SBML Model Report

Model name: “Chen2006 - Nitric Oxide Release from Endothelial Cells”

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 February 20th 2018 at 6:04 p. m. and last time modified at February 21st 2018 at 1:46 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	1
species types	0	species	15
events	0	constraints	0
reactions	17	function definitions	2
global parameters	21	unit definitions	2
rules	0	initial assignments	0

Model Notes

Chen2006 - Nitric Oxide Release fromEndothelial Cells

This model is described in the article:Theoretical analysis of biochemical pathways of nitric oxide release from vascular endothelial cells.Chen K, Popel AS.Free Radic. Biol. Med. 2006 Aug; 41(4): 668-680

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Abstract:

Vascular endothelium expressing endothelial nitric oxide synthase (eNOS) produces nitric oxide (NO), which has a number of important physiological functions in the microvasculature. The rate of NO production by the endothelium is a critical determinant of NO distribution in the vascular wall. We have analyzed the biochemical pathways of NO synthesis and formulated a model to estimate NO production by the microvascular endothelium under physiological conditions. The model quantifies the NO produced by eNOS based on the kinetics of NO synthesis and the availability of eNOS and its intracellular substrates. The predicted NO production from microvessels was in the range of 0.005-0.1 microM/s. This range of predicted values is in agreement with some experimental values but is much lower than other rates previously measured or estimated from experimental data with the help of mathematical modeling. Paradoxical discrepancies between the model predictions and previously reported results based on experimental measurements of NO concentration in the vicinity of the arteriolar wall suggest that NO can also be released through eNOS-independent mechanisms, such as catalysis by neuronal NOS (nNOS). We also used our model to test the sensitivity of NO production to substrate availability, eNOS concentration, and potential rate-limiting factors. The results indicated that the predicted low level of NO production can be attributed primarily to a low expression of eNOS in the microvascular endothelial cells.

This model is hosted on BioModels Database and identified by: BIOMD0000000676.

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 three are predefined by SBML and not mentioned in the model.

2.1 Unit `volume`

Name volume

Definition ml

2.2 Unit `substance`

Name substance

Definition µmol

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
`Endothelium`	Endothelium		3	1	litre	☑	

3.1 Compartment `Endothelium`

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

Name Endothelium

4 Species

This model contains 15 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 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
`Arg`	Arg	`Endothelium`	$\mu mol \cdot ml^{-1}$	☑	☑
`Fe3__enos`	Fe3+(enos)	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`Fe3__Arg`	Fe3+_Arg	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`Fe2`	Fe2+	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`Fe2__Arg`	Fe2+_Arg	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`Fe3__NO`	Fe3+_NO	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`NO`	NO	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`Fe2__NO`	Fe2+_NO	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`Fe3__NOHA`	Fe3+_NOHA	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`NOHA`	NOHA	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`Fe2__NOHA`	Fe2+_NOHA	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`O2`	O2	`Endothelium`	$\mu mol \cdot ml^{-1}$	☑	☑
`Fe3__O2__Arg`	Fe3+_O2-_Arg	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`Fe3__O2__NOHA`	Fe3+_O2-_NOHA	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟
`Citrulline`	Citrulline	`Endothelium`	$\mu mol \cdot ml^{-1}$	⊟	⊟

5 Parameters

This model contains 21 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.100		☑
k1_prime	k1_prime		0.100		☑
k4	k4		1.890		☑
k4_prime	k4_prime		11.400		☑
S	S		0.000		☑
k2	k2		0.910		☑
k14	k14		53.900		☑
k13	k13		0.033		☑
k8	k8		0.100		☑
k8_prime	k8_prime		0.100		☑
k3	k3		0.910		☑
k9	k9		11.400		☑
k9_prime	k9_prime		1.890		☑
k5	k5		2.580		☑
k5_prime	k5_prime		98.000		☑
k6	k6		12.600		☑
k7	k7		0.910		☑
k10	k10		3.330		☑
k10_prime	k10_prime		89.900		☑
k11	k11		29.400		☑
k12	k12		0.910		☑

6 Function definitions

This is an overview of two function definitions.

