SBML Model Report

Model name: "Teusink1998_Glycolysis_TurboDesign"

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Kieran Smallbone[1] at July 20th 2010 at no o' clock in the morning. and last time modified at December second 2010 at 10:45 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	6
events	0	constraints	0
reactions	4	function definitions	0
global parameters	15	unit definitions	4
rules	8	initial assignments	0

Model Notes

This is the model described in the article:
The danger of metabolic pathways with turbo design
Teusink B, Walsh MC, van Dam K, Westerhoff HV Trends Biochem. Sci. 1998 May; Volume: 23 (Issue: 5): 162-9 9612078 ,

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Abstract:
Many catabolic pathways begin with an ATP-requiring activation step, after which further metabolism yields a surplus of ATP. Such a 'turbo' principle is useful but also contains an inherent risk. This is illustrated by a detailed kinetic analysis of a paradoxical Saccharomyces cerevisiae mutant; the mutant fails to grow on glucose because of overactive initial enzymes of glycolysis, but is defective only in an enzyme (trehalose 6-phosphate synthase) that appears to have little relevance to glycolysis. The ubiquity of pathways that possess an initial activation step, suggests that there might be many more genes that, when deleted, cause rather paradoxical regulation phenotypes (i.e. growth defects caused by enhanced utilization of growth substrate).

The model represents the wild-type cell: 'guarded' glycolysis, which is the inhibition of the HK module by hexose monophosphate. The model reproduces figures 3c and 3d of the reference publication.

To reproduce unguarded glycolysis, set parameter wild_type to '0'.

2 Unit Definitions

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

2.1 Unit `substance`

Name mmol

Definition mmol

2.2 Unit `time`

Name min

Definition 60 s

2.3 Unit `mM`

Name mM

Definition $\mathrm{mmol} \cdot \mathrm{l}^{-1}$

2.4 Unit mM_per_min

Name mM per min

Definition $\mathrm{mmol} \cdot \mathrm{l}^{-1} \cdot (60\ \mathrm{s})^{-1}$

2.5 Unit volume

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

Definition l

2.6 Unit area

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

Definition m^2

2.7 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`	cell		3	1	litre	☑	

3.1 Compartment cell

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

Name cell

4 Species

This model contains six species. The boundary condition of three of these species is set to `true` so that these species' amount cannot be changed by any reaction. 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
`HMP`	hexose monophosphate	`cell`	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
`Fru16P2`	fructose 1,6-bisphosphate	`cell`	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
`ATP`	ATP	`cell`	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☐
`Glc`	glucose	`cell`	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☑
`Tre6P`	trehalose 6-phosphate	`cell`	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☑
`ADP`	ADP	`cell`	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☐	☑

5 Parameters

This model contains 15 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
lambda1			0.000		☐
lambda2			0.000		☐
lambda3			0.000		☐
R			0.000		☐
T			0.000		☐
L			0.000		☐
KRHMP		0000194	1.000	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
gR			10.000		☑
c1			$5 \cdot 10^{-4}$		☑
L0			1000.000		☑
KRATP		0000194	0.060	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
gT			1.000		☑
c2			1.000		☑
KiATP		0000261	10.000	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
ci			10.000		☑

6 Rules

This is an overview of eight rules.

6.1 Rule Tre6P

Rule Tre6P is an assignment rule for species Tre6P:

$$\mathrm{Tre6P} = [\mathrm{HMP}]^2 \tag{1}$$

Derived unit $\mathrm{mmol}^2 \cdot \mathrm{l}^{-2}$

6.2 Rule ADP

Rule ADP is an assignment rule for species ADP:

$$\mathrm{ADP} = 5 - [\mathrm{ATP}] \tag{2}$$

6.3 Rule `lambda1`

Rule `lambda1` is an assignment rule for parameter `lambda1`:

$$\text{lambda1} = \frac{[\text{HMP}]}{\text{KRHMP}} \tag{3}$$

Derived unit dimensionless

6.4 Rule `lambda2`

Rule `lambda2` is an assignment rule for parameter `lambda2`:

$$\text{lambda2} = \frac{[\text{ATP}]}{\text{KRATP}} \tag{4}$$

Derived unit dimensionless

6.5 Rule `lambda3`

Rule `lambda3` is an assignment rule for parameter `lambda3`:

$$\text{lambda3} = \frac{[\text{ATP}]}{\text{KiATP}} \tag{5}$$

Derived unit dimensionless

6.6 Rule `R`

Rule `R` is an assignment rule for parameter `R`:

$$\text{R} = 1 + \text{lambda1} + \text{lambda2} + \text{gR} \cdot \text{lambda1} \cdot \text{lambda2} \tag{6}$$

