Electronic Supplementary Information

Aggregation, structure and water permeability of membrane-embedded helical Aβ oligomers

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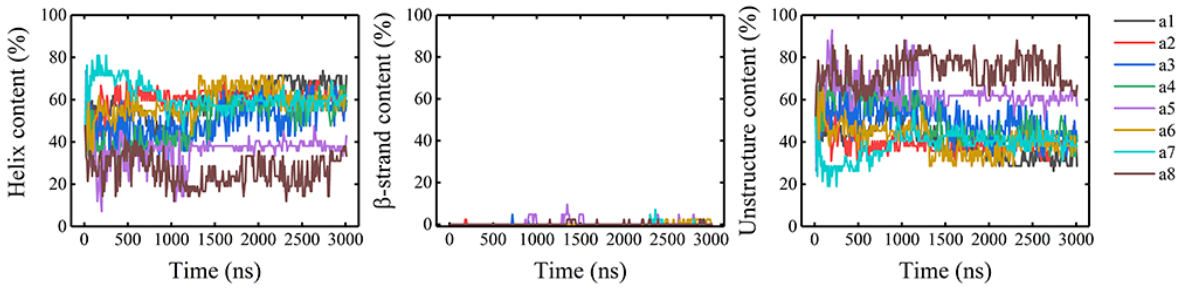

Fig. S1 Time evolution of the secondary structure content for each monomer of rep1. (A) Time evolution of the helix content for each monomer. The sum of the fraction for 3-10 helix, *α*-helix and Pi helix are taken as the helix fraction. (B) Time evolution of the β-strand content for each monomer. The sum of the fraction for parallel β-sheet and anti-parallel β-sheet structure are taken as the β-strand fraction. (C) Time evolution of the unstructured content for each monomer. The sum of the fraction for coil, turn and bend structure are taken as the unstructured fraction. Eight monomers are labeled as a1, a2, a3, a4, a5, a6, a7 and a8 respectively.

