SBML Model Report

Model name: "Nijhout2004_Folate_Cycle"

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by Michal Galdzicki[1] at March 25th 2009 at 1:33 p. m. and last time modified at April eighth 2016 at 4:02 p. 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	14
events	0	constraints	0
reactions	12	function definitions	0
global parameters	38	unit definitions	0
rules	0	initial assignments	0

Model Notes

This is an SBML version of the folate cycle model model from:
A mathematical model of the folate cycle: new insights into folate homeostasis.
Nijhout HF, Reed MC, Budu P, Ulrich CM J. Biol. Chem.,2004, **279** (53),55008-16
pubmedID: 15496403
Abstract:
A mathematical model is developed for the folate cycle based on standard biochemical kinetics. We use the model to provide new insights into several different mechanisms of folate homeostasis. The model reproduces the known pool sizes of folate substrates and the fluxes through each

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of the loops of the folate cycle and has the qualitative behavior observed in a variety of experimental studies. Vitamin B(12) deficiency, modeled as a reduction in the V(max) of the methionine synthase reaction, results in a secondary folate deficiency via the accumulation of folate as 5-methyltetrahydrofolate (the „methyl trap„). One form of homeostasis is revealed by the fact that a 100-fold up-regulation of thymidylate synthase and dihydrofolate reductase (known to occur at the G(1)/S transition) dramatically increases pyrimidine production without affecting the other reactions of the folate cycle. The model also predicts that an almost total inhibition of dihydrofolate reductase is required to significantly inhibit the thymidylate synthase reaction, consistent with experimental and clinical studies on the effects of methotrexate. Sensitivity to variation in enzymatic parameters tends to be local in the cycle and inversely proportional to the number of reactions that interconvert two folate substrates. Another form of homeostasis is a consequence of the nonenzymatic binding of folate substrates to folate enzymes. Without folate binding, the velocities of the reactions decrease approximately linearly as total folate is decreased. In the presence of folate binding and allosteric inhibition, the velocities show a remarkable constancy as total folate is decreased.
This model was encoded by Michal Galdzicki from a MatLab file send to him by Prof. Michael Reed. There some differences in this model compared to the one described in the article, possible due to typos in the publication:
1) reaction NE (THF + H2CO <=> 5,10-CH2-THF) in the article has H2C=O as areactant and is mentioned to display pseudo first order mass actionkinetics, while in the matlab file formic acid, also used in reaction FTS, is included in the rate law for the forward reaction.
2) the reaction MS is modeled after Reed et al. 2004, which is notexplicitly mentioned in the article, although Kd and the parametersfrom Reed et al. 2004 are given.
3) in the kinetic law of the SHTM reaction (THF + Ser <=>5,10-CH2-THF + Gly), there are separate values given for Km,Glyand Km,5,10-CH2-THF in the article. in the matlab file and the SBMLmodel Km,Ser and Km,THF are used instead of Km,Gly and Km,5,10-CH2-THFfor the backwards reaction.

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
`compartment`		0000290	3	1	litre	☑	

3.1 Compartment `compartment`

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

SBO:0000290 physical compartment

4 Species

This model contains 14 species. The boundary condition of eight of these species is set to `true` so that these 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
_5mTHF		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
THF		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
DHF		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
_5_10_CH2THF		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
_5_10_CHTHF		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
_10fTHF		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
Ser		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
Gly		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
dUMP		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
GAR		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
AICAR		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
HCOOH		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
NADPH		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑
Hcy		compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☑

