Supplemental Information

Unassisted N-Acetyl-Phenylalanine-Amide Transport across Membrane with Varying Lipid Size and Composition: Kinetic Measurements and Atomistic Molecular Dynamics Simulation.

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Electron Density Profile.

The electron density profiles for the DOPC 50 and POPC 50 systems studied throughout this article are plotted below in Figure 3.13. Experimental data was obtained from the article by Liu and Nagle.[58]
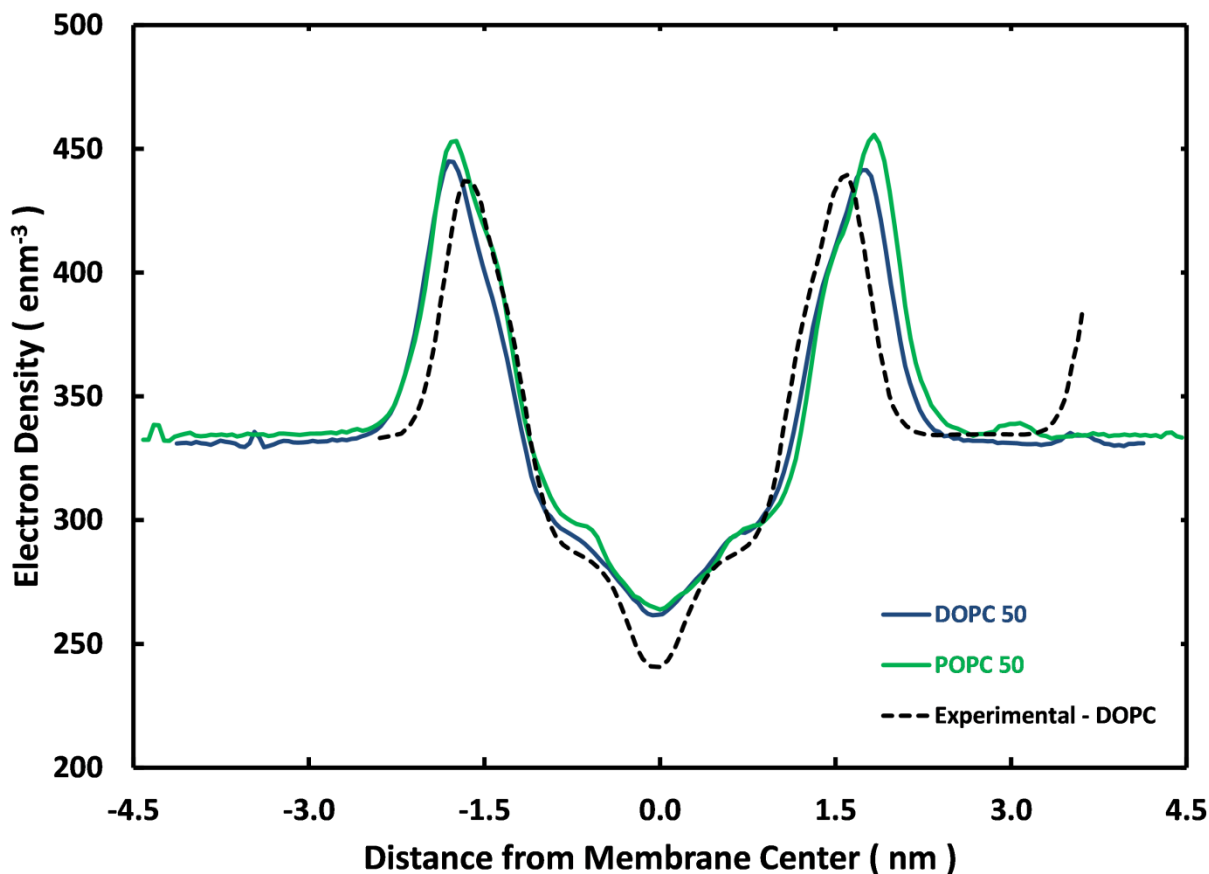

Figure 1. Electron density profiles for the DOPC and POPC 50 simulation systems.

