Table S2. List of reactions and the rate equations for the model of tau pathophysiology.

Reaction Type	Description	Kinetic Law	Reactants	Products	Params	Units
Synthesis of 3R tau	Tau synthesis	r(1) = k(1);	-	Tau0	k(1)	$\mu M \cdot s^{-1}$
Phosphorylation & dephosphorylation of free 3R tau	Phosphorylation of newly synthesized tau	r(2) = k(2)*x(1)*x(23)/(k(3)+x(1));	Tau0, ATP	TauN, ADP	k(2) k(3)	$\mu M^{-1} \cdot s^{-1}$ uM
	Dephosphorylation of normally phosphorylated tau	r(3) = k(4)*x(2)/(k(5)+x(2));	TauN	Tau0	k(4) k(5)	s^{-1} uM
	Phosphorylation of normally phosphorylated tau	r(4) = k(6)*x(2)*x(23)/(k(7)+x(2));	TauN, ATP	TauH, ADP	k(6) k(7)	$\mu M^{-1} \cdot s^{-1}$ uM
	Dephosphorylation of abnormal/misfolded tau	r(5) = k(8)*x(3)/(k(9)+x(3));	TauH	TauN	k(8) k(9)	s^{-1} uM
Microtubule binding and release of 3R tau species	Conformation change favoring MT binding	r(6) = k(10)*x(1);	Tau0	Tau0*	k(10)	s^{-1}
	Conformational change back to original	r(7) = k(11)*x(7);	Tau0*	Tau0	k(11)	s^{-1}
	Binding of newly synthesized tau to MT	r(8) = k(12)*x(7)*x(10);	Tau0*, MT	Tau0*-MT	k(12)	$\mu M^{-1} \cdot s^{-1}$
	Release of newly synthesized tau from MT	r(9) = k(13)*x(4);	Tau0*-MT	Tau0*, MT	k(13)	s^{-1}
	Conformation change favoring MT binding	r(10) = k(14)*x(2);	TauN	TauN*	k(14)	s^{-1}
	Conformational change back to original	r(11) = k(15)*x(8);	TauN*	TauN	k(15)	s^{-1}
	Binding of normally phosphorylated tau to MT	r(12) = k(16)*x(8)*x(10);	TauN*, MT	TauN*-MT	k(16)	$\mu M^{-1} \cdot s^{-1}$
	Release of normally phosphorylated tau from MT	r(13) = k(17)*x(5);	TauN*-MT	TauN*, MT	k(17)	s^{-1}
	Conformation change favoring MT binding	r(14) = k(18)*x(3);	TauH	TauH*	k(18)	s^{-1}
	Conformational change back to original	r(15) = k(19)*x(9);	TauH*	TauH	k(19)	s^{-1}
	Binding of misfolded tau to MT	r(16) = k(20)*x(9)*x(10);	TauH*, MT	TauH*-MT	k(20)	$\mu M^{-1} \cdot s^{-1}$
	Release of misfolded tau from microtubules	r(17) = k(21)*x(6);	TauH*-MT	TauH*, MT	k(21)	s^{-1}
Free 3R tau degradation by non-ubiquitin dependent proteasome	Degradation of newly synthesized tau	r(18) = k(22)*x(1)*x(21)*x(23);	Tau0, 20S, ATP	ADP, 20S	k(22)	$\mu M^{-2} \cdot s^{-1}$
	Degradation of phosphorylated tau	r(19) = k(23)*x(2)*x(21)*x(23);	TauN, 20S, ATP	ADP, 20S	k(23)	$\mu M^{-2} \cdot s^{-1}$
	Degradation of misfolded tau	r(20) = k(24)*x(3)*x(21)*x(23);	TauH, 20S, ATP	ADP, 20S	k(24)	$\mu M^{-2} \cdot s^{-1}$
