Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Folding dynamics of Aβ42 monomer in pH=4.0-7.5 with/without physiological salt condition - either β1 or β2 region folds first?

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Supporting information

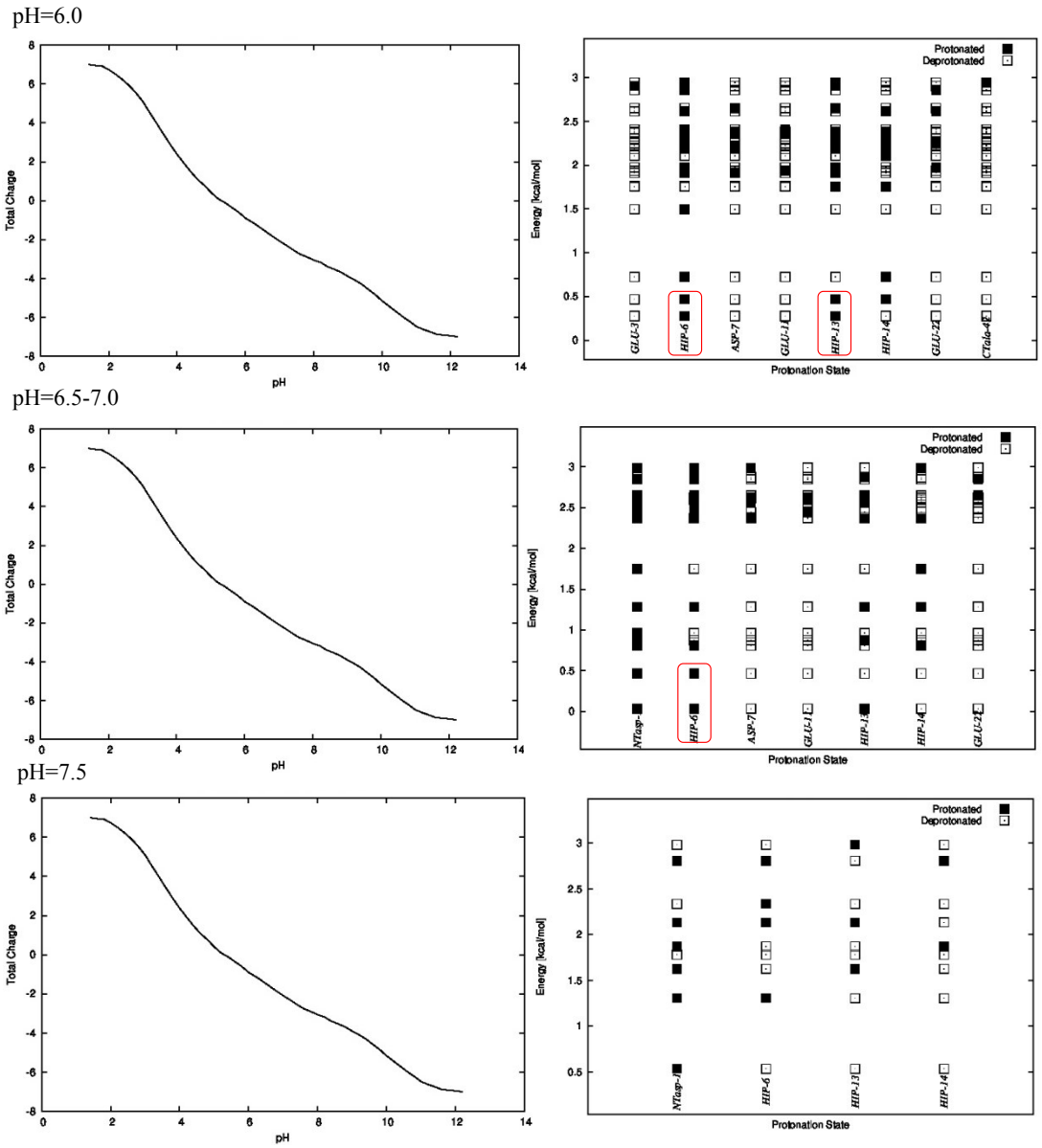


Figure S1. Only the titration curves (left panels) and corresponding of energies (kcal/mol) diagram of protonation microstates (right panels) in three pH states are displayed as the representatives for measurement the protonated residues in the Aβ42 monomer. The protonation residues are boxed in red.

