Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Investigation of interaction of amyloid β peptide (11-42) oligomers with POPC (1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine) membrane by molecular dynamics simulation

Ning Xiang[a], *Yuan Lyu*[a], *Xiao Zhu*[b] *and Ganesan Narsimhan*[a,*]
[a] Department of Agricultural and Biological Engineering
[b] Research Computing, Rosen Center for Advanced Computing
Purdue University
West Lafayette, IN 47907

Initial conformation for pulling simulation

Equilibrium MD simulations were used to generate the starting configurations for pulling simulations. Three different pulling simulations were performed, namely (i) a single peptide removed from lipid bilayer both in the presence as well as in the absence of cholesterol (ii) a trimer removed from lipid bilayer and (iii) a peptide is withdrawn from a trimer (leaving the other two intact) in lipid bilayer. To obtain the initial configuration for these pulling simulations, in each case, three peptides were first placed inside the lipid bilayer and equilibrated (using the same methodology described in section 2.1 in main manuscript) for 200 ns, and the end of equilibrium simulation trajectories were used as the starting configurations for the above pulling simulations. In case of pulling simulation for 1 Aβ in POPC membrane, two of the three Aβ peptides were removed and the other remaining peptide was restrained, followed by equilibrating the system for 100 ns under an NPT ensemble, using the same methodology described in section 2.1, which was then followed by removing the restraint.

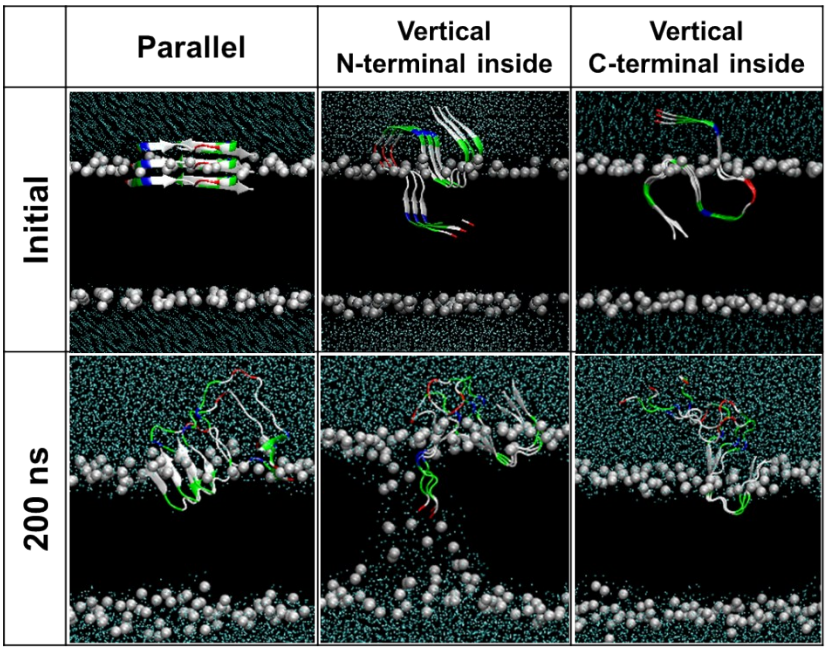


Figure S1. MD simulation snapshots of Aβ oligomer (3 peptides) placed with POPC bilayer for initial and 200 ns for three different orientations. Color code: silver, POPC lipid heads; blue, water molecules; deep blue, charged residues; green, polar residues; white, nonpolar residues. Lipid tails not shown for clarity.

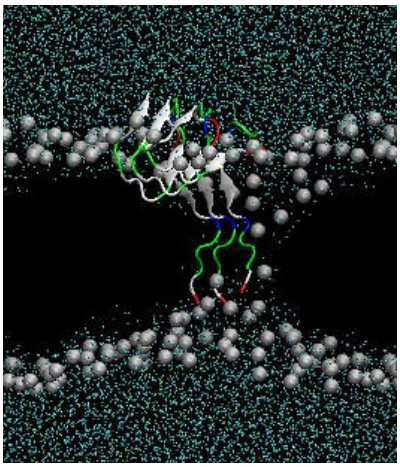


Figure S2. MD simulation snapshots at 500 ns for Aβ trimer placed vertical with N-terminal inside bilayer. A continuation of Figure S1 middle lower panel. Color code: the same as Figure S1. This orientation is stable inside the POPC membrane with lipid heads bending and water channel formation for 500 ns simulation time.