6.1 Function definition Constant_flux__irreversible

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$v \tag{1}$$

6.2 Function definition function_for_modified_reactions

Name function for modified reactions

Arguments k, modifier, substrate

Mathematical Expression

$$\mathrm{k} \cdot \mathrm{modifier} \cdot \mathrm{substrate} \tag{2}$$

7 Reactions

This model contains 17 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	Fe3__Arg_synthesis	Fe3+_Arg synthesis	$\text{Arg} + \text{Fe3\_\_enos} \rightleftharpoons \text{Fe3\_\_Arg}$	
2	Fe2__Arg_synthesis_dissociation	Fe2+_Arg synthesis/dissociation	$\text{Arg} + \text{Fe2} \rightleftharpoons \text{Fe2\_\_Arg}$	
3	Arginine_synthesis	Arginine synthesis	$\emptyset \longrightarrow \text{Arg}$	
4	Fe2__formation	Fe2+ formation	$\text{Fe3\_\_enos} \longrightarrow \text{Fe2}$	
5	Fe3__and_NO_formation	Fe3+ and NO formation	$\text{Fe3\_\_NO} \longrightarrow \text{Fe3\_\_enos} + \text{NO}$	
6	Fe3__formation	Fe3+ formation	$\text{Fe2\_\_NO} \xrightarrow{\text{O2}} \text{Fe3\_\_enos}$	
7	Fe3__NOHA_formation_degradation	Fe3+_NOHA formation/degradation	$\text{Fe3\_\_NOHA} \rightleftharpoons \text{Fe3\_\_enos} + \text{NOHA}$	
8	Fe2__Arg_formation	Fe2+_Arg formation	$\text{Fe3\_\_Arg} \longrightarrow \text{Fe2\_\_Arg}$	
9	Fe2__NOHA_formation	Fe2+_NOHA formation	$\text{Fe2\_\_NOHA} \rightleftharpoons \text{Fe2} + \text{NOHA}$	

№	Id	Name	Reaction Equation	SBO
10	`Fe3__O2_Arg-_formation-_with_Oxygen-_activation`	Fe3+_O2-Arg formation with Oxygen activation	Fe2__Arg $\xrightarrow{\mathrm{O2}}$ Fe3__O2__Arg	
11	`Fe3__O2_Arg-_degradation`	Fe3+_O2-Arg degradation	Fe3__O2__Arg $\longrightarrow$ Fe2__Arg	
12	`Fe3__NOHA-_synthesis`	Fe3+_NOHA synthesis	Fe3__O2__Arg $\longrightarrow$ Fe3__NOHA	
13	`Fe2__NOHA-_synthesis`	Fe2+_NOHA synthesis	Fe3__NOHA $\longrightarrow$ Fe2__NOHA	
14	`Fe3__O2__NOHA-_synthesis-_with_Oxygen-_activation`	Fe3+_O2-_NOHA synthesis with Oxygen activation	Fe2__NOHA $\xrightarrow{\mathrm{O2}}$ Fe3__O2__NOHA	
15	`Fe3__NO_and-_Citrulline-_synthesis`	Fe3+_NO and Citrulline synthesis	Fe3__O2__NOHA $\longrightarrow$ Fe3__NO + Citrulline	
16	`Fe2__NO-_synthesis`	Fe2+_NO synthesis	Fe3__NO $\longrightarrow$ Fe2__NO	
17	`Fe3__O2__NOHA-_degradation`	Fe3+_O2-_NOHA degradation	Fe3__O2__NOHA $\longrightarrow$ Fe2__NOHA	

7.1 Reaction Fe3__Arg_synthesis

This is a reversible reaction of two reactants forming one product.

Name Fe3+_Arg synthesis

Reaction equation

$$\text{Arg} + \text{Fe3\_\_enos} \rightleftharpoons \text{Fe3\_\_Arg} \tag{3}$$

Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
Arg	Arg	
Fe3__enos	Fe3+(enos)	

Product

Table 7: Properties of each product.

Id	Name	SBO
Fe3__Arg	Fe3+_Arg	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}\left(\text{Endothelium}\right) \cdot \left(\text{k1} \cdot [\text{Arg}] \cdot [\text{Fe3\_\_enos}] - \text{k1\_prime} \cdot [\text{Fe3\_\_Arg}]\right) \tag{4}$$

7.2 Reaction Fe2__Arg_synthesis_dissociation

This is a reversible reaction of two reactants forming one product.

