SBML Model Report

Model name: “Reed2004 - Methionine Cycle”

May 17, 2018

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Catherine Lloyd[1] and Matthew Grant Roberts[2] at May eighth 2018 at 11:26 a. m. and last time modified at May nineth 2018 at 9:32 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	7
events	0	constraints	0
reactions	9	function definitions	8
global parameters	22	unit definitions	3
rules	3	initial assignments	0

Model Notes

Reed2004 - Methionine Cycle

This model is described in the article:A mathematical model of the methionine cycle.Reed MC, Nijhout HF, Sparks R, Ulrich CM.J. Theor. Biol. 2004 Jan; 226(1): 33-43

Abstract:

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Building on the work of Martinov et al. (2000), a mathematical model is developed for the methionine cycle. A large amount of information is available about the enzymes that catalyse individual reaction steps in the cycle, from methionine to S-adenosylmethionine to S-adenosylhomocysteine to homocysteine, and the removal of mass from the cycle by the conversion of homocysteine to cystathionine. Nevertheless, the behavior of the cycle is very complicated since many substrates alter the activities of the enzymes in the reactions that produce them, and some can also alter the activities of other enzymes in the cycle. The model consists of four differential equations, based on known reaction kinetics, that can be solved to give the time course of the concentrations of the four main substrates in the cycle under various circumstances. We show that the behavior of the model in response to genetic abnormalities and dietary deficiencies is similar to the changes seen in a wide variety of experimental studies. We conduct computational „experiments„ that give understanding of the regulatory behavior of the methionine cycle under normal conditions and the behavior in the presence of genetic variation and dietary deficiencies.

This model is hosted on BioModels Database and identified by: BIOMD0000000698.

To cite BioModels Database, please use: Chelliah V et al. BioModels: ten-year anniversary. Nucl. Acids Res. 2015, 43(Database issue):D542-8.

2 Unit Definitions

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

2.1 Unit `volume`

Name volume

Definition ml

2.2 Unit `time`

Name time

Definition 3600 s

2.3 Unit `substance`

Name substance

Definition µmol

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
`Compartment`	Compartment		3	1	litre	☑	

3.1 Compartment `Compartment`

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

Name Compartment

4 Species

This model contains seven species. The boundary condition of two of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 9 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
`Metin`	Metin	`Compartment`	$\mu mol \cdot ml^{-1}$	☐	☑
`Methionine`	Methionine	`Compartment`	$\mu mol \cdot ml^{-1}$	☐	☐
`AdoMet`	AdoMet	`Compartment`	$\mu mol \cdot ml^{-1}$	☐	☐
`AdoHcy`	AdoHcy	`Compartment`	$\mu mol \cdot ml^{-1}$	☐	☐
`Homocysteine`	Homocysteine	`Compartment`	$\mu mol \cdot ml^{-1}$	☐	☐
`_5mTHF`	5mTHF	`Compartment`	$\mu mol \cdot ml^{-1}$	☑	☑
`Cystathionine`	Cystathionine	`Compartment`	$\mu mol \cdot ml^{-1}$	☐	☐

5 Parameters

This model contains 22 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`V_max_MATI`	V_max_MATI		561.000		☑
`K_m_MATI`	K_m_MATI		41.000		☑
`K_i_MATI`	K_i_MATI		50.000		☑
`V_max_MATIII`	V_max_MATIII		22870.000		☑
`K_m1_MATIII`	K_m1_MATIII		16689.375		⊟
`K_m2_MATIII`	K_m2_MATIII		21.100		☑
`V_max_GNMT`	V_max_GNMT		10600.000		☑
`K_m_GNMT`	K_m_GNMT		4500.000		☑
`K_i_GNMT`	K_i_GNMT		20.000		☑
`V_max_METH`	V_max_METH		4521.000		☑
`K_m1_METH`	K_m1_METH		4.300		⊟
`K_m2_METH_A`	K_m2_METH_A		10.000		☑
`alpha_1`	alpha_1		100.000		☑
`alpha_2`	alpha_2		10.000		☑
`beta_1`	beta_1		1.700		☑
`beta_2`	beta_2		30.000		☑
`V_max_MS`	V_max_MS		500.000		☑
`K_m_Hcy_MS`	K_m_Hcy_MS		0.100		☑
`K_m_5mTHF_MS`	K_m_5mTHF_MS		25.000		☑
`K_d_MS`	K_d_MS		1.000		☑
`V_max_BHMT`	V_max_BHMT		2500.000		☑
`K_m_BHMT`	K_m_BHMT		12.000		☑

6 Function definitions

This is an overview of eight function definitions.

