

SBML Model Report

Model name: “Ma2002_cAMP_oscillations”



May 6, 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 Chelliah¹ and Lan Ma² at August 18th 2009 at 3:45 p. m. and last time modified at April eighth 2016 at 4:03 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	1
species types	0	species	7
events	0	constraints	0
reactions	14	function definitions	0
global parameters	14	unit definitions	0
rules	0	initial assignments	0

Model Notes

This a model from the article:

Quantifying robustness of biochemical network models.

Ma L, Iglesias PA. *BMC Bioinformatics*.2002 Dec 13;3:38. [12482327](#),

Abstract:

BACKGROUND: Robustness of mathematical models of biochemical networks is important

¹EMBL-EBI, viji@ebi.ac.uk

²Department of Electrical and Computer Engineering, The Johns Hopkins University, Baltimore, MD USA, lma@jhu.edu

for validation purposes and can be used as a means of selecting between different competing models. Tools for quantifying parametric robustness are needed. **RESULTS:** Two techniques for describing quantitatively the robustness of an oscillatory model were presented and contrasted. Single-parameter bifurcation analysis was used to evaluate the stability robustness of the limit cycle oscillation as well as the frequency and amplitude of oscillations. A tool from control engineering—the structural singular value (SSV)—was used to quantify robust stability of the limit cycle. Using SSV analysis, we find very poor robustness when the model’s parameters are allowed to vary. **CONCLUSION:** The results show the usefulness of incorporating SSV analysis to single parameter sensitivity analysis to quantify robustness.

This model is originally proposed by Laub and Loomis (1998).[Laub MT, Loomis WF (1998). A molecular network that produces spontaneous oscillations in excitable cells of Dictyostelium. Mol Biol Cell. 9(12):3521-32. PubMed: [12482327](#).

The parameters used in this model (Ma and Iglesias, 2002), are different from that used in the original model (Laub and Loomis, 1998), because of the typographical errors in the original paper. The parameters used in the model presented by Ma and Iglesias, are obtained directly from the authors of original publication (Laub and Loomis, 1998). These parameters are also used in the website for the Laub-Loomis model, <http://www-biology.ucsd.edu/labs/loomis/network/laubloomis.html>. By using this model, Kim et al., 2006 [Kim J, Bates DG, Postlethwaite I, Ma L, Iglesias PA. (2006) Robustness analysis of biochemical network models. Syst Biol (Stevenage). 153(3):96-104. PubMed: [16984084](#)], validate and extend the analysis approach proposed by Ma and Iglesias (2002), by showing how hybrid optimisation can be used to compute worst-case parameter combinations in the model.

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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 m²

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	compartment		3	1	litre	<input checked="" type="checkbox"/>	

3.1 Compartment `compartment`

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

Name compartment

4 Species

This model contains seven 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 Condi- tion
ACA	ACA	compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
CAR1	CAR1	compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
PKA	PKA	compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
incAMP	incAMP	compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
ERK2	ERK2	compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
REGA	REGA	compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square
excAMP	excAMP	compartment	$\text{mol} \cdot \text{l}^{-1}$	\square	\square

5 Parameters

This model contains 14 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		2.0		<input checked="" type="checkbox"/>
k2	k2		0.9		<input checked="" type="checkbox"/>
k3	k3		2.5		<input checked="" type="checkbox"/>
k4	k4		1.5		<input checked="" type="checkbox"/>
k5	k5		0.6		<input checked="" type="checkbox"/>
k6	k6		0.8		<input checked="" type="checkbox"/>
k7	k7		1.0		<input checked="" type="checkbox"/>
k8	k8		1.3		<input checked="" type="checkbox"/>
k9	k9		0.3		<input checked="" type="checkbox"/>
k10	k10		0.8		<input checked="" type="checkbox"/>
k11	k11		0.7		<input checked="" type="checkbox"/>
k12	k12		4.9		<input checked="" type="checkbox"/>
k13	k13		23.0		<input checked="" type="checkbox"/>
k14	k14		4.5		<input checked="" type="checkbox"/>

