Supporting Material

Carbon nanotube inhibits the formation of β-sheet-rich oligomers of the Alzheimer's amyloid-β(16-22) peptide

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This material includes the estimation of the integrated autocorrelation time of the potential energy, description of the analysis parameters, calculation of the chain-independent C_α-RMSD, and six figures.

Estimation of the integrated autocorrelation time of the potential energy

To calculate the autocorrelation time of the potential energy of the system, we have performed a 20-ns MD simulation at 310 K starting from the structure in Fig. 1A. The potential energy U is recorded at Δt=0.02 ps intervals. Using the same method as used in previous computational study (1), the integrated autocorrelation time $\tau_{\mathrm{int},U}$ is computed with

$$\tau_{int\,U} = \Delta t\left(\frac{1}{2} + \sum_{t=1}^{\infty}\frac{C_U(t)}{C_U(0)}\right) \quad (1)$$

Where $C_U(t)$ is the autocorrelation function of U, which is defined by

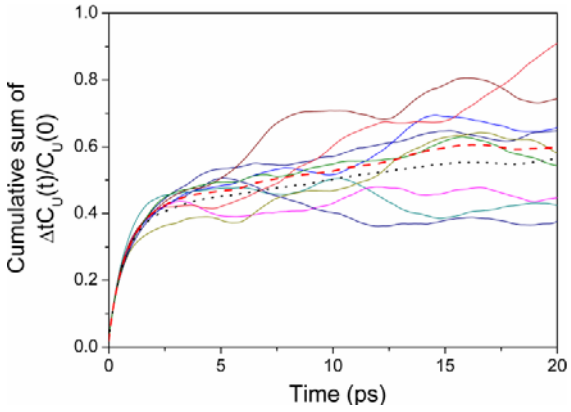
$$C_U(t) = < U(\tau)U(\tau + t) > \quad (2)$$

The autocorrelation function $C_U(t)$ is calculated over the time range $\{0 \ldots P\Delta t\}$ from a simulation fragment of length $Q\Delta$t (with $P \le Q/2$) using

$$C_U(j\Delta t) = \frac{1}{P}\sum_{i=0}^{Q-1-P} U(i\,\Delta t)U\left[(i+j)\Delta t\right] \quad (3)$$

The series $C_U(t)$ are truncated when $C_U(t)$ first becomes negative value to avoid the noisy behavior.

The product of the sampling interval Δt and the cumulative sum ($\Sigma C_U(t)/C_U(0)$) of the potential energy autocorrelation time $C_U(t)$ is plotted below against time t for 0-20 ps. Plots for 0.5 ns autocorrelation functions based on 10 disjointed 1-ns fragments are shown as solid lines and the average of the 10 fragments is shown in red dashed line. The 5 ns autocorrelation function based on the last 10 ns is shown as a black dotted line.



Plot of the product of the sampling interval Δt and the cumulative sum of the potential energy autocorrelation function $C_U(t)$ against time t for 0-20 ps.

Applying Eq.1 with time truncated at t=10 ps (the value of $C_U(t)$ first becomes negative at 15.72 ps and 4.61 ps, respectively, for the 5-ns autocorrelation and the average of the 10 1-ns autocorrelation functions), we obtain $\tau_{\text{int},U}$=0.51 ps for the average of the 10 1-ns autocorrelation functions. Similar value of $\tau_{\text{int},U}$ is obtained (0.52 ps) using the whole 20-ns simulation data.

Description of the analysis parameters

The free energy surfaces are constructed using –RT*logH(x,y), where H(x,y) is the histogram of two selected parameters x and y. The β-sheet size is the number of strands in an *n*-stranded β-sheet, e.g., the β-sheet size of a four-stranded β-sheet is four. Two chains are considered to form a β-sheet if (i) at least two consecutive residues in each chain visit the β-strand state; (ii) they have at least two inter-peptide H-bonds. One H-bond is taken as formed if the N…O distance is less than 0.35 nm and the N-H…O angle is greater than 150°.