Name Fe2+_Arg synthesis/dissociation

Reaction equation

$$\text{Arg} + \text{Fe2} \rightleftharpoons \text{Fe2\_\_Arg} \tag{5}$$

Reactants

Table 8: Properties of each reactant.

Id	Name	SBO
Arg	Arg	
Fe2	Fe2+	

Product

Table 9: Properties of each product.

Id	Name	SBO
Fe2__Arg	Fe2+_Arg	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \left(\mathrm{k4} \cdot [\mathrm{Arg}] \cdot [\mathrm{Fe2}] - \mathrm{k4\_prime} \cdot [\mathrm{Fe2\_\_Arg}]\right) \tag{6}$$

7.3 Reaction Arginine_synthesis

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

Name Arginine synthesis

Reaction equation

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

Product

Table 10: Properties of each product.

Id	Name	SBO
Arg	Arg	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{S}\right) \tag{8}$$

$$\text{Constant\_flux\_\_irreversible}\left(\text{v}\right) = \text{v} \tag{9}$$

$$\text{Constant\_flux\_\_irreversible}\left(\text{v}\right) = \text{v} \tag{10}$$

7.4 Reaction `Fe2__formation`

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

Name Fe2+ formation

Reaction equation

$$\text{Fe3\_\_enos} \longrightarrow \text{Fe2} \tag{11}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
`Fe3__enos`	Fe3+(enos)	

Product

Table 12: Properties of each product.

Id	Name	SBO
`Fe2`	Fe2+	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}\left(\text{Endothelium}\right) \cdot \text{k2} \cdot [\text{Fe3\_\_enos}] \tag{12}$$

7.5 Reaction `Fe3__and_NO_formation`

This is an irreversible reaction of one reactant forming two products.

Name Fe3+ and NO formation

Reaction equation

$$\text{Fe3\_\_NO} \longrightarrow \text{Fe3\_\_enos} + \text{NO} \tag{13}$$

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
Fe3__NO	Fe3+_NO	

Products

Table 14: Properties of each product.

Id	Name	SBO
Fe3__enos	Fe3+(enos)	
NO	NO	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \mathrm{k14} \cdot [\mathrm{Fe3\_\_NO}] \tag{14}$$

7.6 Reaction Fe3__formation

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

Name Fe3+ formation

Reaction equation

$$\mathrm{Fe2\_\_NO} \xrightarrow{\mathrm{O2}} \mathrm{Fe3\_\_enos} \tag{15}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
Fe2__NO	Fe2+_NO	

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
O2	O2	

Product

Table 17: Properties of each product.

Id	Name	SBO
Fe3__enos	Fe3+(enos)	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \mathrm{function\_for\_modified\_reactions}\left(\mathrm{k13}, [\mathrm{O2}], [\mathrm{Fe2\_\_NO}]\right) \quad (16)$$

$$\mathrm{function\_for\_modified\_reactions}\left(\mathrm{k}, \mathrm{modifier}, \mathrm{substrate}\right) = \mathrm{k} \cdot \mathrm{modifier} \cdot \mathrm{substrate} \quad (17)$$

$$\mathrm{function\_for\_modified\_reactions}\left(\mathrm{k}, \mathrm{modifier}, \mathrm{substrate}\right) = \mathrm{k} \cdot \mathrm{modifier} \cdot \mathrm{substrate} \quad (18)$$

7.7 Reaction Fe3__NOHA_formation_degradation

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

Name Fe3+_NOHA formation/degradation

Reaction equation

$$\mathrm{Fe3\_\_NOHA} \rightleftharpoons \mathrm{Fe3\_\_enos} + \mathrm{NOHA} \quad (19)$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
Fe3__NOHA	Fe3+_NOHA	

Products

Table 19: Properties of each product.

Id	Name	SBO
Fe3__enos	Fe3+(enos)	
NOHA	NOHA	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \left(\mathrm{k8} \cdot [\mathrm{Fe3\_\_NOHA}] - \mathrm{k8\_prime} \cdot [\mathrm{Fe3\_\_enos}] \cdot [\mathrm{NOHA}]\right) \quad (20)$$

7.8 Reaction Fe2__Arg_formation

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

Name Fe2+_Arg formation

Reaction equation

$$\mathrm{Fe3\_\_Arg} \longrightarrow \mathrm{Fe2\_\_Arg} \quad (21)$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
Fe3__Arg	Fe3+_Arg	

Product

Table 21: Properties of each product.

