**SBML Model Report**

# Model name: "Chen2007_NeuronalEndothelialNOS"

SBML2LaTeX

May 6, 2016

## 1 General Overview

This is a document in SBML Level 2 Version 3 format. 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 | 0 |
| events | 0 | constraints | 0 |
| reactions | 0 | function definitions | 0 |
| global parameters | 35 | unit definitions | 4 |
| rules | 15 | initial assignments | 0 |

### Model Notes

This a model from the article:
**Vascular and perivascular nitric oxide release and transport: biochemical pathways of neuronal nitric oxide synthase (NOS1) and endothelial nitric oxide synthase (NOS3).**
Chen K, Popel AS Free Radic Biol Med. 2007 Mar 15;42(6):811-22. 17320763 ,
**Abstract:**
Nitric oxide (NO) derived from nitric oxide synthase (NOS) is an important paracrine effector that maintains vascular tone. The release of NO mediated by NOS isozymes under various O(2) conditions critically determines the NO bioavailability in tissues. Because of experimental difficulties, there has been no direct information on how enzymatic NO production and distribution

change around arterioles under various oxygen conditions. In this study, we used computational models based on the analysis of biochemical pathways of enzymatic NO synthesis and the availability of NOS isozymes to quantify the NO production by neuronal NOS (NOS1) and endothelial NOS (NOS3). We compared the catalytic activities of NOS1 and NOS3 and their sensitivities to the concentration of substrate O(2). Based on the NO release rates predicted from kinetic models, the geometric distribution of NO sources, and mass balance analysis, we predicted the NO concentration profiles around an arteriole under various O(2) conditions. The results indicated that NOS1-catalyzed NO production was significantly more sensitive to ambient O(2) concentration than that catalyzed by NOS3. Also, the high sensitivity of NOS1 catalytic activity to O(2) was associated with significantly reduced NO production and therefore NO concentrations, upon hypoxia. Moreover, the major source determining the distribution of NO was NOS1, which was abundantly expressed in the nerve fibers and mast cells close to arterioles, rather than NOS3, which was expressed in the endothelium. Finally, the perivascular NO concentration predicted by the models under conditions of normoxia was paradoxically at least an order of magnitude lower than a number of experimental measurements, suggesting a higher abundance of NOS1 or NOS3 and/or the existence of other enzymatic or nonenzymatic sources of NO in the microvasculature.

This model was taken from the CellML repository and automatically converted to SBML.
The original model was: **Chen K, Popel AS (2007) - version02**
The original CellML model was created by:
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To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler L, Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novre N, Laibe C (2010) BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

## 2 Unit Definitions

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

### 2.1 Unit micromolar

**Name** micromolar

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

### 2.2 Unit first_order_rate_constant

**Name** first_order_rate_constant

**Definition** $\text{s}^{-1}$

### 2.3 Unit second_order_rate_constant

**Name** second_order_rate_constant

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

### 2.4 Unit micromolar_per_second

**Name** micromolar_per_second

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

### 2.5 Unit substance

**Notes** Mole is the predefined SBML unit for `substance`.

**Definition** mol

### 2.6 Unit volume

**Notes** Litre is the predefined SBML unit for `volume`.

**Definition** l

### 2.7 Unit area

**Notes** Square metre is the predefined SBML unit for `area` since SBML Level 2 Version 1.

**Definition** $\text{m}^2$

### 2.8 Unit length

**Notes** Metre is the predefined SBML unit for `length` since SBML Level 2 Version 1.

**Definition** m

## 2.9 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 | | | 3 | 1 | | ☑ | |

## 3.1 Compartment Compartment

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

# 4 Parameters

This model contains 35 global parameters.

Table 3: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| Fe3 | Fe3 | | 0.30 | $\mu mol \cdot l^{-1}$ | ☐ |
| Fe3_Arg | Fe3_Arg | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| Fe2 | Fe2 | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| Fe2_Arg | Fe2_Arg | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| Fe3_02_Arg | Fe3_O2_Arg | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| Fe3_NOHA | Fe3_NOHA | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| Fe2_NOHA | Fe2_NOHA | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| Fe3_02_NOHA | Fe3_O2_NOHA | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| Fe3_NO | Fe3_NO | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| Fe2_NO | Fe2_NO | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| NO | NO | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| dNOdt | dNOdt | | 0.00 | $\mu mol \cdot l^{-1} \cdot s^{-1}$ | ☐ |
| citrulline | citrulline | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| NO3 | NO3 | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| NOHA | NOHA | | 0.00 | $\mu mol \cdot l^{-1}$ | ☐ |
| 02 | O2 | | 100.00 | $\mu mol \cdot l^{-1}$ | ☑ |

