The Molecular Determinants of Membrane Viscosity

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Abstract

Lipid membrane viscosity is critical to biological function. Bacterial cells grown in different environments have been shown to alter their lipid composition in order to maintain a specific viscosity, and membrane viscosity has been linked to the rate of cellular respiration. In order to understand the factors which determine the viscosity of a membrane, we ran equilibrium all-atom simulations of single component lipid bilayers and calculated their viscosities. The viscosity was calculated via a Green-Kubo relation, with the stress tensor autocorrelation function fit to a stretched exponential by a maximum-likelihood Markov chain Monte Carlo method. By simulating a series of lipids at different temperatures, we establish the dependence of viscosity on several aspects of lipid chemistry, including hydrocarbon chain length, unsaturation and backbone structure. Sphingomyelin is found to have a remarkably high viscosity, roughly 10-20 times that of DPPC.

Notation

η	3d shear viscosity	$(\mathrm{Pa\,s})$
μ	2d surface shear viscosity	$(\mathrm{Pa\,m\,s})$
P_{xy}	xy-component of pressure tensor	(Pa)
T_m	$L_\alpha - L_\beta$ transition temperature	(K)

Theory

Green-Kubo Relation

The overall goal was to employ a Green-Kubo relation for viscosity to equilibrium lipid bilayer simulations in order to determine their viscosities:

$$\eta(\tau^\star) \;=\; \frac{V}{k_B T}\int_0^{\tau^\star} \langle P_{xy}(t)P_{xy}(t+\tau)\rangle_t \,\mathrm{d}\tau$$

Stretched Exponential

Autocorrelation functions are often fit to stretched exponentials [3]. In this particular case:

$$\langle P_{xy}(t)P_{xy}(t+\tau)\rangle \;\approx\; \exp\left[-\left(\frac{\tau}{\tau_0}\right)^{1/\beta}\right]$$

Fitting the integrals

It proved more useful in this analysis to fit the *integral* of the stretched exponential:

$$\eta(\tau^\star) \quad\approx\quad \frac{V}{k_B T}\int_0^{\tau^\star} \exp\left[-\left(\frac{\tau}{\tau_0}\right)^{1/\beta}\right]\mathrm{d}\tau \quad\propto\quad \gamma\left[\beta, \left(\frac{\tau^\star}{\tau_0}\right)^{1/\beta}\right]$$

where $\gamma[\beta, x]$ is the lower incomplete gamma function.

References

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[3] J. C. Phillips. "Reports on Progress in Physics Related content Stretched exponential relaxation in molecular and electronic glasses". In: *Rep. Prog. Phys.* (1996). ISSN: 1097-2765.

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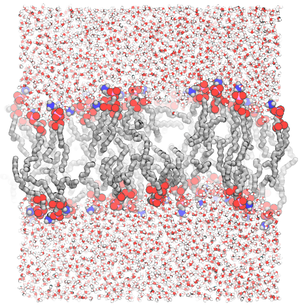
[5] Malcolm L. Williams, Robert F. Landel, and John D. Ferry. "The Temperature Dependence of Relaxation Mechanisms in Amorphous Polymers and Other Glass-forming Liquids". In: *Journal of the American Chemical Society* 77.14 (1955), pp. 3701–3707. ISSN: 0002-7863. DOI: 10.1021/ja01619a008.

Simulation Setup

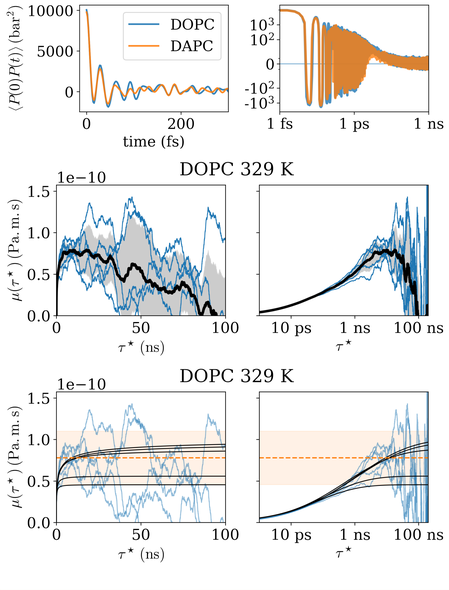
Five replicas of all of the following lipids were run at the listed temperatures, in roughly $(10\,\mathrm{nm})^3$ simulation boxes. After equilibrating under NPT, the simulations were run for 150-200 ns under NVT.