6.1 Function definition `function_for_V_MATI`

Name function for V_MATI

Arguments V_max_mati, K_m_mati, MET, [AdoMet], K_i_meti

Mathematical Expression

$$\frac{\mathrm{V\_max\_mati}}{1+\frac{\mathrm{K\_m\_mati}}{\mathrm{MET}}\cdot\left(1+\frac{[\mathrm{AdoMet}]}{\mathrm{K\_i\_meti}}\right)} \tag{1}$$

6.2 Function definition `function_for_V_MATIII`

Name function for V_MATIII

Arguments V_max_matiii, Met, K_m1_MATIII, K_m2_MATIII

Mathematical Expression

$$\frac{\mathrm{V\_max\_matiii}}{1+\frac{\mathrm{K\_m1\_MATIII}\cdot\mathrm{K\_m2\_MATIII}}{\mathrm{Met}^2+\mathrm{Met}\cdot\mathrm{K\_m2\_MATIII}}} \tag{2}$$

6.3 Function definition `function_for_V_GMNT`

Name function for V_GMNT

Arguments V_max_GMNT, K_m_GMNT, [AdoMet], [AdoHcy], K_i_GMNT

Mathematical Expression

$$\frac{\mathrm{V\_max\_GMNT}}{1+\left(\frac{\mathrm{K\_m\_GMNT}}{[\mathrm{AdoMet}]}\right)^{2.3}}\cdot\frac{1}{1+\frac{[\mathrm{AdoHcy}]}{\mathrm{K\_i\_GMNT}}} \tag{3}$$

6.4 Function definition `function_for_V_METH`

Name function for V_METH

Arguments V_max_METH, [AdoMet], K_m2_METH_A, K_m1_METH

Mathematical Expression

$$\frac{\mathrm{V\_max\_METH}}{1+\frac{\mathrm{K\_m1\_METH}}{[\mathrm{AdoMet}]}+\mathrm{K\_m2\_METH\_A}+\frac{\mathrm{K\_m2\_METH\_A}\cdot\mathrm{K\_m1\_METH}}{[\mathrm{AdoMet}]}} \tag{4}$$

6.5 Function definition `function_for_V_MS`

Name function for V_MS

Arguments V_max_MS, mTHF, Hcy, K_d_MS, K_m_Hcy_MS, K_m_mTHF_MS

Mathematical Expression

$$\frac{\mathrm{V\_max\_MS}\cdot\mathrm{mTHF}\cdot\mathrm{Hcy}}{\mathrm{K\_d\_MS}\cdot\mathrm{K\_m\_Hcy\_MS}+\mathrm{K\_m\_Hcy\_MS}\cdot\mathrm{mTHF}+\mathrm{K\_m\_mTHF\_MS}\cdot\mathrm{Hcy}+\mathrm{mTHF}\cdot\mathrm{Hcy}} \tag{5}$$

6.6 Function definition function_for_V_CBS

Name function for V_CBS

Arguments beta1, [AdoMet], [AdoHcy], beta2, Hcy

Mathematical Expression

$$(\text{beta1} \cdot ([\text{AdoMet}] + [\text{AdoHcy}]) - \text{beta2}) \cdot \text{Hcy} \tag{6}$$

6.7 Function definition function_for_V_BHMT

Name function for V_BHMT

Arguments [AdoMet], [AdoHcy], V_max_bhmt, Hcy, K_m_BHMT

Mathematical Expression

$$(0.7 - 0.025 \cdot ([\text{AdoMet}] + [\text{AdoHcy}] - 150)) \cdot \frac{\text{V\_max\_bhmt} \cdot \text{Hcy}}{\text{K\_m\_BHMT} + \text{Hcy}} \tag{7}$$

6.8 Function definition function_for_V_AH

Name function for V_AH

Arguments alpha1, [AdoHcy], alpha2, Hcy

Mathematical Expression

$$\text{alpha1} \cdot ([\text{AdoHcy}] - \text{alpha2} \cdot \text{Hcy}) \tag{8}$$

7 Rules

This is an overview of three rules.