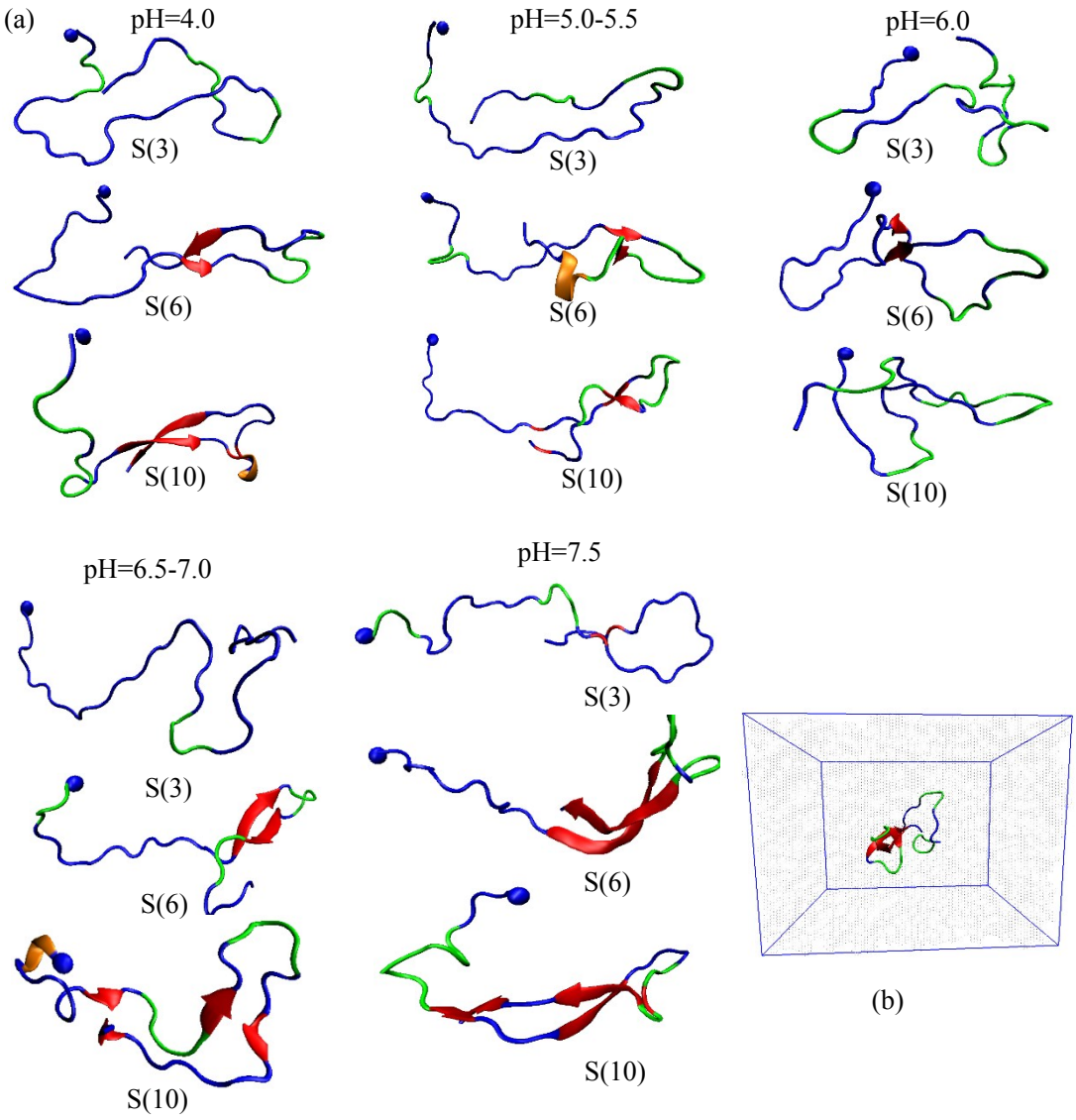


Figure S2. (a) The conformations of initial S(3), S(6) and S(10) under the condition of 130 mM NaCl with different pH values. Clustered structure β-sheet is in red, coil in blue, turn in green and helix in orange, respectively. Blue balls represent N-termini. (b) The position of an Aβ42 unit in the box (pH4.0). The blue space is size of rectangular box, colored chain is Aβ42 model, and the white ball around Aβ42 is water.

