SBML Model Report

Model name: "Yildirim2003_Lac_Operon"

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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 three authors: Harish Dharuri[1], Adam Halasz[2] and Vijayalakshmi Chelliah[3] at June 21st 2006 at 2:47 p. m. and last time modified at February twelveth 2014 at 4:36 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	9
events	0	constraints	0
reactions	16	function definitions	0
global parameters	23	unit definitions	2
rules	0	initial assignments	0

Model Notes

This a model from the article:
Feedback regulation in the lactose operon: a mathematical modeling study and comparison with experimental data.
Yildirim N, Mackey MC Biophys. J. 2003 12719218 ,
Abstract:

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A mathematical model for the regulation of induction in the lac operon in Escherichia coli is presented. This model takes into account the dynamics of the permease facilitating the internalization of external lactose; internal lactose; beta-galactosidase, which is involved in the conversion of lactose to allolactose, glucose and galactose; the allolactose interactions with the lac repressor; and mRNA. The final model consists of five nonlinear differential delay equations with delays due to the transcription and translation process. We have paid particular attention to the estimation of the parameters in the model. We have tested our model against two sets of beta-galactosidase activity versus time data, as well as a set of data on beta-galactosidase activity during periodic phosphate feeding. In all three cases we find excellent agreement between the data and the model predictions. Analytical and numerical studies also indicate that for physiologically realistic values of the external lactose and the bacterial growth rate, a regime exists where there may be bistable steady-state behavior, and that this corresponds to a cusp bifurcation in the model dynamics.

The model reproduces the time profile of beta-galactosidase activity as shown in Fig 3 of the paper. The delay functions for transcription (M) and translation (B and P) have been implemented by introducing intermediates (I1, I2 and I3) in the reaction scheme which then give their respective products (I1-> M, I2 ->B and I3 ->P) after an appropriate length of time. The steady state values, attained upon simulation of model equations, for Allolactose (A), mRNA (M), beta-galactosidase (B), Lactose (L), and Permease (P) match with those predicted by the paper. The model was successfully tested on Jarnac, MathSBML and COPASI

2 Unit Definitions

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

2.1 Unit `time`

Name minute

Definition 60 s

2.2 Unit `substance`

Name millimoles

Definition mmol

2.3 Unit `volume`

Notes Litre is the predefined SBML unit for `volume`.

Definition l

2.4 Unit `area`

Notes Square metre is the predefined SBML unit for `area` since SBML Level 2 Version 1.

Definition m^2

2.5 Unit `length`

Notes Metre is the predefined SBML unit for `length` since SBML Level 2 Version 1.

Definition m

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`cell`			3	1	litre	☑	

3.1 Compartment `cell`

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

4 Species

This model contains nine 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
M	mRNA	cell	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
B	Betagalactosidase	cell	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
A	allolactose	cell	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
L	lactose_internal	cell	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
P	permease	cell	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
I1	PartialmRNA	cell	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
I2	PartialBetagalactosidase	cell	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
I3	PartialPermease	cell	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
L_e	External_Lactose	cell	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑	☑

5 Parameters

This model contains 23 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
mu			0.023		☑
gamma_M			0.411		☑
gamma_B			$8.33 \cdot 10^{-4}$		☑
gamma_A			0.520		☑
gamma_0			$7.25 \cdot 10^{-7}$		☑
K			7200.000		☑
alpha_M			$9.97 \cdot 10^{-4}$		☑
tau_B			2.000		☑
alpha_A			17600.000		☑
K_L1			1.810		☑
alpha_B			0.017		☑
K_A			1.950		☑
beta_A			21500.000		☑
tau_M			0.100		☑
K_L			0.970		☑
gamma_L			0.000		☑
gamma_P			0.650		☑
alpha_L			2880.000		☑
alpha_P			10.000		☑
tau_P			0.830		☑
beta_L1			2650.000		☑
K_Le			0.260		☑
K_1			25200.000		☑

6 Reactions

This model contains 16 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_m1	Basal_mRNA_Synthesis	$\emptyset \longrightarrow M$	
2	r_m2	mRNA_Degradation	$M \longrightarrow \emptyset$	
3	r_m3_i1	allolactose_controlled_mRNA_synthesis	$I1 \longrightarrow M$	
4	r_i1	allolactose_controlled_partial_mRNA-_synthesis	$\emptyset \xrightarrow{A} I1$	
5	r_b1	Beta_galactosidase_Degradation	$B \longrightarrow \emptyset$	
6	r_b2_i2	Beta_galactosidase_synthesis	$I2 \longrightarrow B$	
7	r_i2	Partial_Beta_galactosidase_synthesis	$\emptyset \xrightarrow{M} I2$	
8	r_a1	Basal_Allolactose_Degradation	$A \longrightarrow \emptyset$	
9	r_a2	Betagalactosidase_mediated_Allolactose-_Degradation	$A \xrightarrow{B} \emptyset$	
10	r_a3_l1	Beta_galactosidase_reaction	$L \xrightarrow{B} A$	
11	r_l2	lactose_degradation	$L \longrightarrow \emptyset$	
12	r_l3	Lactose_transport_out	$L \xrightarrow{P} \emptyset$	
13	r_l4	Lactose_transport_in	$\emptyset \xrightarrow{P,\ L\_e} L$	
14	r_p1	permease_degradation	$P \longrightarrow \emptyset$	
15	r_p2_i3	permease_synthesis	$I3 \longrightarrow P$	
16	r_i3	partial_permease_synthesis	$\emptyset \xrightarrow{M} I3$	

