SBML Model Report

Model name: “Kuznetsov2016(II) - -syn aggregation kinetics in Parkinson’s Disease”

December 1, 2016

1 General Overview

This is a document in SBML Level 3 Version 1 format. This model was created by Thawfeek Varusai[1] at August 15th 2016 at 2:02 p. m. and last time modified at August 18th 2016 at 2:07 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	4
events	0	constraints	0
reactions	17	function definitions	17
global parameters	12	unit definitions	5
rules	0	initial assignments	0

Model Notes

Kuznetsov2016(II) - -syn aggregationkinetics in Parkinson’s

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This theoretical model uses 2-step Finke-Watzky (FW) kinetics
todescribe the production, misfolding, aggregation, transport and
degradation of -syn that may lead to Parkinson’s Disease
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(PD). Deregulated -syn degradation is predicted to be
crucialfor PD pathogenesis.

This model is described in the article:What can trigger the onset of Parkinson's disease - A modeling study based on a compartmental model of ?-synuclein transport and aggregation in neurons.Kuznetsov IA, Kuznetsov AV.Math Biosci 2016 Aug; 278: 22-29

Abstract:

The aim of this paper is to develop a minimal model describing events leading to the onset of Parkinson's disease (PD). The model accounts for ?-synuclein (?-syn) production in the soma, transport toward the synapse, misfolding, and aggregation. The production and aggregation of polymeric ?-syn is simulated using a minimalistic 2-step Finke-Watzky model. We utilized the developed model to analyze what changes in a healthy neuron are likely to lead to the onset of ?-syn aggregation. We checked the effects of interruption of ?-syn transport toward the synapse, entry of misfolded (infectious) ?-syn into the somatic and synaptic compartments, increasing the rate of ?-syn synthesis in the soma, and failure of ?-syn degradation machinery. Our model suggests that failure of ?-syn degradation machinery is probably the most likely cause for the onset of ?-syn aggregation leading to PD.

2 Unit Definitions

This is an overview of five unit definitions.

2.1 Unit `length`

Name length

Definition m

2.2 Unit `area`

Name area

Definition m^2

2.3 Unit volume

Name volume

Definition l

2.4 Unit time

Name time

Definition s

2.5 Unit substance

Name substance

Definition mol

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
default_compartment	Neuron	0000410	3	1		☑	

3.1 Compartment default_compartment

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

Name Neuron

SBO:0000410 implicit compartment

4 Species

This model contains four species. 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
As	As	default_compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Bs	Bs	default_compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Asyn	Asyn	default_compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
Bsyn	Bsyn	default_compartment	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains twelve global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
nA	nA		$2.91 \cdot 10^{-20}$		☑
k1	k1		$3 \cdot 10^{-7}$		☑
k2	k2		$2 \cdot 10^{-9}$		☑
qA	qA		$4.17 \cdot 10^{-8}$		☑
QBs	QBs		0.000		☑
QBsyn	QBsyn		0.000		☑
TAh1	TAh1		72000.000		☑
TBh1	TBh1		720000.000		☑
Vs	Vs		$4.19 \cdot 10^{-15}$		☑
Vsyn	Vsyn		$4.19 \cdot 10^{-15}$		☑
t1	t1		0.000		☑
t2	t2		0.000		☑

6 Function definitions

This is an overview of 17 function definitions.