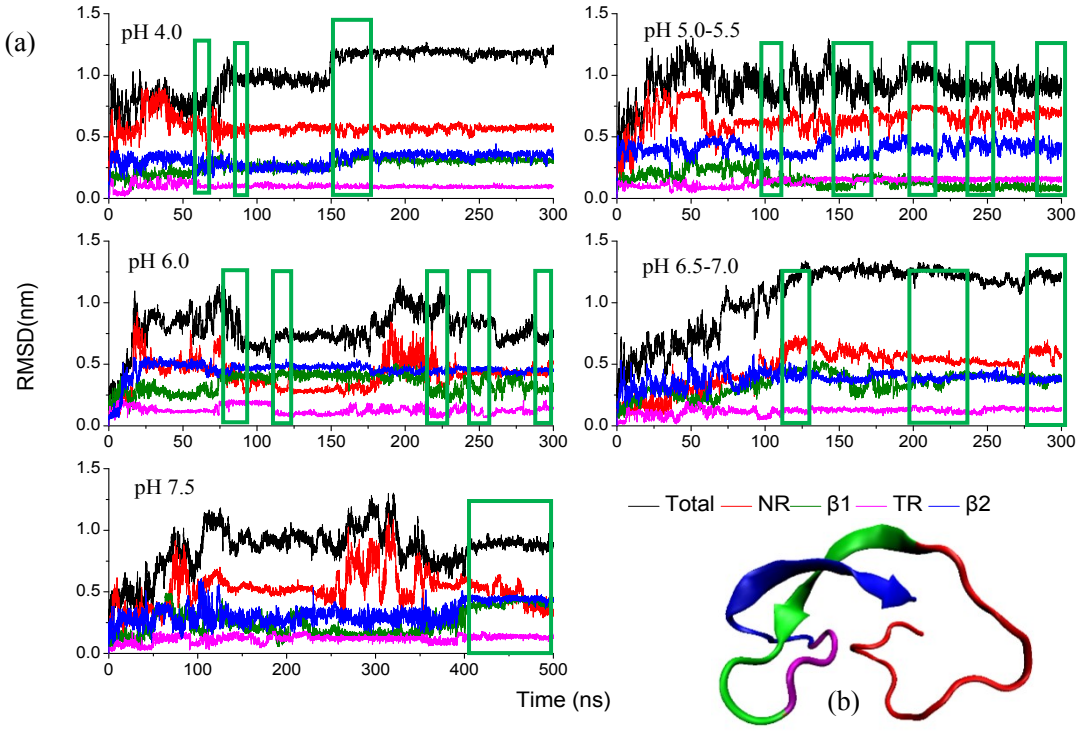


Figure.S3 (a) RMSDs of both Aβ42 monomer and its four regions under the condition of 130 mM NaCl in combination with different pH values, by calculating the backbone atom under different pH conditions. The metastable states in the RMSD trajectories are highlighted in green box. (b) Four region NR/β1/TR/β2 are colored red/green/magenta/blue, respectively.

