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Supplemental Information

Folding and Lipid Composition Determine Membrane Interaction of the Disordered Protein COR15A

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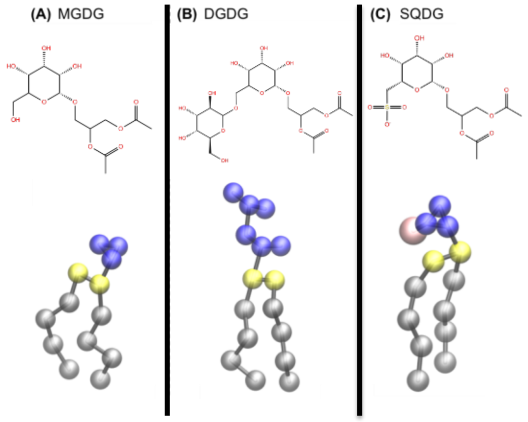
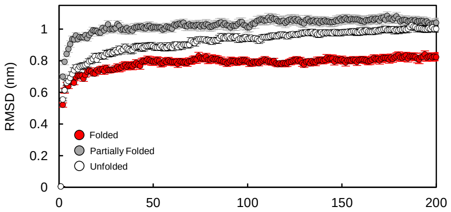


Figure S1. Sketch (top) and CG representation (bottom) of the lipids MGDG **(A)**, DGDG **(B)** and SQDG **(C)**. Blue and pink beads in the CG representation represent the headgroup, yellow the glycerol backbone and acyl esters section and grey beads the fatty acyl chains.

(A) all simulations



(B) only simulations with bound COR15A

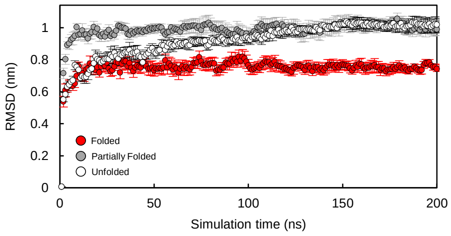


Figure S2. Analysis of protein structural flexibility expressed as the root-mean-square deviation (RMSD) of all beads in the protein backbone during 200 ns CGMD simulations. Data represent the mean ± SE of 50 simulations in **(A)**, while in **(B)** only those simulations were included that resulted in binding of COR15A to the membranes (see Table S1 for details).

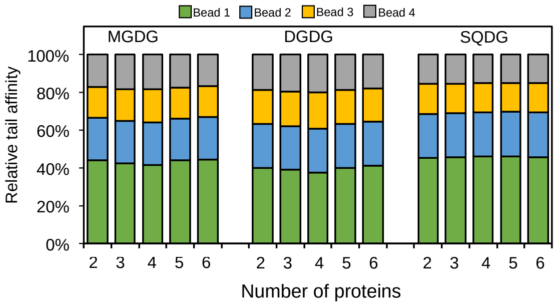


Figure S3. Affinity of COR15A for the four different beads making up the fatty acyl chains of the lipids MGDG(U), DGDG and SQDG in ICMM membranes. The beads are denoted as Bead 1 to Bead 4 from the surface to the center of the bilayer.

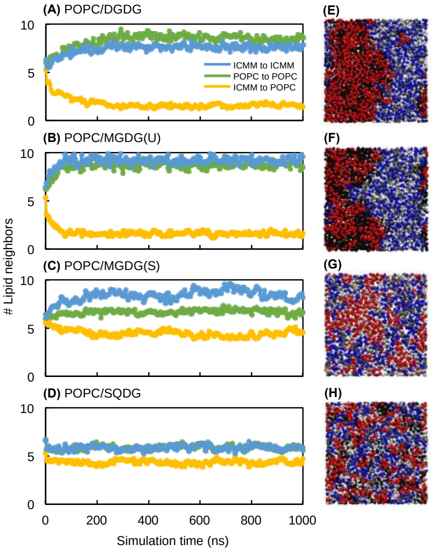


Figure S4. Phase separation in bilayers containing equimolar mixtures of POPC/DGDG **(A** and **E)**, POPC/MGDG(U) **(B** and **F**), POPC/MGDG(S) **(C** and **G)** and POPC/SQDG **(D** and **H)**. **A**, **B**, **C** and **D** show the average number of neighbors with respect to each lipid. Images **E**, **F**, **G** and **H** represent a top view of the distribution of the lipids across each bilayer. Red and blue represent the headgroup and acylester beads of the glycolipids and POPC, respectively. White, gray and black represent the fully saturated (16:0), mono-unsaturated (18:1) and fully unsaturated (18:3) fatty acyl chains.

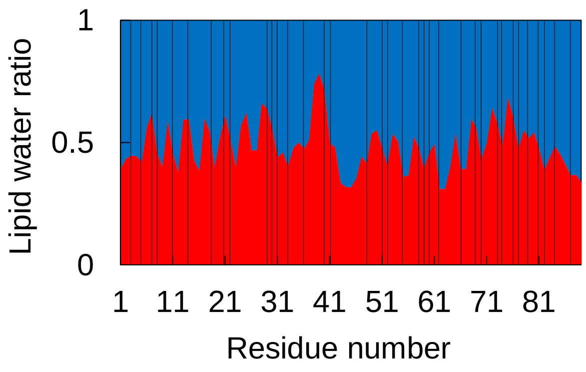


Figure S5. Lipid affinity ratio across the protein considering COR15A in a folded state in the presence of 50% POPC/50% MGDG(U). Perpendicular black lines represent the position of hydrophobic amino acids in the protein.

Supplemental Table 1. Adsorption statistics for folded COR15A to membranes of different lipid composition.

Membrane composition (%)				Adsorption
POPC	DGDG	MGDG	SQDG	
100	0	0	0	0/50 (0%)
90	0	10	0	0/50 (0%)
80	0	20	0	3/50 (6%)
70	0	30	0	24/50 (48%)
60	0	40	0	38/50 (76%)
50	0	50	0	46/50 (92%)
50	0	50*	0	3/50 (6%)
50	50	0	0	37/50 (74%)
50	0	0	50	0/50 (0%)

The adsorption column shows the number of adsorption events and its respective percent. The asterisk (*) indicates the presence of MGDG(S). Otherwise MGDG(U) was present in the indicated concentrations.