Supporting Material

Molecular mechanism of fullerene-inhibited aggregation of Alzheimer's amyloid-β peptide fragment

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This material includes the description of REMD simulations, analysis parameters, AFM images of Aβ(16-22) aggregation in the absence and presence of C_{60} nanoparticle, and three figures.

Description of REMD simulations and analysis parameters

Our REMD simulations include 40 replicas. Exchanges between two neighboring replicas were tried every 2 ps. The acceptance ratio for the three systems is ~18 %. Constraints were applied to bond lengths using the SETTLE algorithm for water[1] and the LINCS method for the peptides,[2] allowing an integration time step of 2 fs. Non-bonded pair lists were updated every 5 integration time steps. The peptide, fullerene and water groups were separately coupled to an external heat bath with a relaxation time of 0.1 ps using velocity rescaling coupling method.[3] The pressure was kept at 1 bar using Parrinello-Rahman method[4] with a coupling time constant of 1.0 ps. Electrostatic interactions were treated with the particle mesh Ewald method with a real space cutoff of 1.0 nm. The van der Waals interactions were calculated using a cutoff of 1.4 nm.

The free energy surfaces (or potential of mean force, PMF) were constructed using the relation -RT logH(x, y), where H(x, y) is the histogram of two selected reaction coordinates, x and y. In this study, the x coordinate is the number of inter-peptide hydrogen bonds (H-bonds) and the y coordinate is the radius of gyration of the Aβ(16-22) octamers. The DSSP program[5] was used to identify the secondary structure content. The percentage of various sizes of β-sheet was calculated. The size of a β-sheet is the number of strands in an n-stranded β-sheet, e.g., the β-sheet size of a two-stranded β-sheet is two. 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 hydrogen bonds (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,[6, 7] we used a topological parameter-connectivity length (CL) to characterize the structures of Aβ(16-22) octamers. CL is defined as the sum over the square root of the β-sheet size and the number of disordered chains in each configuration. Thus, the more disordered the aggregate is, the larger the connectivity length becomes. For example, the CL of a 4 + 4 β-sheet bilayer is sqrt(4) + sqrt(4) = 4, with 4 + 4 being its configuration type (CT). The Daura cluster analysis method[8] was used to cluster the conformations sampled in the REMD simulations with a C_α-root mean square deviation (C_α-RMSD) cutoff of 0.3 nm using residues L17-A21, with K16 and E22 excluded because of their high flexibilities. The chain-independent C_α-RMSD is calculated by completely neglecting the chain identifier in the coordinate file of Aβ(16-22) octamers to obtain the smallest RMSD as the eight chains are topologically identical.[9] The inter-peptide interactions were estimated by the probability of residue-residue contacts. A contact is defined when the aliphatic carbon atoms of two non-sequential main chains (or side chains) come within 0.54 nm or any other atoms of two non-sequential main chains (or side chains) lie within 0.46 nm. Fullerenes C_{60} and C_{180} have a diameter of 0.71 and 1.21 nm respectively.

The area of the molecular surface buried in contact between two molecules is called as contact area calculated as $S_{contact\ area} = 1/2\,((SASA_{pep} + SASA_{ful}) - SASA_{complex})$, where $SASA_{pep}$ and $SASA_{ful}$ are solvent accessible surface area of the isolated Aβ(16-22) octamer and fullerene (C_{60}, $3C_{60}$ and C_{180}) respectively, and $SASA_{complex}$ is the SASA of the fullerene-octamer complex. To probe the Aβ-fullerenes interactions in detail, we analyzed the π-stacking interactions between the peptides and the fullerenes surface by calculating the PDF of the distance between the centroids of the Phe aromatic ring and its closest carbon ring of fullerenes nanoparticles, and the PDF of the angle between the two rings. We calculated the interplanar angle by determining the angle between the surface normals of the two rings.

AFM imaging of Aβ(16-22) aggregation in the absence and presence of C_{60} nanoparticles

The morphology of Aβ(16-22) at different incubation periods was evaluated by utilizing commercial SPM equipment (Multimode V, Bruker Nano Surface, USA). The topography images of all dried samples were obtained by AFM in tapping mode with Si tips at a scanning rate of 1 Hz. All images were shown without any image processing except the flattening. To prepare the samples for AFM imaging, about 10 μL Aβ(16-22) solution with or without C_{60} nanoparticles was dropped on a freshly cleaved mica surface. The droplet was left on the substrate for 30 s with parafilm covered, and then dried under a gentle stream of nitrogen. All the AFM images were collected under ambient conditions at 25 °C and room humidity < 35 %.

