Modulation of Alzheimer's Aβ protofilament-membrane interactions by lipid headgroups

Supporting Information

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Movie S1. Animation (MPG movie) showing a representative trajectory of favorable interactions between the Aβ system S2 and a model POPE membrane. This SI movie is available via the Internet at http://pubs.acs.org.

Movie S2. Animation (MPG movie) showing a representative trajectory of unfavorable interactions between the Aβ system S1b and a model POPC membrane. The fibrilar oligomer is clearly dissociated from the POPC membrane at the end of the 55ns trajectory. This SI movie is available via the Internet at http://pubs.acs.org.

Table S1. Details of the MD parameters used for the atomistic model of the POPC bilayer interacting with the various Aβ -POPC systems

System name	No. of atoms	Initial Volume (Å^3)	Minimization/ Heating	NPT
POPC	73,749 (9X9 =81 lipids/leaflet)	87.25X79.31 X102.67	20,000 steps/ 201ps	0.5ns
S1a	80,783	89X78X130	20,000 steps/ 507ps	60ns
S1b	80,084 More water removed, closer to the membrane	89X78X130	10,000 steps/ 507ps	55ns
S2a	80,813	89X78X130	20,000 steps/ 507ps	150ns
S2b	81,215 (S2 closer to membrane)	89X78X130	20,000steps/ 827ps	53ns
S2c	80,813 (S2 equilibrated longer)	89X78X130	20,000 steps/ 637ps	45ns
S3a	87,965	89X78X140	20,000 steps 833ps	25ns
S3b	89,720 atoms	89X79X140	20,000 steps/ 827ps	30ns
S3c	81,299 atoms	89X79X140	20,000 steps/ 827ps	29ns
S4a	89,942 atoms	89X79X140	20,000 steps/ 827ps	50ns

Table S2. Parameters used for the Steered MD (MD) simulations

System name	Number of lipids	Number of atoms	Minimization/Heating (ps)	NPT (ns)
S2-POPE	98	42,567	20 /201	115
S2-POPC	162	59,759	20/600	107

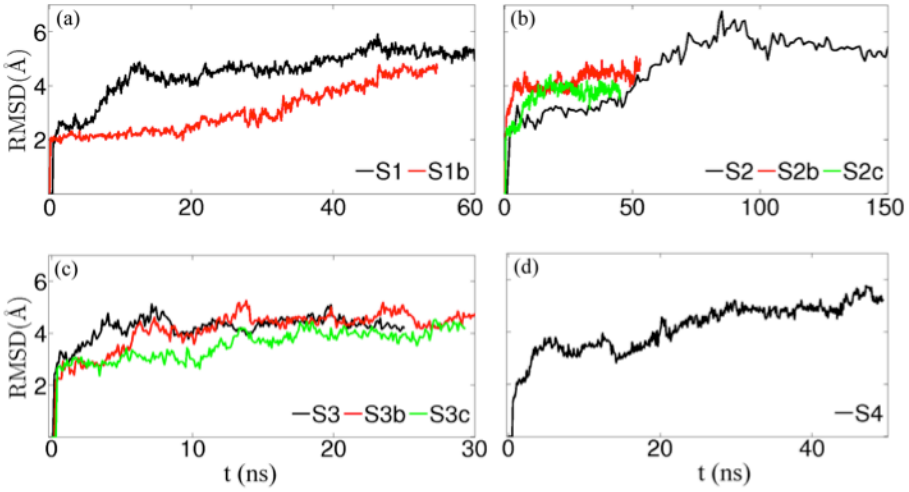

Figure S1. Root mean square deviation (RMSD) for the C_α atoms with respect to the initial structures ($RMSD_0$).