Lipid	Tail(s)	T_m (from [4])	T_{sim}
DLPC	12:0	271	286, 329
DMPC	14:0	297	312, 329
DPPC	16:0	314	329
POPC	16:0/18:1	271	283, …, 329
DSPC	18:0	327	343
DOPC	18:1	256	283, 329
DAPC	20:4	204	329
PSM	16:0/SM(d18:1)	314	329

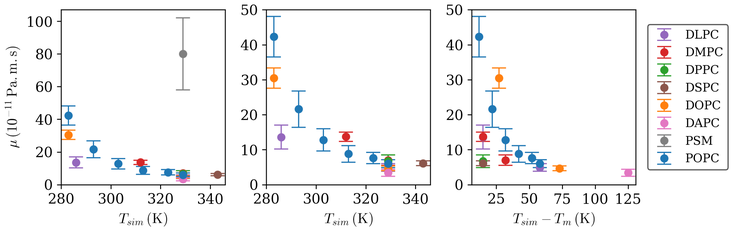


Example frame from one DPPC simulation.

Autocorrelation Function and Integral

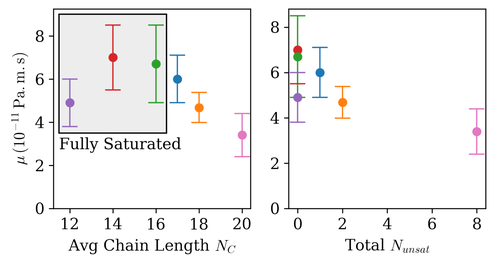


Viscosity vs. Temperature Across Lipid Types



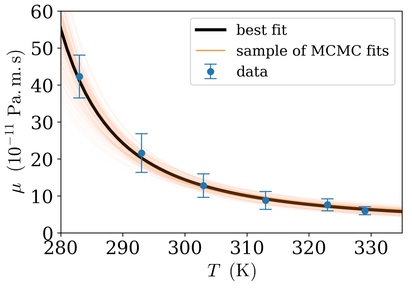
Left: All results, showing the much higher viscosity of PSM **Center:** All results, excluding PSM **Right:** Shifted x-axis, showing degrees above T_m

Viscosity Dependence on Chain Length and Unsaturation



The $329\,\mathrm{K}$ series, excluding PSM. The rightmost plot is a good illustration that the transition temperature T_m is a function of both N_C and N_{unsat}.

Temperature Dependence of POPC Viscosity



Viscosity from the POPC temperature series. The curve fit is a an Arrhenius-like Vogel-Fulcher-Tammann (VFT) model [1] of the form

$$\eta(T) = a\,\exp\left[\frac{b}{T-c}\right]$$

If a more physically meaningful fit were required, the VFT model can be converted directly to a Williams-Landel-Ferry ("WLF") model [5].

Supporting Information

"Subtracting" the Water Viscosity

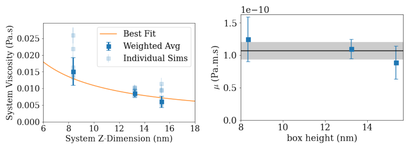
The direct output of the simulation is the pressure tensor for the entire simulation box. It is a very accurate approximation to assume that the simulation box is a slab of lipids of thickness h, and a slab of water of thickness $H-h$. The stresses within the simulation box add in a very simple manner:

$$H\,P^{xy}_{\mathrm{sys}} = h\,P^{xy}_{\mathrm{mem}} + (H-h)\,P^{xy}_{\mathrm{T3P}}$$

which implies

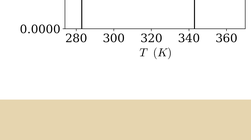
$$\mu_{\mathrm{mem}} = H\,\eta_{\mathrm{sys}} - (H-h)\,\eta_{\mathrm{T3P}}(T)\,.$$

To evaluate this approximation, and to ascertain the independence of box height, a series of DMPC simulations was run with box heights of roughly 8, 13, and $15\,\mathrm{nm}$. The viscosities for all three thicknesses were in clear agreement:



Water Viscosity

TIP3P viscosity data from [2] was fit to a VFT (Arrhenius-like) model [1] for interpolation to other temperatures, with great success.



Summary of Results

- This method was successful at measuring surface viscosity in simulation.
- Viscosity was found to decrease with temperature, and was accurately fit with a VFT model.
- At constant temperature, viscosity increased with chain length, and decreased with unsaturation.

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