References:

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Three Supplemental Figures:

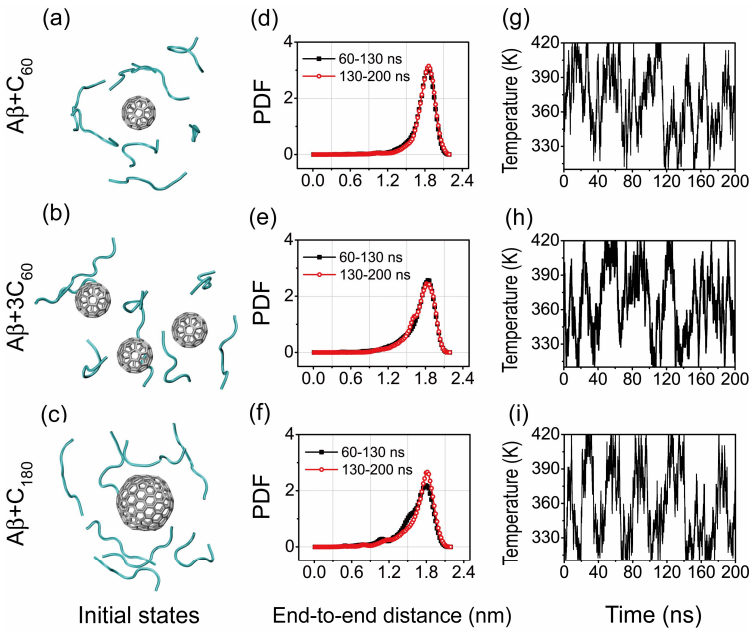

Figure S1: The initial random states and convergence check for the REMD runs of Aβ+C_{60}, Aβ+3C_{60} and Aβ+C_{180} systems at 310 K. Initial states for the REMD run of eight Aβ(16-22) chains with C_{60} (a), 3C_{60} (b) and C_{180} (c). Probability density function (PDF) of end-to-end distance (C_α-C_α distance between K16 and E22) (d, e and f) of Aβ(16-22) octamers within the time intervals of 60-130 ns and 130-200 ns and the time evolution of temperature swapping of one representative replica in temperature space (g, h and i) for the three systems.

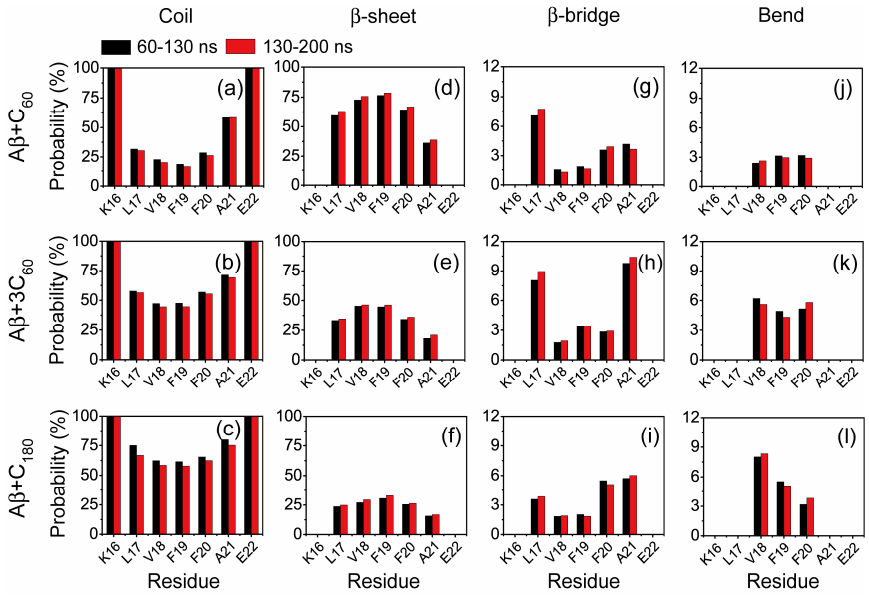

Figure S2: The calculated secondary structure probability of each residue in the REMD runs within the time intervals of 60-130 ns and 130-200 ns for Aβ(16-22) octamers in the presence of C_{60}, $3C_{60}$ and C_{180} at 310 K for (a, b and c) coil, (d, e and f) β-sheet, (g, h and i) β-bridge, and (j, k and l) bend structure.

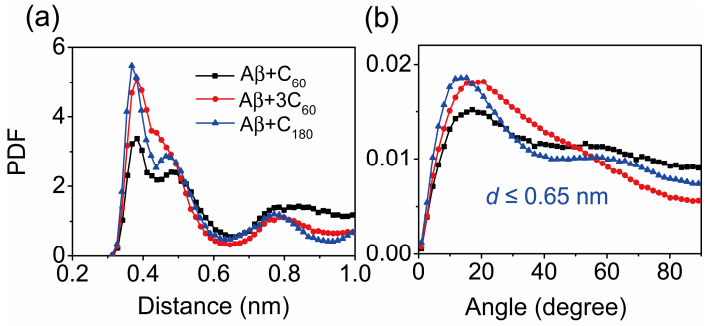

Figure S3: The PDF of the centroid distance (d) between the aromatic rings of Phe residues (each Phe residue is considered) and its closest carbon rings (a) and the PDF of the angle between the two rings with a centroid distance of $d \leq 0.65$ nm (b) in Aβ+C_{60}, Aβ+$3C_{60}$ and Aβ+C_{180} systems at 310 K.