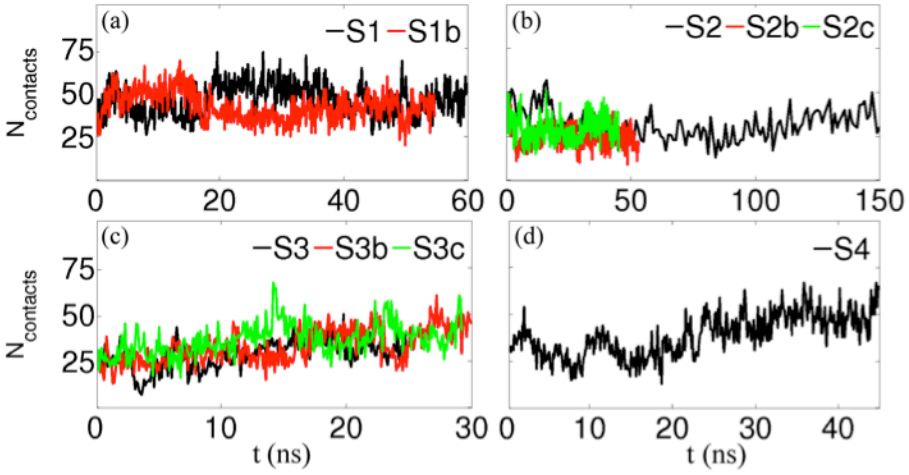

Figure S2. The number of inter-strand C-termini contacts ($N_{contacts}$) versus time for systems in all S1-S4 conformations.

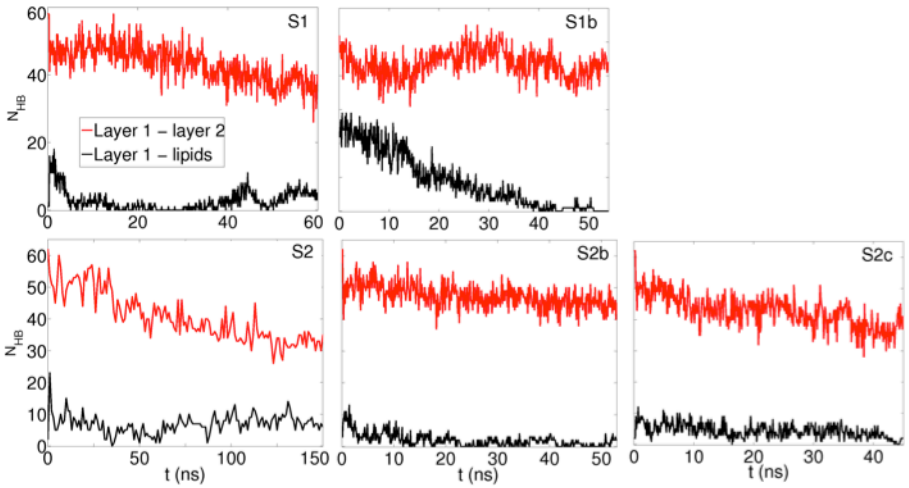

Figure S3. Hydrogen bonds between Layer 1 and Layer 2 (the first two layers in the protofilament closest to the membrane; red line) and between the Layer 1 in the protofilament and the lipids (black line) for systems in conformations S1 and S2.

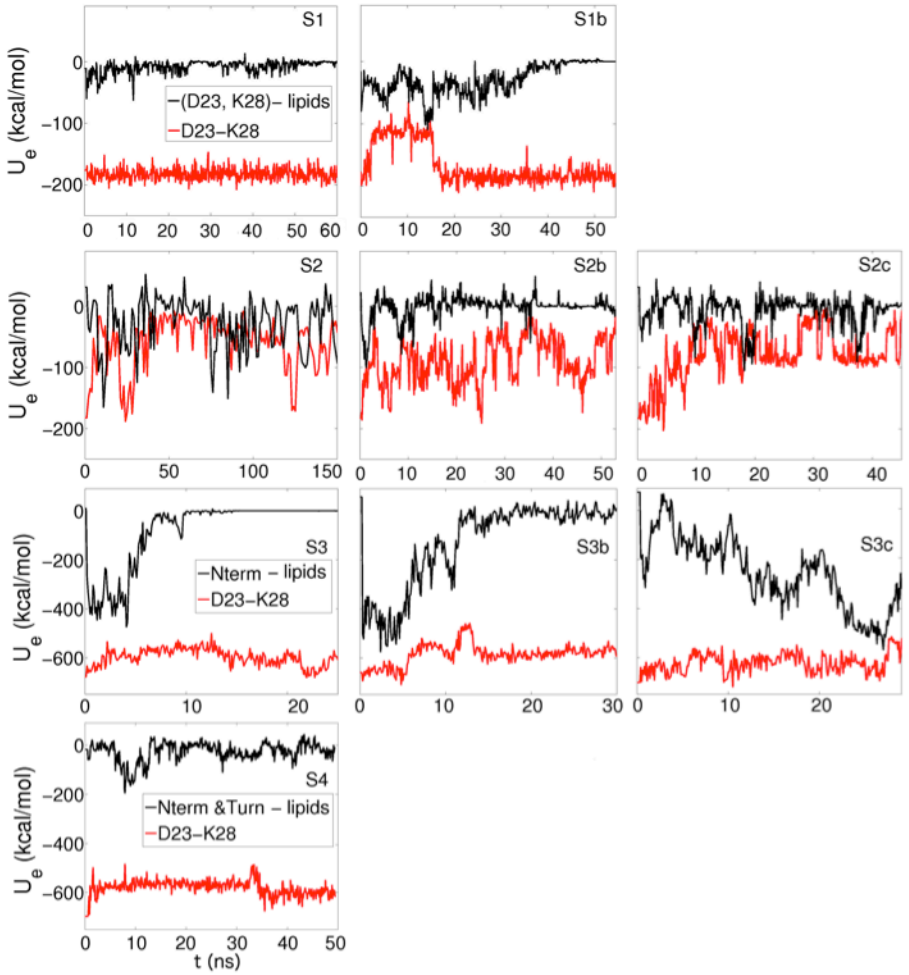

Figure S4. Electrostatic energies for all systems, with focus on the salt-bridge residues (D_{23} and K_{28}). The plots of the values for the interaction energies between D_{23}, K_{28} and lipids versus time are represented as black lines, and between D_{23} and K_{28} as red lines.

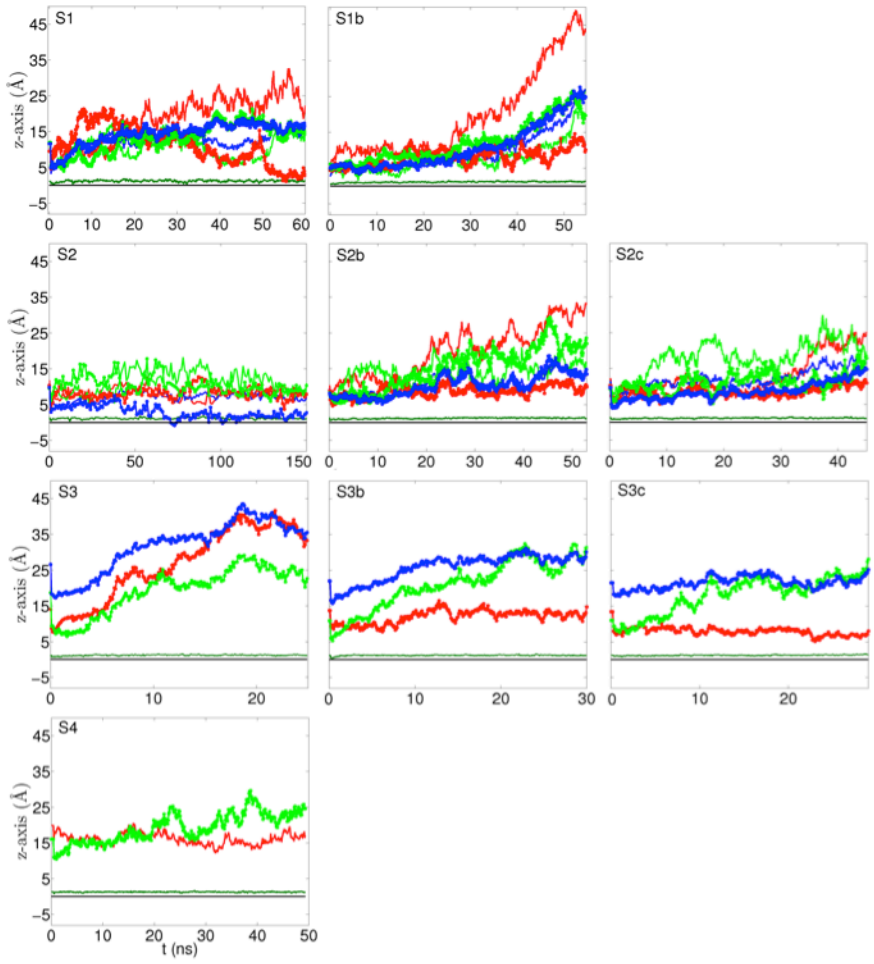

Figure S5. Z-axis position relative to the phosphorus atoms plane for charged residues in the N-terminus region (red), for charged residues in the turn region (bright green) and for the C-terminus (blue). The horizontal black line represents the phosporus atoms plane and the dark-green line is the relative nitrogen atoms plane.

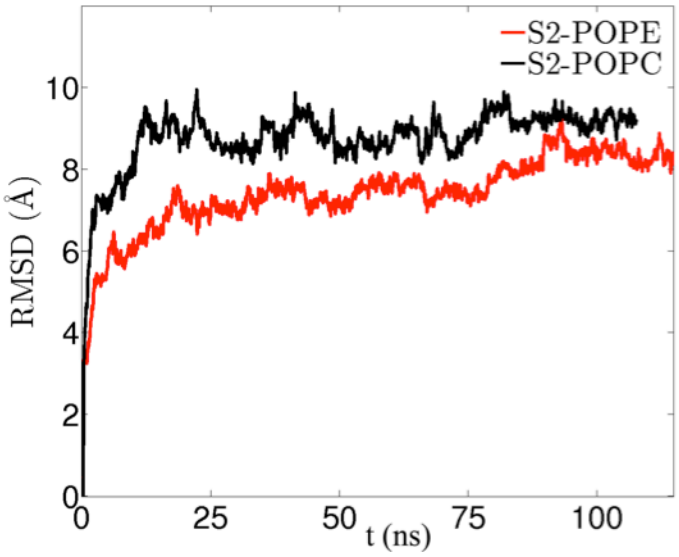

Figure S6. $RMSD_0$ plot for S2-POPE and S2-POPC systems during the Steered Molecular Dynamics simulations. The plot lines have rougher aspects than in our previous MD simulations. The maximum values reached are 8 Å for S2-POPE and 9 Å for S2-POPC.

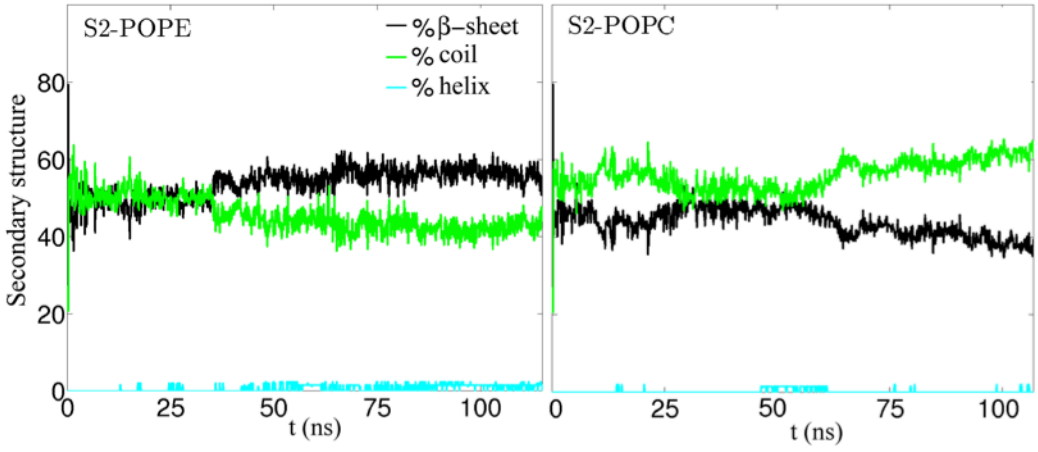

Figure S7. Secondary structure percentage of β-sheet, helix and coil during simulations of systems S2-POPE and S2-POPC.