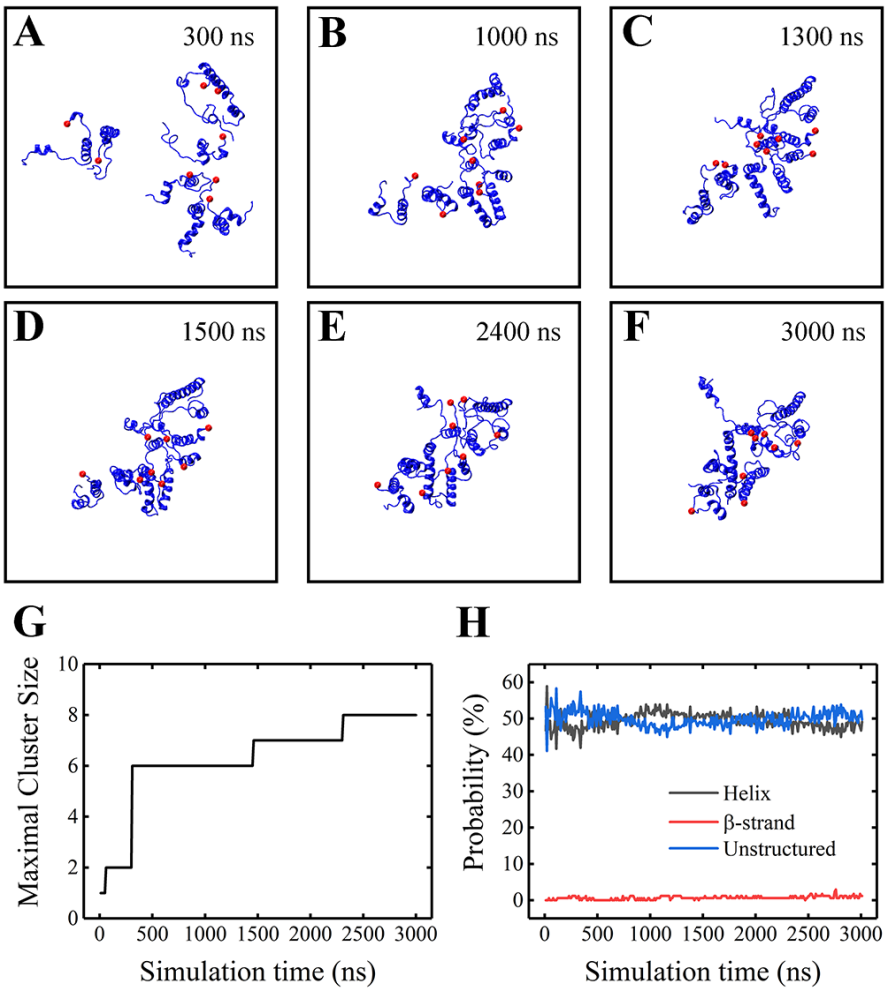

Fig. S2 Aggregating process of the peptides of replica 2. (A-F) Snapshots of the eight membrane-embedded monomers at 300 ns (A), 1000 ns (B), 1300 ns (C), 1500 ns (D), 2400 ns (E) and 3000 ns (F). The peptides are shown in blue and the Cα atom of the first residues of all peptides are shown in red. (G) Maximal cluster size as a function of time, which is defined as the number of peptides in the maximal cluster. (H) Secondary structure fraction of the Aβ42 peptide averaging over the eight peptides. The sum of the fraction for 3-10 helix, α-helix and Pi helix are taken as the helix fraction. The sum of the fraction for parallel β-sheet and anti-parallel β-sheet structure are taken as the β-strand fraction. The sum of the fraction for coil, turn and bend structure are taken as the unstructured fraction.