7.1 Rule Metin

Rule `Metin` is an assignment rule for species `Metin`:

$$\text{Metin} = \begin{cases} 200 & \text{if } (\text{time} < 2) \lor (\text{time} \geq 8) \\ \begin{cases} 300 & \text{if } (\text{time} \geq 2) \land (\text{time} < 5) \\ \begin{cases} 100 & \text{if } (\text{time} \geq 5) \land (\text{time} < 8) \\ 200 & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} & \text{otherwise} \end{cases} \tag{9}$$

7.2 Rule K_m1_MATIII

Rule K_m1_MATIII is an assignment rule for parameter K_m1_MATIII:

$$\mathrm{K\_m1\_MATIII} = \frac{20000}{1 + 5.7 \cdot \left(\frac{[\mathrm{AdoMet}]}{[\mathrm{AdoMet}]+600}\right)^2} \tag{10}$$

7.3 Rule K_m1_METH

Rule K_m1_METH is an assignment rule for parameter K_m1_METH:

$$\mathrm{K\_m1\_METH} = 1 \cdot \left(1 + \frac{[\mathrm{AdoHcy}]}{4}\right) \tag{11}$$

8 Reactions

This model contains nine 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_MAT_I	V_MAT-I	Methionine $\longrightarrow$ AdoMet	
2	V_MAT_III	V_MAT-III	Methionine $\longrightarrow$ AdoMet	
3	V_METH	V_METH	AdoMet $\longrightarrow$ AdoHcy	
4	V_GNMT	V_GNMT	AdoMet $\longrightarrow$ AdoHcy	
5	V_AH	V_AH	AdoHcy $\rightleftharpoons$ Homocysteine	
6	V_MS	V_MS	Homocysteine + _5mTHF $\longrightarrow$ Methionine	
7	V_BHMT	V_BHMT	Homocysteine $\xrightarrow{\text{AdoMet, AdoHcy}}$ Methionine	
8	V_CBS	V_CBS	Homocysteine $\xrightarrow{\text{AdoMet, AdoHcy}}$ Cystathionine	
9	METIN	METIN	Metin $\longrightarrow$ Methionine	

8.1 Reaction V_MAT_I

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

Name V_MAT-I

Reaction equation

$$\text{Methionine} \longrightarrow \text{AdoMet} \tag{12}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
Methionine	Methionine	

Product

Table 7: Properties of each product.

Id	Name	SBO
AdoMet	AdoMet	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{Compartment}) \cdot \text{function\_for\_V\_MATI}(\text{V\_max\_MATI}, \text{K\_m\_MATI}, [\text{Methionine}], [\text{AdoMet}], \text{K\_i\_MATI}) \tag{13}$$

$$\text{function\_for\_V\_MATI}(\text{V\_max\_mati}, \text{K\_m\_mati}, \text{MET}, [\text{AdoMet}], \text{K\_i\_meti}) = \frac{\text{V\_max\_mati}}{1 + \frac{\text{K\_m\_mati}}{\text{MET}} \cdot \left(1 + \frac{[\text{AdoMet}]}{\text{K\_i\_meti}}\right)} \tag{14}$$

$$\text{function\_for\_V\_MATI}(\text{V\_max\_mati}, \text{K\_m\_mati}, \text{MET}, [\text{AdoMet}], \text{K\_i\_meti}) = \frac{\text{V\_max\_mati}}{1 + \frac{\text{K\_m\_mati}}{\text{MET}} \cdot \left(1 + \frac{[\text{AdoMet}]}{\text{K\_i\_meti}}\right)} \tag{15}$$

8.2 Reaction V_MAT_III

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

Name V_MAT-III

Reaction equation

$$\text{Methionine} \longrightarrow \text{AdoMet} \tag{16}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
Methionine	Methionine	

Product

Table 9: Properties of each product.

Id	Name	SBO
AdoMet	AdoMet	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}(\text{Compartment}) \cdot \text{function\_for\_V\_MATIII}(\text{V\_max\_MATIII}, [\text{Methionine}], \text{K\_m1\_MATIII}, \text{K\_m2\_MATIII}) \tag{17}$$

$$\text{function\_for\_V\_MATIII}(\text{V\_max\_matiii}, \text{Met}, \text{K\_m1\_MATIII}, \text{K\_m2\_MATIII}) = \frac{\text{V\_max\_matiii}}{1 + \frac{\text{K\_m1\_MATIII} \cdot \text{K\_m2\_MATIII}}{\text{Met}^2 + \text{Met} \cdot \text{K\_m2\_MATIII}}} \tag{18}$$

$$\text{function\_for\_V\_MATIII}(\text{V\_max\_matiii}, \text{Met}, \text{K\_m1\_MATIII}, \text{K\_m2\_MATIII}) = \frac{\text{V\_max\_matiii}}{1 + \frac{\text{K\_m1\_MATIII} \cdot \text{K\_m2\_MATIII}}{\text{Met}^2 + \text{Met} \cdot \text{K\_m2\_MATIII}}} \tag{19}$$

8.3 Reaction V_METH

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

Name V_METH

Reaction equation

$$\text{AdoMet} \longrightarrow \text{AdoHcy} \tag{20}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
AdoMet	AdoMet	

Product

Table 11: Properties of each product.