6.1 Function definition Function_for_R8

Name Function for R8

Arguments [As], [Bs], ModelValue_2, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_2} \cdot [\text{As}] \cdot [\text{Bs}]}{\text{vol}\,(\text{default\_compartment})} \tag{1}$$

6.2 Function definition Function_for_R17

Name Function for R17

Arguments [Bsyn], ModelValue_7, vol (default_compartment)

Mathematical Expression

$$\frac{\frac{[\text{Bsyn}] \cdot \ln 2}{\text{ModelValue\_7}}}{\text{vol}\,(\text{default\_compartment})} \tag{2}$$

6.3 Function definition Function_for_R1

Name Function for R1

Arguments ModelValue_3, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_3}}{\text{vol}\,(\text{default\_compartment})} \tag{3}$$

6.4 Function definition Function_for_R5

Name Function for R5

Arguments [As], ModelValue_0, ModelValue_8, vol (default_compartment)

Mathematical Expression

$$\frac{\frac{\text{ModelValue\_0}\cdot[\text{As}]}{\text{ModelValue\_8}}}{\text{vol}\,(\text{default\_compartment})} \tag{4}$$

6.5 Function definition Function_for_R9

Name Function for R9

Arguments [Bs], ModelValue_7, vol (default_compartment)

Mathematical Expression

$$\frac{\frac{[\text{Bs}]\cdot\ln 2}{\text{ModelValue\_7}}}{\text{vol}\,(\text{default\_compartment})} \tag{5}$$

6.6 Function definition Function_for_R2

Name Function for R2

Arguments [As], ModelValue_1, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_1}\cdot[\text{As}]}{\text{vol}\,(\text{default\_compartment})} \tag{6}$$

6.7 Function definition Function_for_R16

Name Function for R16

Arguments [Asyn], [Bsyn], ModelValue_2, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_2} \cdot [\text{Asyn}] \cdot [\text{Bsyn}]}{\text{vol}\,(\text{default\_compartment})} \tag{7}$$

6.8 Function definition Function_for_R15

Name Function for R15

Arguments [Asyn], ModelValue_1, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_1} \cdot [\text{Asyn}]}{\text{vol}\,(\text{default\_compartment})} \tag{8}$$

6.9 Function definition Function_for_R4

Name Function for R4

Arguments [As], ModelValue_6, vol (default_compartment)

Mathematical Expression

$$\frac{\frac{[\text{As}] \cdot \ln 2}{\text{ModelValue\_6}}}{\text{vol}\,(\text{default\_compartment})} \tag{9}$$

6.10 Function definition Function_for_R11

Name Function for R11

Arguments [Asyn], ModelValue_1, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_1} \cdot [\text{Asyn}]}{\text{vol}\,(\text{default\_compartment})} \tag{10}$$

6.11 Function definition Function_for_R6

Name Function for R6

Arguments ModelValue_4, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_4}}{\text{vol}\,(\text{default\_compartment})} \tag{11}$$

6.12 Function definition Function_for_R12

Name Function for R12

Arguments [Asyn], [Bsyn], ModelValue_2, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_2} \cdot [\text{Asyn}] \cdot [\text{Bsyn}]}{\text{vol}\,(\text{default\_compartment})} \tag{12}$$

6.13 Function definition Function_for_R7

Name Function for R7

Arguments [As], ModelValue_1, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_1} \cdot [\text{As}]}{\text{vol}\,(\text{default\_compartment})} \tag{13}$$

6.14 Function definition Function_for_R13

Name Function for R13

Arguments [Asyn], ModelValue_6, vol (default_compartment)

Mathematical Expression

$$\frac{\frac{[\text{Asyn}] \cdot \ln 2}{\text{ModelValue\_6}}}{\text{vol}\,(\text{default\_compartment})} \tag{14}$$

6.15 Function definition Function_for_R14

Name Function for R14

Arguments ModelValue_5, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_5}}{\text{vol}\,(\text{default\_compartment})} \tag{15}$$

6.16 Function definition Function_for_R3

Name Function for R3

Arguments [As], [Bs], ModelValue_2, vol (default_compartment)

Mathematical Expression

$$\frac{\text{ModelValue\_2} \cdot [\text{As}] \cdot [\text{Bs}]}{\text{vol}\,(\text{default\_compartment})} \tag{16}$$

6.17 Function definition Function_for_R10

Name Function for R10

Arguments [As], ModelValue_0, ModelValue_9, vol (default_compartment)

