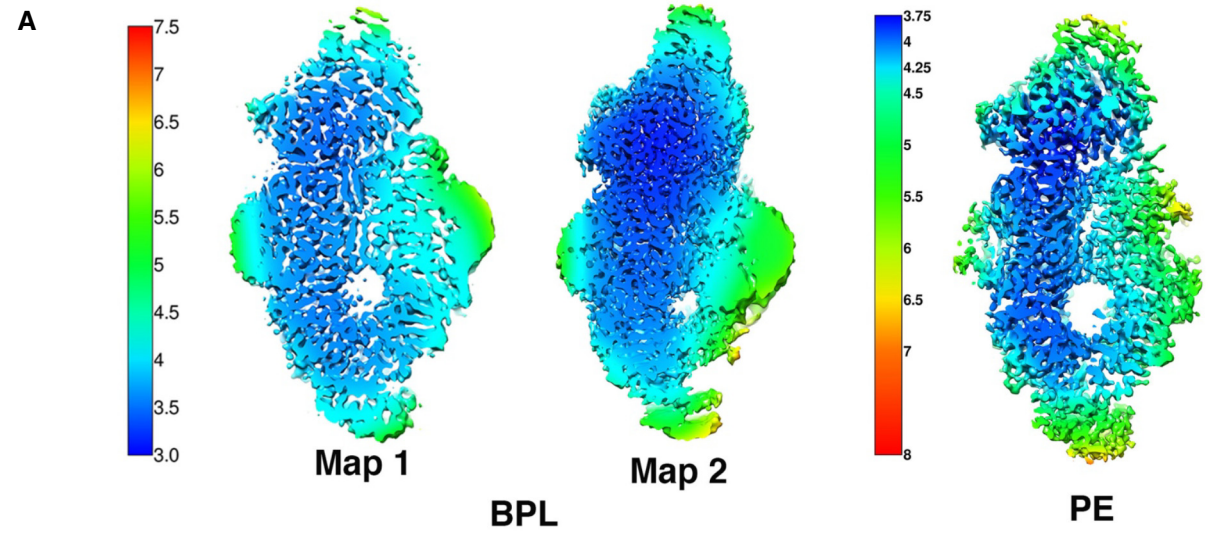
Expanded View Figures



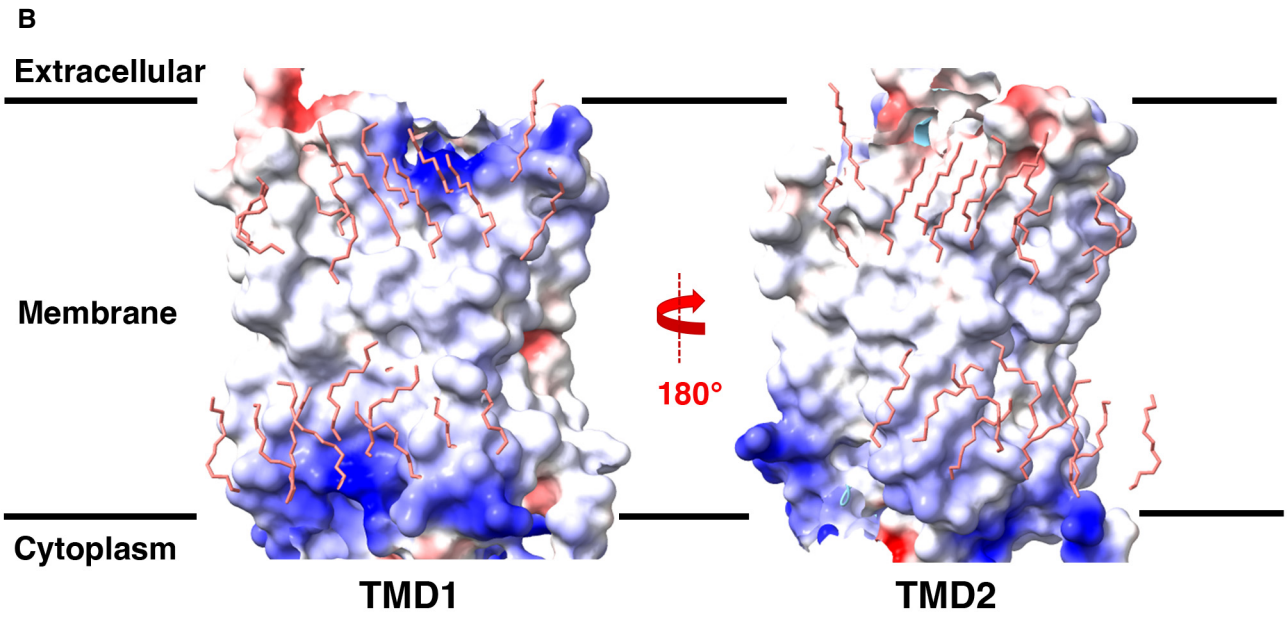


Figure EV1. Variation in local resolution and TMD electrostatics.

A Local resolution maps of $ABCA7_{BPL}$ and $ABCA7_{PE}$ structures. Color keys are indicated on the left of each set of maps with numbers representing resolution (Å).