Id	Name	SBO
AdoHcy	AdoHcy	

Kinetic Law

Derived unit contains undeclared units

$$\begin{aligned} v_3 = \text{vol}\left(\text{Compartment}\right) \cdot \text{function\_for\_V\_METH}\left(\text{V\_max\_METH}, [\text{AdoMet}],\right. \\ \left.\text{K\_m2\_METH\_A}, \text{K\_m1\_METH}\right) \end{aligned} \tag{21}$$

$$\begin{aligned} &\text{function\_for\_V\_METH}\left(\text{V\_max\_METH}, [\text{AdoMet}], \text{K\_m2\_METH\_A}, \text{K\_m1\_METH}\right) \\ &= \frac{\text{V\_max\_METH}}{1 + \frac{\text{K\_m1\_METH}}{[\text{AdoMet}]} + \text{K\_m2\_METH\_A} + \frac{\text{K\_m2\_METH\_A} \cdot \text{K\_m1\_METH}}{[\text{AdoMet}]}} \end{aligned} \tag{22}$$

$$\begin{aligned} &\text{function\_for\_V\_METH}\left(\text{V\_max\_METH}, [\text{AdoMet}], \text{K\_m2\_METH\_A}, \text{K\_m1\_METH}\right) \\ &= \frac{\text{V\_max\_METH}}{1 + \frac{\text{K\_m1\_METH}}{[\text{AdoMet}]} + \text{K\_m2\_METH\_A} + \frac{\text{K\_m2\_METH\_A} \cdot \text{K\_m1\_METH}}{[\text{AdoMet}]}} \end{aligned} \tag{23}$$

8.4 Reaction V_GNMT

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

Name V_GNMT

Reaction equation

$$\text{AdoMet} \longrightarrow \text{AdoHcy} \tag{24}$$

Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
AdoMet	AdoMet	

Product

Table 13: Properties of each product.

Id	Name	SBO
AdoHcy	AdoHcy	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}\left(\text{Compartment}\right) \cdot \text{function\_for\_V\_GMNT}\left(\text{V\_max\_GNMT}, \text{K\_m\_GNMT}, [\text{AdoMet}], [\text{AdoHcy}], \text{K\_i\_GNMT}\right) \tag{25}$$

$$\text{function\_for\_V\_GMNT}\left(\text{V\_max\_GMNT}, \text{K\_m\_GMNT}, [\text{AdoMet}], [\text{AdoHcy}], \text{K\_i\_GMNT}\right) = \frac{\text{V\_max\_GMNT}}{1 + \left(\frac{\text{K\_m\_GMNT}}{[\text{AdoMet}]}\right)^{2.3}} \cdot \frac{1}{1 + \frac{[\text{AdoHcy}]}{\text{K\_i\_GMNT}}} \tag{26}$$

$$\text{function\_for\_V\_GMNT}\left(\text{V\_max\_GMNT}, \text{K\_m\_GMNT}, [\text{AdoMet}], [\text{AdoHcy}], \text{K\_i\_GMNT}\right) = \frac{\text{V\_max\_GMNT}}{1 + \left(\frac{\text{K\_m\_GMNT}}{[\text{AdoMet}]}\right)^{2.3}} \cdot \frac{1}{1 + \frac{[\text{AdoHcy}]}{\text{K\_i\_GMNT}}} \tag{27}$$

8.5 Reaction V_AH

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

Name V_AH

Reaction equation

$$\text{AdoHcy} \rightleftharpoons \text{Homocysteine} \tag{28}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
AdoHcy	AdoHcy	

Product

Table 15: Properties of each product.