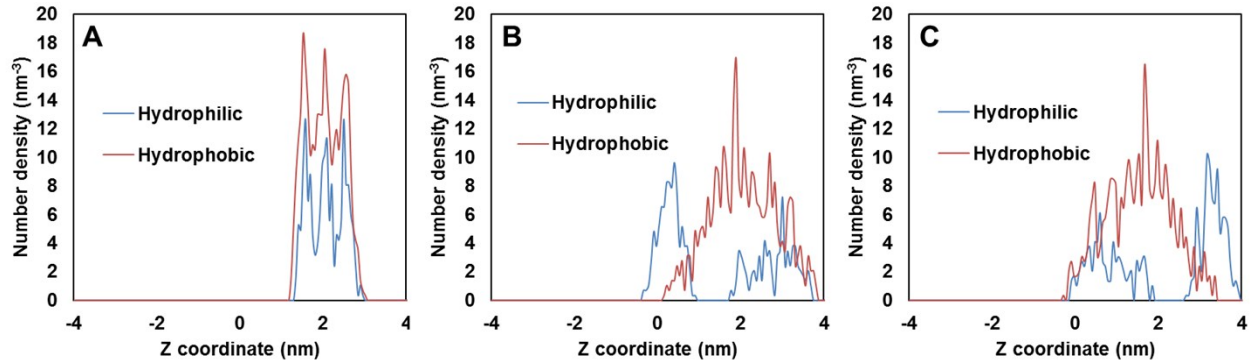
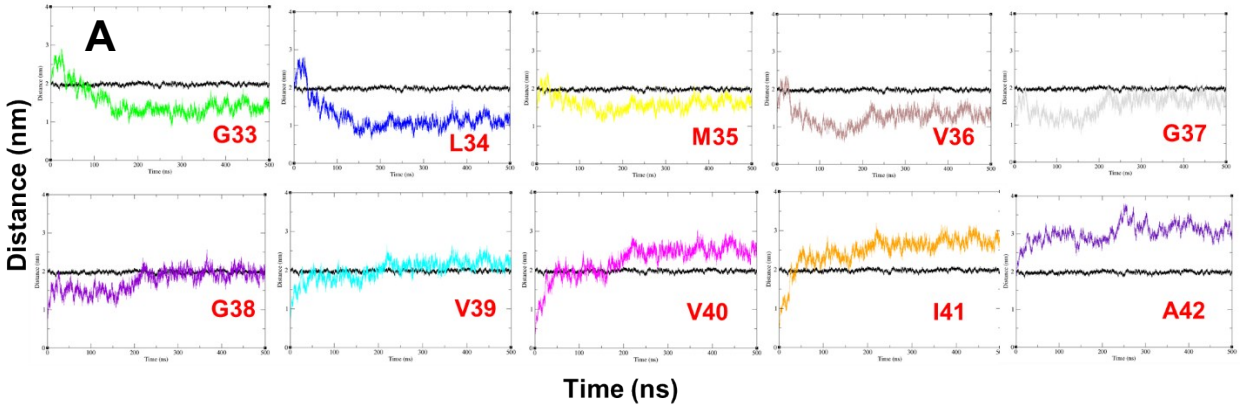


Figure S3. Initial position of the hydrophobic and hydrophilic residues of the Aβ oligomer placed on the top of the bilayer. Three different orientations: A. parallel; B. Vertical with residue 11 (GLU) inside the bilayer; C. Vertical with residue 42 (ALA) inside the bilayer. Blue: hydrophilic residues; Red: hydrophobic residues.



