SBML Model Report

Model name: "Palini2011_Minimal_2_Feedback_Model"

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1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Lukas Endler[1] and Santhosh Palani[2] at March 31st 2011 at 4:12 a. m. and last time modified at November 29th 2011 at 12:07 a. 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	6
events	0	constraints	0
reactions	10	function definitions	0
global parameters	15	unit definitions	0
rules	0	initial assignments	0

Model Notes

This is the model of the minmal 2 feedback switch described in the article:
Synthetic conversion of a graded receptor signal into a tunable, reversible switch.
Santhosh Palani and Casim A. Sarkar, 2011, Molecular Systems Biology 7:480; doi: 10.1038/msb.2011.13

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The ability to engineer an all-or-none cellular response to a given signaling ligand is important in applications ranging from biosensing to tissue engineering. However, synthetic gene network switches have been limited in their applicability and tunability due to their reliance on specific components to function. Here, we present a strategy for reversible switch design that instead relies only on a robust, easily constructed network topology with two positive feedback loops and we apply the method to create highly ultrasensitive (nH420), bistable cellular responses to a synthetic ligand/receptor complex. Independent modulation of the two feedback strengths enables rational tuning and some decoupling of steady-state (ultrasensitivity, signal amplitude, switching threshold, and bistability) and kinetic (rates of system activation and deactivation) response properties.Our integrated computational and synthetic biology approach elucidates design rules for building cellular switches with desired properties, which may be of utility in engineering signal-transduction pathways.

This model is parametrised for a transcription factor and receptor feedback strength of 3, TFs = 3 and Rs = 3. To reproduce figure 1 E, the parameters TFs and Rs have to be varied accordingly.

Nomenclature for the model:
L : Ligand
R : Receptor
C : Ligand-Receptor Complex
I : Inactive Transcription Factor
X : C bound to I
A : Active Transcription Factor

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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
`cell`		0000290	3	1	litre	☑	

3.1 Compartment `cell`

This is a three dimensional compartment with a constant size given in litre.

SBO:0000290 physical compartment

4 Species

This model contains six species. The boundary condition of one of these species is set to `true` so that this species' amount cannot be changed by any reaction. 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
L		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
R		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
C		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
I		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
X		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
A		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐

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5 Parameters

This model contains 15 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
BR		0000485	0.005		☑
Rs		0000186	3.000		☑
KD		0000027	200.000		☑
kdegR		0000356	0.005		☑
kon		0000339	0.001		☑
koff		0000338	0.050		☑
kdegC		0000356	0.010		☑
k1		0000339	1.000		☑
k2		0000338	5.000		☑
k3		0000035	45.000		☑
kdegX		0000356	0.005		☑
kdegA		0000356	0.005		☑
BI		0000485	0.005		☑
TFs		0000186	3.000		☑
kdegI		0000356	0.005		☑

6 Reactions

This model contains ten 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	R_expression		$\emptyset \xrightarrow{A} R$	0000205
2	R_degradation		$R \longrightarrow \emptyset$	0000179
3	R_L_binding		$R + L \rightleftharpoons C$	0000177
4	C_degradation		$C \longrightarrow \emptyset$	0000179
5	C_I_binding		$C + I \rightleftharpoons X$	0000177
6	I_activation		$X \longrightarrow C + A$	0000216
7	X_degradation		$X \longrightarrow \emptyset$	0000179
8	A_degradation		$A \longrightarrow \emptyset$	0000179
9	I_expression		$\emptyset \xrightarrow{A} I$	0000205
10	I_degradation		$I \longrightarrow \emptyset$	0000179

Produced by SBML2LaTeX

6.1 Reaction R_expression

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

SBO:0000205 composite biochemical process

Reaction equation

$$\emptyset \xrightarrow{\mathrm{A}} \mathrm{R} \tag{1}$$

Modifier

Table 6: Properties of each modifier.

Id	Name	SBO
A		0000459

Product

Table 7: Properties of each product.

Id	Name	SBO
R		

Kinetic Law

SBO:0000001 rate law

Derived unit contains undeclared units

$$v_1 = \mathrm{vol}\,(\mathrm{cell}) \cdot \left(\mathrm{BR} + \frac{\mathrm{Rs} \cdot [\mathrm{A}]}{\mathrm{KD} + [\mathrm{A}]} \right) \tag{2}$$

6.2 Reaction R_degradation

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

SBO:0000179 degradation

Reaction equation

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

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
R		

Kinetic Law

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{kdegR} \cdot [\mathrm{R}] \tag{4}$$

6.3 Reaction R_L_binding

This is a reversible reaction of two reactants forming one product.

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{R} + \mathrm{L} \rightleftharpoons \mathrm{C} \tag{5}$$

Reactants

Table 9: Properties of each reactant.

Id	Name	SBO
R		
L		

Product

Table 10: Properties of each product.

Id	Name	SBO
C		

Kinetic Law

SBO:0000101 mass action rate law for second order forward, first order reverse, reversible reactions, two reactants, continuous scheme

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\,(\mathrm{cell}) \cdot (\mathrm{kon} \cdot [\mathrm{L}] \cdot [\mathrm{R}] - \mathrm{koff} \cdot [\mathrm{C}]) \tag{6}$$

6.4 Reaction C_degradation

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

SBO:0000179 degradation

Reaction equation

$$\mathrm{C} \longrightarrow \emptyset \tag{7}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
C		

Kinetic Law

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{kdegC} \cdot [\mathrm{C}] \tag{8}$$

6.5 Reaction C_I_binding

This is a reversible reaction of two reactants forming one product.

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{C} + \mathrm{I} \rightleftharpoons \mathrm{X} \tag{9}$$

Reactants

Table 12: Properties of each reactant.

