SBML Model Report

Model name: "Montaez2008_Arginine_catabolism"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by the following six authors: Lukas Endler[1], Armando Reyes-Palomares[2], Carlos Rodrguez-Caso[3], Raul Montaez[4], Francisca Snchez-Jimnez[5] and Miguel A. Medina[6] at November 27th 2008 at 11:36 a. m. and last time modified at April eighth 2016 at 3:45 p. m. Table 1 shows 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	2
species types	0	species	3
events	0	constraints	0
reactions	5	function definitions	0
global parameters	0	unit definitions	4
rules	0	initial assignments	0

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Model Notes

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http://asp.uma.es

In silico analysis of arginine catabolism as a source of nitric oxide or polyamines in endothelial cells.

Montaez, R et al.: Amino Acids. 2008 Feb;34(2):223-9.

The model reproduces the dynamical behavior of the arginine catabolism and transport in relation to the nitric oxide production. In this model there are some additions and corrections to the publication. All perturbations and analysis have produced results very close to the published experiments. The model was successfully tested on CoPaSi v.4.4 (build 26).

Erratum: parameters values modificated respect to the publication to reach the steady-state:

Kmodc=90 M (60 M in the paper)

Kiornhat (is equivalent to the parameter Kmefflhat Eq) = 360 M (380 M in the paper)

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 `time`

Definition 60 s

2.2 Unit `substance`

Definition µmol

2.3 Unit microM

Name microM

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

2.4 Unit microMpermin

Name microMpermin

Definition $\mu\text{mol} \cdot \text{l}^{-1} \cdot (60\ \text{s})^{-1}$

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 Compartments

This model contains two compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
extracellular	extracellular	0000290	3	1	litre	☑	
cytosol	cytosol	0000290	3	1	litre	☑	

3.1 Compartment extracellular

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

Name extracellular

SBO:0000290 physical compartment

3.2 Compartment `cytosol`

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

Name cytosol

SBO:0000290 physical compartment

4 Species

This model contains three 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 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
`ARGex`	Arginine ex	`extracellular`	$\mu mol \cdot l^{-1}$	☑	☑
`ORN`	Ornithine	`cytosol`	$\mu mol \cdot l^{-1}$	☐	☐
`ARGin`	Arginine in	`cytosol`	$\mu mol \cdot l^{-1}$	☐	☐

5 Reactions

This model contains five 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	Arginase	Arginase	$\mathrm{ARGin} \xrightarrow{\mathrm{ORN}} \mathrm{ORN}$	0000211
2	Arginine_transport	Arginine transport	$\mathrm{ARGex} \xrightarrow{\mathrm{ORN}} \mathrm{ARGin}$	0000185
3	Ornithine_efflux	Ornithine efflux	$\mathrm{ORN} \xrightarrow{\mathrm{ARGex,\ ARGin}} \emptyset$	0000185
4	NOS	Nitric oxide synthase	$\mathrm{ARGin} \longrightarrow \emptyset$	0000211
5	ODC	Ornithine decarboxylase	$\mathrm{ORN} \longrightarrow \emptyset$	0000211

5.1 Reaction `Arginase`

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

Name Arginase

SBO:0000211 removal of a chemical group

Reaction equation

$$\text{ARGin} \xrightarrow{\text{ORN}} \text{ORN} \tag{1}$$

Reactant

Table 5: Properties of each reactant.

Id	Name	SBO
`ARGin`	Arginine in	

Modifier

Table 6: Properties of each modifier.

Id	Name	SBO
`ORN`	Ornithine	

Product

Table 7: Properties of each product.