B

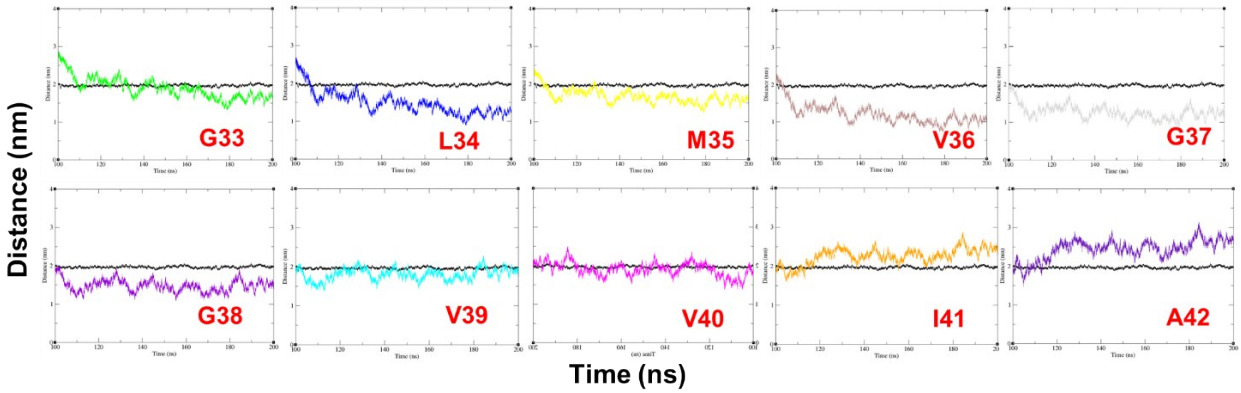


Figure S4. The evolution of distance between center of mass (COM) of C-terminal individual residues (33-42) and lipid bilayer. A and B are independent duplicates with simulation time of 500 ns and 200 ns respectively. Color code: black: COM of upper leaflet phospholipid heads, all other colors: corresponding residues.

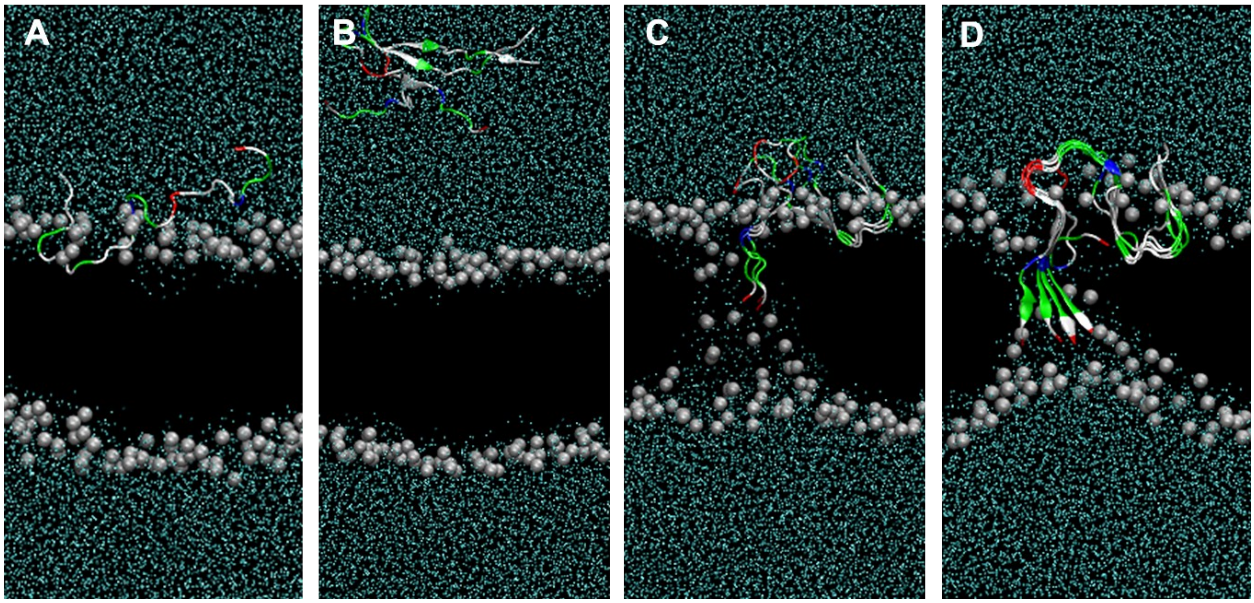


Figure S5. MD simulation snapshots at 200 ns for different number of Aβ peptides. A. 1 Aβ; B. 2β; C. 3β; D. 5β. Color codes are the same as Figure S1.