B Analysis of TMD electrostatics of $ABCA7_{PE}$ with electrostatic potential maps for TMD1 (left) and TMD2 (right) shown along with modeled lipids (pink sticks).

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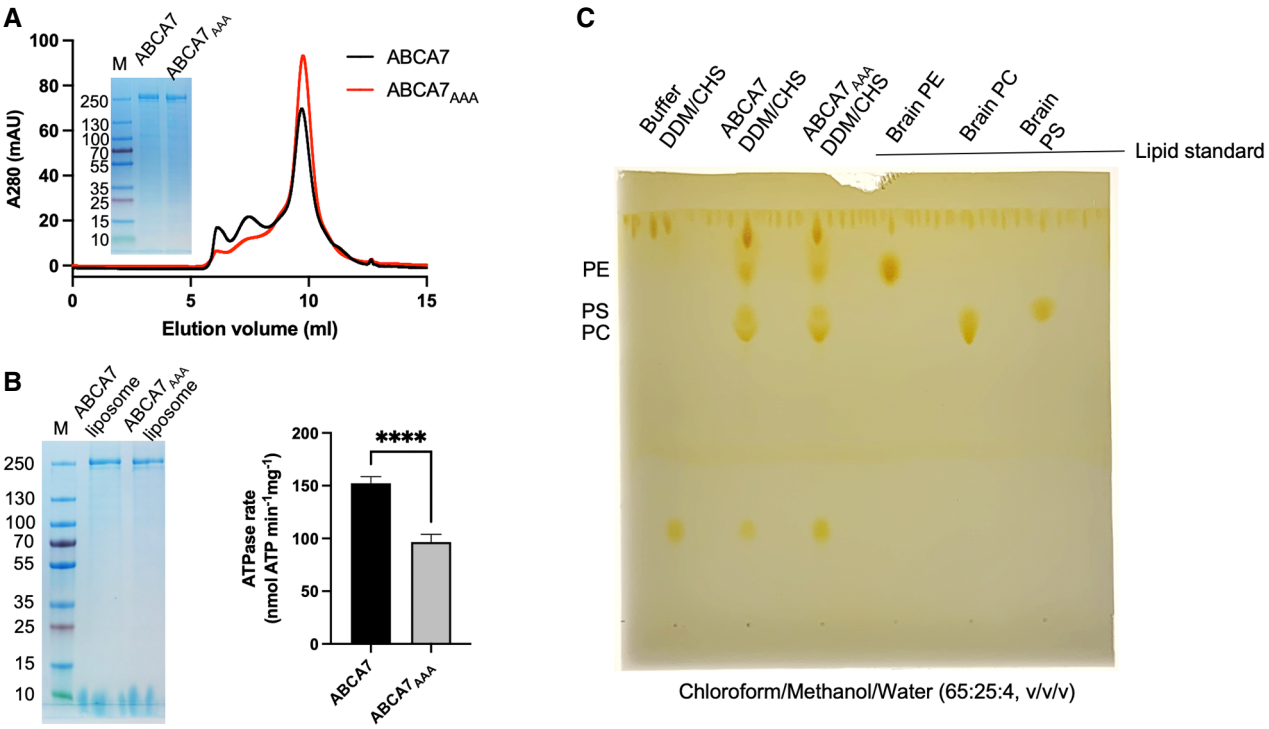

