SBML Model Report

Model name: "Kyrylov2005_HPAaxis"

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	44	unit definitions	6
rules	20	initial assignments	0

Model Notes

This a model from the article:
Modeling robust oscillatory behavior of the hypothalamic-pituitary-adrenal axis.
Kyrylov V, Severyanova LA, Vieira A. IEEE Trans Biomed Eng. 2005 Dec;52(12):1977-83. 16366221 ,
Abstract:
A mathematical model of the hypothalamic-pituitary-adrenal (HPA) axis of the human endocrine system is proposed. This new model provides an improvement over previous models by introducing two nonlinear factors with physiological relevance: 1) a limit to gland size; 2) rejection of negative hormone concentrations. The result is that the new model is by far the most robust;

e.g., it can tolerate at least -50% and +100% perturbations to any of its parameters. This high degree of robustness allows one, for the first time, to model features of the system such as circadian rhythm and response to hormone injections. In addition, relative to its closest predecessor, the model is simpler; it contains only about half of the parameters, and yet achieves more functions. The new model provides opportunities for teaching endocrinology within a biological or medical school context; it may also have applications in modeling and studying HPA axis disorders, for example, related to gland size dynamics, abnormal hormone levels, or stress influences.

This model was taken from the CellML repository and automatically converted to SBML.
The original model was: **Kyrylov V, Severyanova LA, Vieira A. (2005) - version02**
The original CellML model was created by:
Lloyd, Catherine, May
c.lloyd@aukland.ac.nz
The University of Auckland
The Bioengineering Institute

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

2.1 Unit `minute`

Name minute

Definition 60 s

2.2 Unit `hour`

Name hour

Definition 3600 s

2.3 Unit `microg_l`

Name microg_l

Definition $\mu g \cdot l^{-1}$

2.4 Unit `microg_l_min`

Name microg_l_min

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

2.5 Unit `first_order_rate_constant`

Name first_order_rate_constant

Definition $(60\ s)^{-1}$

2.6 Unit `time`

Name minute

Definition 60 s

2.7 Unit `substance`

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

Definition mol

2.8 Unit `volume`

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

Definition l

2.9 Unit `area`

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

Definition m^2

2.10 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			3	1		☑	

3.1 Compartment Compartment

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

4 Parameters

This model contains 44 global parameters.

Table 3: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
y0	y0		0.400	$\mu g \cdot l^{-1}$	⊟
g0	g0		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
r0	r0		0.000	dimensionless	⊟
h0	h0		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
S0	S0		0.010	dimensionless	☑
y1	y1		1.400	$\mu g \cdot l^{-1}$	⊟
g1	g1		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
r1	r1		0.000	dimensionless	⊟
h1	h1		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
S1	S1		0.010	dimensionless	☑
y2	y2		1.170	$\mu g \cdot l^{-1}$	⊟
g2	g2		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
r2	r2		0.000	dimensionless	⊟
h2	h2		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
S2	S2		0.010	dimensionless	☑
y3	y3		0.950	$\mu g \cdot l^{-1}$	⊟
g3	g3		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
r3	r3		0.000	dimensionless	⊟
h3	h3		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
S3	S3		0.010	dimensionless	☑
y4	y4		0.650	$\mu g \cdot l^{-1}$	⊟

Id	Name	SBO	Value	Unit	Constant
g4	g4		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
r4	r4		0.000	dimensionless	⊟
h4	h4		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	⊟
S4	S4		0.010	dimensionless	☑
a00	a00		−0.008	$(60\ s)^{-1}$	☑
a02	a02		−0.440	$(60\ s)^{-1}$	☑
a10	a10		0.082	$(60\ s)^{-1}$	☑
a11	a11		−0.004	$(60\ s)^{-1}$	☑
a12	a12		−0.067	$(60\ s)^{-1}$	☑
a20	a20		0.000	$(60\ s)^{-1}$	☑
a21	a21		0.031	$(60\ s)^{-1}$	☑
a22	a22		−0.096	$(60\ s)^{-1}$	☑
a23	a23		0.058	$(60\ s)^{-1}$	☑
a24	a24		$3.25 \cdot 10^{-4}$	$(60\ s)^{-1}$	☑
a32	a32		0.009	$(60\ s)^{-1}$	☑
a33	a33		−0.009	$(60\ s)^{-1}$	☑
a42	a42		$1.39 \cdot 10^{-4}$	$(60\ s)^{-1}$	☑
a44	a44		$-1.43 \cdot 10^{-4}$	$(60\ s)^{-1}$	☑
c0	c0		0.443	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	☑
e0	e0		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	☑
e1	e1		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	☑
e2	e2		0.000	$\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$	☑
epsilon	epsilon		0.500	$\mu g \cdot l^{-1}$	☑

5 Rules

This is an overview of 20 rules.