Mathematical Expression

$$\frac{\frac{\text{ModelValue\_0} \cdot [\text{As}]}{\text{ModelValue\_9}}}{\text{vol}\,(\text{default\_compartment})} \tag{17}$$

7 Reactions

This model contains 17 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	R1	R1	$\emptyset \rightleftharpoons As$	
2	R2	R2	$As \rightleftharpoons \emptyset$	
3	R3	R3	$As \overset{Bs}{\rightleftharpoons} \emptyset$	
4	R4	R4	$As \rightleftharpoons \emptyset$	
5	R5	R5	$As \rightleftharpoons \emptyset$	
6	R6	R6	$\emptyset \rightleftharpoons Bs$	
7	R7	R7	$\emptyset \overset{As}{\rightleftharpoons} Bs$	
8	R8	R8	$\emptyset \overset{As}{\rightleftharpoons} Bs$	
9	R9	R9	$Bs \rightleftharpoons \emptyset$	
10	R10	R10	$\emptyset \overset{As}{\rightleftharpoons} Asyn$	
11	R11	R11	$Asyn \rightleftharpoons \emptyset$	
12	R12	R12	$Asyn \overset{Bsyn}{\rightleftharpoons} \emptyset$	
13	R13	R13	$Asyn \rightleftharpoons \emptyset$	
14	R14	R14	$\emptyset \rightleftharpoons Bsyn$	
15	R15	R15	$\emptyset \overset{Asyn}{\rightleftharpoons} Bsyn$	
16	R16	R16	$\emptyset \overset{Asyn}{\rightleftharpoons} Bsyn$	
17	R17	R17	$Bsyn \rightleftharpoons \emptyset$	

7.1 Reaction R1

This is a reversible reaction of no reactant forming one product.

Name R1

Reaction equation

$$\emptyset \rightleftharpoons \mathrm{As} \tag{18}$$

Product

Table 6: Properties of each product.

Id	Name	SBO
As	As	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R1}\left(\mathrm{qA}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{19}$$

$$\mathrm{Function\_for\_R1}\left(\mathrm{ModelValue\_3}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_3}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{20}$$

$$\mathrm{Function\_for\_R1}\left(\mathrm{ModelValue\_3}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_3}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{21}$$

7.2 Reaction R2

This is a reversible reaction of one reactant forming no product.

Name R2

Reaction equation

$$\mathrm{As} \rightleftharpoons \emptyset \tag{22}$$

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
As	As	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R2}\left(\left[\mathrm{As}\right], \mathrm{k1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \quad (23)$$

$$\mathrm{Function\_for\_R2}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_1} \cdot \left[\mathrm{As}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \quad (24)$$

$$\mathrm{Function\_for\_R2}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_1} \cdot \left[\mathrm{As}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \quad (25)$$

7.3 Reaction R3

This is a reversible reaction of one reactant forming no product influenced by one modifier.

Name R3

Reaction equation

$$\mathrm{As} \overset{\mathrm{Bs}}{\rightleftharpoons} \emptyset \quad (26)$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
As	As	

Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
Bs	Bs	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R3}\left(\left[\mathrm{As}\right], \left[\mathrm{Bs}\right], \mathrm{k2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{27}$$

$$\begin{aligned} &\mathrm{Function\_for\_R3}\left(\left[\mathrm{As}\right], \left[\mathrm{Bs}\right], \mathrm{ModelValue\_2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \\ &= \frac{\mathrm{ModelValue\_2} \cdot \left[\mathrm{As}\right] \cdot \left[\mathrm{Bs}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \end{aligned} \tag{28}$$

$$\begin{aligned} &\mathrm{Function\_for\_R3}\left(\left[\mathrm{As}\right], \left[\mathrm{Bs}\right], \mathrm{ModelValue\_2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \\ &= \frac{\mathrm{ModelValue\_2} \cdot \left[\mathrm{As}\right] \cdot \left[\mathrm{Bs}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \end{aligned} \tag{29}$$

7.4 Reaction R4

This is a reversible reaction of one reactant forming no product.

