# **SBML Model Report**

# Model name: "Yuraszeck2010 - Vulnerabilities in the Tau Network in Tau Pathophysiology"



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<sup>1</sup> at August 15<sup>th</sup> 2014 at eleven o' clock in the morning. and last time modified at September 23<sup>rd</sup> 2014 at 6:41 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	45
events	0	constraints	0
reactions	84	function definitions	6
global parameters	93	unit definitions	2
rules	4	initial assignments	0

## **Model Notes**

Yuraszeck2010 - Vulnerabilities in the TauNetwork in Tau Pathophysiology

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This model is described in the article: Vulnerabilities in the tau network and the role of ultrasensitive points in tau pathophysiology. Yuraszeck TM, Neveu P, Rodriguez-Fernandez M, Robinson A, Kosik KS, Doyle FJ 3rd.PLoS Comput. Biol. 2010; 6(11): e1000997

Abstract:

The multifactorial nature of disease motivates the use of systems-level analyses to understand their pathology. We used a systems biology approach to study tau aggregation, one of the hallmark features of Alzheimer's disease. A mathematical model was constructed to capture the current state of knowledge concerning tau's behavior and interactions in cells. The model was implemented in silico in the form of ordinary differential equations. The identifiability of the model was assessed and parameters were estimated to generate two cellular states: a population of solutions that corresponds to normal tau homeostasis and a population of solutions that displays aggregation-prone behavior. The model of normal tau homeostasis was robust to perturbations, and disturbances in multiple processes were required to achieve an aggregation-prone state. The aggregation-prone state was ultrasensitive to perturbations in diverse subsets of networks. Tau aggregation requires that multiple cellular parameters are set coordinately to a set of values that drive pathological assembly of tau. This model provides a foundation on which to build and increase our understanding of the series of events that lead to tau aggregation and may ultimately be used to identify critical intervention points that can direct the cell away from tau aggregation to aid in the treatment of tau-mediated (or related) aggregation diseases including Alzheimer's.

This model is hosted on BioModels Database and identified by: BIOMD0000000542.

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

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## 2 Unit Definitions

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

## 2.1 Unit volume

Name volume

**Definition** ml

#### 2.2 Unit substance

Name substance

**Definition** mmol

## 2.3 Unit area

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

**Definition** m<sup>2</sup>

# 2.4 Unit length

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

**Definition** m

## 2.5 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
Brain	Brain		3	1	litre	Ø	

# **3.1 Compartment Brain**

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

Name Brain

# 4 Species

This model contains 45 species. The boundary condition of four of these species is set to true so that these 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 Condi- tion
ADP	ADP	Brain	$\operatorname{mmol}\cdot\operatorname{ml}^{-1}$		
ATP	ATP	Brain	$mmol \cdot ml^{-1}$		
MT	MT	Brain	$mmol \cdot ml^{-1}$		
_20S	20S	Brain	$mmol \cdot ml^{-1}$		
_205 Hsc70	Hsc70	Brain	$mmol \cdot ml^{-1}$		
Hsp90	Hsp90	Brain	$mmol \cdot ml^{-1}$		
CHIP	CHIP	Brain	$mmol \cdot ml^{-1}$		
			mmol·ml <sup>-1</sup>		
Bag2	Bag2	Brain			
_26S	26S	Brain	$\text{mmol} \cdot \text{ml}^{-1}$		$\square$
TauH3RUb	TauH3RUb	Brain	$\text{mmol}\cdot\text{ml}^{-1}$		
TauH4RUb	TauH4RUb	Brain	$\text{mmol}\cdot\text{ml}^{-1}$		
Nucleus3	Nucleus3	Brain	$\operatorname{mmol} \cdot \operatorname{ml}^{-1}$		
Nucleus4	Nucleus4	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$	$\Box$	
Agg33	Agg33	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
Ар	Ap	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		$\square$
Agg43	Agg43	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
Вр	Вр	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		$\square$
Tau03R	Tau03R	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
TauN3R	TauN3R	Brain	$\text{mmol}\cdot\text{ml}^{-1}$		
TauH3R	TauH3R	Brain	$\text{mmol}\cdot\text{ml}^{-1}$		
Tau0_3R	Tau0*3R	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
Tau03RMT	Tau03RMT	Brain	$\operatorname{mmol}\cdot\operatorname{ml}^{-1}$		
TauN_3R	TauN*3R	Brain	$mmol \cdot ml^{-1}$		
TauN3RMT	TauN3RMT		$mmol \cdot ml^{-1}$		
TauH_3R	TauH*3R	Brain	mmol·ml <sup>-1</sup>		
		Brain			
TauH3RMT	TauH3RMT	Brain	$\operatorname{mmol} \cdot \operatorname{ml}^{-1}$		
TauH3R_Hsc70	TauH3R-Hsc70	Brain	$\operatorname{mmol} \cdot \operatorname{ml}^{-1}$		
TauH3R_Hsp90	TauH3R-Hsp90	Brain	$\text{mmol} \cdot \text{ml}^{-1}$		
Tau03R_Hsp90	Tau03R-Hsp90	Brain	$\text{mmol} \cdot \text{ml}^{-1}$		
TauH3R_CHIP_Hsc70	TauH3R-CHIP-Hsc70	Brain	$\operatorname{mmol} \cdot \operatorname{ml}^{-1}$		
TauH3R_CHIP-	TauH3R-CHIP-Hsc70-Bag2	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		$\Box$
_Hsc70_Bag2					
Tau04R	Tau04R	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
TauN4R	TauN4R	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
TauH4R	TauH4R	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
$Tau0_4R$	Tau0*4R	Brain	$mmol \cdot ml^{-1}$		
Tau04RMT	Tau04RMT	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
TauN_4R	TauN*4R	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
TauN4RMT	TauN4RMT	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
TauH_4R	TauH*4R	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
TauH4RMT	TauH4RMT	Brain	$\text{mmol}\cdot\text{ml}^{-1}$		
TauH4R_Hsc70	TauH4R-Hsc70	Brain	$\text{mmol}\cdot\text{ml}^{-1}$		
TauH4R_Hsp90	TauH4R-Hsp90	Brain	$\operatorname{mmol} \cdot \operatorname{ml}^{-1}$		
Tau04R_Hsp90	Tau04R-Hsp90	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
TauH4R_CHIP_Hsc70	TauH4R-CHIP-Hsc70	Brain	$\operatorname{mmol} \cdot \operatorname{ml}^{-1}$		
TauH4R_CHIP-	TauH4R-CHIP-Hsc70-Bag2	Brain	$\mathrm{mmol}\cdot\mathrm{ml}^{-1}$		
_Hsc70_Bag2		•	•	]	

# **5 Parameters**

This model contains 93 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO Value Unit	Constant
k1	k1	0.037	
k2	k2	0.392	$\overline{Z}$
k3	k3	27.567	$\overline{\mathbf{Z}}$
k4	k4	6.066	$\overline{\mathbf{Z}}$
k5	k5	7.996	$\overline{\mathbf{Z}}$
k6	k6	0.142	$\overline{\mathbf{Z}}$
k7	k7	21.911	
k8	k8	0.608	$\overline{\mathbf{Z}}$
k9	k9	5.760	$\overline{\mathbf{Z}}$
k10	k10	7.119	
k11	k11	15.000	
k12	k12	9.634	$\square$
k13	k13	0.163	
k14	k14	1.541	
k15	k15	9.220	
k16	k16	50.662	
k17	k17	0.202	
k18	k18	3.940	$\checkmark$
k19	k19	8.052	$\square$
k20	k20	19.770	$\square$
k21	k21	7.249	$\square$
k22	k22	0.173	$\checkmark$
k23	k23	0.075	
k24	k24	0.039	$\checkmark$
k25	k25	0.066	
k26	k26	0.145	$\checkmark$
k27	k27	0.473	
k28	k28	12.630	$\checkmark$
k29	k29	0.006	
k30	k30	16.566	$\square$
k31	k31	3.992	
k32	k32	7.130	
k33	k33	0.009	
k34	k34	$1.11 \cdot 10^{-4}$	
k35	k35	0.146	
k36	k36	0.006	$\checkmark$
k37	k37	1.070	$\mathbf{Z}$

Id	Name	SBO Value Unit	Constant
k38	k38	0.029	$\mathbf{Z}$
k39	k39	1.164	$\mathbf{Z}$
k40	k40	0.051	
k41	k41	0.279	$\mathbf{Z}$
k42	k42	0.025	$\mathbf{Z}$
k43	k43	3.690	
k44	k44	27.567	$\mathbf{Z}$
k45	k45	0.217	
k46	k46	7.996	$\mathbf{Z}$
k47	k47	2.802	$\mathbf{Z}$
k48	k48	21.911	
k49	k49	0.003	
k50	k50	5.760	$\mathbf{Z}$
k51	k51	7.119	$ \overline{\mathbf{Z}} $
k52	k52	15.000	$ \overline{\mathbf{Z}} $
k53	k53	9.634	$   \overline{\mathbf{Z}} $
k54	k54	0.054	$\overline{\mathbf{Z}}$
k55	k55	1.541	$\overline{\mathbf{Z}}$
k56	k56	9.220	$\overline{\mathbf{Z}}$
k57	k57	50.662	$\overline{\mathbf{Z}}$
k58	k58	0.067	$\overline{\mathbf{Z}}$
k59	k59	3.940	$\overline{\mathbf{Z}}$
k60	k60	8.052	$\overline{\mathbb{Z}}$
k61	k61	19.770	$\overline{\mathbb{Z}}$
k62	k62	2.416	$\overline{\mathbb{Z}}$
k63	k63	0.212	$\overline{\mathbb{Z}}$
k64	k64	0.074	$\overline{\mathbf{Z}}$
k65	k65	0.001	$\overline{\mathbf{Z}}$
k66	k66	0.029	$\overline{\mathbf{Z}}$
k67	k67	0.145	
k68	k68	0.004	$\overline{\mathbf{Z}}$
k69	k69	12.630	$\overline{\mathbb{Z}}$
k70	k70	0.073	$\overline{\mathbf{Z}}$
k71	k71	16.566	$\overline{\mathbf{Z}}$
k72	k72	0.014	$\overline{\mathbf{Z}}$
k73	k73	7.130	$\overline{\mathbb{Z}}$
k74	k74	$1.61 \cdot 10^{-4}$	$\overline{\mathbb{Z}}$
k75	k75	$8.57 \cdot 10^{-5}$	$\overline{\mathbb{Z}}$
k76	k76	0.284	$\overline{\mathbf{Z}}$
k77	k77	1.186	$\mathbf{Z}$
k78	k78	0.005	$\mathbf{Z}$
k79	k79	0.347	$\mathbf{Z}$

Id	Name	SBO	Value	Unit	Constant
k80	k80		0.552		
k81	k81		$5.59 \cdot 10^{-5}$		$   \overline{\mathscr{L}} $
k82	k82		0.645		
k83	k83		0.007		$   \overline{\mathscr{L}} $
k84	k84		0.680		$   \overline{\mathscr{L}} $
k85	k85		0.015		
k86	k86		$5 \cdot 10^{-6}$		
k87	k87		0.001		
k88	k88		$5 \cdot 10^{-6}$		
k89	k89		0.060		
k90	k90		0.095		
k91	k91		0.005		$   \overline{\mathscr{L}} $
k92	k92		0.095		$   \overline{\mathscr{L}} $
k93	k93		0.019		$   \overline{\mathscr{L}} $

# **6 Function definitions**

This is an overview of six function definitions.

# **6.1 Function definition** Constant\_flux\_\_irreversible

Name Constant flux (irreversible)

Argument v

**Mathematical Expression** 

v (1)

## **6.2 Function definition** Henri\_Michaelis\_Menten\_\_irreversible

Name Henri-Michaelis-Menten (irreversible)

Arguments substrate, Km, V

**Mathematical Expression** 

$$\frac{V \cdot substrate}{Km + substrate} \tag{2}$$

## **6.3 Function definition Mass\_Action**

Name Mass Action\*

Arguments k1, x1, x2

## **Mathematical Expression**

$$k1 \cdot x1 \cdot x2 \tag{3}$$

# **6.4 Function definition Michaelis\_Menten**

Name Michaelis-Menten\*

Arguments k1, x1, x2, k2

**Mathematical Expression** 

$$\frac{\mathbf{k}\mathbf{1} \cdot \mathbf{x}\mathbf{1} \cdot \mathbf{x}\mathbf{2}}{\mathbf{k}\mathbf{2} + \mathbf{x}\mathbf{1}} \tag{4}$$

## 6.5 Function definition Mass\_Action\_

Name Mass Action\*\*

Arguments K1, x1, x2, x3

**Mathematical Expression** 

$$K1 \cdot x1 \cdot x2 \cdot x3 \tag{5}$$

## **6.6 Function definition Nucleation**

Name Nucleation

Arguments k1, x1

**Mathematical Expression** 

$$k1 \cdot x1^2 \tag{6}$$

# 7 Rules

This is an overview of four rules.

