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

Effects of Applied Surface-tension on Membrane-assisted Aβ Aggregation

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Protein model

The coarse grained peptide model consists of three primary bead types — charged (sidechains of LYS and GLU), polar (peptide backbone) and hydrophobic (others). The polar bead-types have explicit dummy-charges added to them to represent molecular polarization. These dummies can lead to induced-dipole effects and therefore introduce directionality to interactions. The impact of these dummy-charges in protein structural transitions has been explored in previous publications.[1] The cross-interactions between these bead-types have been defined from free-energies of solvation and partitioning (hexadecane-water). Further details about forcefield parameters, details of parametrization and model validation are provided in Ganesan *et al.*,[2] with minor modifications listed in Sahoo *et al.*[3] Previous publications have used this model to study membrane/surface-assisted peptide folding and role of headgroup charge on membrane-assisted Aβ aggregation.[2,3]

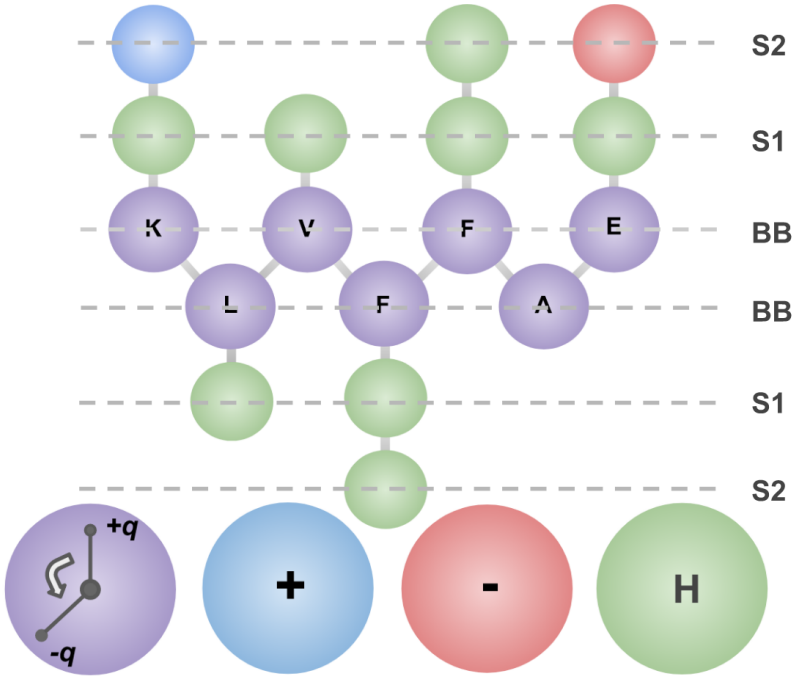

Figure S1: A schematic description of peptide coarse-grained model. Colors: green- hydrophobic bead; violet, polarizable beads ; red, negatively charged bead; blue, positively charged bead. Image reproduced from Ganesan *et.al.*[3] with permission from the PCCP Owner Societies.

Membrane model

The lipid model follows a 4:1 form of coarse-grained mapping scheme, with a single POPC molecule represented by 13 CG-beads. The Phosphate (PO4) and Choline (NC3) are charged CG-beads mapping to the headgroup atoms, and the glycerol-esters are represented with polarizable beads, similar to the ones introduced in the peptide model. The lipid tails are mapped as strings of hydrophobic beads. The membrane model can reproduce accurate electrostatic — dipole moment and headgroup bridging; and structural features — line tension and membrane compressibility.[4]