Id	Name	SBO
Fe2__Arg	Fe2+_Arg	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \mathrm{k3} \cdot [\mathrm{Fe3\_\_Arg}] \tag{22}$$

7.9 Reaction `Fe2__NOHA_formation`

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

Name Fe2+_NOHA formation

Reaction equation

$$\mathrm{Fe2\_\_NOHA} \rightleftharpoons \mathrm{Fe2} + \mathrm{NOHA} \tag{23}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
`Fe2__NOHA`	Fe2+_NOHA	

Products

Table 23: Properties of each product.

Id	Name	SBO
`Fe2`	Fe2+	
`NOHA`	NOHA	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \left(\mathrm{k9} \cdot [\mathrm{Fe2\_\_NOHA}] - \mathrm{k9\_prime} \cdot [\mathrm{Fe2}] \cdot [\mathrm{NOHA}]\right) \tag{24}$$

7.10 Reaction `Fe3__O2_Arg_formation_with_Oxygen_activation`

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

Name Fe3+_O2-Arg formation with Oxygen activation

Reaction equation

$$\text{Fe2\_\_Arg} \xrightarrow{\text{O2}} \text{Fe3\_\_O2\_\_Arg} \tag{25}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
`Fe2__Arg`	Fe2+_Arg	

Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
`O2`	O2	

Product

Table 26: Properties of each product.

Id	Name	SBO
`Fe3__O2__Arg`	Fe3+_O2-_Arg	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{vol}(\text{Endothelium}) \cdot \text{function\_for\_modified\_reactions}(\text{k5}, [\text{O2}], [\text{Fe2\_\_Arg}]) \tag{26}$$

$$\text{function\_for\_modified\_reactions}(\text{k}, \text{modifier}, \text{substrate}) = \text{k} \cdot \text{modifier} \cdot \text{substrate} \tag{27}$$

$$\text{function\_for\_modified\_reactions}(\text{k}, \text{modifier}, \text{substrate}) = \text{k} \cdot \text{modifier} \cdot \text{substrate} \tag{28}$$

7.11 Reaction `Fe3__O2_Arg_degradation`

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

Name Fe3+_O2-Arg degradation

Reaction equation

$$\text{Fe3\_\_O2\_\_Arg} \longrightarrow \text{Fe2\_\_Arg} \tag{29}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
Fe3__O2__Arg	Fe3+_O2-_Arg	

Product

Table 28: Properties of each product.

Id	Name	SBO
Fe2__Arg	Fe2+_Arg	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \mathrm{k5\_prime} \cdot [\mathrm{Fe3\_\_O2\_\_Arg}] \tag{30}$$

7.12 Reaction Fe3__NOHA_synthesis

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

Name Fe3+_NOHA synthesis

Reaction equation

$$\text{Fe3\_\_O2\_\_Arg} \longrightarrow \text{Fe3\_\_NOHA} \tag{31}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
Fe3__O2__Arg	Fe3+_O2-_Arg	

Product

Table 30: Properties of each product.

Id	Name	SBO
Fe3__NOHA	Fe3+_NOHA	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \mathrm{k6} \cdot [\mathrm{Fe3\_\_O2\_\_Arg}] \tag{32}$$

7.13 Reaction Fe2__NOHA_synthesis

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

Name Fe2+_NOHA synthesis

Reaction equation

$$\mathrm{Fe3\_\_NOHA} \longrightarrow \mathrm{Fe2\_\_NOHA} \tag{33}$$

Reactant

Table 31: Properties of each reactant.

Id	Name	SBO
Fe3__NOHA	Fe3+_NOHA	

Product

Table 32: Properties of each product.

Id	Name	SBO
Fe2__NOHA	Fe2+_NOHA	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}\,(\mathrm{Endothelium}) \cdot \mathrm{k7} \cdot [\mathrm{Fe3\_\_NOHA}] \quad (34)$$

7.14 Reaction Fe3__O2__NOHA_synthesis_with_Oxygen_activation

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

Name Fe3+_O2-_NOHA synthesis with Oxygen activation

Reaction equation

$$\mathrm{Fe2\_\_NOHA} \xrightarrow{\mathrm{O2}} \mathrm{Fe3\_\_O2\_\_NOHA} \quad (35)$$

Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
Fe2__NOHA	Fe2+_NOHA	

Modifier

Table 34: Properties of each modifier.