5 Parameters

This model contains 38 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
NE_k1			0.15		☑
NE_k2			12.00		☑
MS_Vmax			500.00		☑
MS_Km_5mTHF			25.00		☑
MS_Km_Hcy			0.10		☑
MS_Kd			1.00		☑
MTHFR_Vmax			6000.00		☑
MTHFR_Km_NADPH			16.00		☑
MTHFR_Km_5_10_CH2THF			50.00		☑
FTD_Vmax			14000.00		☑
FTD_Km_10fTHF			20.00		☑
FTS_Vmax			2000.00		☑
FTS_Km_HCOOH			43.00		☑
FTS_Km_THF			3.00		☑
AICART_Vmax			45000.00		☑
AICART_Km_AICAR			100.00		☑
AICART_Km_10fTHF			5.90		☑
PGT_Vmax			16200.00		☑
PGT_Km_GAR			520.00		☑
PGT_Km_10fTHF			4.90		☑
TS_Vmax			50.00		☑
TS_Km_dUMP			6.30		☑
TS_Km_5_10_CH2THF			14.00		☑
DHFR_Vmax			50.00		☑
DHFR_Km_NADPH			4.00		☑
DHFR_Km_DHF			0.50		☑
MTCH_VmaxF			800000.00		☑
MTCH_Km_5_10_CHTHF			250.00		☑

Id	Name	SBO	Value	Unit	Constant
MTCH_VmaxR			20000.00		☑
MTCH_Km_10fTHF			100.00		☑
SHMT_VmaxF			40000.00		☑
SHMT_Km_Ser			600.00		☑
SHMT_Km_THF			50.00		☑
SHMT_VmaxR			25000.00		☑
MTD_VmaxF			200000.00		☑
MTD_Km_5_10_CH2THF			2.00		☑
MTD_VmaxR			594000.00		☑
MTD_Km_5_10_CHTHF			10.00		☑

6 Reactions

This model contains twelve 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	V_NE		$\mathrm{THF} \xrightarrow{\mathrm{HCOOH}} \mathrm{\_5\_10\_CH2THF}$	0000210
2	V_MS		$\mathrm{\_5mTHF} \xrightarrow{\mathrm{Hcy}} \mathrm{THF}$	0000402
3	V_MTHFR		$\mathrm{\_5\_10\_CH2THF} \xrightarrow{\mathrm{NADPH}} \mathrm{\_5mTHF}$	0000202
4	V_FTD		$\mathrm{\_10fTHF} \longrightarrow \mathrm{THF}$	0000402
5	V_FTS		$\mathrm{THF} \xrightarrow{\mathrm{HCOOH}} \mathrm{\_10fTHF}$	0000402
6	V_AICART		$\mathrm{\_10fTHF} \xrightarrow{\mathrm{AICAR}} \mathrm{THF}$	0000402
7	V_PGT		$\mathrm{\_10fTHF} \xrightarrow{\mathrm{GAR}} \mathrm{THF}$	0000402
8	V_TS		$\mathrm{\_5\_10\_CH2THF} \xrightarrow{\mathrm{dUMP}} \mathrm{DHF}$	0000402
9	V_DHFR		$\mathrm{DHF} \xrightarrow{\mathrm{NADPH}} \mathrm{THF}$	0000202
10	V_MTCH		$\mathrm{\_5\_10\_CHTHF} \longrightarrow \mathrm{\_10fTHF}$	0000376
11	V_SHMT		$\mathrm{THF} \xrightarrow{\mathrm{Ser,\ Gly}} \mathrm{\_5\_10\_CH2THF}$	0000402
12	V_MTD		$\mathrm{\_5\_10\_CH2THF} \longrightarrow \mathrm{\_5\_10\_CHTHF}$	0000201

6.1 Reaction V_NE

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

SBO:0000210 addition of a chemical group

Reaction equation

$$\mathrm{THF} \xrightarrow{\mathrm{HCOOH}} \mathrm{\_5\_10\_CH2THF} \tag{1}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
THF		

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
HCOOH		

Product

Table 8: Properties of each product.

Id	Name	SBO
_5_10_CH2THF		

Kinetic Law

Derived unit contains undeclared units

$$v_1 = [\mathrm{HCOOH}] \cdot \mathrm{NE\_k1} \cdot [\mathrm{THF}] - \mathrm{NE\_k2} \cdot [\mathrm{\_5\_10\_CH2THF}] \tag{2}$$

6.2 Reaction V_MS

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

SBO:0000402 transfer of a chemical group

Reaction equation

$$\text{\_5mTHF} \xrightarrow{\text{Hcy}} \text{THF} \tag{3}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
_5mTHF		

Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
Hcy		

Product

Table 11: Properties of each product.