Following our previous work (2), the structures of Aβ(16-22) octamers are characterized by a topological parameter, the connectivity length (CL), defined as the sum over the square root of the β-sheet size and the number of disordered chains in each configuration. In our notation, an aggregate of eight disordered chains without any β-sheet is assigned a CL of 8×sqrt(1)=8, and a bilayer of two 4-stranded β-sheets by a CL of sqrt(4)＋sqrt(4)=4. Therefore, the higher the connectivity length, the more random and disordered the aggregate is.

Calculation of the chain-independent C_α-RMSD

The chain-independent C_α-RMSD is calculated by completely neglecting the chain identifier in the coordinate file of Aβ(16-22) octamer as the 8 chains are topologically identical. In the coordinate files, each chain has a fixed identifier. As the 8 chains are not covalently connected, their relative spatial positions in one conformation may be different from those in another conformation. In this case, the RMSD value calculated using the coordinate file directly from the REMD run may not be the smallest, thus this RMSD value can't be used for structure similarity comparison. In the calculation, we keep the

identifier of each chain in the reference conformation fixed. For the conformation of which C_α-RMSD to be calculated, we change the chain identifier by permutation. Then we get 8! (8×7×6×5×4×3×2×1) different coordinate files (the x, y, z values of all the atoms are unchanged, only the numbering order of the atoms are changed). The C_α-RMSD is calculated for each coordinate file with respect to the reference structure and the smallest C_α-RMSD is taken for structure clustering. The smallest RMSD is the chain-independent RMSD.

References

1. Abraham, M. J., and J. E. Gready. 2008. Ensuring mixing efficiency of replica-exchange molecular dynamics simulations. J. Chem. Theory Comput. 4:1119-1128.
2. Lu, Y., P. Derreumaux, Z. Guo, N. Mousseau, and G. Wei. 2009. Thermodynamics and dynamics of amyloid peptide oligomerization are sequence dependent. Proteins 75:954-963.

Six figures:

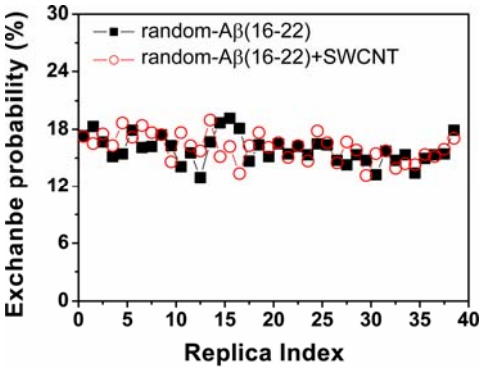


Figure S1: Exchange probability between each two neighboring replicas in the REMD runs of Aβ(16-22) and Aβ(16-22) +SWCNT.

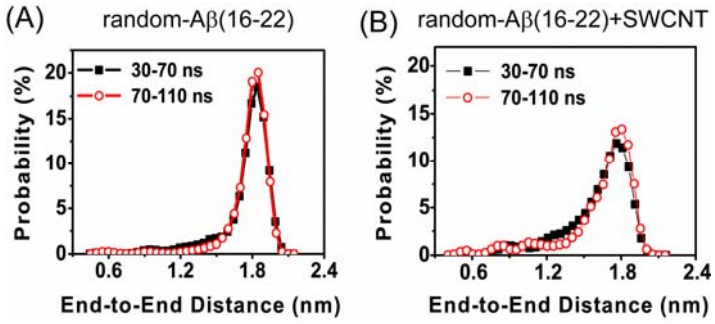


Figure S2: Convergence check of the REMD runs of Aβ(16-22) and Aβ(16-22)+SWCNT. Probability distribution of end-to-end distance (the C_α-C_α distance between K16 and E22) of Aβ(16-22) peptide in (A) Aβ(16-22) system and (B) Aβ(16-22)+SWCNT system within the time intervals 30-70 ns and 70-110 ns.

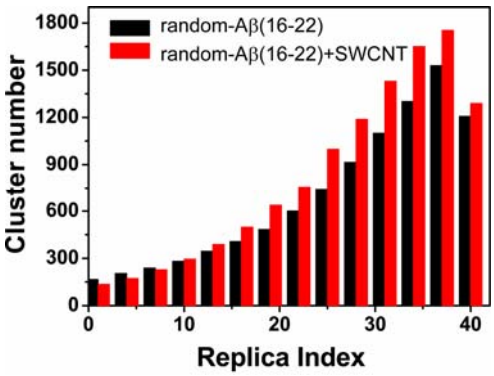


Figure S3: Number of clusters for Aβ(16-22) octamers in Aβ(16-22) system and Aβ(16-22)+SWCNT complex as function of replica index. Replica 1 is at 310 K and replica 40 is at 420 K. The increase of replica index corresponds to an increase of temperature.

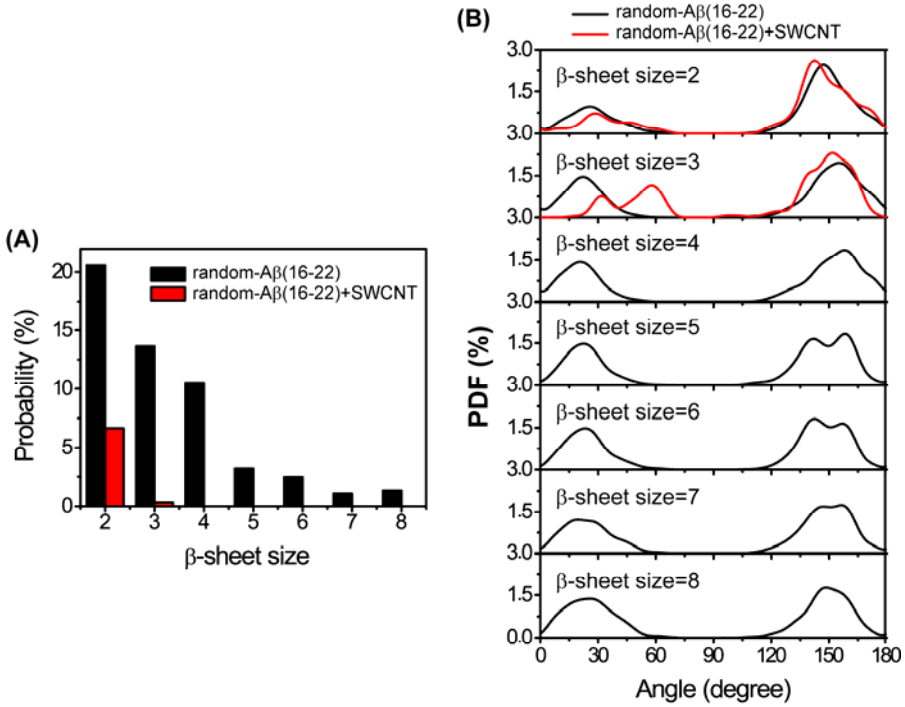


Figure S4: (A) Probability of different sizes of β-sheet and (B) the probability density function (PDF) of the angle between two neighboring strands in each size of β-sheet for Aβ(16-22) octamers in Aβ(16-22) and Aβ(16-22)+SWCNT systems at 310 K.

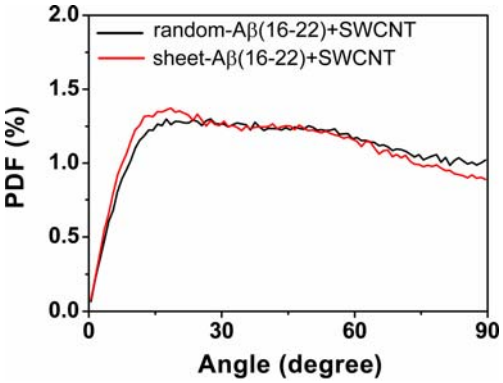


Figure S5: Probability density function (PDF) of the angle between Phe planar ring and its closest SWCNT carbon ring for a ring centroid-centroid distance greater than 0.3 nm in the two REMD runs with SWCNT.