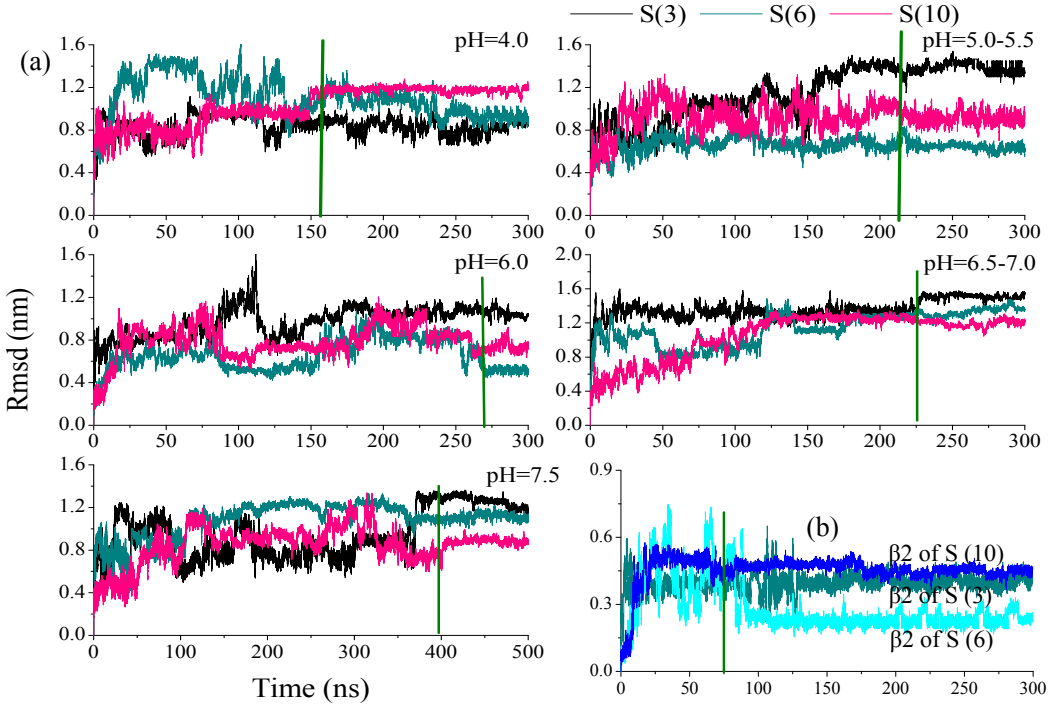


Figure. S4 (a) RMSDs of Aβ42 monomers from three SA samplings, S(3), S(6), and S(10) under the condition of 130 mM NaCl in combination with different pH values, by calculating the backbone atoms. The green vertical lines represent the equilibrium period. (b) RMSDs of β2 region of S(3), S(6) and S(10) under pH6.0. The green vertical lines represent the equilibrium period of S (10) after 70ns.

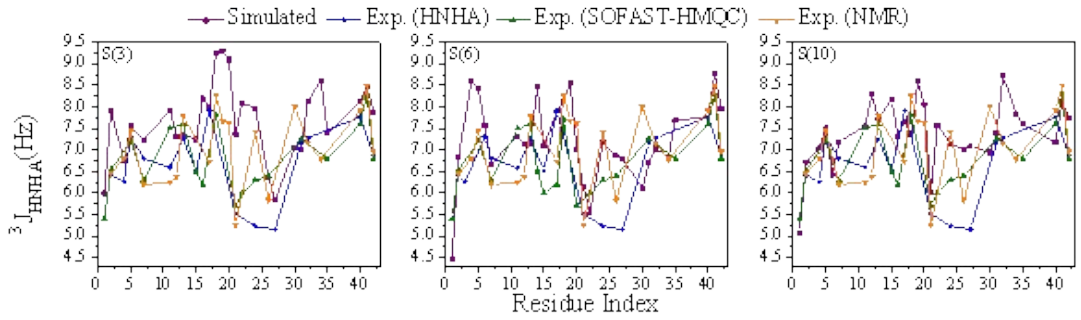


Fig. S5 Validation of 3JHNHA couplings. Direct comparison of present $^3J_{HNHA}$ couplings (colored purple) calculated over the production period with experimentally determined counterparts for S(3), S(6), and S(10), shown as a function of residue number. Three experimentally determined dates are derived from HNHA experiment, the J-resolved SOFAST-HMQC experiment and NMR data quantitatively.[1-3] J-couplings are calculated over 20ns/step. Glycine residues are not included, since the experimental values of the $^3J_{HNHA}$ constants for these residues are ambiguous.

