

SI - An integrative modelling approach to the mitochondrial cristae

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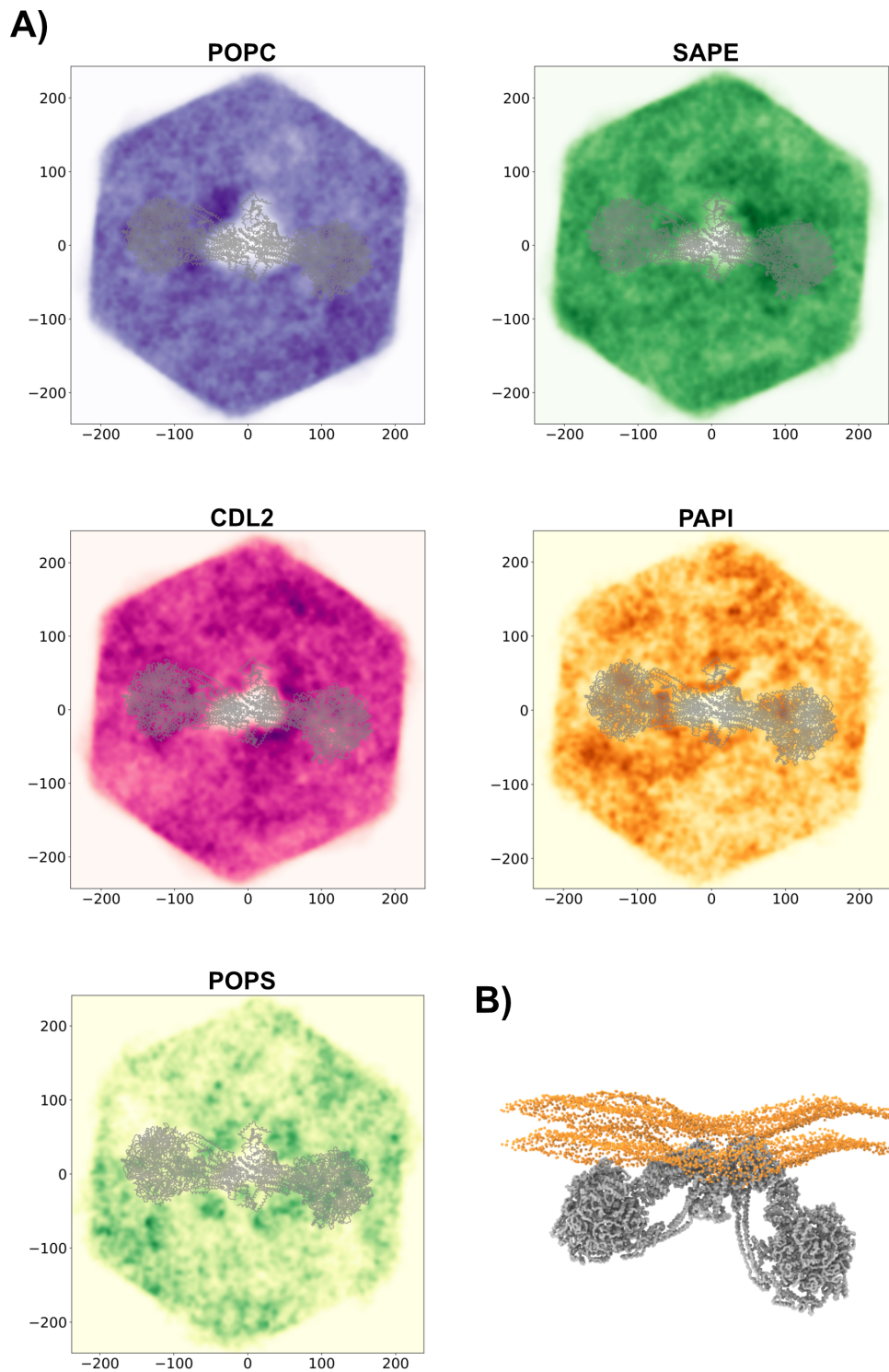
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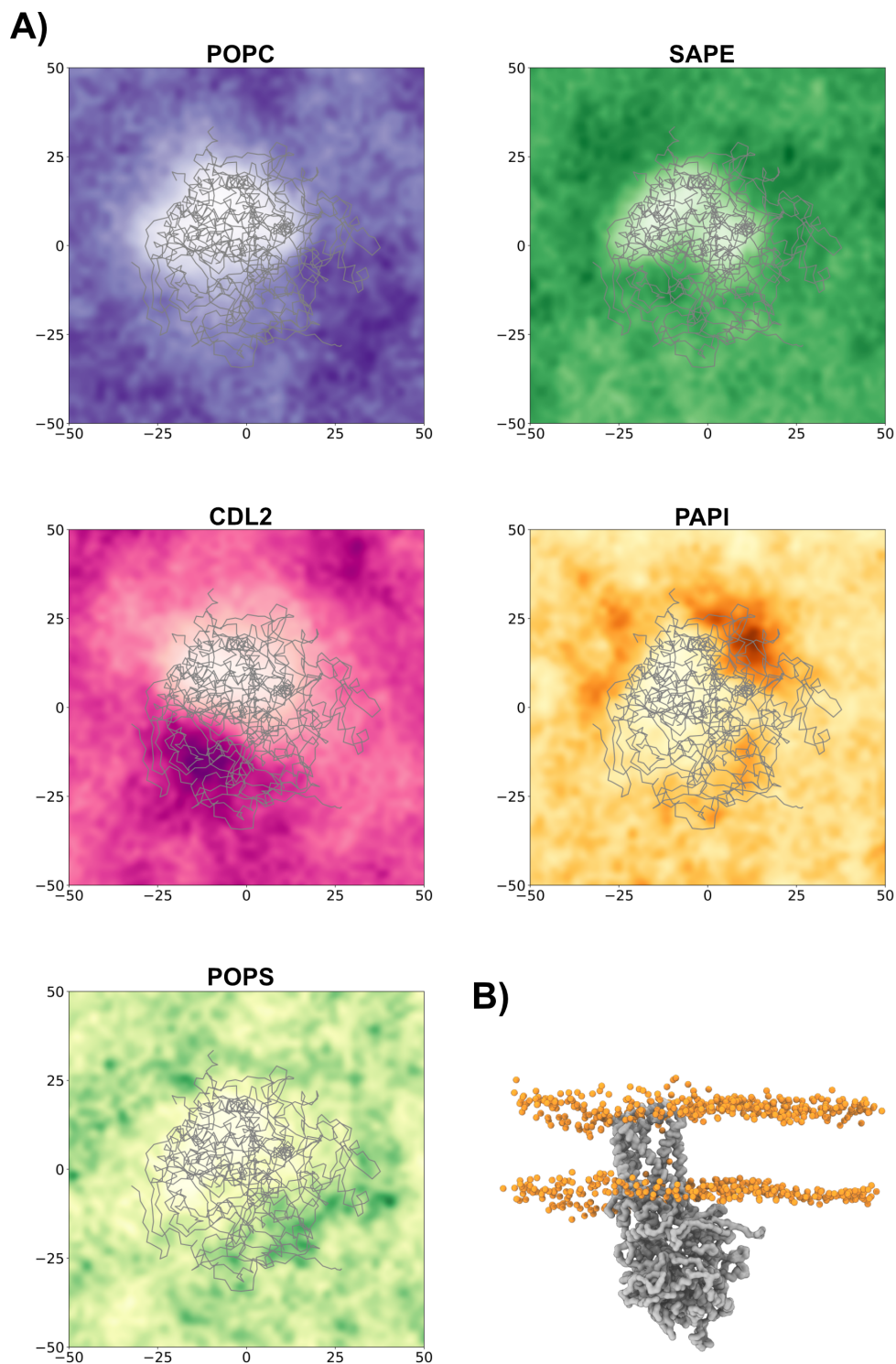
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Protein (complex)	Original structure (PDB ID): organism	Method used in this study
ATPase	8H9S: Human (overlayed with 7AJB: Bovine)	Overlaid human monomer on bovine dimer
Respiratory supercomplex	8UGH: Porcine	AlphaFold2 replacement
Respiratory complex II	8GS8: Human	AlphaFold2 replacement
ANT1	2C3E: Bovine	AlphaFold2 Database
ANT2	N/A	AlphaFold2 Database
MIC60 subcomplex	N/A	AlphaFold 3 online server
TIM22 complex	7CGP: Human	AlphaFold2 replacement
TIM23 complex	8SCX: Yeast	AlphaFold2 online server
TOM complex	7VD2: Human	AlphaFold2 replacement
SAM complex	7E4H: Yeast	AlphaFold2 replacement
VDAC1	6TIQ: Human	Use original structure

