Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

A α–helix mimetic oligopyridylamide ADH–31 modulates $A\beta_{42}$ monomer aggregation and destabilize protofibril structure: Insights from molecular dynamics simulations

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Table of contents

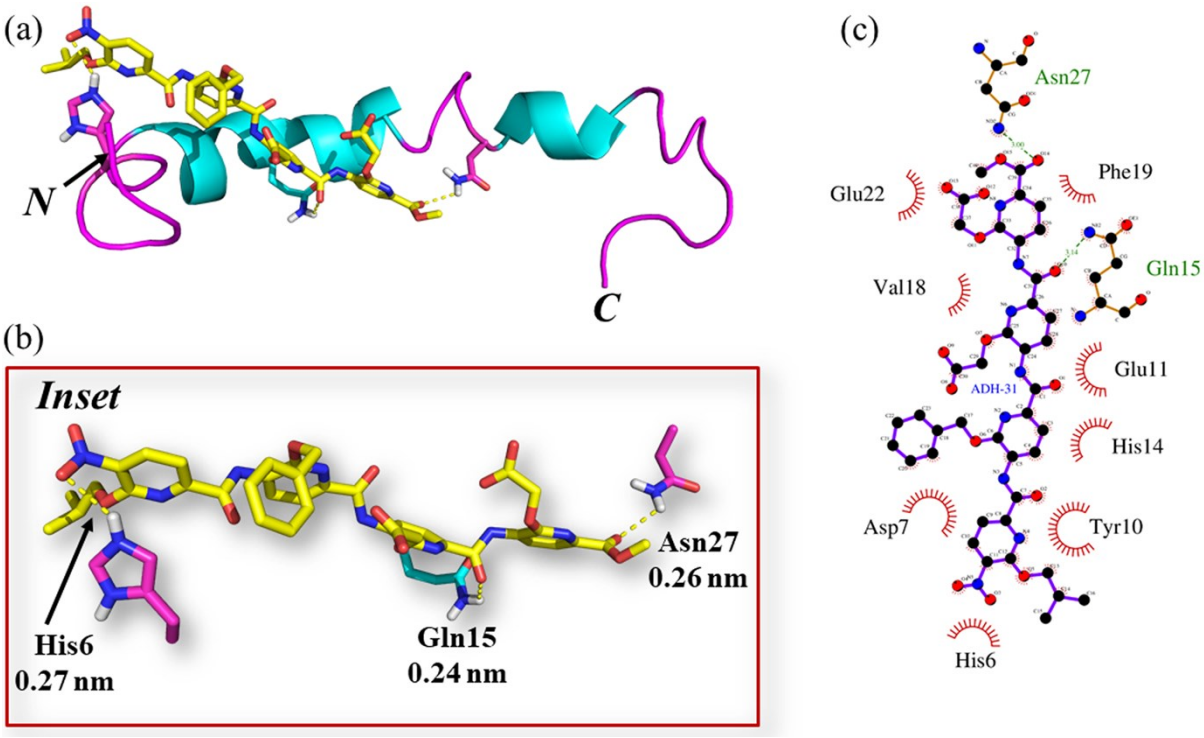

Fig. S1: The docked complex of ADH–31 with $A\beta_{42}$ monomer (PDB: 1Z0Q) highlighting the best–docked conformation is shown in panel a. The $A\beta_{42}$ structure is shown in the cartoon representation and ADH–31 is shown in the stick representation. The inset view of hydrogen bonds formed are represented as yellow dashed lines in panel b. The 2D interaction maps displaying the hydrophobic contacts of ADH–31 with $A\beta_{42}$ monomer is shown in panel c. The maps were generated using LigPlot+ software. The green dashed lines depict the hydrogen bonds between $A\beta_{42}$ monomer + ADH–31 complex.