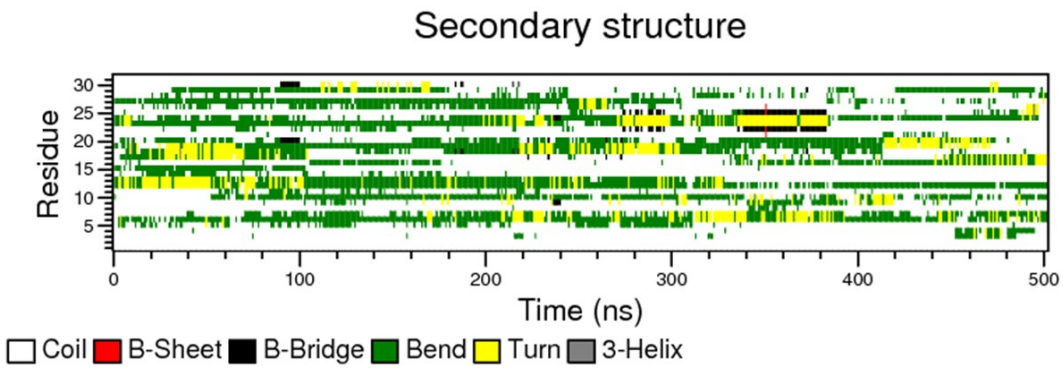


Figure S6. Secondary structure details of Aβ (11-42) monomer over 500 ns.

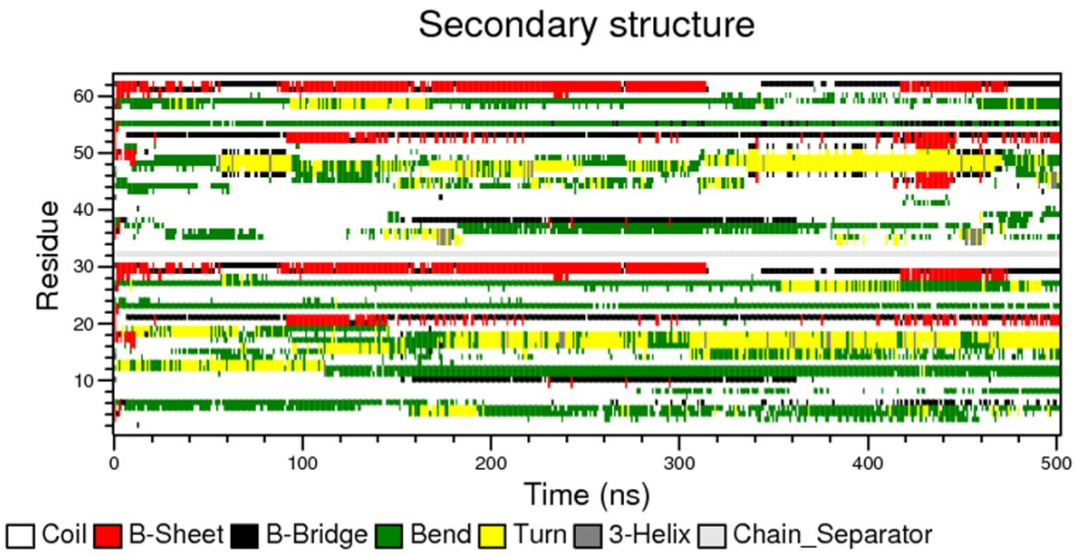


Figure S7. Secondary structure details of Aβ (11-42) dimer over 500 ns.