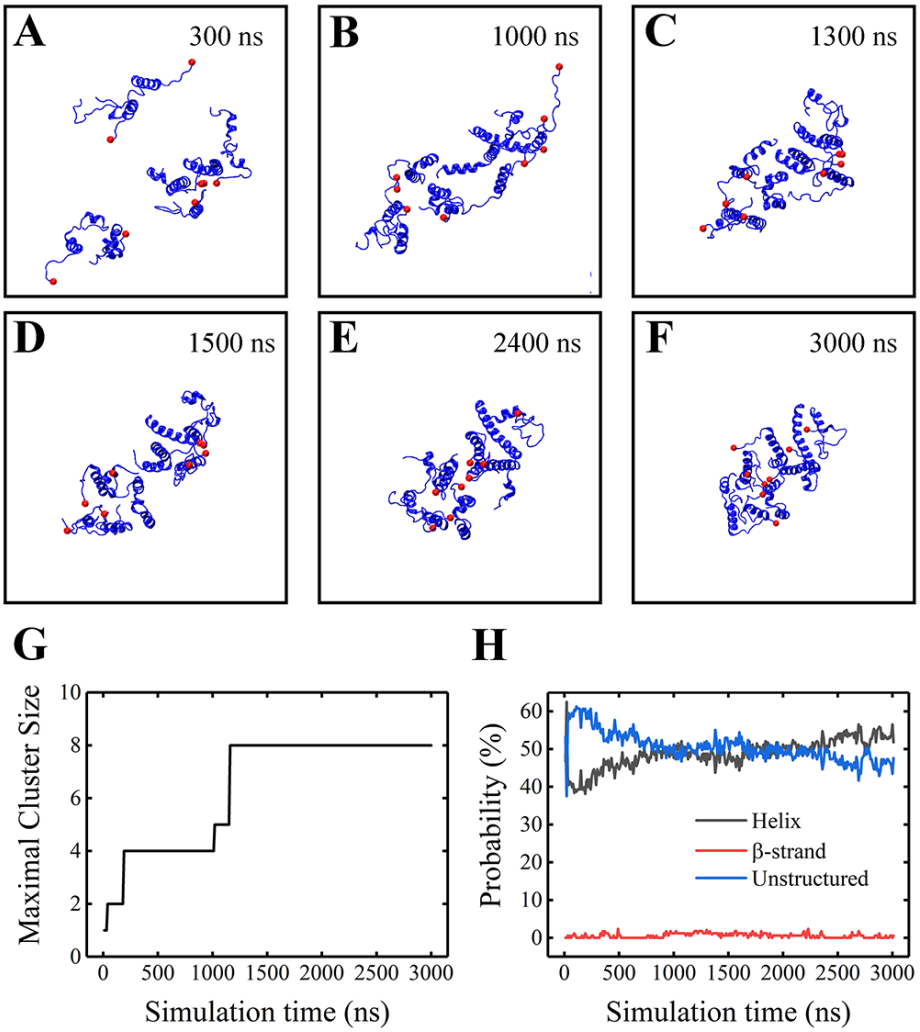

Fig. S3 Aggregating process of the peptides of replica 3. (A-F) Snapshots of the eight membrane-embedded monomers at 300 ns (A), 1000 ns (B), 1300 ns (C), 1500 ns (D), 2400 ns (E) and 3000 ns (F). The peptides are shown in blue and the Cα atom of the first residues of all peptides are shown in red. (G) Maximal cluster size as a function of time, which is defined as the number of peptides in the maximal cluster. (H) Secondary structure fraction of the Aβ42 peptide averaging over the eight peptides. The sum of the fraction for 3-10 helix, α-helix and Pi helix are taken as the helix fraction. The sum of the fraction for parallel β-sheet and anti-parallel β-sheet structure are taken as the β-strand fraction. The sum of the fraction for coil, turn and bend structure are taken as the unstructured fraction.

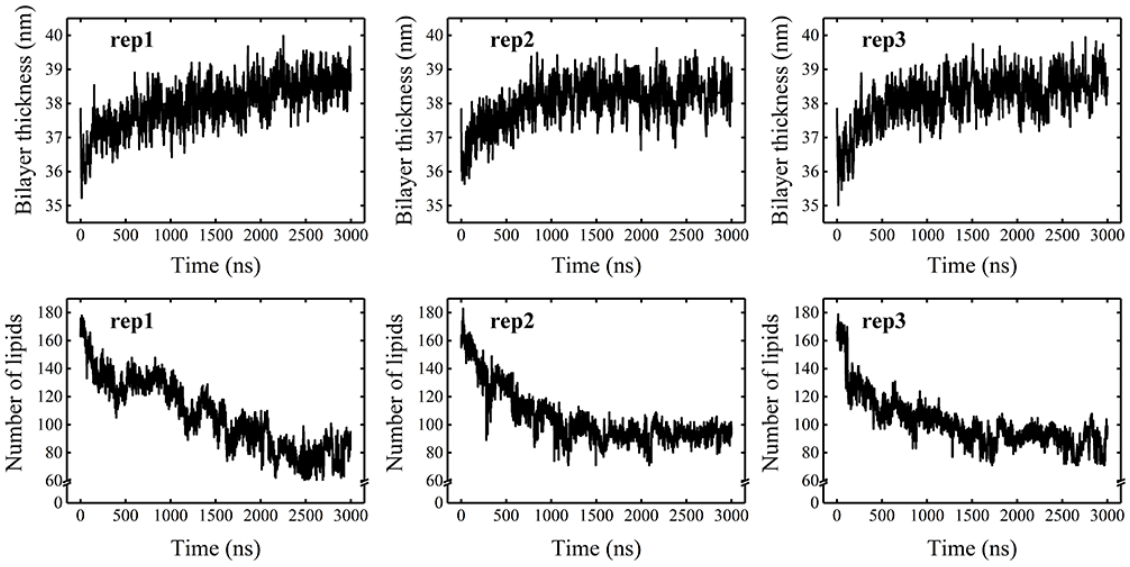

Fig. S4 Time evolution of bilayer thickness (upper panel) and number of number of lipids within 0.5 nm distance to the peptides (lower panel) for replica 1 (rep1), replica 2 (rep2) and replica 3 (rep3).

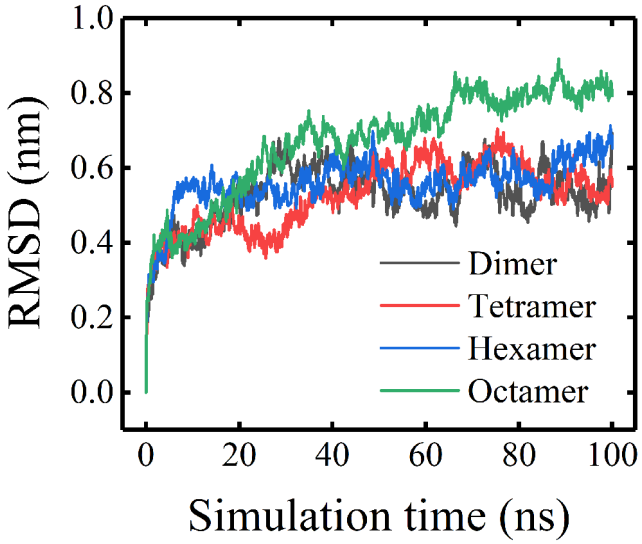

Fig. S5 The time evolution of the RMSD of the protein with respect to the initial structure of four oligomers.

