Supporting Information

The Misfolding and Self-assembly Dynamics of Microtubule-binding Repeats of the Alzheimer-related Protein Tau

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Table S1. The average secondary structure contents of unstructured (coil and bend), β-sheet, helix and turn conformation for each repeat in one- and two-peptide simulation during last 400 ns and 800 ns .

System		Coil&Bend	β-sheet	Helix	Turn
R1	1-peptide	0.771	0.034	0.107	0.088
	2-peptide	0.760	0.051	0.103	0.086
R2	1-peptide	0.779	0.045	0.092	0.084
	2-peptide	0.747	0.106	0.072	0.075
R3	1-peptide	0.750	0.183	0.005	0.062
	2-peptide	0.599	0.346	0.004	0.051
R4	1-peptide	0.717	0.069	0.131	0.083
	2-peptide	0.683	0.124	0.114	0.079

Table S2 The probability distribution of monomer and dimer in two-peptide simulation for each repeat.

Oligomer	R1	R2	R3	R4
Monomer	0.531	0.501	0.012	0.453
Dimer	0.469	0.499	0.988	0.547

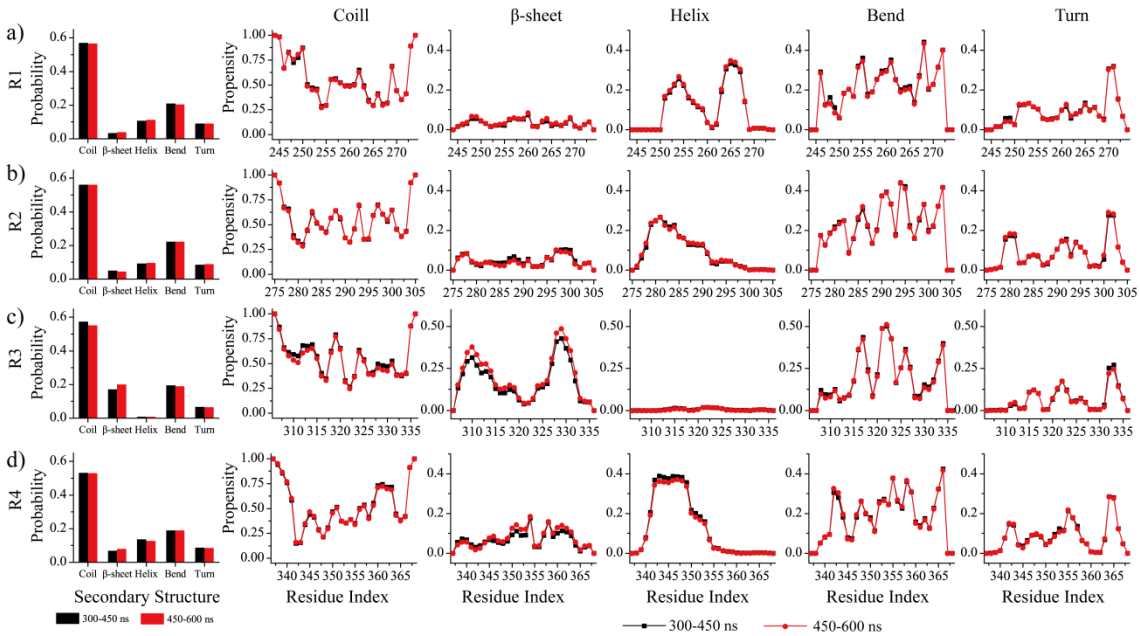

Figure S1. The convergence assessments for the single-peptide simulation of each repeat. The averaged secondary structure probability for each repeat and the propensity of each residue from every repeat adopting different secondary structures using 300-450 ns (black) and 450-600 ns (red) intervals.