6.7 Rule `T`

Rule `T` is an assignment rule for parameter `T`:

$$\text{T} = 1 + \text{c1} \cdot \text{lambda1} + \text{c2} \cdot \text{lambda2} + \text{gT} \cdot \text{c1} \cdot \text{lambda1} \cdot \text{c2} \cdot \text{lambda2} \tag{7}$$

6.8 Rule `L`

Rule `L` is an assignment rule for parameter `L`:

$$\text{L} = \text{L0} \cdot \left(\frac{1 + \text{ci} \cdot \text{lambda3}}{1 + \text{lambda3}} \right)^2 \tag{8}$$

7 Reactions

This model contains four 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	HK	hexokinase	$\mathrm{Glc} + \mathrm{ATP} \xrightarrow{\mathrm{Tre6P}} \mathrm{HMP}$	0000176
2	PFK	phosphofructokinase	$\mathrm{HMP} + \mathrm{ATP} \longrightarrow \mathrm{Fru16P2}$	0000176
3	lower	lower	$\mathrm{Fru16P2} + 4\,\mathrm{ADP} \longrightarrow 4\,\mathrm{ATP}$	0000176
4	ATPase	ATPase	$\mathrm{ATP} \longrightarrow \mathrm{ADP}$	0000176

7.1 Reaction HK

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

Name hexokinase

SBO:0000176 biochemical reaction

Reaction equation

$$\mathrm{Glc} + \mathrm{ATP} \xrightarrow{\mathrm{Tre6P}} \mathrm{HMP} \tag{9}$$

Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
Glc	glucose	
ATP	ATP	

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
Tre6P	trehalose 6-phosphate	

Product

Table 8: Properties of each product.

Id	Name	SBO
HMP	hexose monophosphate	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{\frac{\mathrm{vol(cell)} \cdot \mathrm{VHK} \cdot [\mathrm{Glc}] \cdot [\mathrm{ATP}]}{\mathrm{KGlc} \cdot \mathrm{KATP}}}{\left(1 + \frac{[\mathrm{Glc}]}{\mathrm{KGlc}} + \frac{\mathrm{wild\_type} \cdot [\mathrm{Tre6P}]}{\mathrm{KiTre6P}}\right) \cdot \left(1 + \frac{[\mathrm{ATP}]}{\mathrm{KATP}}\right)} \tag{10}$$

Table 9: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
VHK		0000324	68.000	$\text{mmol} \cdot \text{l}^{-1} \cdot (60\ \text{s})^{-1}$	☑
KATP		0000322	0.150	$\text{mmol} \cdot \text{l}^{-1}$	☑
KGlc		0000322	1.000	$\text{mmol} \cdot \text{l}^{-1}$	☑
KiTre6P		0000261	4.422	$\text{mmol} \cdot \text{l}^{-1}$	☑
wild_type			1.000	dimensionless	☑

7.2 Reaction PFK

This is an irreversible reaction of two reactants forming one product.

Name phosphofructokinase

SBO:0000176 biochemical reaction

Reaction equation

$$\text{HMP} + \text{ATP} \longrightarrow \text{Fru16P2} \tag{11}$$

Reactants

Table 10: Properties of each reactant.

Id	Name	SBO
HMP	hexose monophosphate	
ATP	ATP	

Product

Table 11: Properties of each product.

Id	Name	SBO
Fru16P2	fructose 1,6-bisphosphate	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \frac{\text{vol}\,(\text{cell}) \cdot \text{VPFK} \cdot \text{gR} \cdot \text{lambda1} \cdot \text{lambda2} \cdot \text{R}}{\text{R}^2 + \text{L} \cdot \text{T}^2} \tag{12}$$

Table 12: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
VPFK		0000324	30.0	mmol · 1^{-1} · $(60\ \mathrm{s})^{-1}$	☑

7.3 Reaction lower

This is an irreversible reaction of two reactants forming one product.

Name lower

SBO:0000176 biochemical reaction

Reaction equation

$$\mathrm{Fru16P2} + 4\,\mathrm{ADP} \longrightarrow 4\,\mathrm{ATP} \tag{13}$$

Reactants

Table 13: Properties of each reactant.