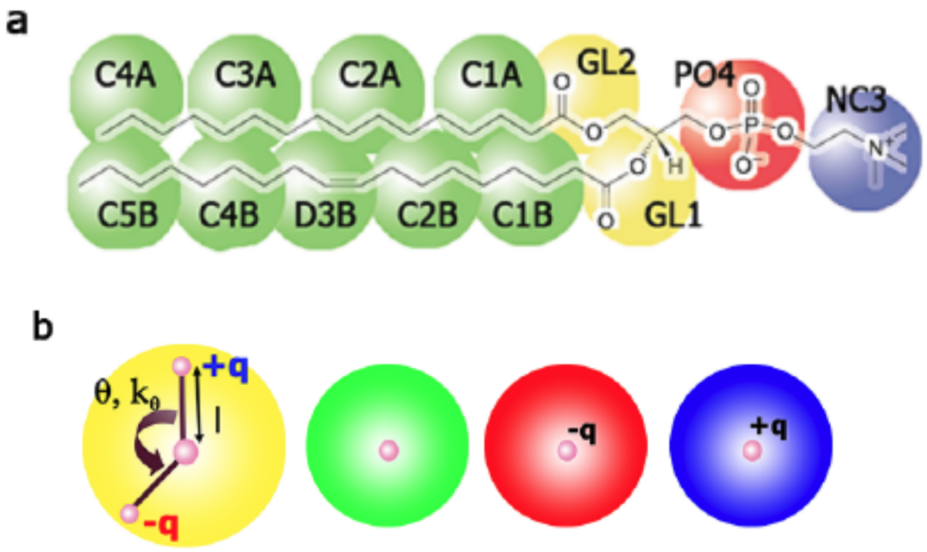

Figure S2: (a) Mapping scheme for POPC coarse-grained lipids; colors: green, hydrophobic bead; yellow, polarizable beads ; red, negatively charged bead; blue, positively charged bead. Image adapted and modified from Ganesan *et.al.*[4] with permission from the PCCP Owner Societies.

Simulation Protocol

All the simulation-systems studied in this article have followed exactly same simulation protocol and the simulations have been performed with Gromacs 4.5.7.[5] The initial membrane systems were created with lipid molecules and water molecules placed in a grid, with an adapted version of insane python script.[6] The membrane was energy minimized and equilibrated over 10 ns, with constant number, pressure and temperature (NPT) ensemble. Nose-Hoover thermostat was used to maintain temperature at 300K, with time constant 1 ps.[7] The Parinello-Rahman barostat with time constant 1 ps and compressibility $3.5X10^{-5}$/bar was used with semiisotropic pressure coupling to maintain a pressure of 1 bar.[8] The long range electrostatics is determined through Particle-Mesh Ewald method with relative dielectric constant of 2.5 and cutoff distance at 1.6 nm.[9] The Lennard-Jones interactions were scaled down from 0.9 nm to 1.2 nm with the Gromacs shift scheme. This initial phase allowed the membrane to be equilibrated.

After that peptides were added to the aqueous phase randomly away from the membrane.

The system was again energy minimized, and then equilibrated for 50 ns with position restraints on the backbone bead of the central Phenylalanine. At this stage, different values of surface-tension was applied on different systems with the Berendsen barostat,[10] with other parameters and simulation conditions fixed. Finally, the position restraints were removed, and the peptides were allowed to interact among themselves and the membrane.

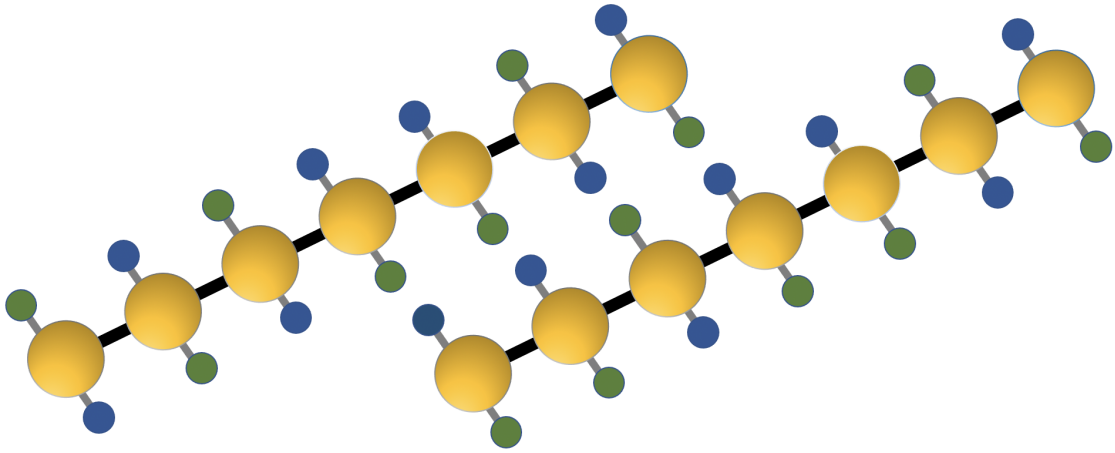

Figure S3: A schematic description of the metric used to determine ordered aggregation. The yellow spheres represent peptide backbones; and the green (positive) and blue (negative) spheres represent charged dummies. A peptide is classified as forming an ordered aggregate, if *at-least* 3 backbone dummies align with another peptide.