PMF Quartiles.

The Potential of Mean Force (PMF) data reported within the primary article was calculated from the last half of the simulation trajectory, and the standard error was calculated using the Bootstrap method. However, these errors were

substantially smaller than the variation witnessed when the PMF was calculated over each quarter of the simulation, and varied between 1 and 20 kJmol^{-1} for the membrane interface and between 2 and 10 kJmol^{-1} for the central barrier. These PMFs are plotted below. The lightest line represents the 1st quarter, and the darkest line represents the PMF for the 4th and last quarter.
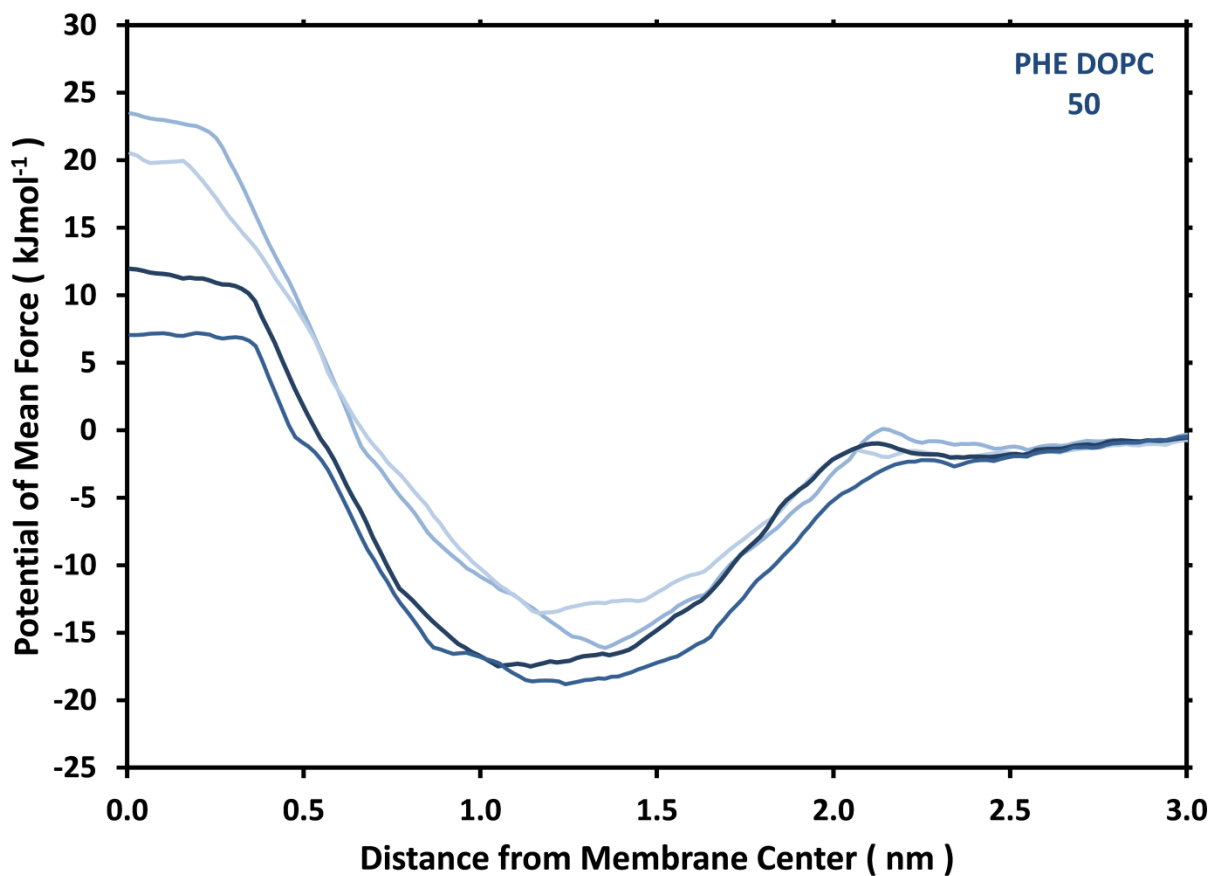

Figure 2. Potential of mean force quartiles for the phenylalanine dipeptide in the DOPC 50 system.