Name R4

Reaction equation

$$\mathrm{As} \rightleftharpoons \emptyset \tag{30}$$

Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
As	As	

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R4}\left(\left[\mathrm{As}\right], \mathrm{TAh1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{31}$$

$$\mathrm{Function\_for\_R4}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_6}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\left[\mathrm{As}\right] \cdot \ln 2}{\mathrm{ModelValue\_6}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{32}$$

$$\mathrm{Function\_for\_R4}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_6}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\left[\mathrm{As}\right] \cdot \ln 2}{\mathrm{ModelValue\_6}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{33}$$

7.5 Reaction R5

This is a reversible reaction of one reactant forming no product.

Name R5

Reaction equation

$$\mathrm{As} \rightleftharpoons \emptyset \tag{34}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
As	As	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R5}\left(\left[\mathrm{As}\right], \mathrm{nA}, \mathrm{Vs}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{35}$$

$$\mathrm{Function\_for\_R5}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_0}, \mathrm{ModelValue\_8}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\mathrm{ModelValue\_0} \cdot \left[\mathrm{As}\right]}{\mathrm{ModelValue\_8}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{36}$$

$$\mathrm{Function\_for\_R5}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_0}, \mathrm{ModelValue\_8}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\mathrm{ModelValue\_0} \cdot \left[\mathrm{As}\right]}{\mathrm{ModelValue\_8}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{37}$$

7.6 Reaction R6

This is a reversible reaction of no reactant forming one product.

Name R6

Reaction equation

$$\emptyset \rightleftharpoons \mathrm{Bs} \tag{38}$$

Product

Table 12: Properties of each product.

Id	Name	SBO
Bs	Bs	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R6}\left(\mathrm{QBs}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{39}$$

$$\mathrm{Function\_for\_R6}\left(\mathrm{ModelValue\_4}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_4}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{40}$$

$$\mathrm{Function\_for\_R6}\left(\mathrm{ModelValue\_4}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_4}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{41}$$

7.7 Reaction R7

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name R7

Reaction equation

$$\emptyset \overset{\mathrm{As}}{\rightleftharpoons} \mathrm{Bs} \tag{42}$$

Modifier

Table 13: Properties of each modifier.

Id	Name	SBO
As	As	

Product

Table 14: Properties of each product.

Id	Name	SBO
Bs	Bs	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R7}\left(\left[\mathrm{As}\right], \mathrm{k1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \quad (43)$$

$$\mathrm{Function\_for\_R7}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_1} \cdot \left[\mathrm{As}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \quad (44)$$

$$\mathrm{Function\_for\_R7}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_1} \cdot \left[\mathrm{As}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \quad (45)$$

7.8 Reaction R8

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name R8

Reaction equation

$$\emptyset \underset{}{\overset{\mathrm{As}}{\rightleftharpoons}} \mathrm{Bs} \quad (46)$$

Modifier

Table 15: Properties of each modifier.

Id	Name	SBO
As	As	

Product

Table 16: Properties of each product.

Id	Name	SBO
Bs	Bs	

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R8}\left([\mathrm{As}], [\mathrm{Bs}], \mathrm{k2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{47}$$

$$\begin{aligned} &\mathrm{Function\_for\_R8}\left([\mathrm{As}], [\mathrm{Bs}], \mathrm{ModelValue\_2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \\ &= \frac{\mathrm{ModelValue\_2} \cdot [\mathrm{As}] \cdot [\mathrm{Bs}]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \end{aligned} \tag{48}$$

$$\begin{aligned} &\mathrm{Function\_for\_R8}\left([\mathrm{As}], [\mathrm{Bs}], \mathrm{ModelValue\_2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \\ &= \frac{\mathrm{ModelValue\_2} \cdot [\mathrm{As}] \cdot [\mathrm{Bs}]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \end{aligned} \tag{49}$$

7.9 Reaction R9

This is a reversible reaction of one reactant forming no product.