5.1 Rule y0

Rule y0 is a rate rule for parameter y0:

$$\frac{d}{dt} y0 = g0 + c0 + e0 \tag{1}$$

Derived unit $\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$

5.2 Rule y1

Rule y1 is a rate rule for parameter y1:

$$\frac{d}{dt} y1 = g1 + e1 \tag{2}$$

Derived unit $\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$

5.3 Rule y2

Rule y2 is a rate rule for parameter y2:

$$\frac{d}{dt} y2 = g2 + e2 \tag{3}$$

Derived unit $\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$

5.4 Rule y3

Rule y3 is a rate rule for parameter y3:

$$\frac{d}{dt} y3 = g3 \tag{4}$$

Derived unit $\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$

5.5 Rule y4

Rule y4 is a rate rule for parameter y4:

$$\frac{d}{dt} y4 = g4 \tag{5}$$

Derived unit $\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$

5.6 Rule g0

Rule g0 is an assignment rule for parameter g0:

$$g0 = h0 \cdot r0 \tag{6}$$

Derived unit $\mu g \cdot l^{-1} \cdot (60\ s)^{-1}$

5.7 Rule h0

Rule h0 is an assignment rule for parameter h0:

$$h0 = \begin{cases} \dfrac{a00 \cdot y0 + a02 \cdot y2}{1 + \frac{a00 \cdot y0 + a02 \cdot y2}{S0} \cdot \left(1 - \exp\left(\left(\frac{a00 \cdot y0 + a02 \cdot y2}{S0}\right)\right)\right)} & \text{if } a00 \cdot y0 + a02 \cdot y2 > 0 \\ a00 \cdot y0 + a02 \cdot y2 & \text{if } a00 \cdot y0 + a02 \cdot y2 \leq 0 \end{cases} \tag{7}$$

5.8 Rule r0

Rule r0 is an assignment rule for parameter r0:

$$\mathrm{r0} = \begin{cases} 1 - \exp\left(\dfrac{\mathrm{S0} \cdot \mathrm{y0}^2}{(\mathrm{a00} \cdot \mathrm{y0} + \mathrm{a02} \cdot \mathrm{y2}) \cdot (\mathrm{epsilon} - \mathrm{y0})^2}\right) & \text{if } (\mathrm{y0} < \mathrm{epsilon}) \wedge (\mathrm{a00} \cdot \mathrm{y0} + \mathrm{a02} \cdot \mathrm{y2} < 0) \\ 1 & \text{otherwise} \end{cases} \tag{8}$$

5.9 Rule g1

Rule g1 is an assignment rule for parameter g1:

$$\mathrm{g1} = \mathrm{h1} \cdot \mathrm{r1} \tag{9}$$

Derived unit $\mu\mathrm{g} \cdot \mathrm{l}^{-1} \cdot (60\ \mathrm{s})^{-1}$

5.10 Rule h1

Rule h1 is an assignment rule for parameter h1:

$$\mathrm{h1} = \begin{cases} \dfrac{\mathrm{a10} \cdot \mathrm{y0} + \mathrm{a11} \cdot \mathrm{y1} + \mathrm{a12} \cdot \mathrm{y2}}{1 + \frac{\mathrm{a10} \cdot \mathrm{y0} + \mathrm{a11} \cdot \mathrm{y1} + \mathrm{a12} \cdot \mathrm{y2}}{\mathrm{S1}} \cdot \left(1 - \exp\left(\left(\frac{\mathrm{a10} \cdot \mathrm{y0} + \mathrm{a11} \cdot \mathrm{y1} + \mathrm{a12} \cdot \mathrm{y2}}{\mathrm{S1}}\right)\right)\right)} & \text{if } \mathrm{a10} \cdot \mathrm{y0} + \mathrm{a11} \cdot \mathrm{y1} + \mathrm{a12} \cdot \mathrm{y2} > 0 \\ \mathrm{a10} \cdot \mathrm{y0} + \mathrm{a11} \cdot \mathrm{y1} + \mathrm{a12} \cdot \mathrm{y2} & \text{if } \mathrm{a10} \cdot \mathrm{y0} + \mathrm{a11} \cdot \mathrm{y1} + \mathrm{a12} \cdot \mathrm{y2} \leq 0 \end{cases} \tag{10}$$

