SBML Model Report

Model name: “Stone1996 - activation of soluble guanylate cyclase by nitric oxide”

March 3, 2017

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by the following four authors: Lukas Endler[1], Vijayalakshmi Chelliah[2], James R Stone[3] and Michael A Marletta[4] at October 21st 2008 at 3:19 p. m. and last time modified at May 16th 2012 at ten o’ clock in the morning. Table 1 gives 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	12
events	0	constraints	0
reactions	7	function definitions	0
global parameters	16	unit definitions	6
rules	3	initial assignments	0

Model Notes

Stone1996 - activation of soluble guanylatecyclase by nitric oxideThis features the two step binding ofNO to soluble Guanylyl Cyclase as proposed by StoneJR, Marletta MA. Biochemistry

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(1996) 35(4):1093-9 . There is afast step binding scheme and a slow step binding scheme. Thedifference lies in the binding of a NO to a non-heme site on sGC,which may not necessarily be the same site of binding during theinitial binding. The rates have been directly used models.

This model is described in the article:Spectral and kinetic studies on the activation of soluble guanylate cyclase by nitric oxide.Stone JR, Marletta MA.Biochemistry 1996 Jan; 35(4): 1093-1099

Abstract:

The soluble form of guanylate cyclase (sGC) is the only definitive receptor for the signaling agent nitric oxide (.NO). The enzyme is a heterodimer of homologous subunits in which each subunit binds 1 equiv of 5-coordinate high-spin heme. .NO increases the Vmax of sGC up to 400-fold and has previously been shown to bind to the heme to form a 5-coordinate complex. Using stopped-flow spectrophotometry, it is demonstrated that the binding of .NO to the heme of sGC is a complex process. .NO first binds to the heme to form a 6-coordinate nitrosyl complex, which then converts to a 5-coordinate nitrosyl complex through one of two ways. For 28 +/- 4% of the heme, the 6-coordinate nitrosyl complex rapidly (approximately 20 s-1) converts to the 5-coordinate complex. For the remaining 72 +/- 4% of the heme, the conversion of the 6-coordinate nitrosyl complex to a 5-coordinate nitrosyl complex is slow (0.1-1.0 s-1) and is dependent upon the interaction of .NO with an unidentified non-heme site on the protein. The heme (200 nM) was completely converted to the 5-coordinate state with as little as 500 nM .NO, and the equilibrium dissociation constant of .NO for activating the enzyme was determined to be < or = 250 nM. Gel-filtration analysis indicates that the binding of .NO to the heme has no effect on the native molecular mass of the protein. Correlation of electronic absorption spectra with activity measurements indicates that the 5-coordinate nitrosyl form of the enzyme is activated relative to the resting 5-coordinate ferrous form of the enzyme.

This model is hosted on BioModels Database and identified by: BIOMD0000000198.

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models.

2 Unit Definitions

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

2.1 Unit `substance`

Name micromole

Definition μmol

2.2 Unit peruMpersec

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

2.3 Unit uM

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

2.4 Unit persec

Definition s^{-1}

2.5 Unit peruMpercm

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

2.6 Unit percm

Definition cm^{-1}

2.7 Unit volume

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

Definition 1

2.8 Unit area

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

Definition m^2

2.9 Unit length

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

Definition m

2.10 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
`cytosol`			3	1	litre	☑	

3.1 Compartment `cytosol`

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

4 Species

This model contains twelve 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 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
NO		cytosol	$\mu mol \cdot l^{-1}$	⊟	☑
sGCfast		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
NO_sGCfast		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
NO_sGCfast_6coord		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
NO_sGCfast_5coord		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
sGCslow		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
NO_sGCslow		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
NO_sGCslow_6coord		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
NO_sGCslow_6coord_NO_int		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
NO_sGCslow_5coord		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
NO_sGC_5coord_tot		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟
sGC_inact_tot		cytosol	$\mu mol \cdot l^{-1}$	⊟	⊟