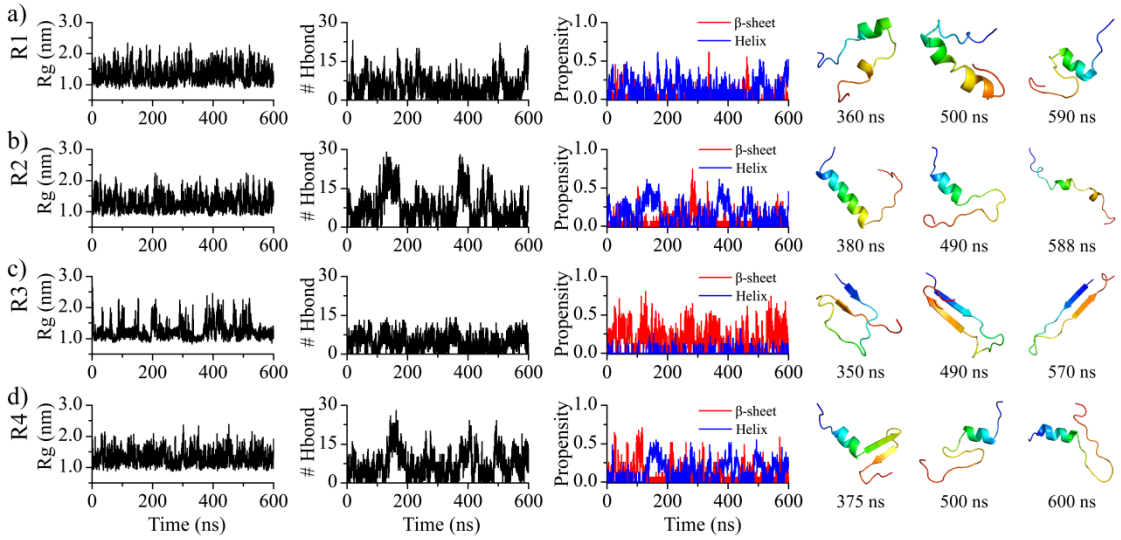

Figure S2. The conformational sampling efficiency assessments for the single-peptide simulation of each repeat. The time evolution of radius gyration (Rg), number of hydrogen bonds formed by main-chain atoms (#Hbond), and β-sheet and helix structure content for each monomer repeat. Three well-defined transient structures were also presented on the left. For each molecular system only one trajectory were selected from 40 independent DMD runs.

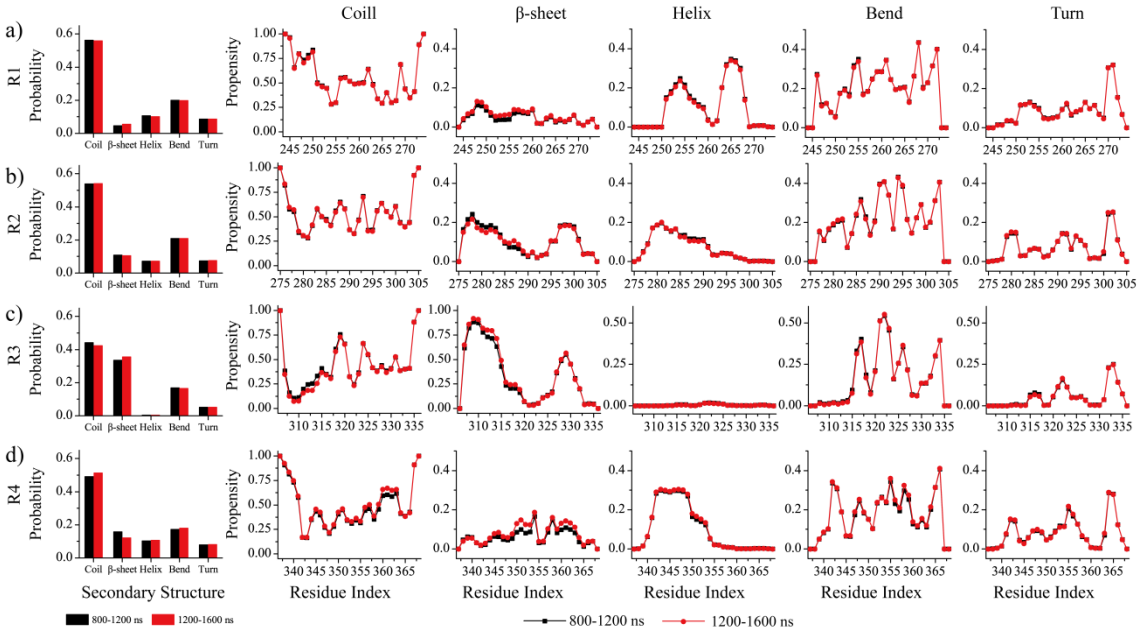

Figure S3. Simulation convergence assessments for two-peptide simulations of each repeat. The average secondary structure probability of each repeat and the secondary structure propensity of each amino acid from every repeat based on the conformations generated within 800-1200 and 1200-1600 ns time intervals.

