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Supplemental Information

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Supporting Information

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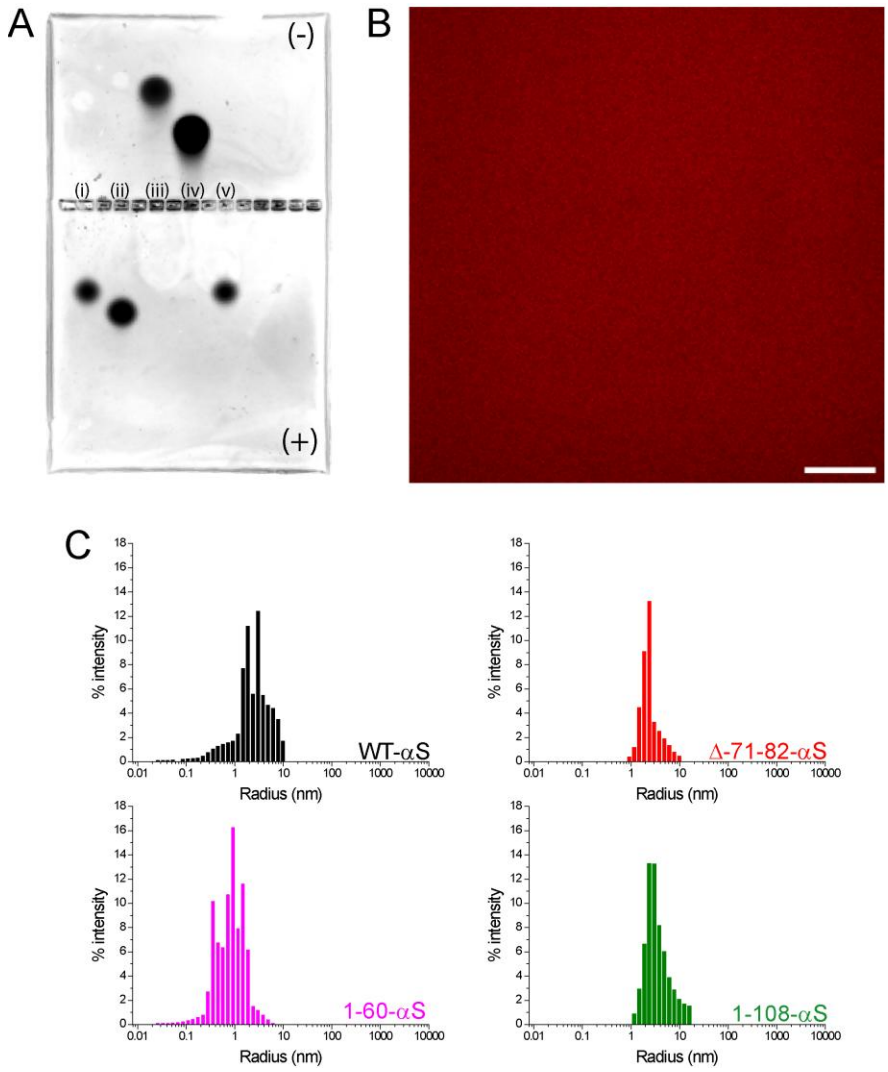


Fig S1: Characterization of monomeric state of αS and effect of bare glass. A) Non-denaturing agarose gel for WT-αS (lane i and v) and deletion variants. 10 µM of αS samples were aliquoted into wells in a 0.5% Agarose gel in Tris-Glycine buffer at pH 8. Since 1-60-αS (lane iii) and 1-108-αS (lane iv) deletion variants have a net positive charge at pH 7.4, an agarose gel was run with wells in middle to allow migration to both charged poles. The Δ71-82-αS deletion variant is shown in lane ii. B) Fluorescence image of 10 µM monomeric WT-αS (10% labeled AlexaFluor647 labeled WT-αS) on bare glass surface. Images were acquired within 1 minute of αS incubation on the glass slide. The scale bar is 10 µm. All experiments were performed in 50 mM HEPES, 0.1 mM EDTA, pH 7.4 buffer at room temperature. C) Distributions of hydrodynamic radii of WT-αS and αS deletion variants obtained by dynamic light scattering confirming absence of higher ordered species.