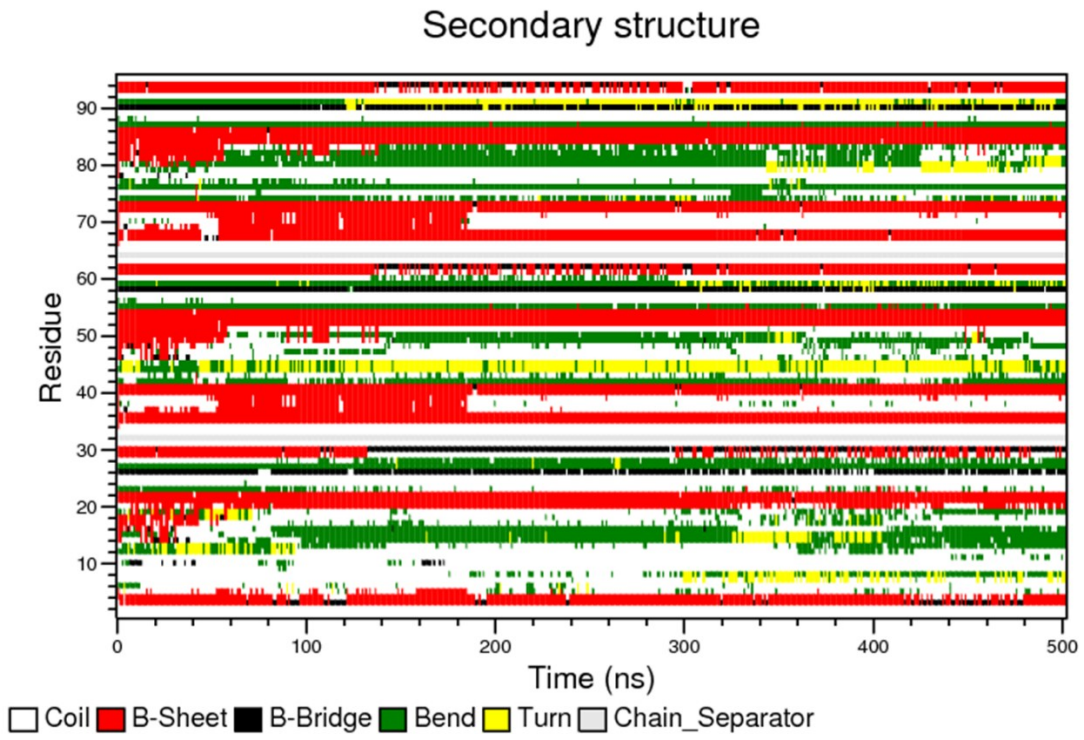


Figure S8. Secondary structure details of Aβ (11-42) trimer over 500 ns.

