`alpha`	alpha	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
`beta`	beta	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
`gamma`	gamma	`cell`	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains nine global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
r31	r31		1.00		☑
r24	r24		1.00		☑
Chi14	Chi14		1.10		☑
Ks1	Ks1		0.01		☑
Ks2	Ks2		0.01		☑
Ks3	Ks3		0.01		☑
Ks4	Ks4		0.01		☑
Vm1	Vm1		1.00		☑
p	p		1.00		☑

6 Reactions

This model contains four 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	v1	v1	alpha $\rightleftharpoons$ beta	
2	v2	v2	beta $\overset{\text{gamma}}{\rightleftharpoons}$ alpha	
3	v3	v3	beta $\overset{\text{alpha}}{\rightleftharpoons}$ gamma	
4	v4	v4	gamma $\longrightarrow$ beta	

6.1 Reaction v1

This is a reversible reaction of one reactant forming one product.

Name v1

Reaction equation

$$\text{alpha} \rightleftharpoons \text{beta} \tag{1}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
alpha	alpha	

Product

Table 7: Properties of each product.

Id	Name	SBO
beta	beta	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{\text{Vm1} \cdot \frac{[\text{alpha}]}{\text{Ks1}}}{1 + \frac{[\text{alpha}]}{\text{Ks1}} + \frac{[\text{beta}]}{\text{Ks3}}} \tag{2}$$

6.2 Reaction v2

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Name v2

Reaction equation

$$\text{beta} \overset{\text{gamma}}{\rightleftharpoons} \text{alpha} \tag{3}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
beta	beta	

Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
gamma	gamma	

Product

Table 10: Properties of each product.

Id	Name	SBO
alpha	alpha	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \frac{\text{r24} \cdot \frac{\text{Vm1}}{\text{Chi14}} \cdot \frac{[\text{beta}]}{\text{Ks2}}}{1 + \frac{[\text{gamma}]}{\text{Ks4}} + \frac{[\text{beta}]}{\text{Ks2}}} \tag{4}$$

6.3 Reaction v3

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Name v3

Reaction equation

$$\text{beta} \underset{}{\overset{\text{alpha}}{\rightleftharpoons}} \text{gamma} \tag{5}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
beta	beta	

Modifier

Table 12: Properties of each modifier.

Id	Name	SBO
alpha	alpha	

Product

Table 13: Properties of each product.

Id	Name	SBO
gamma	gamma	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \frac{\mathrm{r31} \cdot \mathrm{Vm1} \cdot \frac{[\mathrm{beta}]}{\mathrm{Ks3}}}{1 + \frac{[\mathrm{alpha}]}{\mathrm{Ks1}} + \frac{[\mathrm{beta}]}{\mathrm{Ks3}}} \tag{6}$$

6.4 Reaction v4

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

Name v4

Reaction equation

$$\mathrm{gamma} \longrightarrow \mathrm{beta} \tag{7}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
gamma	gamma	

Product

Table 15: Properties of each product.

Id	Name	SBO
beta	beta	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \frac{\frac{\mathrm{Vm1}}{\mathrm{Chi14}} \cdot \frac{[\mathrm{gamma}]}{\mathrm{Ks4}}}{1 + \frac{[\mathrm{gamma}]}{\mathrm{Ks4}} + \frac{[\mathrm{beta}]}{\mathrm{Ks2}}} \tag{8}$$

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.

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.

7.1 Species `alpha`

Name alpha

SBO:0000252 polypeptide chain

Initial concentration $0.462\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in `v1` and as a product in `v2` and as a modifier in `v3`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{alpha} = v_2 - v_1 \tag{9}$$

7.2 Species beta

Name beta

SBO:0000252 polypeptide chain

Initial concentration $0.2\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in v2, v3 and as a product in v1, v4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{beta} = v_1 + v_4 - v_2 - v_3 \tag{10}$$

7.3 Species gamma

Name gamma

SBO:0000252 polypeptide chain

Initial concentration $0.338\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in v4 and as a product in v3 and as a modifier in v2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{gamma} = v_3 - v_4 \tag{11}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000252 polypeptide chain: Naturally occurring macromolecule formed by the repetition of amino-acid residues linked by peptidic bonds. A polypeptide chain is synthesized by the ribosome. CHEBI:1654

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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