#### **7.1 Rule** \_20S

Rule \_20S is a rate rule for species \_20S:

$$\frac{\mathrm{d}}{\mathrm{d}t} - 20\mathrm{S} = 0 \tag{7}$$

## **7.2 Rule** \_26S

Rule \_26S is a rate rule for species \_26S:

$$\frac{\mathrm{d}}{\mathrm{d}t} \cdot 26S = 0 \tag{8}$$

# **7.3 Rule** Ap

Rule Ap is a rate rule for species Ap:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Ap} = \mathrm{r77} \tag{9}$$

Derived unit  $mmol \cdot s^{-1}$ 

# **7.4 Rule** Bp

Rule Bp is a rate rule for species Bp:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Bp} = \mathrm{r}82\tag{10}$$

Derived unit  $mmol \cdot s$ 

# 8 Reactions

This model contains 84 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

N⁰	Id	Name	Reaction Equation	SBO
1	r1	r1	$\emptyset \longrightarrow Tau03R$	
2	r2	r2	$Tau03R + ATP \xrightarrow{Tau03R, ATP} TauN3R + ADP$	
3	r3	r3	$TauN3R \xrightarrow{TauN3R} Tau03R$	
4	r4	r4	$TauN3R + ATP \xrightarrow{TauN3R, ATP} TauH3R + ADP$	
5	r5	r5	$TauH3R \xrightarrow{TauH3R} TauN3R$	
6	r6	r6	$Tau03R \xrightarrow{Tau03R} Tau0\_3R$	
7	r7	r7	$Tau0\_3R \xrightarrow{Tau0\_3R} Tau03R$	
8	r8	r8	$Tau0_3R + MT \xrightarrow{Tau0_3R, MT} Tau03RMT$	
9	r9	r9	$Tau03RMT \xrightarrow{Tau03RMT} Tau0\_3R + MT$	
10	r10	r10	$TauN3R \xrightarrow{TauN3R} TauN_3R$	
11	r11	r11	$TauN_{3}R \xrightarrow{TauN_{3}R} TauN_{3}R$	
12	r12	r12	$TauN_{3}R + MT \xrightarrow{TauN_{3}R, MT} TauN_{3}RMT$	
13	r13	r13	$TauN3RMT \xrightarrow{TauN3RMT} TauN_3R + MT$	
14	r14	r14	$TauH3R \xrightarrow{TauH3R} TauH\_3R$	
15	r15	r15	$TauH\_3R \xrightarrow{TauH\_3R} TauH3R$	
16	r16	r16	$TauH_3R + MT \xrightarrow{TauH_3R, MT} TauH3RMT$	
17	r17	r17	$TauH3RMT \xrightarrow{TauH3RMT} TauH\_3R + MT$	

12	N₀	Id	Name	Reaction Equation	SBO
	18	r18	r18	Tau03R + _20S + ATP $\xrightarrow{\text{Tau03R, } 20S, \text{ ATP}} \text{ADP} + _20S$	
	19	r19	r19	$ \frac{\text{TauN3R} + 20\text{S} + \text{ATP}}{20\text{S}} \xrightarrow{\text{TauN3R}, 20\text{S}, \text{ATP}} \text{ADP} + 20\text{S} $	
	20	r20	r20	$TauH3R + 20S + ATP \xrightarrow{TauH3R, 20S, ATP} 20S + ADP$	
	21	r21	r21	$Tau03RMT + ATP \xrightarrow{Tau03RMT, ATP} TauN3RMT + ADP$	
Proc	22	r22	r22	TauN3RMT Tau03RMT	
Produced by SBML2PTEX	23	r23	r23	$ TauN3RMT + ATP \xrightarrow{TauN3RMT, ATP} TauH3RMT + ADP $	
88	24	r24	r24	$TauH3RMT \xrightarrow{TauH3RMT} TauN3RMT$	
	25	r25	r25	$TauH3R + Hsc70 \xrightarrow{TauH3R, Hsc70} TauH3R \cdot Hsc70$	
ATEX	26	r26	r26	$TauH3R\_Hsc70 \xrightarrow{TauH3R\_Hsc70} TauH3R + Hsc70$	
	27	r27	r27	TauH3R_Hsc70+Hsp90 TauH3R_Hsc70, Hsp90 → TauHsc70	H3R_Hsp90+
	28	r28	r28	$TauH3R\_Hsp90 \xrightarrow{TauH3R\_Hsp90} Tau03R\_Hsp90$	
	29	r29	r29	$Tau03R\_Hsp90 \xrightarrow{Tau03R\_Hsp90} Hsp90 + Tau03R$	
	30	r30	r30	TauH3R_Hsc70+CHIP TauH3R_Hsc70, CHIP TauH	
	31	r31	r31	TauH3R_CHIP_Hsc70 TauH3R_CHIP_Hsc70 TauH3I Hsc70 + CHIP	RUb+
	32	r32	r32	TauH3R_CHIP_Hsc70 + Bag2 TauH3R_CHIP_Hsc70, Bag2 TauH3R_CHIP_H	sc70_Bag2

Id	Name	Reaction Equation SBO	
20	-22	TauH3R_CHIP_Hsc70_Bag2	1170
r33	133		_Hsc/U
~2 <i>1</i>	r34	E .	
134	134	TauH3RUb, 26S, ATP	
0.5	-25		
r35	133		
r36	r36	·	
r37	r37	$TauN4R \xrightarrow{TauN4R} Tau04R$	
r38	r38	$TauN4R + ATP \xrightarrow{TauN4R, ATP} TauH4R + ADP$	
r39	r39	$TauH4R \xrightarrow{TauH4R} TauN4R$	
r40	r40	$Tau04R \xrightarrow{Tau04R} Tau0_{-}4R$	
r41	r41	$Tau0_4R \xrightarrow{Tau0_4R} Tau04R$	
r42	r42	·	
r43	r43	·	
r44	r44		
r45	r45	$TauN_{-}4R \xrightarrow{TauN_{-}4R} TauN4R$	
r46	r46	$TauN_4R + MT \xrightarrow{TauN_4R, MT} TauN4RMT$	
r47	r47	$TauN4RMT \xrightarrow{TauN4RMT} TauN_{-}4R + MT$	
r48	r48	$TauH4R \xrightarrow{TauH4R} TauH_4R$	
r49	r49	$TauH_{-}4R \xrightarrow{TauH_{-}4R} TauH_{-}4R$	
r50	r50		
r51	r51	$TauH4RMT \xrightarrow{TauH4RMT} TauH_4R + MT$	
	r33 r34 r35 r36 r37 r38 r39 r40 r41 r42 r43 r44 r45 r46 r47 r48 r49 r50	r33 r34 r34 r34 r35 r35 r36 r36 r37 r37 r37 r38 r38 r39 r39 r40 r40 r41 r41 r42 r42 r42 r43 r44 r44 r45 r45 r45 r46 r46 r47 r47 r48 r48 r49 r50 r50 r50	r33       TauH3R.CHIP.Hsc70.Bag2       TauH4R.ADP         r35       r35       0 — TauO4R.ATP       TauO4R.ATP       TauUA4R.ATP       TauH4R.ADP       TauH4R.ADP       TauH4R.ADP       TauH4R.ADP       TauH4R.ADP       TauH4R.ADP       TauO4R.ATP       TauO4R.AT

14	N⁰	Id	Name	Reaction Equation	SBO
	52	r52	r52	Tau04R + _20S + ATP $\xrightarrow{\text{Tau04R, } 20S, \text{ ATP}}$ ADP + _20S	
	53	r53	r53	$ \frac{\text{TauN4R} + 20\text{S} + \text{ATP}}{20\text{S}} \xrightarrow{\text{TauN4R}, 20\text{S}, \text{ATP}} \text{ADP} + 20\text{S} $	
	54	r54	r54	TauH4R + $\_20S$ + ATP $\xrightarrow{\text{TauH4R}, } \_20S$ , ATP $\xrightarrow{\text{ADP}}$ ADP + $\_20S$	
	55	r55	r55	$Tau04RMT + ATP \xrightarrow{Tau04RMT, ATP} TauN4RMT + ADP$	
Proc	56	r56	r56	TauN4RMT Tau04RMT	
Produced by SBML2PTEX	57	r57	r57	$\begin{array}{c} \text{TauN4RMT} + \text{ATP} \xrightarrow{\text{TauN4RMT}, \text{ ATP}} \text{TauH4RMT} + \\ \text{ADP} \end{array}$	
88	58	r58	r58	$TauH4RMT \xrightarrow{TauH4RMT} TauN4RMT$	
<u>∑</u>	59	r59	r59	$TauH4R + Hsc70 \xrightarrow{TauH4R, Hsc70} TauH4R \cdot Hsc70$	
ATEX	60	r60	r60	$TauH4R\_Hsc70 \xrightarrow{TauH4R\_Hsc70} TauH4R + Hsc70$	
	61	r61	r61	TauH4R_Hsc70+Hsp90 TauH4R_Hsc70, Hsp90 TauHsc70	H4R_Hsp90+
	62	r62	r62	$TauH4R\_Hsp90 \xrightarrow{TauH4R\_Hsp90} Tau04R\_Hsp90$	
	63	r63	r63	$Tau04R\_Hsp90 \xrightarrow{Tau04R\_Hsp90} Hsp90 + Tau04R$	
	64	r64	r64	TauH4R_Hsc70+CHIP TauH4R_Hsc70, CHIP TauH	
	65	r65	r65	TauH4R_CHIP_Hsc70 TauH4R_CHIP_Hsc70 TauH4l	RUb+
	66	r66	r66	$\begin{array}{c} \text{Hsc70} + \text{CHIP} \\ \text{TauH4R\_CHIP\_Hsc70} & + \\ \text{Bag2} \xrightarrow{\text{TauH4R\_CHIP\_Hsc70, Bag2}} \text{TauH4R\_CHIP\_H} \end{array}$	sc70_Bag2

N⁰	Id	Name	Reaction Equation SBO
67	r67	r67	TauH4R_CHIP_Hsc70_Bag2 TauH4R_CHIP_Hsc70_Bag2 TauH4R_Hsc70+CHIP+Bag2
68	r68	r68	$ \begin{array}{cccc} TauH4RUb & + & 26S & + \\ ATP & \xrightarrow{TauH4RUb, 26S, ATP} & ADP + 26S \end{array} $
69	r69	r69	$ADP \xrightarrow{ADP} ATP$
70	r70	r70	$ATP \xrightarrow{ATP} ADP$
71	r71	r71	2 TauH3RUb TauH3RUb Nucleus3
72	r72	r72	Nucleus $3 \xrightarrow{\text{Nucleus } 3} 2 \text{ TauH} 3 \text{RUb}$
73	r73	r73	2 TauH4RUb TauH4RUb Nucleus4
74	r74	r74	Nucleus4 $\xrightarrow{\text{Nucleus4}}$ 2 TauH4RUb
75	r75	r75	Nucleus3+TauH3RUb Nucleus3, TauH3RUb Agg33
76	r76	r76	$Agg33 \xrightarrow{Agg33} Nucleus3 + TauH3RUb$
77	r77	r77	$TauH3RUb + Agg33 \xrightarrow{TauH3RUb, Agg33} Ap$
78	r78	r78	$TauH3RUb + Ap \xrightarrow{TauH3RUb, Ap} Ap$
79	r79	r79	$Ap \xrightarrow{Ap} TauH3RUb + Ap$
80	r80	r80	Nucleus4+TauH4RUb Nucleus4, TauH4RUb Agg43
81	r81	r81	$Agg43 \xrightarrow{Agg43} Nucleus4 + TauH4RUb$
82	r82	r82	$TauH4RUb + Agg43 \xrightarrow{TauH4RUb, Agg43} Bp$
83	r83	r83	$TauH4RUb + Bp \xrightarrow{TauH4RUb, Bp} Bp$
84	r84	r84	$Bp \xrightarrow{Bp} TauH4RUb + Bp$

## 8.1 Reaction r1

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

Name r1

Notes Tau synthesis

# **Reaction equation**

$$\emptyset \longrightarrow Tau03R$$
 (11)

## **Product**

Table 6: Properties of each product.

Id	Name	SBO
Tau03R	Tau03R	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_1 = \text{vol}\left(\text{Brain}\right) \cdot \text{Constant\_flux\_irreversible}\left(\text{k1}\right)$$
 (12)

$$Constant\_flux\_irreversible(v) = v$$
 (13)

Constant\_flux\_irreversible 
$$(v) = v$$
 (14)

## 8.2 Reaction r2

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name r2

Notes Phosphorylation of newly synthesized tau

## **Reaction equation**

$$Tau03R + ATP \xrightarrow{Tau03R, ATP} TauN3R + ADP$$
 (15)

Table 7: Properties of each reactant.

Id	Name	SBO
Tau03R	Tau03R	
ATP	ATP	

Table 8: Properties of each modifier.

Id	Name	SBO
Tau03R	Tau03R	
ATP	ATP	

#### **Products**

Table 9: Properties of each product.

Id	Name	SBO
TauN3R	TauN3R	
ADP	ADP	

## **Kinetic Law**

Derived unit contains undeclared units

$$v_2 = \text{vol}(\text{Brain}) \cdot \text{Michaelis\_Menten}(k2, [\text{Tau03R}], [\text{ATP}], k3)$$
 (16)

$$Michaelis\_Menten(k1, x1, x2, k2) = \frac{k1 \cdot x1 \cdot x2}{k2 + x1}$$
 (17)

$$Michaelis\_Menten(k1,x1,x2,k2) = \frac{k1 \cdot x1 \cdot x2}{k2 + x1}$$
 (18)

# 8.3 Reaction r3

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

## Name r3

Notes dephosphosrylation of normally phosphorylated tau

#### **Reaction equation**

$$TauN3R \xrightarrow{TauN3R} Tau03R \tag{19}$$

#### Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
TauN3R	TauN3R	

#### **Modifier**

Table 11: Properties of each modifier.

Id	Name	SBO
TauN3R	TauN3R	

#### **Product**

Table 12: Properties of each product.

Id	Name	SBO
Tau03R	Tau03R	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_3 = \text{vol}(\text{Brain}) \cdot \text{Henri\_Michaelis\_Menten\_irreversible}([\text{TauN3R}], \text{k5}, \text{k4})$$
 (20)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{21}$$

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{22}$$

## 8.4 Reaction r4

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Name r4

Notes Phosphorylation of normally phosphorylated tau

# **Reaction equation**

$$TauN3R + ATP \xrightarrow{TauN3R, ATP} TauH3R + ADP$$
 (23)

#### **Reactants**

Table 13: Properties of each reactant.

Id	Name	SBO
TauN3R	TauN3R	
ATP	ATP	

#### **Modifiers**

Table 14: Properties of each modifier.

Id	Name	SBO
TauN3R	TauN3R	
ATP	ATP	

## **Products**

Table 15: Properties of each product.

Id	Name	SBO
TauH3R	TauH3R	
ADP	ADP	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_4 = \text{vol}(\text{Brain}) \cdot \text{Michaelis\_Menten}(k6, [\text{TauN3R}], [\text{ATP}], k7)$$
 (24)

$$Michaelis\_Menten(k1, x1, x2, k2) = \frac{k1 \cdot x1 \cdot x2}{k2 + x1}$$
 (25)

$$Michaelis\_Menten\left(k1,x1,x2,k2\right) = \frac{k1\cdot x1\cdot x2}{k2+x1} \tag{26}$$

## 8.5 Reaction r5

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

#### Name r5

Notes Dephosphorylation of abnormal/misfolded tau

## **Reaction equation**

$$TauH3R \xrightarrow{TauH3R} TauN3R \tag{27}$$

#### Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
TauH3R	TauH3R	

#### **Modifier**

Table 17: Properties of each modifier.

Id	Name	SBO
TauH3R	TauH3R	

#### **Product**

Table 18: Properties of each product.

Id	Name	SBO
TauN3R	TauN3R	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_5 = \text{vol}(\text{Brain}) \cdot \text{Henri\_Michaelis\_Menten\_irreversible}([\text{TauH3R}], \text{k9}, \text{k8})$$
 (28)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{29}$$

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{30}$$

## 8.6 Reaction r6

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r6

Notes Conformation change favoring MT binding

# **Reaction equation**

$$Tau03R \xrightarrow{Tau03R} Tau0_3R \tag{31}$$

#### Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
Tau03R	Tau03R	

#### **Modifier**

Table 20: Properties of each modifier.

