SBML Model Report

Model name: "Fung2005_Metabolic_Oscillator"

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 1 format. This model was created by Harish Dharuri[1] at August 28th 2006 at 8:43 a. m. and last time modified at May 16th 2012 at 10:20 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	8
events	0	constraints	0
reactions	13	function definitions	0
global parameters	21	unit definitions	0
rules	0	initial assignments	0

Model Notes

A Synthetic Gene-Metabolic Oscillator

Reference: *Fung et al; Nature (2005) 435:118-122*

Name of kinetic law	Reaction

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

Glycolytic flux, V_gly:	nil -> AcCoA;
Flux to TCA cycle/ETOH, V_TCA:	AcCoA -> TCA/EtOH;
HOAc ex/import,reversible, V_out:	HOAc -> HOAc_E
V_Pta:	AcCoA + Pi -> AcP + CoA
reversible, V_Ack:	AcP + ADP -> OAc + ATP
V_Acs:	OAC + ATP -> AcCoA +PPi
Acetic acid-base equillibrium, reversible, V_Ace:	OAC + H -> HOAc
Expression of LacI, R_LacI:	nil -> LacI
Expression of Acs, R_Acs:	nil -> Acs
Expression of Pta, R_Pta:	nil -> Pta
LacI degradation, R_dLacI:	LacI -> nil
Acs degradation, R_dAcs:	Acs -> nil
Pta degradation, R_dPta:	Pta -> nil

For this model the differential equation for V_Ace was changed from:
C*(AcP*H-K_eq*OAC) with C = 100 in the supplemental material
to C*(OAc*H-K_eq*HOAc) with C = 100, as in *Bulter et. al; PNAS(2004),101,2299-2304* , and a value for K_eq of 5*10^-4 after communication with the authors.

translated to SBML by:
Lukas Endler(luen at tbi.univie.ac.at), Christoph Flamm (xtof at tbi.univie.ac.at)

Biomodels Curation The model reproduces 3a of the paper for glycolytic flux Vgly = 0.5. The authors have agreed that the values on Y-axis are marked wrong and hence there is a discrepancy between model simulation results and the figure. Also, note that the values of concentration and time are in dimensionless units. The model was successfully tested on MathSBML and Jarnac.

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 3: Properties of all compartments.

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

3.1 Compartment `compartment`

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

Name Intracellular

4 Species

This model contains eight 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 4: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
AcCoA	Acetyl-CoA	compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
AcP	Acetyl phosphate	compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
OAc	Acetate	compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
HOAc	protonated acetate	compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
LacI	lac repressor	compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Acs	Acetyl-CoA synthase	compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Pta	Phosphate acetyl transferase	compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
HOAc_E	acetate export	compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	☑

Produced by SBML2LaTeX

5 Parameters

This model contains 21 global parameters.

Table 5: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
S0			0.500		☑
kTCA			10.000		☑
k1			80.000		☑
KM1			0.060		☑
k2			0.800		☑
KM2			0.100		☑
kAck_f			1.000		☑
kAck_r			1.000		☑
C			100.000		☑
H			10^{-7}		☑
Keq			$5 \cdot 10^{-4}$		☑
k3			0.010		☑
alpha0			0.000		☑
alpha1			0.100		☑
alpha2			2.000		☑
alpha3			2.000		☑
Kg1			10.000		☑
Kg2			10.000		☑
Kg3			0.001		☑
n			2.000		☑
kd			0.060		☑

6 Reactions

This model contains 13 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 6: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	V_gly	Glycolytic flux	$\emptyset \longrightarrow$ AcCoA	
2	V_TCA	Flux to TCA cycle	AcCoA $\longrightarrow \emptyset$	
3	V_out	Intercellular transport of Acetate	HOAc $\rightleftharpoons$ HOAc_E	
4	V_Pta	Phosphate acetyl transferase flux	AcCoA $\xrightarrow{\text{Pta}}$ AcP	
5	V_Ack	Acetate kinase	AcP $\rightleftharpoons$ OAc	
6	V_Acs	Acetyl-CoA synthase flux	OAc $\xrightarrow{\text{Acs}}$ AcCoA	
7	V_Ace	Acid-base equilibrium	OAc $\rightleftharpoons$ HOAc	
8	R_LacI	LacI synthesis	$\emptyset \xrightarrow{\text{AcP}}$ LacI	
9	R_Acs	Acetyl-CoA synthase synthesis	$\emptyset \xrightarrow{\text{AcP}}$ Acs	
10	R_Pta	Phosphate acetyl transferase synthase	$\emptyset \xrightarrow{\text{LacI}}$ Pta	
11	R_dLacI	LacI degradation	LacI $\longrightarrow \emptyset$	
12	R_dAcs	Acs degradation	Acs $\longrightarrow \emptyset$	
13	R_dPta	Pta degradation	Pta $\longrightarrow \emptyset$	

Produced by SBML2LaTeX

6.1 Reaction V_gly

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

Name Glycolytic flux

Reaction equation

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

Product

Table 7: Properties of each product.