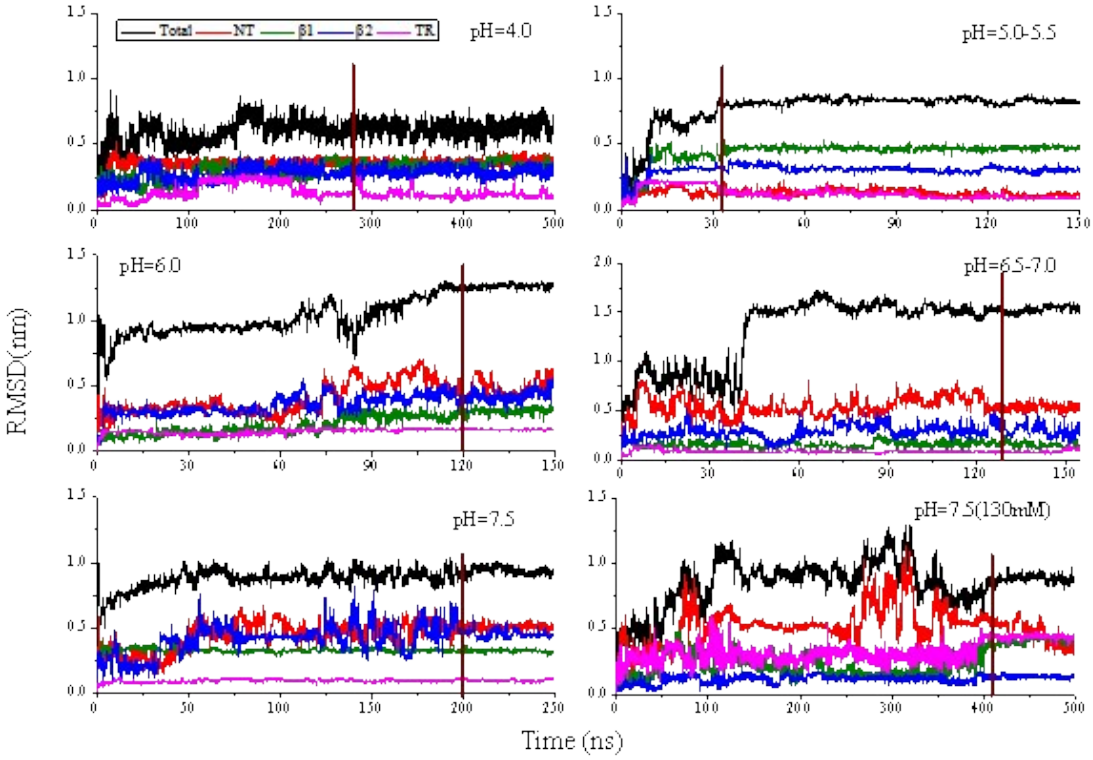
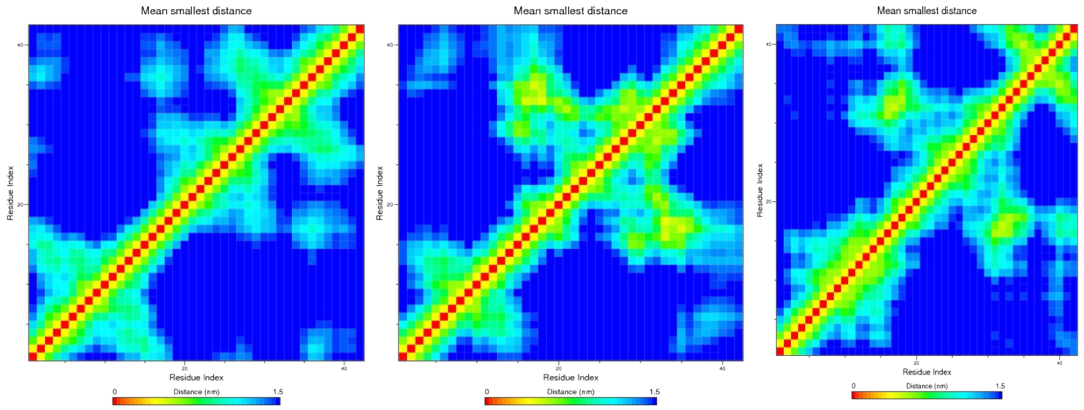


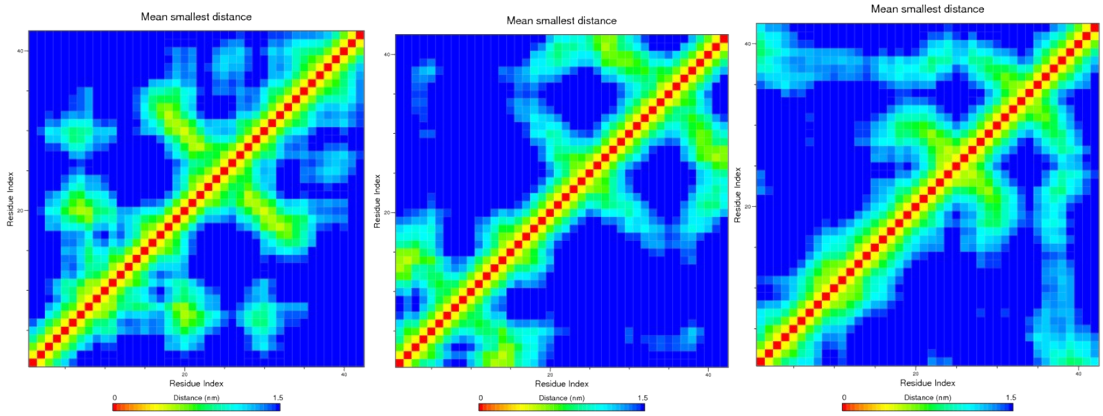
Figure S6 RMSDs of $A\beta_{42}$ monomer and the corresponding contributions from NT, β1, β2 and turn regions under the condition of different pH values but without 130 mM NaCl. Vertical garnet line represents threshold of equilibration. The result is from ref[4]