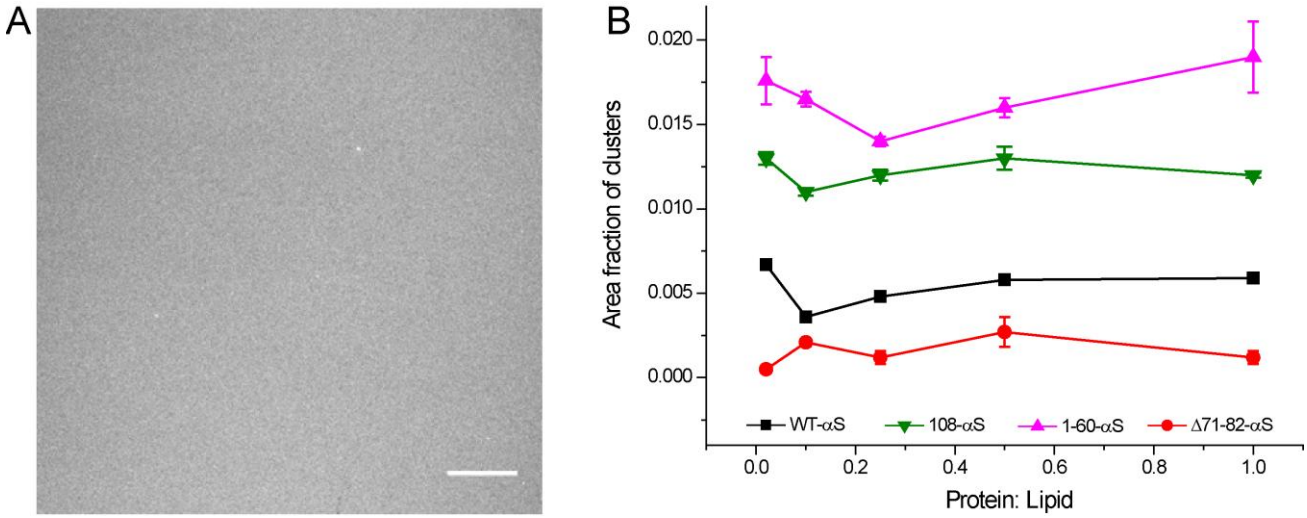
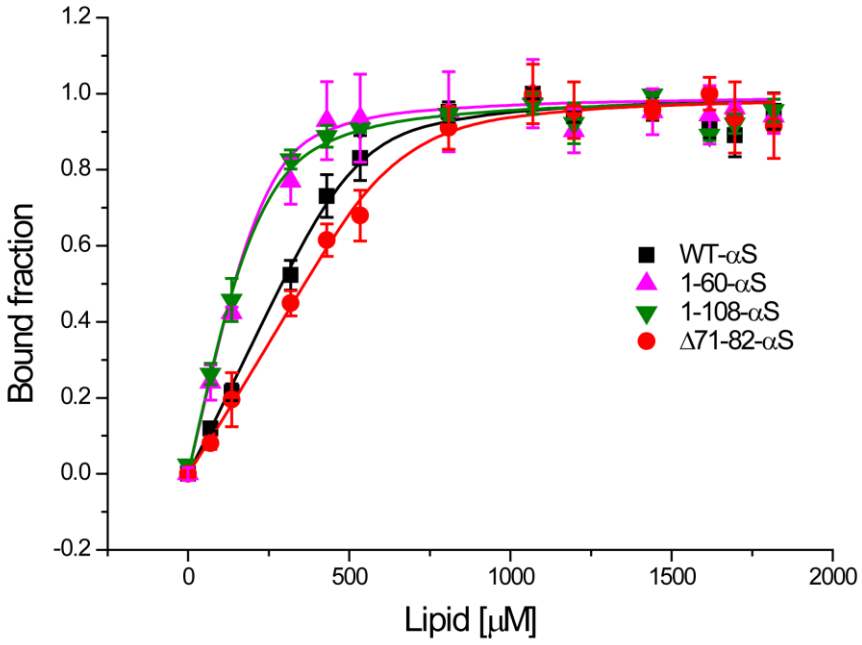


Fig S2: A) Fluorescence image of SLBs obtained before addition of αS. B) Overview of area fractions of αS clusters on POPC:POPG SLBs. The above plot depicts area fraction of αS clusters obtained from fluorescent images after image processing (see methods) starting from a protein:lipid ratio of 0.02.