Id	Name	SBO
AcCoA	Acetyl-CoA	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \mathrm{vol}\,(\mathrm{compartment}) \cdot \mathrm{S0} \tag{2}$$

6.2 Reaction V_TCA

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

Name Flux to TCA cycle

Reaction equation

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

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
AcCoA	Acetyl-CoA	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{compartment}) \cdot \mathrm{kTCA} \cdot [\mathrm{AcCoA}] \tag{4}$$

6.3 Reaction V_out

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

Name Intercellular transport of Acetate

Reaction equation

$$\mathrm{HOAc} \rightleftharpoons \mathrm{HOAc\_E} \tag{5}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
HOAc	protonated acetate	

Product

Table 10: Properties of each product.

Id	Name	SBO
HOAc_E	acetate export	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\,(\mathrm{compartment}) \cdot \mathrm{k3} \cdot ([\mathrm{HOAc}] - [\mathrm{HOAc\_E}]) \tag{6}$$

6.4 Reaction V_Pta

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

Name Phosphate acetyl transferase flux

Reaction equation

$$\mathrm{AcCoA} \xrightarrow{\mathrm{Pta}} \mathrm{AcP} \tag{7}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
AcCoA	Acetyl-CoA	

Modifier

Table 12: Properties of each modifier.

Id	Name	SBO
Pta	Phosphate acetyl transferase	

Product

Table 13: Properties of each product.

Id	Name	SBO
AcP	Acetyl phosphate	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \frac{\mathrm{vol}\,(\mathrm{compartment}) \cdot \mathrm{k1} \cdot [\mathrm{Pta}] \cdot [\mathrm{AcCoA}]}{\mathrm{KM1} + [\mathrm{AcCoA}]} \tag{8}$$

6.5 Reaction V_Ack

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

Name Acetate kinase

Reaction equation

$$\mathrm{AcP} \rightleftharpoons \mathrm{OAc} \tag{9}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
AcP	Acetyl phosphate	

Product

Table 15: Properties of each product.

Id	Name	SBO
OAc	Acetate	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\,(\mathrm{compartment}) \cdot (\mathrm{kAck\_f} \cdot [\mathrm{AcP}] - \mathrm{kAck\_r} \cdot [\mathrm{OAc}]) \tag{10}$$

6.6 Reaction V_Acs

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

Name Acetyl-CoA synthase flux

Reaction equation

$$\mathrm{OAc} \xrightarrow{\mathrm{Acs}} \mathrm{AcCoA} \tag{11}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
OAc	Acetate	

Modifier

Table 17: Properties of each modifier.

Id	Name	SBO
Acs	Acetyl-CoA synthase	

Product

Table 18: Properties of each product.

Id	Name	SBO
AcCoA	Acetyl-CoA	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \frac{\mathrm{vol}\,(\mathrm{compartment}) \cdot \mathrm{k2} \cdot [\mathrm{Acs}] \cdot [\mathrm{OAc}]}{\mathrm{KM2} + [\mathrm{OAc}]} \tag{12}$$

6.7 Reaction V_Ace

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

Name Acid-base equilibrium

Reaction equation

$$\mathrm{OAc} \rightleftharpoons \mathrm{HOAc} \tag{13}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
OAc	Acetate	

Product

Table 20: Properties of each product.

Id	Name	SBO
HOAc	protonated acetate	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\,(\mathrm{compartment}) \cdot \mathrm{C} \cdot ([\mathrm{OAc}] \cdot \mathrm{H} - \mathrm{Keq} \cdot [\mathrm{HOAc}]) \tag{14}$$

6.8 Reaction R_LacI

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

Name LacI synthesis

Reaction equation

$$\emptyset \xrightarrow{\text{AcP}} \text{LacI} \tag{15}$$

Modifier

Table 21: Properties of each modifier.

Id	Name	SBO
AcP	Acetyl phosphate	

Product

Table 22: Properties of each product.