Id	Name	SBO
O2	O2	

Product

Table 35: Properties of each product.

Id	Name	SBO
Fe3__O2__NOHA	Fe3+_O2-_NOHA	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\,(\mathrm{Endothelium}) \cdot \mathrm{function\_for\_modified\_reactions}\,(\mathrm{k10}, [\mathrm{O2}], [\mathrm{Fe2\_\_NOHA}]) \quad (36)$$

$$\mathrm{function\_for\_modified\_reactions}\,(\mathrm{k}, \mathrm{modifier}, \mathrm{substrate}) = \mathrm{k} \cdot \mathrm{modifier} \cdot \mathrm{substrate} \quad (37)$$

$$\mathrm{function\_for\_modified\_reactions}\left(\mathrm{k}, \mathrm{modifier}, \mathrm{substrate}\right) = \mathrm{k} \cdot \mathrm{modifier} \cdot \mathrm{substrate} \tag{38}$$

7.15 Reaction `Fe3__NO_and_Citrulline_synthesis`

This is an irreversible reaction of one reactant forming two products.

Name Fe3+_NO and Citrulline synthesis

Reaction equation

$$\mathrm{Fe3\_\_O2\_\_NOHA} \longrightarrow \mathrm{Fe3\_\_NO} + \mathrm{Citrulline} \tag{39}$$

Reactant

Table 36: Properties of each reactant.

Id	Name	SBO
`Fe3__O2__NOHA`	Fe3+_O2-_NOHA	

Products

Table 37: Properties of each product.

Id	Name	SBO
`Fe3__NO`	Fe3+_NO	
`Citrulline`	Citrulline	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \mathrm{k11} \cdot [\mathrm{Fe3\_\_O2\_\_NOHA}] \tag{40}$$

7.16 Reaction `Fe2__NO_synthesis`

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

Name Fe2+_NO synthesis

Reaction equation

$$\mathrm{Fe3\_\_NO} \longrightarrow \mathrm{Fe2\_\_NO} \tag{41}$$

Reactant

Table 38: Properties of each reactant.

Id	Name	SBO
Fe3__NO	Fe3+_NO	

Product

Table 39: Properties of each product.

Id	Name	SBO
Fe2__NO	Fe2+_NO	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{vol}\,(\mathrm{Endothelium}) \cdot \mathrm{k12} \cdot [\mathrm{Fe3\_\_NO}] \tag{42}$$

7.17 Reaction Fe3__O2__NOHA_degradation

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

Name Fe3+_O2-_NOHA degradation

Reaction equation

$$\mathrm{Fe3\_\_O2\_\_NOHA} \longrightarrow \mathrm{Fe2\_\_NOHA} \tag{43}$$

Reactant

Table 40: Properties of each reactant.

Id	Name	SBO
Fe3__O2__NOHA	Fe3+_O2-_NOHA	

Product

Table 41: Properties of each product.

Id	Name	SBO
Fe2__NOHA	Fe2+_NOHA	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}\left(\mathrm{Endothelium}\right) \cdot \mathrm{k10\_prime} \cdot [\mathrm{Fe3\_\_O2\_\_NOHA}] \tag{44}$$

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.

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.

8.1 Species `Arg`

Name Arg

Initial concentration $100\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

This species takes part in three reactions (as a reactant in `Fe3__Arg_synthesis`, `Fe2__Arg_synthesis_dissociation` and as a product in `Arginine_synthesis`), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t} \mathrm{Arg} = 0 \tag{45}$$

8.2 Species `Fe3__enos`

Name Fe3+(enos)

Initial concentration $0.015\ \mu\mathrm{mol} \cdot \mathrm{ml}^{-1}$

This species takes part in five reactions (as a reactant in `Fe3__Arg_synthesis`, `Fe2__formation` and as a product in `Fe3__and_NO_formation`, `Fe3__formation`, `Fe3__NOHA_formation_degradation`).