5.11 Rule r1

Rule r1 is an assignment rule for parameter r1:

$$\mathrm{r1} = \begin{cases} 1 - \exp\left(\dfrac{\mathrm{S1} \cdot \mathrm{y1}^2}{(\mathrm{a10} \cdot \mathrm{y0} + \mathrm{a11} \cdot \mathrm{y1} + \mathrm{a12} \cdot \mathrm{y2}) \cdot (\mathrm{epsilon} - \mathrm{y1})^2}\right) & \text{if } (\mathrm{y1} < \mathrm{epsilon}) \wedge (\mathrm{a10} \cdot \mathrm{y0} + \mathrm{a11} \cdot \mathrm{y1} + \mathrm{a12} \\ 1 & \text{otherwise} \end{cases} \tag{11}$$

5.12 Rule g2

Rule g2 is an assignment rule for parameter g2:

$$\mathrm{g2} = \mathrm{h2} \cdot \mathrm{r2} \tag{12}$$

Derived unit $\mu\mathrm{g} \cdot \mathrm{l}^{-1} \cdot (60\ \mathrm{s})^{-1}$

5.13 Rule h2

Rule h2 is an assignment rule for parameter h2:

$$\mathrm{h2} = \begin{cases} \dfrac{\mathrm{a20}\cdot\mathrm{y0}+\mathrm{a21}\cdot\mathrm{y1}+\mathrm{a22}\cdot\mathrm{y2}+\mathrm{a23}\cdot\mathrm{y3}+\mathrm{a24}\cdot\mathrm{y4}}{1+\frac{\mathrm{a20}\cdot\mathrm{y0}+\mathrm{a21}\cdot\mathrm{y1}+\mathrm{a22}\cdot\mathrm{y2}+\mathrm{a23}\cdot\mathrm{y3}+\mathrm{a24}\cdot\mathrm{y4}}{\mathrm{S2}}\cdot\left(1-\exp\left(\left(\frac{\mathrm{a20}\cdot\mathrm{y0}+\mathrm{a21}\cdot\mathrm{y1}+\mathrm{a22}\cdot\mathrm{y2}+\mathrm{a23}\cdot\mathrm{y3}+\mathrm{a24}\cdot\mathrm{y4}}{\mathrm{S2}}\right)\right)\right)} & \text{if } \mathrm{a20}\cdot\mathrm{y0}+\mathrm{a21}\cdot\mathrm{y1}+ \\ \mathrm{a20}\cdot\mathrm{y0}+\mathrm{a21}\cdot\mathrm{y1}+\mathrm{a22}\cdot\mathrm{y2}+\mathrm{a23}\cdot\mathrm{y3}+\mathrm{a24}\cdot\mathrm{y4} & \text{if } \mathrm{a20}\cdot\mathrm{y0}+\mathrm{a21}\cdot\mathrm{y1}+ \end{cases} \tag{13}$$

5.14 Rule r2

Rule r2 is an assignment rule for parameter r2:

$$\mathrm{r2} = \begin{cases} 1-\exp\left(\dfrac{\mathrm{S2}\cdot\mathrm{y2}^2}{(\mathrm{a20}\cdot\mathrm{y0}+\mathrm{a21}\cdot\mathrm{y1}+\mathrm{a22}\cdot\mathrm{y2}+\mathrm{a23}\cdot\mathrm{y3}+\mathrm{a24}\cdot\mathrm{y4})\cdot(\mathrm{epsilon}-\mathrm{y2})^2}\right) & \text{if } (\mathrm{y2}<\mathrm{epsilon})\wedge(\mathrm{a20} \\ 1 & \text{otherwise} \end{cases} \tag{14}$$