Phosphorylation & dephosphorylation of microtubule-bound 3R tau	Phosphorylation of MT-bound newly synthesized tau	r(21) = k(25)*x(4)*x(23)/(k(26)+x(4));	Tau0*-MT, ATP	TauN*-MT	k(25) k(26)	$\mu M^{-1} \cdot s^{-1}$ uM
	Dephosphorylation of MT-bound normally phosphorylated tau	r(22) = k(27)*x(5)/(k(28)+x(5));	TauN*-MT	Tau0*-MT	k(27) k(28)	s^{-1} uM
	Phosphorylation of MT-bound normally phosphorylated tau	r(23) = k(29)*x(5)*x(23)/(k(30)+x(5));	TauN*-MT, ATP	TauH-MT	k(29) k(30)	$\mu M^{-1} \cdot s^{-1}$ uM
	Dephosphorylation of MT-bound abnormal/misfolded tau	r(24) = k(31)*x(6)/(k(32)+x(6));	TauH-MT	TauN*-MT	k(31) k(32)	s^{-1} uM
3R Tau loading by Hsp70	Association of misfolded tau with Hsp70	r(25) = k(33)*x(3)*x(11);	TauH, Hsp70	TauH-Hsp70	k(33)	$\mu M^{-1} \cdot s^{-1}$
	Hsp70 release	r(26) = k(34)*x(15);	TauH-Hsp70	TauH, Hsp70	k(34)	s^{-1}
3R Tau Refolding	Exchange of Hsp70 for Hsp90	r(27) = k(35)*x(15)*x(12);	TauH-Hsc70, Hsp90	TauH-Hsp90, Hsc70	k(35)	$\mu M^{-1} \cdot s^{-1}$
	Restoration of TauH to Tau0 via Hsp90	r(28) = k(8)*x(16)/(k(9)+x(16));	TauH-Hsc90	Tau0-Hsp90	k(8) k(9)	s^{-1} uM
	Release of Tau0 from Hsp90	r(29) = k(36)*x(17);	Tau0-Hsp90	Hsp90, Tau0	k(36)	s^{-1}
Degradation of 3R tau by chaperones	Exchange of Hsc70 for CHIP	r(30) = k(37)*x(15)*x(14);	TauH-Hsc70, CHIP	TauH-Hsc70-CHIP	k(37)	$\mu M^{-1} \cdot s^{-1}$
	Ubiquitination of tau	r(31) = k(38)*x(18);	TauH-Hsc70-CHIP	TauHUb, Hsc70, CHIP	k(38)	s^{-1}
	Binding of Bag-2 to the degradation complex	r(32) = k(39)*x(18)*x(13);	TauH-Hsc70-CHIP, Bag2	TauH-Hsc70-CHIP-Bag2	k(39)	$\mu M^{-1} \cdot s^{-1}$
	Rescue from degradation by Bag2	r(33) = k(40)*x(19);	TauH-Hsc70-CHIP-Bag2	TauH-Hsc70, CHIP, Bag2	k(40)	s^{-1}
	Degradation of ubiquitinated tau	r(34) = k(41)*x(20)*x(22)*x(23);	TauHUb, 26S, ATP	ADP, 26S	k(41)	$\mu M^{-2} \cdot s^{-1}$
Synthesis of 4R tau	Synthesis of 4R tau	r(35) = k(42);	-	Tau0	k(42)	$\mu M \cdot s^{-1}$
Phosphorylation & dephosphorylation of free 4R tau	Phosphorylation of newly synthesized tau	r(36) = k(43)*x(25)*x(23)/(k(44)+x(25));	Tau0, ATP	TauN, ADP	k(43) k(44)	$\mu M^{-1} \cdot s^{-1}$ uM
	Dephosphorylation of normally phosphorylated tau	r(37) = k(45)*x(26)/(k(46)+x(26));	TauN	Tau0	k(45) k(46)	s-1 uM
	Phosphorylation of normally phosphorylated tau	r(38) = k(47)*x(26)*x(23)/(k(48)+x(26));	TauN, ATP	TauH, ADP	k(47) k(48)	$\mu M^{-1} \cdot s^{-1}$ uM
	Dephosphorylation of abnormal/misfolded tau	r(39) = k(49)*x(27)/(k(50)+x(27));	TauH	TauN	k(49) k(50)	s^{-1} uM
Microtubule binding and release of 4R tau species	Conformation change favoring MT binding	r(40) = k(51)*x(25);	Tau0	Tau0*	k(51)	s^{-1}
