

Table S1. List of states, differential equations governing the time evolution of the states, and initial conditions for each state.

#	State	Species	Description	Differential Equation Governing the Time Evolution of the State	$[C]_{0, healthy} (\mu M)$	Source
1	x(1)	Tau03R	Newly synthesized 3R tau, unphosphorylated	$dxdt(1) = r1 + r2 + r3 - r6 + r7 - r18 + r29;$	0	*Results are independent of the initial condition for 3R tau.
2	x(2)	TauN3R	Normally phosphorylated 3R tau	$dxdt(2) = r2 + r3 + r4 + r5 + r10 + r11 - r19;$	0	
3	x(3)	TauH3R	Misfolded 3R tau prone to aggregation	$dxdt(3) = r4 + r5 - r14 + r15 - r20 - r25 + r26;$	0	
4	x(4)	Tau03RMT	Unphosphorylated 3R tau bound to microtubule	$dxdt(4) = r8 + r9 - r21 + r22;$	0	
5	x(5)	TauN3RMT	Normal 3R tau bound to microtubule	$dxdt(5) = r12 - r13 + r21 - r22 - r23 + r24;$	0	
6	x(6)	TauH3RMT	Misfolded 3R tau bound to microtubule	$dxdt(6) = r16 - r17 + r23 - r24;$	0	
7	x(7)	Tau0*3R	Conformationally altered, unphosphorylated, 3R tau with affinity for MT	$dxdt(7) = r6 - r7 - r8 + r9;$	0	
8	x(8)	TauN*3R	Conformationally altered, normal, 3R tau with affinity for MT	$dxdt(8) = r10 - r11 - r12 + r13;$	0	
9	x(9)	TauH*3R	Conformationally altered, misfolded, 3R tau with affinity for MT	$dxdt(9) = r14 - r15 - r16 + r17;$	0	
10	x(10)	MT	Microtubules	$dxdt(10) = -r8 + r9 - r12 + r13 - r16 + r17 - r42 + r43 - r46 + r47 - r50 + r51;$	15	
11	x(11)	Hsc70	Chaperone	$dxdt(11) = -r25 + r26 + r27 + r31 - r59 + r60 + r61 + r65;$	0.1	Assumed
12	x(12)	Hsp90	Refolding chaperone	$dxdt(12) = -r27 + r29 - r61 + r63;$	0.1	Assumed
13	x(13)	Bag2	Bag2	$dxdt(13) = -r32 + r33 - r66 + r67;$	0.1	Assumed
14	x(14)	CHIP	Degrading chaperone	$dxdt(14) = -r30 + r31 + r33 - r64 + r65 + r67;$	0.1	Assumed
15	x(15)	TauH3R-Hsc70	Protein triage complex, 3R tau	$dxdt(15) = r25 - r26 - r27 - r30 + r33;$	0	
16	x(16)	TauH3R-Hsp90	Refolding complex, 3R tau	$dxdt(16) = r27 - r28;$	0	
17	x(17)	Tau03R-Hsp90	Refolding complex with restored substrate, 3R tau	$dxdt(17) = r28 - r29;$	0	
18	x(18)	TauH3R-CHIP-Hsc70	Degradation complex, 3R tau	$dxdt(18) = r30 - r31 - r32;$	0	
19	x(19)	TauH3R-CHIP-Hsc70-Bag2	Protein triage complex, 3R tau	$dxdt(19) = r32 - r33;$	0	
20	x(20)	TauH3RUB	Ubiquitinated 3R tau	$dxdt(20) = r31 - r34 - 2*r71 + 2*r72 - r75 + r76 - r77 - r78 + r79;$	0	
21	x(21)	20S	20S proteasome	$dxdt(21) = 0;$	1	Assumed
22	x(22)	26S	26S proteasome	$dxdt(22) = 0;$	1	Assumed
23	x(23)	ATP	Energy	$dxdt(23) = (-1)*(r2 + r4 + r18 + r19 + r20 + r21 + r23 + r34 + r36 + r38 + r52 + r53 + r54 + r55 + r57 + r68 - r69 + r70);$	0	
24	x(24)	ADP	Energy	$dxdt(24) = r2 + r4 + r18 + r19 + r20 + r21 + r23 + r34 + r36 + r38 + r52 + r53 + r54 + r55 + r57 + r68 - r69 + r70;$	1	
25	x(25)	Tau04R	Newly synthesized 4R tau, unphosphorylated	$dxdt(25) = r35 - r40 + r41 - r36 + r37 - r52 + r63;$	0	*Results are independent of the initial condition for 4R tau.
