Supporting Information for:

Dodecyl Maltoside Protects Membrane Proteins *In Vacuo*

Sarah L. Rouse, Julien Marcoux, Carol V. Robinson, and Mark S.P. Sansom

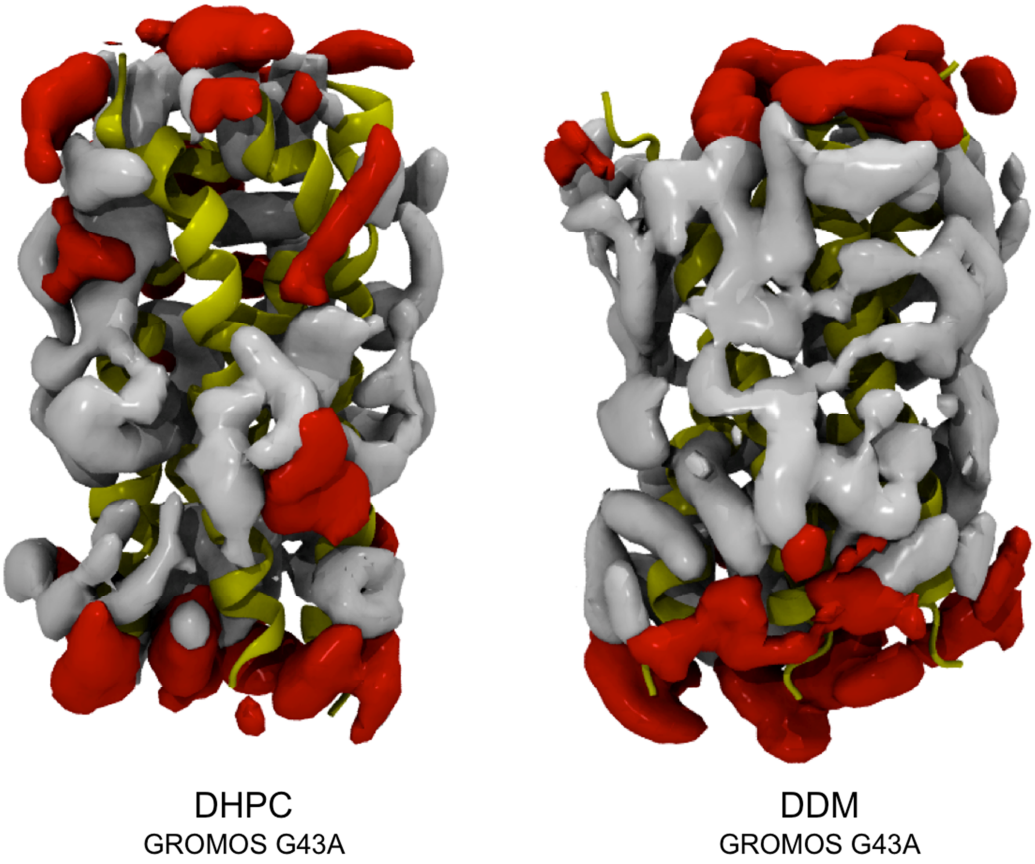

Figure S1. Arrangement of DHPC and DDM micelles about protein during steered MD simulation using the GROMOS G43A force field. Isosurfaces correspond to the mean distribution of detergent headgroup (red) and tail (grey) atoms within 4 Å of the protein surface. The protein is shown in yellow. The behaviour of protein-DHPC and –DDM complexes during transition from solution to vacuum is qualitatively similar to that observed using the OPLS-AA force field (Fig. 3). The loss of regular solution phase detergent arrangement is observed for DHPC, where headgroups are observed to interact with hydrophobic regions of the protein, but largely retained in the case of DDM.

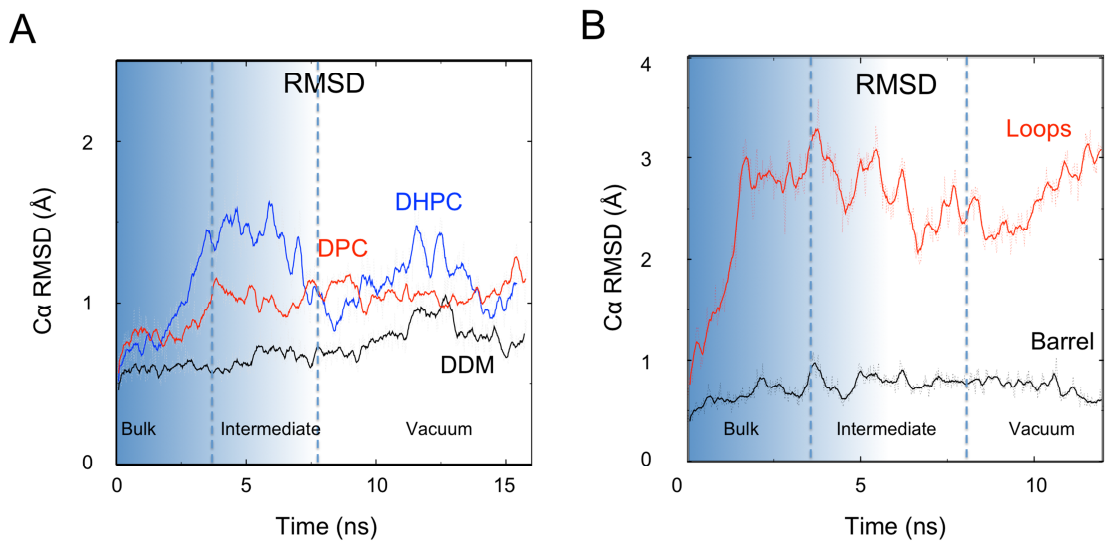

Figure S2. BM2 stability vs. OmpA during steered molecular dynamics simulations. A: Cα RMSD of BM2 in DPC (red), DHPC (blue trace) and DDM (black trace) protein-detergent complexes. B: Cα RMSD of the OmpA residues initially in β-sheet conformation (black trace) and those in loop, turn or unstructured conformations (red trace) for the OmpA-DPC simulation. In each case the location of the dashed lines indicates the approximate boundaries at which the protein-detergent complex is first exposed to vacuum and when it is free from bulk solution. Most of the structural deviation in the OmpA simulation is confined to the loop regions.

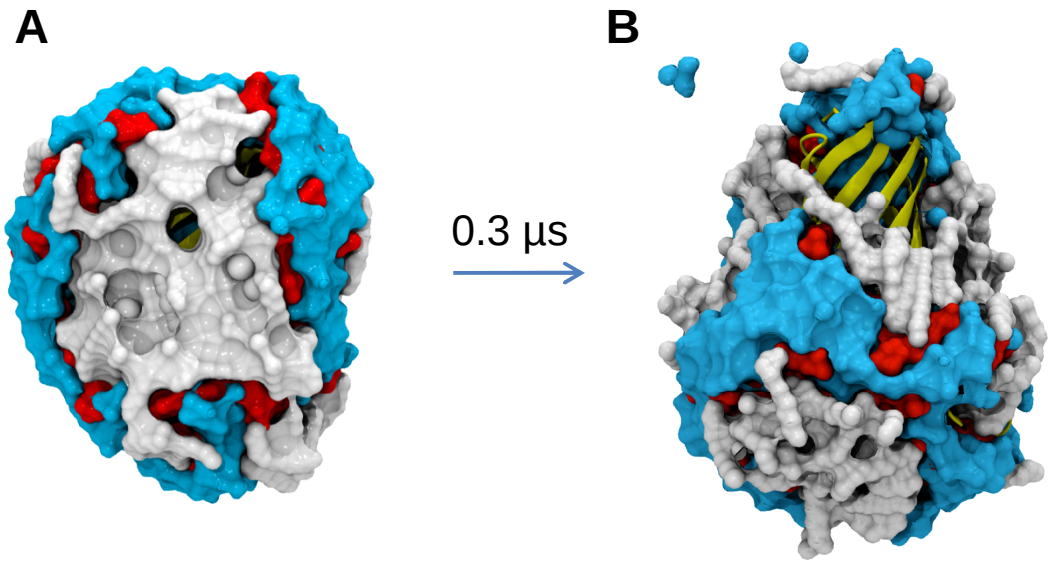

Figure S3. Structure of the OmpA-DPC complex following transfer to vacuum environment. **Left:** The sparingly solvated complex generated from steered MD simulation. DPC headgroups (red), tails (grey), and those water molecules within 5 Å of the complex (cyan) are shown as coloured surfaces, and the protein as a yellow cartoon representation. Thewaters are observed to co-localize with the DPC headgroups. **Right:** The OmpA-DPC complex following a 0.3 µs simulation of the sparingly solvated complex in vacuum. Further rearrangement over the simulation is observed.

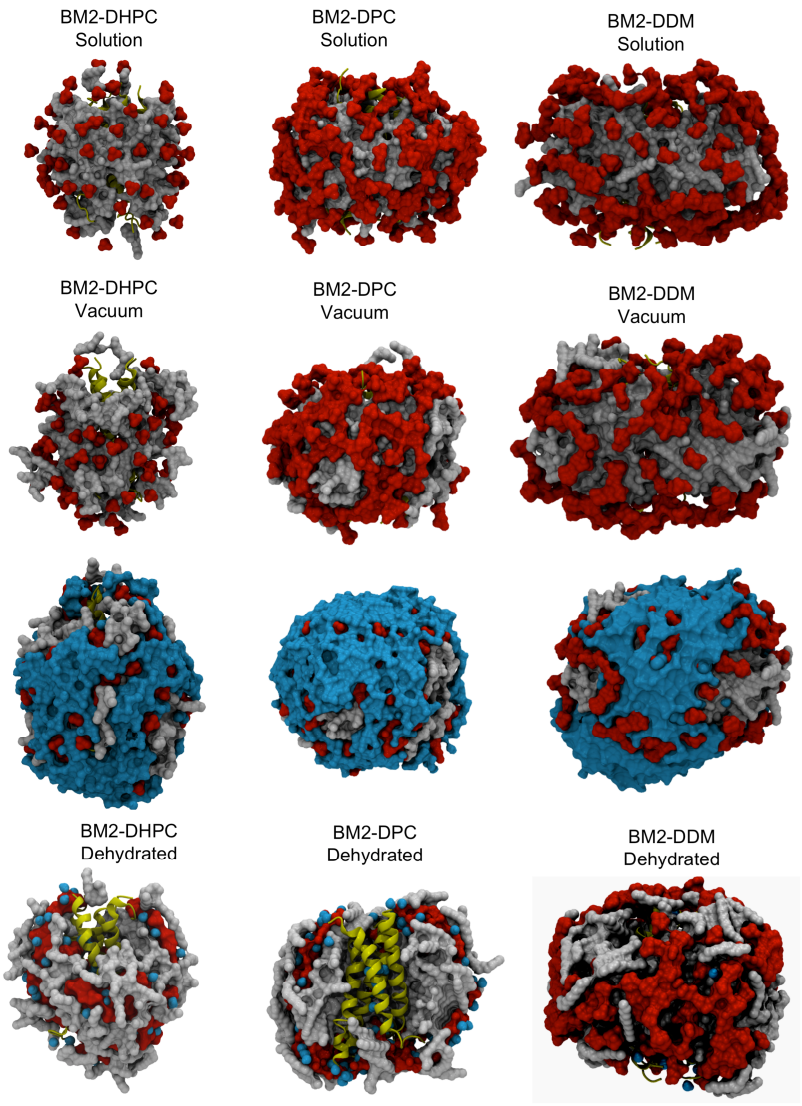

Figure S4. Changes in packing of detergent molecules upon transfer from solution to vacuum. The protein-detergent complexes are shown at the beginning ("Solution") and end ("Vacuum") of the steered molecular dynamics (SMD) trajectories, and following extended simulation under dehydrating conditions ("Dehydrated"). Water is omitted in the top two panels for clarity. The detergent headgroups are shown in red and detergent tails in grey. Only one ring of the DDM headgroups are shown for clarity. The protein is shown in yellow cartoon format. The rearrangement of DHPC detergent molecules during the SMD trajectory leads to partial exposure of the protein to vacuum. During loss of water further rearrangement is observed, more pronounced in the case of DHPC and DPC compared to DDM.

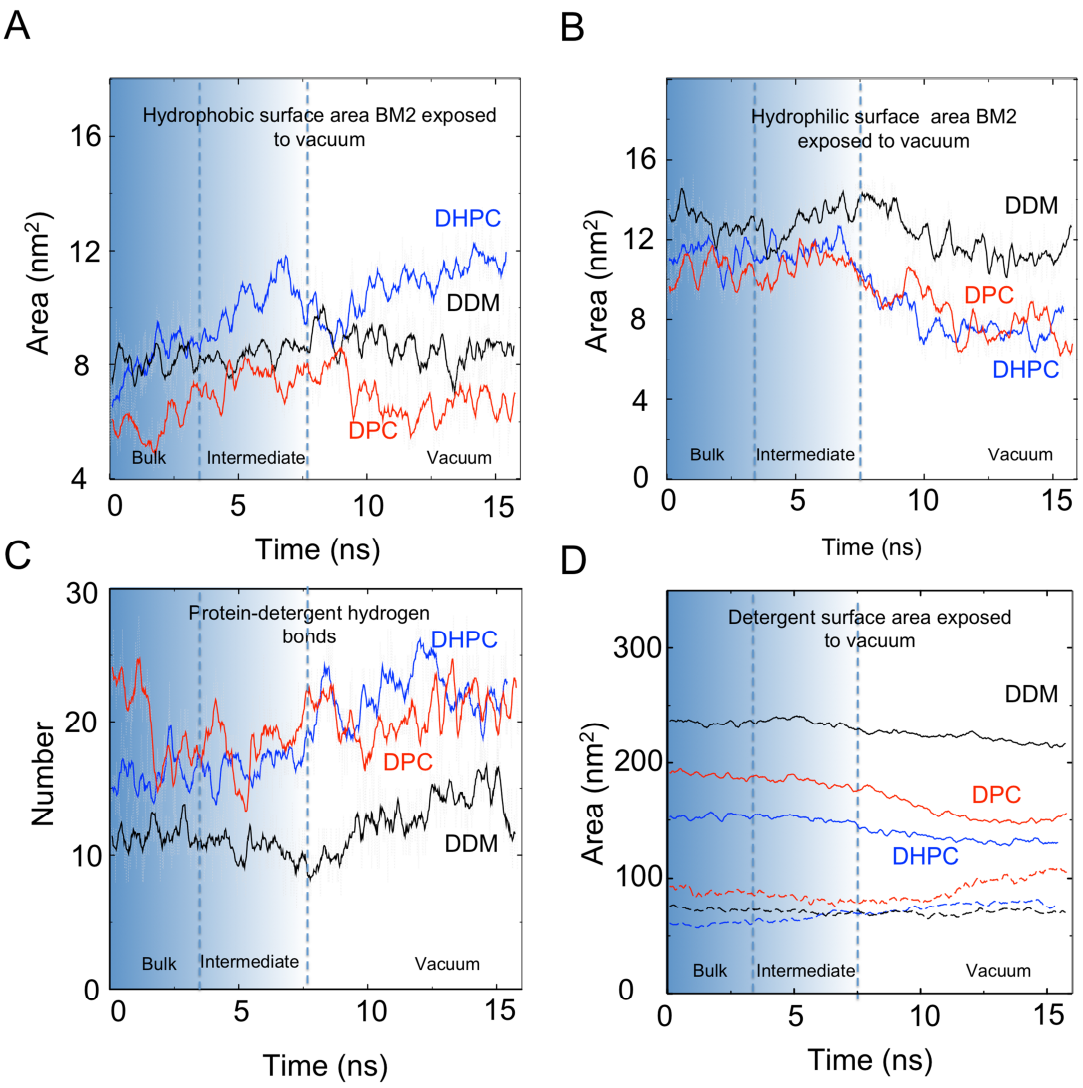

Figure S5. Properties of protein-detergent complexes during transfer from solution to vacuum. Surface area of the protein not covered by detergent of A: hydrophobic residues and B: hydrophilic residues. C: Protein-detergent hydrogen bonds. D: Surface area of detergent exposed to vacuum (ie not in contact with protein). Solid lines correspond to the hydrophilic surface area and dashed lines hydrophobic surface area. In each case the location of the dashed lines indicates the approximate boundaries at which the protein-detergent complex is first exposed to vacuum and when it is free from bulk solution. Black, blue and red traces correspond to DDM, DHPC and DPC data, respectively. A general trend in which hydrophilic regions become more buried and hydrophobic area more exposed is observed for both protein and detergent.

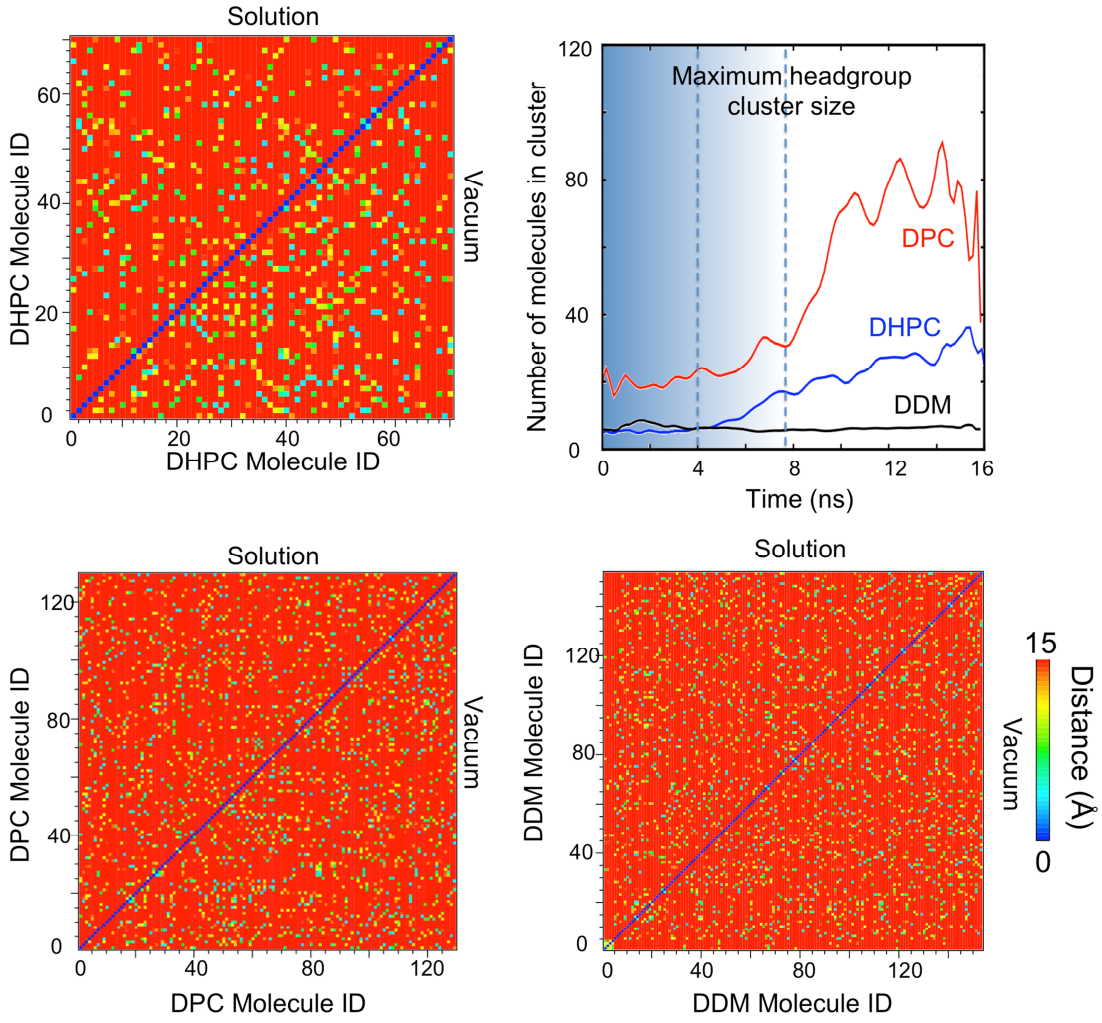

Figure S6. Changes in clustering of detergent headgroups during SMD simulation. Top: The maximum detergent headgroup cluster size is shown in green for DHPC and black for DDM. A detergent headgroup was assigned to a cluster if any atom is within 3.5 Å of any other atom within the cluster. For DDM only the first ring (distal to the tail) is considered in the calculations as the extensive hydrogen bonding network between headgroups means all headgroups belong to a single cluster. The data shown is a mean of the SMD simulations using the OPLS-AA force field, with the trace a running average over 10 data points (shown as circles). Lower: Comparison of minimum pair wise headgroup-headgroup distances in solution and vacuum for DHPC (left) and DDM (right).

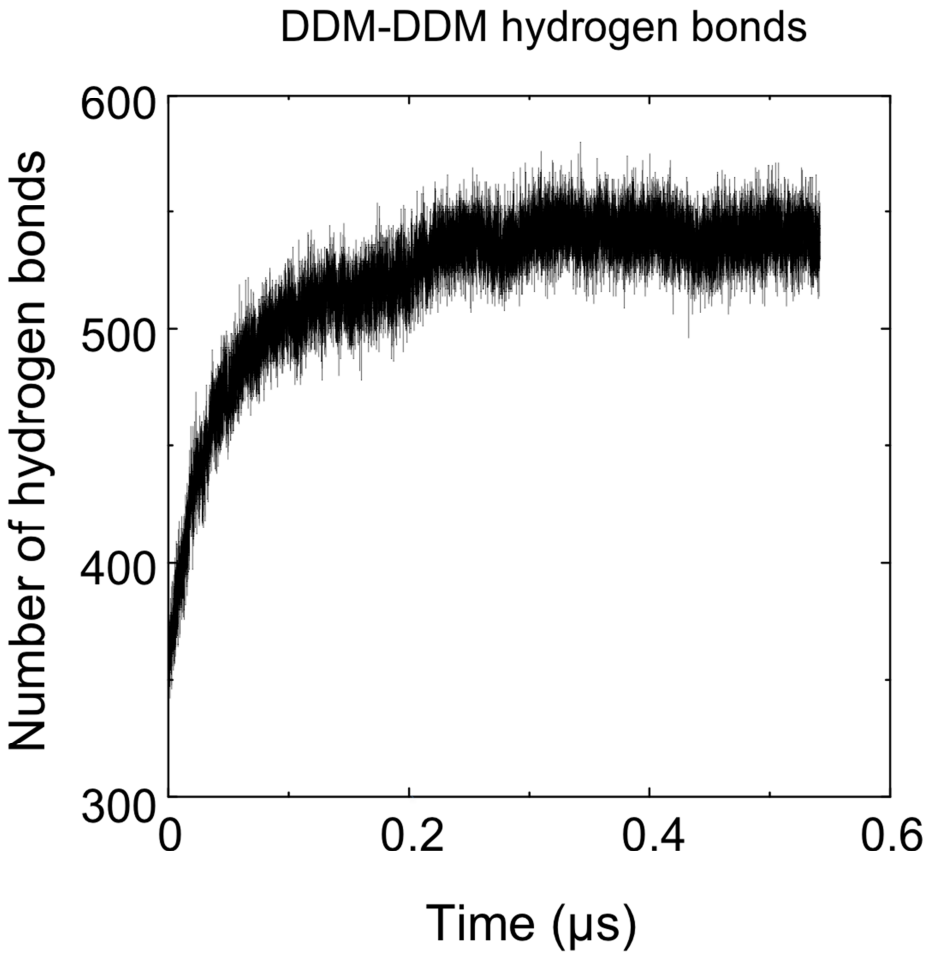

Figure S7. Hydrogen bonds between DDM detergent molecules during extended simulation under dehydrating conditions. The criteria for presence of a hydrogen bond were an acceptor-donor distance cut-off of 3.5 Å and a maximum acceptor-donor-hydrogen angle of 30°. Hydrogen bonds between detergent sugar-based headgroups increase on the same timescale as the loss of water molecules.

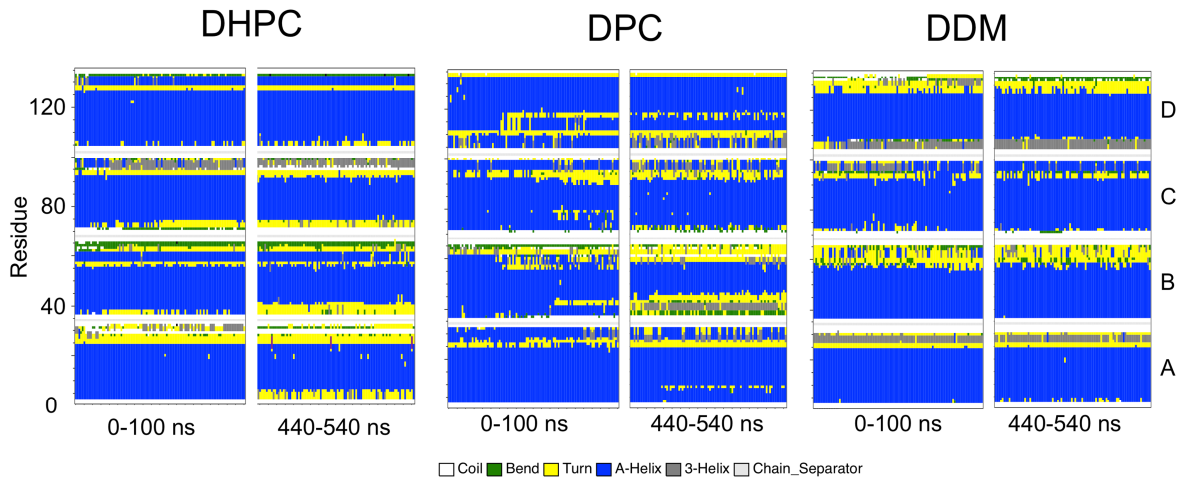

Figure S8. Evolution of BM2 secondary structure in complex with each detergent under dehydrating conditions. Minor disruption in α-helicity in all cases is observed within the first 100 ns. For DHPC this is mainly at the N- and C- termini of chain B, for DPC unfolding occurs at the N- and C-termini of chain B and the N-termini of chains C and D. These initial losses in α-helicity are part of a general trend towards loss in secondary structure and these regions remain non α-helical at the end of the simulations whilst other regions unfold (eg the N-terminus of chain A). In the case of DDM some initial structural loss is observed at the N- and C-termini of chain C, however this is restored within the first 100 ns and persists for the remainder of the simulation.

Protein	Detergent	Force field	Type	Number of simulations	Temperature / K	Duration / ns
BM2	DHPC	OPLS-AA	SMD	3	323	25
BM2	DHPC	OPLS-AA	SMD	1	300	25
BM2	DHPC	OPLS-UA	SMD	1	323	25
BM2	DHPC	GROMOS	SMD	1	323	25
BM2	DHPC	OPLS-AA	Vacuum	1	323	600
BM2	DHPC	OPLS-AA	Vacuum	1	300	250
BM2	DHPC	OPLS-AA	Vacuum	1	323	250
BM2	DDM	OPLS-AA	SMD	2	323	25
BM2	DDM	GROMOS	SMD	1	323	25
BM2	DDM	OPLS-AA	Vacuum	1	323	500
BM2	DDM	OPLS-AA	Vacuum	1	323	150
BM2	DPC	OPLS-AA	SMD	2	323	25
BM2	DPC	OPLS-AA	Vacuum	1	323	500
OmpA	DPC	OPLS-AA	SMD	2	323	25
OmpA	DPC	OPLS-AA	Vacuum +PBC	1	323	300

Table S1. Summary of simulations performed.

Property	BM2-DHPC		BM2-DPC		BM2-DDM	
	Start	End	Start	End	Start	End
# waters	1100	95	1709	119	1504	35
rmsd Cα (Å)	–	2.8	–	3.2	–	1.5
SS count	88	78	104	81	88	89
HB_{pp}	118	115	113	105	119	128
HB_{pd}	23.1	39.5	21.3	45.4	13	35.1
A_p ($Å^2$)	1990	1700	1420	2444	2090	1210
A_d ($Å^2$)	20750	15310	26230	18860	27330	23510
$A_{P,\ hydrophobic\ (\%)}$	61.4	77.8	46.8	90.3	45.1	74.8
$A_{d,\ hydrophobic\ (\%)}$	38.1	52.8	45.7	83.4	25.8	34.6
$R_{g,protein}$ (Å)	16.9	16.6	16.9	16.4	16.8	16.6
$R_{g,detergent\text{-}HG}$ (Å)	23.1	20.4	26.1	22.5	30.4	28.9
$R_{g,detergent\text{-}tail}$ (Å)	22.3	22.2	22.9	23.8	23.3	24.0

Table S2. Structural properties of each BM2-detergent complex in simulations under dehydrating conditions The properties described are as follows: number of water molecules present (# waters); the Cα RMSD of the protein (rmsd Cα); protein-protein hydrogen bond count (HB_{pp}); hydrogen bonds between protein and detergent (HB_{pd}); surface area of protein exposed to vacuum (A_p); surface area of detergent exposed to vacuum (A_d); percentage of A_p that is hydrophobic ($A_{p,\ hydrophobic}$); percentage of A_d that is hydrophobic ($A_{d,\ hydrophobic}$); radius of gyration of protein ($R_{g,protein}$); radius of gyration of detergent headgroups ($R_{g,detergent\text{-}HG}$); radius of gyration of detergent tails ($R_{g,detergent\text{-}tails}$). Values correspond to means over the first 10 ns (“Start”) and final 10 ns (“End”) of simulations, respectively.