Id	Name	SBO
`ORN`	Ornithine	

Kinetic Law

SBO:0000260 enzymatic rate law for simple competitive inhibition of irreversible unireactant enzymes by one inhibitor

Derived unit contains undeclared units

$$v_1 = \text{vol}\,(\text{cytosol}) \cdot \frac{\text{Vmaxarg} \cdot [\text{ARGin}]}{\text{Kmarg} \cdot \left(1 + \frac{[\text{ORN}]}{\text{Kioarg}}\right) + [\text{ARGin}]} \tag{2}$$

Table 8: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Vmaxarg		0000324	110.0	$\mu mol \cdot l^{-1} \cdot (60\ s)^{-1}$	☑
Kmarg		0000322	1500.0	$\mu mol \cdot l^{-1}$	☑
Kioarg		0000261	1000.0	$\mu mol \cdot l^{-1}$	☑

5.2 Reaction Arginine_transport

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

Name Arginine transport

SBO:0000185 transport reaction

Reaction equation

$$\text{ARGex} \xrightarrow{\text{ORN}} \text{ARGin} \tag{3}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
ARGex	Arginine ex	0000015

Modifier

Table 10: Properties of each modifier.

Id	Name	SBO
ORN	Ornithine	0000207

Product

Table 11: Properties of each product.

Id	Name	SBO
ARGin	Arginine in	0000011

Kinetic Law

SBO:0000277 enzymatic rate law for non-competitive inhibition of irreversible unireactant enzymes by two exclusively binding inhibitors

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{extracellular}) \cdot \left(\frac{[\mathrm{ARGex}]}{\mathrm{Kmhat} + [\mathrm{ARGex}]} \cdot \frac{\mathrm{Vmaxhat}}{1 + \frac{[\mathrm{ORN}]}{\mathrm{Kiornhat}} + \frac{[\mathrm{ARGin}]}{\mathrm{Kmhat}}} + \frac{[\mathrm{ARGex}]}{\mathrm{Kmlat} + [\mathrm{ARGex}]} \cdot \frac{\mathrm{Vmaxlat}}{1 + \frac{[\mathrm{ORN}]}{\mathrm{Kiornhat}} + \frac{[\mathrm{ARGin}]}{\mathrm{Kmlat}}} \right) \tag{4}$$

Table 12: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Kmhat`		0000322	70.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑
`Vmaxhat`		0000324	160.5	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑
`Kmlat`		0000322	847.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑
`Vmaxlat`		0000324	420.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1} \cdot (60\ \mathrm{s})^{-1}$	☑
`Kiornhat`		0000261	360.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑

5.3 Reaction `Ornithine_efflux`

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

Name Ornithine efflux

SBO:0000185 transport reaction

Reaction equation

$$\mathrm{ORN} \xrightarrow{\mathrm{ARGex},\ \mathrm{ARGin}} \emptyset \tag{5}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
`ORN`	Ornithine	0000015

Modifiers

Table 14: Properties of each modifier.

Id	Name	SBO
ARGex	Arginine ex	0000207
ARGin	Arginine in	0000206

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\,(\mathrm{cytosol}) \cdot \left(\frac{\mathrm{Vmaxefflhat}}{1 + \frac{[\mathrm{ARGex}]}{\mathrm{Kmhat}}} \cdot \frac{[\mathrm{ORN}]}{\mathrm{Kiornhat} \cdot \left(1 + \frac{[\mathrm{ARGin}]}{\mathrm{Kmhat}}\right) + [\mathrm{ORN}]} + \frac{\mathrm{Vmaxeffllat}}{1 + \frac{[\mathrm{ARGex}]}{\mathrm{Kmlat}}} \cdot \frac{[\mathrm{ORN}]}{\mathrm{Kmeffllat} \cdot \left(1 + \frac{[\mathrm{ARGin}]}{\mathrm{Kmlat}}\right) + [\mathrm{ORN}]} \right) \tag{6}$$

Table 15: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Kmhat		0000261	70.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑
Kmlat		0000261	847.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑
Vmaxefflhat		0000324	160.5	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1} \cdot (60\ \mathrm{s})^{-1}$	☑
Vmaxeffllat		0000324	420.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1} \cdot (60\ \mathrm{s})^{-1}$	☑
Kmeffllat		0000322	847.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑
Kiornhat		0000261	360.0	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑

5.4 Reaction NOS

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

Name Nitric oxide synthase

SBO:0000211 removal of a chemical group

Reaction equation

$$\mathrm{ARGin} \longrightarrow \emptyset \tag{7}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
ARGin	Arginine in	0000015

Kinetic Law

SBO:0000028 enzymatic rate law for irreversible non-modulated non-interacting unireactant enzymes