6 Reactions

This model contains 14 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

Nº	Id	Name	Reaction Equation	SBO
1	v1	v1	$\emptyset \xrightarrow{\text{CAR1}} \text{ACA}$	
2	v2	v2	$\text{ACA} \xrightarrow{\text{PKA}} \emptyset$	
3	v3	v3	$\emptyset \xrightarrow{\text{incAMP}} \text{PKA}$	
4	v4	v4	$\text{PKA} \rightleftharpoons \emptyset$	
5	v5	v5	$\emptyset \xrightarrow{\text{CAR1}} \text{ERK2}$	
6	v6	v6	$\text{ERK2} \xrightarrow{\text{PKA}} \emptyset$	
7	v7	v7	$\emptyset \rightleftharpoons \text{REGA}$	
8	v8	v8	$\text{REGA} \xrightarrow{\text{ERK2}} \emptyset$	
9	v9	v9	$\emptyset \xrightarrow{\text{ACA}} \text{incAMP}$	
10	v10	v10	$\text{incAMP} \xrightarrow{\text{REGA}} \emptyset$	
11	v11	v11	$\emptyset \xrightarrow{\text{ACA}} \text{excAMP}$	
12	v12	v12	$\text{excAMP} \rightleftharpoons \emptyset$	
13	v13	v13	$\emptyset \xrightarrow{\text{excAMP}} \text{CAR1}$	
14	v14	v14	$\text{CAR1} \rightleftharpoons \emptyset$	

6.1 Reaction v1

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name v1

Reaction equation



Modifier

Table 6: Properties of each modifier.

Id	Name	SBO
CAR1	CAR1	

Product

Table 7: Properties of each product.

Id	Name	SBO
ACA	ACA	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = k_1 \cdot [\text{CAR1}] \quad (2)$$

6.2 Reaction v2

This is a reversible reaction of one reactant forming no product influenced by one modifier.

Name v2

Reaction equation



Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
ACA	ACA	

Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
PKA	PKA	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = k_2 \cdot [ACA] \cdot [PKA] \quad (4)$$

6.3 Reaction v3

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name v3

Reaction equation



Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
incAMP	incAMP	

Product

Table 11: Properties of each product.

Id	Name	SBO
PKA	PKA	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = k_3 \cdot [\text{incAMP}] \quad (6)$$

6.4 Reaction v4

This is a reversible reaction of one reactant forming no product.

Name v4

Reaction equation



Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
PKA	PKA	

Kinetic Law

Derived unit contains undeclared units

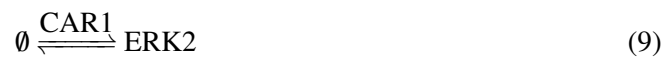
$$v_4 = k_4 \cdot [\text{PKA}] \quad (8)$$

6.5 Reaction v5

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name v5

Reaction equation



Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
CAR1	CAR1	

Product

Table 14: Properties of each product.

Id	Name	SBO
ERK2	ERK2	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = k_5 \cdot [\text{CAR1}] \quad (10)$$

6.6 Reaction v6

This is a reversible reaction of one reactant forming no product influenced by one modifier.

Name v6

Reaction equation



Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
ERK2	ERK2	

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
PKA	PKA	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = k_6 \cdot [\text{PKA}] \cdot [\text{ERK2}] \quad (12)$$

6.7 Reaction v7

This is a reversible reaction of no reactant forming one product.

Name v7

Reaction equation



Product

Table 17: Properties of each product.

Id	Name	SBO
REGA	REGA	

Kinetic Law

Derived unit not available

$$v_7 = k_7 \quad (14)$$

6.8 Reaction v8

This is a reversible reaction of one reactant forming no product influenced by one modifier.

Name v8

Reaction equation



Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
REGA	REGA	

Modifier

Table 19: Properties of each modifier.

Id	Name	SBO
ERK2	ERK2	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = k_8 \cdot [\text{ERK2}] \cdot [\text{REGA}] \quad (16)$$

6.9 Reaction v9

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name v9

Reaction equation



Modifier

Table 20: Properties of each modifier.

Id	Name	SBO
ACA	ACA	

Product

Table 21: Properties of each product.

Id	Name	SBO
incAMP	incAMP	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = k_9 \cdot [ACA] \quad (18)$$

6.10 Reaction v10

This is a reversible reaction of one reactant forming no product influenced by one modifier.

Name v10

Reaction equation



Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
incAMP	incAMP	

Modifier

Table 23: Properties of each modifier.

Id	Name	SBO
REGA	REGA	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = k_{10} \cdot [\text{REGA}] \cdot [\text{incAMP}] \quad (20)$$

6.11 Reaction v11

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name v11

Reaction equation



Modifier

Table 24: Properties of each modifier.

Id	Name	SBO
ACA	ACA	

Product

Table 25: Properties of each product.

Id	Name	SBO
excAMP	excAMP	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = k_{11} \cdot [\text{ACA}] \quad (22)$$

6.12 Reaction v12

This is a reversible reaction of one reactant forming no product.