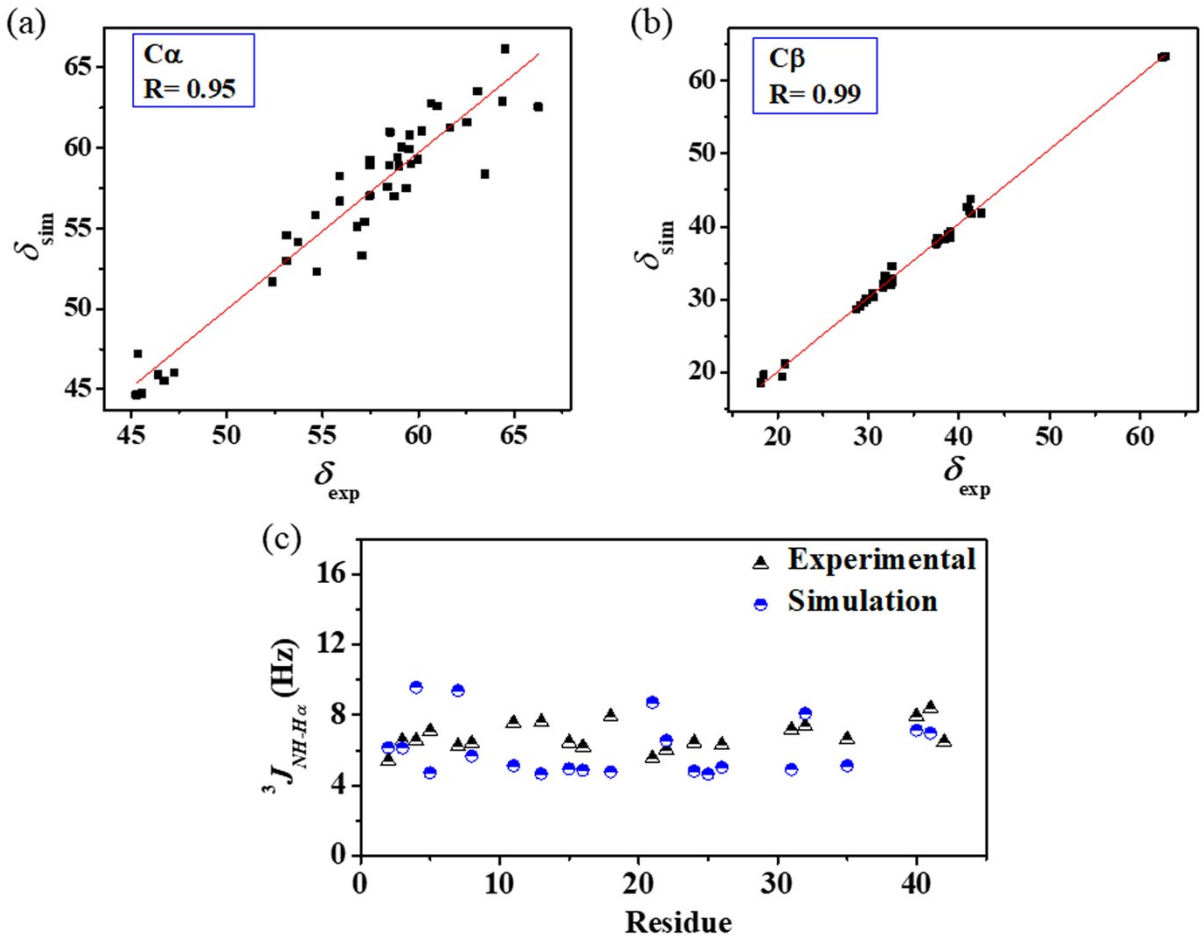

Fig. S2: Comparison of (a) Cα chemical shifts (b) Cβ chemical shifts (c) $^{3}J_{NH-H\alpha}$ coupling constants of simulated with the experimental data of $A\beta_{42}$ monomer.