	Conformational change back to original	r(41) = k(52)*x(31);	Tau0*	Tau0	k(52)	s^{-1}
	Binding of newly synthesized tau to MT	r(42) = k(53)*x(31)*x(10);	Tau0*, MT	Tau0*-MT	k(53)	$\mu M^{-1} \cdot s^{-1}$
	Release of newly synthesized tau from MT	r(43) = k(54)*x(28);	Tau0*-MT	Tau0*, MT	k(54)	s^{-1}
	Conformation change favoring MT binding	r(44) = k(55)*x(26);	TauN	TauN*	k(55)	s^{-1}
	Conformational change back to original	r(45) = k(56)*x(32);	TauN*	TauN	k(56)	s^{-1}
	Binding of normally phosphorylated tau to MT	r(46) = k(57)*x(32)*x(10);	TauN*, MT	TauN*-MT	k(57)	$\mu M^{-1} \cdot s^{-1}$
	Release of normally phosphorylated tau from MT	r(47) = k(58)*x(29);	TauN*-MT	TauN*, MT	k(58)	s^{-1}
	Conformation change favoring MT binding	r(48) = k(59)*x(27);	TauH	TauH*	k(59)	s^{-1}
	Conformational change back to original	r(49) = k(60)*x(33);	TauH*	TauH	k(60)	s^{-1}
	Binding of misfolded tau to MT	r(50) = k(61)*x(33)*x(10);	TauH*, MT	TauH*-MT	k(61)	$\mu M^{-1} \cdot s^{-1}$
	Release of misfolded tau from microtubules	r(51) = k(62)*x(30);	TauH*-MT	TauH*, MT	k(62)	s^{-1}
Free 4R tau degradation by non-ubiquitin dependent proteasome	Degradation of newly synthesized tau	r(52) = k(63)*x(25)*x(23)*x(21);	Tau0, 20S, ATP	ADP, 20S	k(63)	$\mu M^{-2} \cdot s^{-1}$
	Degradation of phosphorylated tau	r(53) = k(64)*x(26)*x(23)*x(21);	TauN, 20S, ATP	ADP, 20S	k(64)	$\mu M^{-2} \cdot s^{-1}$
	Degradation of misfolded tau	r(54) = k(65)*x(27)*x(23)*x(21);	TauH, 20S, ATP	ADP, 20S	k(65)	$\mu M^{-2} \cdot s^{-1}$
Phosphorylation & dephosphorylation of microtubule-bound 4R tau	Phosphorylation of MT-bound newly synthesized tau	r(55) = k(66)*x(28)*x(23)/(k(67)+x(28));	Tau0*-MT, ATP	TauN*-MT	k(66) k(67)	$\mu M^{-1} \cdot s^{-1}$ uM
	Dephosphorylation of MT-bound normally phosphorylated tau	r(56) = k(68)*x(29)/(k(69)+x(29));	TauN*-MT	Tau0*-MT	k(68) k(69)	s^{-1} uM
	Phosphorylation of MT-bound normally phosphorylated tau	r(57) = k(70)*x(29)*x(23)/(k(71)+x(29));	TauN*-MT, ATP	TauH-MT	k(70) k(71)	$\mu M^{-1} \cdot s^{-1}$ uM
	Dephosphorylation of MT-bound abnormal/misfolded tau	r(58) = k(72)*x(30)/(k(73)+x(30));	TauH-MT	TauN*-MT	k(72) k(73)	s^{-1} uM
4R Tau loading by Hsp70	Association of misfolded tau with Hsp70	r(59) = k(74)*x(27)*x(11);	TauH, Hsp70	TauH-Hsp70	k(74)	$\mu M^{-1} \cdot s^{-1}$
	Hsp70 release	r(60) = k(75)*x(34);	TauH-Hsp70	TauH, Hsp70	k(75)	s^{-1}
4R Tau Refolding	Exchange of Hsp70 for Hsp90	r(61) = k(76)*x(34)*x(12);	TauH-Hsc70, Hsp90	TauH-Hsp90, Hsc70	k(76)	$\mu M^{-1} \cdot s^{-1}$
