Table S1. NMR acquisition parameters

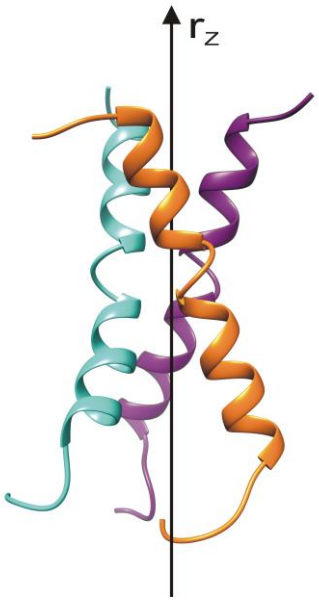
DHPC titration					
Experiment	Spectral widths and chemical shift evolution times		No. of scans	Inter-scan delay (s)	Duration of the experiment
2D ^{1}H-^{15}N TROSY-HSQC	2200 Hz (^{15}N) 58.2 ms	10800 Hz ($^{1}H^{N}$) 95.0 ms	56	1.5	5 hours 40 min
τ_c measurements					
Experiment	Spectral width and acquisition time		No. of scans	Inter-scan delay (s)	Duration of the experiment
1D ^{1}H-^{15}N TRACT	10800 Hz ($^{1}H^{N}$) 95.0 ms		800	1.5	25 min
Gd-DOTA titrations					
Experiment	Spectral widths and chemical shift evolution times		No. of scans	Inter-scan delay (s)	Duration of the experiment
2D ^{1}H-^{15}N TROSY-HSQC	2200 Hz (^{15}N) 58.2 ms	9600 Hz ($^{1}H^{N}$) 106.5 ms	8	3.5	2 hours 10 min

Table S2. Residue-specific PRE_{amp} of the human Fas TMD

	q = 0.7		q = 0.5		q = 0.3	
Residue	PRE_{amp}	R^2_{adj}	PRE_{amp}	R^2_{adj}	PRE_{amp}	R^2_{adj}
ASN 173	0.957±0.023	0.995	0.952±0.026	0.993	0.923±0.031	0.989
LEU 174	0.915±0.030	0.993	0.930±0.012	0.998	0.956±0.013	0.998
GLY 175	0.923±0.059	0.983	0.920±0.012	0.999	0.956±0.012	0.999
TRP 176	-	-	0.866±0.035	0.992	0.917±0.043	0.987
LEU 177	0.820±0.032	0.994	0.852±0.025	0.993	0.915±0.022	0.994
SER 178	0.795±0.050	0.980	0.836±0.019	0.996	0.876±0.031	0.995
LEU 179	0.796±0.028	0.994	0.812±0.033	0.985	0.880±0.032	0.991
LEU 180	0.750±0.035	0.986	0.815±0.020	0.995	0.889±0.036	0.987
LEU 181	0.751±0.028	0.991	0.809±0.023	0.992	0.884±0.043	0.987
LEU 182	0.783±0.035	0.987	0.800±0.022	0.992	0.876±0.038	0.985
ILE 184	0.727±0.037	0.979	0.785±0.031	0.986	0.844±0.030	0.991
LEU 186	0.728±0.042	0.980	0.781±0.025	0.992	0.859±0.038	0.990
ILE 187	0.769±0.038	0.987	0.813±0.023	0.993	0.877±0.035	0.987
VAL 188	0.767±0.024	0.994	0.815±0.023	0.993	0.877±0.030	0.990
TRP 189	0.761±0.052	0.977	0.826±0.021	0.994	0.909±0.028	0.994
VAL 190	0.771±0.042	0.981	0.819±0.023	0.993	0.925±0.029	0.991
LYS 191	0.800±0.037	0.984	0.865±0.019	0.996	0.943±0.025	0.994
ARG 192	0.829±0.033	0.988	0.873±0.016	0.997	0.950±0.017	0.996
LYS 193	0.867±0.024	0.995	0.907±0.020	0.995	0.960±0.018	0.998
GLU 194	0.878±0.022	0.995	0.919±0.011	0.999	0.962±0.017	0.998
VAL 195	0.949±0.024	0.996	0.923±0.012	0.998	0.966±0.014	0.998
GLN 196	0.916±0.043	0.989	0.934±0.016	0.997	0.969±0.014	0.999
LYS 197	0.900±0.048	0.989	0.921±0.021	0.995	0.943±0.015	0.998
THR 198	0.961±0.013	0.998	0.910±0.021	0.995	0.957±0.012	0.999

