SBML Model Report

Model name: "Kim2007_CellularMemory-_SymmetricModel"

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by Harish Dharuri[1] at August 14th 2008 at 3:16 a.m. and last time modified at April seventh 2014 at 0:33 a.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	8
events	0	constraints	0
reactions	20	function definitions	0
global parameters	20	unit definitions	1
rules	2	initial assignments	0

Model Notes

This model is from the article:
Interlinked mutual inhibitory positive feedbacks induce robust cellular memory effects.
Kim TH, Jung SH, Cho KH FEBS Lett.2007 Oct; 581(25) 17892872,
Abstract:
Mutual inhibitory positive feedback (MIPF), or double-negative feedback, is a key regulatory

[1]California Institute of Technology, hdharuri@cds.caltech.edu

motif of cellular memory with the capability of maintaining switched states for transient stimuli. Such MIPFs are found in various biological systems where they are interlinked in many cases despite a single MIPF can still realize such a memory effect. An intriguing question then arises about the advantage of interlinking MIPFs instead of exploiting an isolated single MIPF to realize the memory effect. We have investigated the advantages of interlinked MIPF systems through mathematical modeling and computer simulations. Our results revealed that interlinking MIPFs expands the parameter range of achieving the memory effect, or the memory region, thereby making the system more robust to parameter perturbations. Moreover, the minimal duration and amplitude of an external stimulus required for off-to-on state transition are increased and, as a result, external noises can more effectively be filtered out. Hence, interlinked MIPF systems can realize more robust cellular memories with respect to both parameter perturbations and external noises. Our study suggests that interlinked MIPF systems might be an evolutionary consequence acquired for a more reliable memory effect by enhancing robustness against noisy cellular environments.

Note: The model reproduces the simulation result for the symmetric model as depicted in Fig 3H of the paper. Model successfully tested on MathSBML

2 Unit Definitions

This is an overview of five unit definitions of which four are predefined by SBML and not mentioned in the model.

2.1 Unit `substance`

Name dimensionless

Definition item

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 eight 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
R1		compartment	item	⊟	⊟
P1		compartment	item	⊟	⊟
P1_prime		compartment	item	⊟	⊟
R2		compartment	item	⊟	⊟
P2		compartment	item	⊟	⊟
P2_prime		compartment	item	⊟	⊟
P3_prime		compartment	item	⊟	⊟
P4_prime		compartment	item	⊟	⊟

5 Parameters

This model contains 20 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
i1			0.000		⊟
d_R1			0.235		☑
sP1R1			0.473		☑
d_P1			0.224		☑
sP1_prime_P1			0.287		☑
s1			0.400		☑
n			9.000		☑
s3			0.200		☑
d_P1_prime			0.370		☑
i2			1.000		⊟
d_R2			0.235		☑
sP2R2			0.473		☑
d_P2			0.224		☑
sP2_prime_P2			0.287		☑
s2			0.300		☑
d_P2_prime			0.370		☑
sP3_prime-_P2_prime			0.500		☑
d_P3_prime			0.370		☑
d_P4_prime			0.370		☑
sP4_prime-_P1_prime			0.500		☑

6 Rules

This is an overview of two rules.

6.1 Rule i2

Rule i2 is an assignment rule for parameter i2:

$$i2 = \begin{cases} 1 & \text{if } (t \geq 175) \wedge (t \leq 225) \\ 0 & \text{otherwise} \end{cases} \tag{1}$$

6.2 Rule i1

Rule i1 is an assignment rule for parameter i1:

$$
i1 = \begin{cases} 1 & \text{if } (t \geq 50) \wedge (t \leq 100) \\ 0 & \text{otherwise} \end{cases} \tag{2}
$$

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7 Reactions

This model contains 20 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	React1		$\emptyset \longrightarrow R1$	
2	React2		$R1 \longrightarrow \emptyset$	
3	React3		$\emptyset \xrightarrow{R1} P1$	
4	React4		$P1 \longrightarrow \emptyset$	
5	React5		$\emptyset \xrightarrow{P1} P1\_prime$	
6	React6		$\emptyset \xrightarrow{P2\_prime} P1\_prime$	
7	React7		$\emptyset \xrightarrow{P3\_prime} P1\_prime$	
8	React8		$P1\_prime \longrightarrow \emptyset$	
9	React9		$\emptyset \longrightarrow R2$	
10	React10		$R2 \longrightarrow \emptyset$	
11	React11		$\emptyset \xrightarrow{R2} P2$	
12	React12		$P2 \longrightarrow \emptyset$	
13	React13		$\emptyset \xrightarrow{P2} P2\_prime$	
14	React14		$\emptyset \xrightarrow{P1\_prime} P2\_prime$	
15	React15		$P2\_prime \longrightarrow \emptyset$	
16	React16		$\emptyset \xrightarrow{P2\_prime} P3\_prime$	
17	React17		$P3\_prime \longrightarrow \emptyset$	
18	React18		$\emptyset \xrightleftharpoons{P4\_prime} P2\_prime$	

№	Id	Name	Reaction Equation	SBO
19	React19		$\emptyset \xrightleftharpoons{\text{P1\_prime}} \text{P4\_prime}$	
20	React20		$\text{P4\_prime} \rightleftharpoons \emptyset$	

7.1 Reaction `React1`

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

Reaction equation

$$\emptyset \longrightarrow R1 \tag{3}$$

Product

Table 6: Properties of each product.