$$\frac{\mathrm{d}}{\mathrm{d}t} \mathrm{Fe3\_\_enos} = v_5 + v_6 + v_7 - v_1 - v_4 \tag{46}$$

8.3 Species Fe3__Arg

Name Fe3+_Arg

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

This species takes part in two reactions (as a reactant in Fe2__Arg_formation and as a product in Fe3__Arg_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Fe3\_\_Arg} = v_1 - v_8 \tag{47}$$

8.4 Species Fe2

Name Fe2+

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

This species takes part in three reactions (as a reactant in Fe2__Arg_synthesis_dissociation and as a product in Fe2__formation, Fe2__NOHA_formation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Fe2} = v_4 + v_9 - v_2 \tag{48}$$

8.5 Species Fe2__Arg

Name Fe2+_Arg

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

This species takes part in four reactions (as a reactant in Fe3__O2_Arg_formation_with_Oxygen_activation and as a product in Fe2__Arg_synthesis_dissociation, Fe2__Arg_formation, Fe3__O2_Arg_degradation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Fe2\_\_Arg} = v_2 + v_8 + v_{11} - v_{10} \tag{49}$$

8.6 Species Fe3__NO

Name Fe3+_NO

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

This species takes part in three reactions (as a reactant in Fe3__and_NO_formation, Fe2__NO_synthesis and as a product in Fe3__NO_and_Citrulline_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Fe3\_\_NO} = v_{15} - v_5 - v_{16} \tag{50}$$

8.7 Species NO

Name NO

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

This species takes part in one reaction (as a product in Fe3__and_NO_formation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NO} = v_5 \tag{51}$$

8.8 Species Fe2__NO

Name Fe2+_NO

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

This species takes part in two reactions (as a reactant in Fe3__formation and as a product in Fe2__NO_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Fe2\_\_NO} = v_{16} - v_6 \tag{52}$$

8.9 Species Fe3__NOHA

Name Fe3+_NOHA

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

This species takes part in three reactions (as a reactant in Fe3__NOHA_formation_degradation, Fe2__NOHA_synthesis and as a product in Fe3__NOHA_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Fe3\_\_NOHA} = v_{12} - v_7 - v_{13} \tag{53}$$

8.10 Species NOHA

Name NOHA

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

This species takes part in two reactions (as a product in Fe3__NOHA_formation_degradation, Fe2__NOHA_formation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NOHA} = v_7 + v_9 \tag{54}$$

8.11 Species Fe2__NOHA

Name Fe2+_NOHA

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

This species takes part in four reactions (as a reactant in Fe2__NOHA_formation, Fe3__O2__NOHA_synthesis_with_Oxygen_activation and as a product in Fe2__NOHA_synthesis, Fe3__O2__NOHA_degradation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Fe2\_\_NOHA} = v_{13} + v_{17} - v_{9} - v_{14} \tag{55}$$

8.12 Species O2

Name O2

Initial concentration $150\ \mu\text{mol} \cdot \text{ml}^{-1}$

This species takes part in three reactions (as a modifier in Fe3__formation, Fe3__O2_Arg_formation_with_Oxygen_activation, Fe3__O2__NOHA_synthesis_with_Oxygen_activation), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{O2} = 0 \tag{56}$$

8.13 Species Fe3__O2__Arg

Name Fe3+_O2-_Arg

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

This species takes part in three reactions (as a reactant in Fe3__O2_Arg_degradation, Fe3__NOHA_synthesis and as a product in Fe3__O2_Arg_formation_with_Oxygen_activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Fe3\_\_O2\_\_Arg} = v_{10} - v_{11} - v_{12} \tag{57}$$

8.14 Species Fe3__O2__NOHA

Name Fe3+_O2-_NOHA

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

This species takes part in three reactions (as a reactant in Fe3__NO_and_Citrulline_synthesis, Fe3__O2__NOHA_degradation and as a product in Fe3__O2__NOHA_synthesis_with_Oxygen_activation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Fe3\_\_O2\_\_NOHA} = v_{14} - v_{15} - v_{17} \tag{58}$$

8.15 Species Citrulline

Name Citrulline

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

This species takes part in one reaction (as a product in Fe3_NO_and_Citrulline_synthesis).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Citrulline} = v_{15} \tag{59}$$

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