	Restoration of TauH to Tau0 via Hsp90	r(62) = k(77)*x(35)/(k(9)+x(35));	TauH-Hsc90	Tau0-Hsp90	k(77) = k(8) k(9)	s^{-1} uM
	Release of Tau0 from Hsp90	r(63) = k(78)*x(36);	Tau0-Hsp90	Hsp90, Tau0	k(78)	s^{-1}
Degradation of 4R tau by chaperones	Exchange of Hsc70 for CHIP	r(64) = k(79)*x(34)*x(14);	TauH-Hsc70, CHIP	TauH-Hsc70-CHIP	k(79)	$\mu M^{-1} \cdot s^{-1}$
	Ubiquitination of tau	r(65) = k(80)*x(37);	TauH-Hsc70-CHIP	TauHUb, Hsc70, CHIP	k(80)	s^{-1}
	Binding of Bag-2 to the degradation complex	r(66) = k(81)*x(37)*x(13);	TauH-Hsc70-CHIP, Bag2	TauH-Hsc70-CHIP-Bag2	k(81)	$\mu M^{-1} \cdot s^{-1}$
	Rescue from degradation by Bag2	r(67) = k(82)*x(38);	TauH-Hsc70-CHIP-Bag2	TauH-Hsc70, CHIP, Bag2	k(82)	s^{-1}
	Degradation of ubiquitinated tau	r(68) = k(83)*x(39)*x(22)*x(23);	TauHUb, 26S, ATP	ADP, 26S	k(83)	$\mu M^{-2} \cdot s^{-1}$
ATP generation and use by other processes	Generation of ATP	r(69) = k(84)*x(24);	ADP	ATP	k(84)	s^{-1}
	Use of ATP by other processes	r(70) = k(85)*x(23);	ATP	ADP	k(85)	s^{-1}
Aggregation of 3R and 4R tau	Nucleation of Tau3	r(71) = k(86)*x(20).^2;	TauH3RUb (2)	Nucleus3	k(86)	$\mu M^{-1} \cdot s^{-1}$
	Dissociation of Tau3 Nucleus	r(72) = k(87)*x(40);	Nucleus3	TauH3RUb (2)	k(87)	s^{-1}
	Nucleation of Tau4	r(73) = k(88)*x(39).^2;	TauH4RUb (2)	Nucleus4	k(88)	$\mu M^{-1} \cdot s^{-1}$
	Dissociation of Tau4 Nucleus	r(74) = k(89)*x(41);	Nucleus4	TauH4RUb (2)	k(89)	s^{-1}
	Formation of Tau3, length 3	r(75) = k(90)*x(20)*x(40);	Nucleus3, TauH3RUB	Agg33	k(90)	$\mu M^{-1} \cdot s^{-1}$
	Dissociation	r(76) = k(91)*x(42);	Agg33	Nucleus3, TauH3RUB	k(91)	s^{-1}
	Formation of Tau3, l > 3 from Tau3 aggregate of length 3	r(77) = k(90)*x(20)*x(42);	TauH3RUB, Agg33	Ap	k(90)	$\mu M^{-1} \cdot s^{-1}$
	Formation of agg of l > 3 from aggregates of l > 3	r(78) = k(90)*x(20)*x(43);	TauH3RUB, Ap	Ap	k(90)	$\mu M^{-1} \cdot s^{-1}$
	Dissociation of aggregates l>3	r(79) = k(91)*x(43);	Ap	TauH3RUB, Ap	k(91)	s^{-1}
	Formation of Tau4, length 3	r(80) = k(92)*x(39)*x(41);	Nucleus4, TauH4RUB	Agg43	k(92)	$\mu M^{-1} \cdot s^{-1}$
	Dissociation	r(81) = k(93)*x(44);	Agg43	Nucleus4, TauH4RUB	k(93)	s^{-1}
	Formation of Tau4, l > 3 from Tau3 aggregate of length 3	r(82) = k(92)*x(39)*x(44);	TauH4RUb, Agg43	Bp	k(92)	$\mu M^{-1} \cdot s^{-1}$
	Formation of agg of l > 3 from aggregates of l > 3	r(83) = k(92)*x(39)*x(45);	TauH4RUb,Bp	Bp	k(92)	$\mu M^{-1} \cdot s^{-1}$
	Dissociation of aggregates l>3	r(84) = k(93)*x(45);	Bp	TauH4RUb, Bp	k(93)	s^{-1}