Table S1 Hydrogen bonds and their occupancy formed in sole oligomers of dimer, tetramer, hexamer and octamer.

Oligomers	Donor	Acceptor	Occupancy
Dimer	a2: LYS16-Side	a1: GLU3-Side	53.85%
	a1: LYS28-Side	a2: GLU22-Side	38.46%
Tetramer	a2: LYS16-Side	a1: GLU22-Side	59.62%
	a4: LYS16-Side	a3: GLU22-Side	34.62%
	a3: GLY9-Main	a4: ASP7-Side	34.62%
	a3: LYS28-Side	a2: GLU22-Side	23.08%
	a3: LYS16-Side	a2: ASP23-Side	23.08%
Hexamer	a4: TYR10-Side	a5: GLU11-Side	71.15%
	a4: LYS16-Side	a3: GLU22-Side	53.85%
	a5: LYS28-Side	a6: ASP23-Side	50.00%
	a2: SER26-Side	a1: ASP23-Side	48.08%
	a5: LYS28-Side	a6: GLU22-Side	46.15%
	a1: LYS16-Side	a2: GLU22-Side	44.23%
	a2: LYS16-Side	a1: GLU3-Side	44.23%
	a3: SER8-Main	a4: ASP7-Side	40.38%
	a5: GLN15-Side	a3: VAL36-Main	38.46%
	a4: LYS28-Side	a1: GLU22-Side	30.77%
	a3: GLY9-Main	a4: ASP7-Side	28.85%

	a4: LYS16-Side	a1: ASP23-Side	26.92%
	a3: TYR10-Side	a4: HSD14-Side	26.92%
	a3: SER8-Side	a4: GLU11-Side	25.00%
Octamer	a2: ARG5-Side	a1: ASP7-Side	84.62%
	a2: LYS16-Side	a1: GLU22-Side	59.62%
	a4: LYS16-Side	a3: ALA42-Side	50.00%
	a5: ILE31-Main	a4: VAL39-Main	44.23%
	a4: LYS16-Side	a5: GLU22-Side	40.38%
	a7: LYS16-Side	a6: GLU22-Side	38.46%
	a6: LYS16-Side	a3: ALA42-Side	32.69%
	a6: LYS16-Side	a5: GLU22-Side	32.69%
	a8: LYS28-Side	a7: ASP23-Side	32.69%
	a1: VAL39-Main	a2: ASN27-Side	30.77%
	a4: GLN15-Side	a3: GLN15-Side	28.85%
	a7: ARG5-Side	a5: GLU11-Side	28.85%
	a8: ALA30-Main	a7: GLY28-Main	28.85%
	a1: TYR10-Side	a2: HSD14-Side	23.08%
	a2: ASP1-Main	a3: GLU3-Side	21.15%

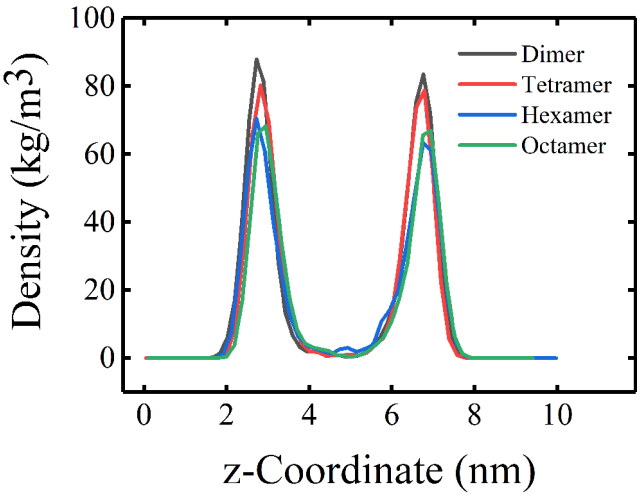

Fig. S6 One-dimensional density distribution of phosphorus atoms for the structure ensemble of dimer, tetramer, hexamer and octamer.

