Methods

Preparation of Aβ40 and the mutants. The peptides utilized were synthesized on a PS3 solid phase peptide synthesizer (Protein Technologies Inc., Woburn, MA) using standard Fmoc strategy**.** The crude peptides were purified by reversed phase high-performance liquid chromatography (RP-HPLC) using a C18 reverse phase column and characterized by matrix-assisted laser desorption ionization (MALDI) mass spectrometry. The peptides were monomerized before being used. Briefly, lyophilized Aβ40 powder was dissolved in aqueous NaOH solution (2 mM) and the pH was adjusted to 11 by adding 100 mM NaOH solution. The solution was sonicated for 1 h in an ice-water bath, then filtered through a 0.22-μm filter (Millipore) and kept on ice before use. The concentration of the peptide solution was determined by using the tyrosine UV absorbance at 280 nm (ε = 1,280 $M^{-1}cm^{-1}$).

Kinetic aggregation assay of Aβ40 using ThT fluorescence. The monomerized Aβ40 peptide solution was diluted to a specific final concentration of 10 μM in pH 7.4 Tris buffer (50 mM Tris, 150 mM NaCl). The solution also contained ThT with a final concentration of 20 μM. 100 μL solution was transferred into a well of a 96-well microplate (Costar black, clear bottom). The plate was sealed with a microplate cover and loaded into a Gemini SpectraMax EM fluorescence plate reader (Molecular Devices, Sunnyvale, CA), where it was incubated at 37 °C. The fluorescence of ThT was measured every 10 min after shaking for 5 s with excitation wavelength of 440 nm and emission wavelength of 480 nm. The same procedure was followed for monitoring the kinetics of Aβ40 mutants.

Atomic force microscopy (AFM) measurement. The peptide samples (100 μL) of 30 μM Aβ40 in pH 7.4 Tris buffer (50 mM Tris, 150 mM NaCl) were incubated on a mixer plate for 6 d at 37 °C. An aliquot of 20 μL was adsorbed onto the surface of freshly cleaved mica (10×10 mm) for 5

min at room temperature. The liquid was wicked off by absorption into filter paper. Salts and unbound materials were removed by washing with 20 μL Milli-Q water for three times. The samples were dried overnight and AFM images were acquired in tapping mode using an Asylum Research MFP 3D AFM system with MikroMasch NSC15/Al BS cantilevers.

Preparation of liposome model system. The POPC small unilamellar vesicles (SUVs) were prepared using a membrane extrusion method. POPC powder was dissolved in chloroform at 5mg/mL. Appropriate amount of the solution was dispensed into a glass scintillation vial, and organic solvent was evaporated overnight under vacuum to ensure removal of any residual chloroform. The sample was hydrated by adding pH 7.4 Tris buffer (10 mM Tris, 150 mM NaCl) buffer, and then vortexed vigorously and sonicated for 30 min. The POPC SUVs were prepared by downsizing the liposomes using membrane extrusion (0.05 μm pore size). Extrusion was repeated 20 times to ensure sample homogeneity. The liposome samples were stored at 4 °C for up to 14 d with no significant difference in size or population distribution.

QCM-D measurement. The deposition and remobilization experiments of peptides on model cell membranes were performed on the platform of a QCM-D system (E1, Q-Sense, Västra Frölunda, Sweden). Silica-coated 5 MHz AT-cut quartz crystals (QSX303, Q-Sense) were used as the oscillating sensors. The oscillating frequency and energy dissipation at 1st, 3rd, 5th, 7th, 9th, 11th, and 13th harmonics were measured constantly during QCM-D experiments. Before experiments, the crystal sensor and the flow module were soaked in 2% Hellmanex III cleaning solution (Hellma GmbH & Co. KG, Müllheim, Germany) for 30 min, followed by thorough rinsing with ample 2% Hellmanex III solution and then DI water. After drying under ultrapure nitrogen, the crystal sensor was further cleaned in a UV-ozone chamber (Procleaner^{TM} 110, BioForce Nanosciences, Inc., Ames, IA) for 20 min to remove organic residuals. During QCM-D experiments, a supported

POPC phospholipid bilayer was first formed on silica surface by introduction of 0.1 g/L POPC vesicles in Tris buffer (10 mM Tris, 150 mM NaCl, pH 7.4). The formation of a continuous supported phospholipid bilayer is evidenced by the signature profiles of frequency and dissipation,[1] as shown in Figure S3. Then, 10 μM peptides dispersed in Tris buffer were directed across the surface of the supported POPC bilayer to induce deposition of peptides on membranes (Section 5 in Figure S2). Following deposition, the reversibility test was performed by subsequently rinsing deposited peptides with Tris buffer and DI water (Sections 6 and 7, respectively, in Figure S2). The flow rate was maintained at 0.1 mL/min during QCM-D experiments, at which laminar flow is expected in the flow module. Temperature was set to be 25 °C.

