Balancing force field protein-lipid interactions to capture transmembrane helix-helix association

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Table S1: The positions and spring constants used in defining umbrella sampling simulation of all-atom GpA TM fragment

Umbrella center (nm)	Umbrella spring constant (kJ/mol/nm^2)	Umbrella center (nm)	Umbrella spring constant (kJ/mol/nm^2)
0.033	10000	0.550	1000
0.066	10000	0.636	1000
0.099	10000	0.722	1000
0.133	10000	0.809	1000
0.140	50000	0.895	1000
0.150	50000	0.981	1000
0.160	50000	1.068	1000
0.166	10000	1.154	1000
0.170	50000	1.240	1000
0.180	50000	1.327	1000
0.199	10000	1.413	1000
0.233	10000	1.500	1000
0.266	10000	1.530	200
0.299	10000	1.668	200
0.333	10000	1.807	200
0.366	10000	1.945	200
0.399	10000	2.084	200
0.433	10000	2.222	200
0.466	10000	2.361	200
0.500	10000	2.500	200

Table S2: Example values showing the relationship between λ and T_{eff}, $\lambda = T_0/T_i$

λ	T_{eff}
1.0	300
0.75	400
0.5	600
0.375	800

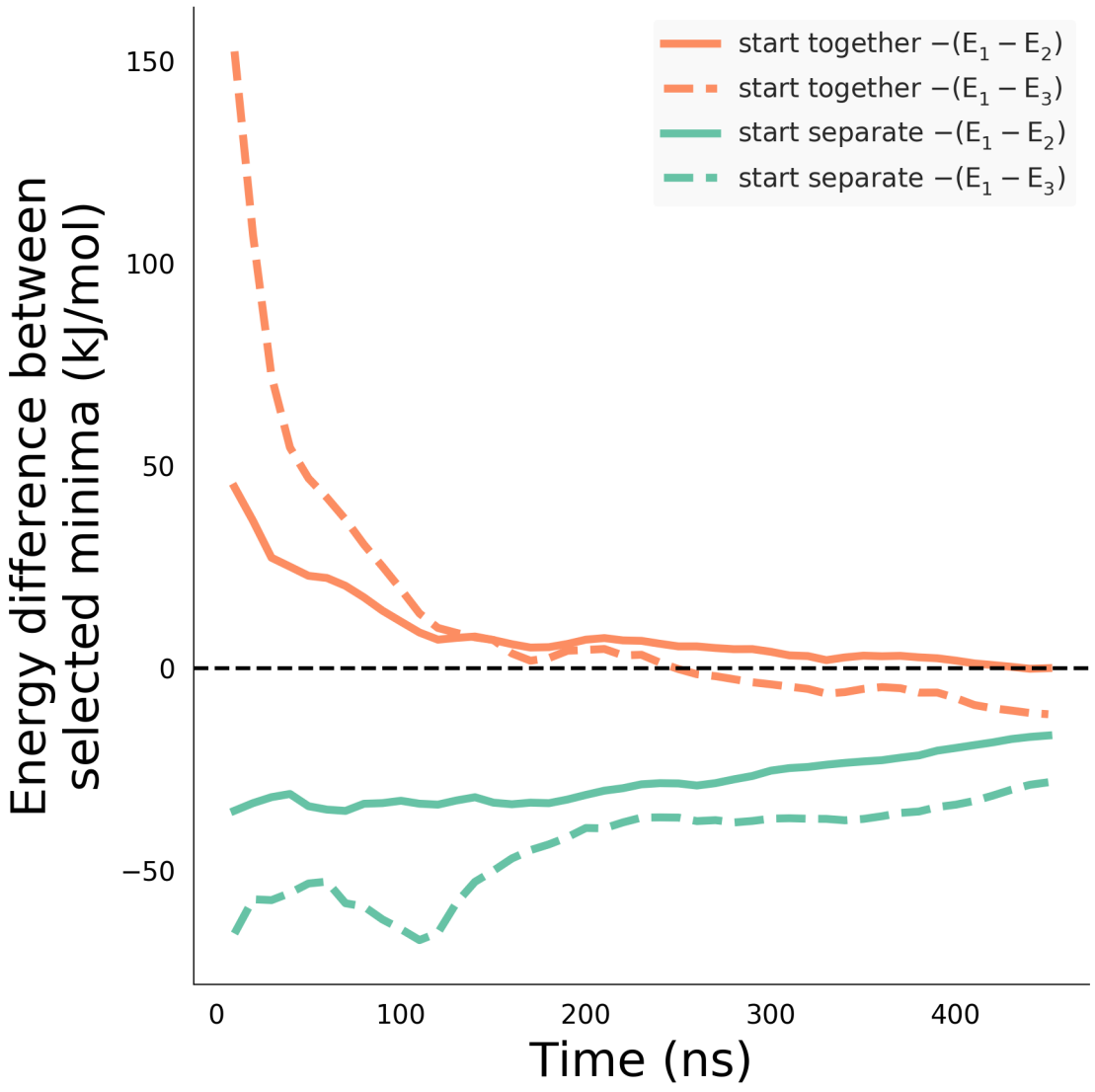

Figure S1: Energy differences between minima on the PMF, as a function of simulation length, for the two different initial conditions. E_1, E_2 and E_3 are the energies of minima 1, 2 and 3 respectively.

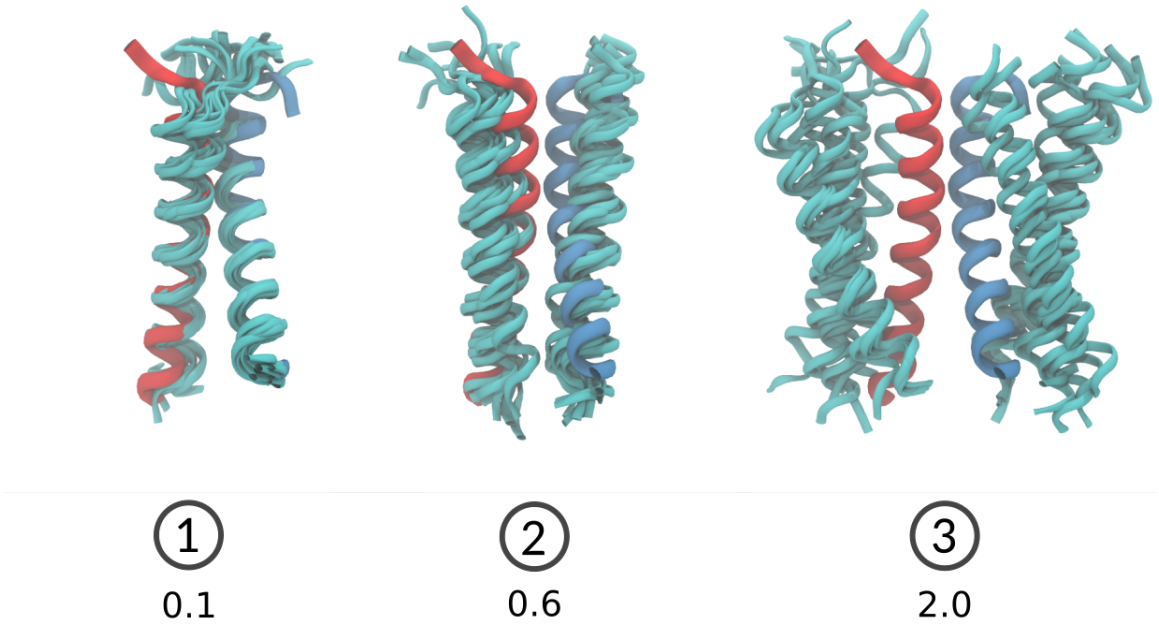

Figure S2: Ensembles of representative structures for minima (1), (2),(3) identified along the PMF at positions 0.1, 0.6 and 2.0 nm D_{RMS} from native. The representative structures are visually tightly clustered for minima (1), (2).

