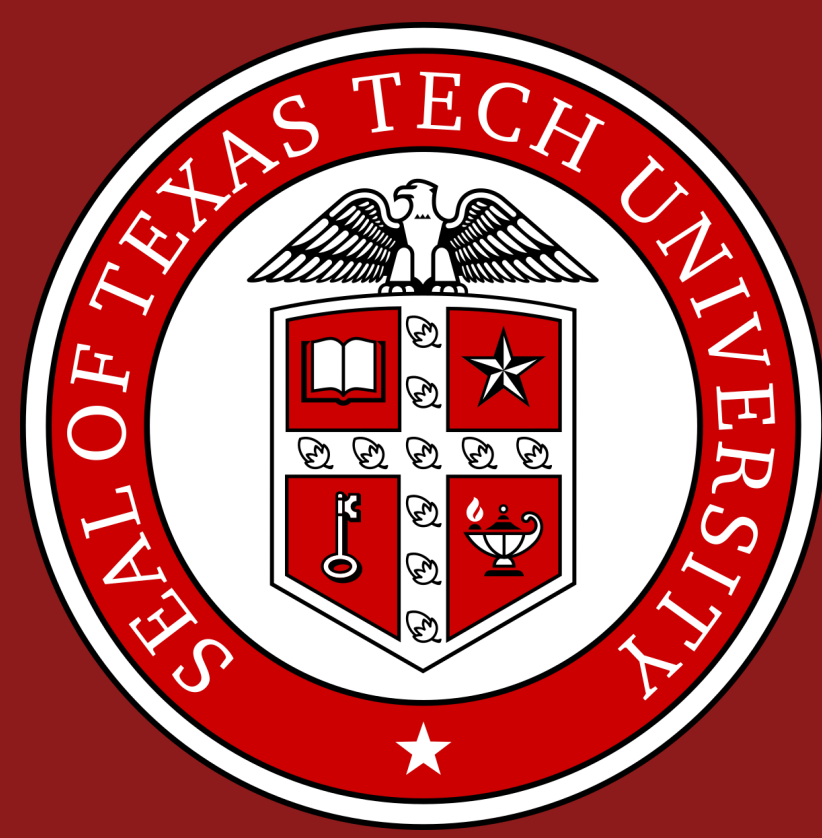




Ion-Specific Effects of KCl and NaCl on the Structural Properties of DPPC Lipid Bilayers

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Introduction

Dipalmitoylphosphatidylcholine (DPPC) is a phospholipid commonly found in lung surfactant and is widely used as a model system to investigate lipid membrane structure and dynamics. DPPC consists of two saturated acyl chains and exhibits distinct structural phases depending on temperature, including the gel phase, ripple gel phase, and liquid-crystalline phase. [1]

Temperature and dissolved ions can influence lipid packing, acyl-chain ordering, and overall bilayer structure. These changes can be characterized through measurements of area per lipid, acyl-chain order parameters, bilayer thickness, and mass density.

In this study, molecular dynamics (MD) simulations were performed to investigate the effects of temperature and ionic environments on DPPC bilayers. Pure DPPC systems were examined at 298 K, 310 K, and 325 K, while additional simulations containing NaCl and KCl were conducted at 310 K to evaluate ion-specific effects on membrane structure.

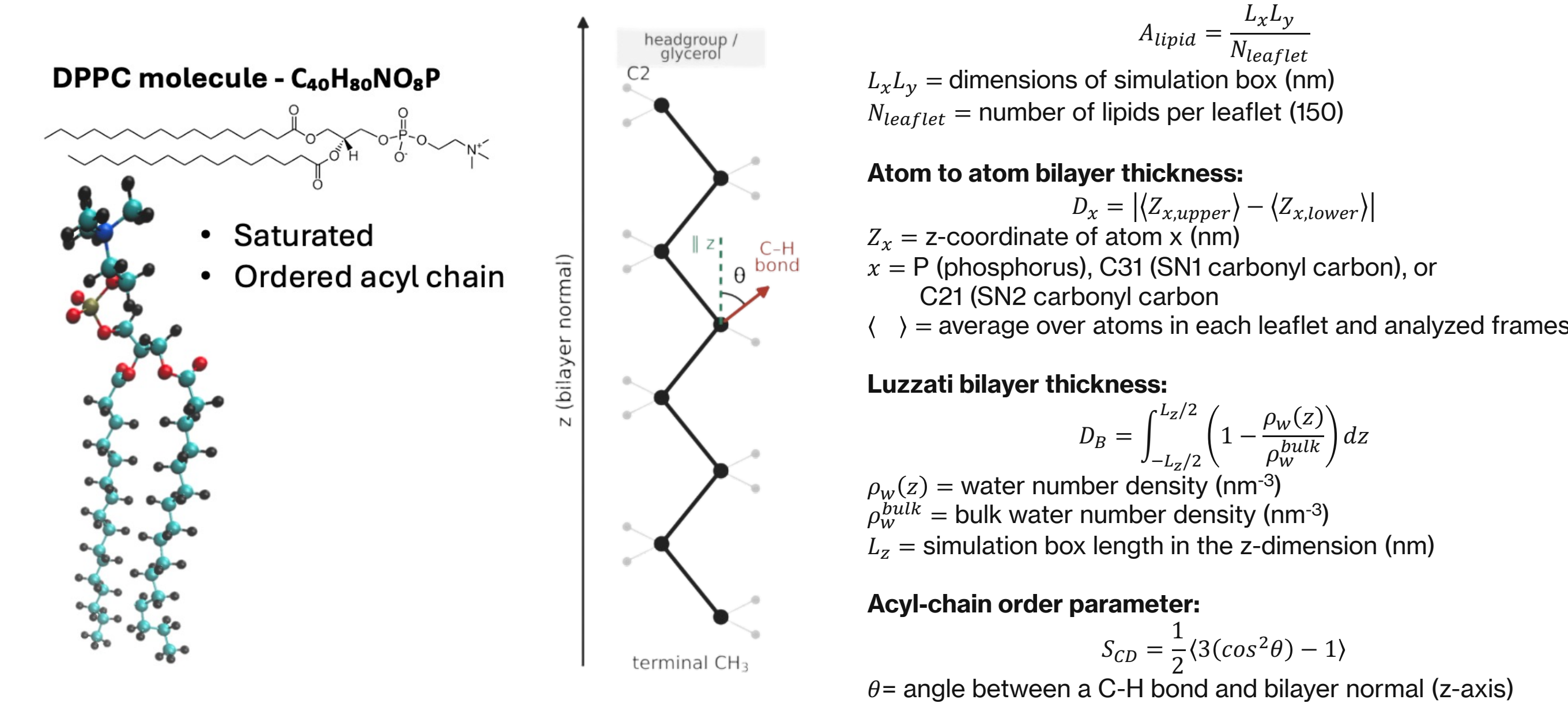


Fig 1 – DPPC molecule ($C_{40}H_{80}NO_8P$) and the structural parameters used in the analysis

Methodology

- DPPC bilayers prepared with CHARMM-GUI [2] and simulated using GROMACS 2024.3. [3]
- Systems were equilibrated under NVT and NPT conditions before production dynamics.
- Structural analysis used the final 50 ns of the trajectories.
- Area per lipid (APL), SN1/SN2 acyl-chain order parameters (S_{CD}), bilayer thickness, and mass-density profiles were evaluated.
- Thickness was estimated using phosphate–phosphate (P–P), carbonyl–carbonyl (SN1 and SN2), and Luzzati definitions.

Temperature series

Pure DPPC at 298, 310 and 325 K
Compare thermal changes in membrane structure

Ionic series (310 K)

Pure DPPC, DPPC + NaCl, DPPC + KCl
Compare ion-dependent changes at 310 K

DPPC Bilayer

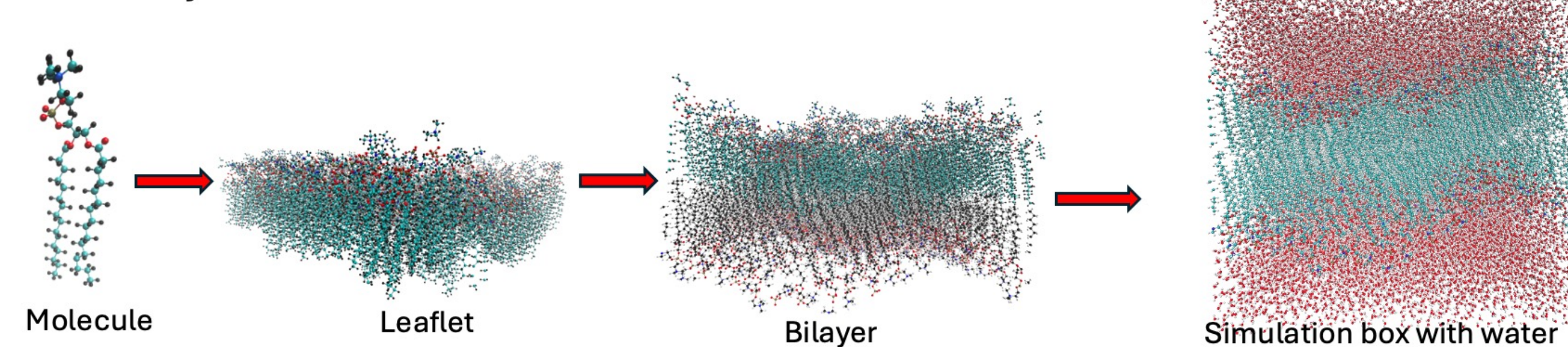


Fig 2 – Building DPPC bilayer boxes using CHARMM-GUI

Energy minimization
Removes clashes and bad contacts

NVT equilibration
Constant volume; stabilizes temperature

NPT equilibration
Constant pressure; relaxes density and box size

Production run
400 ns; final 50 ns analysed

Fig 3 – GROMACS simulation workflow used for every system

Analysis

A. Temperature behavior (pure DPPC: 298, 310, 325 K)

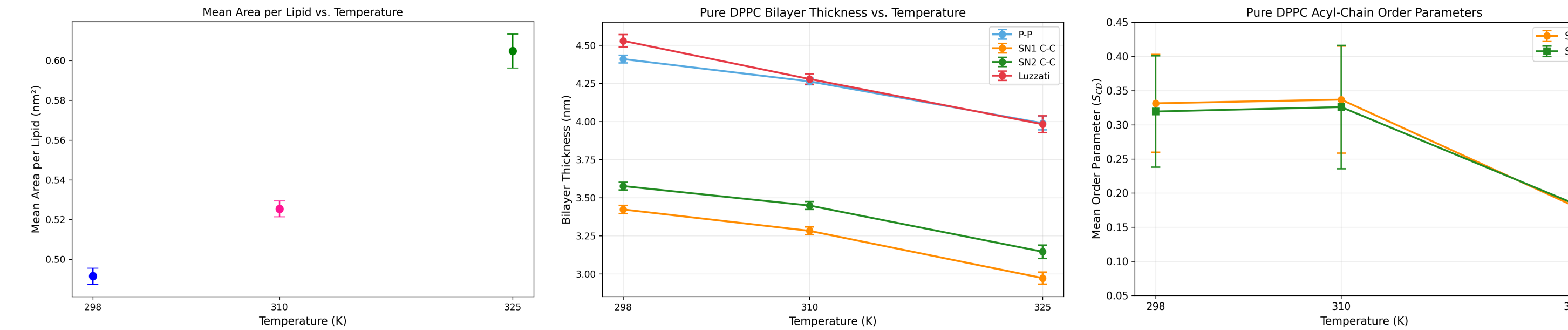


Fig 4 – Pure DPPC vs temperature: mean area per lipid (left), bilayer thickness by four definitions (centre) and mean SN1/SN2 order parameter (right)

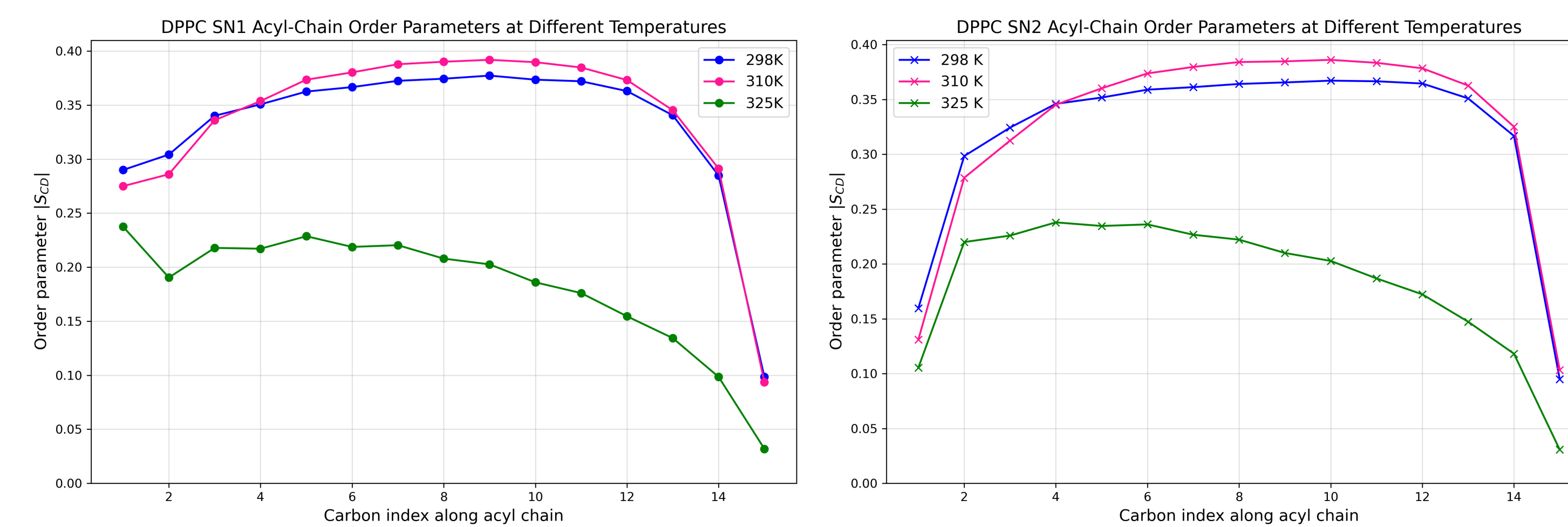


Fig 5 – Carbon-resolved order parameter S_{CD} along the SN1 (left) and SN2 (right) acyl chains at 298, 310 and 325 K

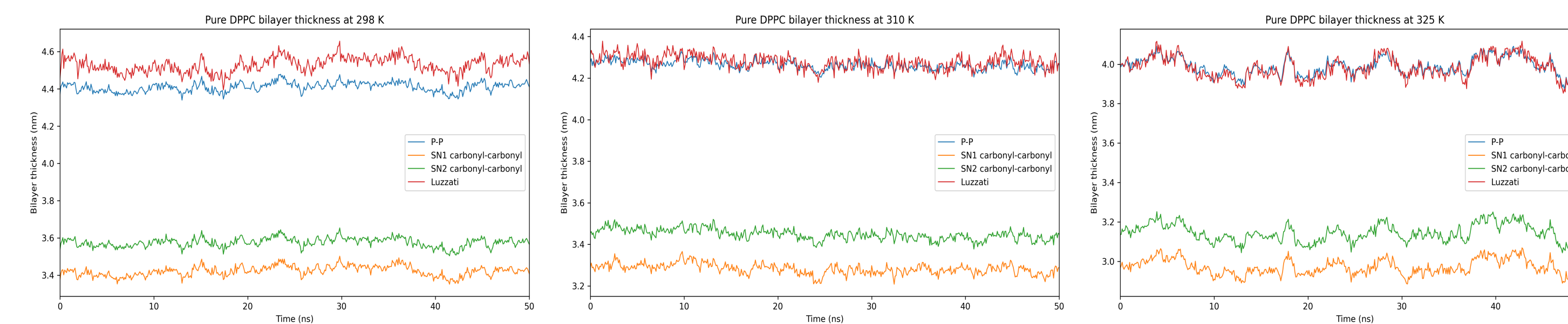


Fig 6 – Time series of P–P, Luzzati, SN1 and SN2 bilayer thickness at 298 K (left), 310 K (centre) and 325 K (right)

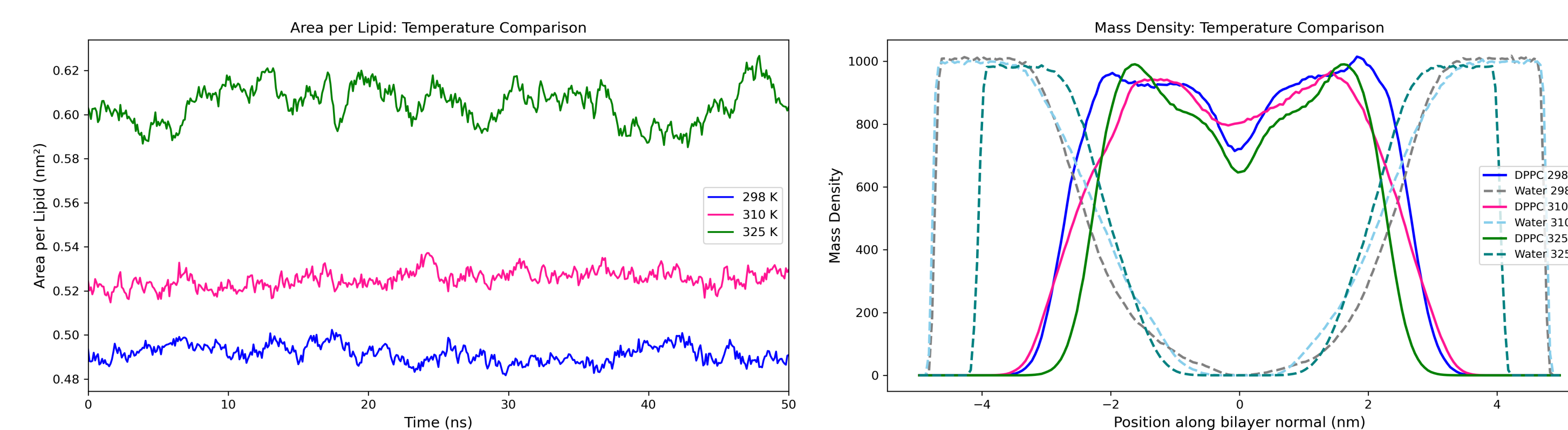


Fig 7 – Area per lipid over time (left) and DPPC/water mass-density profiles along the bilayer normal (right) at each temperature

Increasing temperature resulted in an increase in area per lipid (APL), consistent with the transition of DPPC from the gel phase to the liquid-crystalline phase. At 325 K, the acyl-chain order parameters decreased substantially, indicating increased lipid disorder and chain mobility. Mass-density profiles also exhibited changes in peak shape and distribution at 325 K, reflecting structural reorganization of the bilayer. Additionally, phosphate–phosphate (P–P) and Luzzati thickness measurements showed a noticeable separation at 298 K but converged at 310 K and 325 K, suggesting temperature-dependent changes in bilayer structure.

B. Ion-specific effects at 310 K (NaCl vs KCl)

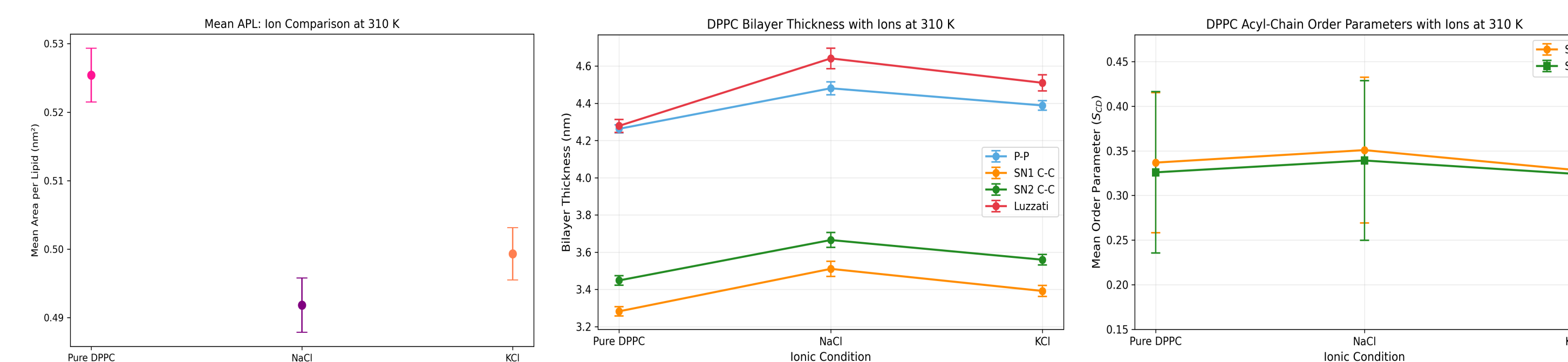


Fig 8 – Pure DPPC, DPPC + NaCl and DPPC + KCl at 310 K: mean area per lipid (left), bilayer thickness (centre) and mean order parameter (right)

Analysis (Contd.)

B. Ion-specific effects at 310 K (continued)

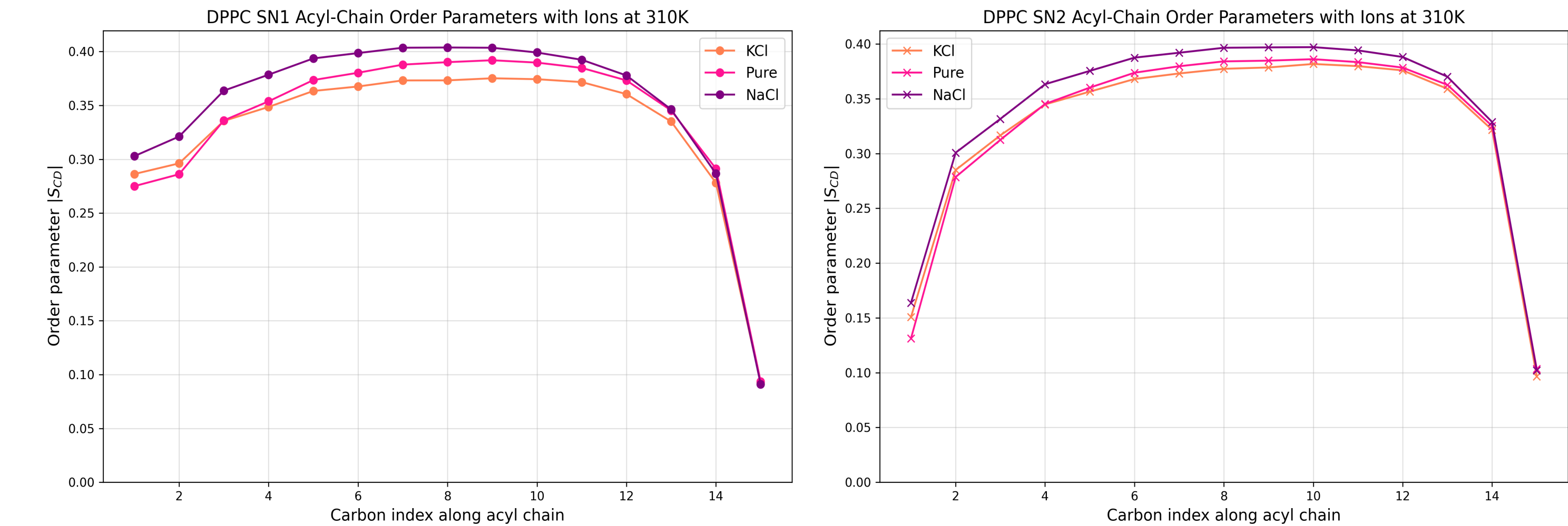


Fig 9 – Carbon-resolved order parameter S_{CD} along the SN1 (left) and SN2 (right) acyl chains for each ionic condition at 310 K

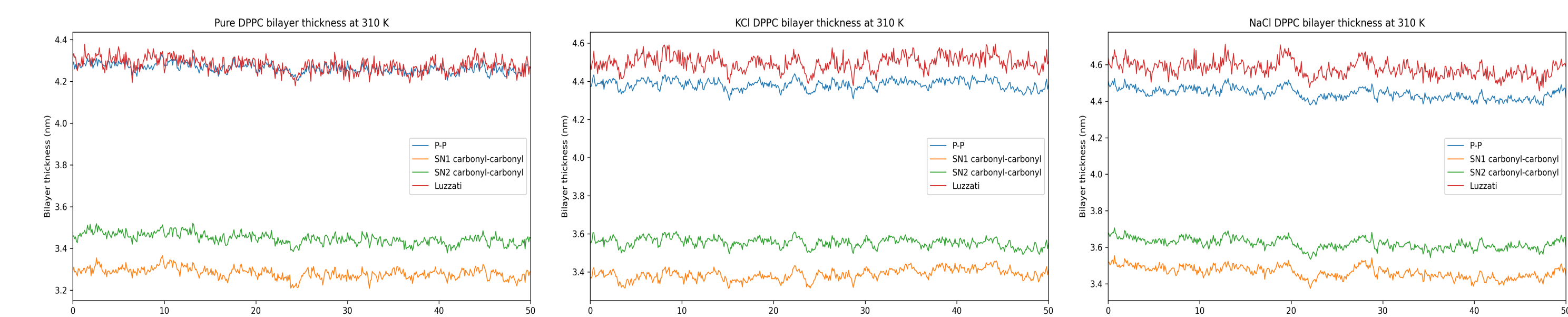


Fig 10 – Time series of P–P, Luzzati, SN1 and SN2 bilayer thickness for pure DPPC (left), DPPC + KCl (centre) and DPPC + NaCl (right)

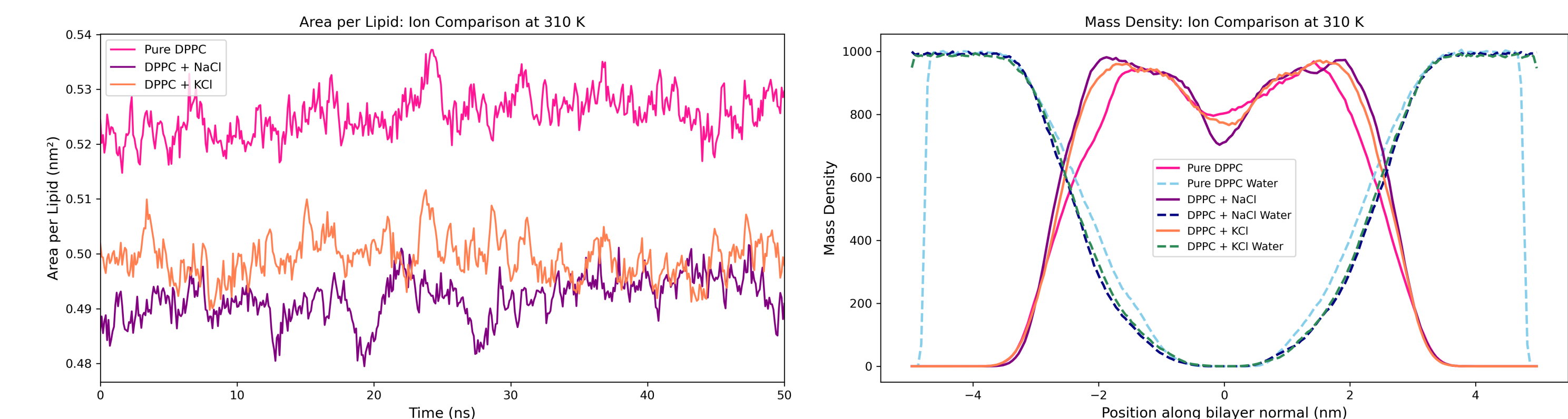


Fig 11 – Area per lipid over time (left) and DPPC/water mass-density profiles along the bilayer normal (right) for each ionic condition

The addition of NaCl and KCl resulted in a decrease in area per lipid (APL) compared to pure DPPC at 310 K, suggesting increased lipid packing. Phosphate–phosphate (P–P) and Luzzati thickness measurements exhibited similar values in pure DPPC but showed greater separation following the addition of ions, indicating ion-dependent changes in bilayer structure. Minor variations in the acyl-chain order parameters were also observed, suggesting subtle changes in lipid organization. Additionally, mass-density profiles exhibited slight shifts in peak positions and distributions, reflecting changes in the bilayer structure associated with the presence of ions.

Conclusion

- Temperature:** Increasing temperature increases area per lipid (APL) and decreases bilayer thickness, with a substantial reduction in acyl-chain order at 325 K, consistent with the transition to the liquid-crystalline phase.
- Ions at 310 K:** The addition of NaCl and KCl decreases APL and increases bilayer thickness relative to pure DPPC, suggesting tighter lipid packing. Minor changes in acyl-chain order parameters and mass-density profiles indicate subtle ion-specific effects on membrane structure.
- Future Work:** Investigate the effects of electric fields on DPPC membrane structure in the presence and absence of NaCl and KCl.

References

- [1] Nagle, J. F., & Tristram-Nagle, S. (2000). Structure of lipid bilayers. *Biochimica et Biophysica Acta*, 1469, 159–195. [https://doi.org/10.1016/S0304-4157\(00\)00016-2](https://doi.org/10.1016/S0304-4157(00)00016-2)
- [2] S. Jo, T. Kim, V.G. Iyer, and W. Im (2008) CHARMM-GUI: A Web-based Graphical User Interface for CHARMM. *J. Comput. Chem.* 29:1859-1865
- [3] GROMACS 2024.3 molecular simulation package <https://doi.org/10.5281/zenodo.13457083>