Id	Name	SBO
Fru16P2	fructose 1,6-bisphosphate	
ADP	ADP	

Product

Table 14: Properties of each product.

Id	Name	SBO
ATP	ATP	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \frac{\frac{\mathrm{vol(cell)} \cdot \mathrm{Vlower} \cdot [\mathrm{Fru16P2}] \cdot [\mathrm{ADP}]}{\mathrm{KFru16P2} \cdot \mathrm{KADP}}}{\left(1 + \frac{[\mathrm{Fru16P2}]}{\mathrm{KFru16P2}}\right) \cdot \left(1 + \frac{[\mathrm{ADP}]}{\mathrm{KADP}}\right)} \tag{14}$$

Table 15: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Vlower`		0000324	20.0	$\text{mmol} \cdot \text{l}^{-1} \cdot (60\ \text{s})^{-1}$	☑
`KFru16P2`		0000322	1.0	$\text{mmol} \cdot \text{l}^{-1}$	☑
`KADP`		0000322	0.1	$\text{mmol} \cdot \text{l}^{-1}$	☑

7.4 Reaction `ATPase`

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

Name ATPase

SBO:0000176 biochemical reaction

Reaction equation

$$\text{ATP} \longrightarrow \text{ADP} \tag{15}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
`ATP`	ATP	

Product

Table 17: Properties of each product.

Id	Name	SBO
`ADP`	ADP	

Kinetic Law

Derived unit $0.0010\ \text{mol} \cdot (60\ \text{s})^{-1}$

$$v_4 = \frac{\text{vol}\,(\text{cell}) \cdot \text{VATPase} \cdot [\text{ATP}]}{\text{KATP} + [\text{ATP}]} \tag{16}$$

Table 18: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
VATPase		0000324	68.0	$\text{mmol} \cdot \text{l}^{-1} \cdot (60\ \text{s})^{-1}$	☑
KATP		0000322	3.0	$\text{mmol} \cdot \text{l}^{-1}$	☑

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.

8.1 Species HMP

Name hexose monophosphate

SBO:0000247 simple chemical

Initial concentration $0.1\ \text{mmol} \cdot \text{l}^{-1}$

This species takes part in two reactions (as a reactant in PFK and as a product in HK).

$$\frac{\text{d}}{\text{d}t}\text{HMP} = v_1 - v_2 \tag{17}$$

8.2 Species Fru16P2

Name fructose 1,6-bisphosphate

SBO:0000247 simple chemical

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

This species takes part in two reactions (as a reactant in lower and as a product in PFK).

$$\frac{\text{d}}{\text{d}t}\text{Fru16P2} = v_2 - v_3 \tag{18}$$

8.3 Species ATP

Name ATP

SBO:0000247 simple chemical

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

This species takes part in four reactions (as a reactant in HK, PFK, ATPase and as a product in lower).

$$\frac{\text{d}}{\text{d}t}\text{ATP} = 4v_3 - v_1 - v_2 - v_4 \tag{19}$$

8.4 Species Glc

Name glucose

SBO:0000247 simple chemical

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Glc} = 0 \tag{20}$$

8.5 Species Tre6P

Name trehalose 6-phosphate

SBO:0000247 simple chemical

Involved in rule Tre6P

This species takes part in one reaction (as a modifier in HK). Not this but one rule determines the species' quantity because this species is on the boundary of the reaction system.

8.6 Species ADP

Name ADP

SBO:0000247 simple chemical

Involved in rule ADP

This species takes part in two reactions (as a reactant in lower and as a product in ATPase). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

A Glossary of Systems Biology Ontology Terms

SBO:0000176 biochemical reaction: An event involving one or more chemical entities that modifies the electrochemical structure of at least one of the participants.

SBO:0000194 pseudo-dissociation constant: Dissociation constant equivalent to an intrinsic microscopic dissociation constant, but obtained from an averaging process, for instance by extracting the root of a Hill constant.

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

SBO:0000261 inhibitory constant: Dissociation constant of a compound from a target of which it inhibits the function.

SBO:0000322 Michaelis constant for substrate: Substrate concentration at which the velocity of product production by the forward activity of a reversible enzyme is half its maximum.

SBO:0000324 forward maximal velocity: Limiting maximal velocity of the forward reaction of a reversible enzyme, reached when the substrate is in large excess and all the enzyme is complexed.

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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