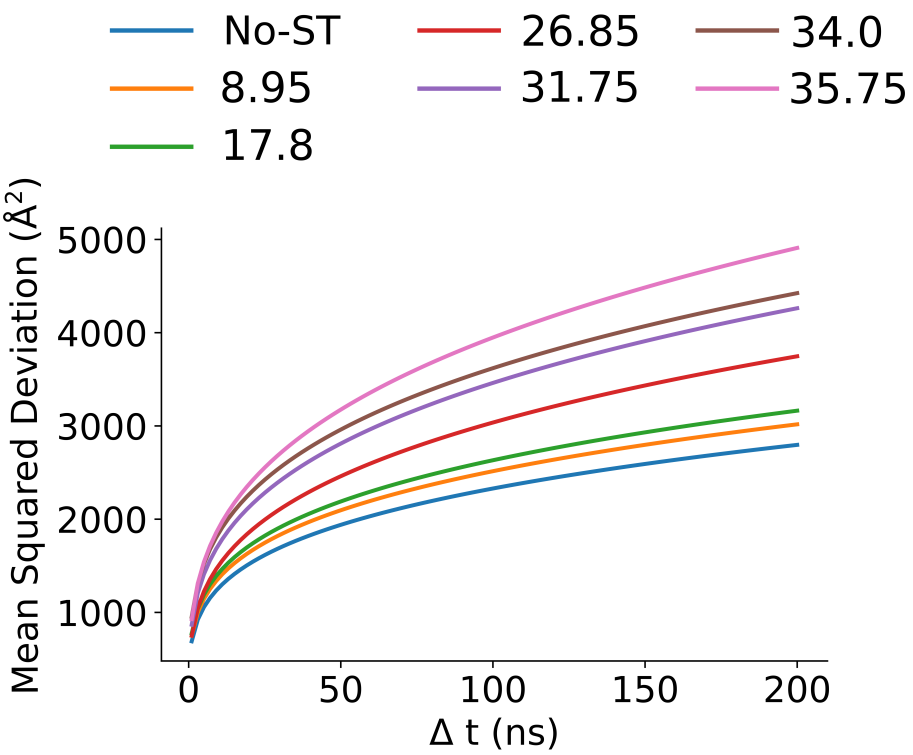

Figure S4: Mean squared deviation of a single peptide in presence of the membranes at different surface-tension.

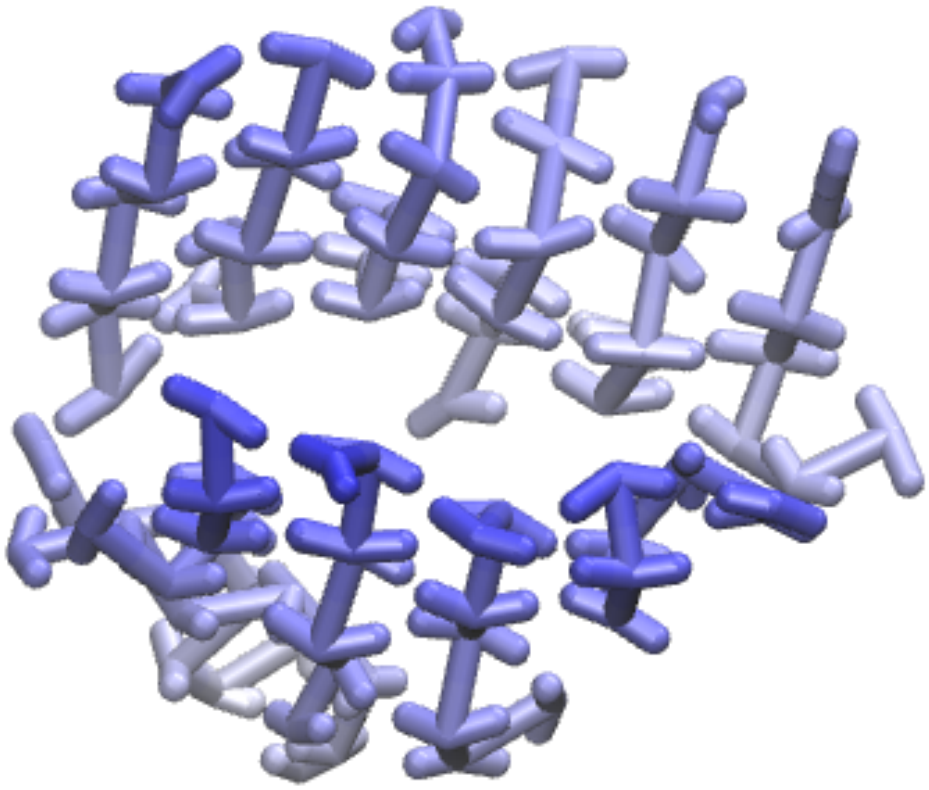

Figure S5: Molecular snapshot of peptide aggregate in aqueous solution. Colors: Peptide backbone and associated dummies in blue.

References

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