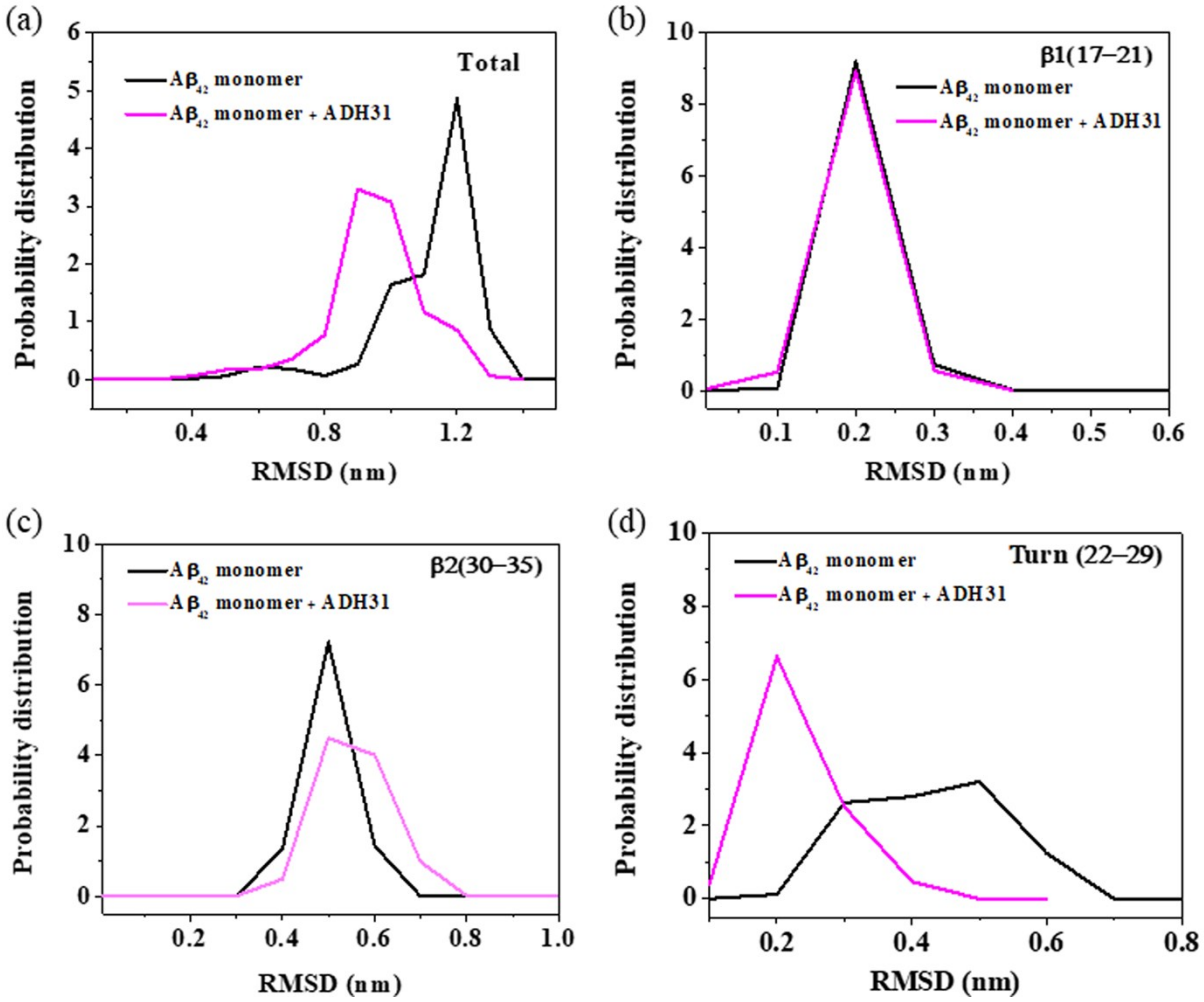

Fig. S3: The probability distribution graph of RMSD for total (full length), β1 (17–21), β2 (30–35) and turn (22–29) region of $A\beta_{42}$ monomer and $A\beta_{42}$ monomer + ADH–31 complex are shown in panel a, b, c and d, respectively.