Deposited mass of peptides during deposition process was obtained through Voigt modeling,[2] using frequency and dissipation shifts at 3rd, 5th, 7th, and 9th harmonies as fitted raw data, and using deposited mass, shear modulus, and viscosity of the peptide layer as the fitting parameters (QTools 3 software, Q-Sense).[3] The fluid density and viscosity were fixed at 1.00×10^3 kg/m^3 and 1.00×10^{-3} kg/(m·s), respectively. The density of the peptide layers was fixed at 1.05×10^3 kg/m^3. The increase rate of deposited mass of peptides during the first 5 min of deposition periods were calculated using linear least squares regression and termed initial deposition rate. The frequency increase due to remobilization of peptides ($\Delta f_{release}$) was calculated by subtracting the frequency decrease due to buffer effect of switching solution from DI water to Tris buffer (between section 2 and 1, Figure S2) from frequency increase during the remobilization process (between section 7 and 6, Figure S2). The reversibility of peptide deposition (%) was calculated by dividing $\Delta f_{release}$ of the peptides with the value of frequency decrease during peptide deposition (section 5 in Figure S2).

Table S1. The physical properties of Aβ40 and the mutants.

Peptide	Net Charge at pH 7.4	Isoelectric point	Hydrophobicity
Aβ40	-2.9	5.17	0.0575
Aβ40-M1 (E11Q)	-1.9	5.78	0.0575
Aβ40-M2 (E11Orn)	-0.9	6.35	0.0475
Aβ40-M3 (D7N)	-1.9	5.79	0.0575
Aβ40-M4 (D7Dab)	-0.9	6.35	0.0325
Aβ40-M5 (K16Nle)	-3.9	4.61	0.2675
Aβ40-M6 (K16E)	-4.9	4.36	0.0675
Aβ40-M7 (R5Nle)	-3.9	4.61	0.2650
Aβ40-M8 (R5E)	-4.9	4.36	0.0575

The net charge value at pH 7.4 and the isoelectric point were calculated according to ref. 4. The hydrophobicity (GRAVY value) was calculated using the online ExPASy peptide calculator, https://web.expasy.org/compute_pi.

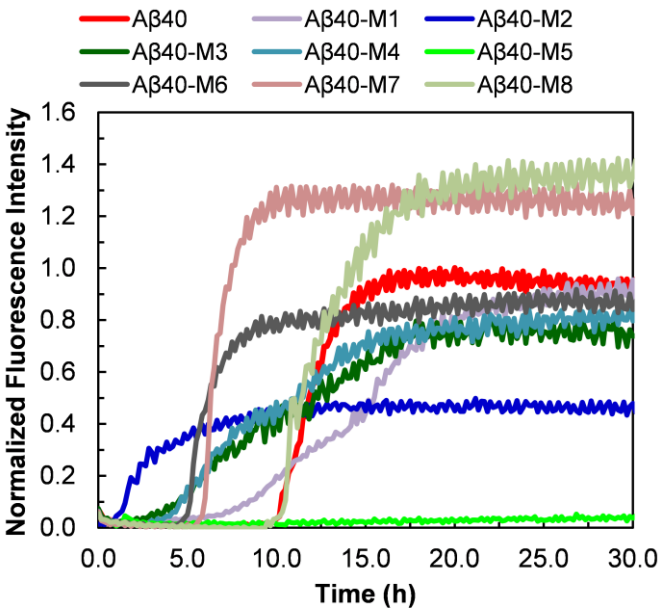

Figure S1. Aggregation kinetics of Aβ40 and the mutants (10 μM) followed by ThT fluorescence at 37 ^{o}C in pH 7.4 Tris buffer (50 mM Tris, 150 mM NaCl).