pH=6.0



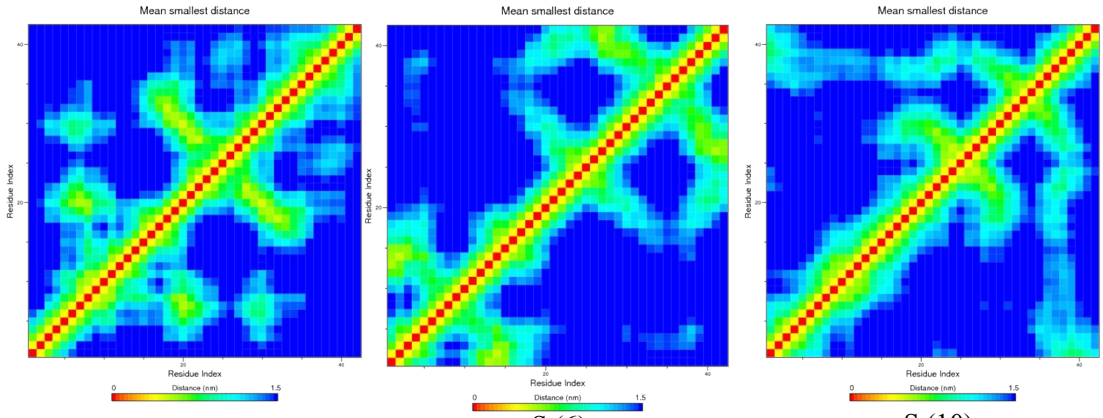
S (3) S (6) S (10)

pH=6.5-7.0



S (3) S (6) S (10)

pH=7.5



S (3) S (6) S (10)

Figure S7. Three sample tertiary structures of pH6.0/6.5-7.0/7.5 with 130 mM NaCl.