Id	Name	SBO
R1		

Kinetic Law

Derived unit not available

$$v_1 = \text{i1} \tag{4}$$

7.2 Reaction `React2`

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

Reaction equation

$$R1 \longrightarrow \emptyset \tag{5}$$

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
R1		

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{d\_R1} \cdot R1 \tag{6}$$

7.3 Reaction `React3`

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

Reaction equation

$$\emptyset \xrightarrow{\text{R1}} \text{P1} \tag{7}$$

Modifier

Table 8: Properties of each modifier.

Id	Name	SBO
R1		

Product

Table 9: Properties of each product.

Id	Name	SBO
P1		

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{sP1R1} \cdot \text{R1} \tag{8}$$

7.4 Reaction `React4`

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

Reaction equation

$$\text{P1} \longrightarrow \emptyset \tag{9}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
P1		

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{d\_P1} \cdot \text{P1} \tag{10}$$

7.5 Reaction `React5`

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

Reaction equation

$$\emptyset \xrightarrow{\text{P1}} \text{P1\_prime} \tag{11}$$

Modifier

Table 11: Properties of each modifier.

Id	Name	SBO
P1		

Product

Table 12: Properties of each product.

Id	Name	SBO
P1_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{sP1\_prime\_P1} \cdot \text{P1} \tag{12}$$

7.6 Reaction `React6`

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

Reaction equation

$$\emptyset \xrightarrow{\text{P2\_prime}} \text{P1\_prime} \tag{13}$$

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
P2_prime		

Product

Table 14: Properties of each product.

Id	Name	SBO
P1_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \frac{s1}{1 + \text{P2\_prime}^n} \qquad (14)$$

7.7 Reaction `React7`

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

Reaction equation

$$\emptyset \xrightarrow{\text{P3\_prime}} \text{P1\_prime} \qquad (15)$$

Modifier

Table 15: Properties of each modifier.

Id	Name	SBO
P3_prime		

Product

Table 16: Properties of each product.

Id	Name	SBO
P1_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \frac{s3}{1 + \text{P3\_prime}^n} \tag{16}$$

7.8 Reaction `React8`

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

Reaction equation

$$\text{P1\_prime} \longrightarrow \emptyset \tag{17}$$

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
P1_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{d\_P1\_prime} \cdot \text{P1\_prime} \tag{18}$$

7.9 Reaction `React9`

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

Reaction equation

$$\emptyset \longrightarrow \text{R2} \tag{19}$$

Product

Table 18: Properties of each product.

Id	Name	SBO
R2		

Kinetic Law

Derived unit not available

$$v_9 = i2 \tag{20}$$

7.10 Reaction `React10`

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

Reaction equation

$$R2 \longrightarrow \emptyset \tag{21}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
R2		

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = d\_R2 \cdot R2 \tag{22}$$

7.11 Reaction `React11`

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

Reaction equation

$$\emptyset \xrightarrow{R2} P2 \tag{23}$$

Modifier

Table 20: Properties of each modifier.

Id	Name	SBO
R2		

Product

Table 21: Properties of each product.

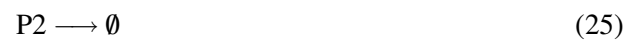| Id	Name	SBO
P2		

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{sP2R2} \cdot \text{R2} \tag{24}$$

7.12 Reaction `React12`

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

Reaction equation

$$\text{P2} \longrightarrow \emptyset \tag{25}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
P2		

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{d\_P2} \cdot \text{P2} \tag{26}$$

7.13 Reaction `React13`

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

Reaction equation

$$\emptyset \xrightarrow{\text{P2}} \text{P2\_prime} \tag{27}$$

Modifier

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Table 23: Properties of each modifier.

Id	Name	SBO
P2		

Product

Table 24: Properties of each product.

Id	Name	SBO
P2_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{sP2\_prime\_P2} \cdot \text{P2} \qquad (28)$$

7.14 Reaction `React14`

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

Reaction equation

$$\emptyset \xrightarrow{\text{P1\_prime}} \text{P2\_prime} \qquad (29)$$

Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
P1_prime		

Product

Table 26: Properties of each product.