Figure EV2. Purification and characterization of ABCA7 and ABCA7$_{AAA}$.

A SEC chromatograms and SDS-PAGE analysis of ABCA7 and ABCA7$_{AAA}$ in DDM/CHS.

B SDS-PAGE gel and ATPase activity comparison of ABCA7 and ABCA7$_{AAA}$ reconstituted in liposomes. Experimental replicates (n) = 6 and error bars represent standard deviation (s.d.). Statistical significance by unpaired, two-tailed t-test P-value of < 0.0001 is indicated by ****.

C Detection of endogenous lipids co-purified with ABCA7 and ABCA7$_{AAA}$ by thin-layer chromatography (TLC).

Source data are available online for this figure.

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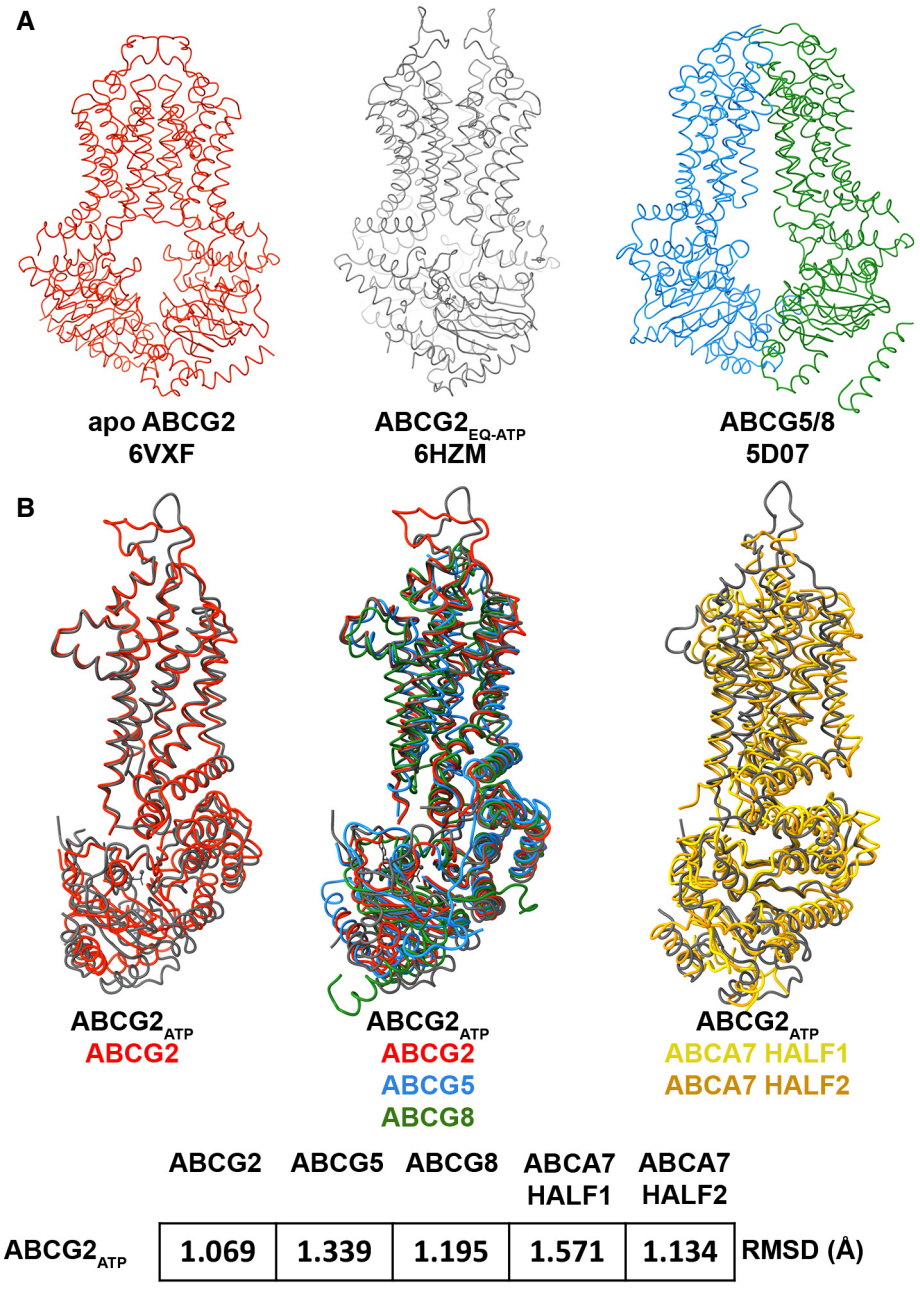