Name R9

Reaction equation

$$\mathrm{Bs} \rightleftharpoons \emptyset \tag{50}$$

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
Bs	Bs	

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R9}\left(\left[\mathrm{Bs}\right], \mathrm{TBh1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{51}$$

$$\mathrm{Function\_for\_R9}\left(\left[\mathrm{Bs}\right], \mathrm{ModelValue\_7}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\left[\mathrm{Bs}\right] \cdot \ln 2}{\mathrm{ModelValue\_7}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{52}$$

$$\mathrm{Function\_for\_R9}\left(\left[\mathrm{Bs}\right], \mathrm{ModelValue\_7}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\left[\mathrm{Bs}\right] \cdot \ln 2}{\mathrm{ModelValue\_7}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{53}$$

7.10 Reaction R10

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name R10

Reaction equation

$$\emptyset \overset{\mathrm{As}}{\rightleftharpoons} \mathrm{Asyn} \tag{54}$$

Modifier

Table 18: Properties of each modifier.

Id	Name	SBO
As	As	

Product

Table 19: Properties of each product.

Id	Name	SBO
Asyn	Asyn	

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R10}\left(\left[\mathrm{As}\right], \mathrm{nA}, \mathrm{Vsyn}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{55}$$

$$\mathrm{Function\_for\_R10}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_0}, \mathrm{ModelValue\_9}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\mathrm{ModelValue\_0} \cdot \left[\mathrm{As}\right]}{\mathrm{ModelValue\_9}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{56}$$

$$\mathrm{Function\_for\_R10}\left(\left[\mathrm{As}\right], \mathrm{ModelValue\_0}, \mathrm{ModelValue\_9}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\mathrm{ModelValue\_0} \cdot \left[\mathrm{As}\right]}{\mathrm{ModelValue\_9}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{57}$$

7.11 Reaction R11

This is a reversible reaction of one reactant forming no product.

Name R11

Reaction equation

$$\mathrm{Asyn} \rightleftharpoons \emptyset \tag{58}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
Asyn	Asyn	

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R11}\left(\left[\mathrm{Asyn}\right], \mathrm{k1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{59}$$

$$\mathrm{Function\_for\_R11}\left(\left[\mathrm{Asyn}\right], \mathrm{ModelValue\_1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_1} \cdot \left[\mathrm{Asyn}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{60}$$

$$\mathrm{Function\_for\_R11}\left(\left[\mathrm{Asyn}\right], \mathrm{ModelValue\_1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_1} \cdot \left[\mathrm{Asyn}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{61}$$

7.12 Reaction R12

This is a reversible reaction of one reactant forming no product influenced by one modifier.

Name R12

Reaction equation

$$\mathrm{Asyn} \underset{}{\overset{\mathrm{Bsyn}}{\rightleftharpoons}} \emptyset \tag{62}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
Asyn	Asyn	

Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
Bsyn	Bsyn	

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R12}\left(\left[\mathrm{Asyn}\right], \left[\mathrm{Bsyn}\right], \mathrm{k2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{63}$$

$$\begin{aligned}&\text{Function\_for\_R12}\left([\text{Asyn}], [\text{Bsyn}], \text{ModelValue\_2}, \text{vol}\left(\text{default\_compartment}\right)\right)\\&= \frac{\text{ModelValue\_2} \cdot [\text{Asyn}] \cdot [\text{Bsyn}]}{\text{vol}\left(\text{default\_compartment}\right)}\end{aligned} \tag{64}$$

$$\begin{aligned}&\text{Function\_for\_R12}\left([\text{Asyn}], [\text{Bsyn}], \text{ModelValue\_2}, \text{vol}\left(\text{default\_compartment}\right)\right)\\&= \frac{\text{ModelValue\_2} \cdot [\text{Asyn}] \cdot [\text{Bsyn}]}{\text{vol}\left(\text{default\_compartment}\right)}\end{aligned} \tag{65}$$

7.13 Reaction R13

This is a reversible reaction of one reactant forming no product.