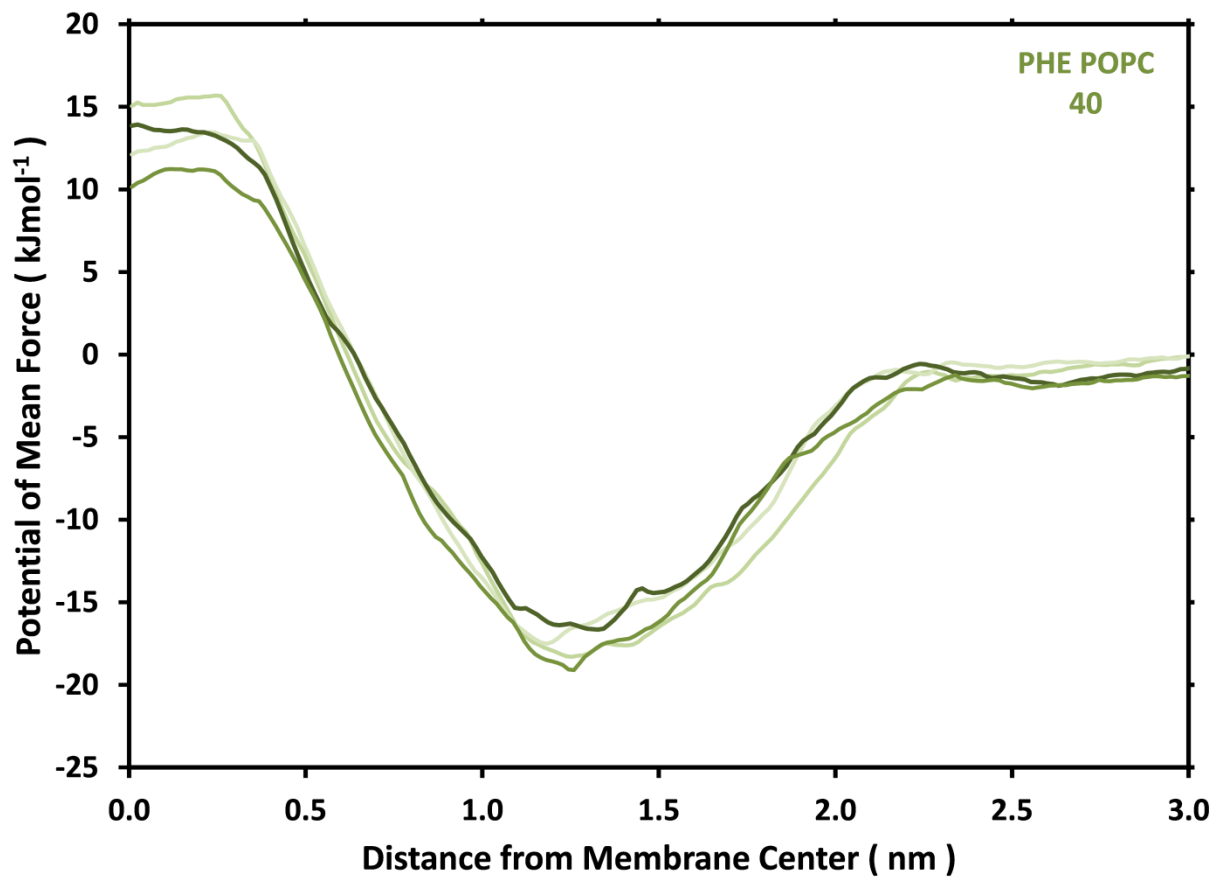
Figure 3. Potential of mean force quartiles for the phenylalanine dipeptide in the POPC 40 system.