Id	Name	SBO
Homocysteine	Homocysteine	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}\left(\text{Compartment}\right) \cdot \text{function\_for\_V\_AH}\left(\text{alpha\_1}, [\text{AdoHcy}], \text{alpha\_2}, [\text{Homocysteine}]\right) \tag{29}$$

$$\text{function\_for\_V\_AH}\left(\text{alpha1}, [\text{AdoHcy}], \text{alpha2}, \text{Hcy}\right) = \text{alpha1} \cdot \left([\text{AdoHcy}] - \text{alpha2} \cdot \text{Hcy}\right) \tag{30}$$

$$\text{function\_for\_V\_AH}\left(\text{alpha1}, [\text{AdoHcy}], \text{alpha2}, \text{Hcy}\right) = \text{alpha1} \cdot \left([\text{AdoHcy}] - \text{alpha2} \cdot \text{Hcy}\right) \tag{31}$$

8.6 Reaction V_MS

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

Name V_MS

Reaction equation

$$\text{Homocysteine} + \text{\_5mTHF} \longrightarrow \text{Methionine} \tag{32}$$

Reactants

Table 16: Properties of each reactant.

Id	Name	SBO
`Homocysteine`	Homocysteine	
`_5mTHF`	5mTHF	

Product

Table 17: Properties of each product.

Id	Name	SBO
`Methionine`	Methionine	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{vol}\left(\text{Compartment}\right) \cdot \text{function\_for\_V\_MS}\left(\text{V\_max\_MS}, [\text{\_5mTHF}], [\text{Homocysteine}], \text{K\_d\_MS}, \text{K\_m\_Hcy\_MS}, \text{K\_m\_5mTHF\_MS}\right) \tag{33}$$

$$\text{function\_for\_V\_MS}\left(\text{V\_max\_MS}, \text{mTHF}, \text{Hcy}, \text{K\_d\_MS}, \text{K\_m\_Hcy\_MS}, \text{K\_m\_mTHF\_MS}\right) = \frac{\text{V\_max\_MS} \cdot \text{mTHF} \cdot \text{Hcy}}{\text{K\_d\_MS} \cdot \text{K\_m\_Hcy\_MS} + \text{K\_m\_Hcy\_MS} \cdot \text{mTHF} + \text{K\_m\_mTHF\_MS} \cdot \text{Hcy} + \text{mTHF} \cdot \text{Hcy}} \tag{34}$$

$$\text{function\_for\_V\_MS}\left(\text{V\_max\_MS}, \text{mTHF}, \text{Hcy}, \text{K\_d\_MS}, \text{K\_m\_Hcy\_MS}, \text{K\_m\_mTHF\_MS}\right) = \frac{\text{V\_max\_MS} \cdot \text{mTHF} \cdot \text{Hcy}}{\text{K\_d\_MS} \cdot \text{K\_m\_Hcy\_MS} + \text{K\_m\_Hcy\_MS} \cdot \text{mTHF} + \text{K\_m\_mTHF\_MS} \cdot \text{Hcy} + \text{mTHF} \cdot \text{Hcy}} \tag{35}$$

8.7 Reaction `V_BHMT`

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

Name V_BHMT

Reaction equation

$$\text{Homocysteine} \xrightarrow{\text{AdoMet, AdoHcy}} \text{Methionine} \tag{36}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
`Homocysteine`	Homocysteine	

Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
`AdoMet`	AdoMet	
`AdoHcy`	AdoHcy	

Product

Table 20: Properties of each product.

Id	Name	SBO
`Methionine`	Methionine	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{Compartment}\right) \cdot \mathrm{function\_for\_V\_BHMT}\left([\mathrm{AdoMet}], [\mathrm{AdoHcy}], \mathrm{V\_max\_BHMT}, [\mathrm{Homocysteine}], \mathrm{K\_m\_BHMT}\right) \tag{37}$$

$$\mathrm{function\_for\_V\_BHMT}\left([\mathrm{AdoMet}], [\mathrm{AdoHcy}], \mathrm{V\_max\_bhmt}, \mathrm{Hcy}, \mathrm{K\_m\_BHMT}\right) = \left(0.7 - 0.025 \cdot \left([\mathrm{AdoMet}] + [\mathrm{AdoHcy}] - 150\right)\right) \cdot \frac{\mathrm{V\_max\_bhmt} \cdot \mathrm{Hcy}}{\mathrm{K\_m\_BHMT} + \mathrm{Hcy}} \tag{38}$$

$$
\begin{aligned}
&\text{function\_for\_V\_BHMT}\left([\text{AdoMet}], [\text{AdoHcy}], \text{V\_max\_bhmt}, \text{Hcy}, \text{K\_m\_BHMT}\right) \\
&= (0.7 - 0.025 \cdot ([\text{AdoMet}] + [\text{AdoHcy}] - 150)) \cdot \frac{\text{V\_max\_bhmt} \cdot \text{Hcy}}{\text{K\_m\_BHMT} + \text{Hcy}}
\end{aligned} \quad (39)
$$

8.8 Reaction V_CBS

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

Name V_CBS

Reaction equation

$$\text{Homocysteine} \xrightarrow{\text{AdoMet, AdoHcy}} \text{Cystathionine} \quad (40)$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
Homocysteine	Homocysteine	

Modifiers

Table 22: Properties of each modifier.