αS type	Aggregation into amyloids	Net charge at pH 7.4	Mean residue ellipticity (mdeg.cm^2.dmol^{-1})	% α-helical content,H	Size of helix, amino acids	Lipid concentration at 50% αS binding
Δ71-82-αS	-	-9.9	13077 ± 587	36 ± 2	47 ± 3	359 ± 24
WT-αS	+	-8.9	20758 ± 687	56 ± 3	79 ± 4	293 ± 24
1-60-αS	-	+4.1	18306 ± 971	51 ± 3	31 ± 5	155 ± 10
1-108-αS	+++	+3.1	26684 ± 914	73 ± 3	79 ± 4	144 ± 17

Fig S3: Binding of WT-αS and other truncated variants to POPC:POPG liposomes. The bound fractions were obtained by measuring mean residual ellipticites at 222 nm by CD spectroscopy. The binding curve was quantified by fitting normalized mean residual ellipticity values. The error bars indicate standard deviations from three independent measurements. All experiments were carried out in 50 mM HEPES, 0.1 mM EDTA, pH 7.4 buffer at room temperature. The calculation of helicity was performed as described elsewhere (1). Briefly, $\mathbf{H = 100 * (\theta - \theta_{coil})/(\theta_{\alpha} - \theta_{coil})}$ where H is % helicity, $\boldsymbol{\theta}$ is the measured mean-residual ellipticity at 222 nm, $\boldsymbol{\theta_{\alpha}}$ and $\boldsymbol{\theta_{coil}}$ are the mean residual ellipticites at 222 nm of idealized α-helical and random coil peptides, respectively, calculated as follows: $\boldsymbol{\theta_{\alpha} = -40000 * \left(1 - \frac{2.5}{n}\right) + 100 * t}$; $\boldsymbol{\theta_{coil} = 640 - 45 * t}$ where t is temperature in Celsius and n is the number of amino acids in the peptide. From the values of H, the approximate numbers of residues forming a helix were calculated.