Id	Name	SBO
THF		

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \frac{\text{MS\_Vmax} \cdot \frac{[\text{\_5mTHF}]}{\text{MS\_Km\_5mTHF}} \cdot \frac{[\text{Hcy}]}{\text{MS\_Km\_Hcy}}}{\frac{\text{MS\_Kd}}{\text{MS\_Km\_5mTHF}} + \frac{[\text{\_5mTHF}]}{\text{MS\_Km\_5mTHF}} + \frac{[\text{Hcy}]}{\text{MS\_Km\_Hcy}} + \frac{[\text{\_5mTHF}] \cdot [\text{Hcy}]}{\text{MS\_Km\_5mTHF} \cdot \text{MS\_Km\_Hcy}}} \tag{4}$$

6.3 Reaction V_MTHFR

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

SBO:0000202 reduction

Reaction equation

$$\text{\_5\_10\_CH2THF} \xrightarrow{\text{NADPH}} \text{\_5mTHF} \tag{5}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
_5_10_CH2THF		

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
NADPH		

Product

Table 14: Properties of each product.

Id	Name	SBO
_5mTHF		

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{MTHFR\_Vmax} \cdot \frac{[\text{NADPH}]}{\text{MTHFR\_Km\_NADPH} + [\text{NADPH}]} \cdot \frac{[\text{\_5\_10\_CH2THF}]}{\text{MTHFR\_Km\_5\_10\_CH2THF} + [\text{\_5\_10\_CH2THF}]} \tag{6}$$

6.4 Reaction V_FTD

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

SBO:0000402 transfer of a chemical group

Reaction equation

$$\text{\_10fTHF} \longrightarrow \text{THF} \tag{7}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
_10fTHF		

Product

Table 16: Properties of each product.

Id	Name	SBO
THF		

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{FTD\_Vmax} \cdot \frac{[\text{\_10fTHF}]}{\text{FTD\_Km\_10fTHF} + [\text{\_10fTHF}]} \tag{8}$$

6.5 Reaction V_FTS

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

SBO:0000402 transfer of a chemical group

Reaction equation

$$\text{THF} \xrightarrow{\text{HCOOH}} \text{\_10fTHF} \tag{9}$$

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
THF		

Modifier

Table 18: Properties of each modifier.

Id	Name	SBO
HCOOH		

Id	Name	SBO

Product

Table 19: Properties of each product.

Id	Name	SBO
_10fTHF		

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{FTS\_Vmax} \cdot \frac{[\text{HCOOH}]}{\text{FTS\_Km\_HCOOH} + [\text{HCOOH}]} \cdot \frac{[\text{THF}]}{\text{FTS\_Km\_THF} + [\text{THF}]} \tag{10}$$

6.6 Reaction V_AICART

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

SBO:0000402 transfer of a chemical group

Reaction equation

$$\text{\_10fTHF} \xrightarrow{\text{AICAR}} \text{THF} \tag{11}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
_10fTHF		

Modifier

Table 21: Properties of each modifier.

Id	Name	SBO
AICAR		

Product

Table 22: Properties of each product.

Id	Name	SBO
THF		

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{AICART\_Vmax} \cdot \frac{[\text{AICAR}]}{\text{AICART\_Km\_AICAR} + [\text{AICAR}]} \cdot \frac{[\text{\_10fTHF}]}{\text{AICART\_Km\_10fTHF} + [\text{\_10fTHF}]} \tag{12}$$

6.7 Reaction V_PGT

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

SBO:0000402 transfer of a chemical group

Reaction equation

$$\text{\_10fTHF} \xrightarrow{\text{GAR}} \text{THF} \tag{13}$$

Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
_10fTHF		

Modifier

Table 24: Properties of each modifier.

Id	Name	SBO
GAR		

Product

Table 25: Properties of each product.