	ABCG2	ABCG5	ABCG8	ABCA7 HALF1	ABCA7 HALF2	
$ABCG2_{ATP}$	1.069	1.339	1.195	1.571	1.134	RMSD (Å)

Figure EV3. Conservation of ABCA and ABCG family structural elements.

A Ribbon representation of select ABCG family transporter structures and their respective PDB IDs including apo open ABCG2 (red), closed ATP-bound structure of $ABCG2_{EQ}$ (black), and ABCG5/G8 (blue and green, respectively).

B Alignment of NBD-TMD pairs from open and closed conformations of ABCG2 (left), ABCG2 and ABCG5/G8 (center), and closed ABCG2 with TMD-NBD pairs from ABCA7 half 1 (gold) and half 2 (orange) along with the root mean square deviations (RMSD) of aligned atoms shown at the bottom.

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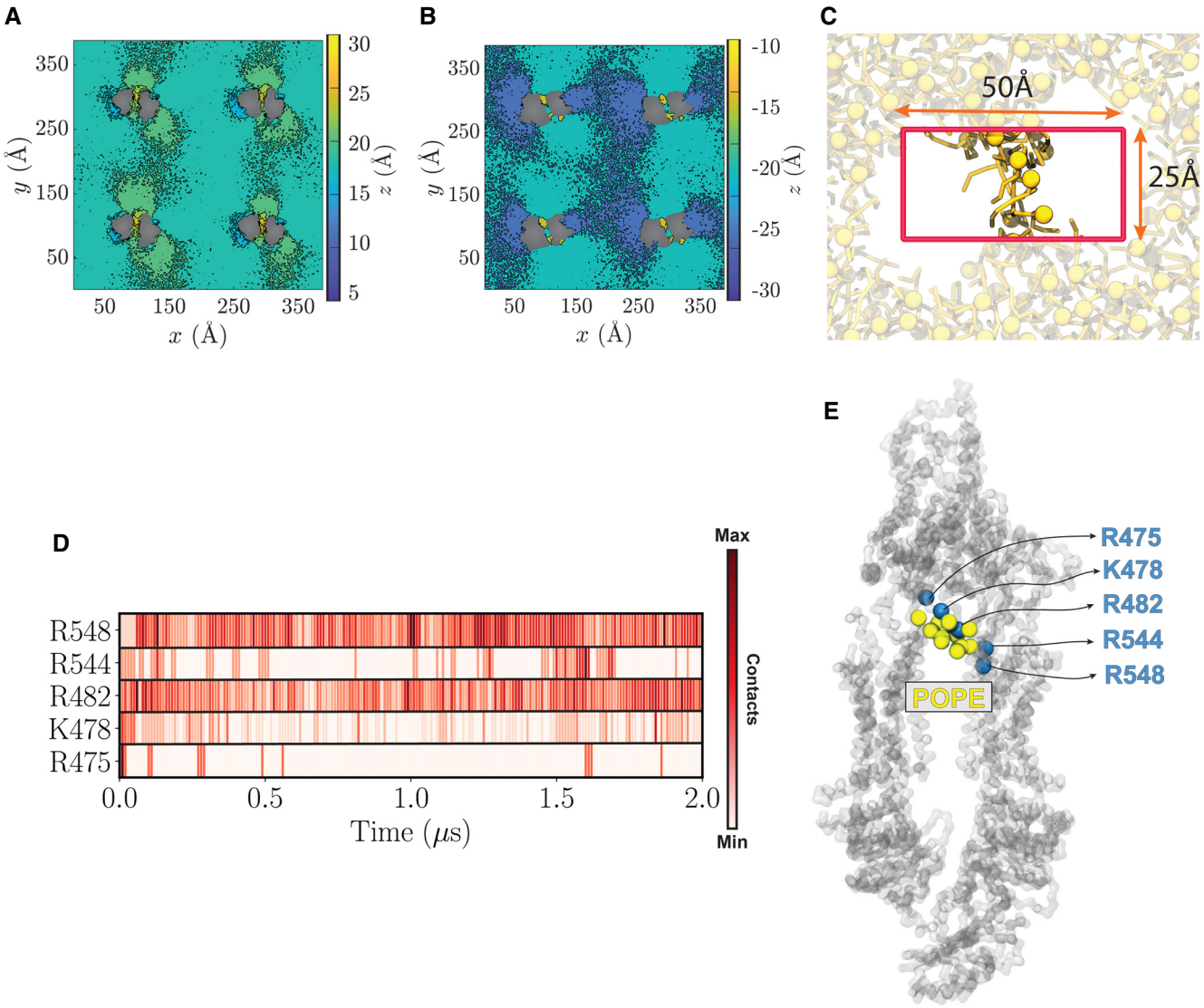

Figure EV4. Lipid configuration induced by protein copies in a bilayer and criteria used for identifying luminal lipids in MD simulations.

A, B POPE headgroup height calculated for extracellular (A) and cytoplasmic (B) leaflets.

C Dimension and position of the box used to calculate the number of phospholipids (yellow) partitioned in the TMD leaflets. The box is centered at the protein center and has dimensions of 50 and 25 Å in *x* and *y* directions, respectively. The ABCA7 transporter is hidden for clarity.

D Contact map, based on the number of POPE headgroups in proximity of each residue throughout the simulation.

E Accumulation of POPE headgroups (yellow spheres) in close proximity of most frequently contacted residues (blue spheres) throughout the simulation. All protein residues are represented as spheres (C_α atoms).