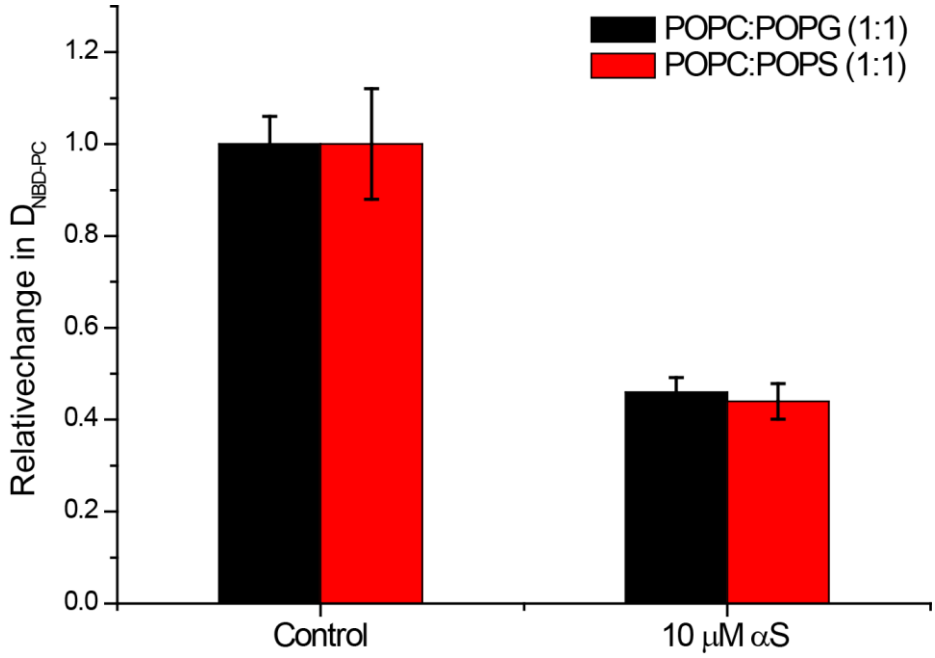


Fig S4: Influence of WT-αS on the D_{NBD-PC} in SLBs with different lipid headgroups. 10 μM of WT-αS was incubated on SLBs composed of equimolar ratios of POPC:POPG (black bars) and POPC:POPS (red bars). The D_{NBD-PC} values were normalized with respect to that obtained in absence of any added protein. All experiments were performed in 50 mM HEPES, 0.1 mM EDTA, pH 7.4 buffer at room temperature.

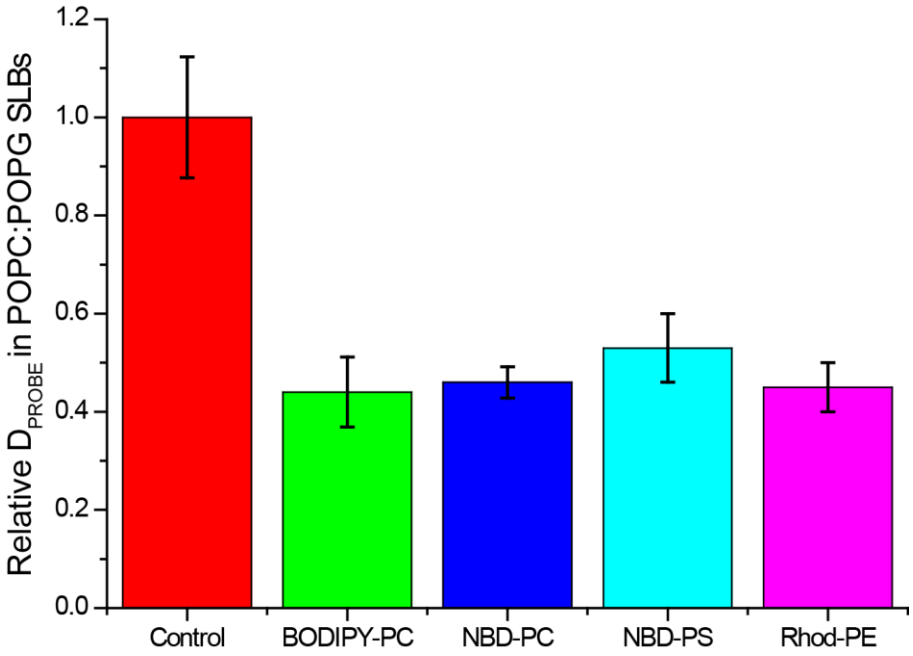


Fig S5: Relative change in the D_{LL} of different probes in POPC:POPG SLBs. POPC:POPG (1:1) SLBs were prepared in 50 mM HEPES, 0.1 mM EDTA, pH 7.4 buffer at room temperature. The fluorescent lipid probe concentration was 0.5 mol% in each case. 10 μM of WT-αS was incubated with POPC:POPG SLBs and D_{PROBE} was measured immediately. NBD-PC and BODIPY-PC have a zwitterionic PC headgroup and the fluorophore is covalently linked in the acyl chain. The Rhod-PE probe is headgroup labeled and negatively charged while the NBD-PS probe is acyl chain labeled and negatively charged. The similar magnitude of change in the D_{PROBE} suggests that the type of fluorescent lipid probe does not influence our observations.

