SBML Model Report

Model name: "Curien2003_MetThr_synthesis"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 1 format. This model was created by the following three authors: Jacky L Snoep[1], Harish Dharuri[2] and Lukas Endler[3] at August 30th 2006 at 9:46 p. 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	9
events	0	constraints	0
reactions	3	function definitions	0
global parameters	0	unit definitions	4
rules	0	initial assignments	0

Model Notes

This a model from the article:
A kinetic model of the branch-point between the methionine and threonine biosynthesis pathways in Arabidopsis thaliana.

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Curien G, Ravanel S, Dumas R Eur. J. Biochem. 2003 Dec; Volume: 270 (Issue: 23)]:4615-27
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Abstract:
This work proposes a model of the metabolic branch-point between the methionine and threonine biosynthesis pathways in Arabidopsis thaliana which involves kinetic competition for phosphohomoserine between the allosteric enzyme threonine synthase and the two-substrate enzyme cystathionine gamma-synthase. Threonine synthase is activated by S-adenosylmethionine and inhibited by AMP. Cystathionine gamma-synthase condenses phosphohomoserine to cysteine via a ping-pong mechanism. Reactions are irreversible and inhibited by inorganic phosphate. The modelling procedure included an examination of the kinetic links, the determination of the operating conditions in chloroplasts and the establishment of a computer model using the enzyme rate equations. To test the model, the branch-point was reconstituted with purified enzymes. The computer model showed a partial agreement with the in vitro results. The model was subsequently improved and was then found consistent with flux partition in vitro and in vivo. Under near physiological conditions, S-adenosylmethionine, but not AMP, modulates the partition of a steady-state flux of phosphohomoserine. The computer model indicates a high sensitivity of cystathionine flux to enzyme and S-adenosylmethionine concentrations. Cystathionine flux is sensitive to modulation of threonine flux whereas the reverse is not true. The cystathionine gamma-synthase kinetic mechanism favours a low sensitivity of the fluxes to cysteine. Though sensitivity to inorganic phosphate is low, its concentration conditions the dynamics of the system. Threonine synthase and cystathionine gamma-synthase display similar kinetic efficiencies in the metabolic context considered and are first-order for the phosphohomoserine substrate. Under these conditions outflows are coordinated.

Biomodels Curation The model simulates the flux for TS and CGS under conditions given in Table 2 and reproduces the dotted lines given in Table 3 of the paper. There is a typo in the equation for the apparent specificity constant for Phser, Kts (equation13). This was changed after communication with the authors to be: Kts = 5.9E-4+6.2E-2*pow(AdoMet,2.9)/(pow(32,2.9)+pow(AdoMet,2.9)). The model was successfully tested on Jarnac and Copasi. Due to a suggestion from Pedro Mendez the parameter AdoMet, TS and CGS where made constant species.

2 Unit Definitions

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

2.1 Unit `substance`

Name micromole

Definition μmol

2.2 Unit `microM`

Name microM

Definition $\mu mol \cdot l^{-1}$

2.3 Unit `sec_inverse`

Name sec_inverse

Definition s^{-1}

2.4 Unit `microM_per_second`

Name microM_per_second

Definition $\mu mol \cdot l^{-1} \cdot s^{-1}$

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

2.8 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`	Cell		3	1	litre	☑	

3.1 Compartment `compartment`

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

Name Cell

4 Species

This model contains nine species. The boundary condition of five of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 6 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
`Phser`	Phosphohomoserine	`compartment`	$\mu mol \cdot l^{-1}$	☐	☐
`Thr`	Threonine	`compartment`	$\mu mol \cdot l^{-1}$	☐	☑
`Cystathionine`	Cystathionine	`compartment`	$\mu mol \cdot l^{-1}$	☐	☑
`Hser`	Homoserine	`compartment`	$\mu mol \cdot l^{-1}$	☐	☑
`Phi`	Inorganic phosphate	`compartment`	$\mu mol \cdot l^{-1}$	☐	☑
`Cys`	Cysteine	`compartment`	$\mu mol \cdot l^{-1}$	☐	☑
`AdoMet`	S-adenosylmethionine	`compartment`	$\mu mol \cdot l^{-1}$	☑	☐
`CGS`	Cystathionine gamma-synthase	`compartment`	$\mu mol \cdot l^{-1}$	☑	☐
`TS`	Threonine synthase	`compartment`	$\mu mol \cdot l^{-1}$	☑	☐

5 Reactions

This model contains three 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 4: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	v1	Phosphohomoserine synthesis	$\mathrm{Hser} \rightleftharpoons \mathrm{Phser}$	
2	vCys	Cystathionine gamma-synthase	$\mathrm{Phser} + \mathrm{Cys} \overset{\mathrm{CGS}}{\rightleftharpoons} \mathrm{Cystathionine} + \mathrm{Phi}$	
3	vThr	Threonine Synthase	$\mathrm{Phser} \overset{\mathrm{AdoMet,\ TS}}{\rightleftharpoons} \mathrm{Thr} + \mathrm{Phi}$	

5.1 Reaction v1

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

Name Phosphohomoserine synthesis

Reaction equation

$$\text{Hser} \rightleftharpoons \text{Phser} \tag{1}$$

Reactant

Table 5: Properties of each reactant.