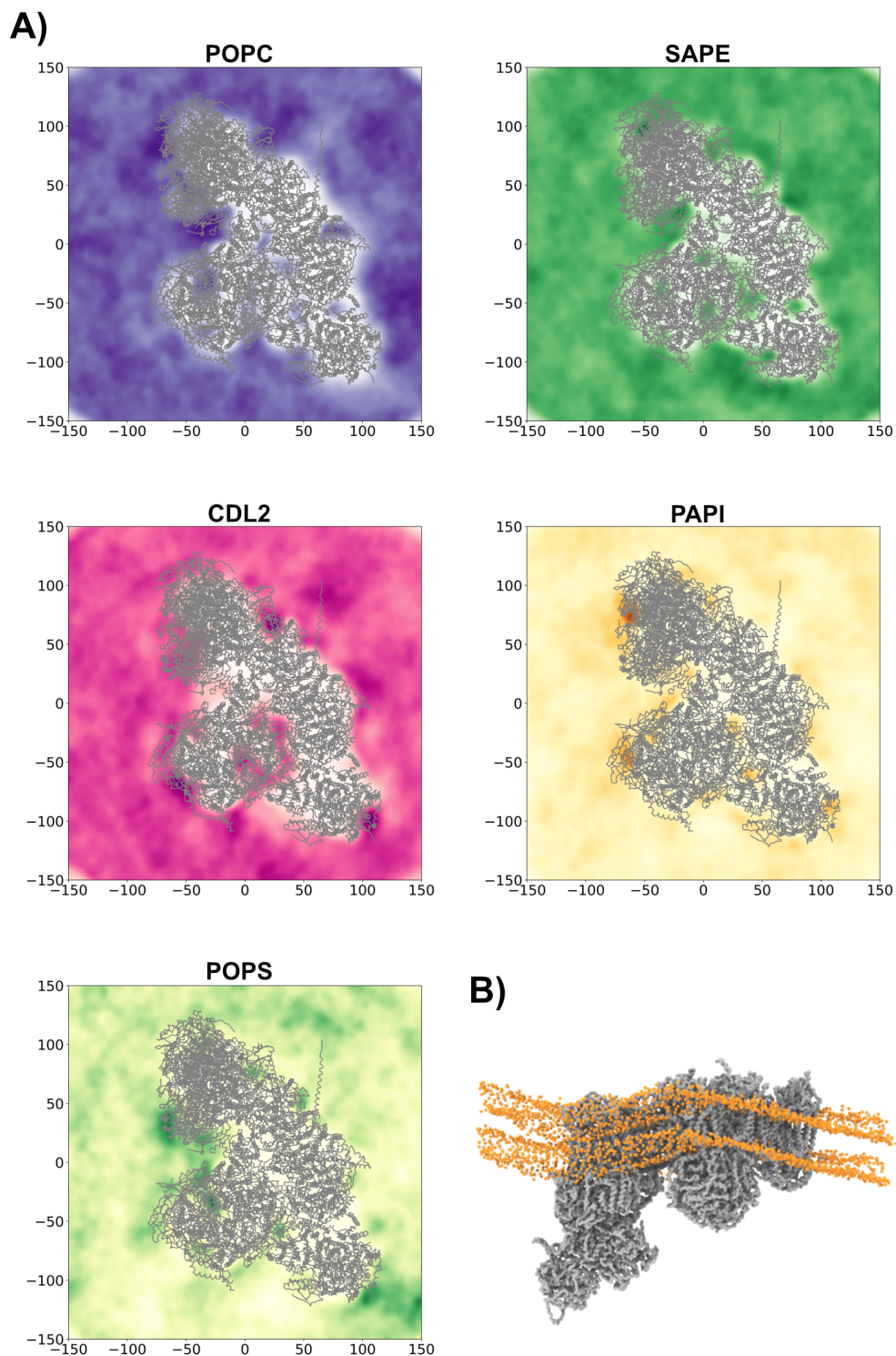
SI Table 1. A table showing the protein (complexes) used in this study, the structure the model was based upon or compared to and the method used to construct the model.



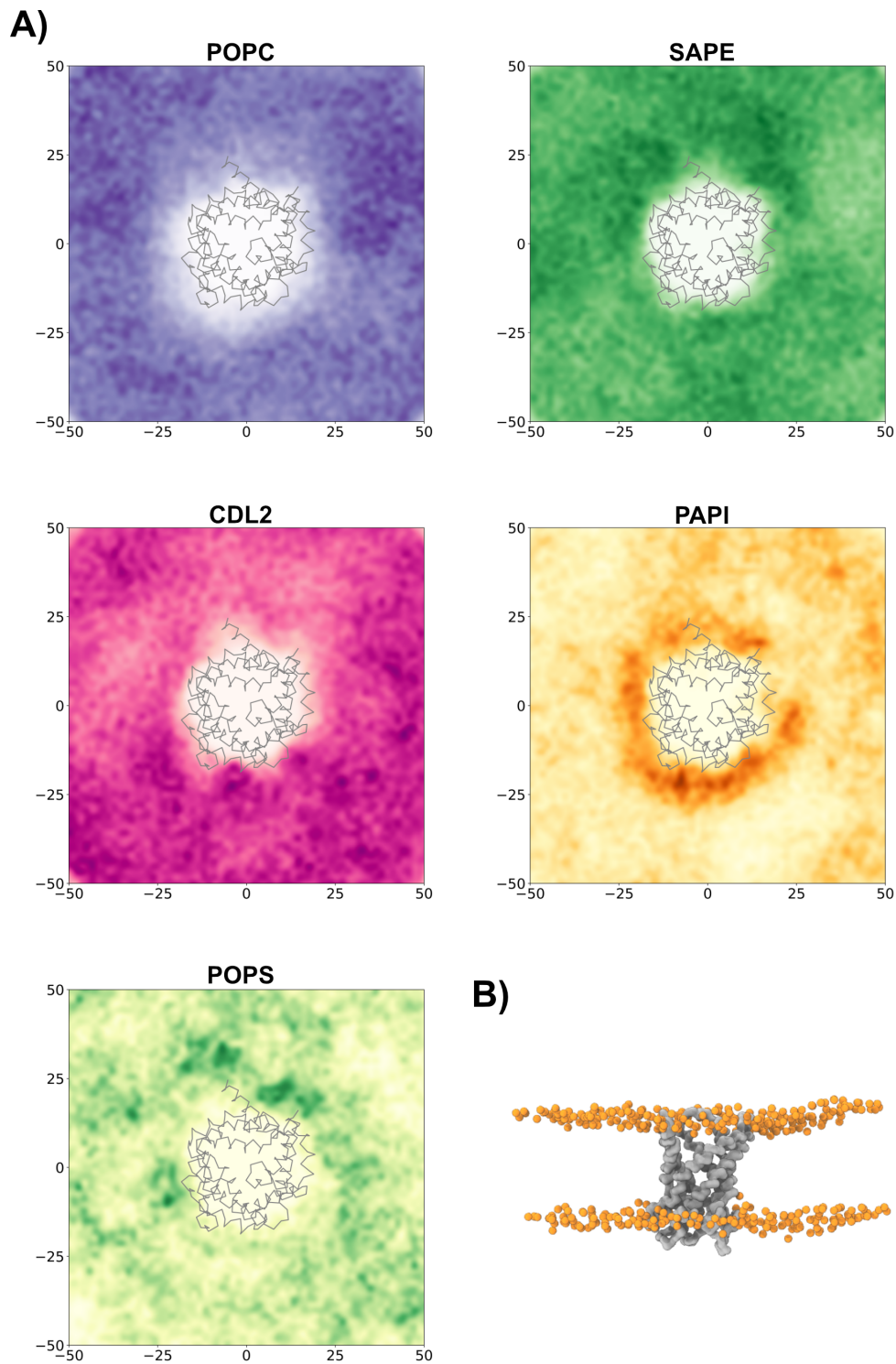
SI Figure 1. ATPase high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.



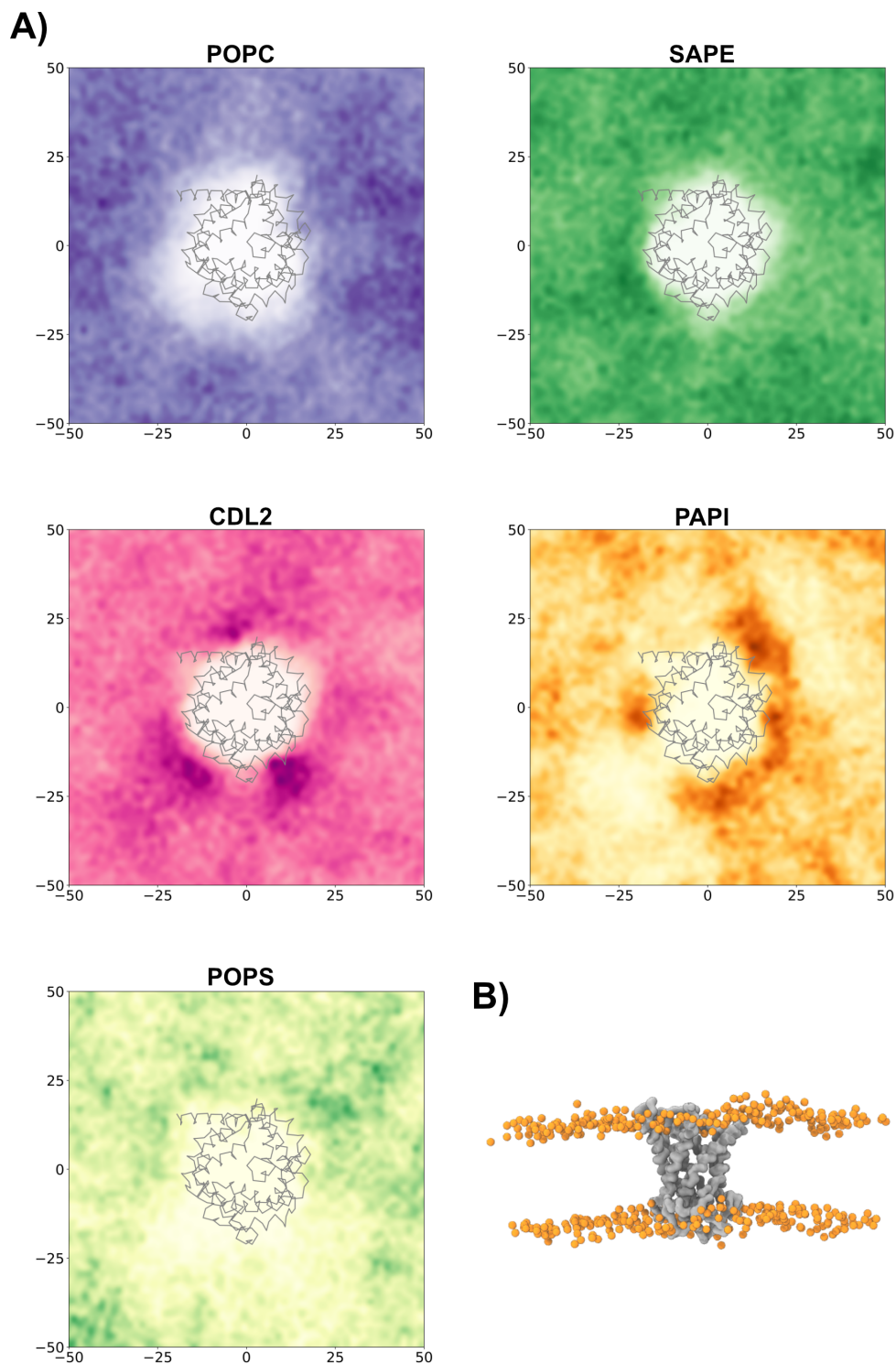
SI Figure 2. Complex II high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.



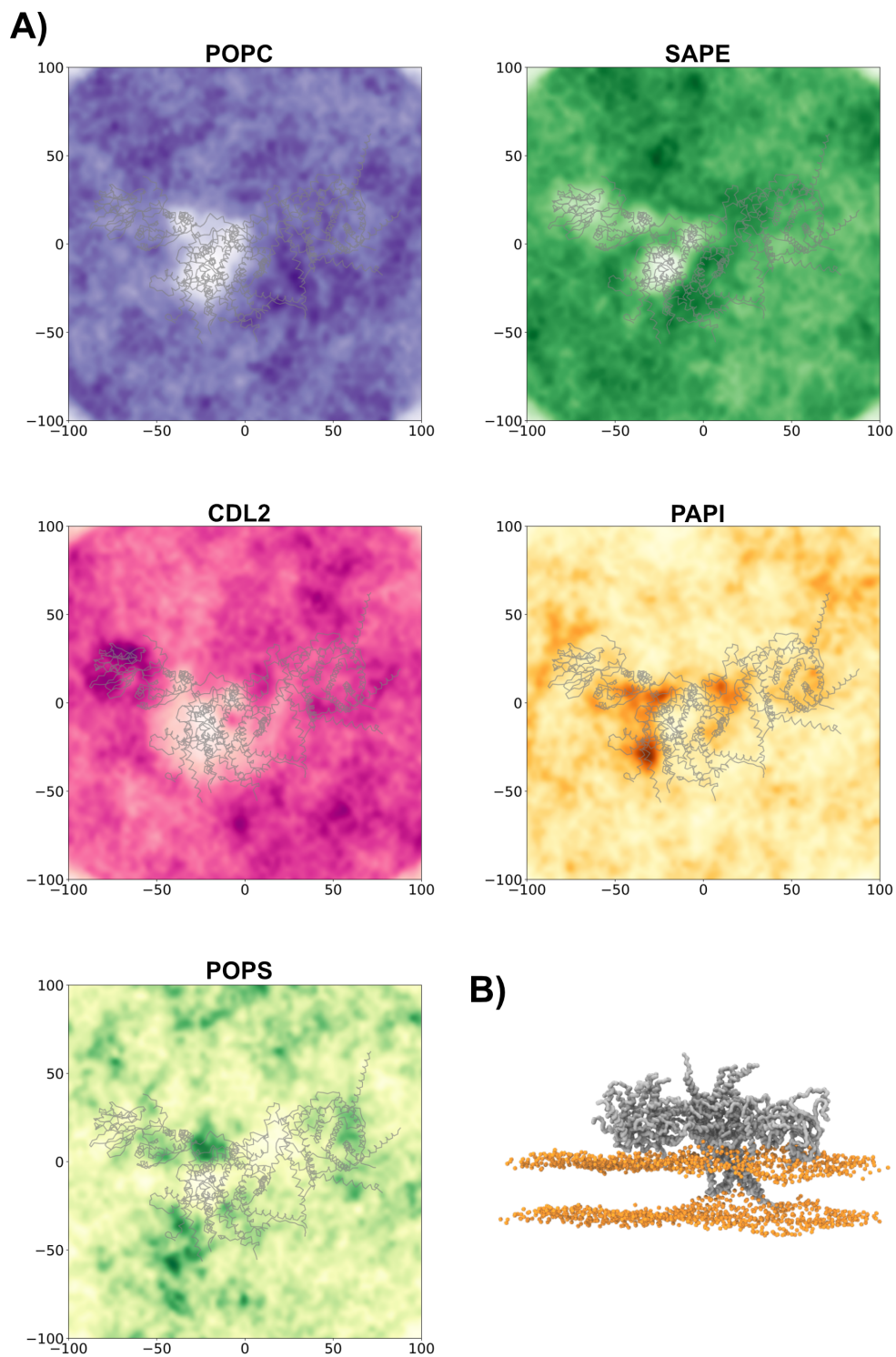
SI Figure 3. Respiratory supercomplex high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.



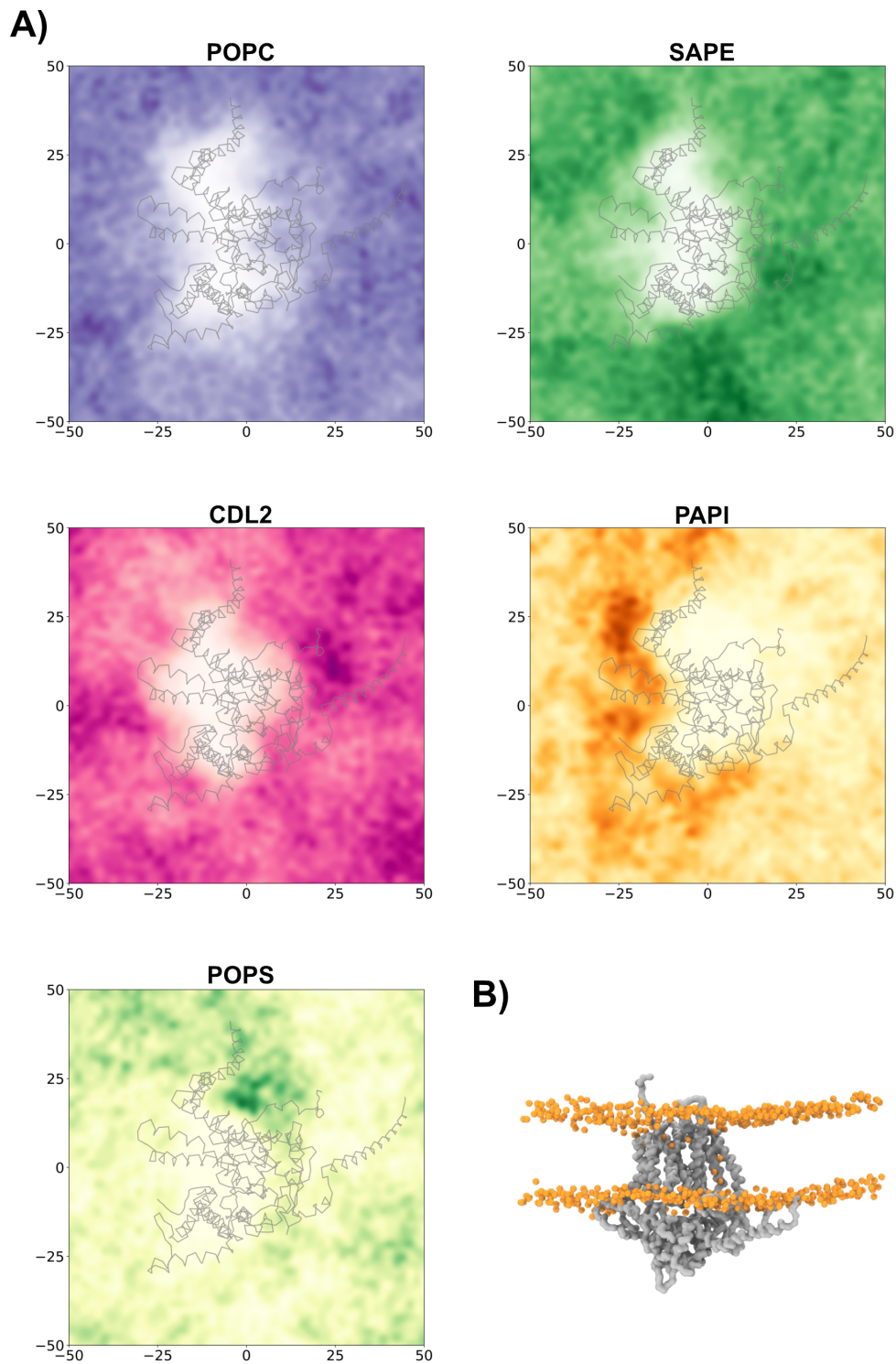
SI Figure 4. ANT1 high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.



