define@key

SBML Model Report

Model name: "Clarke2000 - One-hit model of cell death in neuronal degenerations"

September 9, 2014

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 August seventh 2014 at 11:59 a. m. and last time modified at September eighth 2014 at 1:29 p. m. 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	3
events	0	constraints	0
reactions	0	function definitions	0
global parameters	5	unit definitions	3
rules	3	initial assignments	0

Model Notes

Clarke2000 - One-hit model of cell death inneuronal degenerationsThis one-hit model fits differentneuronal-death associated diseases for different animalmodels.

This model is described in the article:A one-hit model of cell death in inherited neuronal degenerations.Clarke G, Collins RA, Leavitt BR, Andrews DF, Hayden MR, Lumsden CJ, McInnes RR.Nature 2000 Jul; 406(6792): 195-199

[1]EMBL-EBI, lloret@ebi.ac.uk

Abstract:

In genetic disorders associated with premature neuronal death, symptoms may not appear for years or decades. This delay in clinical onset is often assumed to reflect the occurrence of age-dependent cumulative damage. For example, it has been suggested that oxidative stress disrupts metabolism in neurological degenerative disorders by the cumulative damage of essential macromolecules. A prediction of the cumulative damage hypothesis is that the probability of cell death will increase over time. Here we show in contrast that the kinetics of neuronal death in 12 models of photoreceptor degeneration, hippocampal neurons undergoing excitotoxic cell death, a mouse model of cerebellar degeneration and Parkinson's and Huntington's diseases are all exponential and better explained by mathematical models in which the risk of cell death remains constant or decreases exponentially with age. These kinetics argue against the cumulative damage hypothesis; instead, the time of death of any neuron is random. Our findings are most simply accommodated by a 'one-hit' biochemical model in which mutation imposes a mutant steady state on the neuron and a single event randomly initiates cell death. This model appears to be common to many forms of neurodegeneration and has implications for therapeutic strategies.

This model is hosted on BioModels Database and identified by: BIOMD0000000538.

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 three of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 7 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
`ONLnr`	ONLnr	`Brain`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☑
`ONLpcd`	ONLpcd	`Brain`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☑
`ONLrom`	ONLrom	`Brain`	$\mathrm{mmol} \cdot \mathrm{ml}^{-1}$	☐	☑

5 Parameters

This model contains five global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Munr	Munr		0.278		☑
Mupcd	Mupcd		0.223		☑
Rrom	Rrom		0.103		☑
ONLrom_0	ONLrom		40.947		☑
Murom	Murom		0.071		☑

6 Rules

This is an overview of three rules.

6.1 Rule ONLrom

Rule ONLrom is an assignment rule for species ONLrom:

$$\mathrm{ONLrom} = \frac{\mathrm{ONLrom\_0} \cdot \exp\left(\frac{(\exp(\mathrm{Rrom} \cdot \mathrm{time}) - 1) \cdot \mathrm{Murom}}{\mathrm{Rrom}}\right) \cdot 100}{\mathrm{ONLrom\_0}} \tag{1}$$

6.2 Rule ONLnr

Rule ONLnr is a rate rule for species ONLnr:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ONLnr} = \mathrm{Munr} \cdot [\mathrm{ONLnr}] \tag{2}$$

Derived unit $\mathrm{mmol} \cdot \mathrm{ml}^{-1}$

6.3 Rule ONLpcd

Rule ONLpcd is a rate rule for species ONLpcd:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ONLpcd} = \mathrm{Mupcd} \cdot [\mathrm{ONLpcd}] \tag{3}$$

Derived unit $\mathrm{mmol} \cdot \mathrm{ml}^{-1}$

7 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.

7.1 Species ONLnr

Name ONLnr

Notes `Outer nuclear layer in nr/nr mice`
`Constant risk equation, according to the article`

Initial concentration $100 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule ONLnr

One rule determines the species' quantity.

7.2 Species ONLpcd

Name ONLpcd

Notes `Outer nuclear layer in pcd/pcd mice`
`Constant risk equation, according to the article`

Initial concentration $100 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule ONLpcd

One rule determines the species' quantity.

7.3 Species ONLrom

Name ONLrom

Notes `Outer nuclear layer in Rom1-/- mice`
`Exponentially decreasing risk equation, according to supplementary information`

Initial concentration $100 \text{ mmol} \cdot \text{ml}^{-1}$

Involved in rule ONLrom

One rule determines the species' quantity.