Residue-specific PRE_{amp} were determined by fitting I/I_0 vs. [Gd-DOTA] to Eq. 1. The adjusted coefficient of determination (R^2_{adj}) provided an evaluation of the fitting quality. The R^2_{adj} parameter is a measure of how well the model describes the experimental data.

Table S3. Transmembrane partition of the Fas TMD determined in q = 0.5 bicelles



r_z (Å)	Residue (H^N)
15.9±0.5	SER 172
14.7±0.5	ASN 173
16.4±0.5	LEU 174
15.1±0.5	GLY 175
12.6±0.5	TRP 176
11.0±0.5	LEU 177
10.3±0.5	SER 178
8.6±0.5	LEU 179
6.3±0.5	LEU 180
5.0±0.5	LEU 181
3.9±0.5	LEU 182
0	*Membrane Center*
-0.8±0.5	ILE 184
-3.5±0.5	LEU 186
-6.1±0.5	ILE 187
-7.0±0.5	VAL 188
-7.5±0.5	TRP 189
-9.8±0.5	VAL 190
-11.8±0.5	LYS 191
-12.0±0.5	ARG 192
-13.2±0.5	LYS 193
-15.7±0.5	GLU 194
-19.1±0.5	VAL 195
-21.6±0.5	GLN 196
-23.0±0.5	LYS 197
-23.2±0.5	THR 198

Data not available for Arg171 (N-terminus), Pro183 and Pro185

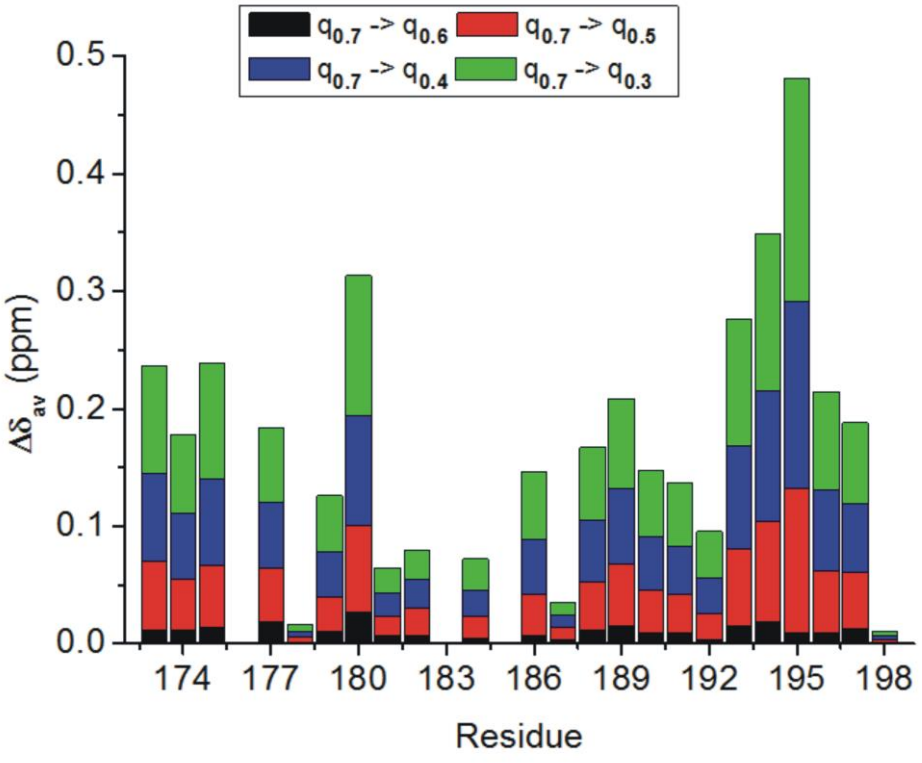


Figure S1. Chemical shift changes upon reducing the *q* from 0.7 to 0.6, 0.5, 0.4 and 0.3 versus residue number. The data are shown as a stack column plot. Essentially no chemical shift changes were detected when changing the *q* from 0.7 to 0.6. Much larger chemical shift changes were observed when further reducing the *q* to 0.5 and below.

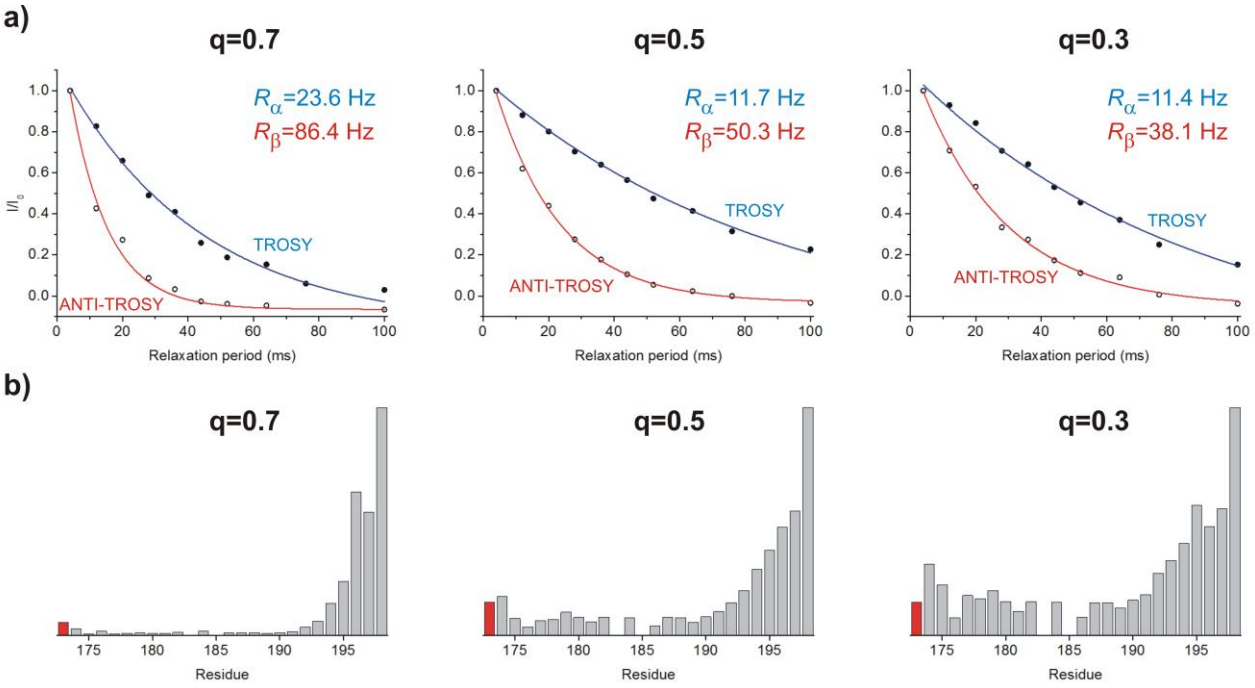


Figure S2. Determination of τ_c at different q. **a**) TROSY (filled circle) and anti-TROSY (empty circle) signal intensity decays for Asn173 of the human Fas TMD reconstituted in q = 0.7, 0.5 and 0.3 bicelles. Exponential fittings (blue for TROSY and red for anti-TROSY) provide the transversal relaxation rates used to estimate τ_c. **b**) Peak intensities in the 2D ^{1}H-^{15}N TROSY-HSQC spectrum of the Fas TMD reconstituted in q = 0.7, 0.5 and 0.3 bicelles. The position of Asn173 is highlighted in red. The plots show that Asn173, despite being at the N-terminus, is not as flexible as the residues near the C-terminus and exhibits similar relaxation properties to those residues buried in the lipid bilayer core. For this reason, in consideration of the fact that this signal is well resolved in the 1D spectrum, it was chosen for the TRACT analysis.

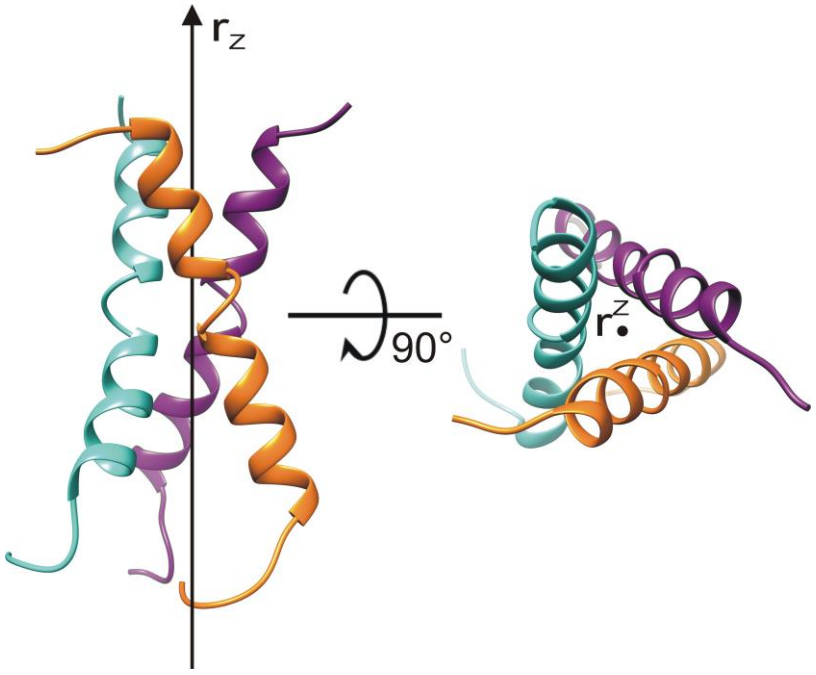


Figure S3. The NMR structure of the human Fas TMD trimer showing the three-fold axis of rotational symmetry. The symmetry axis is parallel to the bilayer normal (not shown). The structure was taken from the *Protein Data Bank* (PDB) (entry 2NA7).

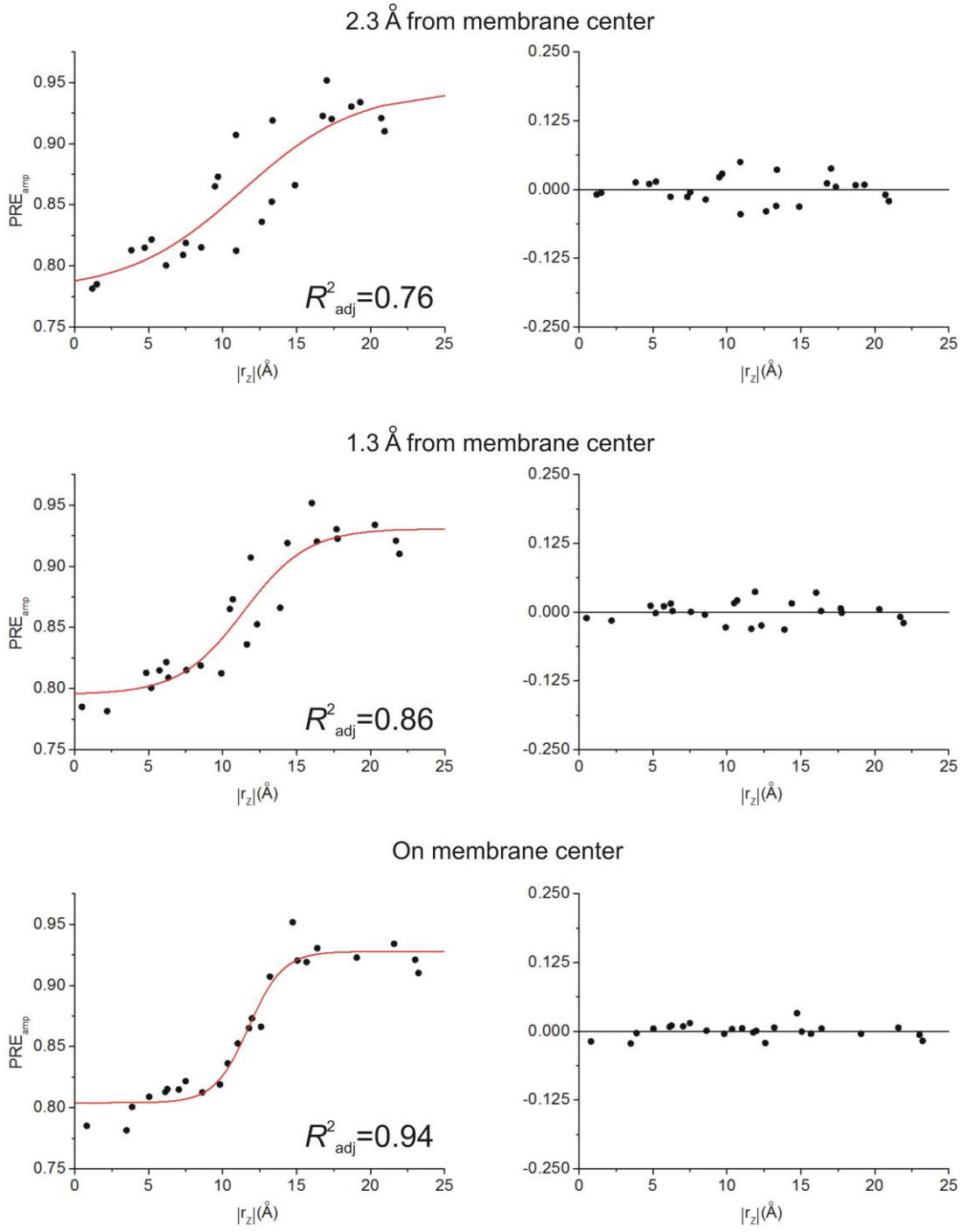


Figure S4. Systematic adjustment of the TMD position for achieving best fit of the PRE data to Eq. 2. At the top of each graph, the offset from the true membrane center (obtained from the best fit) is reported. The fittings to Eq. 2 (left column) include PRE_{amp} vs. r_Z data points from both halves of the lipid bilayer. The residuals from the fitted model are reported on the right. The fitting in the last row shows the best fit, which yields the position of the Fas TMD relative to the lipid bilayer center.