Id	Name	SBO
THF		

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{PGT\_Vmax} \cdot \frac{[\text{GAR}]}{\text{PGT\_Km\_GAR} + [\text{GAR}]} \cdot \frac{[\text{\_10fTHF}]}{\text{PGT\_Km\_10fTHF} + [\text{\_10fTHF}]} \tag{14}$$

6.8 Reaction V_TS

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

SBO:0000402 transfer of a chemical group

Reaction equation

$$\text{\_5\_10\_CH2THF} \xrightarrow{\text{dUMP}} \text{DHF} \tag{15}$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
_5_10_CH2THF		

Modifier

Table 27: Properties of each modifier.

Id	Name	SBO
dUMP		

Product

Table 28: Properties of each product.

Id	Name	SBO
DHF		

Id	Name	SBO

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{TS\_Vmax} \cdot \frac{[\text{dUMP}]}{\text{TS\_Km\_dUMP} + [\text{dUMP}]} \cdot \frac{[\text{\_5\_10\_CH2THF}]}{\text{TS\_Km\_5\_10\_CH2THF} + [\text{\_5\_10\_CH2THF}]} \quad (16)$$

6.9 Reaction V_DHFR

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

SBO:0000202 reduction

Reaction equation

$$\text{DHF} \xrightarrow{\text{NADPH}} \text{THF} \quad (17)$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
DHF		

Modifier

Table 30: Properties of each modifier.

Id	Name	SBO
NADPH		

Product

Table 31: Properties of each product.

Id	Name	SBO
THF		

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{DHFR\_Vmax} \cdot \frac{[\text{NADPH}]}{\text{DHFR\_Km\_NADPH} + [\text{NADPH}]} \cdot \frac{[\text{DHF}]}{\text{DHFR\_Km\_DHF} + [\text{DHF}]} \tag{18}$$

6.10 Reaction V_MTCH

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

SBO:0000376 hydrolysis

Reaction equation

$$\text{\_5\_10\_CHTHF} \longrightarrow \text{\_10fTHF} \tag{19}$$

Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
_5_10_CHTHF		

Product

Table 33: Properties of each product.

Id	Name	SBO
_10fTHF		

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{10} = \text{MTCH\_VmaxF} \cdot \frac{[\text{\_5\_10\_CHTHF}]}{\text{MTCH\_Km\_5\_10\_CHTHF} + [\text{\_5\_10\_CHTHF}]} \\ - \text{MTCH\_VmaxR} \cdot \frac{[\text{\_10fTHF}]}{\text{MTCH\_Km\_10fTHF} + [\text{\_10fTHF}]} \end{aligned} \tag{20}$$

6.11 Reaction V_SHMT

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

SBO:0000402 transfer of a chemical group

Reaction equation

$$\mathrm{THF} \xrightarrow{\text{Ser, Gly}} \mathtt{\_5\_10\_CH2THF} \tag{21}$$

Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
THF		

Modifiers

Table 35: Properties of each modifier.

Id	Name	SBO
Ser		
Gly		

Product

Table 36: Properties of each product.

Id	Name	SBO
_5_10_CH2THF		

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{11} = {} & \mathrm{SHMT\_VmaxF} \cdot \frac{[\mathrm{Ser}]}{\mathrm{SHMT\_Km\_Ser} + [\mathrm{Ser}]} \cdot \frac{[\mathrm{THF}]}{\mathrm{SHMT\_Km\_THF} + [\mathrm{THF}]} \\ & - \mathrm{SHMT\_VmaxR} \cdot \frac{[\mathrm{Gly}]}{\mathrm{SHMT\_Km\_Ser} + [\mathrm{Gly}]} \cdot \frac{[\mathrm{\_5\_10\_CH2THF}]}{\mathrm{SHMT\_Km\_THF} + [\mathrm{\_5\_10\_CH2THF}]} \end{aligned} \tag{22}$$

6.12 Reaction V_MTD

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

SBO:0000201 oxidation

Reaction equation

$$\_5\_10\_CH2THF \longrightarrow \_5\_10\_CHTHF \tag{23}$$

Reactant

Table 37: Properties of each reactant.

Id	Name	SBO
_5_10_CH2THF		

Product

Table 38: Properties of each product.