Id	Name	SBO
Tau03R	Tau03R	

#### **Product**

Table 21: Properties of each product.

Id	Name	SBO
Tau0_3R	Tau0*3R	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_6 = \text{vol}(\text{Brain}) \cdot \text{k10} \cdot [\text{Tau03R}] \tag{32}$$

# 8.7 Reaction r7

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

#### Name r7

Notes Conformational change back to original

# **Reaction equation**

$$Tau0_{3}R \xrightarrow{Tau0_{3}R} Tau0_{3}R$$
 (33)

## Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
Tau0_3R	Tau0*3R	

## **Modifier**

Table 23: Properties of each modifier.

Id	Name	SBO
Tau0_3R	Tau0*3R	

## **Product**

Table 24: Properties of each product.

Id	Name	SBO
Tau03R	Tau03R	

## **Kinetic Law**

Derived unit contains undeclared units

$$v_7 = \text{vol}(\text{Brain}) \cdot \text{k11} \cdot [\text{Tau0}_{-}3\text{R}] \tag{34}$$

#### 8.8 Reaction r8

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

# Name r8

 $oldsymbol{\mathsf{Notes}}$  Binding of newly synthesized tau to MT

## **Reaction equation**

$$Tau0_{3}R + MT \xrightarrow{Tau0_{3}R, MT} Tau0_{3}RMT$$
 (35)

#### **Reactants**

Table 25: Properties of each reactant.

Id	Name	SBO
Tau0_3R	Tau0*3R	
MT	MT	

#### **Modifiers**

Table 26: Properties of each modifier.

Id	Name	SBO
Tau0_3R MT	Tau0*3R MT	

#### **Product**

Table 27: Properties of each product.

Id	Name	SBO
Tau03RMT	Tau03RMT	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_8 = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(k12, [\text{Tau0\_3R}], [\text{MT}])$$
 (36)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{37}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{38}$$

#### 8.9 Reaction r9

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r9

Notes Release of newly synthesized au from MT

## **Reaction equation**

$$Tau03RMT \xrightarrow{Tau03RMT} Tau0_3R + MT$$
 (39)

#### Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
Tau03RMT	Tau03RMT	

#### Modifier

Table 29: Properties of each modifier.

Id	Name	SBO
Tau03RMT	Tau03RMT	

#### **Products**

Table 30: Properties of each product.

Id	Name	SBO
Tau0_3R	Tau0*3R	
MT	MT	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_9 = \text{vol}(\text{Brain}) \cdot \text{k13} \cdot [\text{Tau03RMT}] \tag{40}$$

# **8.10 Reaction** r10

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r10

Notes Conformation chang favoring MT binding

# **Reaction equation**

$$TauN3R \xrightarrow{TauN3R} TauN_3R \tag{41}$$

#### Reactant

Table 31: Properties of each reactant.

Id	Name	SBO
TauN3R	TauN3R	

## **Modifier**

Table 32: Properties of each modifier.

Id	Name	SBO
TauN3R	TauN3R	

## **Product**

Table 33: Properties of each product.

Id	Name	SBO
TauN_3R	TauN*3R	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{10} = \text{vol}(\text{Brain}) \cdot \text{k14} \cdot [\text{TauN3R}] \tag{42}$$

# **8.11 Reaction** r11

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r11

Notes Conformational change back to original

# **Reaction equation**

$$TauN_{3}R \xrightarrow{TauN_{3}R} TauN_{3}R \tag{43}$$

Table 34: Properties of each reactant.

Id	Name	SBO
TauN_3R	TauN*3R	

Table 35: Properties of each modifier.

Id	Name	SBO
TauN_3R	TauN*3R	

## **Product**

Table 36: Properties of each product.

Id	Name	SBO
TauN3R	TauN3R	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{11} = \text{vol}(\text{Brain}) \cdot \text{k15} \cdot [\text{TauN}_{-}3\text{R}] \tag{44}$$

## **8.12 Reaction** r12

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r12

Notes Binding of normally phosphorylated tau to MT

# **Reaction equation**

$$TauN_3R + MT \xrightarrow{TauN_3R, MT} TauN3RMT$$
 (45)

Table 37: Properties of each reactant.

Id	Name	SBO
TauN_3R	TauN*3R	
MT	MT	

Table 38: Properties of each modifier.

Id	Name	SBO
TauN_3R MT	TauN*3R MT	

#### **Product**

Table 39: Properties of each product.

Id	Name	SBO
TauN3RMT	TauN3RMT	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{12} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k16}, [\text{TauN\_3R}], [\text{MT}])$$
 (46)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{47}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{48}$$

## **8.13 Reaction** r13

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

## Name r13

 $oldsymbol{\mathsf{Notes}}$  Release of normally phosphorylated tau from MT

## **Reaction equation**

$$TauN3RMT \xrightarrow{TauN3RMT} TauN_3R + MT$$
 (49)

Table 40: Properties of each reactant.

Id	Name	SBO
TauN3RMT	TauN3RMT	

Table 41: Properties of each modifier.

Id	Name	SBO
TauN3RMT	TauN3RMT	

## **Products**

Table 42: Properties of each product.

Id	Name	SBO
TauN_3R	TauN*3R	
MT	MT	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{13} = \text{vol}(\text{Brain}) \cdot \text{k17} \cdot [\text{TauN3RMT}]$$
 (50)

## 8.14 Reaction r14

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r14

Notes Conformational change favoring MT binding

# **Reaction equation**

$$TauH3R \xrightarrow{TauH3R} TauH_3R \tag{51}$$

Table 43: Properties of each reactant.

Id	Name	SBO
TauH3R	TauH3R	

Table 44: Properties of each modifier.

Id	Name	SBO
TauH3R	TauH3R	

# **Product**

Table 45: Properties of each product.

Id	Name	SBO
TauH_3R	TauH*3R	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{14} = \text{vol}(\text{Brain}) \cdot \text{k18} \cdot [\text{TauH3R}] \tag{52}$$

## **8.15 Reaction** r15

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r15

Notes Conformational change backt to original

# **Reaction equation**

$$TauH_3R \xrightarrow{TauH_3R} TauH_3R \tag{53}$$

Table 46: Properties of each reactant.

Id	Name	SBO
TauH_3R	TauH*3R	

Table 47: Properties of each modifier.

Id	Name	SBO
TauH_3R	TauH*3R	

# **Product**

Table 48: Properties of each product.

Id	Name	SBO
TauH3R	TauH3R	

## **Kinetic Law**

Derived unit contains undeclared units

$$v_{15} = \text{vol}(\text{Brain}) \cdot \text{k19} \cdot [\text{TauH}_{-}3\text{R}] \tag{54}$$

## **8.16 Reaction** r16

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r16

Notes Binding of misfolded tau to MT

# **Reaction equation**

$$TauH_3R + MT \xrightarrow{TauH_3R, MT} TauH3RMT$$
 (55)

Table 49: Properties of each reactant.

Id	Name	SBO
TauH_3R	TauH*3R	
MT	MT	

Table 50: Properties of each modifier.

Id	Name	SBO
TauH_3R	TauH*3R	
MT	MT	

#### **Product**

Table 51: Properties of each product.

Id	Name	SBO
TauH3RMT	TauH3RMT	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{16} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k20}, [\text{TauH\_3R}], [\text{MT}])$$
 (56)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{57}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{58}$$

## **8.17 Reaction** r17

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r17

Notes Release of misfolded tau from microtubules

## **Reaction equation**

$$TauH3RMT \xrightarrow{TauH3RMT} TauH_3R + MT$$
 (59)

Table 52: Properties of each reactant.

Id	Name	SBO
TauH3RMT	TauH3RMT	

Table 53: Properties of each modifier.

Id	Name	SBO
TauH3RMT	TauH3RMT	

## **Products**

Table 54: Properties of each product.

Id	Name	SBO
TauH_3R	TauH*3R	
MT	MT	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{17} = \text{vol}(\text{Brain}) \cdot \text{k21} \cdot [\text{TauH3RMT}] \tag{60}$$

## 8.18 Reaction r18

This is an irreversible reaction of three reactants forming two products influenced by three modifiers.

Name r18

Notes Degradation of newly synthesized tau

# **Reaction equation**

$$Tau03R + 20S + ATP \xrightarrow{Tau03R, 20S, ATP} ADP + 20S$$
 (61)

Table 55: Properties of each reactant.

ame SBO
u03R S
)

Table 56: Properties of each modifier.

Id	Name	SBO
Tau03R	Tau03R	
_20S	20S	
ATP	ATP	

#### **Products**

Table 57: Properties of each product.

Id	Name	SBO
ADP	ADP	
_20S	20S	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{18} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action\_}(\text{k22}, [\text{Tau03R}], [\text{\_20S}], [\text{ATP}])$$
 (62)

$$Mass\_Action\_(K1,x1,x2,x3) = K1 \cdot x1 \cdot x2 \cdot x3 \tag{63}$$

$$Mass\_Action\_(K1,x1,x2,x3) = K1 \cdot x1 \cdot x2 \cdot x3 \tag{64}$$

## **8.19 Reaction** r19

This is an irreversible reaction of three reactants forming two products influenced by three modifiers.

Name r19

Notes Degradation of phosphorlated tau

# **Reaction equation**

$$TauN3R + 20S + ATP \xrightarrow{TauN3R, 20S, ATP} ADP + 20S$$
 (65)

#### **Reactants**

Table 58: Properties of each reactant.

Id	Name	SBO
TauN3R	TauN3R	
_20S	20S	
ATP	ATP	

## **Modifiers**

Table 59: Properties of each modifier.

Id	Name	SBO
TauN3R	TauN3R	
_20S	20S	
ATP	ATP	

## **Products**

Table 60: Properties of each product.

Id	Name	SBO
ADP	ADP	
_20S	20S	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{19} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action\_}(\text{k23}, [\text{TauN3R}], [\text{\_20S}], [\text{ATP}])$$
 (66)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (67)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (68)

# **8.20 Reaction** r20

This is an irreversible reaction of three reactants forming two products influenced by three modifiers.

Name r20

Notes Degradation of misfolded tau

# **Reaction equation**

$$TauH3R + 20S + ATP \xrightarrow{TauH3R, 20S, ATP} 20S + ADP$$
 (69)

### **Reactants**

Table 61: Properties of each reactant.

Id	Name	SBO
TauH3R	TauH3R	
_20S	20S	
ATP	ATP	

## **Modifiers**

Table 62: Properties of each modifier.

Id	Name	SBO
TauH3R 20S	TauH3R 20S	
_205 ATP	ATP	

## **Products**

Table 63: Properties of each product.

Id	Name	SBO
_20S	20S	
ADP	ADP	

## **Kinetic Law**

$$v_{20} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action\_}(\text{k24}, [\text{TauH3R}], [\text{\_20S}], [\text{ATP}])$$
 (70)

$$Mass\_Action\_(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3 \tag{71}$$

$$Mass\_Action\_(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3 \tag{72}$$

# **8.21 Reaction** r21

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Name r21

Notes Phosphorylation of MT-bound newly synthesized tau

## **Reaction equation**

$$Tau03RMT + ATP \xrightarrow{Tau03RMT, ATP} TauN3RMT + ADP$$
 (73)

#### **Reactants**

Table 64: Properties of each reactant.

Id	Name	SBO
Tau03RMT	Tau03RMT	
ATP	ATP	

### **Modifiers**

Table 65: Properties of each modifier.

Id	Name	SBO
Tau03RMT ATP	Tau03RMT ATP	

## **Products**

Table 66: Properties of each product.

Id	Name	SBO
	- 1 (41110	
TauN3RMT	TauN3RMT	

Id	Name	SBO
ADP	ADP	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{21} = \text{vol}(\text{Brain}) \cdot \text{Michaelis\_Menten}(\text{k25}, [\text{Tau03RMT}], [\text{ATP}], \text{k26})$$
 (74)

$$\label{eq:Michaelis_Menten} \begin{aligned} \text{Michaelis\_Menten}\left(k1,x1,x2,k2\right) &= \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \end{aligned} \tag{75}$$

$$\label{eq:Michaelis_Menten} \begin{aligned} \text{Michaelis\_Menten}\left(k1,x1,x2,k2\right) &= \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \end{aligned} \tag{76}$$

## **8.22 Reaction** r22

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r22

Notes Dephosphorylation of MT-bound normally phosphorylated tau

# **Reaction equation**

$$TauN3RMT \xrightarrow{TauN3RMT} Tau03RMT$$
 (77)

### Reactant

Table 67: Properties of each reactant.

Id	Name	SBO
TauN3RMT	TauN3RMT	

### **Modifier**

Table 68: Properties of each modifier.

Id	Name	SBO
TauN3RMT	TauN3RMT	

### **Product**

Table 69: Properties of each product.

Id	Name	SBO
Tau03RMT	Tau03RMT	

### **Kinetic Law**

Derived unit contains undeclared units

$$v_{22} = \text{vol}(\text{Brain}) \cdot \text{Henri\_Michaelis\_Menten\_irreversible}([\text{TauN3RMT}], \text{k28}, \text{k27})$$
 (78)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{79}$$

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{80}$$

## **8.23 Reaction** r23

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name r23

Notes Phosphorylation of MT-bound normally phosphorylated tau

## **Reaction equation**

$$TauN3RMT + ATP \xrightarrow{TauN3RMT, ATP} TauH3RMT + ADP$$
 (81)

### Reactants

Table 70: Properties of each reactant.

Id	Name	SBO
TauN3RMT ATP	TauN3RMT ATP	

### **Modifiers**

Table 71: Properties of each modifier.

Id	Name	SBO
TauN3RMT	TauN3RMT	
ATP	ATP	

### **Products**

Table 72: Properties of each product.

Id	Name	SBO
TauH3RMT ADP	TauH3RMT ADP	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{23} = \text{vol}(\text{Brain}) \cdot \text{Michaelis\_Menten}(\text{k29}, [\text{TauN3RMT}], [\text{ATP}], \text{k30})$$
 (82)

$$Michaelis\_Menten(k1, x1, x2, k2) = \frac{k1 \cdot x1 \cdot x2}{k2 + x1}$$
 (83)

$$\label{eq:Michaelis_Menten} \begin{aligned} \text{Michaelis\_Menten}\left(k1,x1,x2,k2\right) &= \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \end{aligned} \tag{84}$$

### 8.24 Reaction r24

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r24

Notes Dephosphorylation of MT-bound abnormal/midfolded tau

# **Reaction equation**

$$TauH3RMT \xrightarrow{TauH3RMT} TauN3RMT$$
 (85)

## Reactant

Table 73: Properties of each reactant.

Id	Name	SBO
TauH3RMT	TauH3RMT	

### **Modifier**

Table 74: Properties of each modifier.