5 Parameters

This model contains 16 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		700.000	$1 \cdot \mu mol^{-1} \cdot s^{-1}$	☑
k2	k2		800.000	s^{-1}	☑
k3	k3		850.000	s^{-1}	☑
k4	k4		20.000	s^{-1}	☑
k5	k5		0.200	s^{-1}	☑
k6	k6		700.000	$1 \cdot \mu mol^{-1} \cdot s^{-1}$	☑
k7	k7		800.000	s^{-1}	☑
k8	k8		850.000	s^{-1}	☑
k9	k9		5.000	$1 \cdot \mu mol^{-1} \cdot s^{-1}$	☑
k10	k10		25.000	s^{-1}	☑
k11	k11		1.600	s^{-1}	☑
k12	k12		0.020	s^{-1}	☑
e5c	ext_5coord		0.110	$1 \cdot \mu mol^{-1} \cdot cm^{-1}$	☑
e5c_NO	ext_5coord_NO		0.025	$1 \cdot \mu mol^{-1} \cdot cm^{-1}$	☑
e6c_NO	ext_6coord_NO		0.064	$1 \cdot \mu mol^{-1} \cdot cm^{-1}$	☑
ext	extinction		0.000	cm^{-1}	☐

6 Rules

This is an overview of three rules.

6.1 Rule NO_sGC_5coord_tot

Rule NO_sGC_5coord_tot is an assignment rule for species NO_sGC_5coord_tot:

$$\text{NO\_sGC\_5coord\_tot} = [\text{NO\_sGCfast\_5coord}] + [\text{NO\_sGCslow\_5coord}] \quad (1)$$

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

6.2 Rule sGC_inact_tot

Rule sGC_inact_tot is an assignment rule for species sGC_inact_tot:

$$\begin{aligned}\text{sGC\_inact\_tot} = {} & [\text{sGCfast}] + [\text{NO\_sGCfast}] + [\text{NO\_sGCfast\_6coord}] + [\text{sGCslow}] \\ & + [\text{NO\_sGCslow}] + [\text{NO\_sGCslow\_6coord}] + [\text{NO\_sGCslow\_6coord\_NO\_int}]\end{aligned} \quad (2)$$

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

6.3 Rule `ext`

Rule `ext` is an assignment rule for parameter `ext`:

$$\begin{aligned}\text{ext} = {} & \text{e5c} \cdot ([\text{sGCfast}] + [\text{NO\_sGCfast}] + [\text{sGCslow}] + [\text{NO\_sGCslow}]) \\ & + \text{e5c\_NO} \cdot ([\text{NO\_sGCfast\_5coord}] + [\text{NO\_sGCslow\_5coord}]) + \text{e6c\_NO} \\ & \cdot ([\text{NO\_sGCfast\_6coord}] + [\text{NO\_sGCslow\_6coord}] + [\text{NO\_sGCslow\_6coord\_NO\_int}])\end{aligned} \tag{3}$$

Derived unit cm^{-1}

7 Reactions

This model contains seven 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	r1fast	r1fast	$NO + sGCfast \rightleftharpoons NO\_sGCfast$	0000177
2	r2fast	r2fast	$NO\_sGCfast \longrightarrow NO\_sGCfast\_6coord$	0000181
3	r3fast	r3fast	$NO\_sGCfast\_6coord \rightleftharpoons NO\_sGCfast\_5coord$	0000181
4	r1slow	r1slow	$NO + sGCslow \rightleftharpoons NO\_sGCslow$	0000177
5	r2slow	r2slow	$NO\_sGCslow \longrightarrow NO\_sGCslow\_6coord$	0000181
6	r3slow	r3slow	$NO + NO\_sGCslow\_6coord \rightleftharpoons NO\_sGCslow\_6coord\_NO\_int$	0000177
7	r4slow	r4slow	$NO\_sGCslow\_6coord\_NO\_int \rightleftharpoons NO\_sGCslow\_5coord$	0000181

7.1 Reaction r1fast

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

Name r1fast

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{NO} + \mathrm{sGCfast} \rightleftharpoons \mathrm{NO\_sGCfast} \tag{4}$$

Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
NO		
sGCfast		

Product

Table 7: Properties of each product.