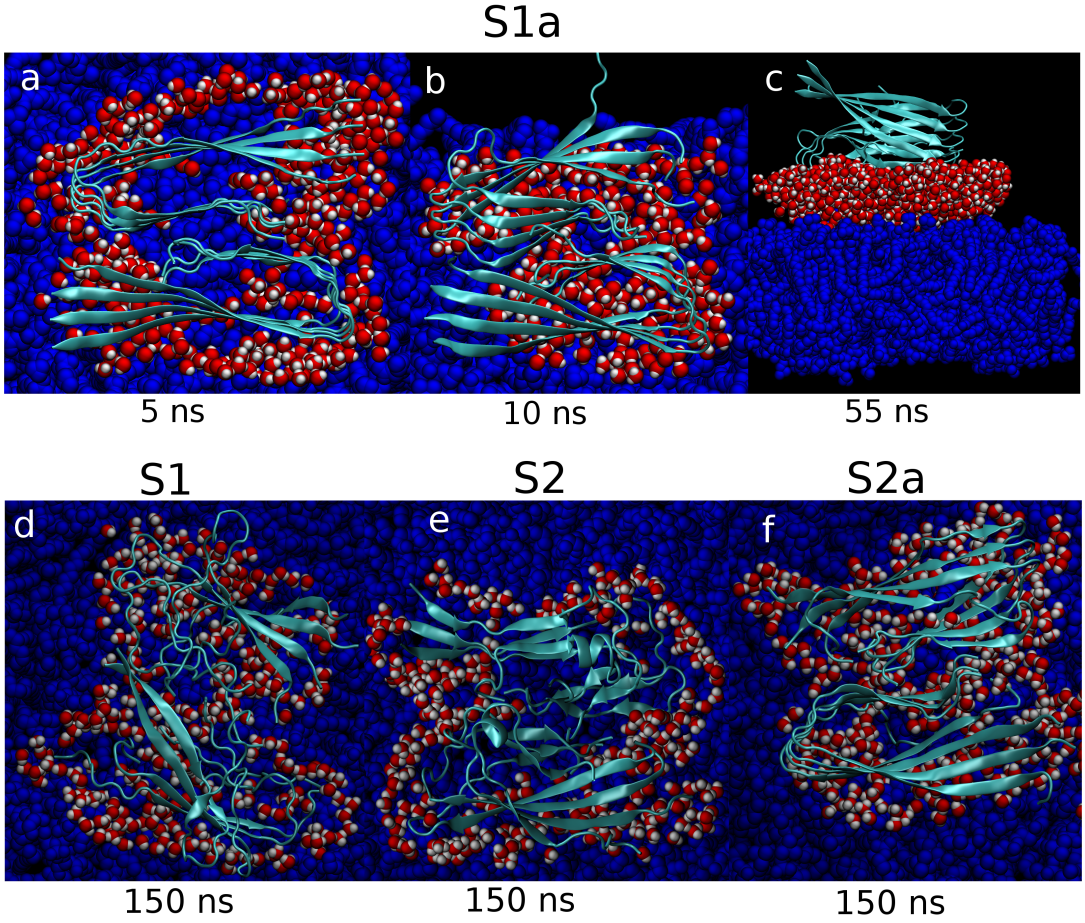

Figure S8. Water dynamics at the Aβ fibril-membrane interface. The comparison here is between a representative system in which the fibril drifts apart (POPC bilayer, representative S1a), and systems in which the fibril maintains its interaction with the lipids (S1, S2/POPE bilayer, and S2a/POPC bilayer) (a) After only 4 to 5 ns, the peptides are still in direct contact with the membrane and the interface is still essentially dry, but (b) after 10 ns the Aβ-lipid interaction becomes weaker and, finally, (c) at about 38 ns the water molecules accumulate between the fibril and the lipids such that the fibrillar oligomer is effectively solvated, as shown at 55ns. This progression is in contrast with cases illustrated in panels (d), (e) and (f) which show that due to the close Aβ-lipid interaction in the POPE case, even after 150 ns of simulation, there are only a few water molecules at the fibril-membrane interface, even though the fibril structure is also lost to a greater extent (e.g., in S1, panel (d)).