Id	Name	SBO
TauH3RMT	TauH3RMT	

### **Product**

Table 75: Properties of each product.

Id	Name	SBO
TauN3RMT	TauN3RMT	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{24} = \text{vol}(\text{Brain}) \cdot \text{Henri\_Michaelis\_Menten\_irreversible}([\text{TauH3RMT}], \text{k32}, \text{k31})$$
 (86)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate}$$
 (87)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate}$$
 (88)

## **8.25 Reaction** r25

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r25

Notes Association of misfolded tau with Hsp70

### **Reaction equation**

$$TauH3R + Hsc70 \xrightarrow{TauH3R, Hsc70} TauH3R - Hsc70$$
 (89)

### Reactants

Table 76: Properties of each reactant.

Id	Name	SBO
TauH3R	TauH3R	
Hsc70	Hsc70	

## **Modifiers**

Table 77: Properties of each modifier.

Id	Name	SBO
TauH3R	TauH3R	
Hsc70	Hsc70	

### **Product**

Table 78: Properties of each product.

Id	Name	SBO
TauH3R_Hsc70	TauH3R-Hsc70	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{25} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k33}, [\text{TauH3R}], [\text{Hsc70}])$$
(90)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{91}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{92}$$

## 8.26 Reaction r26

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r26

Notes Hsc70 release

## **Reaction equation**

$$TauH3R\_Hsc70 \xrightarrow{TauH3R\_Hsc70} TauH3R + Hsc70$$
 (93)

# Reactant

Table 79: Properties of each reactant.

Id	Name	SBO
TauH3R_Hsc70	TauH3R-Hsc70	

## **Modifier**

Table 80: Properties of each modifier.

Id	Name	SBO
TauH3R_Hsc70	TauH3R-Hsc70	

## **Products**

Table 81: Properties of each product.

Id	Name	SBO
TauH3R	TauH3R	_
Hsc70	Hsc70	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{26} = \text{vol}(\text{Brain}) \cdot \text{k34} \cdot [\text{TauH3R\_Hsc70}] \tag{94}$$

## **8.27 Reaction** r27

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name r27

Notes Exchange of Hsc70 for Hsp90

# **Reaction equation**

$$TauH3R\_Hsc70 + Hsp90 \xrightarrow{TauH3R\_Hsc70, Hsp90} TauH3R\_Hsp90 + Hsc70$$
 (95)

## **Reactants**

Table 82: Properties of each reactant.

Id	Name	SBO
TauH3R_Hsc70 Hsp90	TauH3R-Hsc70 Hsp90	

## **Modifiers**

Table 83: Properties of each modifier.

Id	Name	SBO
TauH3R_Hsc70	TauH3R-Hsc70	
Hsp90	Hsp90	

### **Products**

Table 84: Properties of each product.

Id	Name	SBO
TauH3R_Hsp90	TauH3R-Hsp90	
Hsc70	Hsc70	

## **Kinetic Law**

Derived unit contains undeclared units

$$v_{27} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k35}, [\text{TauH3R\_Hsc70}], [\text{Hsp90}]) \tag{96}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{97}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{98}$$

# 8.28 Reaction r28

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r28

Notes Restoration of TauH to TauO via Hsp90

# **Reaction equation**

$$TauH3R\_Hsp90 \xrightarrow{TauH3R\_Hsp90} Tau03R\_Hsp90$$
 (99)

### Reactant

Table 85: Properties of each reactant.

Id	Name	SBO
TauH3R_Hsp90	TauH3R-Hsp90	

### **Modifier**

Table 86: Properties of each modifier.

Id	Name	SBO
TauH3R_Hsp90	TauH3R-Hsp90	

## **Product**

Table 87: Properties of each product.

Id	Name	SBO
Tau03R_Hsp90	Tau03R-Hsp90	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$\textit{v}_{28} = vol\left(Brain\right) \cdot Henri\_Michaelis\_Menten\_irreversible\left([TauH3R\_Hsp90], k9, k8\right) \quad (100)$$

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{101}$$

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{102}$$

## **8.29 Reaction** r29

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r29

Notes Release of Tau0 from Hsp90

## **Reaction equation**

$$Tau03R\_Hsp90 \xrightarrow{Tau03R\_Hsp90} Hsp90 + Tau03R$$
 (103)

### Reactant

Table 88: Properties of each reactant.

Id	Name	SBO
Tau03R_Hsp90	Tau03R-Hsp90	

### **Modifier**

Table 89: Properties of each modifier.

Id	Name	SBO
Tau03R_Hsp90	Tau03R-Hsp90	

## **Products**

Table 90: Properties of each product.

Id	Name	SBO
Hsp90	Hsp90	
Tau03R	Tau03R	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{29} = \text{vol}(\text{Brain}) \cdot \text{k36} \cdot [\text{Tau03R\_Hsp90}] \tag{104}$$

# 8.30 Reaction r30

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r30

Notes Exchange of Hsc70 for CHIP

## **Reaction equation**

$$TauH3R\_Hsc70 + CHIP \xrightarrow{TauH3R\_Hsc70, CHIP} TauH3R\_CHIP\_Hsc70$$
 (105)

### **Reactants**

Table 91: Properties of each reactant.

Id	Name	SBO
TauH3R_Hsc70 CHIP	TauH3R-Hsc70 CHIP	

### **Modifiers**

Table 92: Properties of each modifier.

Id	Name	SBO
TauH3R_Hsc70	TauH3R-Hsc70	
CHIP	CHIP	

### **Product**

Table 93: Properties of each product.

Id	Name	SBO
TauH3R_CHIP_Hsc70	TauH3R-CHIP-Hsc70	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{30} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k37}, [\text{TauH3R\_Hsc70}], [\text{CHIP}])$$
 (106)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{107}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{108}$$

# **8.31 Reaction** r31

This is an irreversible reaction of one reactant forming three products influenced by one modifier.

## Name r31

Notes Ubiquitination of tau

# **Reaction equation**

$$TauH3R\_CHIP\_Hsc70 \xrightarrow{TauH3R\_CHIP\_Hsc70} TauH3RUb + Hsc70 + CHIP$$
 (109)

### Reactant

Table 94: Properties of each reactant.

Id	Name	SBO
TauH3R_CHIP_Hsc70	TauH3R-CHIP-Hsc70	

#### **Modifier**

Table 95: Properties of each modifier.

Id	Name	SBO
TauH3R_CHIP_Hsc70	TauH3R-CHIP-Hsc70	

#### **Products**

Table 96: Properties of each product.

Id	Name	SBO
TauH3RUb	TauH3RUb	
Hsc70	Hsc70	
CHIP	CHIP	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{31} = \text{vol}(\text{Brain}) \cdot \text{k38} \cdot [\text{TauH3R\_CHIP\_Hsc70}]$$
 (110)

## **8.32 Reaction** r32

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r32

Notes Binding of Bag-2 to the degradation complex

# **Reaction equation**

$$TauH3R\_CHIP\_Hsc70 + Bag2 \xrightarrow{TauH3R\_CHIP\_Hsc70, Bag2} TauH3R\_CHIP\_Hsc70\_Bag2 \tag{111}$$

## **Reactants**

Table 97: Properties of each reactant.

Id	Name	SBO
TauH3R_CHIP_Hsc70	TauH3R-CHIP-Hsc70	
Bag2	Bag2	

### **Modifiers**

Table 98: Properties of each modifier.

R-CHIP-Hsc70
,

## **Product**

Table 99: Properties of each product.

Id	Name	SBO
TauH3R_CHIP_Hsc70_Bag2	TauH3R-CHIP-Hsc70-Bag2	

### **Kinetic Law**

$$v_{32} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k39}, [\text{TauH3R\_CHIP\_Hsc70}], [\text{Bag2}])$$
 (112)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{113}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{114}$$

## 8.33 Reaction r33

This is an irreversible reaction of one reactant forming three products influenced by one modifier.

Name r33

Notes Rescue for degradation by Bag2

# **Reaction equation**

$$TauH3R\_CHIP\_Hsc70\_Bag2 \xrightarrow{TauH3R\_CHIP\_Hsc70\_Bag2} TauH3R\_Hsc70 + CHIP + Bag2 \tag{115}$$

### Reactant

Table 100: Properties of each reactant.

Id	Name	SBO
TauH3R_CHIP_Hsc70_Bag2	TauH3R-CHIP-Hsc70-Bag2	

#### **Modifier**

Table 101: Properties of each modifier.

Tuble 101. Froperties of each incumer.		
Id	Name	SBO
TauH3R_CHIP_Hsc70_Bag2	TauH3R-CHIP-Hsc70-Bag2	

### **Products**

Table 102: Properties of each product.

Id	Name	SBO
TauH3R_Hsc70	TauH3R-Hsc70	
CHIP	CHIP	
Bag2	Bag2	

### **Kinetic Law**

$$v_{33} = \text{vol}(\text{Brain}) \cdot \text{k40} \cdot [\text{TauH3R\_CHIP\_Hsc70\_Bag2}]$$
 (116)

## 8.34 Reaction r34

This is an irreversible reaction of three reactants forming two products influenced by three modifiers.

Name r34

Notes Degradation of ubiquitinated tau

# **Reaction equation**

$$TauH3RUb + _26S + ATP \xrightarrow{TauH3RUb, _26S, ATP} ADP + _26S$$
 (117)

### **Reactants**

Table 103: Properties of each reactant.

Id	Name	SBO
TauH3RUb	TauH3RUb	
_26S	26S	
ATP	ATP	

## **Modifiers**

Table 104: Properties of each modifier.

Id	Name	SBO
TauH3RUb	TauH3RUb	
_26S	26S	
ATP	ATP	

## **Products**

Table 105: Properties of each product.

Id	Name	SBO
ADP	ADP	
_26S	26S	

## **Kinetic Law**

$$v_{34} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action\_}(\text{k41}, [\text{TauH3RUb}], [\text{\_26S}], [\text{ATP}])$$
 (118)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (119)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (120)

## 8.35 Reaction r35

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

Name r35

Notes Synthesis of 4R tau

### **Reaction equation**

$$\emptyset \longrightarrow \text{Tau}04R$$
 (121)

### **Product**

Table 106: Properties of each product.

Id	Name	SBO
Tau04R	Tau04R	

### **Kinetic Law**

Derived unit contains undeclared units

$$v_{35} = \text{vol}(\text{Brain}) \cdot \text{Constant\_flux\_irreversible}(\text{k42})$$
 (122)

Constant\_flux\_irreversible 
$$(v) = v$$
 (123)

Constant\_flux\_irreversible 
$$(v) = v$$
 (124)

### **8.36 Reaction** r36

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name r36

Notes Phosphorylation of newly synthesized tau

## **Reaction equation**

$$Tau04R + ATP \xrightarrow{Tau04R, ATP} TauN4R + ADP$$
 (125)

## **Reactants**

Table 107: Properties of each reactant.

Id	Name	SBO
Tau04R	Tau04R	
ATP	ATP	

#### **Modifiers**

Table 108: Properties of each modifier.

Id	Name	SBO
Tau04R	Tau04R	
ATP	ATP	

### **Products**

Table 109: Properties of each product.

Name	SBO
TauN4R ADP	
	TauN4R

# **Kinetic Law**

$$v_{36} = vol\left(Brain\right) \cdot Michaelis\_Menten\left(k43, [Tau04R], [ATP], k44\right) \tag{126}$$

$$\label{eq:Michaelis_Menten} \begin{aligned} \text{Michaelis\_Menten}\left(k1,x1,x2,k2\right) &= \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \end{aligned} \tag{127}$$

$$\mbox{Michaelis\_Menten} \left(k1, x1, x2, k2\right) = \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \eqno(128)$$

## **8.37 Reaction** r37

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r37

Notes Dephosphorylation of normally phosphorylated tau

### **Reaction equation**

$$TauN4R \xrightarrow{TauN4R} Tau04R \tag{129}$$

#### Reactant

Table 110: Properties of each reactant.

Id	Name	SBO
TauN4R	TauN4R	

#### **Modifier**

Table 111: Properties of each modifier.

Id	Name	SBO
TauN4R	TauN4R	

### **Product**

Table 112: Properties of each product.

Id	Name	SBO
Tau04R	Tau04R	

#### **Kinetic Law**

$$v_{37} = \text{vol}(\text{Brain}) \cdot \text{Henri\_Michaelis\_Menten\_irreversible}([\text{TauN4R}], \text{k46}, \text{k45})$$
 (130)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{131}$$

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{132}$$

## 8.38 Reaction r38

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name r38

Notes Phosphorylation of normally phosphorylated tau

# **Reaction equation**

$$TauN4R + ATP \xrightarrow{TauN4R, ATP} TauH4R + ADP$$
 (133)

#### **Reactants**

Table 113: Properties of each reactant.

Id	Name	SBO
	TauN4R	
ATP	ATP	

#### **Modifiers**

Table 114: Properties of each modifier.

Id	Name	SBO
TauN4R	TauN4R	_
ATP	ATP	

# **Products**

Table 115: Properties of each product.

Id	Name	SBO
TauH4R ADP	TauH4R ADP	

## **Kinetic Law**

$$v_{38} = \text{vol}(\text{Brain}) \cdot \text{Michaelis\_Menten}(\text{k47}, [\text{TauN4R}], [\text{ATP}], \text{k48})$$
 (134)

$$\label{eq:Menten} \begin{aligned} \text{Michaelis\_Menten}\left(k1,x1,x2,k2\right) &= \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \end{aligned} \tag{135}$$

$$\label{eq:Menten} \begin{aligned} \text{Michaelis\_Menten}\left(k1,x1,x2,k2\right) &= \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \end{aligned} \tag{136}$$

### 8.39 Reaction r39

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r39

Notes Dephosphorylation of abnormal/misfolded tau

# **Reaction equation**

$$TauH4R \xrightarrow{TauH4R} TauN4R$$
 (137)

## Reactant

Table 116: Properties of each reactant.

Id	Name	SBO
TauH4R	TauH4R	

# **Modifier**

Table 117: Properties of each modifier.

Id	Name	SBO
TauH4R	TauH4R	

## **Product**

Table 118: Properties of each product.

Id	Name	SBO
TauN4R	TauN4R	

## **Kinetic Law**

 $v_{39} = \text{vol}(Brain) \cdot \text{Henri\_Michaelis\_Menten\_irreversible}([TauH4R], k50, k49)$  (138)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{139}$$

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate}$$
 (140)

## **8.40 Reaction** r40

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r40

Notes Conformation change favoring MT binding

## **Reaction equation**

$$Tau04R \xrightarrow{Tau04R} Tau0_4R \tag{141}$$

### Reactant

Table 119: Properties of each reactant.

