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Supporting Material

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Atomic Scale Simulations Confirm that *Soluble* β-Sheet-Rich Peptide Self-Assemblies Provide Amyloid Mimics Presenting Similar Conformational Properties

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MD simulation protocol. All MD simulations were conducted by using the NAMD 2.6 program (1) with the all-atom CHARMM22 force field (2, 3) for the peptide and the modified TIP3P model for water (3) in the NPT ensemble (1 atm and 330 K). The temperature was controlled at 330 K by a Langevin thermostat with a damping coefficient of 5 ps^{-1}, while the pressure was maintained at 1 atm by a Langevin piston with a decay period of 100 fs and a damping time of 50 fs. The simulation temperature of 330 K is slightly higher than room temperature and may aid in avoiding kinetic traps and allow us to probe the stabilities and dynamics of PSAMs more quickly in the limited simulation time. The short-range van der Waals (VDW) interactions were calculated by the switch function with a twin range cutoff of 10.0 and 12.0 Å, and the long-range electrostatic interactions were calculated by the force shift function with a cutoff of 12.0 Å. Periodic boundary condition is applied to all directions. Newton's equation was integrated by the velocity Verlet algorithm with a time step of 2 fs. The SHAKE algorithm was used to constrain all bonds between hydrogen atoms and heavy atoms. Structures were saved every 2 ps for analysis. The simulation systems studied are listed in Table 1. The VMD software was used for Visualization (4).

Figure S1. Structural characterization of four PSAMs with the end-capping proteins derived from experiments. Time evolution of (a) radius of gyration (Rg), (b) backbone root-mean-square-deviation (RMSD) of whole PSAM structures, and (c) backbone RMSD of selected β-hairpin building blocks without the end-caps.

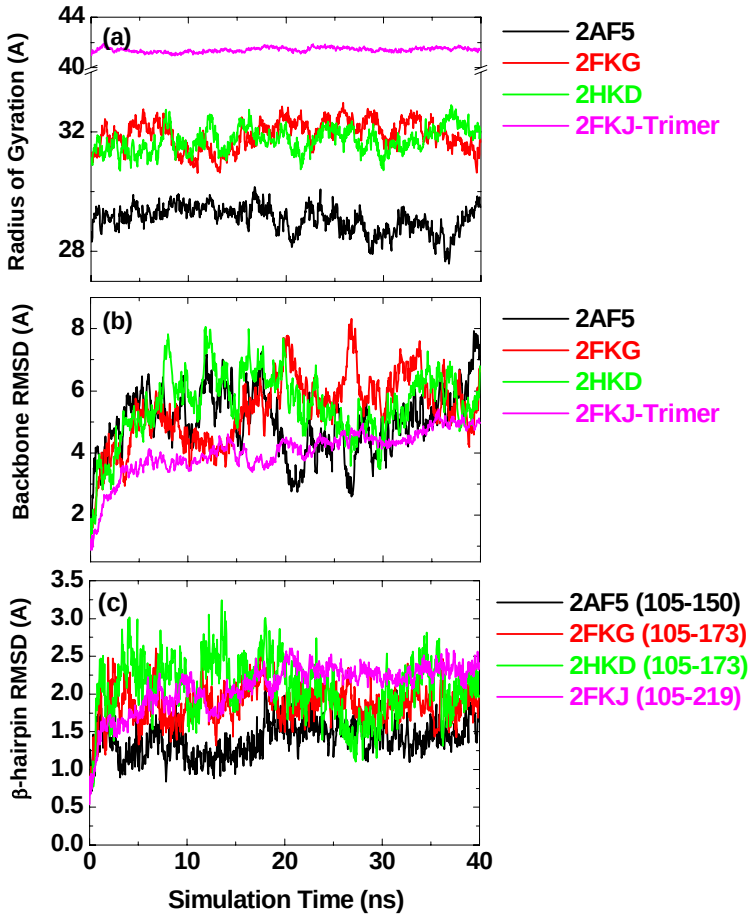


Figure S2. Structural characterization of the single-layer β-sheets without the end-capping proteins for wild type and mutated sequences (Lys→Tyr). Time evolution of (a) backbone RMSD, (b) backbone RMSF, and (c) β-strand population.