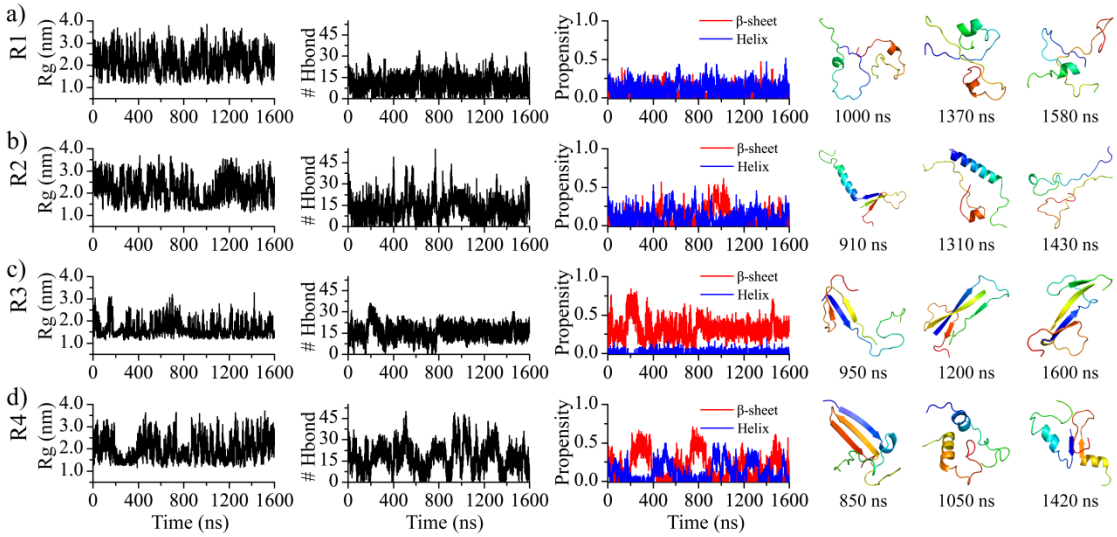

Figure S4. The conformational sampling efficiency assessments for the two-peptide simulation of each repeat. The time evolution of radius gyration (Rg), number of hydrogen bonds formed by main-chain atoms (#Hbond), and β-sheet and helix structure content for each monomer repeat. Three well-defined transient structures were also presented on the left. For each molecular system only one trajectory were selected from 40 independent DMD runs

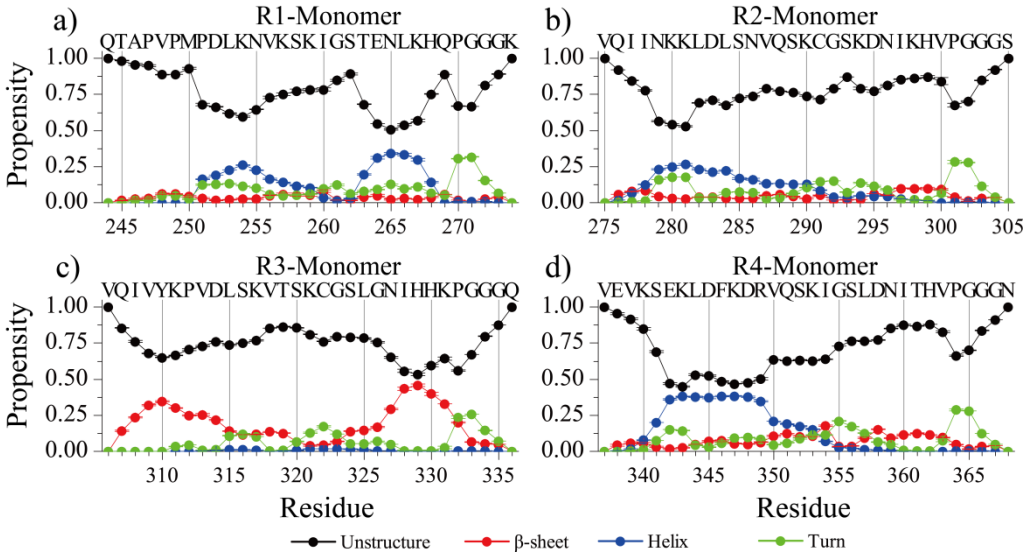

Figure S5. Secondary structure analysis. The averaged propensity of each residue from every tau repeat adopted unstructured (random coil and bend), β-sheet, helix and turn conformation in single-repeat simulation during 400-800 ns (a-d).