| Id | Name | SBO | Value | Unit | Constant |
|---|---|---|---|---|---|
| Arg | Arg | | 100.00 | $\mu mol \cdot l^{-1}$ | ☑ |
| k1 | k1 | | 6.60 | $s^{-1} \cdot \mu mol^{-1} \cdot l$ | ☑ |
| k_1 | k_1 | | 6.60 | $s^{-1}$ | ☑ |
| k2 | k2 | | 20.80 | $s^{-1}$ | ☑ |
| k3 | k3 | | 20.80 | $s^{-1}$ | ☑ |
| k4 | k4 | | 6.60 | $s^{-1} \cdot \mu mol^{-1} \cdot l$ | ☑ |
| k_4 | k_4 | | 6.60 | $s^{-1}$ | ☑ |
| k5 | k5 | | 8.50 | $s^{-1} \cdot \mu mol^{-1} \cdot l$ | ☑ |
| k_5 | k_5 | | 215.60 | $s^{-1}$ | ☑ |
| k6 | k6 | | 175.60 | $s^{-1}$ | ☑ |
| k7 | k7 | | 20.80 | $s^{-1}$ | ☑ |
| k8 | k8 | | 13.20 | $s^{-1} \cdot \mu mol^{-1} \cdot l$ | ☑ |
| k_8 | k_8 | | 13.20 | $s^{-1}$ | ☑ |
| k9 | k9 | | 8.60 | $s^{-1} \cdot \mu mol^{-1} \cdot l$ | ☑ |
| k_9 | k_9 | | 399.20 | $s^{-1}$ | ☑ |
| k10 | k10 | | 39.10 | $s^{-1}$ | ☑ |
| k11 | k11 | | 20.80 | $s^{-1}$ | ☑ |
| k12 | k12 | | 0.01 | $s^{-1} \cdot \mu mol^{-1} \cdot l$ | ☑ |
| k13 | k13 | | 39.90 | $s^{-1}$ | ☑ |

## 5 Rules

This is an overview of 15 rules.

### 5.1 Rule Fe3

Rule Fe3 is a rate rule for parameter Fe3:

$$\frac{d}{dt}\text{Fe3} = \text{k\_1} \cdot \text{Fe3\_Arg} + \text{k13} \cdot \text{Fe3\_NO} + \text{k12} \cdot \text{Fe2\_NO} \cdot \text{O2} - (\text{k1} \cdot \text{Arg} \cdot \text{Fe3} + \text{k2} \cdot \text{Fe3}) \quad (1)$$

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

### 5.2 Rule Fe3_Arg

Rule Fe3_Arg is a rate rule for parameter Fe3_Arg:

$$\frac{d}{dt}\text{Fe3\_Arg} = \text{k1} \cdot \text{Fe3} \cdot \text{Arg} - (\text{k\_1} \cdot \text{Fe3\_Arg} + \text{k3} \cdot \text{Fe3\_Arg}) \quad (2)$$

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

### 5.3 Rule Fe2

Rule Fe2 is a rate rule for parameter Fe2:

$$\frac{d}{dt}\mathrm{Fe2} = \mathrm{k2} \cdot \mathrm{Fe3} + \mathrm{k\_4} \cdot \mathrm{Fe2\_Arg} - \mathrm{k4} \cdot \mathrm{Fe2} \cdot \mathrm{Arg} \tag{3}$$

**Derived unit** $\mathrm{s}^{-1} \cdot \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$

### 5.4 Rule Fe2_Arg

Rule Fe2_Arg is a rate rule for parameter Fe2_Arg:

$$\frac{d}{dt}\mathrm{Fe2\_Arg} = \mathrm{k3} \cdot \mathrm{Fe3\_Arg} + \mathrm{k\_5} \cdot \mathrm{Fe3\_O2\_Arg} + \mathrm{k4} \cdot \mathrm{Fe2} \cdot \mathrm{Arg} - (\mathrm{k5} \cdot \mathrm{Fe2\_Arg} \cdot \mathrm{O2} + \mathrm{k\_4} \cdot \mathrm{Fe2\_Arg}) \tag{4}$$