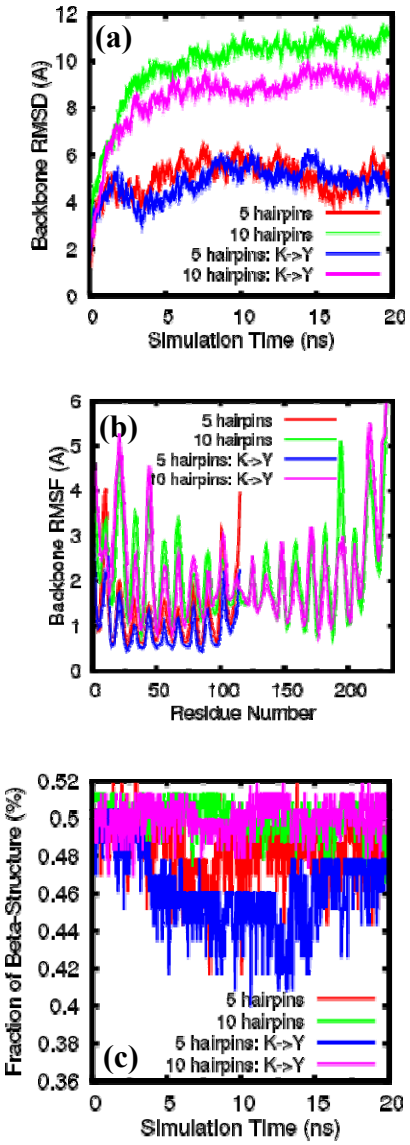


Figure S3. Number of hydrogen bonds between sheets and waters and number of native contacts within the sheet for the (a) five-β-hairpin sheet and (b) ten-β-hairpin sheet. In parallel, the self-interactions of β-sheet and the interaction of β-sheet with waters within 6Å for the (c) five-β-hairpin sheet and (d) ten-β-hairpin sheet. Native contacts consist of hydrogen bonds and sidechain contacts. A hydrogen bond is assigned if the distance between donor D and acceptor A is less than 3.5 Å and the angle D–H. . .A is larger than 120^{o}. A side chain contact is defined if the distance between the center of mass of two side chains is less than 5.5 Å.

