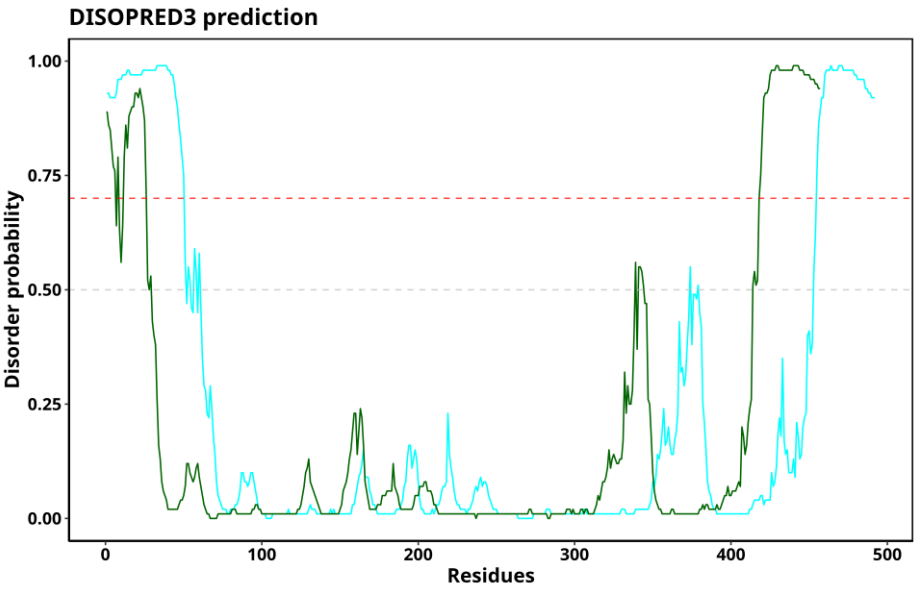
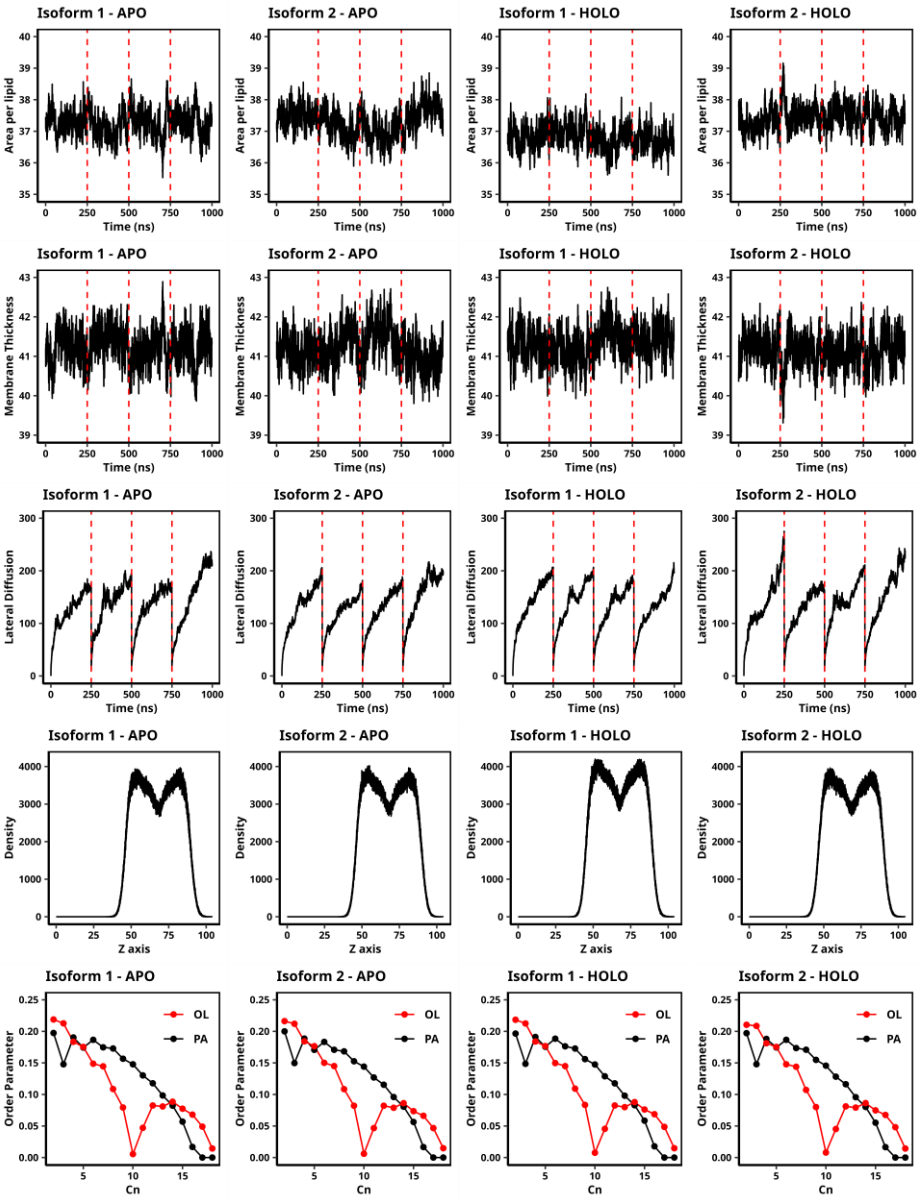
Supplementary material

Supplementary Table 1. Minimized Model structure assessment.

Metrics	MolProbity Score	Ramachandran Favoured	Ramachandran Outliers	QMEANDisCo
Reference value	≈ 0	> 98%	< 0.2%	≈ 1.00
PBD ID 8E3Z (chains P and R)	1.62	96.21	0.0	0.78
VPAC1-iso1-holo	1.86	96.06	1.13	0.65
VPAC1-iso1-apo	0.99	96.05	0.61	0.68
VPAC1-iso2-holo	1.89	96.50	0.81	0.63
VPAC1-iso2-apo	0.82	96.24	0.87	0.65



Supplementary Figure S1. DISOPRED3 disorder prediction for protein isoforms. Disorder probability predictions for Isoform 1 (dark green) and Isoform 2 (cyan) across the protein sequence. The gray dashed line indicates the default DISOPRED3 threshold (0.5), while the red dashed line represents the threshold used in this study (0.7). Both isoforms show similar disorder patterns with high probability regions at the N-terminus (~residues 1-50) and C-terminus (~residues 400-500), while the central region remains largely ordered, but isoform 2 show larger disordered region in the N-terminal.



Supplementary Figure S2. Membrane stability analysis across simulation systems. Temporal evolution of membrane properties for four protein-membrane systems (Isoform 1-APO, Isoform 2-APO, Isoform 1-HOLO, Isoform 2-HOLO) showing: (Row 1) area per lipid over time, (Row 2) membrane thickness, (Row 3) lateral diffusion coefficients, (Row 4) lipid density profiles, and (Row 5) lipid order parameters. Vertical red dashed lines in temporal plots separate simulation replicates. All systems demonstrate stable membrane properties throughout the simulation period, validating the integrity of the lipid bilayer environment.