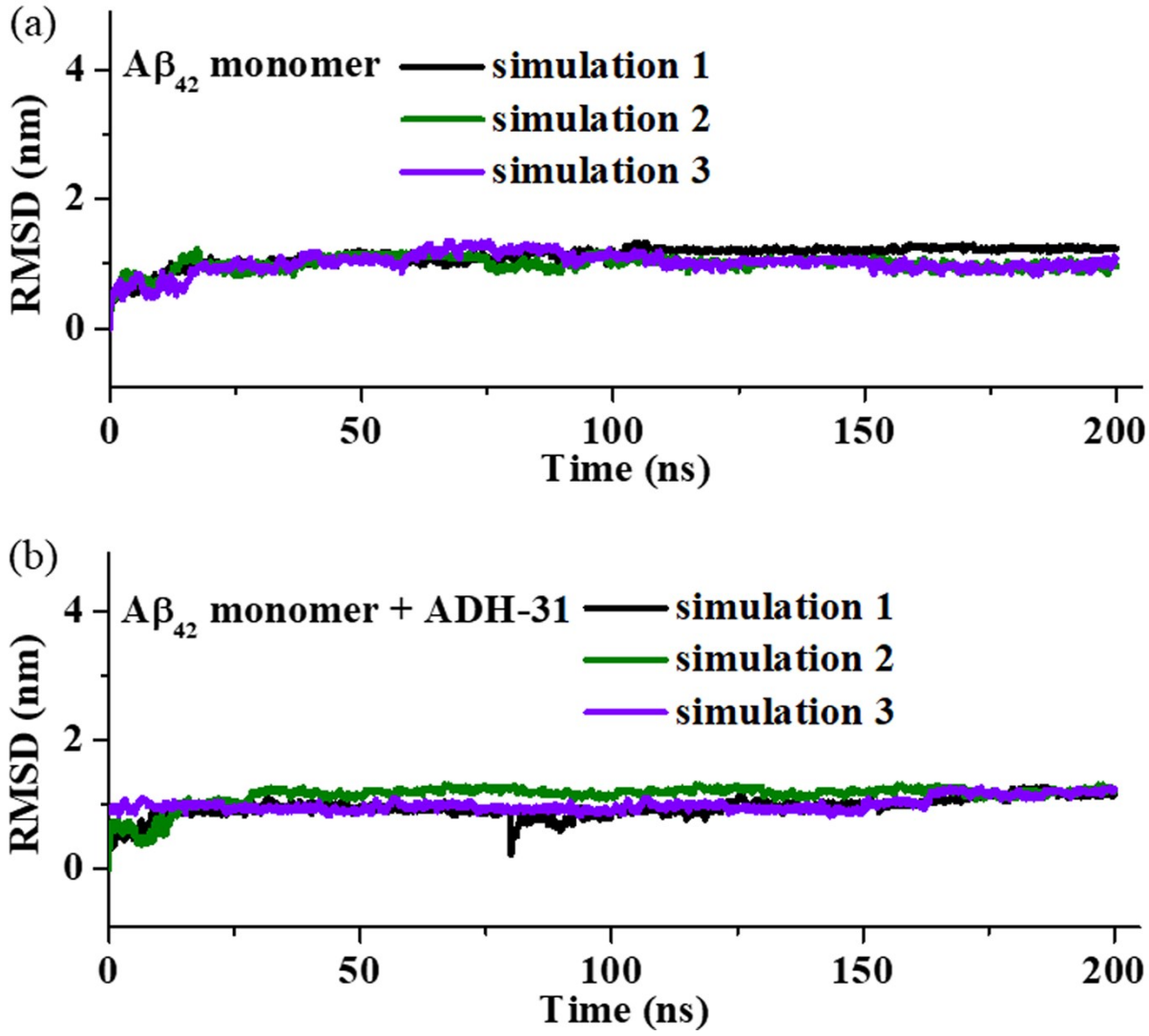

Fig. S4: The RMSD of triplicate simulations for $A\beta_{42}$ monomer and $A\beta_{42}$ monomer + ADH–31 complex, are shown in panel a and b, respectively.

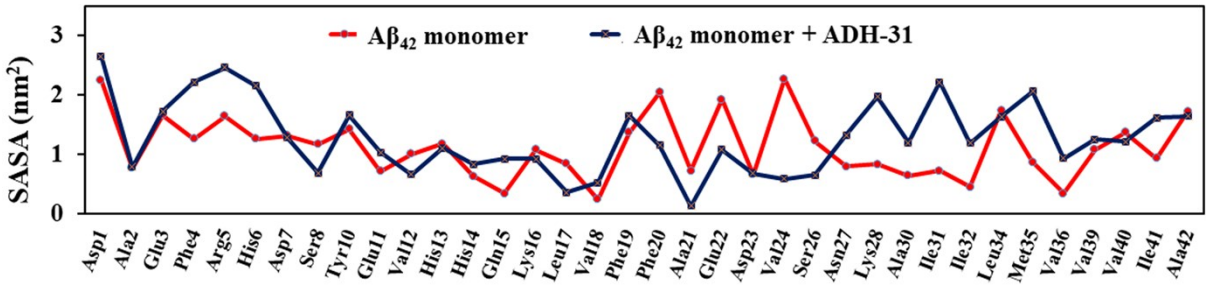

Fig. S5: The solvent accessible surface area (SASA) for the sidechain atoms of $A\beta_{42}$ peptide in $A\beta_{42}$ monomer and $A\beta_{42}$ monomer + ADH–31 complex is shown.