**Derived unit** $\mathrm{s}^{-1} \cdot \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$

### 5.5 Rule Fe3_O2_Arg

Rule Fe3_O2_Arg is a rate rule for parameter Fe3_O2_Arg:

$$\frac{d}{dt}\mathrm{Fe3\_O2\_Arg} = \mathrm{k5} \cdot \mathrm{Fe2\_Arg} \cdot \mathrm{O2} - (\mathrm{k6} \cdot \mathrm{Fe3\_O2\_Arg} + \mathrm{k\_5} \cdot \mathrm{Fe3\_O2\_Arg}) \tag{5}$$

**Derived unit** $\mathrm{s}^{-1} \cdot \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$

### 5.6 Rule Fe3_NOHA

Rule Fe3_NOHA is a rate rule for parameter Fe3_NOHA:

$$\frac{d}{dt}\mathrm{Fe3\_NOHA} = \mathrm{k6} \cdot \mathrm{Fe3\_O2\_Arg} - \mathrm{k7} \cdot \mathrm{Fe3\_NOHA} \tag{6}$$

**Derived unit** $\mathrm{s}^{-1} \cdot \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$

### 5.7 Rule Fe2_NOHA

Rule Fe2_NOHA is a rate rule for parameter Fe2_NOHA:

$$\frac{d}{dt}\mathrm{Fe2\_NOHA} = \mathrm{k7} \cdot \mathrm{Fe3\_NOHA} + \mathrm{k\_9} \cdot \mathrm{Fe3\_O2\_NOHA} + \mathrm{k8} \cdot \mathrm{Fe2} \cdot \mathrm{NOHA} - (\mathrm{k\_8} \cdot \mathrm{Fe2\_NOHA} + \mathrm{k9} \cdot \mathrm{Fe2\_NOHA} \cdot \mathrm{O2}) \tag{7}$$

**Derived unit** $\mathrm{s}^{-1} \cdot \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$

### 5.8 Rule Fe3_O2_NOHA

Rule Fe3_O2_NOHA is a rate rule for parameter Fe3_O2_NOHA:

$$\frac{d}{dt}\text{Fe3\_O2\_NOHA} = \text{k9} \cdot \text{Fe2\_NOHA} \cdot \text{O2} - (\text{k10} \cdot \text{Fe3\_O2\_NOHA} + \text{k\_9} \cdot \text{Fe3\_O2\_NOHA}) \quad (8)$$

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

### 5.9 Rule Fe3_NO

Rule Fe3_NO is a rate rule for parameter Fe3_NO:

$$\frac{d}{dt}\text{Fe3\_NO} = \text{k10} \cdot \text{Fe3\_O2\_NOHA} - (\text{k13} \cdot \text{Fe3\_NO} + \text{k11} \cdot \text{Fe3\_NO}) \quad (9)$$

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

### 5.10 Rule Fe2_NO

Rule Fe2_NO is a rate rule for parameter Fe2_NO:

$$\frac{d}{dt}\text{Fe2\_NO} = \text{k11} \cdot \text{Fe3\_NO} - \text{k12} \cdot \text{Fe2\_NO} \cdot \text{O2} \quad (10)$$

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

### 5.11 Rule NO

Rule NO is a rate rule for parameter NO:

$$\frac{d}{dt}\text{NO} = \text{k13} \cdot \text{Fe3\_NO} \quad (11)$$

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

### 5.12 Rule citrulline

Rule citrulline is a rate rule for parameter citrulline:

$$\frac{d}{dt}\text{citrulline} = \text{k10} \cdot \text{Fe3\_O2\_NOHA} \quad (12)$$

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

### 5.13 Rule NO3

Rule NO3 is a rate rule for parameter NO3:

$$\frac{d}{dt}\text{NO3} = \text{k12} \cdot \text{Fe2\_NO} \cdot \text{O2} \quad (13)$$

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

### 5.14 Rule NOHA

Rule NOHA is a rate rule for parameter NOHA:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NOHA} = \mathrm{k\_8} \cdot \mathrm{Fe2\_NOHA} - \mathrm{k8} \cdot \mathrm{Fe2} \cdot \mathrm{NOHA} \tag{14}$$

**Derived unit** $\mathrm{s}^{-1} \cdot \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$

### 5.15 Rule dNOdt

Rule dNOdt is an assignment rule for parameter dNOdt:

$$\mathrm{dNOdt} = \mathrm{k13} \cdot \mathrm{Fe3\_NO} \tag{15}$$

**Derived unit** $\mathrm{s}^{-1} \cdot \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$