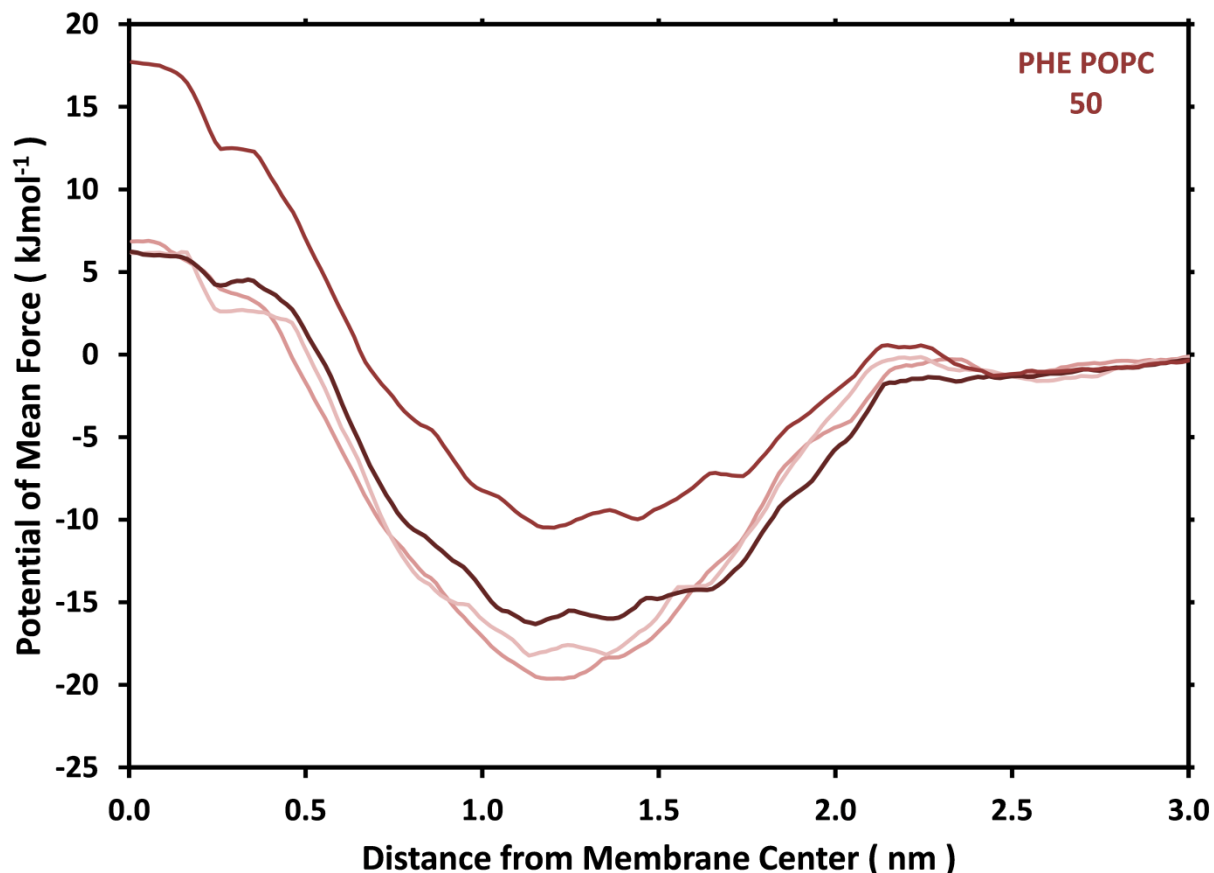
Figure 4. Potential of mean force quartiles for the phenylalanine dipeptide in the POPC 50 system.

Radius of Gyration.