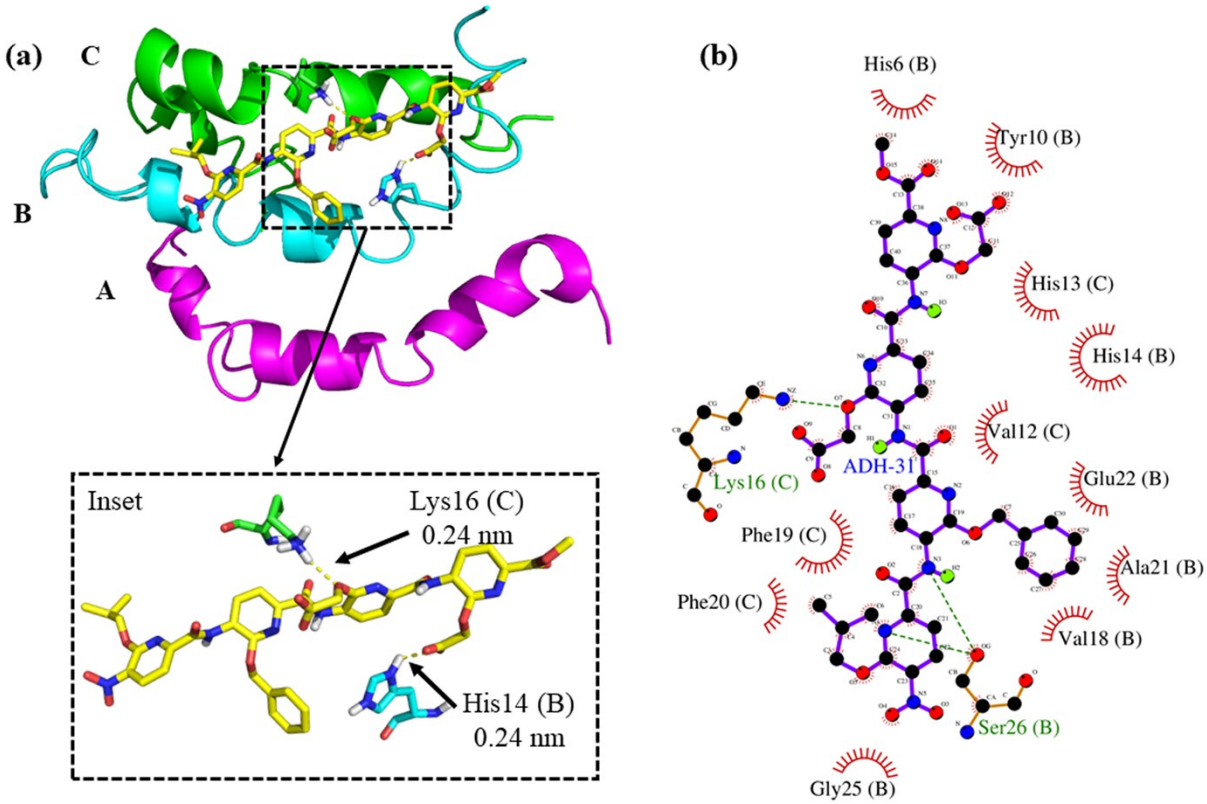

Fig. S6: The best docked conformation of ADH–31 with $A\beta_{42}$ trimer (PDB: 1Z0Q) is shown in panel a. The $A\beta_{42}$ structure is shown in the cartoon representation and ADH–31 is shown in the stick representation. The hydrogen bonds between $A\beta_{42}$ protofibril and ADH–31 are shown as yellow dashed lines with distance in nm (inset). The 2D interaction maps displaying the hydrophobic contacts of ADH–31 with $A\beta_{42}$ trimer is shown in panel b. The maps were generated using LigPlot+ software.