Id	Name	SBO
P2_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \frac{\text{s2}}{1 + \text{P1\_prime}^{\text{n}}} \tag{30}$$

7.15 Reaction `React15`

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

Reaction equation

$$\text{P2\_prime} \longrightarrow \emptyset \tag{31}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
P2_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \text{d\_P2\_prime} \cdot \text{P2\_prime} \tag{32}$$

7.16 Reaction `React16`

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

Reaction equation

$$\emptyset \xrightarrow{\text{P2\_prime}} \text{P3\_prime} \tag{33}$$

Modifier

Table 28: Properties of each modifier.

Id	Name	SBO
P2_prime		

Product

Table 29: Properties of each product.

Id	Name	SBO
P3_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \text{sP3\_prime\_P2\_prime} \cdot \frac{\text{P2\_prime}^n}{1 + \text{P2\_prime}^n} \tag{34}$$

7.17 Reaction `React17`

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

Reaction equation

$$\text{P3\_prime} \longrightarrow \emptyset \tag{35}$$

Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
P3_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \text{d\_P3\_prime} \cdot \text{P3\_prime} \tag{36}$$

7.18 Reaction `React18`

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

Reaction equation
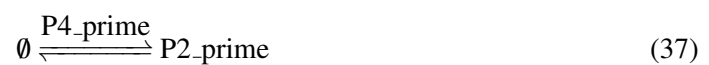
$$\emptyset \xrightleftharpoons{\text{P4\_prime}} \text{P2\_prime} \tag{37}$$

Modifier

Table 31: Properties of each modifier.

Id	Name	SBO
P4_prime		

Product

Table 32: Properties of each product.

Id	Name	SBO
P2_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_{18} = \frac{s3}{1 + P4\_prime^n} \tag{38}$$

7.19 Reaction `React19`

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

Reaction equation

$$\varnothing \xrightleftharpoons{P1\_prime} P4\_prime \tag{39}$$

Modifier

Table 33: Properties of each modifier.

Id	Name	SBO
P1_prime		

Product

Produced by SBML2LATEX

Table 34: Properties of each product.

Id	Name	SBO
P4_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_{19} = \text{sP4\_prime\_P1\_prime} \cdot \frac{\text{P1\_prime}^n}{1 + \text{P1\_prime}^n} \tag{40}$$

7.20 Reaction `React20`

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

Reaction equation
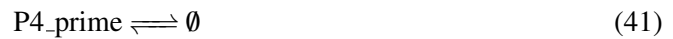
$$\text{P4\_prime} \rightleftharpoons \emptyset \tag{41}$$

Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
P4_prime		

Kinetic Law

Derived unit contains undeclared units

$$v_{20} = \text{d\_P4\_prime} \cdot \text{P4\_prime} \tag{42}$$

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 R1

Initial amount 0.01 item

This species takes part in three reactions (as a reactant in React2 and as a product in React1 and as a modifier in React3).

$$\frac{d}{dt}R1 = v_1 - v_2 \tag{43}$$

8.2 Species P1

Initial amount 0.1 item

This species takes part in three reactions (as a reactant in React4 and as a product in React3 and as a modifier in React5).

$$\frac{d}{dt}P1 = v_3 - v_4 \tag{44}$$

8.3 Species P1_prime

Initial amount 0.1 item

This species takes part in six reactions (as a reactant in React8 and as a product in React5, React6, React7 and as a modifier in React14, React19).

$$\frac{d}{dt}P1\_prime = v_5 + v_6 + v_7 - v_8 \tag{45}$$

8.4 Species R2

Initial amount 0.1 item

This species takes part in three reactions (as a reactant in React10 and as a product in React9 and as a modifier in React11).

$$\frac{d}{dt}R2 = v_9 - v_{10} \tag{46}$$

8.5 Species P2

Initial amount 1 item

This species takes part in three reactions (as a reactant in React12 and as a product in React11 and as a modifier in React13).

$$\frac{d}{dt}P2 = v_{11} - v_{12} \tag{47}$$

8.6 Species `P2_prime`

Initial amount 1 item

This species takes part in six reactions (as a reactant in `React15` and as a product in `React13`, `React14`, `React18` and as a modifier in `React6`, `React16`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{P2\_prime} = v_{13} + v_{14} + v_{18} - v_{15} \tag{48}$$

8.7 Species `P3_prime`

Initial amount 0.1 item

This species takes part in three reactions (as a reactant in `React17` and as a product in `React16` and as a modifier in `React7`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{P3\_prime} = v_{16} - v_{17} \tag{49}$$

8.8 Species `P4_prime`

Initial amount 0.1 item

This species takes part in three reactions (as a reactant in `React20` and as a product in `React19` and as a modifier in `React18`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{P4\_prime} = v_{19} - v_{20} \tag{50}$$