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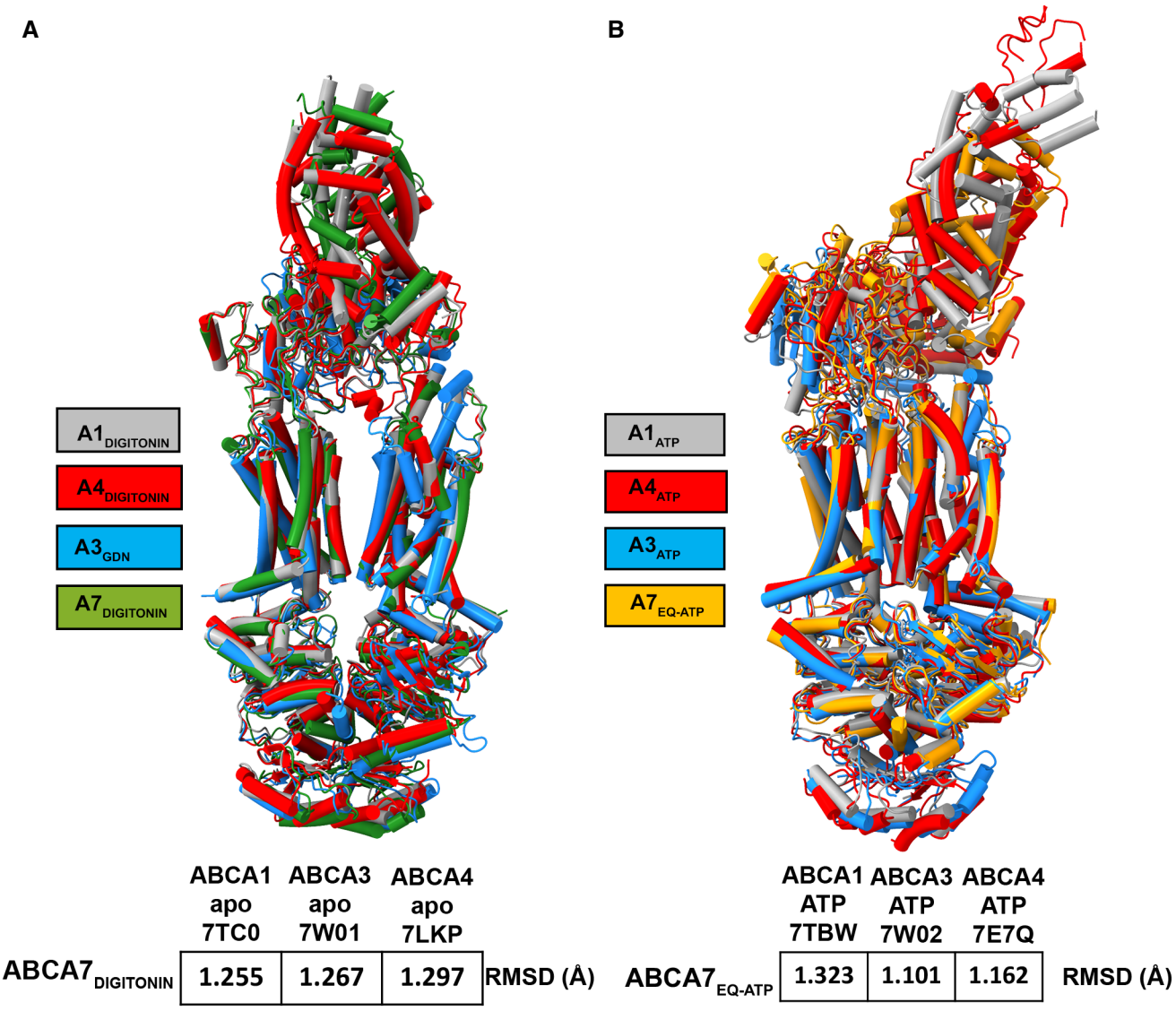

Figure EV5. Structure alignment of ABCA7, ABCA1, ABCA3 and ABCA4.

A, B Superposition of (A) ABCA7 (green, this manuscript), ABCA1 (gray, PDB: 7TC0), ABCA3 (blue, PDB: 7W01), and ABCA4 (red, PDB: 7LKP) structures in detergent and (B) ABCA7 (orange, this manuscript), ABCA1 (gray, PDB: 7TBW), ABCA3 (blue, PDB: 7W02), and ABCA4 (red, PDB: 7E7Q) structures in ATP-bound states. Color keys are indicated on the left and the RMSD of aligned atoms of ABCA7 versus ABCA1, ABCA3, and ABCA4 are displayed at the bottom of each set of structures.

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