Supporting Information

Biophysical Insights into the Membrane Interaction of the Core Amyloid-Forming Aβ$_{40}$ fragment K16-K28 and its Role in the Pathogenesis of Alzheimer's Disease

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Methods of calculating -S$_{CD}$ and area per lipid

Calculation of lipid order parameters −S$_{CD}$ and area per lipid was performed using MEMBPLUGIN module [1]. For the calculation of these parameters, the Desmond trajectories were made converted to Gromacs format using VMD software. Importantly, the system was oriented to make the bilayer normal along the Z-axis and the periodic boundary conditions were removed. The parameter files were introduced by saving the atom name in the pdb format that were finally used for recognition of the system for the calculation. Step size was fixed to 50 frames interval for the calculation.

Table S1: Details of the systems used in MD simulations.

Membrane constitutes	Purpose	Time Scale	Number of trajectories	Number of atoms
POPC	Production run	150 ns	2	13,163
DMPC	Production run	150 ns	2	11,014
GM1*	Equilibrium run**	10 ns	1	41,108
GM1	Equilibrium run**	10 ns	1	41,388
GM1	Production run	200 ns	1	21,027
POPC:POPG:cholesterol:GM1	Equilibrium run**	10 ns	1	58,591
POPC:POPG:cholesterol:GM1	Production run	50 ns	2	59,667
POPC:POPG:cholesterol:GM1* (system without KK13)	Production run	50 ns	1	54,168

MD simulations were processed without the presence of KK13 peptide.

**Equilibrium run was always followed with the removal of water molecules and setting of the system again for the purpose of production run.*

Table S2: Comparison of area per lipid molecule in the presence of peptide.

| Area per lipid molecules (Å²)	Present study	Collected from Experimental or Theoretical studies			
POPC	72.4[#]	65.2[+] [2]	64.3[*] [3]	68.3[*] [4]	68.4[*] [5]
DMPC	67.0[#]	59.9[*] [3]	60.6[*] [4]	60.8[*] [6]	60.0[+] [7]

[#] Computed based on average of two trajectories over last 50 ns time frame.

[+] Data collected from reported MD simulation studies.