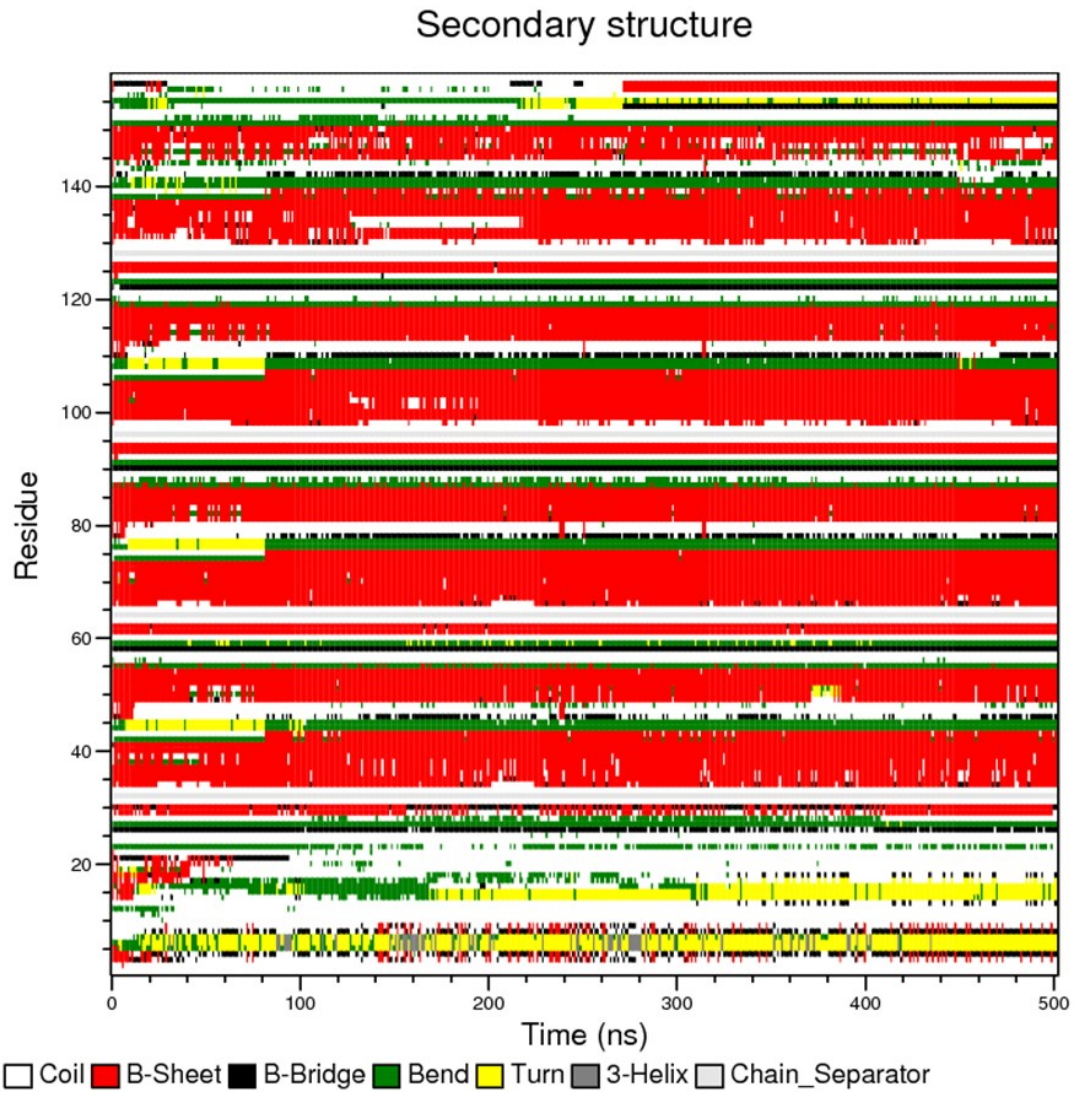


Figure S9. Secondary structure details of Aβ (11-42) pentamer over 500 ns.

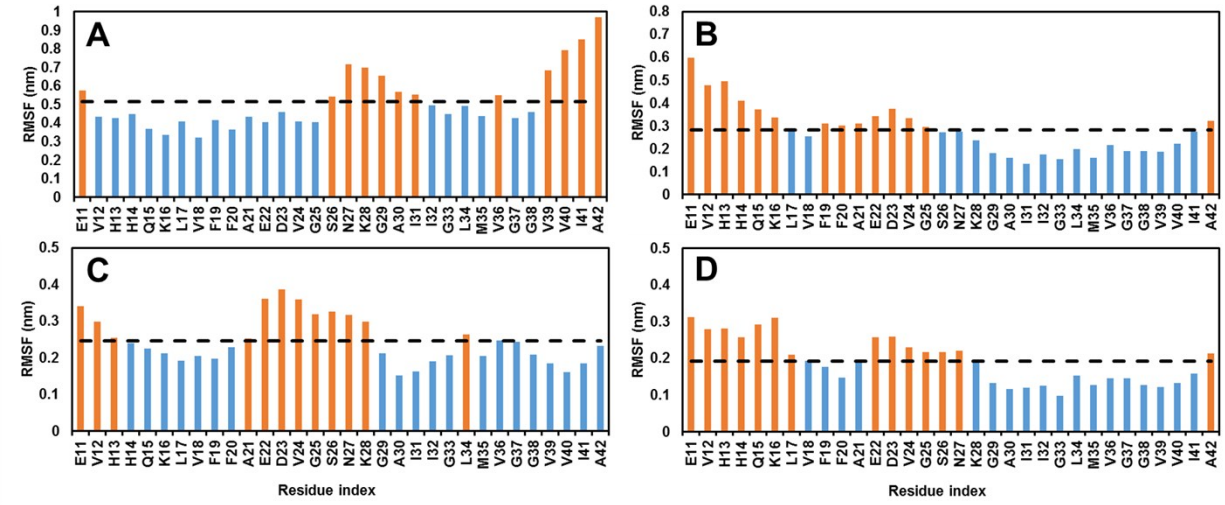


Figure S10. RMSF of Aβ monomer, dimer, trimer and pentamer, averaged over 500 ns simulation time. A. monomer, B. dimer, C. trimer, D. pentamer. Dashed line: average RMSF value. Orange bar: residue with RMSF higher than average RMSF value. Blue bar: residue with RMSF lower than average RMSF value.