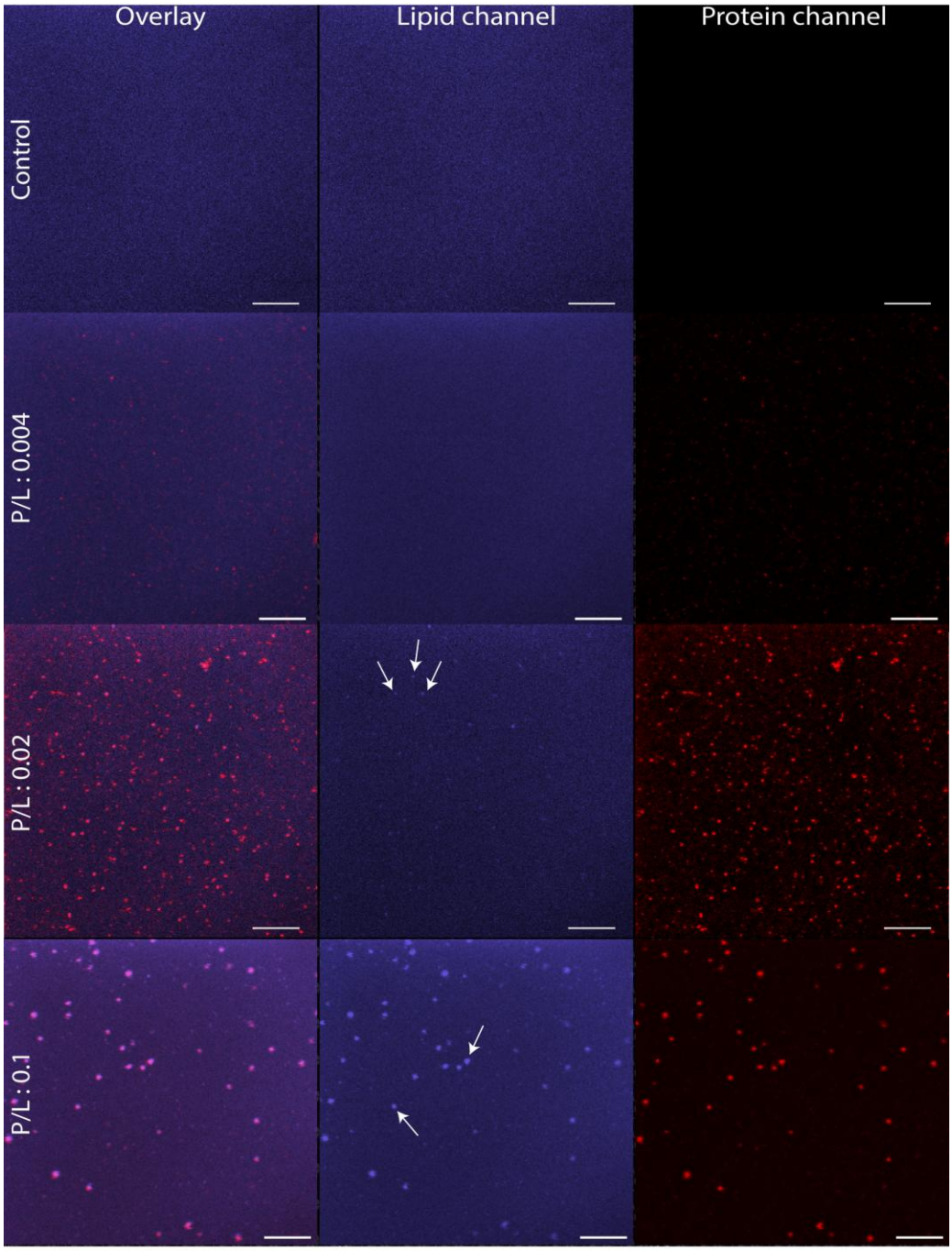


Fig S6: WT-αS induced lipid ordering in POPC:POPG SLBs observed using DPH. Incubation of increasing concentrations of monomeric αS, or increased P/L ratios a shown in figure above resulted in intense fluorescent regions (white arrows in lipid channel) upon larger cluster formation (protein channel). POPC:POPG SLBs were labeled with 1 mol% DPH. All experiments were carried out in 50 mM HEPES buffer, 0.1 mM EDTA, pH 7.4 at room temperature. The scale bar is 10 µm.

Supporting References

1. Scholtz, J. M., H. Qian, E. J. York, J. M. Stewart, and R. L. Baldwin. 1991. Parameters of Helix-Coil Transition Theory for Alanine-Based Peptides of Varying Chain Lengths in Water. Biopolymers 31:1463-1470.