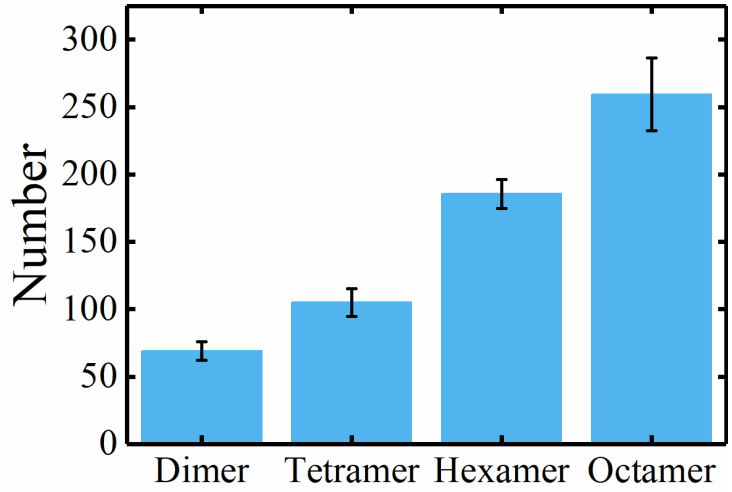

Fig. S7 The average number of water molecules in the membrane within 3 Å around the oligomers.

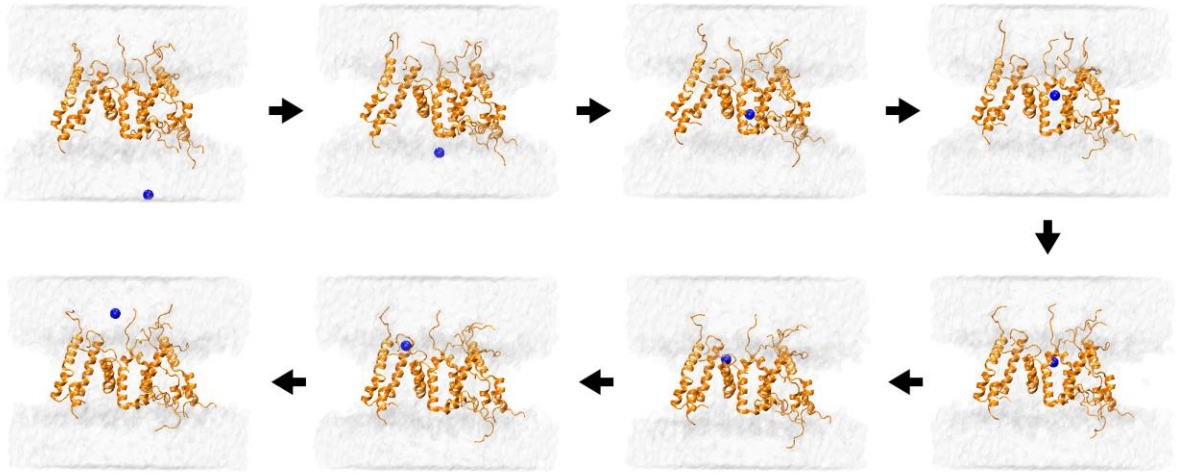

Fig. S8 One water molecule entering and exiting the transmembrane octamer. The black arrows instruct the transmembrane process. In each snapshot, the octamer is shown in orange whereas the oxygen atom of one water molecule is represented by blue ball.