Id	Name	SBO
LacI	lac repressor	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{vol}(\text{compartment}) \cdot \left(\frac{\text{alpha1} \cdot \left(\frac{[\text{AcP}]}{\text{Kg1}} \right)^{\text{n}}}{1 + \left(\frac{[\text{AcP}]}{\text{Kg1}} \right)^{\text{n}}} + \text{alpha0} \right) \tag{16}$$

6.9 Reaction R_Acs

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

Name Acetyl-CoA synthase synthesis

Reaction equation

$$\emptyset \xrightarrow{\text{AcP}} \text{Acs} \tag{17}$$

Modifier

Table 23: Properties of each modifier.

Id	Name	SBO
AcP	Acetyl phosphate	

Product

Table 24: Properties of each product.

Id	Name	SBO
Acs	Acetyl-CoA synthase	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\left(\mathrm{compartment}\right) \cdot \left(\frac{\mathrm{alpha2} \cdot \left(\frac{[\mathrm{AcP}]}{\mathrm{Kg2}}\right)^{\mathrm{n}}}{1 + \left(\frac{[\mathrm{AcP}]}{\mathrm{Kg2}}\right)^{\mathrm{n}}} + \mathrm{alpha0} \right) \tag{18}$$

6.10 Reaction R_Pta

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

Name Phosphate acetyl transferase synthase

Reaction equation

$$\emptyset \xrightarrow{\mathrm{LacI}} \mathrm{Pta} \tag{19}$$

Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
LacI	lac repressor	

Product

Table 26: Properties of each product.

Id	Name	SBO
Pta	Phosphate acetyl transferase	

Kinetic Law

Derived unit not available

$$v_{10} = \frac{\text{alpha3}}{1 + \left(\frac{[\text{LacI}]}{\text{Kg3}}\right)^{\text{n}}} + \text{alpha0} \tag{20}$$

6.11 Reaction R_dLacI

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

Name LacI degradation

Reaction equation

$$\text{LacI} \longrightarrow \emptyset \tag{21}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
LacI	lac repressor	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \text{vol}\,(\text{compartment}) \cdot \text{kd} \cdot [\text{LacI}] \tag{22}$$

6.12 Reaction R_dAcs

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

Name Acs degradation

Reaction equation

$$\text{Acs} \longrightarrow \emptyset \tag{23}$$

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
Acs	Acetyl-CoA synthase	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\,(\mathrm{compartment}) \cdot \mathrm{kd} \cdot [\mathrm{Acs}] \tag{24}$$

6.13 Reaction R_dPta

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

Name Pta degradation

Reaction equation

$$\mathrm{Pta} \longrightarrow \emptyset \tag{25}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
Pta	Phosphate acetyl transferase	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}\,(\mathrm{compartment}) \cdot \mathrm{kd} \cdot [\mathrm{Pta}] \tag{26}$$

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 `AcCoA`

Name Acetyl-CoA

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

This species takes part in four reactions (as a reactant in `V_TCA`, `V_Pta` and as a product in `V_gly`, `V_Acs`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AcCoA} = v_1 + v_6 - v_2 - v_4 \tag{27}$$

7.2 Species `AcP`

Name Acetyl phosphate

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

This species takes part in four reactions (as a reactant in `V_Ack` and as a product in `V_Pta` and as a modifier in `R_LacI`, `R_Acs`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AcP} = v_4 - v_5 \tag{28}$$

7.3 Species `OAc`

Name Acetate

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

This species takes part in three reactions (as a reactant in `V_Acs`, `V_Ace` and as a product in `V_Ack`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{OAc} = v_5 - v_6 - v_7 \tag{29}$$

7.4 Species `HOAc`

Name protonated acetate

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

This species takes part in two reactions (as a reactant in `V_out` and as a product in `V_Ace`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{HOAc} = v_7 - v_3 \tag{30}$$

7.5 Species LacI

Name lac repressor

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

This species takes part in three reactions (as a reactant in R_dLacI and as a product in R_LacI and as a modifier in R_Pta).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{LacI} = v_8 - v_{11} \tag{31}$$

7.6 Species Acs

Name Acetyl-CoA synthase

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

This species takes part in three reactions (as a reactant in R_dAcs and as a product in R_Acs and as a modifier in V_Acs).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Acs} = v_9 - v_{12} \tag{32}$$

7.7 Species Pta

Name Phosphate acetyl transferase

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

This species takes part in three reactions (as a reactant in R_dPta and as a product in R_Pta and as a modifier in V_Pta).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Pta} = v_{10} - v_{13} \tag{33}$$

7.8 Species HOAc_E

Name acetate export

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{HOAc\_E} = 0 \tag{34}$$

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.

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany