Supplementary Figure 1. Attenuation profile of the amide cross peak intensities in the presence of lipids versus the absence of lipids for samples containing αS concentrations of 75 μM (black circles), 150 μM (x marks), and 300 μM (grey circles) αS in the presence of 0.03% SUV.
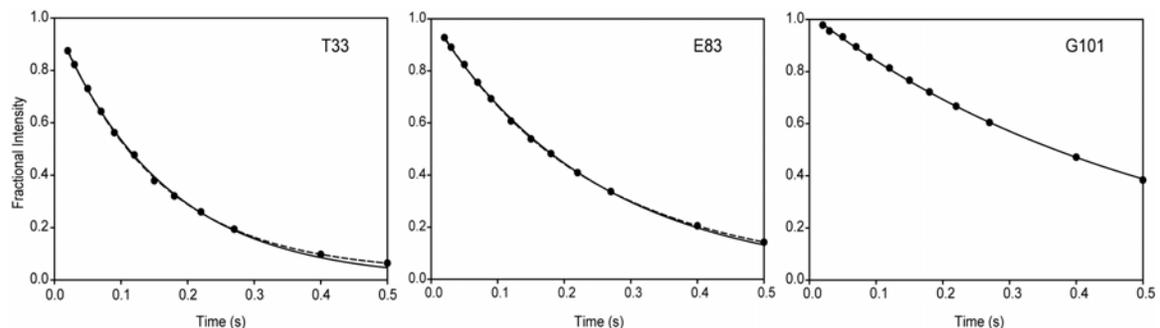
Supplementary Figure 2. Mono-exponential (solid line) and bi-exponential (dashed) fits for the signal decay of residues T33, E83, and G101, as a function of increasing transverse relaxation delay in a TROSY-T_2 experiment. R_2 rates shown in Figure 4 of the main text are derived from such fits and experimental conditions of Figure 4 apply. In practice, the mono-exponential adequately approximates the transverse relaxation rate. Slight bi-exponential character arises for N-terminal residues due to a given residue being involved in different SLn bound forms while maintaining identical chemical shift. This effect is minimal for the 40 C-terminal residues, such that mono- and bi-exponential fits coincide.
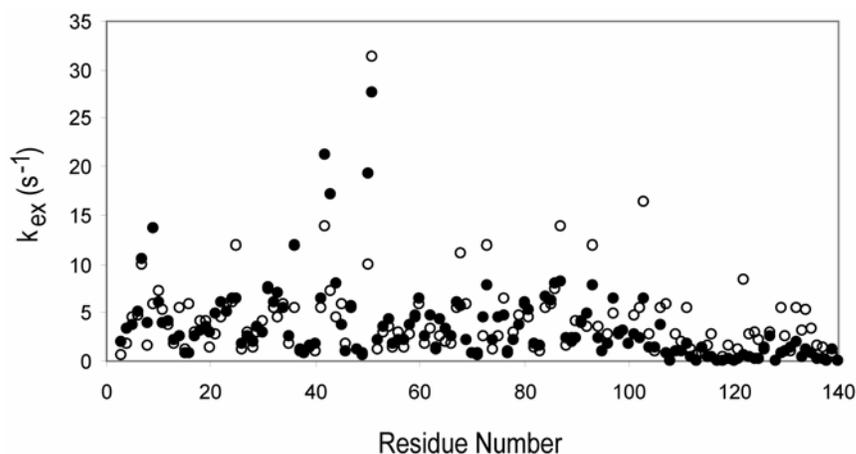
Supplementary Figure 3. Intrinsic hydrogen exchange rates for αS at pH 6.4 and 25 °C measured (filled circles) and predicted (open circles) by the SPHERE program (Bai, Milne, Mayne & Englander, *Proteins* 17: 75-86 (1993). Rates were determined by a water inversion-recovery experiment on perdeuterated αS in the absence of lipids.
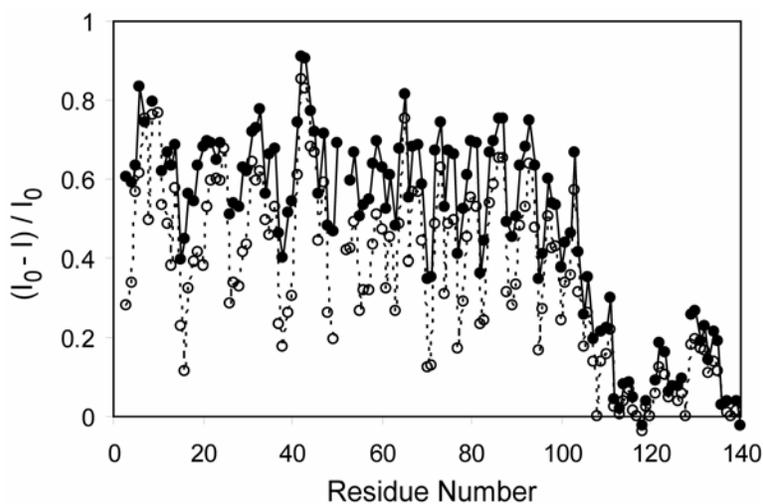
Supplementary Figure 4. Fractional attenuation of amide proton cross peaks for a sample of 150 μM perdeuterated αS in the absence (open circles) or presence (filled circles) of 0.03% SUV, when the HSQC experiment is alternately not preceded (I_o) or preceded (I) by saturation of the H_2O resonance, in order to measure the magnetization exchange between amide protons and water. The experiment is carried out in a difference mode, with 1.5 s presaturation centered at either 4.75 or 40 ppm preceding the recording of the HSQC spectra. Samples are at pH 6.0, and data were acquired at 20 °C.
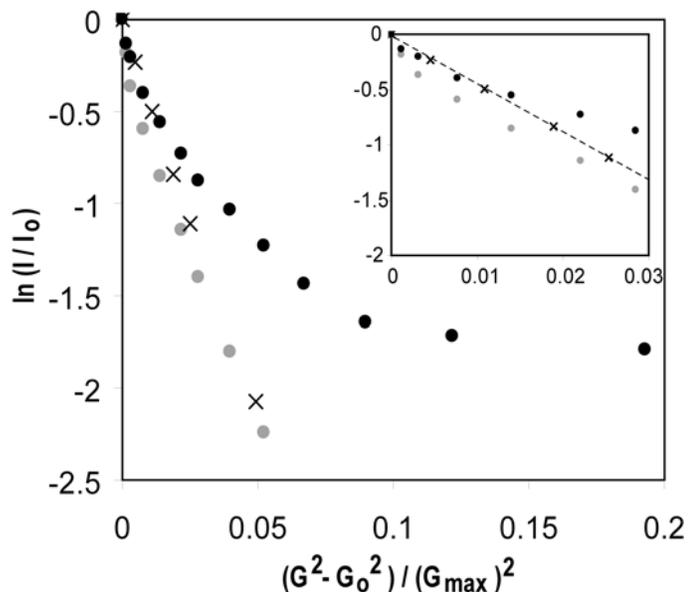
Supplementary Figure 5. Pulsed field gradient diffusion plots for αS and SUVs, isolated and in mixed samples, as shown in Figure 9, main text, but including the weak gradient region, starting from $G_o = 1.7$ G/cm. 150 μM αS in absence of lipid (black x), and in the presence of 0.03% (grey circles) or 2.0% (black circles) lipid is shown. Diffusion delays of 500ms were used and for αS the signal decay of the entire amide envelope region is used for intensity measurement. Data were recorded for pH 6.0 samples at 10 °C. Non-linear behavior at weak gradient strengths, in particular for lipid-containing samples, is attributed to magnetization exchange with rapidly diffusing water, which is more pronounced in the presence than in the absence of lipids (see Supplementary Figure 4). The inset shows the expanded region of the initial decay, showing exponential decay for free αS (dashed line) but non-exponential decay at low gradient strength in the presence of lipids. The impact of water exchange and the degree of non-exponential initial decay decreases for short mixing times (data not shown).