SBML Model Report

Model name: "Ehrenstein1997 - The choline-leakage hypothesis in Alzheimer's disease"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Audald Lloret i Villas[1] at October 20th 2014 at 1:38 p. m. and last time modified at March 17th 2015 at 5:01 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	3
events	0	constraints	0
reactions	4	function definitions	4
global parameters	4	unit definitions	3
rules	1	initial assignments	0

Model Notes

Ehrenstein1997 - The choline-leakagehypothesis in Alzheimer's disease

This model is described in the article:The choline-leakage hypothesis for the loss of acetylcholine in Alzheimer's disease.Ehrenstein G, Galdzicki Z, Lange GD.Biophys. J. 1997 Sep; 73(3): 1276-1280

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Abstract:

We present a hypothesis for the loss of acetylcholine in Alzheimer's disease that is based on two recent experimental results: that beta-amyloid causes leakage of choline across cell membranes and that decreased production of acetylcholine increases the production of beta-amyloid. According to the hypothesis, an increase in beta-amyloid concentration caused by proteolysis of the amyloid precursor protein results in an increase in the leakage of choline out of cells. This leads to a reduction in intracellular choline concentration and hence a reduction in acetylcholine production. The reduction in acetylcholine production, in turn, causes an increase in the concentration of beta-amyloid. The resultant positive feedback between decreased acetylcholine and increased beta-amyloid accelerates the loss of acetylcholine. We compare the predictions of the choline-leakage hypothesis with a number of experimental observations. We also approximate it with a pair of ordinary differential equations. The solutions of these equations indicate that the loss of acetylcholine is very sensitive to the initial rate of beta-amyloid production.

This model is hosted on BioModels Database and identified by: BIOMD0000000553.

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 five unit definitions of which two are predefined by SBML and not mentioned in the model.

2.1 Unit `volume`

Name volume

Definition ml

2.2 Unit `time`

Name time

Definition 86400 s

2.3 Unit `substance`

Name substance

Definition mmol

2.4 Unit `area`

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

Definition m^2

2.5 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
`Brain`	Brain		3	1	litre	☑	

3.1 Compartment `Brain`

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

Name Brain

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 9 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
`a`	a	`Brain`	$\text{mmol} \cdot \text{ml}^{-1}$	⊟	⊟
`b`	b	`Brain`	$\text{mmol} \cdot \text{ml}^{-1}$	⊟	⊟
`aRel`	aRel	`Brain`	$\text{mmol} \cdot \text{ml}^{-1}$	⊟	☑

5 Parameters

This model contains four global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.007		☑
k2	k2		0.330		☑
k3	k3		0.004		☑
k4	k4		0.010		☑

6 Function definitions

This is an overview of four function definitions.

6.1 Function definition Constant_flux__irreversible

Name Constant flux (irreversible)

Argument v

Mathematical Expression

$$v \tag{1}$$

6.2 Function definition Loss_of_intracellular_choline_0

Name Loss of intracellular choline

Arguments k1, [a], [b]

Mathematical Expression

$$k1 \cdot [a] \cdot [b] \tag{2}$$

6.3 Function definition Effect_of_extracellular_ACh_0

Name Effect of extracellular ACh

Arguments k3, [a]

Mathematical Expression

$$k3 \cdot [a] \tag{3}$$

6.4 Function definition Decrease_in_the_extracellular_concentration_of_beta_amyloid_0

Name Decrease in the extracellular concentration of beta-amyloid

Arguments k4, [b]

Mathematical Expression

$$k4 \cdot [b] \tag{4}$$

7 Rule

This is an overview of one rule.

7.1 Rule aRel

Rule aRel is an assignment rule for species aRel:

$$\mathrm{aRel} = \frac{[a]}{50} \tag{5}$$

8 Reactions

This model contains four 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	`Loss_of_intracellular_choline`	Loss of intracellular choline	$a \xrightarrow{b,\, a,\, b} \emptyset$	
2	`Abeta_formation_from_APP`	Abeta formation from APP	$\emptyset \longrightarrow b$	
3	`Effect_of_extracellular_ACh`	Effect of extracellular ACh	$b \xrightarrow{a,\, a} \emptyset$	
4	`Decrease_in_the_extracellular_concentration_of_beta_amyloid`	Decrease in the extracellular concentration of beta-amyloid	$b \xrightarrow{b} \emptyset$	