Id	Name	SBO
C		
I		

Product

Table 13: Properties of each product.

Id	Name	SBO
X		

Kinetic Law

SBO:0000101 mass action rate law for second order forward, first order reverse, reversible reactions, two reactants, continuous scheme

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\,(\mathrm{cell}) \cdot (\mathrm{k1} \cdot [\mathrm{C}] \cdot [\mathrm{I}] - \mathrm{k2} \cdot [\mathrm{X}]) \tag{10}$$

6.6 Reaction I_activation

This is an irreversible reaction of one reactant forming two products.

SBO:0000216 phosphorylation

Reaction equation

$$\mathrm{X} \longrightarrow \mathrm{C} + \mathrm{A} \tag{11}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
X		

Products

Table 15: Properties of each product.

Id	Name	SBO
C		
A		

Kinetic Law

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{k3} \cdot [\mathrm{X}] \tag{12}$$

6.7 Reaction X_degradation

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

SBO:0000179 degradation

Reaction equation

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

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
X		

Kinetic Law

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{kdegX} \cdot [\mathrm{X}] \tag{14}$$

6.8 Reaction A_degradation

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

SBO:0000179 degradation

Reaction equation

$$\mathrm{A} \longrightarrow \emptyset \tag{15}$$

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
A		

Kinetic Law

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{kdegA} \cdot [\mathrm{A}] \tag{16}$$

6.9 Reaction I_expression

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

SBO:0000205 composite biochemical process

Reaction equation

$$\emptyset \xrightarrow{\mathrm{A}} \mathrm{I} \tag{17}$$

Modifier

Table 18: Properties of each modifier.

Id	Name	SBO
A		0000459

Product

Table 19: Properties of each product.

Id	Name	SBO
I		

Kinetic Law

SBO:0000001 rate law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\,(\mathrm{cell}) \cdot \left(\mathrm{BI} + \frac{\mathrm{TFs} \cdot [\mathrm{A}]}{\mathrm{KD} + [\mathrm{A}]} \right) \tag{18}$$

6.10 Reaction `I_degradation`

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

SBO:0000179 degradation

Reaction equation

$$\mathrm{I} \longrightarrow \emptyset \tag{19}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
I		

Kinetic Law

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{kdegI} \cdot [\mathrm{I}] \tag{20}$$

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 L

SBO:0000247 simple chemical

Initial concentration $0.1\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in one reaction (as a reactant in R_L_binding), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{L} = 0 \tag{21}$$

7.2 Species R

SBO:0000252 polypeptide chain

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

This species takes part in three reactions (as a reactant in R_degradation, R_L_binding and as a product in R_expression).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{R} = v_1 - v_2 - v_3 \tag{22}$$

7.3 Species C

SBO:0000297 protein complex

Initial concentration $0\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in C_degradation, C_I_binding and as a product in R_L_binding, I_activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{C} = v_3 + v_6 - v_4 - v_5 \tag{23}$$

7.4 Species I

SBO:0000252 polypeptide chain

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

This species takes part in three reactions (as a reactant in C_I_binding, I_degradation and as a product in I_expression).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{I} = v_9 - v_5 - v_{10} \tag{24}$$

7.5 Species X

SBO:0000297 protein complex

Initial concentration $0\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in I_activation, X_degradation and as a product in C_I_binding).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{X} = v_5 - v_6 - v_7 \tag{25}$$

7.6 Species A

SBO:0000252 polypeptide chain

Initial concentration $0\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in A_degradation and as a product in I_activation and as a modifier in R_expression, I_expression).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{A} = v_6 - v_8 \tag{26}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000001 rate law: mathematical description that relates quantities of reactants to the reaction velocity

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:0000035 forward unimolecular rate constant, continuous case: 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. It is to be used in a reaction modelled using a continuous framework

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme: Reaction scheme where the products are created from the reactants and the change of a product quantity is proportional to the product of reactant activities. The reaction scheme does not include any reverse process that creates the reactants from the products. The change of a product quantity is proportional to the quantity of one reactant. It is to be used in a reaction modelled using a continuous framework.

SBO:0000101 mass action rate law for second order forward, first order reverse, reversible reactions, two reactants, continuous scheme: Reaction scheme where the products are created from the reactants and the change of a product quantity is proportional to the product of reactant activities. The reaction scheme does include a reverse process that creates the reactants from the products. The rate of the forward process is proportional to the product of two reactant quantities. The rate of the reverse process is proportional to the quantity of one product. It is to be used in a reaction modelled using a continuous framework.

SBO:0000177 non-covalent binding: Interaction between several biochemical entities that results in the formation of a non-covalent comple

SBO:0000179 degradation: Complete disappearance of a physical entity

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:0000205 composite biochemical process: Process that involves the participation of chemical or biological entities and is composed of several elementary steps or reactions.

SBO:0000216 phosphorylation: Addition of a phosphate group (-H2PO4) to a chemical entity

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

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

SBO:0000290 physical compartment: Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions

SBO:0000297 protein complex: Macromolecular complex containing one or more polypeptide chains possibly associated with simple chemicals. CHEBI:3608

SBO:0000338 dissociation rate constant: Rate with which a complex dissociates into its components

SBO:0000339 bimolecular association rate constant: Rate with which two components associate into a complex

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:0000459 stimulator: Substance that accelerates the velocity of a chemical reaction without itself being consumed or transformed.

SBO:0000485 basal rate constant: The minimal velocity observed under defined conditions, which may or may not include the presence of an effector. For example in an inhibitory system, this would be the residual velocity observed under full inhibition. In non-essential activation, this would be the velocity in the absence of any activator

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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