Id	Name	SBO
Tau04R	Tau04R	

### **Modifier**

Table 120: Properties of each modifier.

Id	Name	SBO
Tau04R	Tau04R	

#### **Product**

Table 121: Properties of each product.

Id	Name	SBO
Tau0_4R	Tau0*4R	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{40} = \text{vol}(\text{Brain}) \cdot \text{k51} \cdot [\text{Tau04R}] \tag{142}$$

## **8.41 Reaction** r41

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r41

Notes Conformational change back to original

## **Reaction equation**

$$Tau0_{-}4R \xrightarrow{Tau0_{-}4R} Tau0_{-}4R$$
 (143)

### Reactant

Table 122: Properties of each reactant.

Id	Name	SBO
Tau0_4R	Tau0*4R	

### **Modifier**

Table 123: Properties of each modifier.

Id	Name	SBO
Tau0_4R	Tau0*4R	

### **Product**

Table 124: Properties of each product.

Id	Name	SBO
Tau04R	Tau04R	

## **Kinetic Law**

$$v_{41} = \text{vol}(\text{Brain}) \cdot \text{k52} \cdot [\text{Tau0}_{-}4\text{R}] \tag{144}$$

### **8.42 Reaction** r42

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r42

Notes Binding of newly shynthesized tau to MT

# **Reaction equation**

$$Tau0_{-}4R + MT \xrightarrow{Tau0_{-}4R, MT} Tau04RMT$$
 (145)

#### **Reactants**

Table 125: Properties of each reactant.

Id	Name	SBO
Tau0_4R	Tau0*4R	
MT	MT	

## **Modifiers**

Table 126: Properties of each modifier.

Id	Name	SBO
Tau0_4R	Tau0*4R	
MT	MT	

## **Product**

Table 127: Properties of each product.

Id	Name	SBO
Tau04RMT	Tau04RMT	

# **Kinetic Law**

$$v_{42} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k53}, [\text{Tau0\_4R}], [\text{MT}])$$
 (146)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{147}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{148}$$

## 8.43 Reaction r43

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r43

Notes Release of newly shyntesized tau from MT

# **Reaction equation**

$$Tau04RMT \xrightarrow{Tau04RMT} Tau0_{-}4R + MT$$
 (149)

## Reactant

Table 128: Properties of each reactant.

Id	Name	SBO
Tau04RMT	Tau04RMT	

## **Modifier**

Table 129: Properties of each modifier.

Id	Name	SBO
Tau04RMT	Tau04RMT	

### **Products**

Table 130: Properties of each product.

Id	Name	SBO
Tau0_4R	Tau0*4R	
MT	MT	

### **Kinetic Law**

$$v_{43} = \text{vol}(\text{Brain}) \cdot \text{k54} \cdot [\text{Tau04RMT}] \tag{150}$$

### 8.44 Reaction r44

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r44

Notes Conformation change favoring MT binding

# **Reaction equation**

$$TauN4R \xrightarrow{TauN4R} TauN_{-}4R \tag{151}$$

### Reactant

Table 131: Properties of each reactant.

Id	Name	SBO
TauN4R	TauN4R	

## **Modifier**

Table 132: Properties of each modifier.

Id	Name	SBO
TauN4R	TauN4R	

### **Product**

Table 133: Properties of each product.

Id	Name	SBO
TauN_4R	TauN*4R	

## **Kinetic Law**

$$v_{44} = \text{vol}(\text{Brain}) \cdot \text{k55} \cdot [\text{TauN4R}] \tag{152}$$

## **8.45 Reaction** r45

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r45

Notes Conformational change back to original

# **Reaction equation**

$$TauN_{-}4R \xrightarrow{TauN_{-}4R} TauN_{-}4R \tag{153}$$

#### Reactant

Table 134: Properties of each reactant.

Id	Name	SBO
TauN_4R	TauN*4R	

#### **Modifier**

Table 135: Properties of each modifier.

Id	Name	SBO
${\tt TauN\_4R}$	TauN*4R	

### **Product**

Table 136: Properties of each product.

Id	Name	SBO
TauN4R	TauN4R	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{45} = \text{vol}(\text{Brain}) \cdot \text{k56} \cdot [\text{TauN}_{-}4\text{R}]$$
 (154)

### **8.46 Reaction** r46

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

### Name r46

Notes Binding of normally phosphorylated tau to MT

# **Reaction equation**

$$TauN_4R + MT \xrightarrow{TauN_4R, MT} TauN4RMT$$
 (155)

## **Reactants**

Table 137: Properties of each reactant.

Id	Name	SBO
TauN_4R	TauN*4R	
MT	MT	

## **Modifiers**

Table 138: Properties of each modifier.

Id	Name	SBO
TauN_4R	TauN*4R	
MT	MT	

## **Product**

Table 139: Properties of each product.

Id	Name	SBO
TauN4RMT	TauN4RMT	

## **Kinetic Law**

$$v_{46} = vol\left(Brain\right) \cdot Mass\_Action\left(k57, [TauN\_4R], [MT]\right) \tag{156}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{157}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{158}$$

## **8.47 Reaction** r47

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r47

Notes Release of normally phosphorylated tau from MT

# **Reaction equation**

$$TauN4RMT \xrightarrow{TauN4RMT} TauN_{4}R + MT$$
 (159)

#### Reactant

Table 140: Properties of each reactant.

Id	Name	SBO
TauN4RMT	TauN4RMT	

#### **Modifier**

Table 141: Properties of each modifier.

Id	Name	SBO
TauN4RMT	TauN4RMT	

#### **Products**

Table 142: Properties of each product.

Id	Name	SBO
TauN_4R	TauN*4R	
MT	MT	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{47} = \text{vol}(\text{Brain}) \cdot \text{k58} \cdot [\text{TauN4RMT}] \tag{160}$$

### **8.48 Reaction** r48

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r48

Notes Conformation change favoring MT binding

# **Reaction equation**

$$TauH4R \xrightarrow{TauH4R} TauH_{-}4R$$
 (161)

## Reactant

Table 143: Properties of each reactant.

Id	Name	SBO
TauH4R	TauH4R	

## **Modifier**

Table 144: Properties of each modifier.

Id	Name	SBO
TauH4R	TauH4R	

## **Product**

Table 145: Properties of each product.

Id	Name	SBO
TauH_4R	TauH*4R	

## **Kinetic Law**

Derived unit contains undeclared units

$$v_{48} = \text{vol}(\text{Brain}) \cdot \text{k59} \cdot [\text{TauH4R}] \tag{162}$$

### **8.49 Reaction** r49

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r49

Notes Conformational change back to original

## **Reaction equation**

$$TauH_{-}4R \xrightarrow{TauH_{-}4R} TauH_{-}4R \tag{163}$$

#### Reactant

Table 146: Properties of each reactant.

Id	Name	SBO
TauH_4R	TauH*4R	

### **Modifier**

Table 147: Properties of each modifier.

Id	Name	SBO
TauH_4R	TauH*4R	

### **Product**

Table 148: Properties of each product.

Id	Name	SBO
TauH4R	TauH4R	

### **Kinetic Law**

Derived unit contains undeclared units

$$v_{49} = \text{vol}(\text{Brain}) \cdot \text{k60} \cdot [\text{TauH}_{-}4\text{R}] \tag{164}$$

## 8.50 Reaction r50

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r50

 $\ensuremath{\text{Notes}}$  Binding of misfolded tau to MT

## **Reaction equation**

$$TauH_4R + MT \xrightarrow{TauH_4R, MT} TauH4RMT$$
 (165)

# **Reactants**

Table 149: Properties of each reactant.

Id	Name	SBO
TauH_4R	TauH*4R	
MT	MT	

#### **Modifiers**

Table 150: Properties of each modifier.

Id	Name	SBO
TauH_4R	TauH*4R	
MT	MT	

### **Product**

Table 151: Properties of each product.

Id	Name	SBO
TauH4RMT	TauH4RMT	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{50} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k61}, [\text{TauH\_4R}], [\text{MT}])$$
 (166)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{167}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{168}$$

### **8.51 Reaction** r51

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r51

Notes Release of misfolded tau from microtubules

# **Reaction equation**

$$TauH4RMT \xrightarrow{TauH4RMT} TauH_4R + MT$$
 (169)

### Reactant

Table 152: Properties of each reactant.

Id	Name	SBO
TauH4RMT	TauH4RMT	

#### **Modifier**

Table 153: Properties of each modifier.

Id	Name	SBO
TauH4RMT	TauH4RMT	

#### **Products**

Table 154: Properties of each product.

Id	Name	SBO
TauH_4R	TauH*4R	
MT	MT	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{51} = \text{vol}(\text{Brain}) \cdot \text{k62} \cdot [\text{TauH4RMT}] \tag{170}$$

## **8.52 Reaction** r52

This is an irreversible reaction of three reactants forming two products influenced by three modifiers.

Name r52

Notes Degradation of newly shynthesized tau

# **Reaction equation**

$$Tau04R + 20S + ATP \xrightarrow{Tau04R, 20S, ATP} ADP + 20S$$
 (171)

### **Reactants**

Table 155: Properties of each reactant.

Id	Name	SBO
Tau04R	Tau04R	
_20S	20S	
ATP	ATP	

### **Modifiers**

Table 156: Properties of each modifier.

Id	Name	SBO
Tau04R	Tau04R	
_20S	20S	
ATP	ATP	

## **Products**

Table 157: Properties of each product.

Id	Name	SBO
ADP	ADP	
_20S	20S	

## **Kinetic Law**

$$v_{52} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action\_}(\text{k63}, [\text{Tau04R}], [\text{\_20S}], [\text{ATP}])$$
 (172)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (173)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (174)

# 8.53 Reaction r53

This is an irreversible reaction of three reactants forming two products influenced by three modifiers.

Name r53

Notes Degradation of phosphorylated tau

# **Reaction equation**

$$TauN4R + 20S + ATP \xrightarrow{TauN4R, 20S, ATP} ADP + 20S$$
 (175)

### **Reactants**

Table 158: Properties of each reactant.

Id	Name	SBO
TauN4R	TauN4R	
_20S	20S	
ATP	ATP	

## **Modifiers**

Table 159: Properties of each modifier.

Id	Name	SBO
TauN4R _20S ATP	TauN4R 20S ATP	

## **Products**

Table 160: Properties of each product.

Id	Name	SBO
ADP	ADP	
_20S	20S	

## **Kinetic Law**

$$v_{53} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action\_}(\text{k64}, [\text{TauN4R}], [\text{\_20S}], [\text{ATP}])$$
 (176)

$$Mass\_Action\_(K1,x1,x2,x3) = K1 \cdot x1 \cdot x2 \cdot x3 \tag{177}$$

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (178)

# **8.54 Reaction** r54

This is an irreversible reaction of three reactants forming two products influenced by three modifiers.

Name r54

Notes Degradation of misfolded tau

## **Reaction equation**

$$TauH4R + 20S + ATP \xrightarrow{TauH4R, 20S, ATP} ADP + 20S$$
 (179)

#### **Reactants**

Table 161: Properties of each reactant.

Id	Name	SBO
TauH4R	TauH4R	
_20S	20S	
ATP	ATP	

### **Modifiers**

Table 162: Properties of each modifier.

Id	Name	SBO
TauH4R	TauH4R	
_20S	20S	
ATP	ATP	

# **Products**

Table 163: Properties of each product.

Id	Name	SBO
ADP	ADP	
_20S	20S	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{54} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action\_}(\text{k65}, [\text{TauH4R}], [\text{\_20S}], [\text{ATP}])$$
(180)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (181)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (182)

## 8.55 Reaction r55

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name r55

Notes Phosphorylation of MT-bound newly synthesized tau

## **Reaction equation**

$$Tau04RMT + ATP \xrightarrow{Tau04RMT, ATP} TauN4RMT + ADP$$
 (183)

## **Reactants**

Table 164: Properties of each reactant.

Name	SBO
Tau04RMT ATP	
	Tau04RMT

## **Modifiers**

Table 165: Properties of each modifier.

Id	Name	SBO
TauO4RMT	Tau04RMT	
AIP	AIP	

### **Products**

Table 166: Properties of each product.

Id	Name	SBO
TauN4RMT ADP	TauN4RMT ADP	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{55} = \text{vol}(\text{Brain}) \cdot \text{Michaelis\_Menten}(\text{k}66, [\text{Tau}04\text{RMT}], [\text{ATP}], \text{k}67)$$
 (184)

$$Michaelis\_Menten(k1, x1, x2, k2) = \frac{k1 \cdot x1 \cdot x2}{k2 + x1}$$
 (185)

$$\label{eq:Michaelis_Menten} \begin{aligned} \text{Michaelis\_Menten}\left(k1,x1,x2,k2\right) &= \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \end{aligned} \tag{186}$$

### **8.56 Reaction** r56

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r56

Notes Dephosphorylation of MT-bound normally phosphorylated tau

# **Reaction equation**

$$TauN4RMT \xrightarrow{TauN4RMT} Tau04RMT$$
 (187)

### Reactant

Table 167: Properties of each reactant.

Id	Name	SBO
TauN4RMT	TauN4RMT	

# **Modifier**

Table 168: Properties of each modifier.

Id	Name	SBO
TauN4RMT	TauN4RMT	

# **Product**

Table 169: Properties of each product.

Id	Name	SBO
Tau04RMT	Tau04RMT	

### **Kinetic Law**

Derived unit contains undeclared units

$$v_{56} = \text{vol}(Brain) \cdot \text{Henri\_Michaelis\_Menten\_irreversible}([TauN4RMT], k69, k68)$$
 (188)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate}$$
 (189)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{190}$$

### **8.57 Reaction** r57

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name r57

 ${f Notes}$  Phosphorylation of MT-bound normally phosphorylated tau

# **Reaction equation**

$$TauN4RMT + ATP \xrightarrow{TauN4RMT, ATP} TauH4RMT + ADP$$
 (191)

### **Reactants**

Table 170: Properties of each reactant.

Id	Name	SBO
TauN4RMT ATP	TauN4RMT ATP	

#### **Modifiers**

Table 171: Properties of each modifier.

Id	Name	SBO
TauN4RMT	TauN4RMT	
ATP	ATP	

### **Products**

Table 172: Properties of each product.

Id	Name	SBO
TauH4RMT ADP	TauH4RMT ADP	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{57} = \text{vol}(\text{Brain}) \cdot \text{Michaelis\_Menten}(k70, [\text{TauN4RMT}], [\text{ATP}], k71)$$
 (192)

$$Michaelis\_Menten\left(k1,x1,x2,k2\right) = \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \tag{193}$$

$$\label{eq:Michaelis_Menten} \begin{aligned} \text{Michaelis\_Menten}\left(k1,x1,x2,k2\right) &= \frac{k1 \cdot x1 \cdot x2}{k2 + x1} \end{aligned} \tag{194}$$

## 8.58 Reaction r58

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r58

Notes Dephosphorylation of MT-bound abnormal/misfolded tau

$$TauH4RMT \xrightarrow{TauH4RMT} TauN4RMT$$
 (195)

#### Reactant

Table 173: Properties of each reactant.