The radius of gyration with respect to the center of mass of the phenylalanine dipeptide is plotted below with respect to the simulation z-axis. The standard error of each sample mean was calculated and was not plotted since it was around 0.02% of the radius of gyration for all simulation depths. In contrast, the standard error of each sample was plotted in our previous article[56] and is around 3-5% of the radius of gyration, which is similar to these results. Either way, a discernible pattern is not present, as seen below.
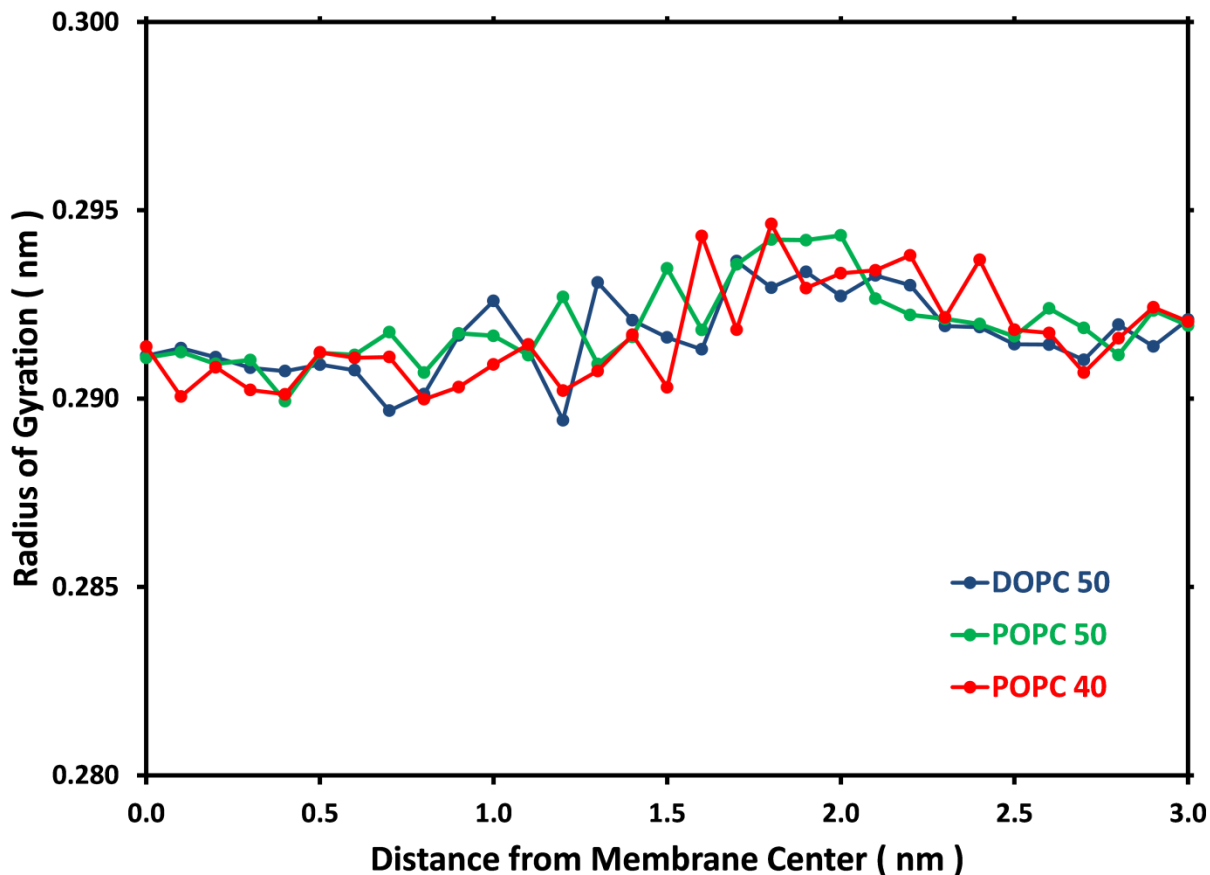
Figure 3. The radius of gyration for the phenylalanine dipeptide in DOPC and POPC lipid bilayers of varying sizes. 95% confidence intervals for the sample mean for each trajectory windows are plotted but are too small to be seen.

Solvent Accessible Surface Area.

The solvent accessible surface area -- hydrophilic, hydrophobic, and total -- can be found below. The standard error for each sample mean at a 95% confidence is also plotted. There is little, if any, variation in all of these surface area measurements.
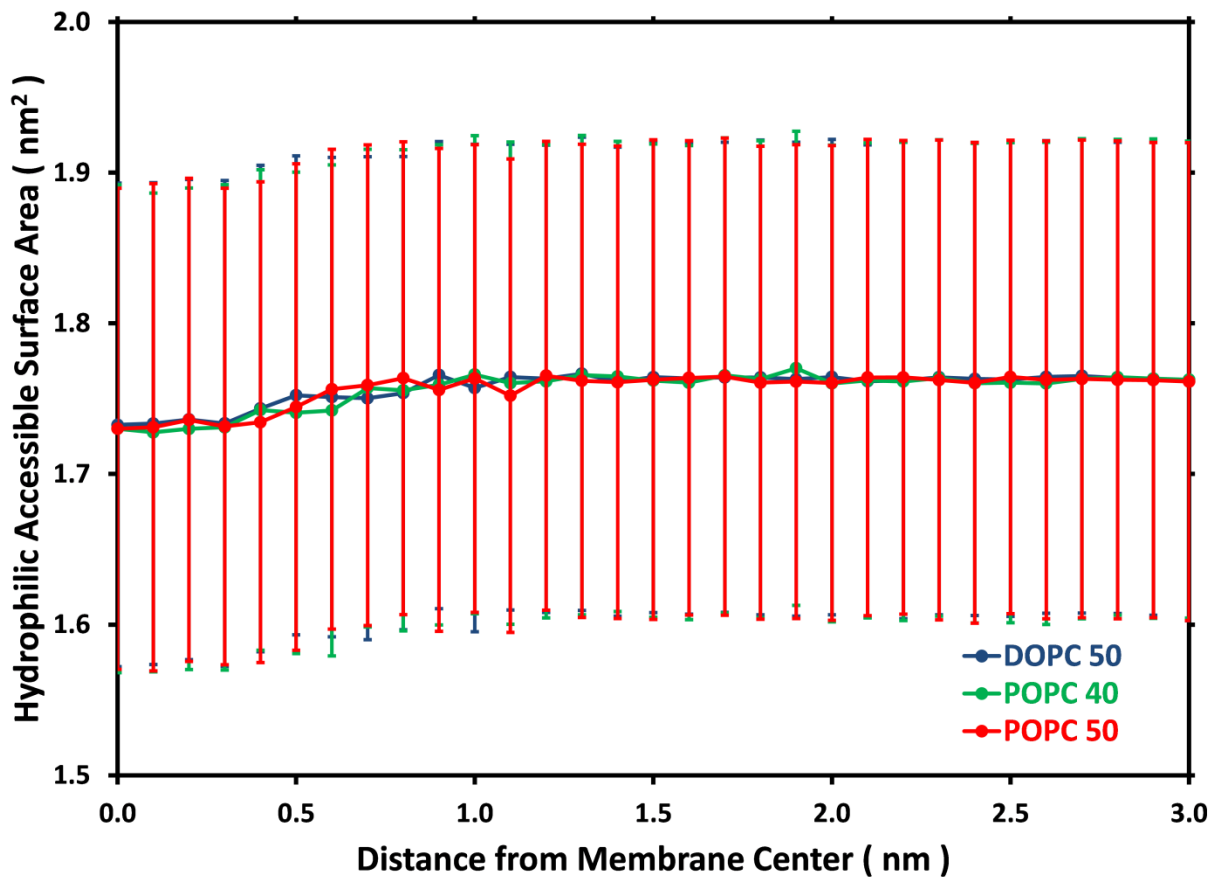
Figure 4. The hydrophilic accessible surface area for the phenylalanine dipeptide in DOPC and POPC lipid bilayers of varying sizes. The standard error (95% confidence) for the sample mean for each umbrella sampling window is plotted.
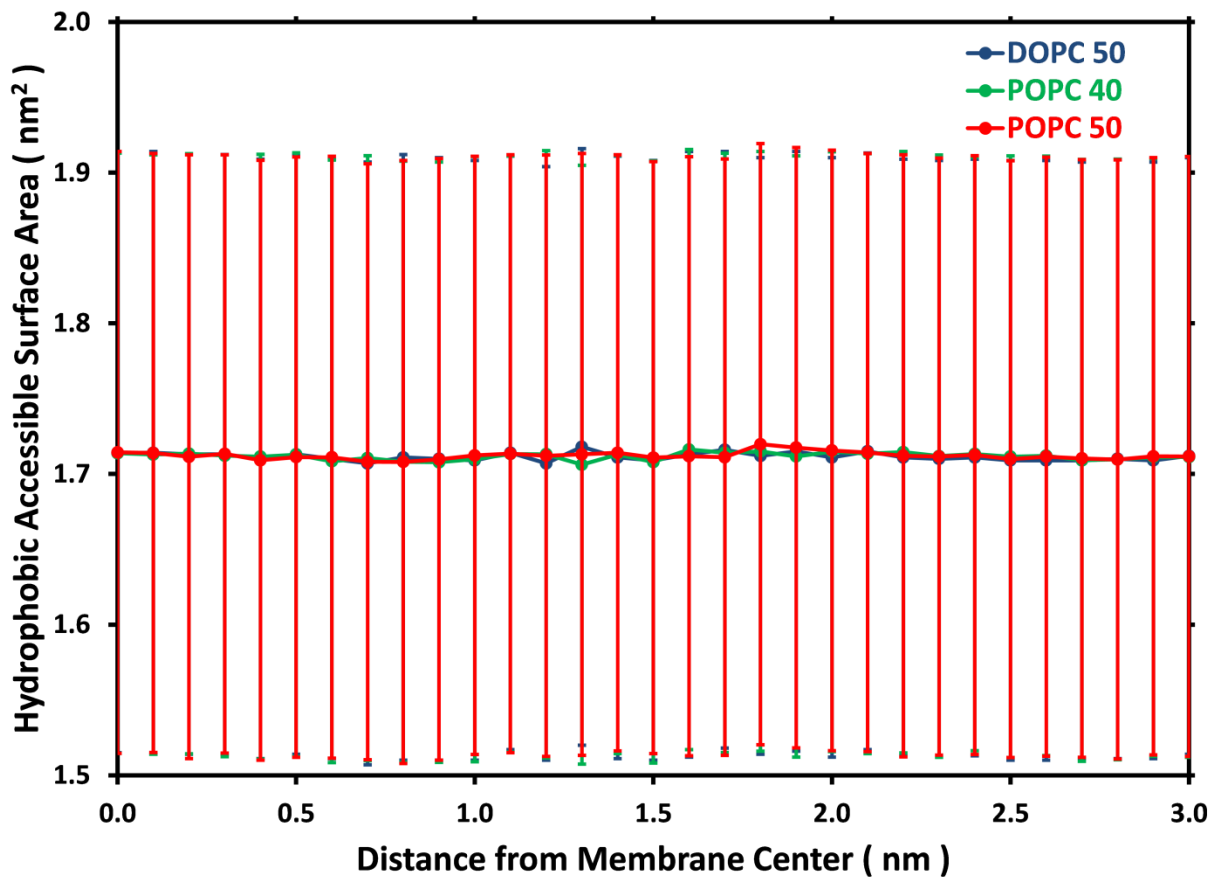
Figure 5. The hydrophobic accessible surface area for the phenylalanine dipeptide in DOPC and POPC lipid bilayers of varying sizes. The standard error (95% confidence) for the sample mean for each umbrella sampling window is plotted.