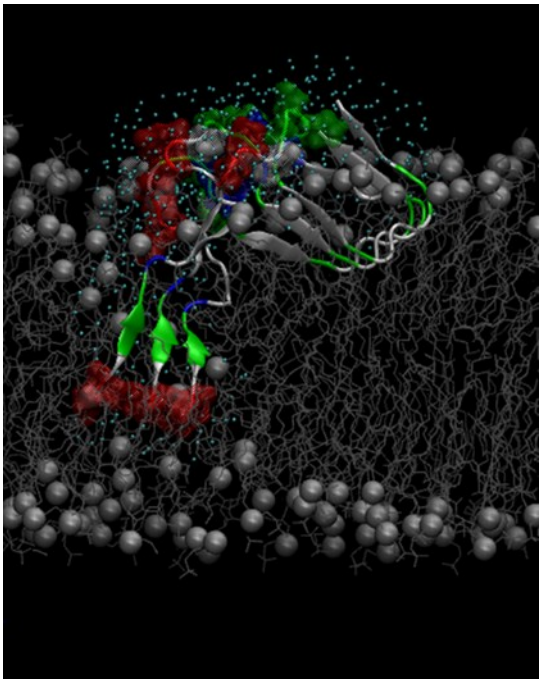


Figure S11. MD simulation snapshot at 500 ns for Aβ (11-42) trimer in POPC lipid bilayer. Color codes are the same as Figure S1. Residues E11, E22, D23, V24, G25, S26, N27 and K28 are shown

with drawing method of SURF. Water molecules that have distance > 5 Å with protein are not shown for clarity.

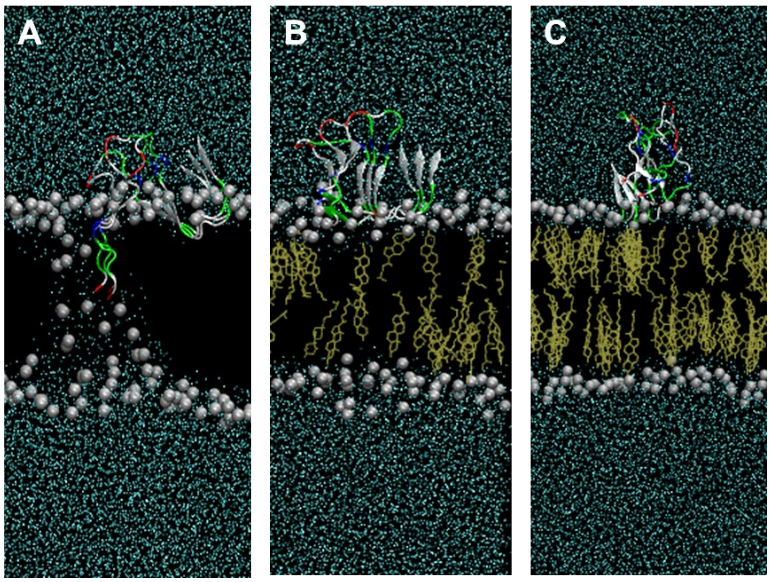


Figure S12. MD simulation snapshots of Aβ oligomer (3 peptides) placed with POPC bilayer at 500 ns for cholesterol concentration of 0%, 20% and 40%. Color codes: Tan, Cholestrol, the rest are the same as Figure S1. Lipid tails are not shown for clarity.