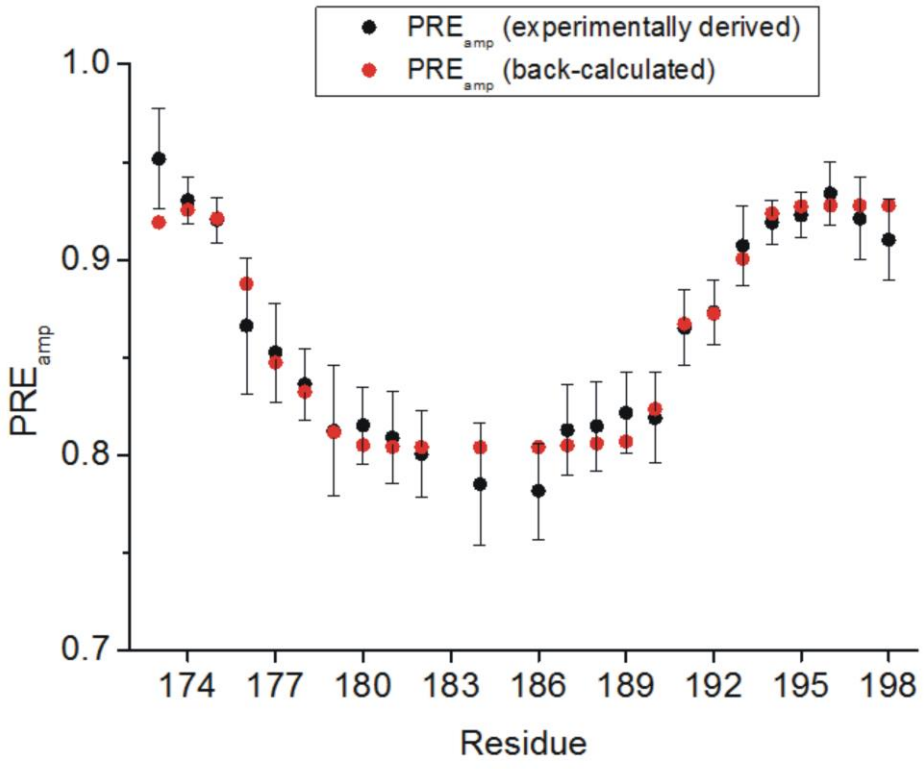


Figure S5. Comparison between experimentally derived and back-calculated PRE_{amp} of the human Fas TMD reconstituted in q = 0.5 bicelles. The high fidelity of the back-calculation indicates that Eq. 2 is a good model to describe the experimental data.

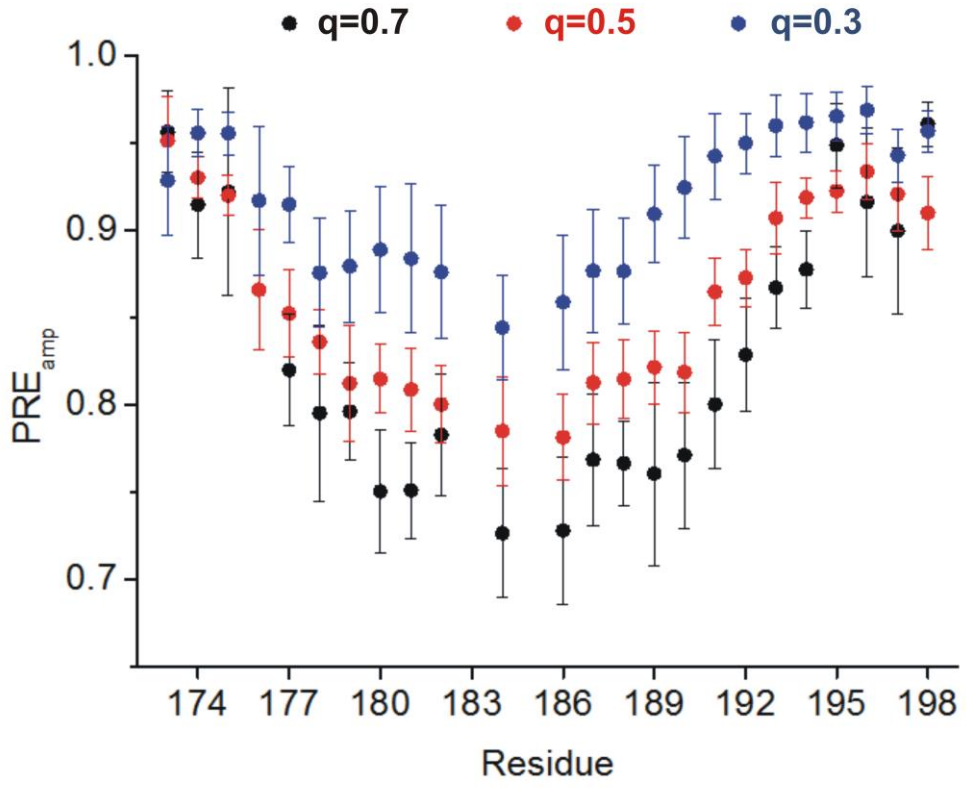


Figure S6. Comparison of experimentally derived PRE_{amp} of the human Fas TMD reconstituted in q = 0.7 (black), 0.5 (red) and 0.3 (blue) bicelles. While q = 0.7 and 0.5 data sets are similar and almost overlapping (within the error), the q = 0.3 data set shows much stronger PRE_{amp}. These results indicate that only q = 0.7 and 0.5 bicelles are large enough to minimize the lateral contributions of the solvent PRE.