Id	Name	SBO
_5_10_CHTHF		

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_{12} = \text{MTD\_VmaxF} \cdot \frac{[\_5\_10\_CH2THF]}{\text{MTD\_Km\_5\_10\_CH2THF} + [\_5\_10\_CH2THF]} \\ - \text{MTD\_VmaxR} \cdot \frac{[\_5\_10\_CHTHF]}{\text{MTD\_Km\_5\_10\_CHTHF} + [\_5\_10\_CHTHF]} \end{aligned} \tag{24}$$

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 _5mTHF

SBO:0000247 simple chemical

Initial concentration 5.16 mol · l^{-1}

This species takes part in two reactions (as a reactant in V_MS and as a product in V_MTHFR).

$$\frac{\mathrm{d}}{\mathrm{d}t}\_5\mathrm{mTHF} = v_3 - v_2 \tag{25}$$

7.2 Species THF

SBO:0000247 simple chemical

Initial concentration 6.73 mol · l^{-1}

This species takes part in eight reactions (as a reactant in V_NE, V_FTS, V_SHMT and as a product in V_MS, V_FTD, V_AICART, V_PGT, V_DHFR).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{THF} = v_2 + v_4 + v_6 + v_7 + v_9 - v_1 - v_5 - v_{11} \tag{26}$$

7.3 Species DHF

SBO:0000247 simple chemical

Initial concentration 0.027 mol · l^{-1}

This species takes part in two reactions (as a reactant in V_DHFR and as a product in V_TS).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{DHF} = v_8 - v_9 \tag{27}$$

7.4 Species _5_10_CH2THF

SBO:0000247 simple chemical

Initial concentration 0.94 mol · l^{-1}

This species takes part in five reactions (as a reactant in V_MTHFR, V_TS, V_MTD and as a product in V_NE, V_SHMT).

$$\frac{\mathrm{d}}{\mathrm{d}t}\_5\_10\_\mathrm{CH2THF} = v_1 + v_{11} - v_3 - v_8 - v_{12} \tag{28}$$

7.5 Species _5_10_CHTHF

SBO:0000247 simple chemical

Initial concentration $1.153\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in V_MTCH and as a product in V_MTD).

$$\frac{\mathrm{d}}{\mathrm{d}t}\_5\_10\_\mathrm{CHTHF} = v_{12} - v_{10} \tag{29}$$

7.6 Species _10fTHF

SBO:0000247 simple chemical

Initial concentration $5.99\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in five reactions (as a reactant in V_FTD, V_AICART, V_PGT and as a product in V_FTS, V_MTCH).

$$\frac{\mathrm{d}}{\mathrm{d}t}\_10\mathrm{fTHF} = v_5 + v_{10} - v_4 - v_6 - v_7 \tag{30}$$

7.7 Species Ser

SBO:0000247 simple chemical

Initial concentration $468\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ser} = 0 \tag{31}$$

7.8 Species Gly

SBO:0000247 simple chemical

Initial concentration $1850\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Gly} = 0 \tag{32}$$

7.9 Species dUMP

SBO:0000247 simple chemical

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{dUMP} = 0 \tag{33}$$

7.10 Species GAR

SBO:0000247 simple chemical

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

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

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

7.11 Species AICAR

SBO:0000247 simple chemical

Initial concentration $2.1\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AICAR} = 0 \tag{35}$$

7.12 Species HCOOH

SBO:0000247 simple chemical

Initial concentration $900\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{HCOOH} = 0 \tag{36}$$

7.13 Species NADPH

SBO:0000247 simple chemical

Initial concentration $50\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NADPH} = 0 \tag{37}$$

7.14 Species Hcy

SBO:0000247 simple chemical

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

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Hcy} = 0 \tag{38}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000201 **oxidation:** Chemical process during which a molecular entity loses electrons

SBO:0000202 **reduction:** Chemical process in which a molecular entity gain electrons

SBO:0000210 **addition of a chemical group:** Covalent reaction that results in the addition of a chemical group on a molecule

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

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:0000376 **hydrolysis:** Decomposition of a compound by reaction with water, where the hydroxyl and H groups are incorporated into different product

SBO:0000402 **transfer of a chemical group:** Covalent reaction that results in the transfer of a chemical group from one molecule to another

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