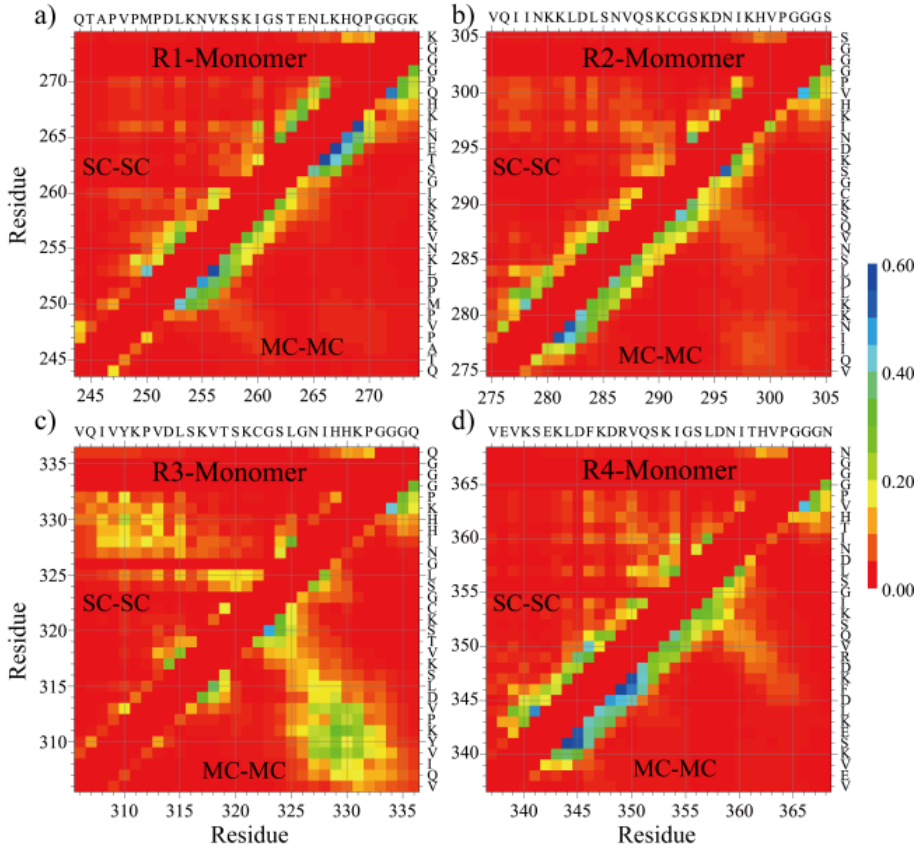

Figure S6. The residue-pairwise interaction analysis. The residue-pairwise inter-molecular contact frequency maps were computed both between main-chain atoms (MC-MC) and between side-chain atoms (SC-SC) in the single-peptides DMD simulations of each repeat. Only the last 400 ns of each 800 ns independent simulation was used for analysis.