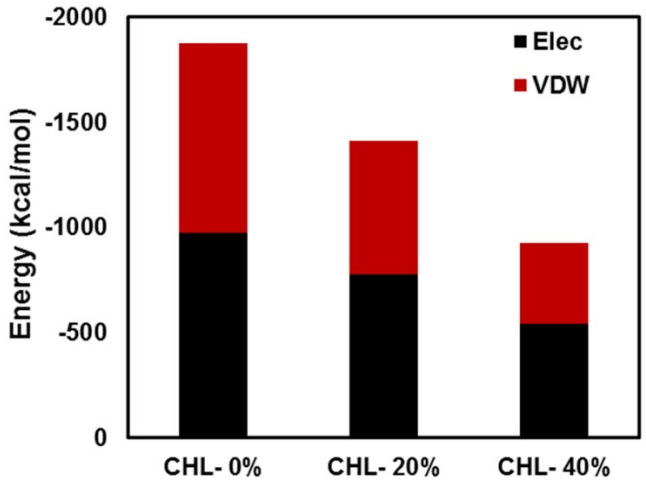


Figure S13. Total binding energy for lipid membranes contain different concentration of cholesterol in the presence of 3 Aβ. Color code: Black, electrostatic interaction; Red, van der Waals interaction.

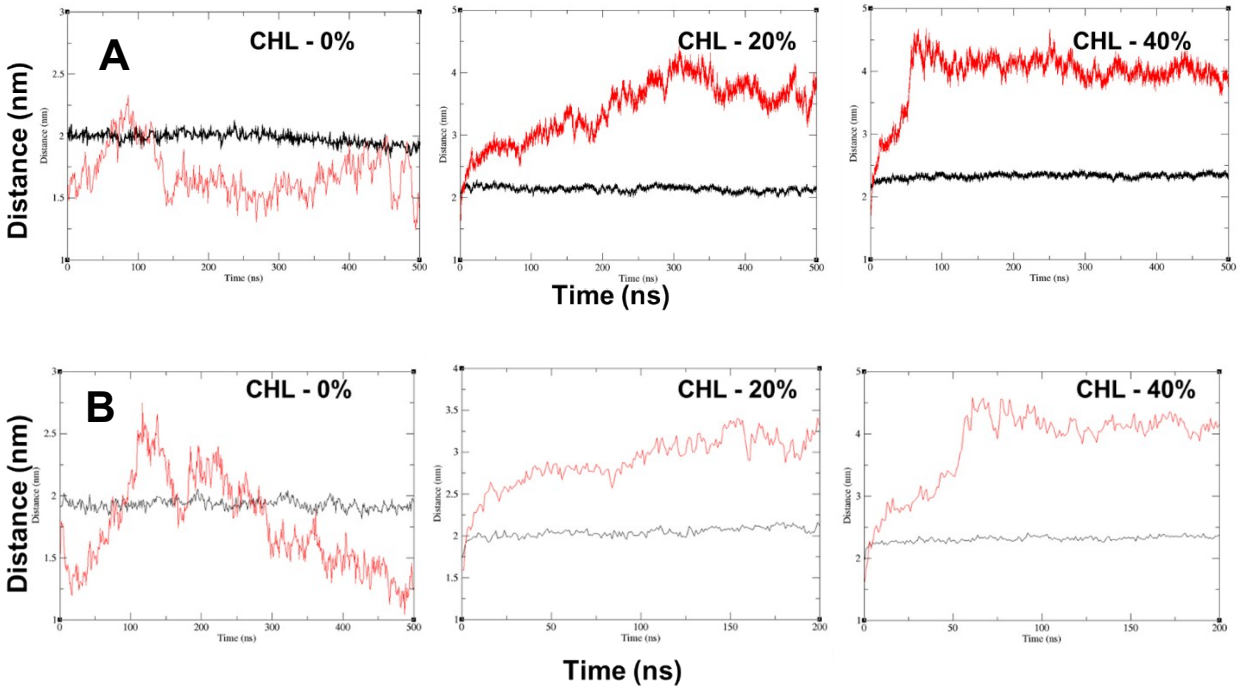


Figure S14. The evolution of distance between center of mass (COM) of residues (17-21) and lipid bilayer. A and B are independent duplicates with simulation time of 500 ns and 200 ns respectively. Color code: black: COM of upper leaflet phospholipid heads, red: COM of residues (17-21).