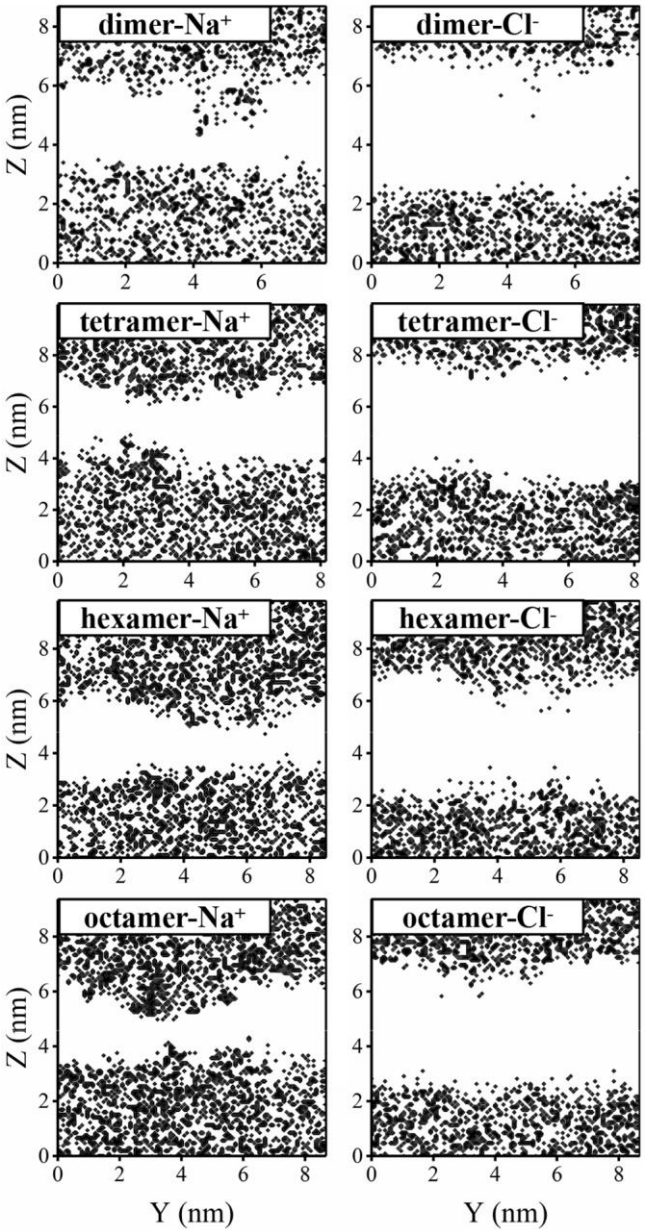

Fig. S9 Spatial density plot of Na^+ (left) and Cl^- (right) for sole oligomers on Y-Z plane. The positions where the ion densities are not zero are colored in black.