Id	Name	SBO
NO_sGCfast		

Kinetic Law

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

$$v_1 = \mathrm{vol}\,(\mathrm{cytosol}) \cdot (\mathrm{k1} \cdot [\mathrm{NO}] \cdot [\mathrm{sGCfast}] - \mathrm{k2} \cdot [\mathrm{NO\_sGCfast}]) \tag{5}$$

7.2 Reaction r2fast

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

Name r2fast

SBO:0000181 conformational transition

Reaction equation

$$\mathrm{NO\_sGCfast} \longrightarrow \mathrm{NO\_sGCfast\_6coord} \tag{6}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
NO_sGCfast		

Product

Table 9: Properties of each product.

Id	Name	SBO
NO_sGCfast_6coord		

Kinetic Law

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

$$v_2 = \mathrm{k3} \cdot \mathrm{vol}\,(\mathrm{cytosol}) \cdot [\mathrm{NO\_sGCfast}] \tag{7}$$

7.3 Reaction r3fast

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

Name r3fast

SBO:0000181 conformational transition

Reaction equation

$$\mathrm{NO\_sGCfast\_6coord} \rightleftharpoons \mathrm{NO\_sGCfast\_5coord} \tag{8}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
NO_sGCfast_6coord		

Product

Table 11: Properties of each product.

Id	Name	SBO
NO_sGCfast_5coord		

Kinetic Law

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

$$v_3 = \mathrm{vol}(\mathrm{cytosol}) \cdot (\mathrm{k4} \cdot [\mathrm{NO\_sGCfast\_6coord}] - \mathrm{k5} \cdot [\mathrm{NO\_sGCfast\_5coord}]) \tag{9}$$

7.4 Reaction r1slow

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

Name r1slow

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{NO} + \mathrm{sGCslow} \rightleftharpoons \mathrm{NO\_sGCslow} \tag{10}$$

Reactants

Table 12: Properties of each reactant.

Id	Name	SBO
NO		
sGCslow		

Product

Table 13: Properties of each product.

Id	Name	SBO
NO_sGCslow		

Kinetic Law

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

$$v_4 = \mathrm{vol}(\mathrm{cytosol}) \cdot (\mathrm{k6} \cdot [\mathrm{NO}] \cdot [\mathrm{sGCslow}] - \mathrm{k7} \cdot [\mathrm{NO\_sGCslow}]) \tag{11}$$

7.5 Reaction r2slow

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

Name r2slow

SBO:0000181 conformational transition

Reaction equation

$$\mathrm{NO\_sGCslow} \longrightarrow \mathrm{NO\_sGCslow\_6coord} \tag{12}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
NO_sGCslow		

Product

Table 15: Properties of each product.

Id	Name	SBO
NO_sGCslow_6coord		

Kinetic Law

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

$$v_5 = \mathrm{k8} \cdot \mathrm{vol}\,(\mathrm{cytosol}) \cdot [\mathrm{NO\_sGCslow}] \tag{13}$$

7.6 Reaction r3slow

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

Name r3slow

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{NO} + \mathrm{NO\_sGCslow\_6coord} \rightleftharpoons \mathrm{NO\_sGCslow\_6coord\_NO\_int} \tag{14}$$

Reactants

Table 16: Properties of each reactant.

Id	Name	SBO
NO		
NO_sGCslow_6coord		

Product

Table 17: Properties of each product.

Id	Name	SBO
NO_sGCslow_6coord_NO_int		

Kinetic Law

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

$$v_6 = \mathrm{vol}\,(\mathrm{cytosol}) \cdot (\mathrm{k9} \cdot [\mathrm{NO}] \cdot [\mathrm{NO\_sGCslow\_6coord}] - \mathrm{k10} \cdot [\mathrm{NO\_sGCslow\_6coord\_NO\_int}]) \tag{15}$$

7.7 Reaction r4slow

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

Name r4slow

SBO:0000181 conformational transition

Reaction equation

$$\mathrm{NO\_sGCslow\_6coord\_NO\_int} \rightleftharpoons \mathrm{NO\_sGCslow\_5coord} \tag{16}$$

Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
NO_sGCslow_6coord_NO_int		

Product

Table 19: Properties of each product.