Id	Name	SBO
TauH4RMT	TauH4RMT	

#### **Modifier**

Table 174: Properties of each modifier.

Id	Name	SBO
TauH4RMT	TauH4RMT	

#### **Product**

Table 175: Properties of each product.

Id	Name	SBO
TauN4RMT	TauN4RMT	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{58} = \text{vol}(Brain) \cdot Henri\_Michaelis\_Menten\_irreversible([TauH4RMT], k73, k72)$$
 (196)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate}$$
 (197)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \qquad (198)$$

### **8.59 Reaction** r59

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r59

Notes Association of misfolded tau with Hsp70

$$TauH4R + Hsc70 \xrightarrow{TauH4R, Hsc70} TauH4R - Hsc70$$
 (199)

#### **Reactants**

Table 176: Properties of each reactant.

Id	Name	SBO
TauH4R	TauH4R	
Hsc70	Hsc70	

#### **Modifiers**

Table 177: Properties of each modifier.

Id	Name	SBO
TauH4R	TauH4R	
Hsc70	Hsc70	

### **Product**

Table 178: Properties of each product.

Id	Name	SBO
TauH4R_Hsc70	TauH4R-Hsc70	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{59} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(k74, [\text{TauH4R}], [\text{Hsc70}])$$
 (200)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{201}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{202}$$

## 8.60 Reaction r60

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r60

Notes Hsc70 release

$$TauH4R\_Hsc70 \xrightarrow{TauH4R\_Hsc70} TauH4R + Hsc70$$
 (203)

#### Reactant

Table 179: Properties of each reactant.

Id	Name	SBO
TauH4R_Hsc70	TauH4R-Hsc70	

### **Modifier**

Table 180: Properties of each modifier.

Id	Name	SBO
TauH4R_Hsc70	TauH4R-Hsc70	

#### **Products**

Table 181: Properties of each product.

Id	Name	SBO
TauH4R	TauH4R	
Hsc70	Hsc70	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{60} = \text{vol}(\text{Brain}) \cdot \text{k75} \cdot [\text{TauH4R\_Hsc70}] \tag{204}$$

# **8.61 Reaction** r61

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Name r61

Notes Exchange of Hsc70 for Hsp90

$$TauH4R\_Hsc70 + Hsp90 \xrightarrow{TauH4R\_Hsc70, Hsp90} TauH4R\_Hsp90 + Hsc70$$
(205)

## **Reactants**

Table 182: Properties of each reactant.

Name	SBO
TauH4R-Hsc70	

### **Modifiers**

Table 183: Properties of each modifier.

Id	Name	SBO
TauH4R_Hsc70	TauH4R-Hsc70	
Hsp90	Hsp90	

### **Products**

Table 184: Properties of each product.

Id	Name	SBO
TauH4R_Hsp90 Hsc70	TauH4R-Hsp90 Hsc70	

### **Kinetic Law**

$$v_{61} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(k76, [\text{TauH4R\_Hsc70}], [\text{Hsp90}])$$
 (206)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{207}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{208}$$

### **8.62 Reaction** r62

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r62

Notes Restoration of TauH to TauO via Hsp90

### **Reaction equation**

$$TauH4R\_Hsp90 \xrightarrow{TauH4R\_Hsp90} Tau04R\_Hsp90$$
 (209)

### Reactant

Table 185: Properties of each reactant.

Id	Name	SBO
TauH4R_Hsp90	TauH4R-Hsp90	

### **Modifier**

Table 186: Properties of each modifier.

Tuble 100: 1 toperties of each modifier:		
Id	Name	SBO
TauH4R_Hsp90	TauH4R-Hsp90	

### **Product**

Table 187: Properties of each product.

Id	Name	SBO
Tau04R_Hsp90	Tau04R-Hsp90	

### **Kinetic Law**

$$v_{62} = \text{vol}(\text{Brain}) \cdot \text{Henri\_Michaelis\_Menten\_irreversible}([\text{TauH4R\_Hsp90}], \text{k9}, \text{k77})$$
 (210)

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{211}$$

$$Henri\_Michaelis\_Menten\_irreversible (substrate, Km, V) = \frac{V \cdot substrate}{Km + substrate} \tag{212}$$

## 8.63 Reaction r63

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r63

Notes Release of Tau0 from Hsp90

# **Reaction equation**

$$Tau04R\_Hsp90 \xrightarrow{Tau04R\_Hsp90} Hsp90 + Tau04R$$
 (213)

### Reactant

Table 188: Properties of each reactant.

Id	Name	SBO
Tau04R_Hsp90	Tau04R-Hsp90	

### **Modifier**

Table 189: Properties of each modifier.

Tuble 105: 1 toperties of each mounter:		
Id	Name	SBO
Tau04R_Hsp90	Tau04R-Hsp90	

## **Products**

Table 190: Properties of each product.

Id	Name	SBO
Hsp90	Hsp90	
Tau04R	Tau04R	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{63} = \text{vol}(\text{Brain}) \cdot \text{k78} \cdot [\text{Tau04R\_Hsp90}] \tag{214}$$

### 8.64 Reaction r64

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

## Name r64

Notes Exchange of Hsc70 for CHIP

# **Reaction equation**

$$TauH4R\_Hsc70 + CHIP \xrightarrow{TauH4R\_Hsc70, CHIP} TauH4R\_CHIP\_Hsc70$$
 (215)

### **Reactants**

Table 191: Properties of each reactant.

Id	Name	SBO
TauH4R_Hsc70 CHIP	TauH4R-Hsc70 CHIP	

## **Modifiers**

Table 192: Properties of each modifier.

Id	Name	SBO
TauH4R_Hsc70 CHIP	TauH4R-Hsc70 CHIP	

## **Product**

Table 193: Properties of each product.

Id	Name	SBO
TauH4R_CHIP_Hsc70	TauH4R-CHIP-Hsc70	

## **Kinetic Law**

$$v_{64} = vol(Brain) \cdot Mass\_Action(k79, [TauH4R\_Hsc70], [CHIP])$$
 (216)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{217}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{218}$$

## **8.65 Reaction** r65

This is an irreversible reaction of one reactant forming three products influenced by one modifier.

Name r65

Notes Ubiquitination of tau

# **Reaction equation**

$$TauH4R\_CHIP\_Hsc70 \xrightarrow{TauH4R\_CHIP\_Hsc70} TauH4RUb + Hsc70 + CHIP$$
 (219)

#### Reactant

Table 194: Properties of each reactant.

Id	Name	SBO
TauH4R_CHIP_Hsc70	TauH4R-CHIP-Hsc70	

#### Modifier

Table 195: Properties of each modifier.

Id	Name	SBO
TauH4R_CHIP_Hsc70	TauH4R-CHIP-Hsc70	

### **Products**

Table 196: Properties of each product.

Id	Name	SBO
TauH4RUb	TauH4RUb	
Hsc70	Hsc70	
CHIP	CHIP	

### **Kinetic Law**

$$v_{65} = \text{vol}(\text{Brain}) \cdot \text{k80} \cdot [\text{TauH4R\_CHIP\_Hsc70}]$$
 (220)

## 8.66 Reaction r66

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r66

Notes Binding of Bag-2 to the degradation complex

# **Reaction equation**

$$TauH4R\_CHIP\_Hsc70 + Bag2 \xrightarrow{TauH4R\_CHIP\_Hsc70, Bag2} TauH4R\_CHIP\_Hsc70\_Bag2 \tag{221}$$

#### **Reactants**

Table 197: Properties of each reactant.

Id	Name	SBO
TauH4R_CHIP_Hsc70 Bag2	TauH4R-CHIP-Hsc70 Bag2	

#### **Modifiers**

Table 198: Properties of each modifier.

Id	Name	SBO
TauH4R_CHIP_Hsc70	TauH4R-CHIP-Hsc70	
Bag2	Bag2	

### **Product**

Table 199: Properties of each product.

Id	Name	SBO
TauH4R_CHIP_Hsc70_Bag2	TauH4R-CHIP-Hsc70-Bag2	

#### **Kinetic Law**

$$v_{66} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k81}, [\text{TauH4R\_CHIP\_Hsc70}], [\text{Bag2}])$$
 (222)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{223}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{224}$$

### **8.67 Reaction** r67

This is an irreversible reaction of one reactant forming three products influenced by one modifier.

Name r67

Notes Rescue from degradation by Bag2

# **Reaction equation**

$$TauH4R\_CHIP\_Hsc70\_Bag2 \xrightarrow{TauH4R\_CHIP\_Hsc70\_Bag2} TauH4R\_Hsc70 + CHIP + Bag2 \tag{225}$$

#### Reactant

Table 200: Properties of each reactant.

Id Name		SBO
TauH4R_CHIP_Hsc70_Bag2	TauH4R-CHIP-Hsc70-Bag2	

#### Modifier

Table 201: Properties of each modifier.

Id	Name	SBO
TauH4R_CHIP_Hsc70_Bag2	TauH4R-CHIP-Hsc70-Bag2	

### **Products**

Table 202: Properties of each product.

Id	Name	SBO
TauH4R_Hsc70	TauH4R-Hsc70	
CHIP	CHIP	
Bag2	Bag2	

### **Kinetic Law**

$$v_{67} = \text{vol}(\text{Brain}) \cdot \text{k82} \cdot [\text{TauH4R\_CHIP\_Hsc70\_Bag2}]$$
 (226)

## 8.68 Reaction r68

This is an irreversible reaction of three reactants forming two products influenced by three modifiers.

Name r68

Notes Degradation of ubiquitinated tau

# **Reaction equation**

$$TauH4RUb + _26S + ATP \xrightarrow{TauH4RUb, _26S, ATP} ADP + _26S$$
 (227)

### **Reactants**

Table 203: Properties of each reactant.

Id	Name	SBO
TauH4RUb	TauH4RUb	
_26S	26S	
ATP	ATP	

## **Modifiers**

Table 204: Properties of each modifier.

Id	Name	SBO
TauH4RUb	TauH4RUb	
_26S	26S	
ATP	ATP	

# **Products**

Table 205: Properties of each product.

Id	Name	SBO
ADP	ADP	
_26S	26S	

## **Kinetic Law**

$$v_{68} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action\_}(\text{k83}, [\text{TauH4RUb}], [\text{\_26S}], [\text{ATP}])$$
 (228)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (229)

Mass\_Action\_
$$(K1, x1, x2, x3) = K1 \cdot x1 \cdot x2 \cdot x3$$
 (230)

# **8.69 Reaction** r69

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r69

Notes Generation of ATP

# **Reaction equation**

$$ADP \xrightarrow{ADP} ATP \tag{231}$$

### Reactant

Table 206: Properties of each reactant.

Id	Name	SBO
ADP	ADP	

## **Modifier**

Table 207: Properties of each modifier.

Id	Name	SBO
ADP	ADP	

### **Product**

Table 208: Properties of each product.

Id	Name	SBO
ATP	ATP	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{69} = \text{vol}(\text{Brain}) \cdot \text{k84} \cdot [\text{ADP}] \tag{232}$$

## **8.70 Reaction** r70

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r70

Notes Use of ATP by other processes

## **Reaction equation**

$$ATP \xrightarrow{ATP} ADP \tag{233}$$

### Reactant

Table 209: Properties of each reactant.

Id	Name	SBO
ATP	ATP	

### **Modifier**

Table 210: Properties of each modifier.

Id	Name	SBO
ATP	ATP	

### **Product**

Table 211: Properties of each product.

Id	Name	SBO
ADP	ADP	

## **Kinetic Law**

$$v_{70} = \text{vol}(\text{Brain}) \cdot \text{k85} \cdot [\text{ATP}] \tag{234}$$

### **8.71 Reaction r71**

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r71

Notes Nucleation of Tau3

# **Reaction equation**

#### Reactant

Table 212: Properties of each reactant.

Id	Name	SBO
TauH3RUb	TauH3RUb	

### **Modifier**

Table 213: Properties of each modifier.

Id	Name	SBO
TauH3RUb	TauH3RUb	

## **Product**

Table 214: Properties of each product.

Id	Name	SBO
Nucleus3	Nucleus3	

### **Kinetic Law**

$$v_{71} = \text{vol}(\text{Brain}) \cdot \text{Nucleation}(\text{k86}, [\text{TauH3RUb}])$$
 (236)

Nucleation 
$$(k1, x1) = k1 \cdot x1^2$$
 (237)

Nucleation 
$$(k1, x1) = k1 \cdot x1^2$$
 (238)

### **8.72 Reaction** r72

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r72

Notes Dissociation of Tau3 Nucleus

# **Reaction equation**

Nucleus 
$$3 \xrightarrow{\text{Nucleus } 3} 2 \text{TauH} 3 \text{RUb}$$
 (239)

### Reactant

Table 215: Properties of each reactant.

Id	Name	SBO
Nucleus3	Nucleus3	

## **Modifier**

Table 216: Properties of each modifier.

Id	Name	SBO
Nucleus3	Nucleus3	

## **Product**

Table 217: Properties of each product.

Id	Name	SBO
TauH3RUb	TauH3RUb	

## **Kinetic Law**

$$v_{72} = \text{vol}(\text{Brain}) \cdot \text{k87} \cdot [\text{Nucleus3}] \tag{240}$$

## **8.73 Reaction** r73

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r73

Notes Nucleation of Tau4

# **Reaction equation**

$$2 \text{ TauH4RUb} \xrightarrow{\text{TauH4RUb}} \text{Nucleus4}$$
 (241)

#### Reactant

Table 218: Properties of each reactant.

Id	Name	SBO
TauH4RUb	TauH4RUb	

#### **Modifier**

Table 219: Properties of each modifier.

Id	Name	SBO
TauH4RUb	TauH4RUb	

### **Product**

Table 220: Properties of each product.

Id	Name	SBO
Nucleus4	Nucleus4	

## **Kinetic Law**

$$v_{73} = \text{vol}(\text{Brain}) \cdot \text{Nucleation}(\text{k88}, [\text{TauH4RUb}])$$
 (242)

Nucleation 
$$(k1, x1) = k1 \cdot x1^2$$
 (243)

Nucleation 
$$(k1, x1) = k1 \cdot x1^2$$
 (244)

## 8.74 Reaction r74

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name r74

Notes Dissociation of Tau4 Nucleus

# **Reaction equation**

Nucleus 
$$4 \xrightarrow{\text{Nucleus 4}} 2 \text{ TauH 4 RUb}$$
 (245)

#### Reactant

Table 221: Properties of each reactant.