8.1 Reaction Loss_of_intracellular_choline

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

Name Loss of intracellular choline

Reaction equation

$$a \xrightarrow{b,\ a,\ b} \emptyset \tag{6}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
a	a	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
b	b	
a	a	
b	b	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \mathrm{vol}\left(\mathrm{Brain}\right) \cdot \mathrm{Loss\_of\_intracellular\_choline\_0}\left(\mathrm{k1}, [\mathrm{a}], [\mathrm{b}]\right) \tag{7}$$

$$\mathrm{Loss\_of\_intracellular\_choline\_0}\left(\mathrm{k1}, [\mathrm{a}], [\mathrm{b}]\right) = \mathrm{k1} \cdot [\mathrm{a}] \cdot [\mathrm{b}] \tag{8}$$

$$\mathrm{Loss\_of\_intracellular\_choline\_0}\left(\mathrm{k1}, [\mathrm{a}], [\mathrm{b}]\right) = \mathrm{k1} \cdot [\mathrm{a}] \cdot [\mathrm{b}] \tag{9}$$

8.2 Reaction Abeta_formation_from_APP

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

Name Abeta formation from APP

Reaction equation

$$\emptyset \longrightarrow \mathrm{b} \tag{10}$$

Product

Table 8: Properties of each product.

Id	Name	SBO
b	b	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\left(\mathrm{Brain}\right) \cdot \mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{k2}\right) \tag{11}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{12}$$

$$\mathrm{Constant\_flux\_\_irreversible}\left(\mathrm{v}\right) = \mathrm{v} \tag{13}$$

8.3 Reaction `Effect_of_extracellular_ACh`

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

Name Effect of extracellular ACh

Reaction equation

$$\mathrm{b} \xrightarrow{\mathrm{a},\,\mathrm{a}} \emptyset \tag{14}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
b	b	

Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
a	a	
a	a	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{Brain}\right) \cdot \mathrm{Effect\_of\_extracellular\_ACh\_0}\left(\mathrm{k3}, [\mathrm{a}]\right) \tag{15}$$

$$\mathrm{Effect\_of\_extracellular\_ACh\_0}\left(\mathrm{k3}, [\mathrm{a}]\right) = \mathrm{k3} \cdot [\mathrm{a}] \tag{16}$$

$$\mathrm{Effect\_of\_extracellular\_ACh\_0}\left(\mathrm{k3}, [\mathrm{a}]\right) = \mathrm{k3} \cdot [\mathrm{a}] \tag{17}$$

8.4 Reaction Decrease_in_the_extracellular_concentration_of_beta_amyloid

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

Name Decrease in the extracellular concentration of beta-amyloid

Reaction equation

$$\mathrm{b} \xrightarrow{\mathrm{b}} \emptyset \tag{18}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
b	b	

Modifier

Table 12: Properties of each modifier.

Id	Name	SBO
b	b	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}(\mathrm{Brain}) \cdot \mathrm{Decrease\_in\_the\_extracellular\_concentration\_of\_beta\_amyloid\_0}(\mathrm{k4}, [\mathrm{b}]) \tag{19}$$

$$\mathrm{Decrease\_in\_the\_extracellular\_concentration\_of\_beta\_amyloid\_0}(\mathrm{k4}, [\mathrm{b}]) = \mathrm{k4} \cdot [\mathrm{b}] \tag{20}$$

$$\mathrm{Decrease\_in\_the\_extracellular\_concentration\_of\_beta\_amyloid\_0}(\mathrm{k4}, [\mathrm{b}]) = \mathrm{k4} \cdot [\mathrm{b}] \tag{21}$$

9 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.

9.1 Species a

Name a

Notes `Extracellular concentration of Acetylcholine (ACh)`

Initial concentration $50 \ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$

This species takes part in four reactions (as a reactant in `Loss_of_intracellular_choline` and as a modifier in `Loss_of_intracellular_choline`, `Effect_of_extracellular_ACh`, `Effect_of_extracellular_ACh`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{a} = -v_1 \tag{22}$$

9.2 Species b

Name b

Notes `Extracellular concentration of -amyloid`

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

This species takes part in six reactions (as a reactant in Effect_of_extracellular_ACh, Decrease_in_the_extracellular_concentration_of_beta_amyloid and as a product in Abeta_formation_from_APP and as a modifier in Loss_of_intracellular_choline, Loss_of_intracellular_choline, Decrease_in_the_extracellular_concentration_of_beta_amyloid).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{b} = v_2 - v_3 - v_4 \tag{23}$$

9.3 Species aRel

Name aRel

Notes Relative concentration of Acetylcholine

Initial concentration $1 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule aRel

One rule determines the species' quantity.

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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