6.1 Reaction r_m1

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

Name Basal_mRNA_Synthesis

Reaction equation

$$\emptyset \longrightarrow \mathrm{M} \tag{1}$$

Product

Table 6: Properties of each product.

Id	Name	SBO
M	mRNA	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{gamma\_0} \tag{2}$$

6.2 Reaction r_m2

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

Name mRNA_Degradation

Reaction equation

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

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
M	mRNA	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{M}] \cdot (\mathrm{gamma\_M} + \mathrm{mu}) \tag{4}$$

6.3 Reaction r_m3_i1

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

Name allolactose_controlled_mRNA_synthesis

Reaction equation

$$\mathrm{I1} \longrightarrow \mathrm{M} \tag{5}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
I1	PartialmRNA	

Product

Table 9: Properties of each product.

Id	Name	SBO
M	mRNA	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \frac{\mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{I1}]}{\mathrm{tau\_M}} \tag{6}$$

6.4 Reaction r_i1

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

Name allolactose_controlled_partial_mRNA_synthesis

Reaction equation

$$\emptyset \xrightarrow{\mathrm{A}} \mathrm{I1} \tag{7}$$

Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
A	allolactose	

Product

Table 11: Properties of each product.

Id	Name	SBO
I1	PartialmRNA	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{alpha\_M} \cdot \frac{\mathrm{K\_1} \cdot \exp\left(\mathrm{mu} \cdot \mathrm{tau\_M} \cdot -2\right) \cdot [\mathrm{A}]^2 + 1}{\mathrm{K} + \mathrm{K\_1} \cdot \exp\left(-2 \cdot \mathrm{mu} \cdot \mathrm{tau\_M}\right) \cdot [\mathrm{A}]^2} \tag{8}$$

6.5 Reaction r_b1

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

Name Beta_galactosidase_Degradation

Reaction equation

$$\mathrm{B} \longrightarrow \emptyset \tag{9}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
B	Betagalactosidase	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{B}] \cdot (\mathrm{gamma\_B} + \mathrm{mu}) \tag{10}$$

6.6 Reaction r_b2_i2

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

Name Beta_galactosidase_synthesis

Reaction equation

$$\mathrm{I2} \longrightarrow \mathrm{B} \tag{11}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
I2	PartialBetagalactosidase	

Product

Table 14: Properties of each product.

Id	Name	SBO
B	Betagalactosidase	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \frac{\mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{I2}]}{\mathrm{tau\_B}} \tag{12}$$

6.7 Reaction r_i2

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

Name Partial_Beta_galactosidase_synthesis

Reaction equation

$$\emptyset \xrightarrow{\mathrm{M}} \mathrm{I2} \tag{13}$$

Modifier

Table 15: Properties of each modifier.

Id	Name	SBO
M	mRNA	

Product

Table 16: Properties of each product.

Id	Name	SBO
I2	PartialBetagalactosidase	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{alpha\_B} \cdot [\mathrm{M}] \cdot \exp\left((\mathrm{mu} \cdot \mathrm{tau\_B})\right) \tag{14}$$

6.8 Reaction r_a1

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

Name Basal_Allolactose_Degradation

Reaction equation

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

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
A	allolactose	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{A}] \cdot (\mathrm{gamma\_A} + \mathrm{mu}) \tag{16}$$

6.9 Reaction r_a2

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

Name Betagalactosidase_mediated_Allolactose_Degradation

Reaction equation

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

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
A	allolactose	

Modifier

Table 19: Properties of each modifier.

Id	Name	SBO
B	Betagalactosidase	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{beta\_A} \cdot [\mathrm{B}] \cdot \frac{[\mathrm{A}]}{\mathrm{K\_A} + [\mathrm{A}]} \tag{18}$$

6.10 Reaction r_a3_l1

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name Beta_galactosidase_reaction

Reaction equation

$$\mathrm{L} \xrightarrow{\mathrm{B}} \mathrm{A} \tag{19}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
L	lactose_internal	

Modifier

Table 21: Properties of each modifier.

Id	Name	SBO
B	Betagalactosidase	

Product

Table 22: Properties of each product.

Id	Name	SBO
A	allolactose	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{alpha\_A} \cdot [\mathrm{B}] \cdot \frac{[\mathrm{L}]}{\mathrm{K\_L} + [\mathrm{L}]} \tag{20}$$

6.11 Reaction r_l2

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

Name lactose_degradation

Reaction equation

$$\mathrm{L} \longrightarrow \emptyset \tag{21}$$

Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
L	lactose_internal	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{L}] \cdot (\mathrm{gamma\_L} + \mathrm{mu}) \tag{22}$$

6.12 Reaction r_l3

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

Name Lactose_transport_out

Reaction equation

$$\mathrm{L} \xrightarrow{\mathrm{P}} \emptyset \tag{23}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
L	lactose_internal	

Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
P	permease	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{beta\_L1} \cdot [\mathrm{P}] \cdot \frac{[\mathrm{L}]}{\mathrm{K\_L1} + [\mathrm{L}]} \tag{24}$$

6.13 Reaction r_l4

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

Name Lactose_transport_in

Reaction equation

$$\emptyset \xrightarrow{\text{P, L\_e}} \text{L} \tag{25}$$

Modifiers

Table 26: Properties of each modifier.

Id	Name	SBO
P	permease	
L_e	External_Lactose	

Product

Table 27: Properties of each product.

Id	Name	SBO
L	lactose_internal	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{vol}\,(\text{cell}) \cdot \text{alpha\_L} \cdot [\text{P}] \cdot \frac{[\text{L\_e}]}{\text{K\_Le} + [\text{L\_e}]} \tag{26}$$

6.14 Reaction r_p1

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

Name permease_degradation

Reaction equation

$$\text{P} \longrightarrow \emptyset \tag{27}$$

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
P	permease	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{P}] \cdot (\mathrm{gamma\_P} + \mathrm{mu}) \tag{28}$$

6.15 Reaction r_p2_i3

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

Name permease_synthesis

Reaction equation

$$\mathrm{I3} \longrightarrow \mathrm{P} \tag{29}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
I3	PartialPermease	

Product

Table 30: Properties of each product.

Id	Name	SBO
P	permease	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \frac{\mathrm{vol}\,(\mathrm{cell}) \cdot [\mathrm{I3}]}{\mathrm{tau\_B} + \mathrm{tau\_P}} \tag{30}$$

6.16 Reaction r_i3

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

Name partial_permease_synthesis

Reaction equation

$$\emptyset \xrightarrow{\mathrm{M}} \mathrm{I3} \tag{31}$$

Modifier

Table 31: Properties of each modifier.

Id	Name	SBO
M	mRNA	

Product

Table 32: Properties of each product.

Id	Name	SBO
I3	PartialPermease	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{vol}(\mathrm{cell}) \cdot \mathrm{alpha\_P} \cdot [\mathrm{M}] \cdot \exp(-1 \cdot \mathrm{mu} \cdot (\mathrm{tau\_B} + \mathrm{tau\_P})) \tag{32}$$

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 M

Name mRNA

Initial concentration $6.26 \cdot 10^{-4}$ mmol $\cdot$ l^{-1}

This species takes part in five reactions (as a reactant in r_m2 and as a product in r_m1, r_m3_i1 and as a modifier in r_i2, r_i3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{M} = v_1 + v_3 - v_2 \tag{33}$$

7.2 Species B

Name Betagalactosidase

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

This species takes part in four reactions (as a reactant in r_b1 and as a product in r_b2_i2 and as a modifier in r_a2, r_a3_l1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{B} = v_6 - v_5 \tag{34}$$

7.3 Species A

Name allolactose

Initial concentration $0.038\ \mathrm{mmol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in r_a1, r_a2 and as a product in r_a3_l1 and as a modifier in r_i1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{A} = v_{10} - v_8 - v_9 \tag{35}$$

7.4 Species L

Name lactose_internal

Initial concentration $0.372\ \mathrm{mmol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in r_a3_l1, r_l2, r_l3 and as a product in r_l4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{L} = v_{13} - v_{10} - v_{11} - v_{12} \tag{36}$$

7.5 Species P

Name permease

Initial concentration $0.0149\ \mathrm{mmol}\cdot\mathrm{l}^{-1}$

This species takes part in four reactions (as a reactant in r_p1 and as a product in r_p2_i3 and as a modifier in r_l3, r_l4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{P} = v_{15} - v_{14} \tag{37}$$

7.6 Species I1

Name PartialmRNA

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

This species takes part in two reactions (as a reactant in r_m3_i1 and as a product in r_i1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{I1} = v_4 - v_3 \tag{38}$$

7.7 Species I2

Name PartialBetagalactosidase

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

This species takes part in two reactions (as a reactant in r_b2_i2 and as a product in r_i2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{I2} = v_7 - v_6 \tag{39}$$

7.8 Species I3

Name PartialPermease

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

This species takes part in two reactions (as a reactant in r_p2_i3 and as a product in r_i3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{I3} = v_{16} - v_{15} \tag{40}$$

7.9 Species L_e

Name External_Lactose

Initial concentration $0.08\ \mathrm{mmol}\cdot\mathrm{l}^{-1}$

This species takes part in one reaction (as a modifier in r_l4), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{L\_e} = 0 \tag{41}$$

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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