Name R13

Reaction equation

$$\text{Asyn} \rightleftharpoons \emptyset \tag{66}$$

Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
Asyn	Asyn	

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{vol}\left(\text{default\_compartment}\right) \cdot \text{Function\_for\_R13}\left([\text{Asyn}], \text{TAh1}, \text{vol}\left(\text{default\_compartment}\right)\right) \tag{67}$$

$$\begin{aligned}&\text{Function\_for\_R13}\left([\text{Asyn}], \text{ModelValue\_6}, \text{vol}\left(\text{default\_compartment}\right)\right)\\&= \frac{\frac{[\text{Asyn}] \cdot \ln 2}{\text{ModelValue\_6}}}{\text{vol}\left(\text{default\_compartment}\right)}\end{aligned} \tag{68}$$

$$\begin{aligned}&\text{Function\_for\_R13}\left([\text{Asyn}], \text{ModelValue\_6}, \text{vol}\left(\text{default\_compartment}\right)\right)\\&= \frac{\frac{[\text{Asyn}] \cdot \ln 2}{\text{ModelValue\_6}}}{\text{vol}\left(\text{default\_compartment}\right)}\end{aligned} \tag{69}$$

7.14 Reaction R14

This is a reversible reaction of no reactant forming one product.

Name R14

Reaction equation

$$\emptyset \rightleftharpoons \mathrm{Bsyn} \tag{70}$$

Product

Table 24: Properties of each product.

Id	Name	SBO
Bsyn	Bsyn	

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R14}\left(\mathrm{QBsyn}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{71}$$

$$\mathrm{Function\_for\_R14}\left(\mathrm{ModelValue\_5}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_5}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{72}$$

$$\mathrm{Function\_for\_R14}\left(\mathrm{ModelValue\_5}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\mathrm{ModelValue\_5}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{73}$$

7.15 Reaction R15

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name R15

Reaction equation

$$\emptyset \overset{\mathrm{Asyn}}{\rightleftharpoons} \mathrm{Bsyn} \tag{74}$$

Modifier

Table 25: Properties of each modifier.

Id	Name	SBO
Asyn	Asyn	

Product

Table 26: Properties of each product.

Id	Name	SBO
Bsyn	Bsyn	

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R15}\left(\left[\mathrm{Asyn}\right], \mathrm{k1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{75}$$

$$\begin{aligned} &\mathrm{Function\_for\_R15}\left(\left[\mathrm{Asyn}\right], \mathrm{ModelValue\_1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \\ &= \frac{\mathrm{ModelValue\_1} \cdot \left[\mathrm{Asyn}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \end{aligned} \tag{76}$$

$$\begin{aligned} &\mathrm{Function\_for\_R15}\left(\left[\mathrm{Asyn}\right], \mathrm{ModelValue\_1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \\ &= \frac{\mathrm{ModelValue\_1} \cdot \left[\mathrm{Asyn}\right]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \end{aligned} \tag{77}$$

7.16 Reaction R16

This is a reversible reaction of no reactant forming one product influenced by one modifier.

Name R16

Reaction equation

$$\emptyset \overset{\mathrm{Asyn}}{\rightleftharpoons} \mathrm{Bsyn} \tag{78}$$

Modifier

Table 27: Properties of each modifier.

Id	Name	SBO
Asyn	Asyn	

Product

Table 28: Properties of each product.