Derived unit $10^{-6}\,\mathrm{mol}\cdot(60\,\mathrm{s})^{-1}$

$$v_4 = \mathrm{vol}\,(\mathrm{cytosol}) \cdot \frac{\mathrm{Vmaxnos1} \cdot [\mathrm{ARGin}]}{\mathrm{Kmnos1} + [\mathrm{ARGin}]} \tag{8}$$

Table 17: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Vmaxnos1		0000324	1.33	$\mu\mathrm{mol}\cdot\mathrm{l}^{-1}\cdot(60\,\mathrm{s})^{-1}$	☑
Kmnos1			16.00	$\mu\mathrm{mol}\cdot\mathrm{l}^{-1}$	☑

5.5 Reaction ODC

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

Name Ornithine decarboxylase

SBO:0000211 removal of a chemical group

Reaction equation

$$\mathrm{ORN} \longrightarrow \emptyset \tag{9}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
ORN	Ornithine	0000015

Kinetic Law

SBO:0000028 enzymatic rate law for irreversible non-modulated non-interacting unireactant enzymes

Derived unit $10^{-6}\ \mathrm{mol} \cdot (60\ \mathrm{s})^{-1}$

$$v_5 = \mathrm{vol}\,(\mathrm{cytosol}) \cdot \frac{\mathrm{Vmaxodc} \cdot [\mathrm{ORN}]}{\mathrm{Kmodc} + [\mathrm{ORN}]} \tag{10}$$

Table 19: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`Vmaxodc`		0000324	0.013	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1} \cdot (60\ \mathrm{s})^{-1}$	☑
`Kmodc`		0000322	90.000	$\mu\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑

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.

6.1 Species `ARGex`

Name Arginine ex

SBO:0000247 simple chemical

Initial concentration $330\ \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in `Arginine_transport` and as a modifier in `Ornithine_efflux`), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

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

6.2 Species `ORN`

Name Ornithine

SBO:0000247 simple chemical

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

This species takes part in five reactions (as a reactant in Ornithine_efflux, ODC and as a product in Arginase and as a modifier in Arginase, Arginine_transport).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ORN} = v_1 - v_3 - v_5 \tag{12}$$

6.3 Species ARGin

Name Arginine in

SBO:0000247 simple chemical

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

This species takes part in four reactions (as a reactant in Arginase, NOS and as a product in Arginine_transport and as a modifier in Ornithine_efflux).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ARGin} = v_2 - v_1 - v_4 \tag{13}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000011 product: Substance that is produced in a reaction. In a chemical equation the Products are the elements or compounds on the right hand side of the reaction equation. A product can be produced and consumed by the same reaction, its global quantity remaining unchanged

SBO:0000015 substrate: Molecule which is acted upon by an enzyme. The substrate binds with the enzyme's active site, and the enzyme catalyzes a chemical reaction involving the substrate

SBO:0000028 enzymatic rate law for irreversible non-modulated non-interacting unireactant enzymes: Kinetics of enzymes that react only with one substance, their substrate. The enzymes do not catalyse the reactions in both directions.

SBO:0000185 transport reaction: Movement of a physical entity without modification of the structure of the entity

SBO:0000206 competitive inhibitor: Substance that decreases the probability of a chemical reaction, without itself being consumed or transformed by the reaction, by stericaly hindering the interaction between reactants

SBO:0000207 non-competitive inhibitor: Substance that decreases the probability of a chemical reaction, without itself being consumed or transformed by the reaction, and without sterically hindering the interaction between reactants.

SBO:0000211 removal of a chemical group: Covalent reaction that results in the removal of a chemical group from a molecule

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

SBO:0000260 enzymatic rate law for simple competitive inhibition of irreversible unireactant enzymes by one inhibitor: Inhibition of a unireactant enzyme by one inhibitor that binds once to the free enzyme and prevents the binding of the substrate. The enzymes do not catalyse the reactions in both directions.

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

SBO:0000277 enzymatic rate law for non-competitive inhibition of irreversible unireactant enzymes by two exclusively binding inhibitors: Inhibition of unireactant enzymes by two inhibitors that can bind to the complex enzyme-substrate and the free enzyme with the same equilibrium constant and totally prevent the catalysis.

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: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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