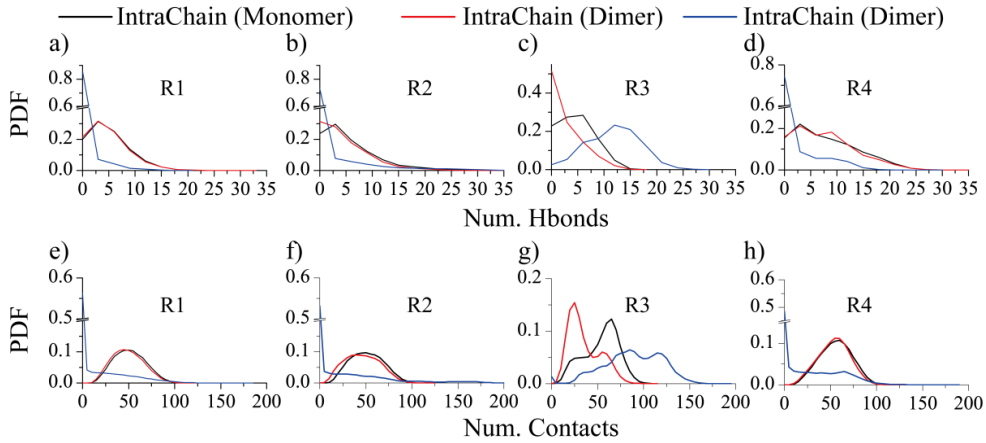

Figure S7. Hydrogen bonds and contact analysis. The probabililty distribution of the number of hydrogen bonds formed by main-chain atom (a-d) and residue-pairwise contact formed by heavy atoms (e-h) for each type of repeat. The trajectories during 400~800 ns from the single-peptide simulation were used to calculate the number of hydrogen bonds and contacts. For the two-peptide systems, the number of inter-molecular hydergen bonds and contacts per chain, and inter-chain hydrogen bonds and contacts were calculated using the last 800 ns from 1600 ns from each two-peptide simulation.

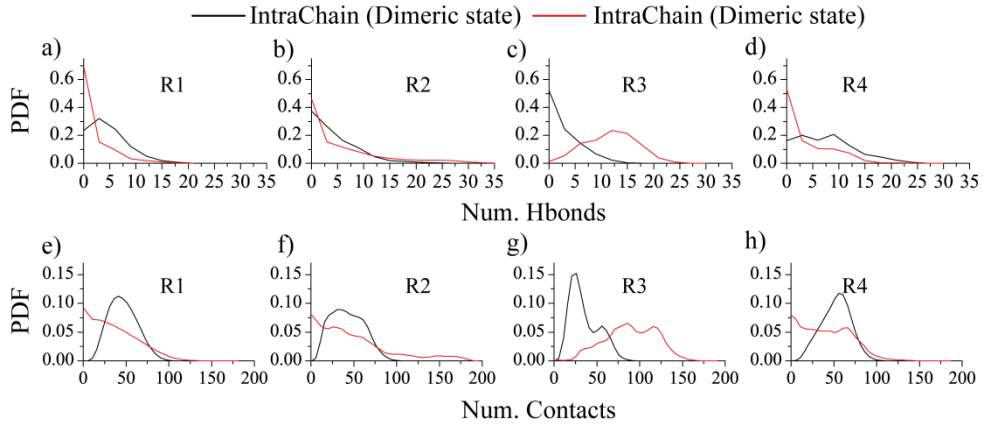

Figure S8. Hydrogen bonds and contact analysis of each repeat in dimeric state. The probability distribution of the number of hydrogen bonds formed by main-chain atoms (a-d) and residue-pairwise contact formed by heavy atoms (e-h) for each type of repeat. For each repeat, only the dimeric conformations, where two peptides were connetcted by at least one inter-molecular contect, were consider during the 800 ns from 1600 ns DMD simulations.

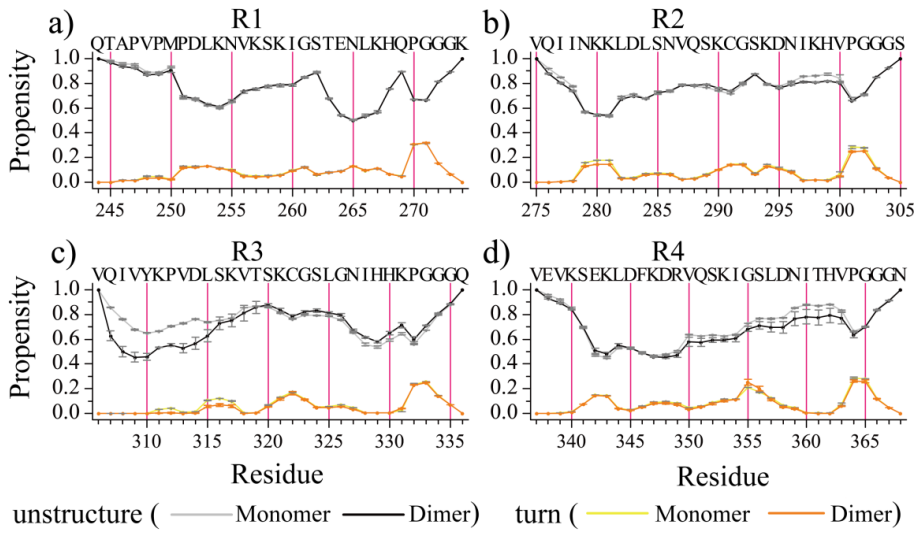

Figure S9. Secondary structure analysis. The averaged propensity of each residue from every tau repeat adopted unstructured and turn conformation in one- and two-peptides DMD simulation.