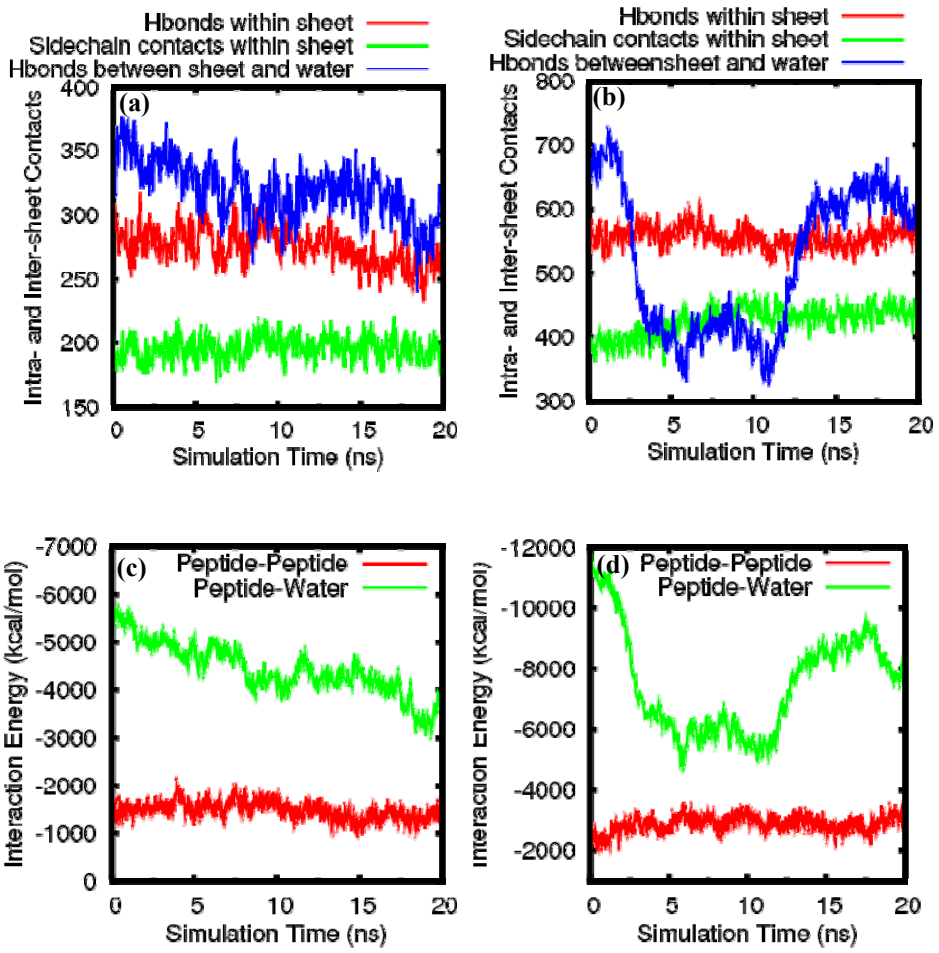


Figure S4. Time evolution of sheet-to-sheet distances for (a) three wild-type models consisting of two, three, and four β-sheets and (b) two mutants consisting of four β-sheets with Phe→Ala or Lys→Tyr mutations.

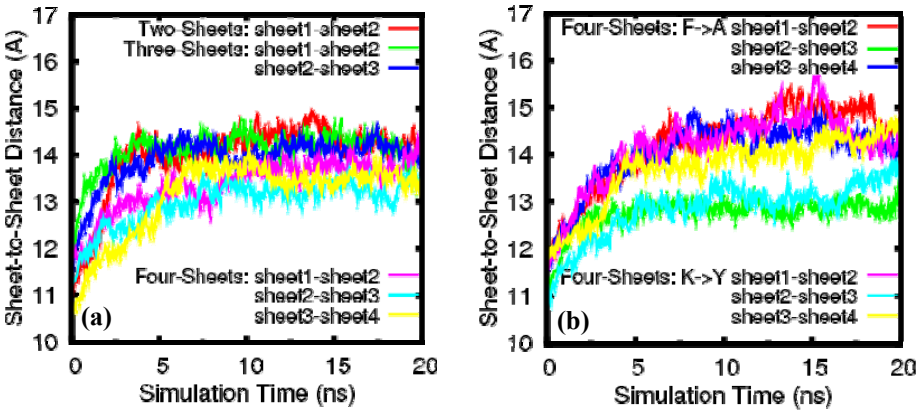


Figure S5. Interstrand distances between edge residues and between center residues, normalized by the number of β-sheets, for (a) two β-sheets, (b) three β-sheets, (c) four β-sheets, (d) four β-sheets with Phe→Ala mutations, and (e) four β-sheets with Lys→Tyr mutations.