[*] Experimental results for POPC and DMPC bilayer at 30° C.
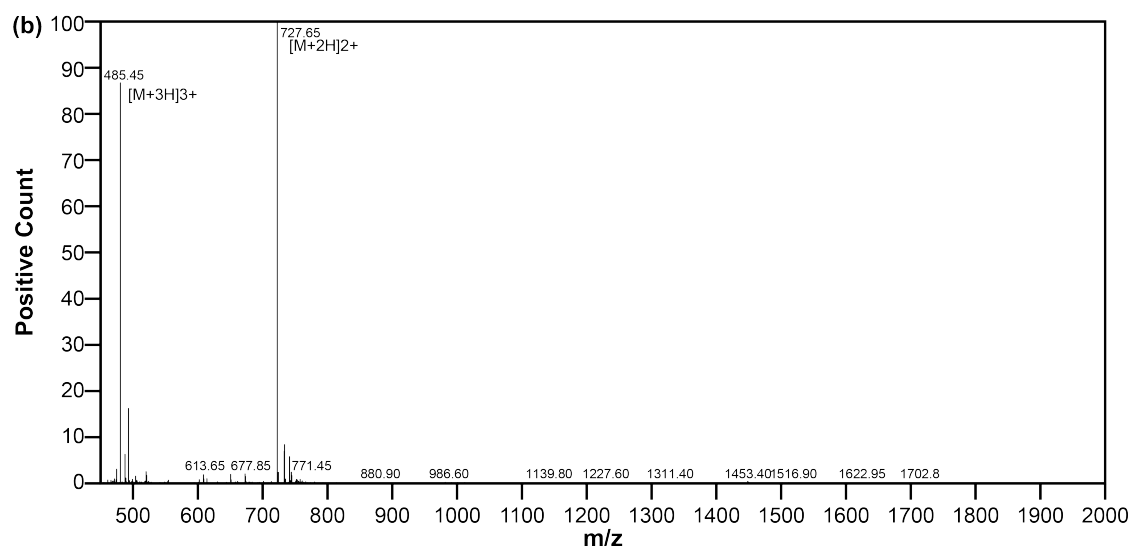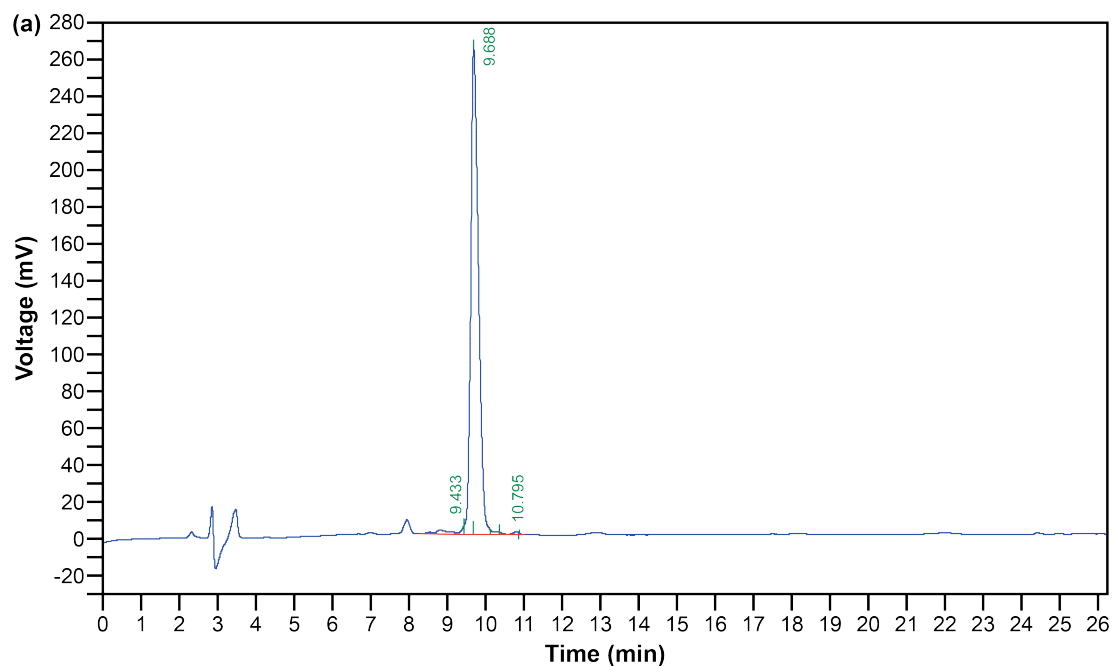
Supporting Figure S1. The HPLC trace (a) and mass spectrum (b) of KK13, obtained from the vendor, GL Biochem (Sanghai, China). The peptide was received at >95% purity and used without further purification.
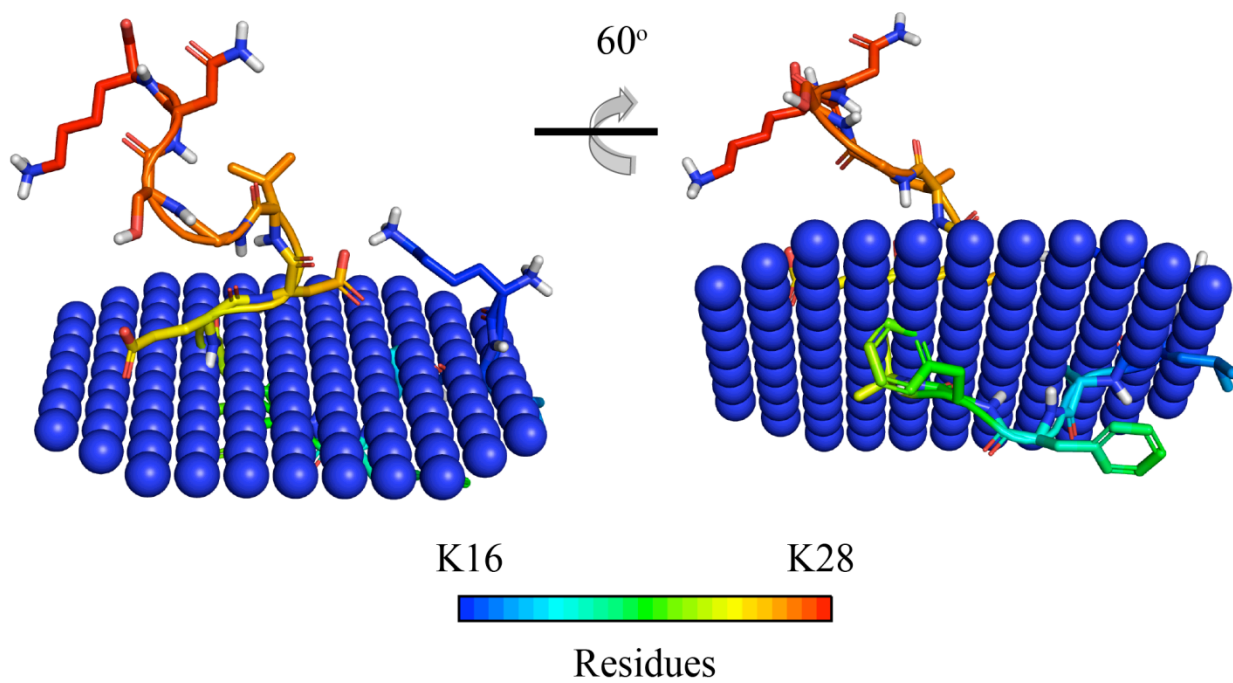
Supporting Figure S2. Alignment of peptide relative to lipid bilayer surface as modelled by the OPM server (http://www.opm.phar.umich.edu).
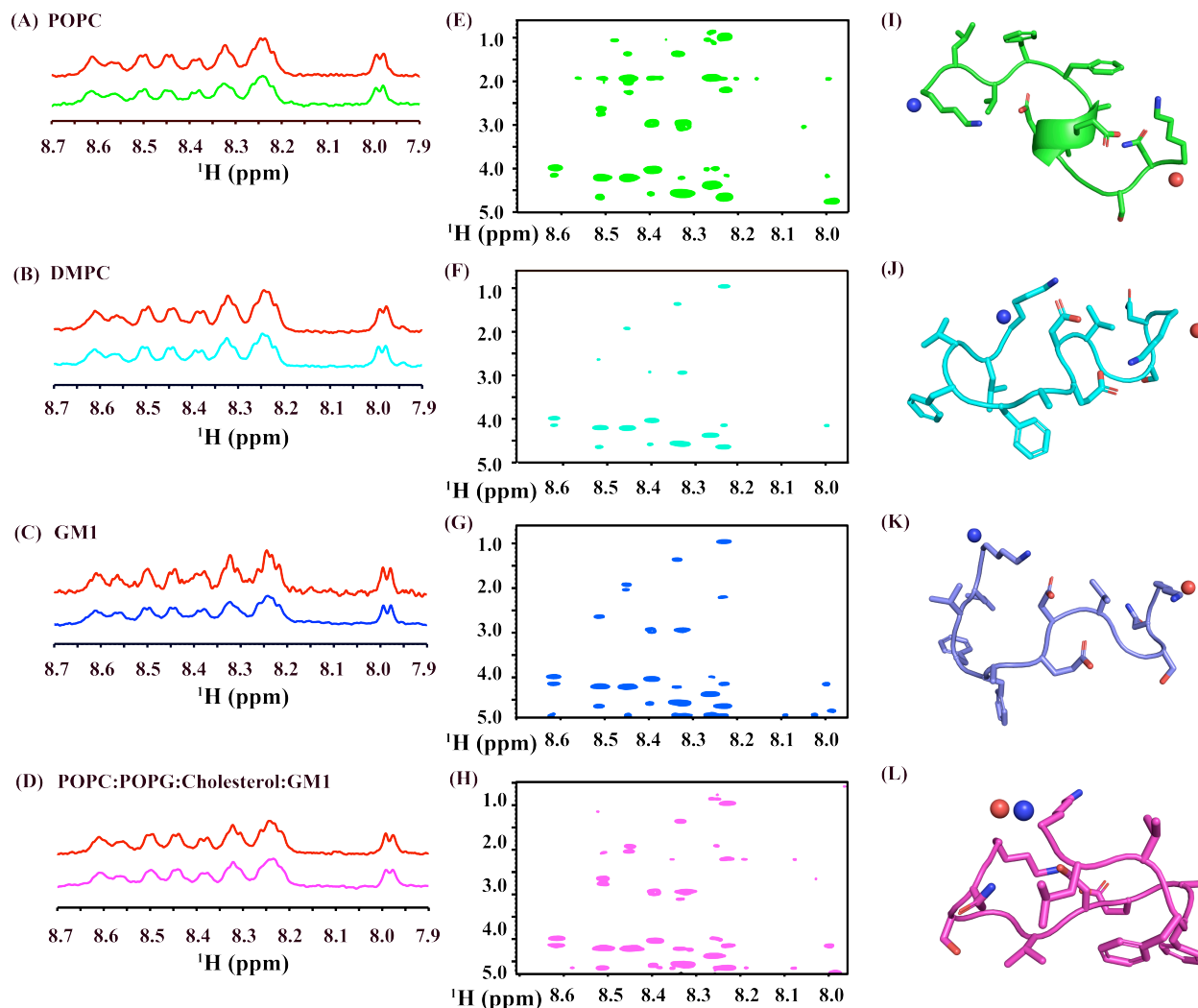
Supporting Figure S3: Proton detected NMR spectra of KK13 in the presence of lipids. (A-D) Amide regions of 1D ^{1}H spectra of KK13 in the absence (red) and the presence (color) of lipid. (E-H) The H$^\alpha$-NH and side chain-NH region of *tr*-NOESY spectra of KK13 in the presence of indicated LUVs. NMR experiments were carried out with 0.5mM peptide in a buffer solution composed of 20mM PO$_4$, 50mM NaCl (pH 7.4) on a 500 MHz Bruker Avance III spectrometer at 283 K. Structural snapshots of KK13 collected from MD simulation (I-L).

References:

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