Id	Name	SBO
Nucleus4	Nucleus4	

#### **Modifier**

Table 222: Properties of each modifier.

Id	Name	SBO
Nucleus4	Nucleus4	

#### **Product**

Table 223: Properties of each product.

Id	Name	SBO
TauH4RUb	TauH4RUb	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{74} = \text{vol}(\text{Brain}) \cdot \text{k89} \cdot [\text{Nucleus4}] \tag{246}$$

# **8.75 Reaction** r75

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

## Name r75

Notes Formation of Tau3, length 3

# **Reaction equation**

Nucleus 
$$3 + \text{TauH} 3\text{RUb} \xrightarrow{\text{Nucleus 3, TauH} 3\text{RUb}} \text{Agg} 33$$
 (247)

### **Reactants**

Table 224: Properties of each reactant.

Id	Name	SBO
Nucleus3	Nucleus3	
TauH3RUb	TauH3RUb	

## **Modifiers**

Table 225: Properties of each modifier.

Id	Name	SBO
Nucleus3	Nucleus3	
TauH3RUb	TauH3RUb	

## **Product**

Table 226: Properties of each product.

Id	Name	SBO
Agg33	Agg33	

## **Kinetic Law**

$$v_{75} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k90}, [\text{Nucleus3}], [\text{TauH3RUb}])$$
 (248)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{249}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{250}$$

## **8.76 Reaction** r76

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r76

Notes Dissociation

# **Reaction equation**

$$Agg33 \xrightarrow{Agg33} Nucleus3 + TauH3RUb$$
 (251)

### Reactant

Table 227: Properties of each reactant.

Id	Name	SBO
Agg33	Agg33	

### **Modifier**

Table 228: Properties of each modifier.

Id	Name	SBO
Agg33	Agg33	

## **Products**

Table 229: Properties of each product.

Id	Name	SBO
Nucleus3	Nucleus3	

## **Kinetic Law**

Derived unit contains undeclared units

$$v_{76} = \text{vol}(\text{Brain}) \cdot \text{k91} \cdot [\text{Agg33}] \tag{252}$$

### **8.77 Reaction** r77

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

### Name r77

Notes Formation of Tau3, 1 \$>\$ 3 from Tau3 aggregate of length 3

# **Reaction equation**

$$TauH3RUb + Agg33 \xrightarrow{TauH3RUb, Agg33} Ap$$
 (253)

#### **Reactants**

Table 230: Properties of each reactant.

Id	Name	SBO
TauH3RUb	TauH3RUb	
Agg33	Agg33	

#### **Modifiers**

Table 231: Properties of each modifier.

Id	Name	SBO
TauH3RUb	TauH3RUb	
Agg33	Agg33	

## **Product**

Table 232: Properties of each product.

Id	Name	SBO
Ap	Ap	

### **Kinetic Law**

$$v_{77} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k}90, [\text{TauH}3\text{RUb}], [\text{Agg}33])$$
 (254)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{255}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{256}$$

## **8.78 Reaction r78**

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r78

Notes Formation of Agg of 1 \$>\$ 3 from aggregaties of 1 \$>\$ 3

# **Reaction equation**

$$TauH3RUb + Ap \xrightarrow{TauH3RUb, Ap} Ap$$
 (257)

### **Reactants**

Table 233: Properties of each reactant.

Id	Name	SBO
TauH3RUb	TauH3RUb	
Ар	Ap	

### **Modifiers**

Table 234: Properties of each modifier.

Id	Name	SBO
TauH3RUb	TauH3RUb	
Ap	Ap	

# **Product**

Table 235: Properties of each product.

Id	Name	SBO
Ap	Ap	

### **Kinetic Law**

$$v_{78} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k90}, [\text{TauH3RUb}], [\text{Ap}])$$
 (258)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{259}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{260}$$

### **8.79 Reaction** r79

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r79

Notes Dissociation of aggregates 1 \$>\$ 3

# **Reaction equation**

$$Ap \xrightarrow{Ap} TauH3RUb + Ap$$
 (261)

#### Reactant

Table 236: Properties of each reactant.

Id	Name	SBO
Ap	Ap	

## **Modifier**

Table 237: Properties of each modifier.

Id	Name	SBO
Ap	Ap	

# **Products**

Table 238: Properties of each product.

Id	Name	SBO
TauH3RUb	TauH3RUb	
Ap	Ap	

### **Kinetic Law**

$$v_{79} = \text{vol}(\text{Brain}) \cdot \text{k91} \cdot [\text{Ap}] \tag{262}$$

## 8.80 Reaction r80

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r80

Notes Formation of Tau4, length 3

# **Reaction equation**

Nucleus4 + TauH4RUb 
$$\xrightarrow{\text{Nucleus4}}$$
 Agg43 (263)

#### **Reactants**

Table 239: Properties of each reactant.

Id	Name	SBO
Nucleus4	Nucleus4	
TauH4RUb	TauH4RUb	

#### **Modifiers**

Table 240: Properties of each modifier.

Id	Name	SBO
Nucleus4	Nucleus4	
TauH4RUb	TauH4RUb	

### **Product**

Table 241: Properties of each product.

Id	Name	SBO
Agg43	Agg43	

## **Kinetic Law**

$$v_{80} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k92}, [\text{Nucleus4}], [\text{TauH4RUb}])$$
 (264)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{265}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{266}$$

## **8.81 Reaction** r81

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r81

Notes Dissociation

# **Reaction equation**

$$Agg43 \xrightarrow{Agg43} Nucleus4 + TauH4RUb$$
 (267)

### Reactant

Table 242: Properties of each reactant.

Id	Name	SBO
Agg43	Agg43	

## **Modifier**

Table 243: Properties of each modifier.

Id	Name	SBO
Agg43	Agg43	

## **Products**

Table 244: Properties of each product.

Id	Name	SBO
Nucleus4	Nucleus4	
TauH4RUb	TauH4RUb	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{81} = \text{vol}(\text{Brain}) \cdot \text{k93} \cdot [\text{Agg43}] \tag{268}$$

### **8.82 Reaction r82**

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

### Name r82

Notes Formation of Tau4, 1 \$>\$ 3 from Tau3 aggreate of length 3

# **Reaction equation**

$$TauH4RUb + Agg43 \xrightarrow{TauH4RUb, Agg43} Bp$$
 (269)

#### **Reactants**

Table 245: Properties of each reactant.

Id	Name	SBO
TauH4RUb	TauH4RUb	
Agg43	Agg43	

#### **Modifiers**

Table 246: Properties of each modifier.

Id	Name	SBO
TauH4RUb	TauH4RUb	
Agg43	Agg43	

## **Product**

Table 247: Properties of each product.

Id	Name	SBO
Вр	Bp	

### **Kinetic Law**

$$v_{82} = \text{vol}(\text{Brain}) \cdot \text{Mass\_Action}(\text{k92}, [\text{TauH4RUb}], [\text{Agg43}])$$
 (270)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{271}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{272}$$

## 8.83 Reaction r83

This is an irreversible reaction of two reactants forming one product influenced by two modifiers.

Name r83

Notes Formation of Agg of 1 \$>\$ 3 from aggregates of 1 \$>\$3

# **Reaction equation**

$$TauH4RUb + Bp \xrightarrow{TauH4RUb, Bp} Bp$$
 (273)

### **Reactants**

Table 248: Properties of each reactant.

Id	Name	SBO
TauH4RUb	TauH4RUb	
Вр	Bp	

### **Modifiers**

Table 249: Properties of each modifier.

Id	Name	SBO
TauH4RUb	TauH4RUb	
Вр	Bp	

# **Product**

Table 250: Properties of each product.

Id	Name	SBO
Вр	Bp	

### **Kinetic Law**

$$v_{83} = \text{vol}(Brain) \cdot Mass\_Action(k92, [TauH4RUb], [Bp])$$
 (274)

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{275}$$

$$Mass\_Action(k1, x1, x2) = k1 \cdot x1 \cdot x2 \tag{276}$$

### 8.84 Reaction r84

This is an irreversible reaction of one reactant forming two products influenced by one modifier.

Name r84

Notes Dissociation of aggregates 1 \$>\$ 3

# **Reaction equation**

$$Bp \xrightarrow{Bp} TauH4RUb + Bp \tag{277}$$

#### Reactant

Table 251: Properties of each reactant.

Id	Name	SBO
Вр	Bp	

## **Modifier**

Table 252: Properties of each modifier.

Вр	Вр	

## **Products**

Table 253: Properties of each product.

	_	
Id	Name	SBO
TauH4RUb	TauH4RUb	
Вр	Bp	

### **Kinetic Law**

$$v_{84} = \text{vol}(\text{Brain}) \cdot \text{k93} \cdot [\text{Bp}] \tag{278}$$

# 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 ADP

Name ADP

Notes Energy

Initial concentration 1 mmol⋅ml<sup>-1</sup>

This species takes part in 19 reactions (as a reactant in r69 and as a product in r2, r4, r18, r19, r20, r21, r23, r34, r36, r38, r52, r53, r54, r55, r57, r68, r70 and as a modifier in r69).

$$\frac{d}{dt}ADP = v_2 + v_4 + v_{18} + v_{19} + v_{20} + v_{21} + v_{23} + v_{34} + v_{36} 
+ v_{38} + v_{52} + v_{53} + v_{54} + v_{55} + v_{57} + v_{68} + v_{70} - v_{69}$$
(279)

## 9.2 Species ATP

Name ATP

Notes Energy

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

This species takes part in 35 reactions (as a reactant in r2, r4, r18, r19, r20, r21, r23, r34, r36, r38, r52, r53, r54, r55, r57, r68, r70 and as a product in r69 and as a modifier in r2, r4, r18, r19, r20, r21, r23, r34, r36, r38, r52, r53, r54, r55, r57, r68, r70).

$$\frac{d}{dt}ATP = v_{69} - v_2 - v_4 - v_{18} - v_{19} - v_{20} - v_{21} - v_{23} - v_{34} 
- v_{36} - v_{38} - v_{52} - v_{53} - v_{54} - v_{55} - v_{57} - v_{68} - v_{70}$$
(280)

## 9.3 Species MT

Name MT

Notes Microtubules

Initial concentration 15 mmol·ml<sup>-1</sup>

This species takes part in 18 reactions (as a reactant in r8, r12, r16, r42, r46, r50 and as a product in r9, r13, r17, r43, r47, r51 and as a modifier in r8, r12, r16, r42, r46, r50).

$$\frac{d}{dt}MT = v_9 + v_{13} + v_{17} + v_{43} + v_{47} + v_{51} - v_8 - v_{12} - v_{16} - v_{42} - v_{46} - v_{50}$$
 (281)

## **9.4 Species** \_20S

Name 20S

Notes 20S proteasome

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

Involved in rule \_20S

This species takes part in 18 reactions (as a reactant in r18, r19, r20, r52, r53, r54 and as a product in r18, r19, r20, r52, r53, r54 and as a modifier in r18, r19, r20, r52, r53, r54). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

### 9.5 Species Hsc70

Name Hsc70

Notes Chaperone

Initial concentration  $0.1 \text{ mmol} \cdot \text{ml}^{-1}$ 

This species takes part in ten reactions (as a reactant in r25, r59 and as a product in r26, r27, r31, r60, r61, r65 and as a modifier in r25, r59).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Hsc70} = |v_{26}| + |v_{27}| + |v_{31}| + |v_{60}| + |v_{61}| + |v_{65}| - |v_{25}| - |v_{59}| \tag{282}$$

## 9.6 Species Hsp90

Name Hsp90

Notes Refolding chaperone

Initial concentration  $0.1 \text{ mmol} \cdot \text{ml}^{-1}$ 

This species takes part in six reactions (as a reactant in r27, r61 and as a product in r29, r63 and as a modifier in r27, r61).

$$\frac{d}{dt}Hsp90 = |v_{29}| + |v_{63}| - |v_{27}| - |v_{61}|$$
(283)

### 9.7 Species CHIP

Name CHIP

Notes Degrading chaperone

Initial concentration  $0.1 \text{ mmol} \cdot \text{ml}^{-1}$ 

This species takes part in eight reactions (as a reactant in r30, r64 and as a product in r31, r33, r65, r67 and as a modifier in r30, r64).

$$\frac{d}{dt}CHIP = |v_{31}| + |v_{33}| + |v_{65}| + |v_{67}| - |v_{30}| - |v_{64}|$$
(284)

# 9.8 Species Bag2

Name Bag2

Notes Bag2

Initial concentration  $0.1 \text{ mmol} \cdot \text{ml}^{-1}$ 

This species takes part in six reactions (as a reactant in r32, r66 and as a product in r33, r67 and as a modifier in r32, r66).

$$\frac{d}{dt}Bag2 = |v_{33}| + |v_{67}| - |v_{32}| - |v_{66}|$$
(285)

### **9.9 Species** \_26S

Name 26S

Notes 26S proteasome

Initial concentration 1 mmol⋅ml<sup>-1</sup>

Involved in rule \_26S

This species takes part in six reactions (as a reactant in r34, r68 and as a product in r34, r68 and as a modifier in r34, r68). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

## 9.10 Species TauH3RUb

Name TauH3RUb

Notes Ubiquitinated 3R tau

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

This species takes part in 14 reactions (as a reactant in r34, r71, r75, r77, r78 and as a product in r31, r72, r76, r79 and as a modifier in r34, r71, r75, r77, r78).

$$\frac{d}{dt} \text{TauH3RUb} = |v_{31}| + 2|v_{72}| + |v_{76}| + |v_{79}| - |v_{34}| - 2|v_{71}| - |v_{75}| - |v_{77}| - |v_{78}|$$
(286)

## 9.11 Species TauH4RUb

Name TauH4RUb

Notes Ubiquitinated 4R tau

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

This species takes part in 14 reactions (as a reactant in r68, r73, r80, r82, r83 and as a product in r65, r74, r81, r84 and as a modifier in r68, r73, r80, r82, r83).

$$\frac{d}{dt} \text{TauH4RUb} = |v_{65}| + 2|v_{74}| + |v_{81}| + |v_{84}| - |v_{68}| - 2|v_{73}| - |v_{80}| - |v_{82}| - |v_{83}|$$
(287)

### 9.12 Species Nucleus3

Name Nucleus3

Notes Nucleus for aggregaion (dimer) from 3R tau

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

This species takes part in six reactions (as a reactant in r72, r75 and as a product in r71, r76 and as a modifier in r72, r75).

$$\frac{d}{dt} \text{Nucleus3} = |v_{71}| + |v_{76}| - |v_{72}| - |v_{75}|$$
(288)