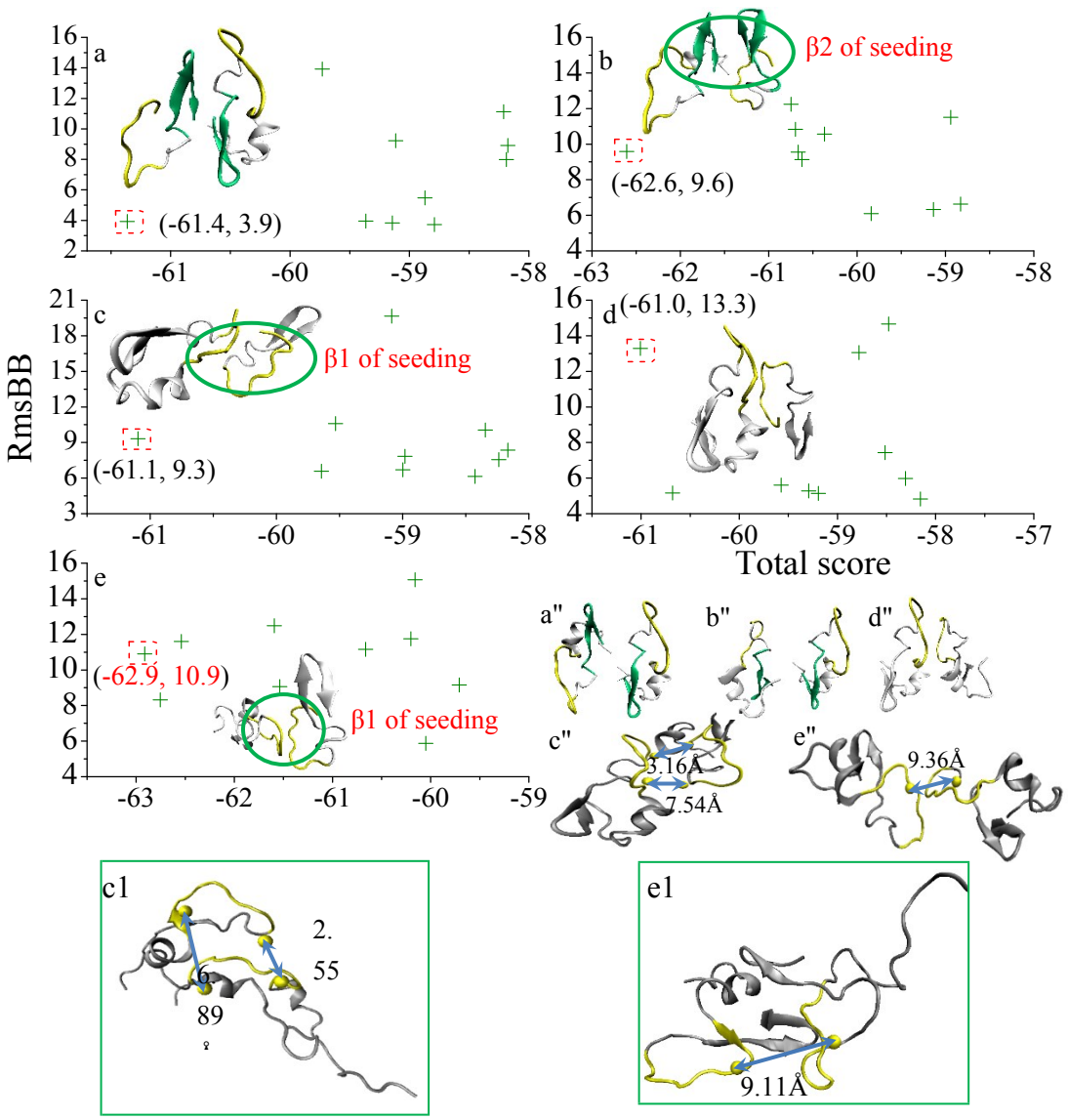


Figure S8. Scores (REU) of Top 10 dimers and top1 conformation in pH=6.0. (c), (d) and (e) are dimers contacted by β1 seeding regions of two Aβ42 monomers with antiparallel (c″), parallel (d″) and cross (e″) preassembly, respectively. (a) and (b) are dimers contacted by β2 seeding regions of two Aβ42 monomers with antiparallel (a″) and parallel (b″) preassembly, respectively, for comparison with their each β2-β2 contacted counterparts (a) and (b). RmsBB in Å. c1/e1 are representative structures of c/e after MD.

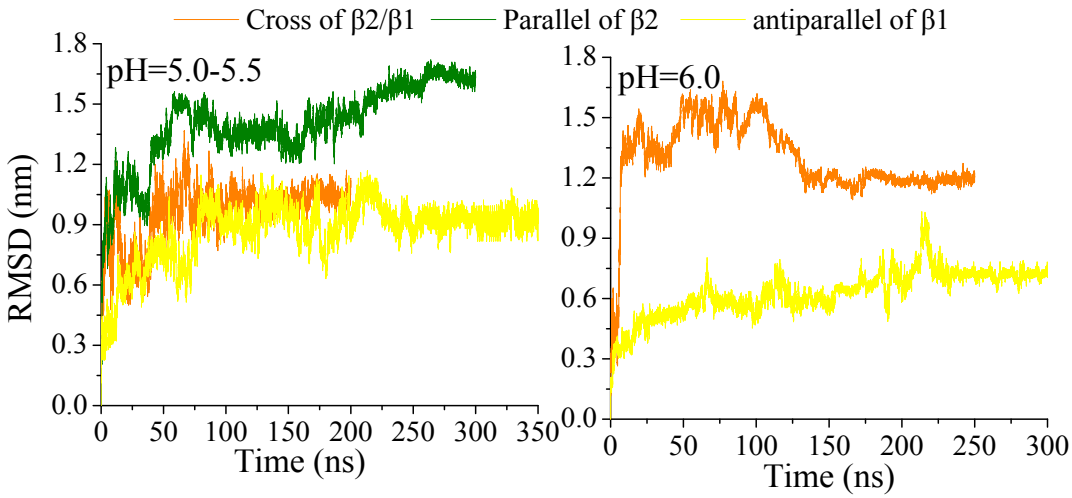


Figure S9 RMSDs of both Aβ42 dimer under the condition of 130 mM NaCl in combination with different pH values (5.0-5.5/6.0), by calculating the backbone atom.