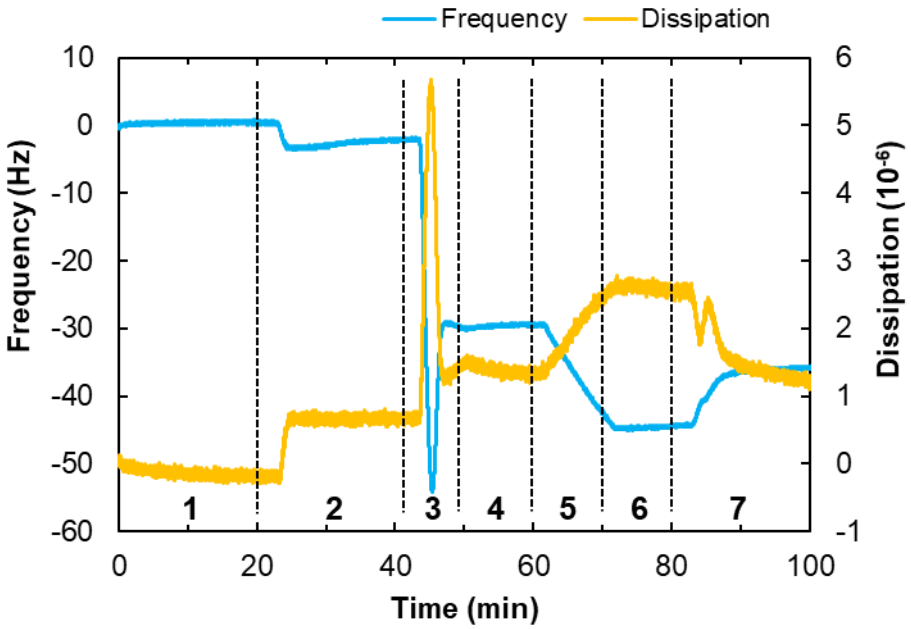

Figure S2. Frequency and dissipation responses in the deposition and remobilization of Aβ40 peptide on the POPC bilayer obtained in QCM-D experiment. Solutions were introduced into the QCM-D chamber in order: 1: DI water; 2: Tris buffer; 3: POPC liposomes in Tris buffer; 4: Tris buffer; 5: Aβ40 (10 μM) in Tris buffer; 6: Tris buffer; 7: DI water. Single lipid bilayer formation of POPC was confirmed by the QCM-D result in Section 3.

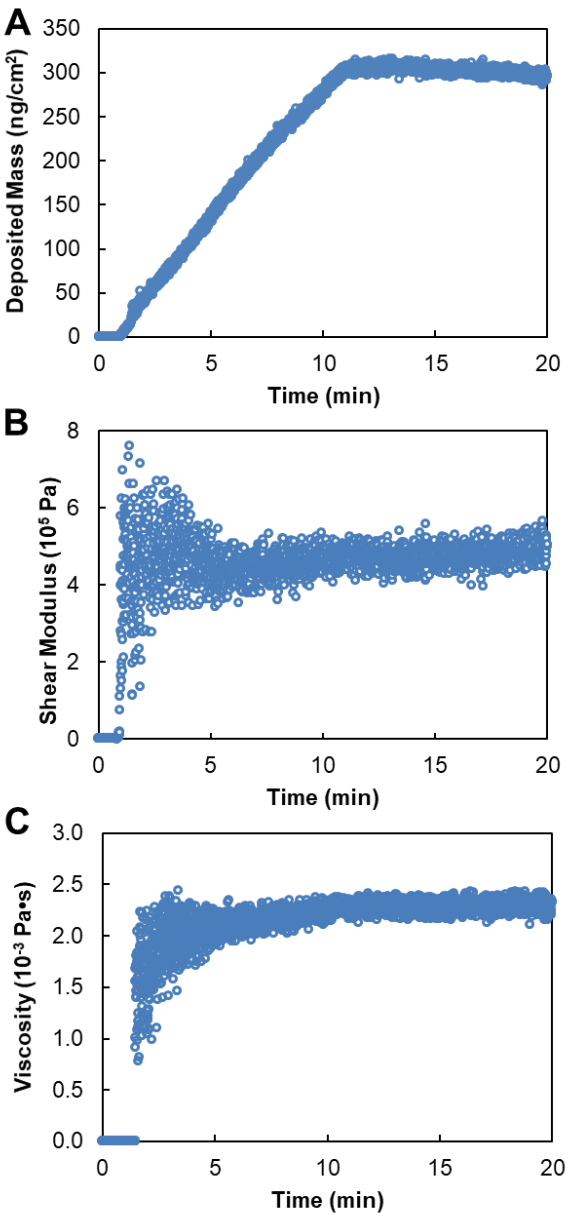

Figure S3. The deposited mass, shear modulus, and viscosity of Aβ40 deposited on supported POPC phospholipid bilayer. The results are obtained through Voigt modeling using 3rd, 5th, 7th, and 9th frequencies and dissipations during the Sections 5 and 6 presented in Figure S2.

References:

[1] R. Richter, A. Mukhopadhyay, A. Brisson, *Biophys. J.* **2003**, *85*, 3035-3047.

[2] M. V. Voinova, M. Rodahl, M. Jonson, B. Kasemo, *Phys. Scr.* **1999**, *59*, 391-396.

[3] P. Yi, K. L. Chen, *Environ. Sci. Technol.* **2013**, *47*, 12211-12218.

[4] L. P. Kozlowski, *Biology Direct.* **2016**, *11*, 55-72.