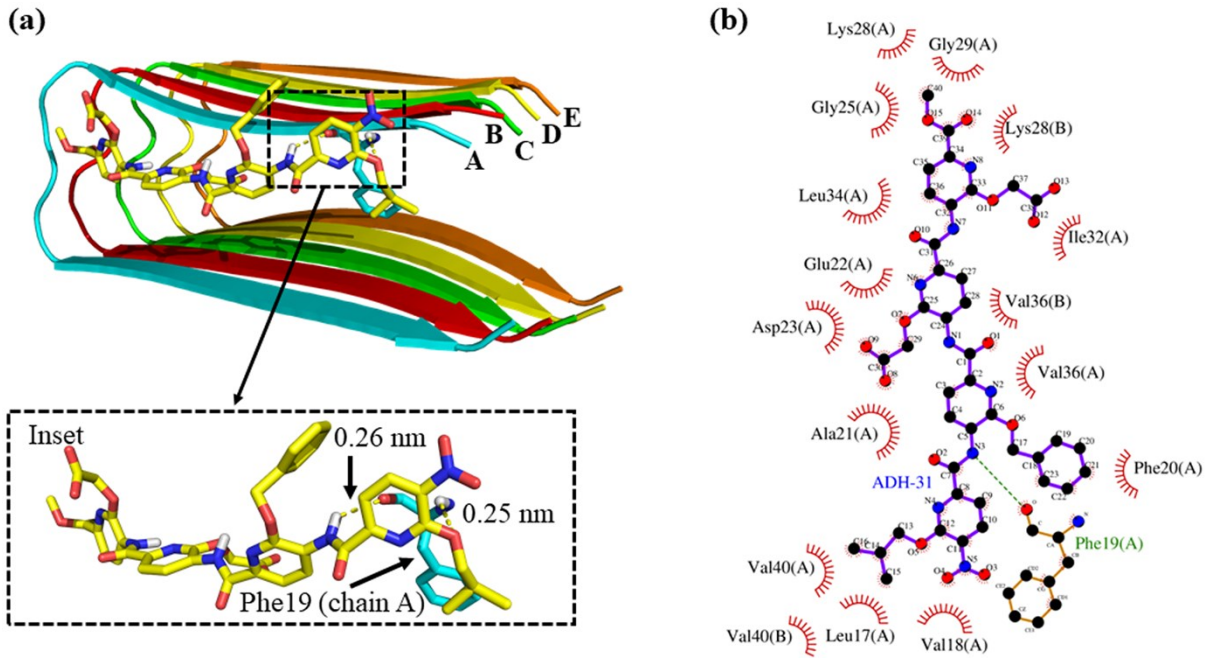

Fig. S7: The best docked conformation of ADH–31 with $A\beta_{42}$ protofibril (PDB: 2BEG) is shown in panel a. The $A\beta_{42}$ structure is shown in cartoon representation and ADH–31 is shown in stick representation. The hydrogen bonds between $A\beta_{42}$ protofibril and ADH–31 are shown as yellow dashed lines with distance in nm (inset). The 2D interaction maps displaying hydrophobic contacts of ADH–31 with $A\beta_{42}$ protofibril is shown in panel b. The maps were generated using LigPlot+ software.

Table S1: The secondary structure component statistics of $A\beta_{42}$ monomer and $A\beta_{42}$ monomer + ADH–31 complex for triplicate simulations.

Model system	Simulation	Secondary structure component (%)				
		Helix[a]	β–sheet[b]	Coil	Bend	Turn
$A\beta_{42}$ monomer	1	38.5 ±0.9	4.5 ±1.1	29.7 ±0.5	11.7 ±1.1	14.7 ±0.9
	2	40.5 ±0.7	3.5 ±1.6	31.7 ±1.1	17.2 ±0.6	6.5 ±1.4
	3	41.5 ±2.2	3.5 ±1.8	33.2 ±1.7	17.2 ±1.2	5.0 ±0.5
$A\beta_{42}$ monomer+ ADH–31	1	50.2 ±2.3	0	31.0 ±1.5	11.7 ±1.4	6.2 ±0.4
	2	50.2 ±0.2	0.7 ±0.2	24.7 ±0.2	18.0 ±0.3	5.7 ±0.4
	3	48.5 ±0.4	0.2 ±0.2	34.2 ±2.4	13.7 ±1.5	2.7 ±0.6

[a]Helix= α–helix+ π–helix+ 3_{10}–helix; [b]β–sheet= β–strand + β–bridge