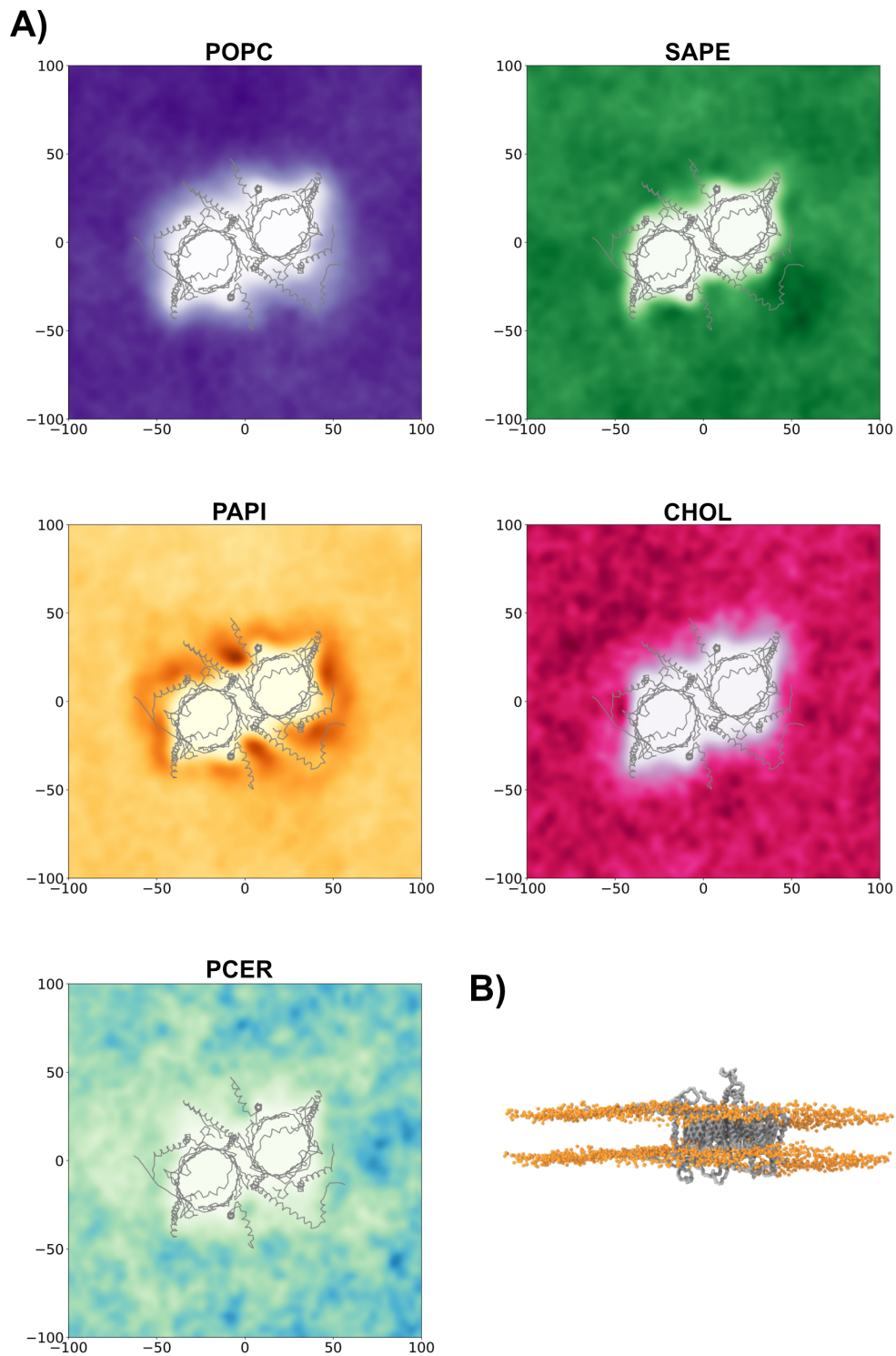
SI Figure 5. ANT2 high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.



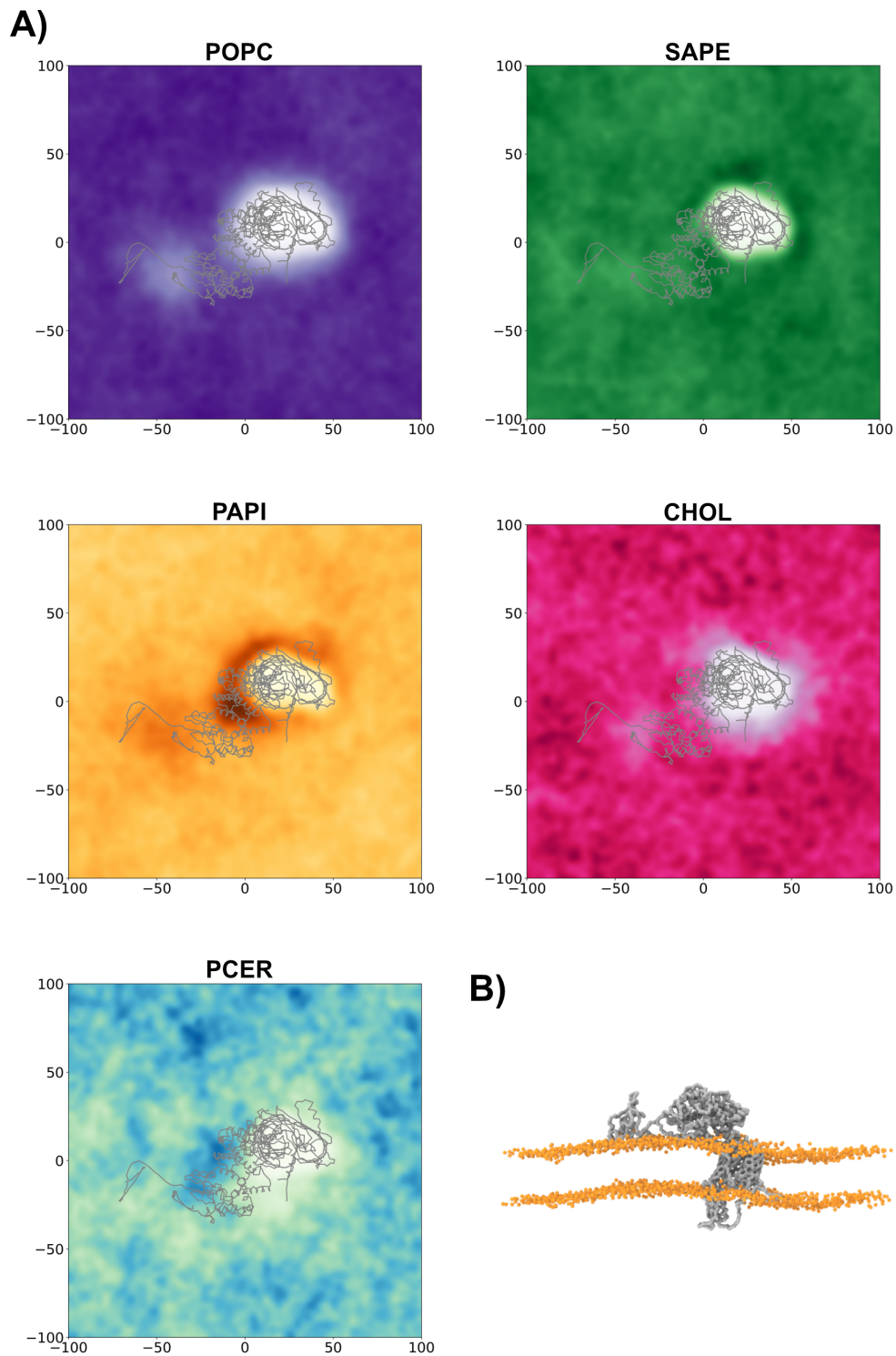
SI Figure 6. TIM22 high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.



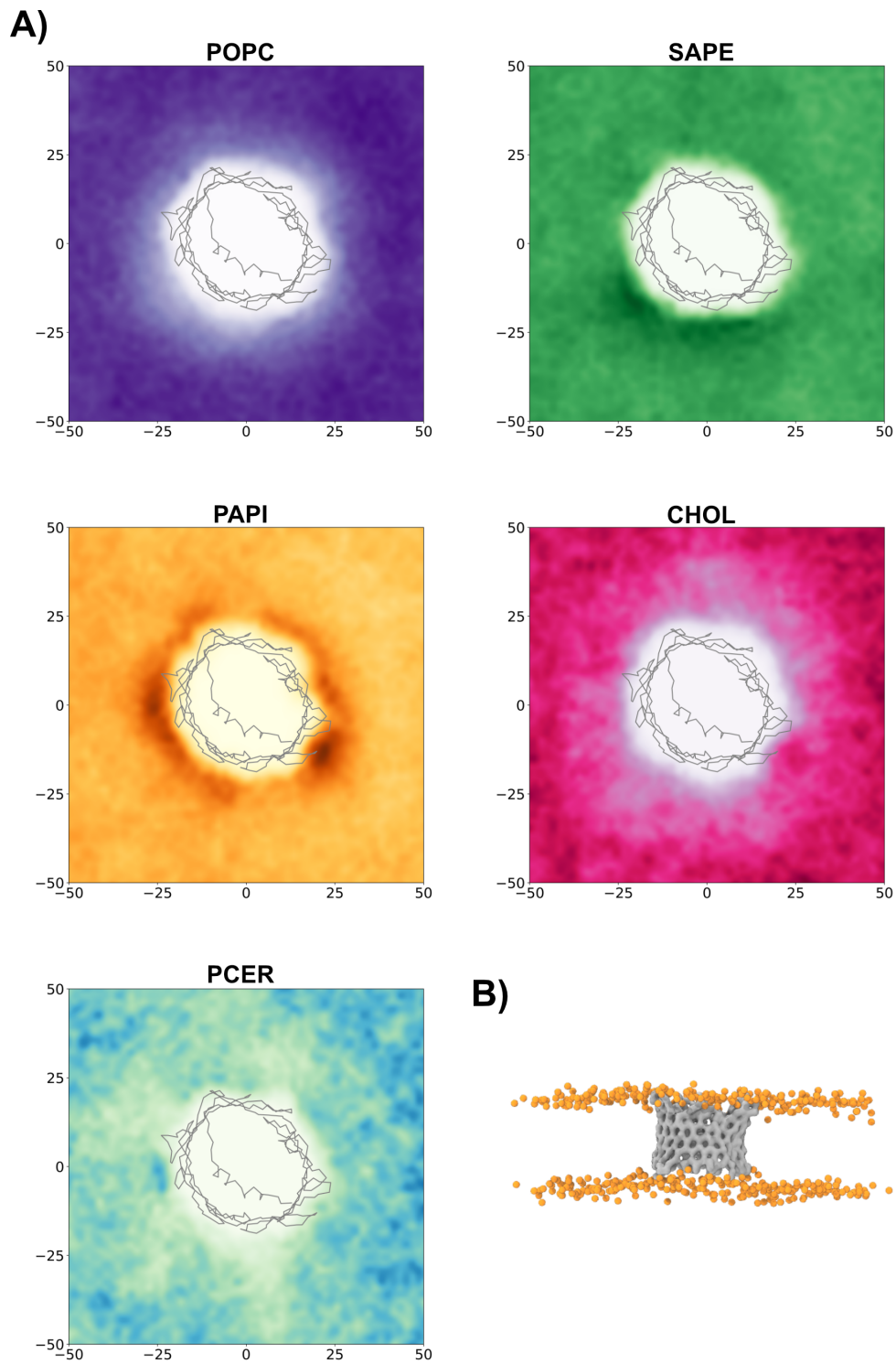
SI Figure 7. TIM23 high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.



SI Figure 8. TOM complex high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.

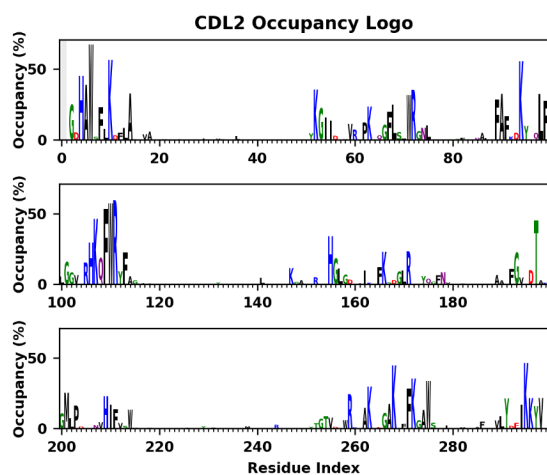
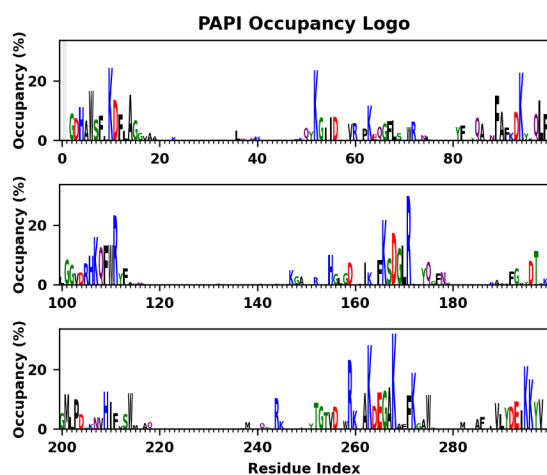


SI Figure 9. SAM complex high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.

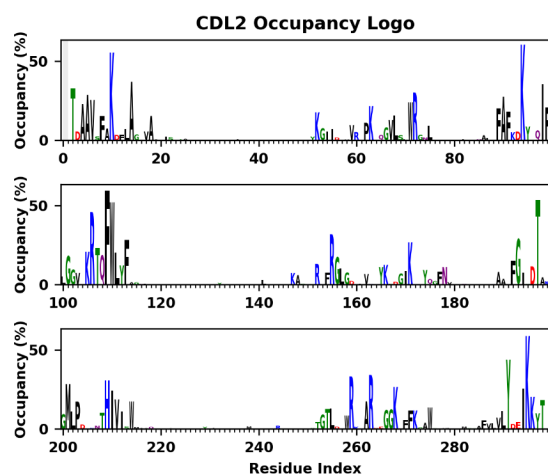
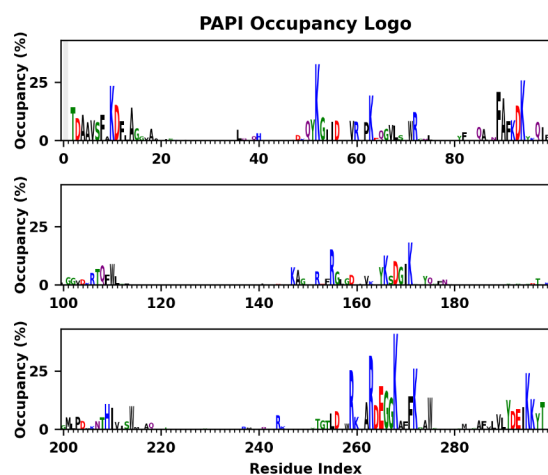


SI Figure 10. VDAC1 high-throughput results. A) Lipid density plots for each lipid in the system. The darker the color indicates the higher the density over all simulations. The protein backbone is shown as gray lines. B) A final frame from a simulation, showing the effect on membrane curvature. The phosphate headgroups are shown as orange spheres and the protein backbone as a gray surface.

ANT1

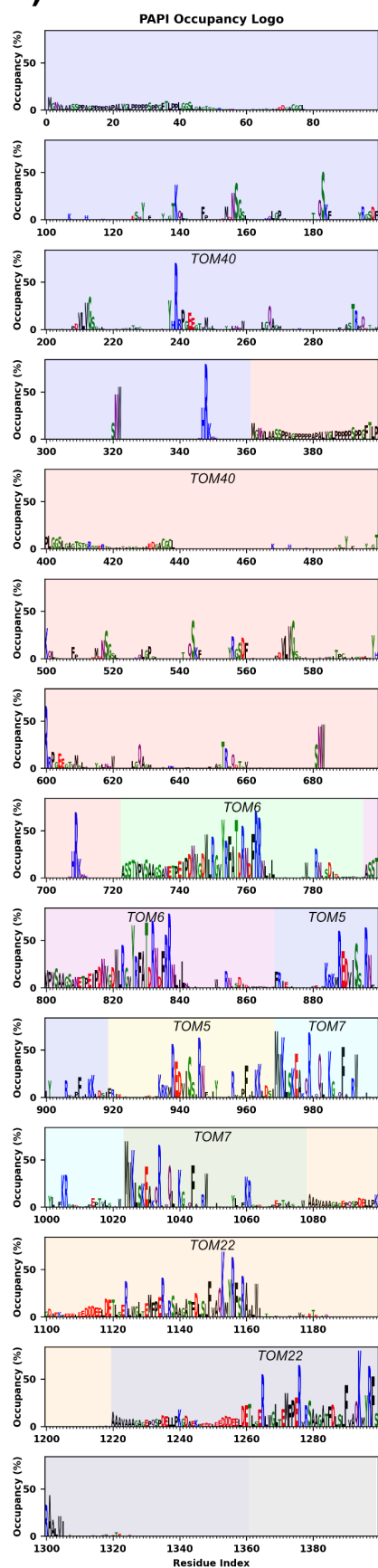


ANT2

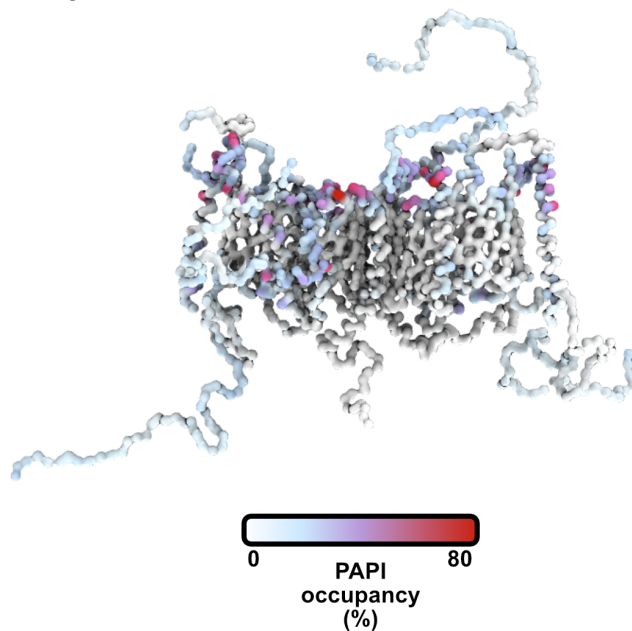


SI Figure 11. ANT1 (left) & ANT2 (right) interaction with PAPI (top) and CDL2 (bottom) in high-throughput simulation. The height of the residue shows the amount of simulation time that the respective lipid headgroup was in contact with that residue. The residue letters are colored by chemistry.

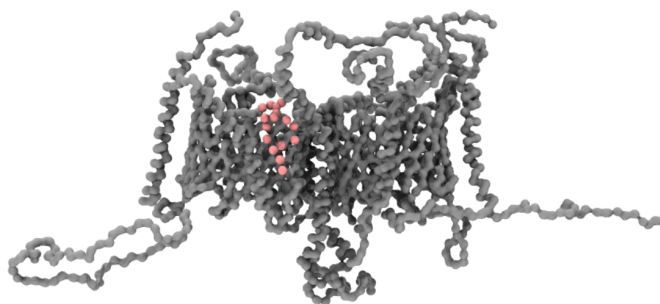
A)



B)

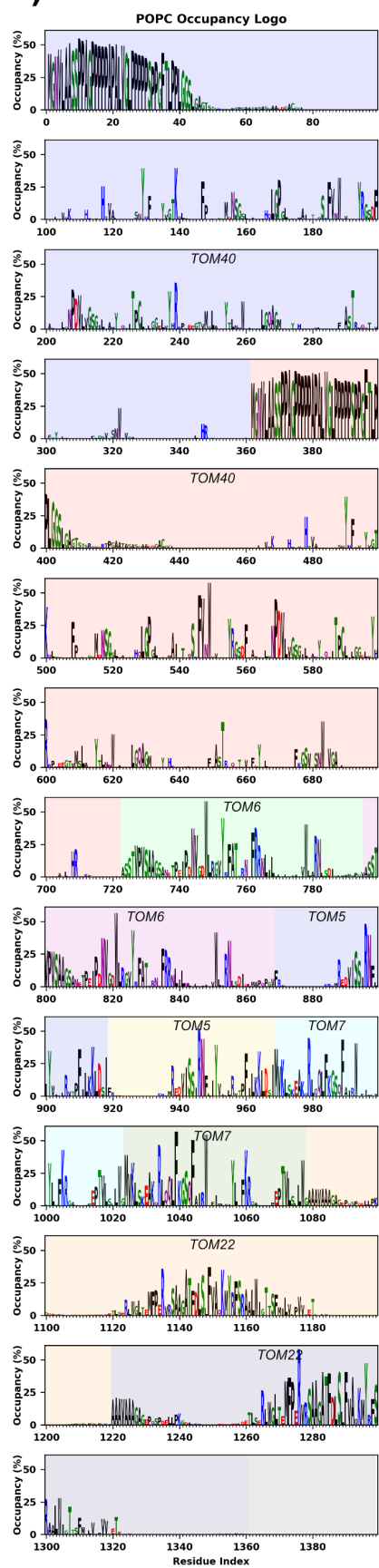


C)

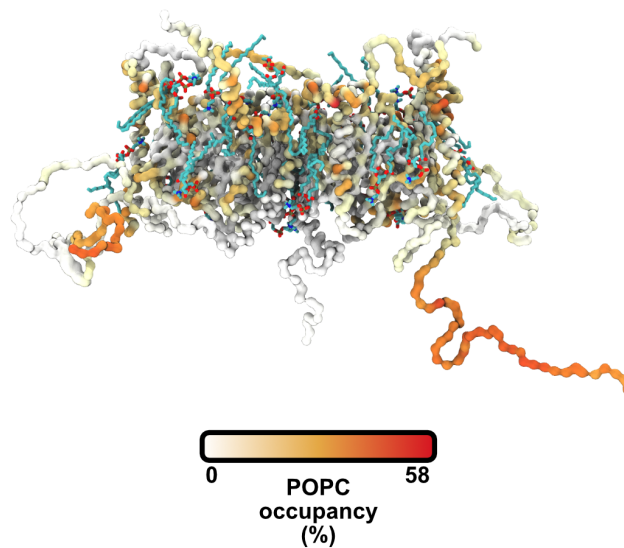


SI Figure 12. TOM complex interaction with PAPI. (A) The PAPI headgroup occupancy averaged over all high-throughput simulations, with the taller residues showing higher occupancy. The separate protein chains have different background color and are labelled as the subunit. The residue letters are colored by chemistry. (B) The TOM complex colored by the contact with the headgroups PAPI. The color shows the amount of contact, with a darker color showing increased lipid occupancy. (C) The TOM complex is shown as a gray surface, and a bound pose predicted by PyLipID shows a PAPI lipid in pink spheres.

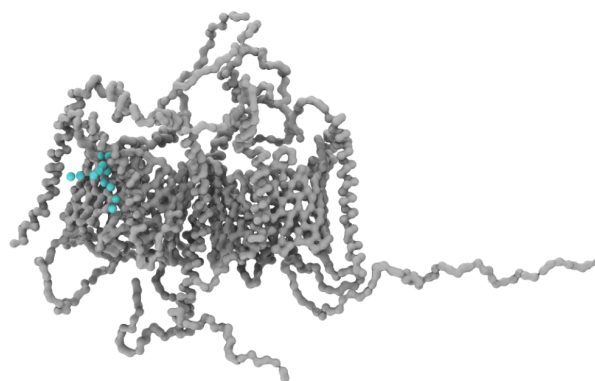
A)



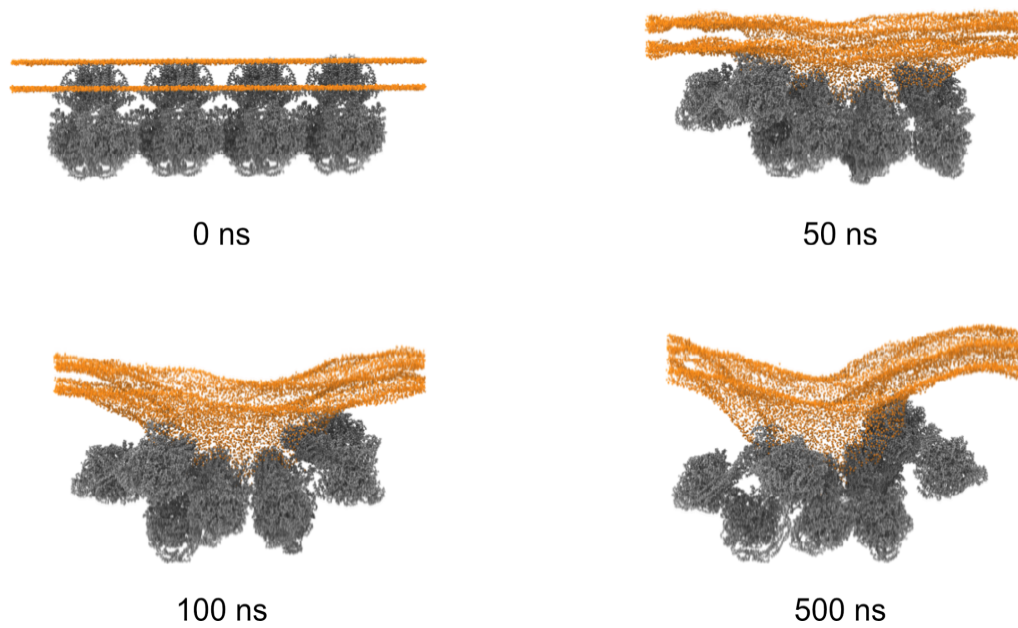
B)



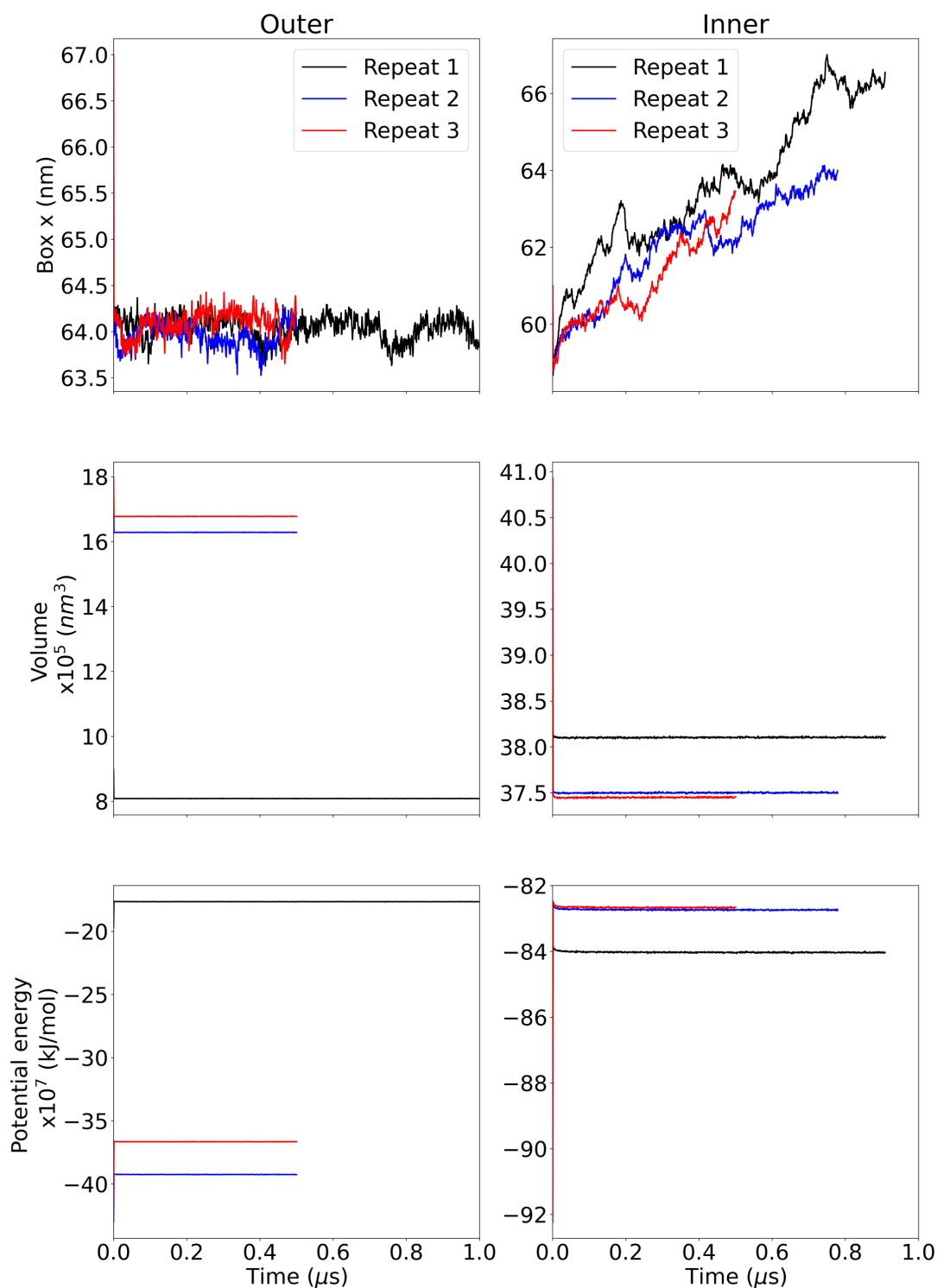
C)



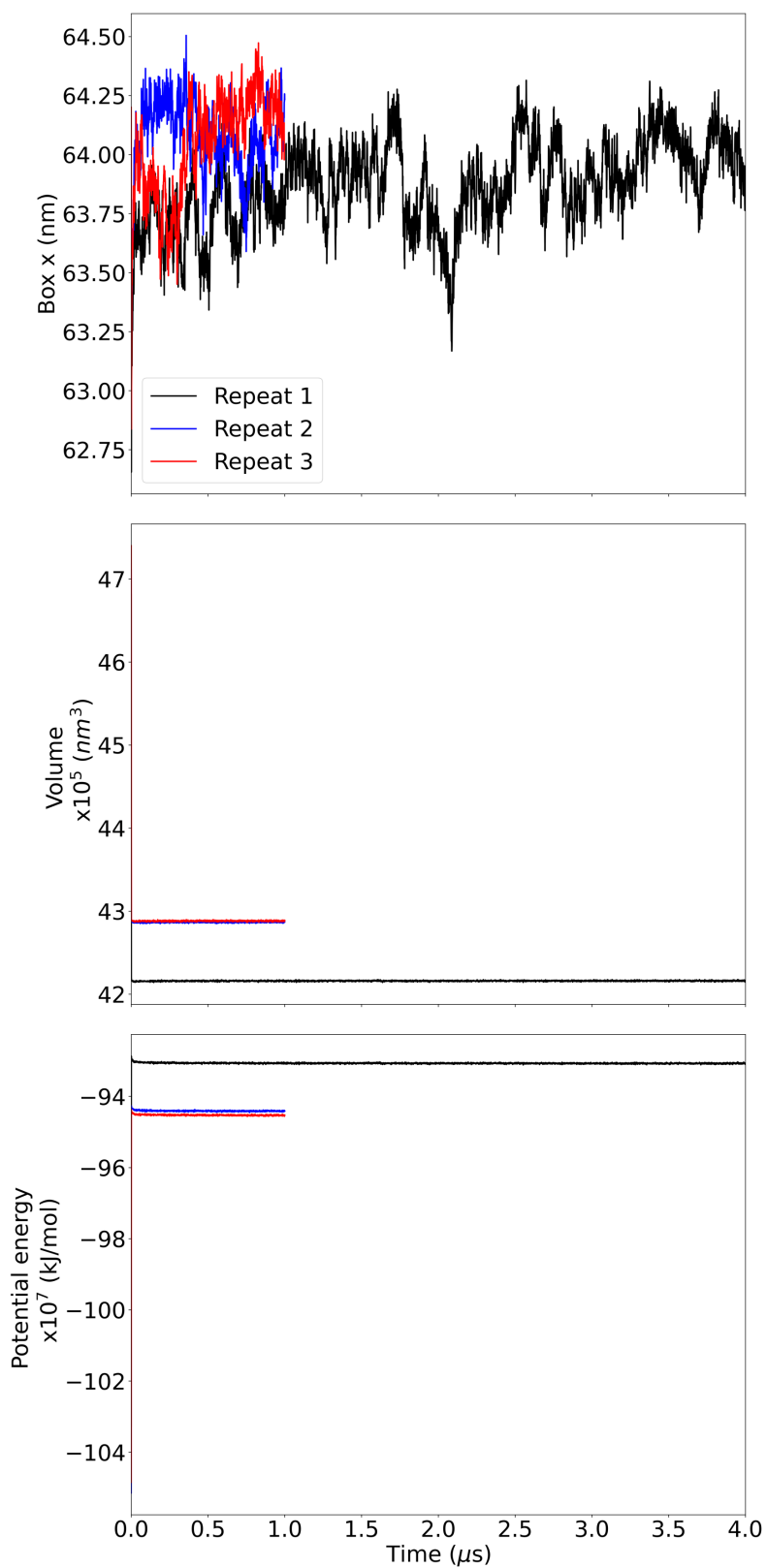
SI Figure 13. TOM complex interaction with POPE. (A) The POPE headgroup occupancy averaged over all high-throughput simulations, with the taller residues showing higher occupancy. The separate protein chains have different background color and are labelled as the subunit. The residue letters are colored by chemistry. The experimentally resolved POPC lipids [PDB ID: 7VD2] are shown as cyan sticks. (B) The TOM complex colored by the contact with the headgroups PAPI. The color shows the amount of contact, with a darker color showing increased lipid occupancy. (C) The TOM complex is shown as a gray surface, and a bound pose predicted by PyLipID shows a POPE lipid in cyan spheres.



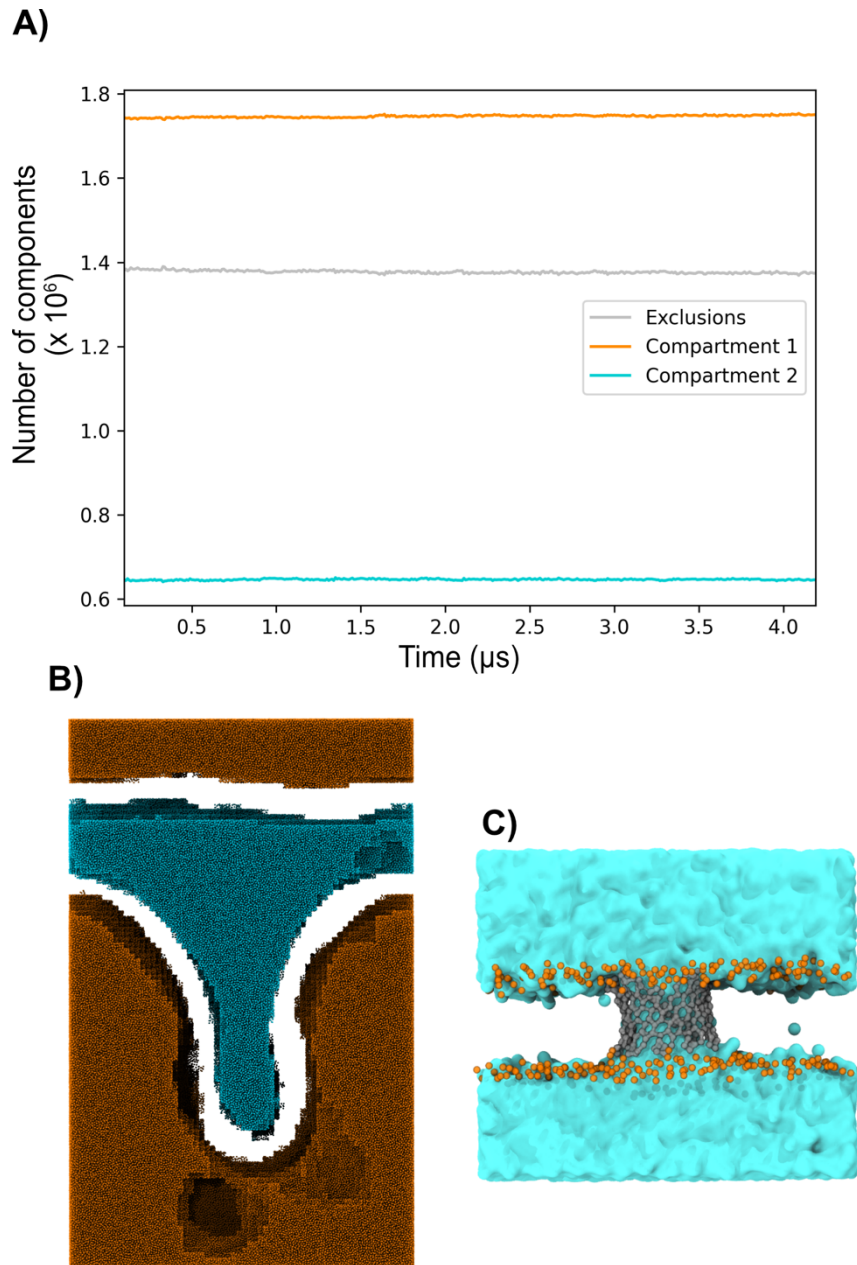
SI Figure 14. Snapshots from a simulation with a row of ATPase dimers. The phosphate head groups are shown as orange spheres and the protein backbone is shown as a gray surface.



SI Figure 15. Analysis of system behaviour for membranes simulated individually. The left graphs show results from the OMM, while the right are from the IMM. Top graph shows the x (equal to y) box dimension, the middle graphs show the volume of the simulation box and the bottom graphs show the potential energy of the system.

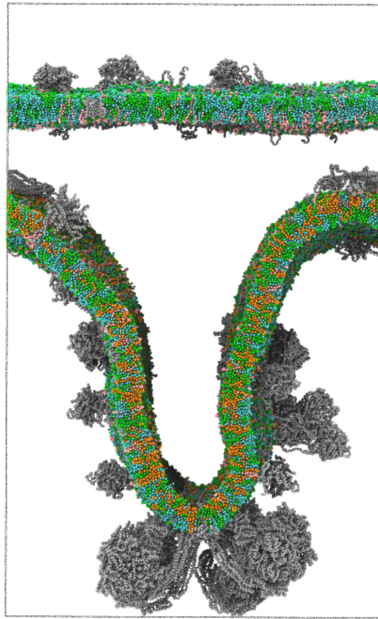


SI Figure 16. Analysis of system behaviour for the crista model. Top graph shows the x (equals y) box dimension, the middle graphs show the volume of the simulation box and the bottom graphs show the potential energy of the system.

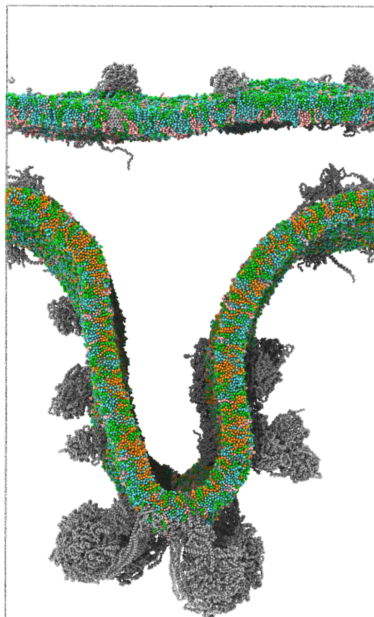


SI Figure 17. Movement of water in the simulation box. A) The fluctuation of the major compartments of water. The simulation box is separated by exclusions, which is comprised of the lipids, proteins and any water molecules within 8 nm of these. The system is then separated into two compartments, which represent the area between the bilayers and the water connected by the periodic conditions above the outer mitochondrial membrane and below the inner mitochondrial membrane, a visual representation can be seen in B). B) A snapshot showing the two compartments (1 in orange and 2 in cyan), which are separated by the exclusion group, not shown here C) A snapshot of a small VDAC1 simulation, showing the ability of water to pass through the β -barrel. The water is shown as a surface, the phosphate headgroups shown as orange spheres and the protein backbone shown as a grey surface.