Id	Name	SBO
Hser	Homoserine	

Product

Table 6: Properties of each product.

Id	Name	SBO
Phser	Phosphohomoserine	

Kinetic Law

Derived unit $\mu\text{mol} \cdot \text{s}^{-1}$

$$v_1 = \text{vol}(\text{compartment}) \cdot \text{V0} \tag{2}$$

Table 7: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
V0			1.0	$\mu\text{mol} \cdot \text{l}^{-1} \cdot \text{s}^{-1}$	☑

5.2 Reaction vCys

This is a reversible reaction of two reactants forming two products influenced by one modifier.

Name Cystathionine gamma-synthase

Reaction equation

$$\mathrm{Phser} + \mathrm{Cys} \overset{\mathrm{CGS}}{\rightleftharpoons} \mathrm{Cystathionine} + \mathrm{Phi} \tag{3}$$

Reactants

Table 8: Properties of each reactant.

Id	Name	SBO
`Phser`	Phosphohomoserine	
`Cys`	Cysteine	

Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
`CGS`	Cystathionine gamma-synthase	

Products

Table 10: Properties of each product.

Id	Name	SBO
`Cystathionine`	Cystathionine	
`Phi`	Inorganic phosphate	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \frac{[\mathrm{CGS}] \cdot \frac{\mathrm{kcat2}}{1+\frac{\mathrm{KmCYS}}{[\mathrm{Cys}]}} \cdot [\mathrm{Phser}]}{[\mathrm{Phser}] + \frac{\mathrm{KmPHSER} \cdot \left(1+\frac{[\mathrm{Phi}]}{\mathrm{Ki2}}\right)}{1+\frac{\mathrm{KmCYS}}{[\mathrm{Cys}]}}} \tag{4}$$

Table 11: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`kcat2`			30.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑

Id	Name	SBO	Value	Unit	Constant
KmCYS			460.0	$\mu mol \cdot l^{-1}$	☑
KmPHSER			2500.0	$\mu mol \cdot l^{-1}$	☑
Ki2			2000.0	$\mu mol \cdot l^{-1}$	☑

5.3 Reaction vThr

This is a reversible reaction of one reactant forming two products influenced by two modifiers.

Name Threonine Synthase

Reaction equation

$$\text{Phser} \xrightleftharpoons{\text{AdoMet, TS}} \text{Thr} + \text{Phi} \tag{5}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
Phser	Phosphohomoserine	

Modifiers

Table 13: Properties of each modifier.

Id	Name	SBO
AdoMet	S-adenosylmethionine	
TS	Threonine synthase	

Products

Table 14: Properties of each product.

Id	Name	SBO
Thr	Threonine	
Phi	Inorganic phosphate	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \frac{[\mathrm{TS}] \cdot \left(5.9E-4 + \frac{0.062 \cdot [\mathrm{AdoMet}]^{2.9}}{32^{2.9} + [\mathrm{AdoMet}]^{2.9}}\right) \cdot [\mathrm{Phser}]}{1 + \frac{[\mathrm{Phi}]}{\mathrm{Ki3}}} \tag{6}$$

Table 15: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Ki3			1000.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑

6 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.

6.1 Species `Phser`

Name Phosphohomoserine

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

This species takes part in three reactions (as a reactant in `vCys`, `vThr` and as a product in `v1`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Phser} = v_1 - v_2 - v_3 \tag{7}$$

6.2 Species `Thr`

Name Threonine

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Thr} = 0 \tag{8}$$

6.3 Species Cystathionine

Name Cystathionine

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Cystathionine} = 0 \tag{9}$$

6.4 Species Hser

Name Homoserine

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

This species takes part in one reaction (as a reactant in v1), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Hser} = 0 \tag{10}$$

6.5 Species Phi

Name Inorganic phosphate

Initial concentration $10000\ \mu\text{mol}\cdot\text{l}^{-1}$

This species takes part in two reactions (as a product in vCys, vThr), which do not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Phi} = 0 \tag{11}$$

6.6 Species Cys

Name Cysteine

Initial concentration $15\ \mu\text{mol}\cdot\text{l}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Cys} = 0 \tag{12}$$

6.7 Species AdoMet

Name S-adenosylmethionine

Initial concentration $20\ \mu\text{mol} \cdot \text{l}^{-1}$

This species takes part in one reaction (as a modifier in vThr).

$$\frac{\text{d}}{\text{d}t}\text{AdoMet} = 0 \tag{13}$$

6.8 Species CGS

Name Cystathionine gamma-synthase

Initial concentration $0.7\ \mu\text{mol} \cdot \text{l}^{-1}$

This species takes part in one reaction (as a modifier in vCys).

$$\frac{\text{d}}{\text{d}t}\text{CGS} = 0 \tag{14}$$

6.9 Species TS

Name Threonine synthase

Initial concentration $5\ \mu\text{mol} \cdot \text{l}^{-1}$

This species takes part in one reaction (as a modifier in vThr).

$$\frac{\text{d}}{\text{d}t}\text{TS} = 0 \tag{15}$$

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