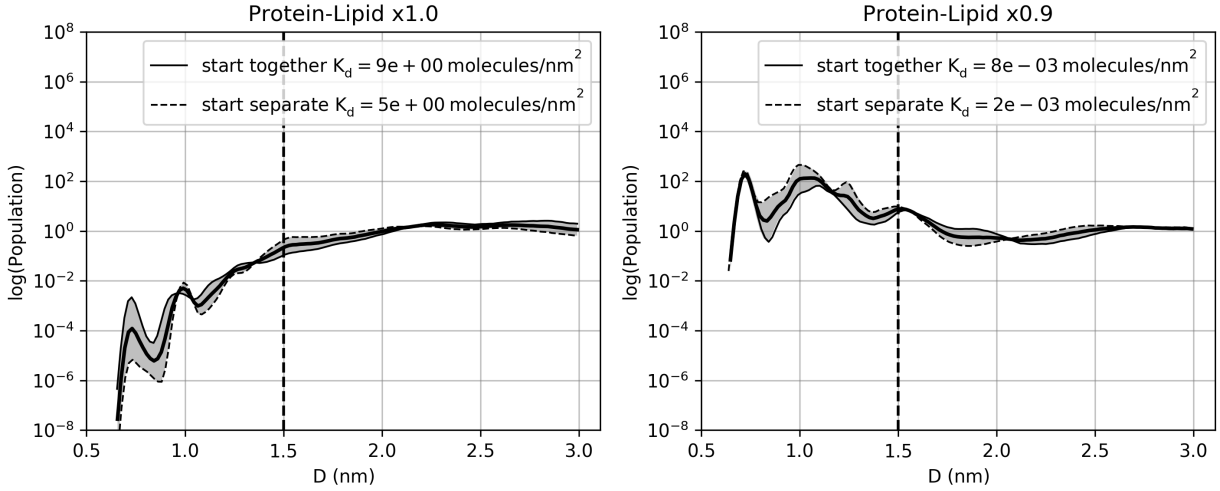

Figure S3: Calculating the helix-helix dimerization K_d from population distribution obtained from the PMF, for both the original force-field (left-hand panel) and the protein-lipid scaled/corrected PL-0.9 model (right-hand panel)

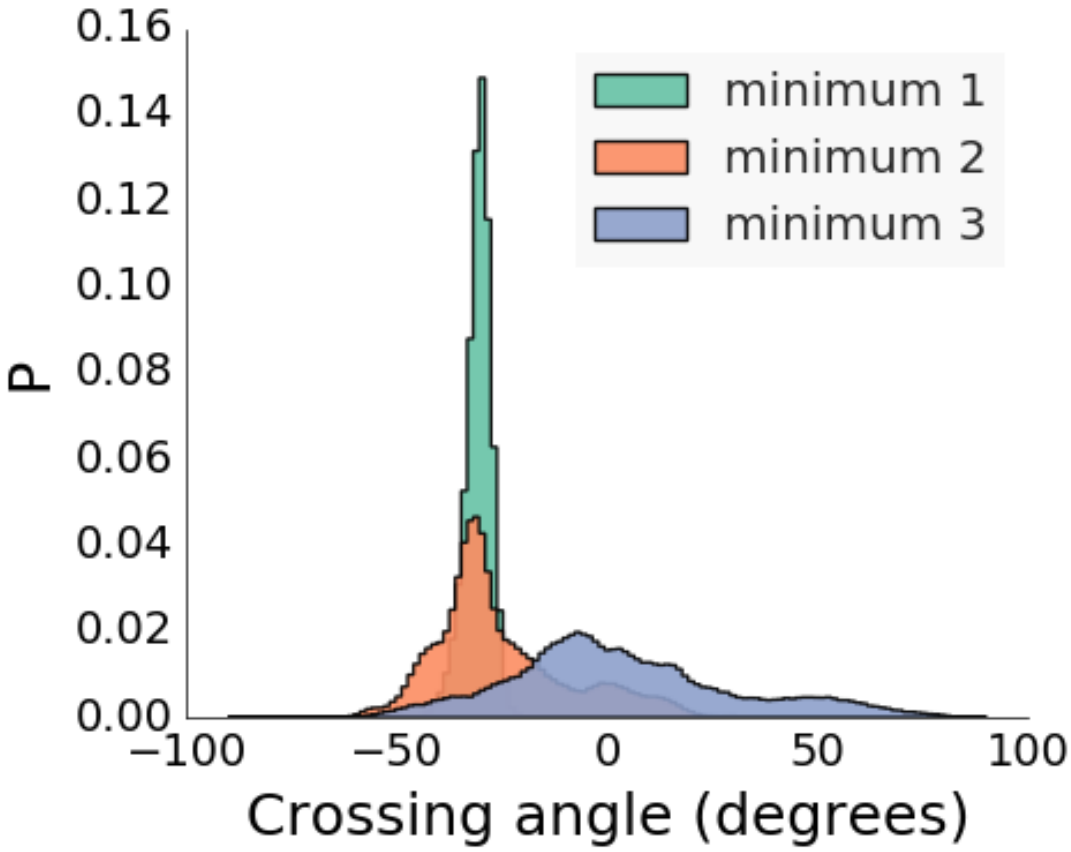

Figure S4: Crossing angle distributions for the PMF minima 1-3.

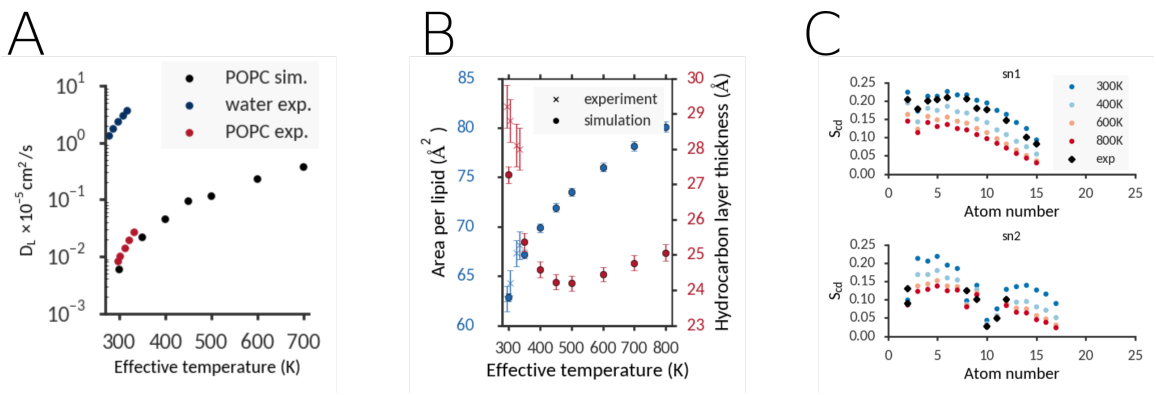

Figure S5: Pure POPC bilayer properties as function of effective temperature (determined from scaling factor λ). Note in all cases that the results from the simulations can strictly only be compared with experiment at the temperature of the neutral replica, i.e. $T_{\text{eff}} = 300$ K. However, because the properties of the lipid dominate the observables here, the results usually compare well at other effective temperatures also. (A) Diffusion coefficient as function of temperature, experimentally for water[1] and POPC.[2] For the POPC simulations, effective temperature was used. (B) Bilayer thickness (red), and area per lipid (blue), experimentally as function of temperature and as function of effective temperature for simulations. Experimental data taken from.[3] (C) Lipid tail deuterium order parameters from simulation and experiment. Experimental NMR data (in black) was collected at 300 K.[4]

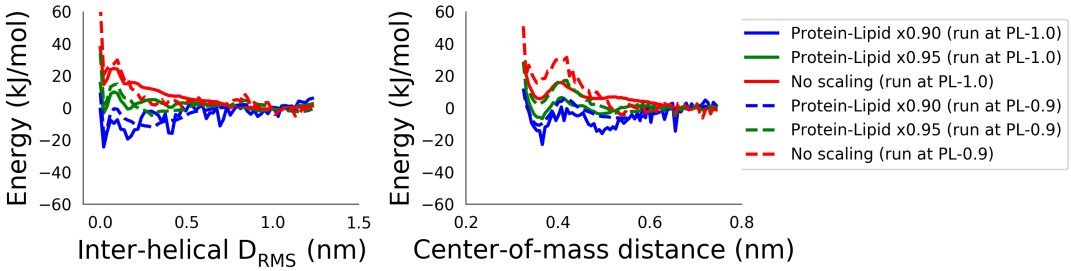

Figure S6: Re-weighting the PMF along two collective variables for simulation run at PL 0.9 and 1.0 (with and without the scaling correction). The projection is done along inter-helical D_{RMS} and D. Upper and lower row are fixes involving protein-lipid interaction scaling and introduction of a C_α-hydrogen bond. The reweightings are consistent: the PMF obtained from simulations run at PL-1.0 and reweighted onto PL-0.9 is similar to the PMF obtained by running the simulation at PL-0.9.

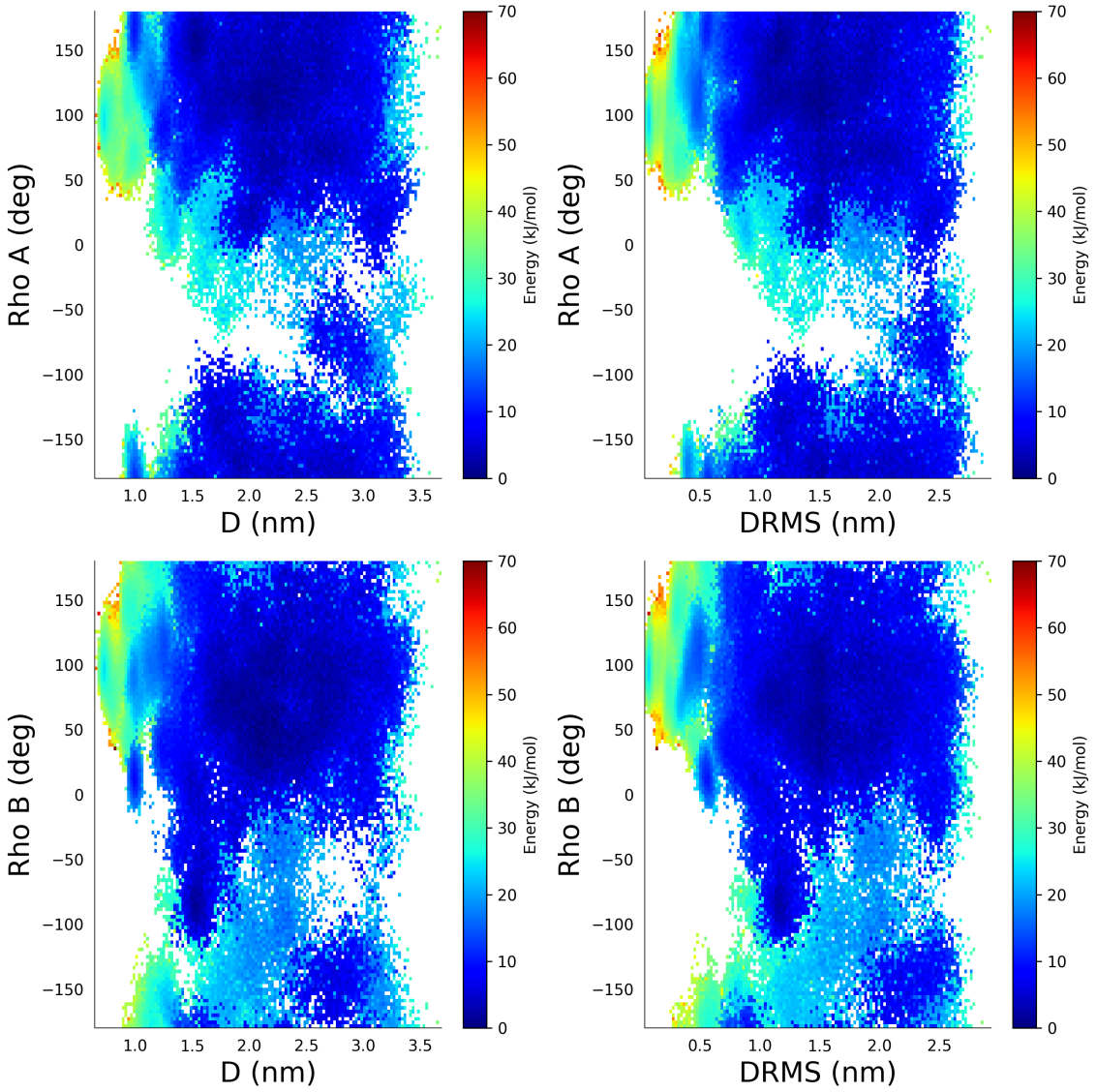

Figure S7: Relative helix rotations projected on a 2D surface along center-of-mass helix-helix distance (left column), and the inter-helical D_{RMS} (right column). The helix-helix relative angles were defined similarly to,[5] as two dihedral angles RhoA and RhoB. RhoA is defined between the four C_α atoms of residues 83, 78 and 88 of chain A and residue 83 of chain B; vice-versa for chain B in case of RhoB.

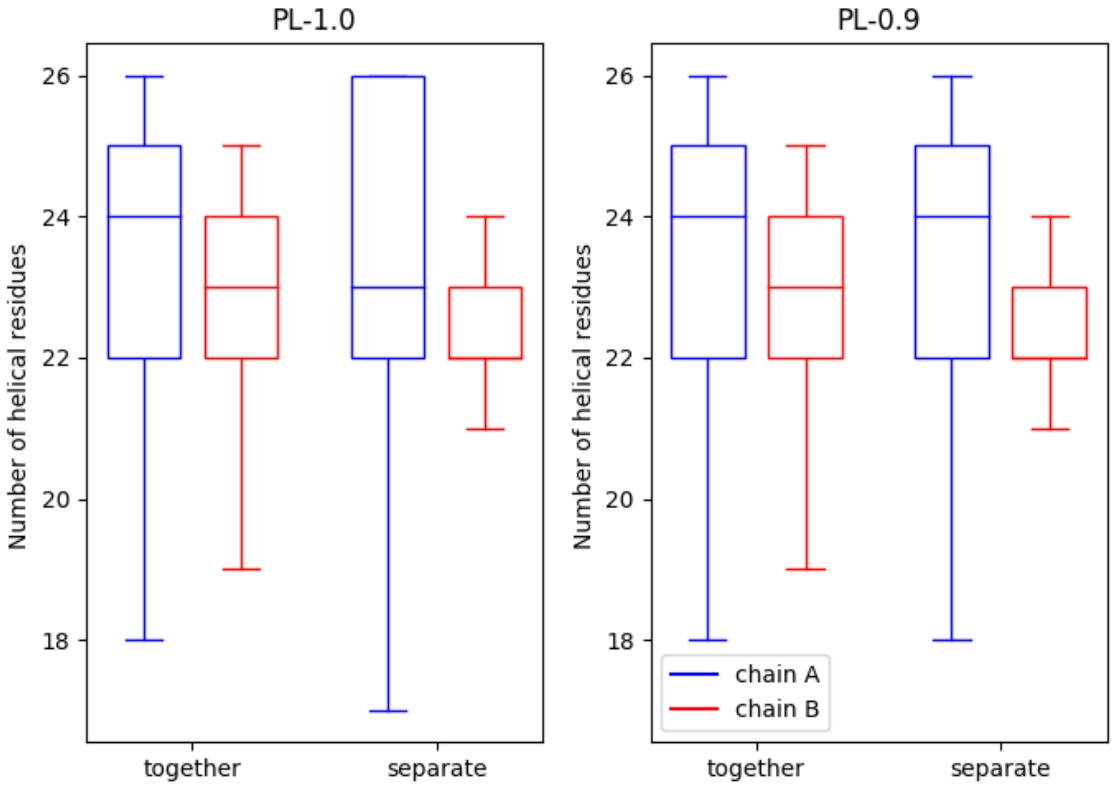

Figure S8: Boxplot showing number of helical residues, as classified by DSSP, in umbrella sampling simulations of GpA. PL-1.0 on the left for the original force field, and PL-0.9 for the scaled force field on the right. Chain A shown in blue and chain B shown in red, for the two initial conditions with all replicas started together or separate.

References

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