Id	Name	SBO
Bsyn	Bsyn	

Kinetic Law

Derived unit contains undeclared units

$$v_{16} = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R16}\left([\mathrm{Asyn}], [\mathrm{Bsyn}], \mathrm{k2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{79}$$

$$\begin{aligned} &\mathrm{Function\_for\_R16}\left([\mathrm{Asyn}], [\mathrm{Bsyn}], \mathrm{ModelValue\_2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \\ &= \frac{\mathrm{ModelValue\_2} \cdot [\mathrm{Asyn}] \cdot [\mathrm{Bsyn}]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \end{aligned} \tag{80}$$

$$\begin{aligned} &\mathrm{Function\_for\_R16}\left([\mathrm{Asyn}], [\mathrm{Bsyn}], \mathrm{ModelValue\_2}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \\ &= \frac{\mathrm{ModelValue\_2} \cdot [\mathrm{Asyn}] \cdot [\mathrm{Bsyn}]}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \end{aligned} \tag{81}$$

7.17 Reaction R17

This is a reversible reaction of one reactant forming no product.

Name R17

Reaction equation

$$\mathrm{Bsyn} \rightleftharpoons \emptyset \tag{82}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
Bsyn	Bsyn	

Kinetic Law

Derived unit contains undeclared units

$$v_{17} = \mathrm{vol}\left(\mathrm{default\_compartment}\right) \cdot \mathrm{Function\_for\_R17}\left(\left[\mathrm{Bsyn}\right], \mathrm{TBh1}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) \tag{83}$$

$$\mathrm{Function\_for\_R17}\left(\left[\mathrm{Bsyn}\right], \mathrm{ModelValue\_7}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\left[\mathrm{Bsyn}\right] \cdot \ln 2}{\mathrm{ModelValue\_7}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{84}$$

$$\mathrm{Function\_for\_R17}\left(\left[\mathrm{Bsyn}\right], \mathrm{ModelValue\_7}, \mathrm{vol}\left(\mathrm{default\_compartment}\right)\right) = \frac{\frac{\left[\mathrm{Bsyn}\right] \cdot \ln 2}{\mathrm{ModelValue\_7}}}{\mathrm{vol}\left(\mathrm{default\_compartment}\right)} \tag{85}$$

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.

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.

8.1 Species `As`

Name As

SBO:0000245 macromolecule

Notes `-syn monomer concentration in the soma`

Initial concentration $0.0060\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in eight reactions (as a reactant in R2, R3, R4, R5 and as a product in R1 and as a modifier in R7, R8, R10).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{As} = v_1 - v_2 - v_3 - v_4 - v_5 \tag{86}$$

8.2 Species Bs

Name Bs

SBO:0000543 protein aggregate

Notes -syn concentration in the misfolded state in the soma

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

This species takes part in five reactions (as a reactant in R9 and as a product in R6, R7, R8 and as a modifier in R3).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Bs} = v_6 + v_7 + v_8 - v_9 \tag{87}$$

8.3 Species Asyn

Name Asyn

SBO:0000245 macromolecule

Notes -syn monomer concentration in the synapse

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

This species takes part in six reactions (as a reactant in R11, R12, R13 and as a product in R10 and as a modifier in R15, R16).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Asyn} = v_{10} - v_{11} - v_{12} - v_{13} \tag{88}$$

8.4 Species Bsyn

Name Bsyn

SBO:0000543 protein aggregate

Notes -syn concentration in the misfolded state in the synapse

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

This species takes part in five reactions (as a reactant in R17 and as a product in R14, R15, R16 and as a modifier in R12).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Bsyn} = v_{14} + v_{15} + v_{16} - v_{17} \tag{89}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000245 macromolecule: Molecular entity mainly built-up by the repetition of pseudo-identical units. CHEBI:3383

SBO:0000410 implicit compartment: A compartment whose existence is inferred due to the presence of known material entities which must be bounded, allowing the creation of material entity pools

SBO:0000543 protein aggregate: A nonspecific coalescence of misfolded proteins which may or may not form a precipitate, depending upon particle size

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