Id	Name	SBO
AdoMet	AdoMet	
AdoHcy	AdoHcy	

Product

Table 23: Properties of each product.

Id	Name	SBO
Cystathionine	Cystathionine	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\left(\mathrm{Compartment}\right) \cdot \mathrm{function\_for\_V\_CBS}\left(\mathrm{beta\_1}, [\mathrm{AdoMet}], [\mathrm{AdoHcy}], \mathrm{beta\_2}, [\mathrm{Homocysteine}]\right) \quad (41)$$

$$\mathrm{function\_for\_V\_CBS}\left(\mathrm{beta1}, [\mathrm{AdoMet}], [\mathrm{AdoHcy}], \mathrm{beta2}, \mathrm{Hcy}\right) = \left(\mathrm{beta1} \cdot \left([\mathrm{AdoMet}] + [\mathrm{AdoHcy}]\right) - \mathrm{beta2}\right) \cdot \mathrm{Hcy} \quad (42)$$

$$\mathrm{function\_for\_V\_CBS}\left(\mathrm{beta1}, [\mathrm{AdoMet}], [\mathrm{AdoHcy}], \mathrm{beta2}, \mathrm{Hcy}\right) = \left(\mathrm{beta1} \cdot \left([\mathrm{AdoMet}] + [\mathrm{AdoHcy}]\right) - \mathrm{beta2}\right) \cdot \mathrm{Hcy} \quad (43)$$

8.9 Reaction `METIN`

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

Name METIN

Reaction equation

$$\mathrm{Metin} \longrightarrow \mathrm{Methionine} \quad (44)$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
`Metin`	Metin	

Product

Table 25: Properties of each product.

Id	Name	SBO
`Methionine`	Methionine	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\left(\mathrm{Compartment}\right) \cdot \mathrm{k1} \cdot [\mathrm{Metin}] \quad (45)$$

Table 26: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		1.0		☑

9 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.

9.1 Species Metin

Name Metin

Initial concentration $200\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

Involved in rule Metin

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

9.2 Species Methionine

Name Methionine

Initial concentration $53.5\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

This species takes part in five reactions (as a reactant in V_MAT_I, V_MAT_III and as a product in V_MS, V_BHMT, METIN).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Methionine} = v_6 + v_7 + v_9 - v_1 - v_2 \tag{46}$$

9.3 Species AdoMet

Name AdoMet

Initial concentration $137.6\ \mu\text{mol}\cdot\text{ml}^{-1}$

This species takes part in six reactions (as a reactant in V_METH, V_GNMT and as a product in V_MAT_I, V_MAT_III and as a modifier in V_BHMT, V_CBS).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{AdoMet} = v_1 + v_2 - v_3 - v_4 \tag{47}$$

9.4 Species AdoHcy

Name AdoHcy

Initial concentration $13.2\ \mu\text{mol}\cdot\text{ml}^{-1}$

This species takes part in five reactions (as a reactant in V_AH and as a product in V_METH, V_GNMT and as a modifier in V_BHMT, V_CBS).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{AdoHcy} = v_3 + v_4 - v_5 \tag{48}$$

9.5 Species Homocysteine

Name Homocysteine

Initial concentration $0.88\ \mu\text{mol}\cdot\text{ml}^{-1}$

This species takes part in four reactions (as a reactant in V_MS, V_BHMT, V_CBS and as a product in V_AH).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Homocysteine} = v_5 - v_6 - v_7 - v_8 \tag{49}$$

9.6 Species _5mTHF

Name 5mTHF

Initial concentration $5.2\ \mu\text{mol}\cdot\text{ml}^{-1}$

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\_5\text{mTHF} = 0 \tag{50}$$

9.7 Species Cystathionine

Name Cystathionine

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

This species takes part in one reaction (as a product in V_CBS).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Cystathionine} = v_8 \tag{51}$$

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