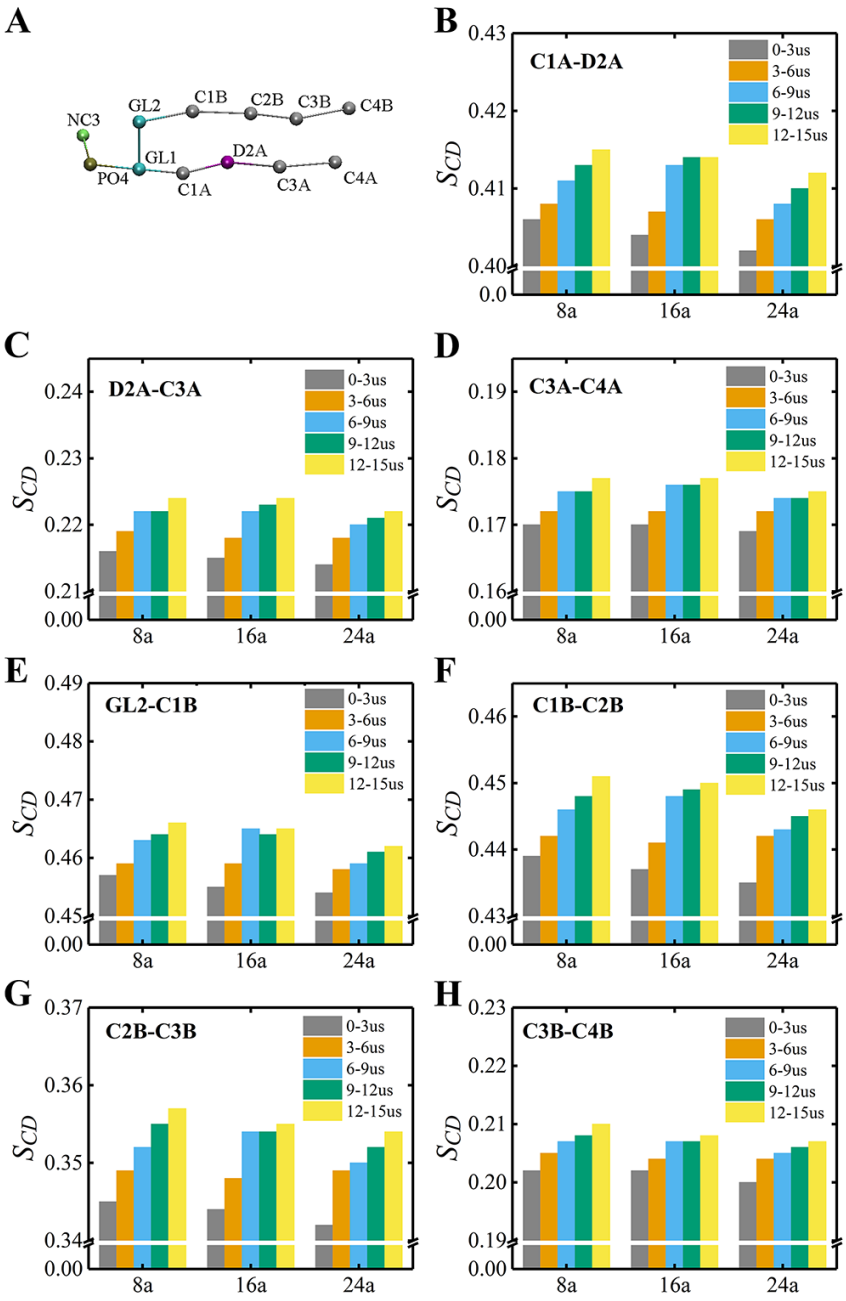

Fig. S10 The representative structure of one POPC lipid of CG representation (A) and order parameter S_{CD} of POPC lipids for the bond vector of C1A-D2A (B), D2A-C3A (C), C3A-C4A (D), GL2-C1B (E), C1B-C2B (F), C2B-C3B (G), C3B-C4B (H) and the bilayer normal for 0-3 μs, 3-6 μs, 6-9 μs, 9-12 μs and 12-15 μs time intervals.

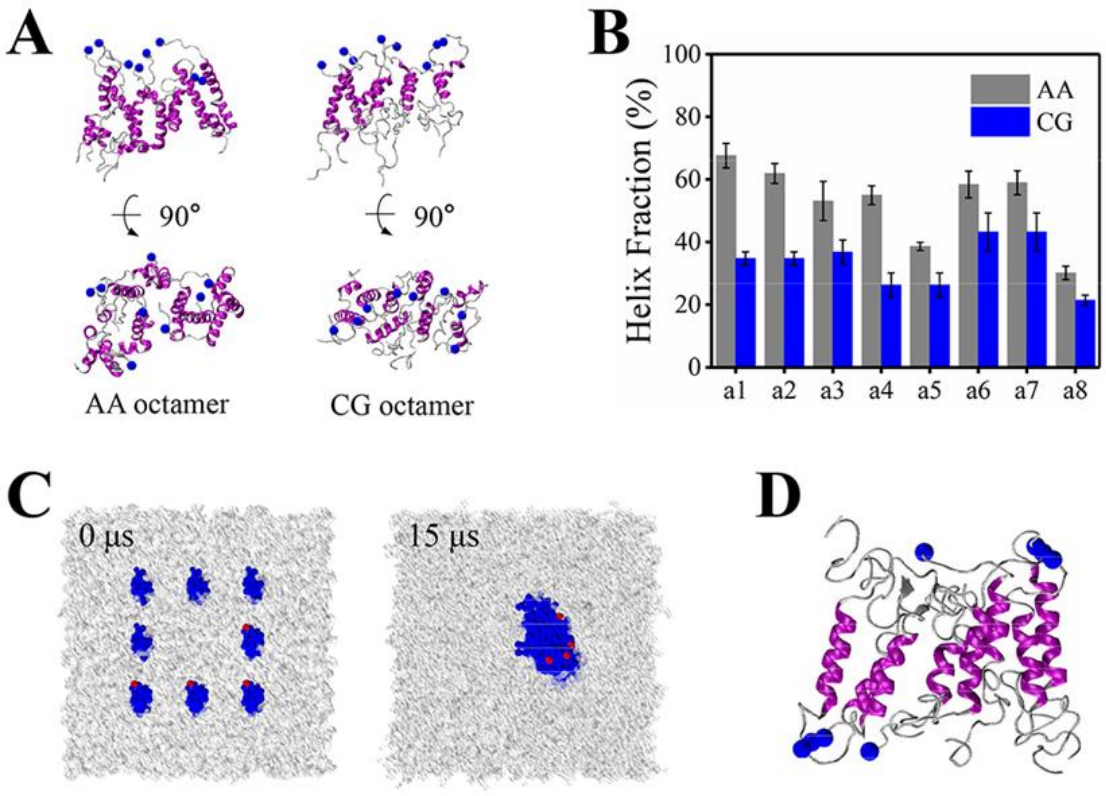

Fig. S11 (A) Comparison of the representative structure for the octamer from the aggregates of AA simulation (left) and the octamer backmapped from CG simulation (right). Side views are shown in upper panel while top views are shown in lower panel. (B) Fraction of helix structure in eight chains for the octamer form AA and CG simulation. (C) Snapshots for the newly oriented 8a model at 0 μs of initial structure (left) and at the end of 15 μs (right). (D) The molecular architecture of the all-atom backmapped assembly at the end of 15 μs for the newly oriented 8a model.