26	x(26)	TauN4R	Normally phosphorylated 4R tau	$dxdt(26) = r36 - r37 - r38 + r39 - r44 + r45 - r53;$	0	
27	x(27)	TauH4R	Misfolded 4R tau prone to aggregation	$dxdt(27) = r38 - r39 - r48 + r49 - r54 - r59 + r60;$	0	
28	x(28)	Tau04MT	Unphosphorylated 4R tau bound to microtubule	$dxdt(28) = r42 - r43 - r55 + r56;$	0	
29	x(29)	TauN4RMT	Normal 4R tau bound to microtubule	$dxdt(29) = r46 - r47 + r55 - r56 - r57 + r58;$	0	
30	x(30)	TauH4RMT	Misfolded 4R tau bound to microtubule	$dxdt(30) = r50 - r51 + r57 - r58;$	0	
31	x(31)	Tau0*4R	Conformationally altered, unphosphorylated, 4R tau with affinity for MT	$dxdt(31) = r40 - r41 - r42 + r43;$	0	
32	x(32)	TauN*4R	Conformationally altered, normal, 4R tau with affinity for MT	$dxdt(32) = r44 - r45 - r46 + r47;$	0	
33	x(33)	TauH*4R	Conformationally altered, misfolded, 4R tau with affinity for MT	$dxdt(33) = r48 - r49 - r50 + r51;$	0	
34	x(34)	TauH4R-Hsc70	Protein triage complex, 4R tau	$dxdt(34) = r59 - r60 - r61 - r64 + r67;$	0	
35	x(35)	TauH4R-Hsp90	Refolding complex, 4R tau	$dxdt(35) = r61 - r62;$	0	
36	x(36)	Tau04R-Hsp90	Refolding complex with restored substrate, 4R tau	$dxdt(36) = r62 - r63;$	0	
37	x(37)	TauH4R-CHIP-Hsc70	Degradation complex, 4R tau	$dxdt(37) = r64 - r65 - r66;$	0	
38	x(38)	TauH4R-CHIP-Hsc70-Bag2	Protein triage complex, 4R tau	$dxdt(38) = r66 - r67;$	0	
39	x(39)	TauH4RUB	Ubiquitinated 4R tau	$dxdt(39) = r65 - r68 - 2*r73 + 2*r74 - r80 + r81 - r82 - r83 + r84;$	0	
40	x(40)	Nucleus (3R tau)	Nucleus for aggregation (dimer) from 3R tau	$dxdt(40) = r71 - r72 - r75 + r76;$	0	
41	x(41)	Nucleus (4R tau)	Nucleus for aggregation (dimer) from 4R tau	$dxdt(41) = r73 - r74 - r80 + r81;$	0	
42	x(42)	Length 3 aggregate of 3R tau	Aggregates of length 3, 3R tau	$dxdt(42) = r75 - r76 - r77;$	0	
43	x(43)	3R aggregates > length 3 (Ap)	Aggregates greater than length 3, 3R tau	$dxdt(43) = r77;$	0	
44	x(44)	Length 3 aggregates of 4R tau	Aggregates of length 3, 4R tau	$dxdt(44) = r80 - r81 - r82;$	0	
45	x(45)	4R aggregates > length 3 (Bp)	Aggregates greater than length 3, 4R tau	$dxdt(45) = r82;$	0	