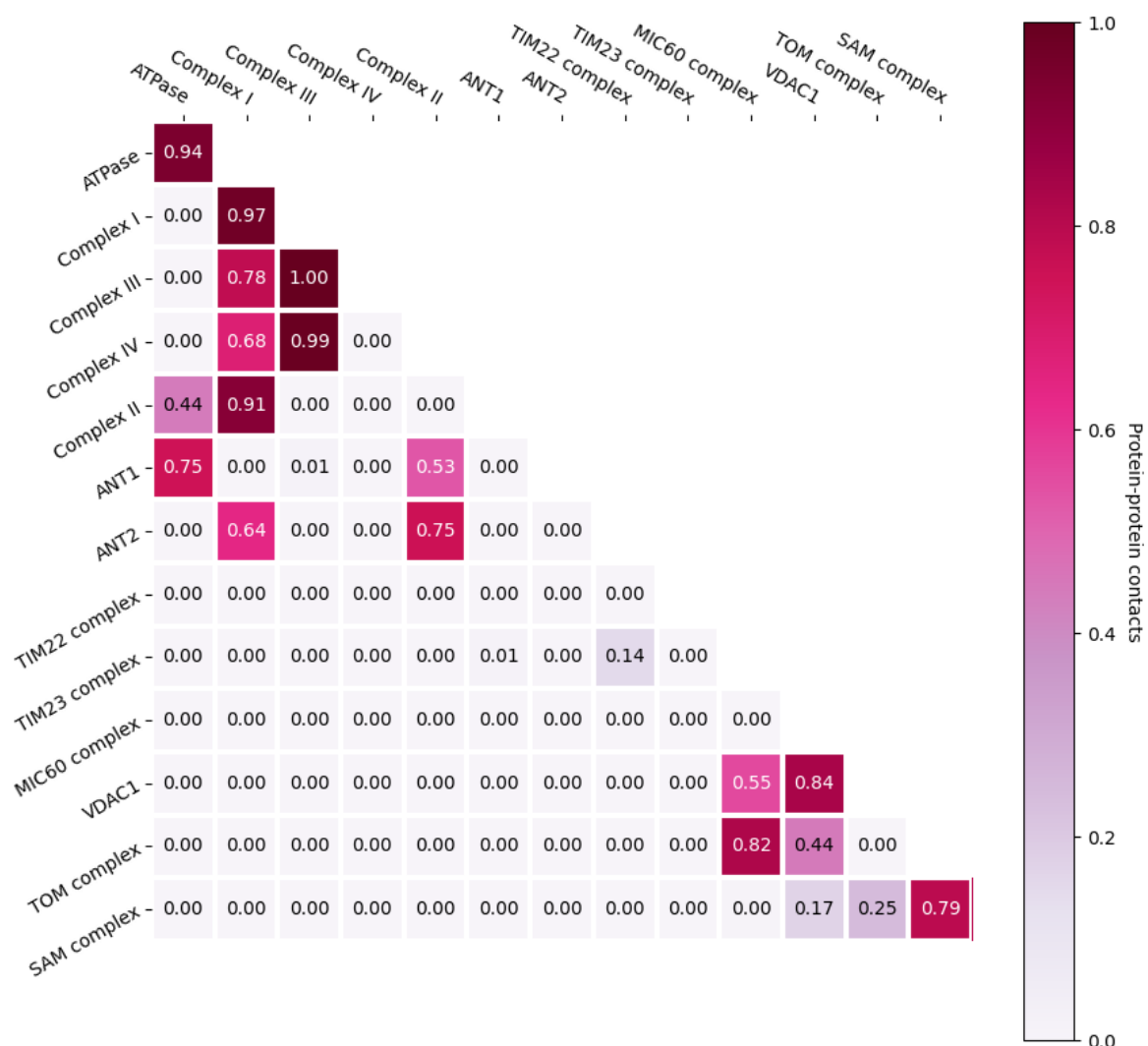
Simulation 2



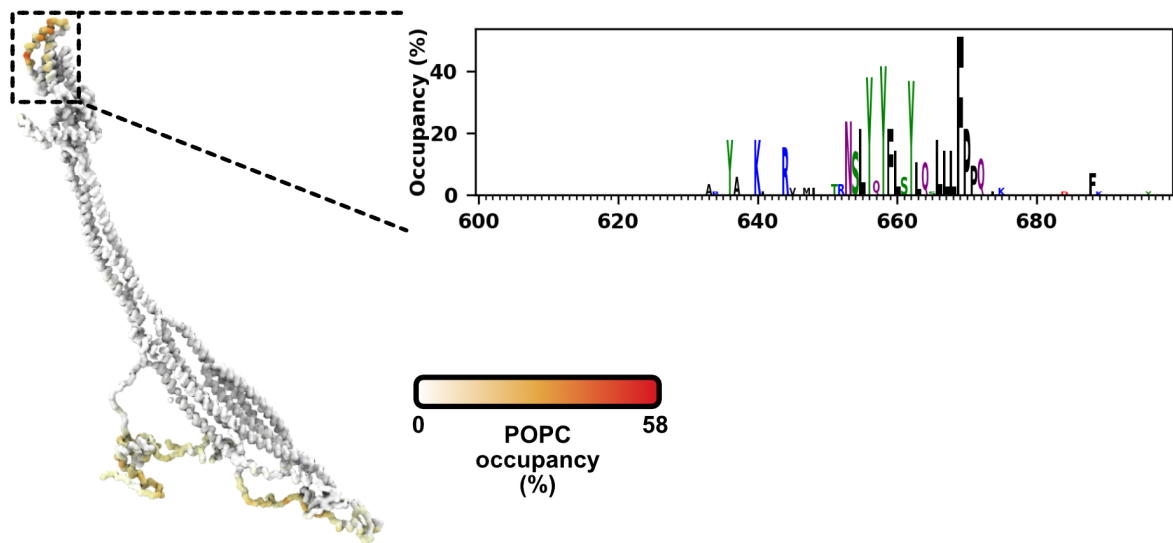
Simulation 3



SI Figure 18. The final frame of the two further independent simulations performed of the cristae model after 1 μ s of simulation. Protein backbone is shown in gray, with lipids shown as colored spheres. These systems contain one copy of the respiratory supercomplex (whereas Simulation 1 contained two copies).

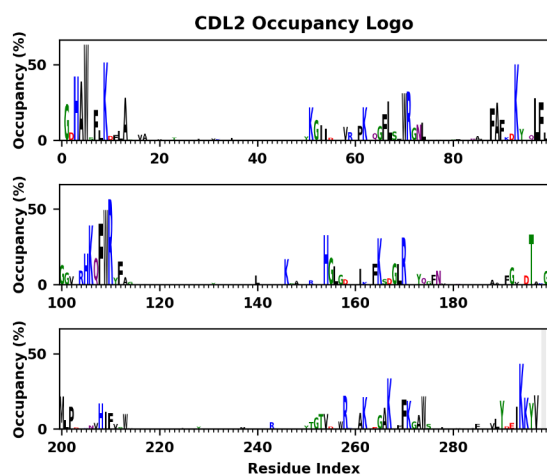
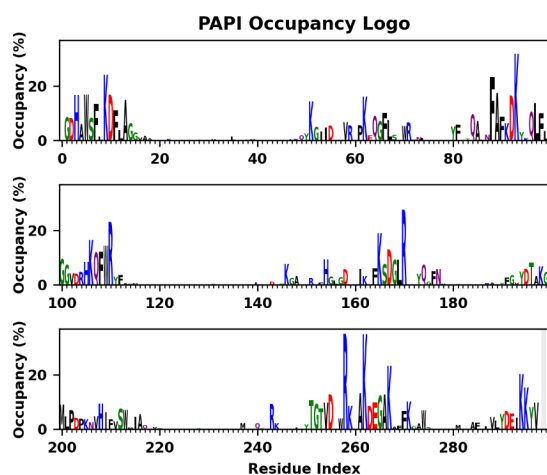


SI Figure 19. Protein-protein contacts for Simulation 1 of the model cristae system averaged over each protein type, and between protein pairs. The darker the color, the more contacts between protein types. A value of 1 would suggest contact (within 8 Å) between at least one copy of the protein pair over the whole simulation.

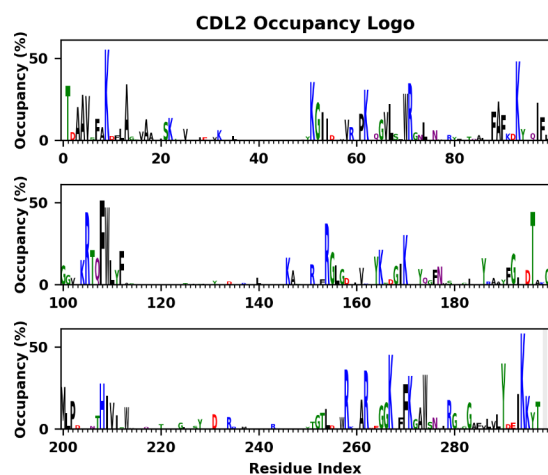
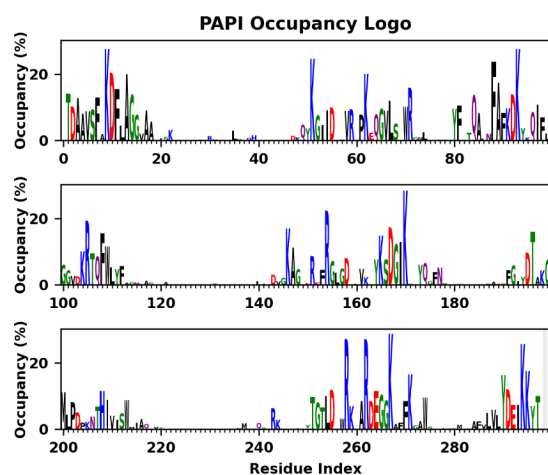


SI Figure 20. MIC60 subcomplex contact with lipids in the full cristae model. On the left, the MIC60 subcomplex colored by the contact with the headgroups POPC, the major lipid in the OMM. The color shows the amount of contact, with a darker color showing increased lipid occupancy. The graph shows the lipid headgroup occupancy averaged over both copies of the MIC60 subcomplex in the system for the highlighted region, coloured by residue chemistry.

ANT1



ANT2



SI Figure 21. ANT1 (left) & ANT2 (right) interaction with PAPI (top) and CDL2 (bottom) in model crista simulation. The height of the residue shows the amount of simulation time that the respective lipid headgroup was in contact with that residue. The residue letters are colored by chemistry.