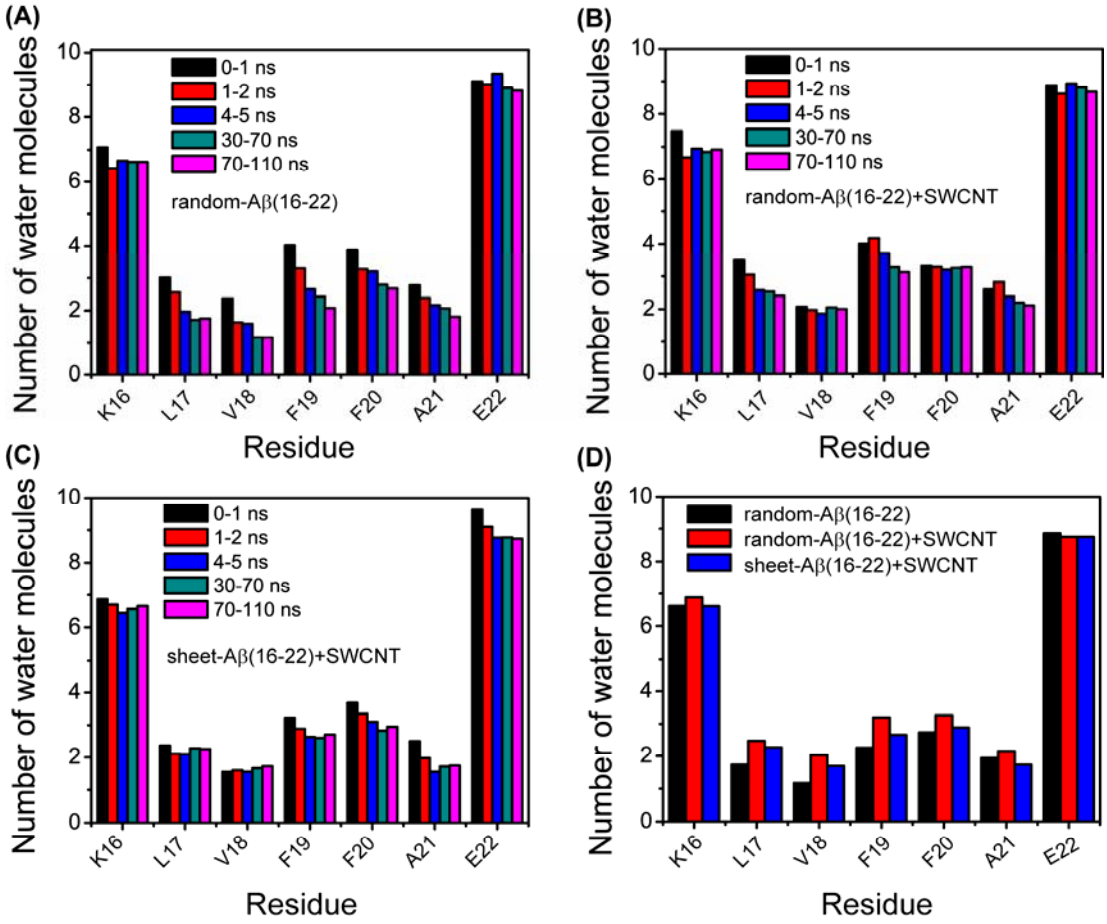


Figure S6: Average number of water molecules within 0.36 nm of any atom of a given residue during the three different REMD simulations. A rapid dehydration process (within 5 ns) is observed in the three different systems: Aβ(16-22), Aβ(16-22)+SWCNT and bilayer-Aβ(16-22)+SWCNT.