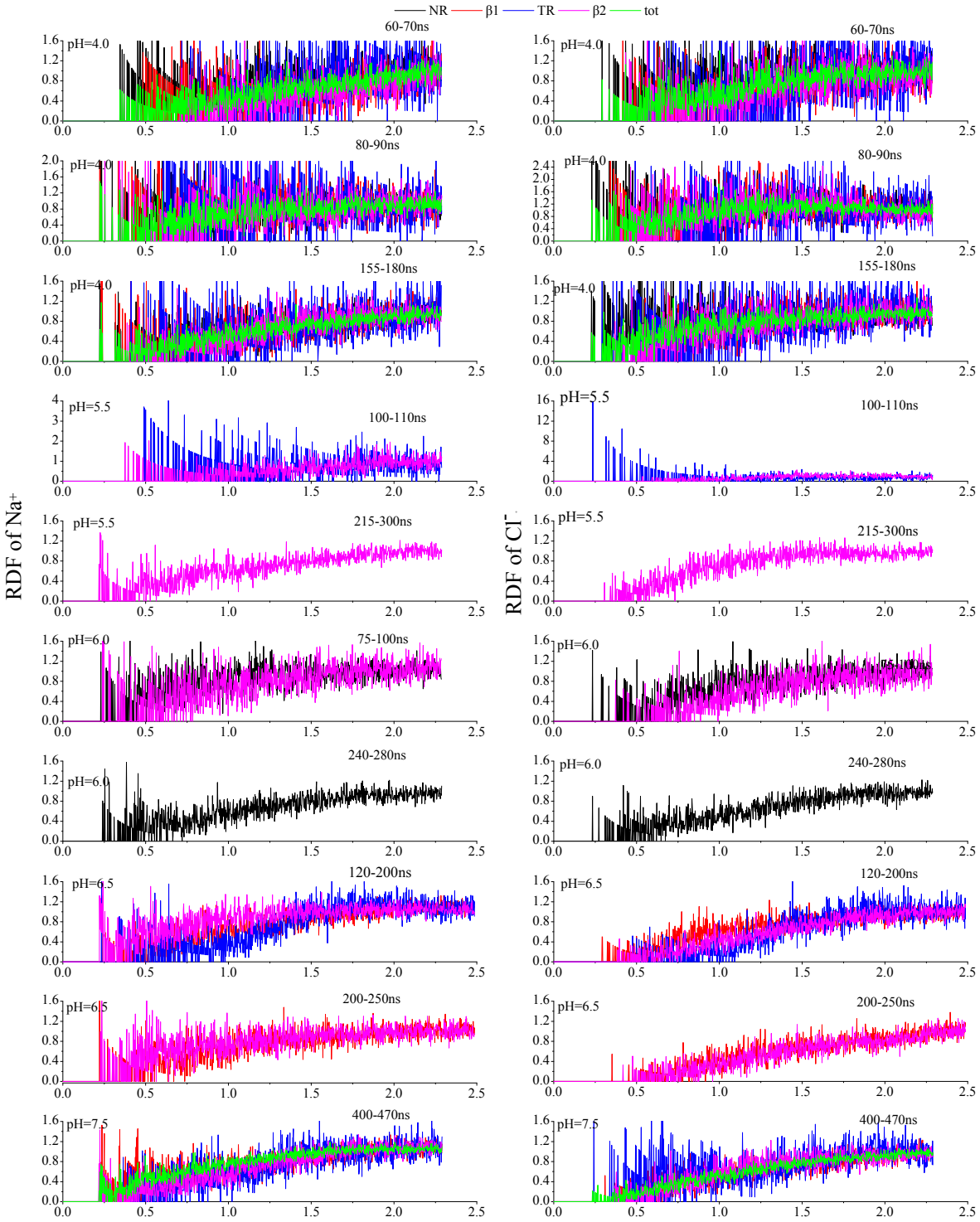


Figure.S10 RDFs of Na^+ and Cl^- around four regions of Aβ42 in different pH during different times.

References

1. Rosenman, D. J.; Connors, C. R.; Chen, W.; Wang, C.; Garcia, A. E., Abeta monomers transiently sample oligomer and fibril-like configurations: ensemble characterization using a combined MD/NMR approach. *J Mol Biol* **2013,** *425* (18), 3338-59.

2. Sgourakis, N. G.; Yan, Y.; McCallum, S. A.; Wang, C.; Garcia, A. E., The Alzheimer's peptides Abeta40 and 42 adopt distinct conformations in water: a combined MD / NMR study. *J Mol Biol* **2007,** *368* (5), 1448-57.

3. Lendel, C.; Damberg, P., 3D J-resolved NMR spectroscopy for unstructured polypeptides: fast measurement of 3JHNHa coupling constants with outstanding spectral resolution.pdf *J Biomol Nmr* **2009,** *44*, 35-42.

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