Name v12

Reaction equation



Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
excAMP	excAMP	

Kinetic Law

Derived unit contains undeclared units

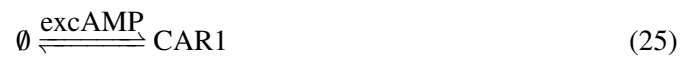
$$v_{12} = k_{12} \cdot [\text{excAMP}] \quad (24)$$

6.13 Reaction v13

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name v13

Reaction equation



Modifier

Table 27: Properties of each modifier.

Id	Name	SBO
excAMP	excAMP	

Product

Table 28: Properties of each product.

Id	Name	SBO
CAR1	CAR1	

Kinetic Law

Derived unit contains undeclared units

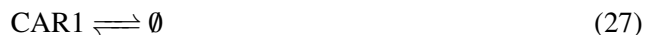
$$v_{13} = k_{13} \cdot [\text{excAMP}] \quad (26)$$

6.14 Reaction v14

This is a reversible reaction of one reactant forming no product.

Name v14

Reaction equation



Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
CAR1	CAR1	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = k_{14} \cdot [\text{CAR1}] \quad (28)$$

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 ACA

Name ACA

SBO:0000014 enzyme

Initial concentration 3.39 mol · l⁻¹

This species takes part in four reactions (as a reactant in [v2](#) and as a product in [v1](#) and as a modifier in [v9](#), [v11](#)).

$$\frac{d}{dt}\text{ACA} = v_1 - v_2 \quad (29)$$

7.2 Species CAR1

Name CAR1

SBO:0000244 receptor

Initial concentration $2.45 \text{ mol} \cdot \text{l}^{-1}$

This species takes part in four reactions (as a reactant in [v14](#) and as a product in [v13](#) and as a modifier in [v1](#), [v5](#)).

$$\frac{d}{dt}\text{CAR1} = v_{13} - v_{14} \quad (30)$$

7.3 Species PKA

Name PKA

SBO:0000014 enzyme

Initial concentration $1.6 \text{ mol} \cdot \text{l}^{-1}$

This species takes part in four reactions (as a reactant in [v4](#) and as a product in [v3](#) and as a modifier in [v2](#), [v6](#)).

$$\frac{d}{dt}\text{PKA} = v_3 - v_4 \quad (31)$$

7.4 Species incAMP

Name incAMP

SBO:0000247 simple chemical

Initial concentration $1.2 \text{ mol} \cdot \text{l}^{-1}$

This species takes part in three reactions (as a reactant in [v10](#) and as a product in [v9](#) and as a modifier in [v3](#)).

$$\frac{d}{dt}\text{incAMP} = v_9 - v_{10} \quad (32)$$

7.5 Species ERK2

Name ERK2

SBO:0000014 enzyme

Initial concentration $1.13 \text{ mol} \cdot \text{l}^{-1}$

This species takes part in three reactions (as a reactant in [v6](#) and as a product in [v5](#) and as a modifier in [v8](#)).

$$\frac{d}{dt}\text{ERK2} = v_5 - v_6 \quad (33)$$

7.6 Species REGA

Name REGA

SBO:0000014 enzyme

Initial concentration $0.9 \text{ mol} \cdot \text{l}^{-1}$

This species takes part in three reactions (as a reactant in [v8](#) and as a product in [v7](#) and as a modifier in [v10](#)).

$$\frac{d}{dt}\text{REGA} = v_7 - v_8 \quad (34)$$

7.7 Species excAMP

Name excAMP

SBO:0000247 simple chemical

Initial concentration $0.48 \text{ mol} \cdot \text{l}^{-1}$

This species takes part in three reactions (as a reactant in [v12](#) and as a product in [v11](#) and as a modifier in [v13](#)).

$$\frac{d}{dt}\text{excAMP} = v_{11} - v_{12} \quad (35)$$

A Glossary of Systems Biology Ontology Terms

SBO:0000014 enzyme: A protein that catalyzes a chemical reaction. The word comes from en “a” or “i”) and simo “leave” or “yeas”)

SBO:0000244 receptor: Participating entity that binds to a specific physical entity and initiates the response to that physical entity. The original concept of the receptor was introduced independently at the end of the 19th century by John Newport Langley (1852-1925) and Paul Ehrlich (1854-1915). Langley JN. On the reaction of cells and of nerve-endings to certain poisons, chiefly as regards the reaction of striated muscle to nicotine and to curari. J Physiol. 1905 Dec 30;33(4-5):374-413

SBO:0000247 simple chemical: Simple, non-repetitive chemical entity

SBML²TeX 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.

^aCenter for Bioinformatics Tübingen (ZBIT), Germany

^bCalifornia Institute of Technology, Beckman Institute BNMC, Pasadena, United States

^cEuropean Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom

^dEML Research gGmbH, Heidelberg, Germany