Id	Name	SBO
NO_sGCslow_5coord		

Kinetic Law

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

$$v_7 = \mathrm{vol}\,(\mathrm{cytosol}) \cdot (\mathrm{k11} \cdot [\mathrm{NO\_sGCslow\_6coord\_NO\_int}] - \mathrm{k12} \cdot [\mathrm{NO\_sGCslow\_5coord}]) \quad (17)$$

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.

8.1 Species NO

SBO:0000247 simple chemical

Initial concentration $0.5\ \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in r1fast, r1slow, r3slow), which do not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NO} = 0 \quad (18)$$

8.2 Species sGCfast

SBO:0000297 protein complex

Initial concentration $0.112\ \mu\mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in one reaction (as a reactant in r1fast).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{sGCfast} = -v_1 \quad (19)$$

8.3 Species NO_sGCfast

SBO:0000297 protein complex

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

This species takes part in two reactions (as a reactant in r2fast and as a product in r1fast).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{NO\_sGCfast} = v_1 - v_2 \quad (20)$$

8.4 Species NO_sGCfast_6coord

SBO:0000297 protein complex

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

This species takes part in two reactions (as a reactant in r3fast and as a product in r2fast).

$$\frac{\text{d}}{\text{d}t}\text{NO\_sGCfast\_6coord} = v_2 - v_3 \tag{21}$$

8.5 Species NO_sGCfast_5coord

SBO:0000297 protein complex

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

This species takes part in one reaction (as a product in r3fast).

$$\frac{\text{d}}{\text{d}t}\text{NO\_sGCfast\_5coord} = v_3 \tag{22}$$

8.6 Species sGCslow

SBO:0000297 protein complex

Initial concentration $0.288\ \mu\text{mol}\cdot\text{l}^{-1}$

This species takes part in one reaction (as a reactant in r1slow).

$$\frac{\text{d}}{\text{d}t}\text{sGCslow} = -v_4 \tag{23}$$

8.7 Species NO_sGCslow

SBO:0000297 protein complex

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

This species takes part in two reactions (as a reactant in r2slow and as a product in r1slow).

$$\frac{\text{d}}{\text{d}t}\text{NO\_sGCslow} = v_4 - v_5 \tag{24}$$

8.8 Species NO_sGCslow_6coord

SBO:0000297 protein complex

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

This species takes part in two reactions (as a reactant in r3slow and as a product in r2slow).

$$\frac{\text{d}}{\text{d}t}\text{NO\_sGCslow\_6coord} = v_5 - v_6 \tag{25}$$

8.9 Species NO_sGCslow_6coord_NO_int

SBO:0000297 protein complex

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

This species takes part in two reactions (as a reactant in r4slow and as a product in r3slow).

$$\frac{\text{d}}{\text{d}t}\text{NO\_sGCslow\_6coord\_NO\_int} = v_6 - v_7 \tag{26}$$

8.10 Species NO_sGCslow_5coord

SBO:0000297 protein complex

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

This species takes part in one reaction (as a product in r4slow).

$$\frac{\text{d}}{\text{d}t}\text{NO\_sGCslow\_5coord} = v_7 \tag{27}$$

8.11 Species NO_sGC_5coord_tot

SBO:0000297 protein complex

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

Involved in rule NO_sGC_5coord_tot

One rule which determines this species' quantity.

8.12 Species sGC_inact_tot

SBO:0000297 protein complex

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

Involved in rule sGC_inact_tot

One rule which determines this species' quantity.

A Glossary of Systems Biology Ontology Terms

SBO:0000177 non-covalent binding: Interaction between several biochemical entities that results in the formation of a non-covalent comple

SBO:0000181 conformational transition: Biochemical reaction that does not result in the modification of covalent bonds of reactants, but rather modifies the conformation of some reactants, that is the relative position of their atoms in space

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

SBO:0000297 protein complex: Macromolecular complex containing one or more polypeptide chains possibly associated with simple chemicals. CHEBI:3608

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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