### 9.13 Species Nucleus4

Name Nucleus4

Notes Nucleus for aggregaion (dimer) from 4R tau

Initial concentration 0 mmol⋅ml<sup>-1</sup>

This species takes part in six reactions (as a reactant in r74, r80 and as a product in r73, r81 and as a modifier in r74, r80).

$$\frac{d}{dt} \text{Nucleus4} = |v_{73}| + |v_{81}| - |v_{74}| - |v_{80}| \tag{289}$$

## 9.14 Species Agg33

Name Agg33

Notes Aggregates of length 3, 3R tau

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

This species takes part in five reactions (as a reactant in r76, r77 and as a product in r75 and as a modifier in r76, r77).

$$\frac{d}{dt}Agg33 = |v_{75}| - |v_{76}| - |v_{77}| \tag{290}$$

# 9.15 Species Ap

Name Ap

Notes Aggregates greater than length 3, 3R tau

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

## Involved in rule Ap

This species takes part in seven reactions (as a reactant in r78, r79 and as a product in r77, r78, r79 and as a modifier in r78, r79). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

## 9.16 Species Agg43

Name Agg43

Notes Aggregates of length 3, 4R tau

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

This species takes part in five reactions (as a reactant in r81, r82 and as a product in r80 and as a modifier in r81, r82).

$$\frac{d}{dt}Agg43 = |v_{80}| - |v_{81}| - |v_{82}| \tag{291}$$

## 9.17 Species Bp

Name Bp

Notes Aggregates greater than length 3, 4R tau

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

### Involved in rule Bp

This species takes part in seven reactions (as a reactant in r83, r84 and as a product in r82, r83, r84 and as a modifier in r83, r84). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

### 9.18 Species Tau03R

Name Tau03R

Notes Newly synthesized 3R tau, unphosphorylated

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

This species takes part in ten reactions (as a reactant in r2, r6, r18 and as a product in r1, r3, r7, r29 and as a modifier in r2, r6, r18).

$$\frac{d}{dt} \text{Tau} 03R = |v_1| + |v_3| + |v_7| + |v_{29}| - |v_2| - |v_6| - |v_{18}|$$
(292)

## 9.19 Species TauN3R

Name TauN3R

Notes Normally phosphorylated 3R tau

Initial concentration 0 mmol⋅ml<sup>-1</sup>

This species takes part in eleven reactions (as a reactant in r3, r4, r10, r19 and as a product in r2, r5, r11 and as a modifier in r3, r4, r10, r19).

$$\frac{d}{dt} \text{TauN3R} = |v_2| + |v_5| + |v_{11}| - |v_3| - |v_4| - |v_{10}| - |v_{19}|$$
(293)

## 9.20 Species TauH3R

Name TauH3R

Notes Misfolded 3R tau prone to aggregation

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

This species takes part in eleven reactions (as a reactant in r5, r14, r20, r25 and as a product in r4, r15, r26 and as a modifier in r5, r14, r20, r25).

$$\frac{\mathrm{d}}{\mathrm{d}t} \text{TauH3R} = |v_4| + |v_{15}| + |v_{26}| - |v_5| - |v_{14}| - |v_{20}| - |v_{25}|$$
(294)

## 9.21 Species Tau0\_3R

Name Tau0\*3R

Notes Conformationally altered, unphosphorylated, 3R tau with afinity for MT Initial concentration  $0 \; \mathrm{mmol} \cdot \mathrm{ml}^{-1}$ 

This species takes part in six reactions (as a reactant in r7, r8 and as a product in r6, r9 and as a modifier in r7, r8).

$$\frac{d}{dt} \text{Tau} 0.3 \text{R} = |v_6| + |v_9| - |v_7| - |v_8| \tag{295}$$

## 9.22 Species Tau03RMT

Name Tau03RMT

Notes Unphosphorylated 3R tau bound to microtubule

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

This species takes part in six reactions (as a reactant in r9, r21 and as a product in r8, r22 and as a modifier in r9, r21).

$$\frac{d}{dt} \text{Tau03RMT} = |v_8| + |v_{22}| - |v_9| - |v_{21}|$$
 (296)

### 9.23 Species TauN\_3R

Name TauN\*3R

Notes Conformationally altered, normal, 3R tau with affinity for MT

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

This species takes part in six reactions (as a reactant in r11, r12 and as a product in r10, r13 and as a modifier in r11, r12).

$$\frac{d}{dt} \text{TauN}_{-3} = v_{10} + v_{13} - v_{11} - v_{12}$$
(297)

## 9.24 Species TauN3RMT

Name TauN3RMT

Notes Normal 3R tau bound to microtubule

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

This species takes part in nine reactions (as a reactant in r13, r22, r23 and as a product in r12, r21, r24 and as a modifier in r13, r22, r23).

$$\frac{d}{dt} \text{TauN3RMT} = |v_{12}| + |v_{21}| + |v_{24}| - |v_{13}| - |v_{22}| - |v_{23}|$$
(298)

## 9.25 Species TauH\_3R

Name TauH\*3R

Notes Conformationally altered, misfolded, 3R tau with affinity for MT

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

This species takes part in six reactions (as a reactant in r15, r16 and as a product in r14, r17 and as a modifier in r15, r16).

$$\frac{d}{dt} \text{TauH}_{-3} R = v_{14} + v_{17} - v_{15} - v_{16}$$
 (299)

## 9.26 Species TauH3RMT

Name TauH3RMT

Notes Misfolded 3R tau bound to microtubule

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

This species takes part in six reactions (as a reactant in r17, r24 and as a product in r16, r23 and as a modifier in r17, r24).

$$\frac{d}{dt} \text{TauH3RMT} = |v_{16}| + |v_{23}| - |v_{17}| - |v_{24}|$$
(300)

### 9.27 Species TauH3R\_Hsc70

Name TauH3R-Hsc70

Notes Protein triage complex, 3R tau

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

This species takes part in eight reactions (as a reactant in r26, r27, r30 and as a product in r25, r33 and as a modifier in r26, r27, r30).

$$\frac{d}{dt} \text{TauH3R\_Hsc70} = |v_{25}| + |v_{33}| - |v_{26}| - |v_{27}| - |v_{30}|$$
(301)

### 9.28 Species TauH3R\_Hsp90

Name TauH3R-Hsp90

Notes Refolding complex, 3R tau

Initial concentration 0 mmol⋅ml<sup>-1</sup>

This species takes part in three reactions (as a reactant in r28 and as a product in r27 and as a modifier in r28).

$$\frac{d}{dt} \text{TauH3R\_Hsp90} = v_{27} - v_{28}$$
 (302)

# 9.29 Species Tau03R\_Hsp90

Name Tau03R-Hsp90

Notes Refolding complex with restored substrate, 3R tau

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

This species takes part in three reactions (as a reactant in r29 and as a product in r28 and as a modifier in r29).

$$\frac{d}{dt} \text{Tau} 03 \text{R.Hsp} 90 = |v_{28}| - |v_{29}|$$
 (303)

## 9.30 Species TauH3R\_CHIP\_Hsc70

Name TauH3R-CHIP-Hsc70

Notes Degradation complex, 3R tau

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

This species takes part in five reactions (as a reactant in r31, r32 and as a product in r30 and as a modifier in r31, r32).

$$\frac{d}{dt} \text{TauH3R\_CHIP\_Hsc70} = |v_{30}| - |v_{31}| - |v_{32}|$$
 (304)

### 9.31 Species TauH3R\_CHIP\_Hsc70\_Bag2

Name TauH3R-CHIP-Hsc70-Bag2

Notes Protein triage complex, 3R tau

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

This species takes part in three reactions (as a reactant in r33 and as a product in r32 and as a modifier in r33).

$$\frac{\mathrm{d}}{\mathrm{d}t} \text{TauH3R\_CHIP\_Hsc70\_Bag2} = v_{32} - v_{33}$$
 (305)

### 9.32 Species Tau04R

Name Tau04R

Notes Newly synthesized 4R tau, unphosphorylated

Initial concentration 0 mmol⋅ml<sup>-1</sup>

This species takes part in ten reactions (as a reactant in r36, r40, r52 and as a product in r35, r37, r41, r63 and as a modifier in r36, r40, r52).

$$\frac{d}{dt} \text{Tau 04R} = |v_{35}| + |v_{37}| + |v_{41}| + |v_{63}| - |v_{36}| - |v_{40}| - |v_{52}|$$
(306)

# 9.33 Species TauN4R

Name TauN4R

Notes Normally phosphorylated 4R tau

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

This species takes part in eleven reactions (as a reactant in r37, r38, r44, r53 and as a product in r36, r39, r45 and as a modifier in r37, r38, r44, r53).

$$\frac{d}{dt} \text{TauN4R} = |v_{36}| + |v_{39}| + |v_{45}| - |v_{37}| - |v_{38}| - |v_{44}| - |v_{53}|$$
(307)

## 9.34 Species TauH4R

Name TauH4R

Notes Misfolded 4R tau prone to aggregation

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

This species takes part in eleven reactions (as a reactant in r39, r48, r54, r59 and as a product in r38, r49, r60 and as a modifier in r39, r48, r54, r59).

$$\frac{\mathrm{d}}{\mathrm{d}t} \text{TauH4R} = |v_{38}| + |v_{49}| + |v_{60}| - |v_{39}| - |v_{48}| - |v_{54}| - |v_{59}|$$
(308)

### 9.35 Species Tau0\_4R

Name Tau0\*4R

Notes Conformationally altered, unphosphorylated, 4R tau with afinity for MT Initial concentration  $0 \ \mathrm{mmol} \cdot \mathrm{ml}^{-1}$ 

This species takes part in six reactions (as a reactant in r41, r42 and as a product in r40, r43 and as a modifier in r41, r42).

$$\frac{\mathrm{d}}{\mathrm{d}t} \mathrm{Tau} 0_{-} 4 \mathrm{R} = |v_{40}| + |v_{43}| - |v_{41}| - |v_{42}| \tag{309}$$

### 9.36 Species Tau04RMT

Name Tau04RMT

Notes Unphosphorylated 4R tau bound to microtubule

Initial concentration 0 mmol⋅ml<sup>-1</sup>

This species takes part in six reactions (as a reactant in r43, r55 and as a product in r42, r56 and as a modifier in r43, r55).

$$\frac{d}{dt} \text{Tau04RMT} = |v_{42}| + |v_{56}| - |v_{43}| - |v_{55}| \tag{310}$$

## 9.37 Species TauN\_4R

Name TauN\*4R

Notes Conformationally altered, normal, 4R tau with affinity for MT

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

This species takes part in six reactions (as a reactant in r45, r46 and as a product in r44, r47 and as a modifier in r45, r46).

$$\frac{d}{dt} \text{TauN}_{-}4R = v_{44} + v_{47} - v_{45} - v_{46}$$
 (311)

## 9.38 Species TauN4RMT

Name TauN4RMT

Notes Normal 4R tau bound to microtubule

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

This species takes part in nine reactions (as a reactant in r47, r56, r57 and as a product in r46, r55, r58 and as a modifier in r47, r56, r57).

$$\frac{d}{dt} \text{TauN4RMT} = |v_{46}| + |v_{55}| + |v_{58}| - |v_{47}| - |v_{56}| - |v_{57}|$$
(312)

### 9.39 Species TauH\_4R

Name TauH\*4R

Notes Conformationally altered, misfolded, 4R tau with affinity for MT

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

This species takes part in six reactions (as a reactant in r49, r50 and as a product in r48, r51 and as a modifier in r49, r50).

$$\frac{d}{dt} \text{TauH}_{-}4\text{R} = |v_{48}| + |v_{51}| - |v_{49}| - |v_{50}|$$
(313)

## 9.40 Species TauH4RMT

Name TauH4RMT

Notes Misfolded 4R tau bound to microtubule

Initial concentration 0 mmol⋅ml<sup>-1</sup>

This species takes part in six reactions (as a reactant in r51, r58 and as a product in r50, r57 and as a modifier in r51, r58).

$$\frac{d}{dt} \text{TauH4RMT} = |v_{50}| + |v_{57}| - |v_{51}| - |v_{58}|$$
(314)

## 9.41 Species TauH4R\_Hsc70

Name TauH4R-Hsc70

Notes Protein triage complex, 4R tau

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

This species takes part in eight reactions (as a reactant in r60, r61, r64 and as a product in r59, r67 and as a modifier in r60, r61, r64).

$$\frac{d}{dt} \text{TauH4R\_Hsc70} = |v_{59}| + |v_{67}| - |v_{60}| - |v_{61}| - |v_{64}|$$
(315)

## 9.42 Species TauH4R\_Hsp90

Name TauH4R-Hsp90

Notes Refolding complex, 4R tau

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

This species takes part in three reactions (as a reactant in r62 and as a product in r61 and as a modifier in r62).

$$\frac{d}{dt} \text{TauH4R\_Hsp90} = v_{61} - v_{62}$$
 (316)

### 9.43 Species Tau04R\_Hsp90

Name Tau04R-Hsp90

Notes Refolding complex with restored substrate, 4R tau

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

This species takes part in three reactions (as a reactant in r63 and as a product in r62 and as a modifier in r63).

$$\frac{d}{dt} \text{Tau} 04 \text{R}_{-} \text{Hsp} 90 = v_{62} - v_{63}$$
 (317)

## 9.44 Species TauH4R\_CHIP\_Hsc70

Name TauH4R-CHIP-Hsc70

Notes Degradation complex, 4R tau

Initial concentration 0 mmol⋅ml<sup>-1</sup>

This species takes part in five reactions (as a reactant in r65, r66 and as a product in r64 and as a modifier in r65, r66).

$$\frac{d}{dt} \text{TauH4R\_CHIP\_Hsc70} = |v_{64}| - |v_{65}| - |v_{66}|$$
(318)

## 9.45 Species TauH4R\_CHIP\_Hsc70\_Bag2

Name TauH4R-CHIP-Hsc70-Bag2

Notes Protein triage complex, 4R tau

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

This species takes part in three reactions (as a reactant in r67 and as a product in r66 and as a modifier in r67).

$$\frac{d}{dt} \text{TauH4R\_CHIP\_Hsc70\_Bag2} = v_{66} - v_{67}$$
(319)

 $\mathfrak{BML2}^{lA}$  was developed by Andreas Dräger<sup>a</sup>, Hannes Planatscher<sup>a</sup>, Dieudonné M Wouamba<sup>a</sup>, Adrian Schröder<sup>a</sup>, Michael Hucka<sup>b</sup>, Lukas Endler<sup>c</sup>, Martin Golebiewski<sup>d</sup> and Andreas Zell<sup>a</sup>. Please see http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX for more information.

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