Figure 6. The total solvent accessible surface area for the phenylalanine dipeptide in DOPC and POPC lipid bilayers of varying sizes. The standard error (95% confidence) for the sample mean for each umbrella sampling window is plotted.
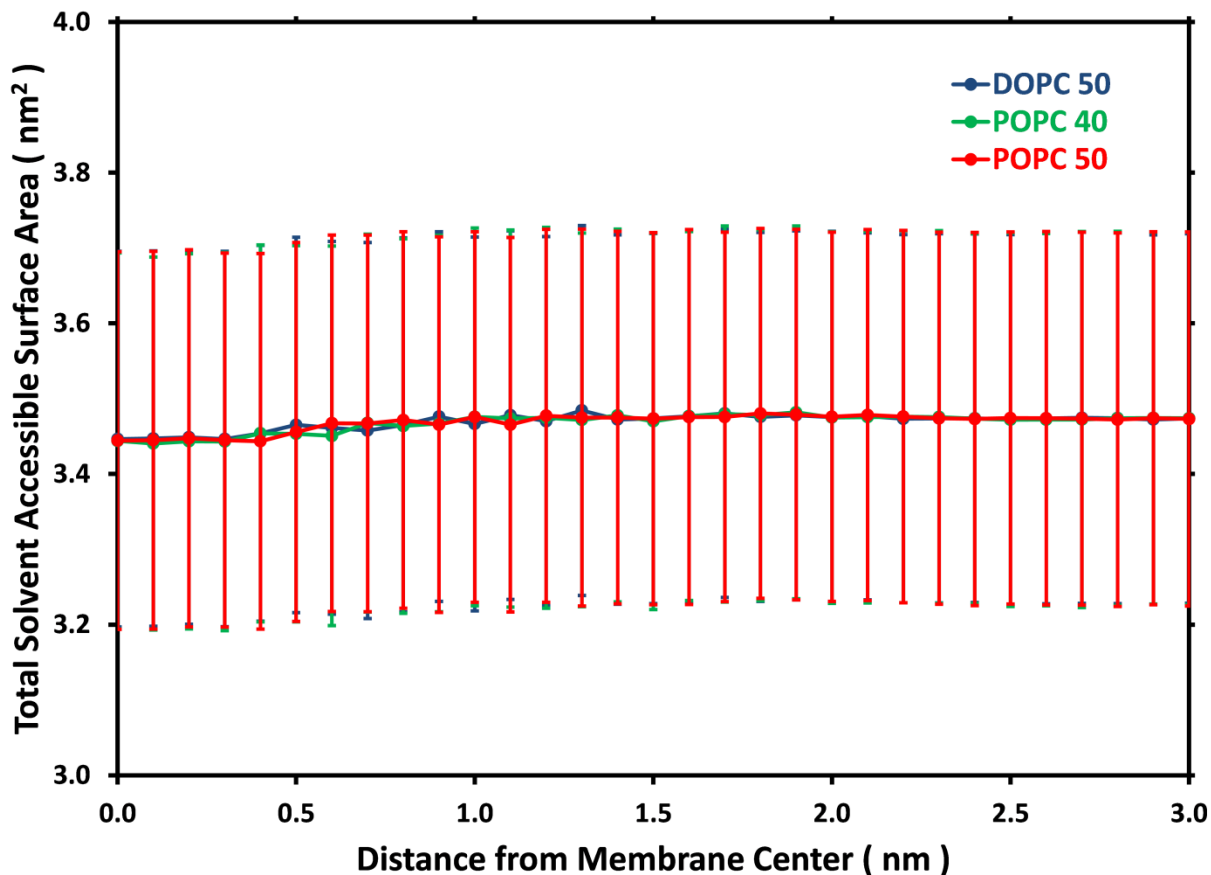
Availability of CODE: Codes used to calculate the diffusion coefficients, permeation coefficients and mean first passage times are available from the authors upon request.