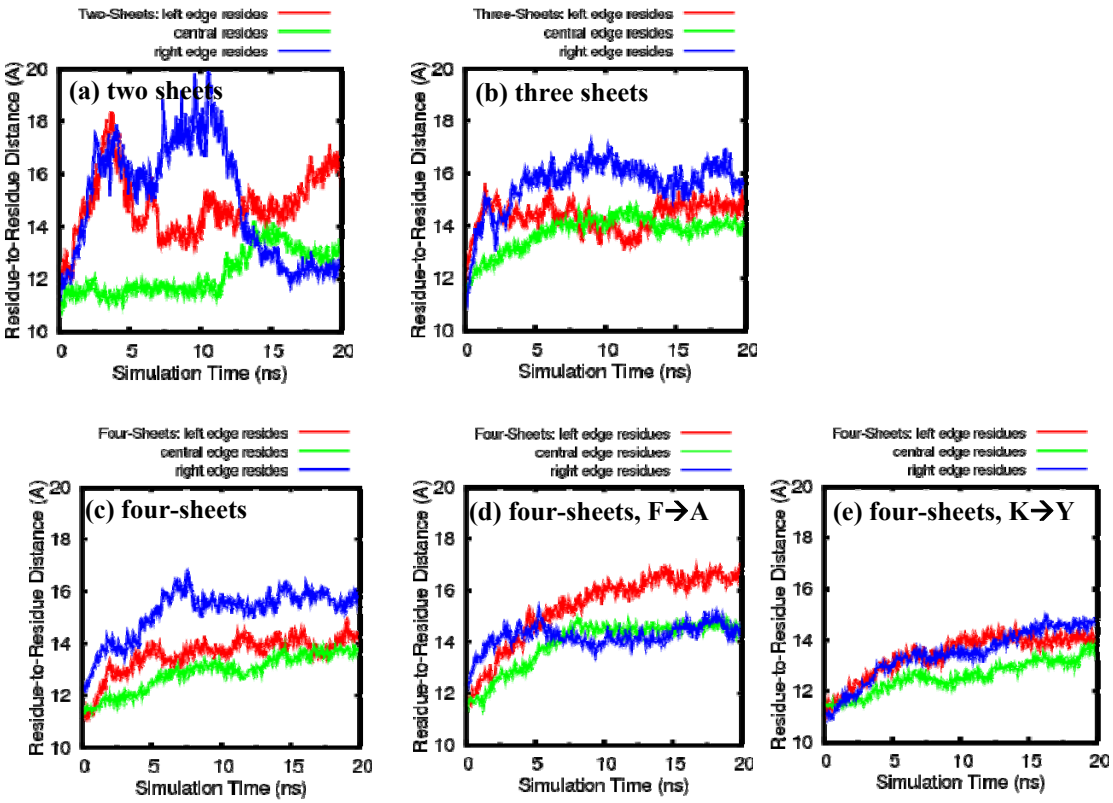


Figure S6. Number of hydrogen bonds between water and residues at the edge and center region of β-sheets for (a) two β-sheets, (b) three β-sheets, and (c) four β-sheets.

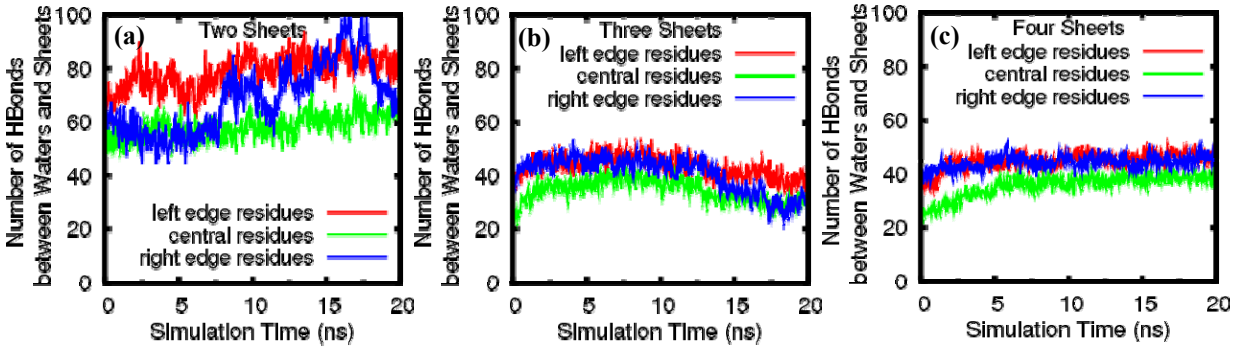
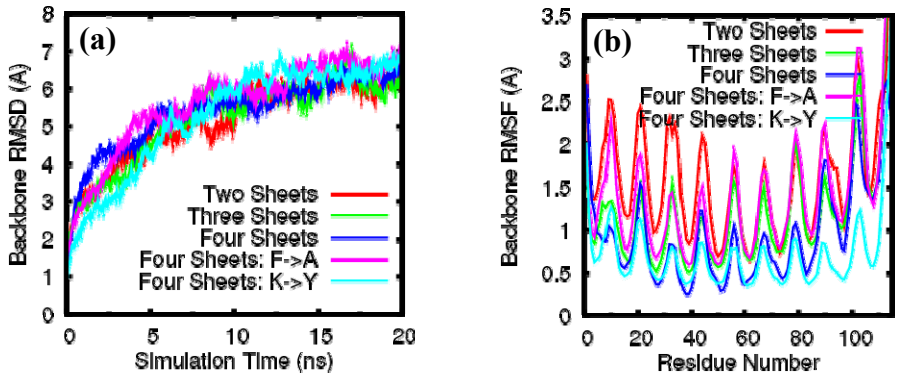


Figure S7. Structural characterization of the multiple-layer β-sheets without the end-capped proteins for wild type and mutated sequences (Phe→Ala or Lys→Tyr). Time evolution of (a) backbone RMSD and (b) backbone RMSF using the second series of MD trajectories with the same initial coordinates, but different initial velocities.



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