5.15 Rule g3

Rule g3 is an assignment rule for parameter g3:

$$\mathrm{g3} = \mathrm{h3}\cdot\mathrm{r3} \tag{15}$$

Derived unit $\mu\mathrm{g}\cdot\mathrm{l}^{-1}\cdot(60\,\mathrm{s})^{-1}$

5.16 Rule h3

Rule h3 is an assignment rule for parameter h3:

$$\mathrm{h3} = \begin{cases} \dfrac{\mathrm{a32}\cdot\mathrm{y2}+\mathrm{a33}\cdot\mathrm{y3}}{1+\frac{\mathrm{a32}\cdot\mathrm{y2}+\mathrm{a33}\cdot\mathrm{y3}}{\mathrm{S3}}\cdot\left(1-\exp\left(\left(\frac{\mathrm{a32}\cdot\mathrm{y2}+\mathrm{a33}\cdot\mathrm{y3}}{\mathrm{S3}}\right)\right)\right)} & \text{if } \mathrm{a32}\cdot\mathrm{y2}+\mathrm{a33}\cdot\mathrm{y3}>0 \\ \mathrm{a32}\cdot\mathrm{y2}+\mathrm{a33}\cdot\mathrm{y3} & \text{if } \mathrm{a32}\cdot\mathrm{y2}+\mathrm{a33}\cdot\mathrm{y3}\leq 0 \end{cases} \tag{16}$$

5.17 Rule r3

Rule r3 is an assignment rule for parameter r3:

$$\mathrm{r3} = \begin{cases} 1-\exp\left(\dfrac{\mathrm{S3}\cdot\mathrm{y3}^2}{(\mathrm{a32}\cdot\mathrm{y2}+\mathrm{a33}\cdot\mathrm{y3})\cdot(\mathrm{epsilon}-\mathrm{y3})^2}\right) & \text{if } (\mathrm{y3}<\mathrm{epsilon})\wedge(\mathrm{a32}\cdot\mathrm{y2}+\mathrm{a33}\cdot\mathrm{y3}<0) \\ 1 & \text{otherwise} \end{cases} \tag{17}$$

5.18 Rule g4

Rule g4 is an assignment rule for parameter g4:

$$\mathrm{g4} = \mathrm{h4} \cdot \mathrm{r4} \tag{18}$$

Derived unit $\mu\mathrm{g} \cdot \mathrm{l}^{-1} \cdot (60\ \mathrm{s})^{-1}$

5.19 Rule h4

Rule h4 is an assignment rule for parameter h4:

$$\mathrm{h4} = \begin{cases} \dfrac{\mathrm{a42} \cdot \mathrm{y2} + \mathrm{a44} \cdot \mathrm{y4}}{1 + \frac{\mathrm{a42} \cdot \mathrm{y2} + \mathrm{a44} \cdot \mathrm{y4}}{\mathrm{S4}} \cdot \left(1 - \exp\left(\left(\frac{\mathrm{a42} \cdot \mathrm{y2} + \mathrm{a44} \cdot \mathrm{y4}}{\mathrm{S4}}\right)\right)\right)} & \text{if } \mathrm{a42} \cdot \mathrm{y2} + \mathrm{a44} \cdot \mathrm{y4} > 0 \\ \mathrm{a42} \cdot \mathrm{y2} + \mathrm{a44} \cdot \mathrm{y4} & \text{if } \mathrm{a42} \cdot \mathrm{y2} + \mathrm{a44} \cdot \mathrm{y4} \leq 0 \end{cases} \tag{19}$$

5.20 Rule r4

Rule r4 is an assignment rule for parameter r4:

$$\mathrm{r4} = \begin{cases} 1 - \exp\left(\dfrac{\mathrm{S4} \cdot \mathrm{y4}^2}{(\mathrm{a42} \cdot \mathrm{y2} + \mathrm{a44} \cdot \mathrm{y4}) \cdot (\mathrm{epsilon} - \mathrm{y4})^2}\right) & \text{if } (\mathrm{y4} < \mathrm{epsilon}) \wedge (\mathrm{a42} \cdot \mathrm{y2} + \mathrm{a44} \cdot \mathrm{y4} < 0) \\ 1 & \text{otherwise} \end{cases} \tag{20}$$

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.

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany