Atomistic Study of Bromoform and Lipid Bilayers: Membrane Traverse of Bromoform and its Influence on the Membrane

Jie Shi, Kevin J. Cheng

Center for Cellular Construction & IBM Almaden Research Center

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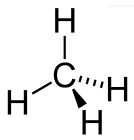
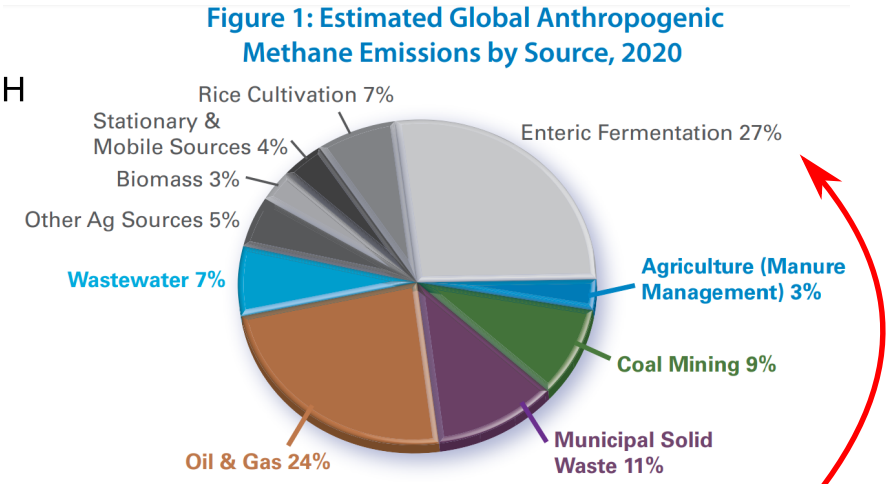
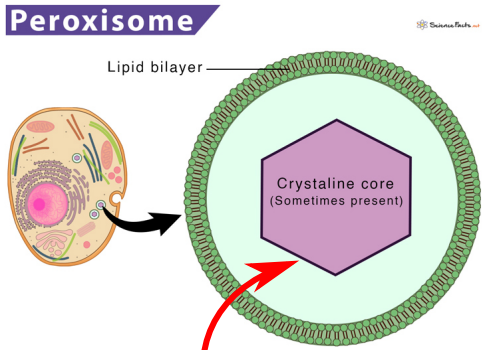
Motivations

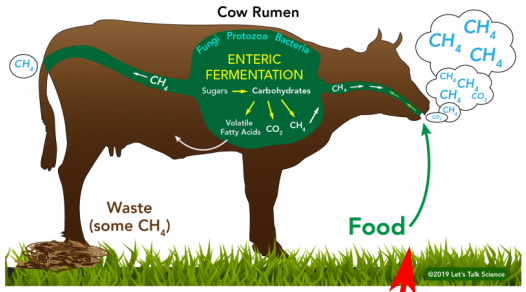
Methane:

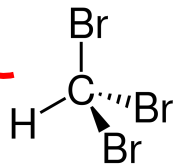
- Second most abundant anthropogenic greenhouse gas
- Much shorter lifespan than CO_2 (12 years vs >100 years)
- Effect on the climate change much faster



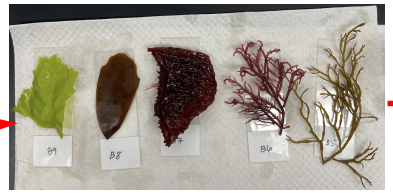








Bromoform
inhibitor of methanogenesis



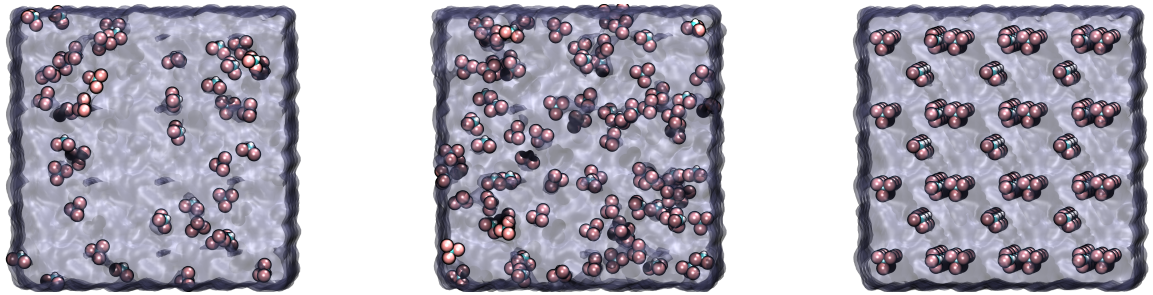
Engineer seaweed with peroxisomes that are able to store more bromoform

Goals

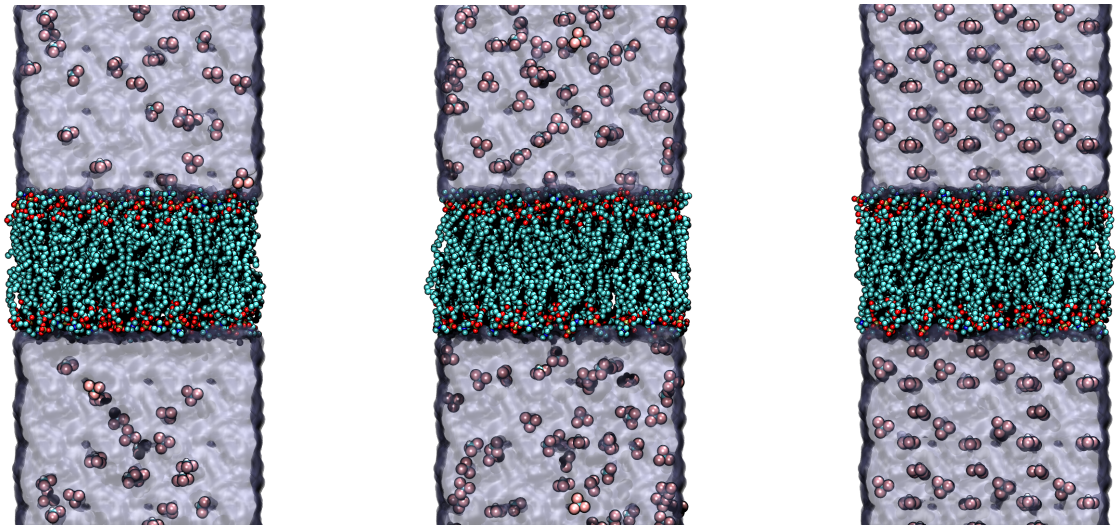
- **Goal of our project**: performing molecular dynamics simulations to study the interplay between bromoform molecules and lipid bilayer membranes
- **Goal of this talk**: sharing our current progresses and having feedback and comments from the experimental and cellular engineering perspectives

Setups of Six Simulation Systems

Bromoform + water



Bromoform + water + POPC Bilayer

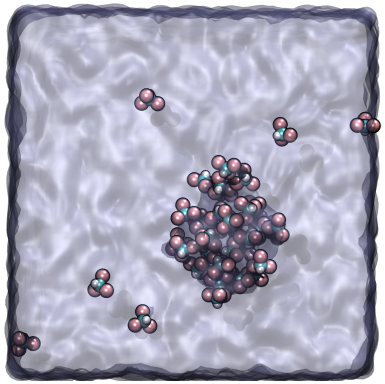


0.2 M Bromoform 0.4 M Bromoform 0.6 M Bromoform

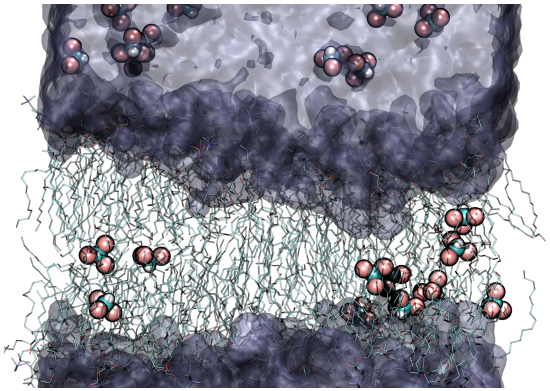
MD simulation in each system has reached ∼400 ns

Behaviour of Bromoform

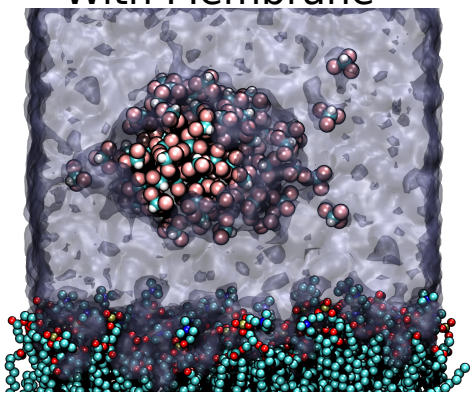
0.2 M Bromoform



0.2 M Bromoform
With Membrane



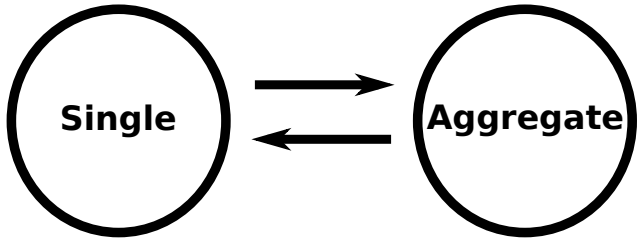
0.6 M Bromoform
With Membrane



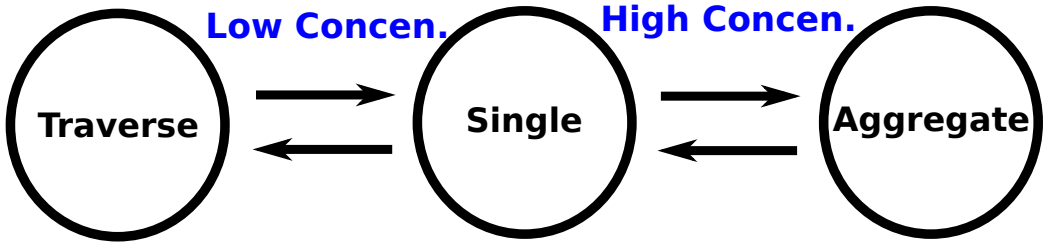
- 5 out of 6 systems form aggregates of bromoform molecules
- Only in 0.2 M with lipid membrane, the individual bromoform molecule doesn't aggregate but instead passively diffuse through lipid bilayer

Equilibrium States Distribution

Without Membrane:



With Membrane:

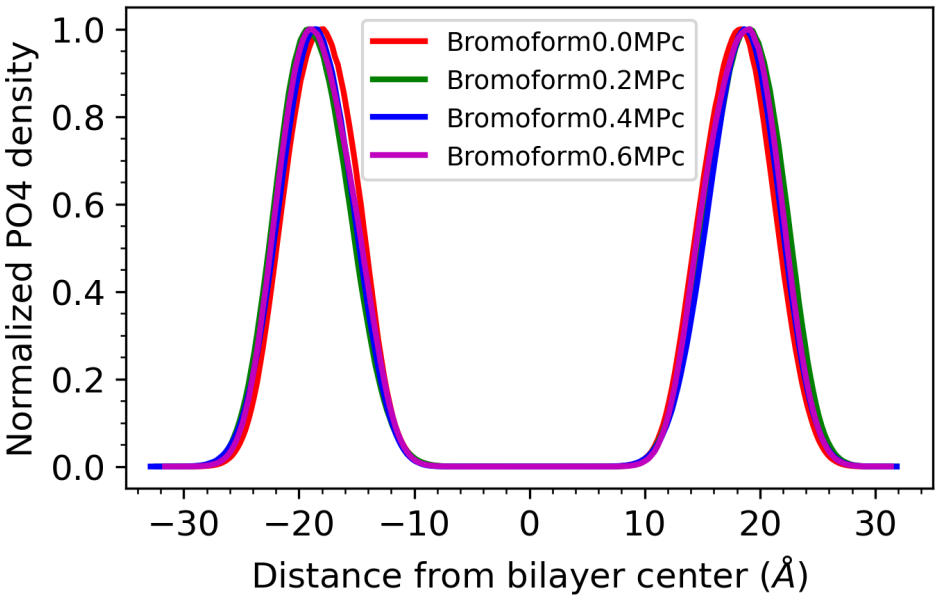


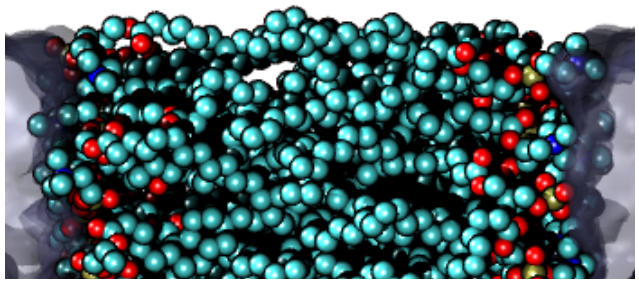
For bromoform molecules to traverse the membrane:

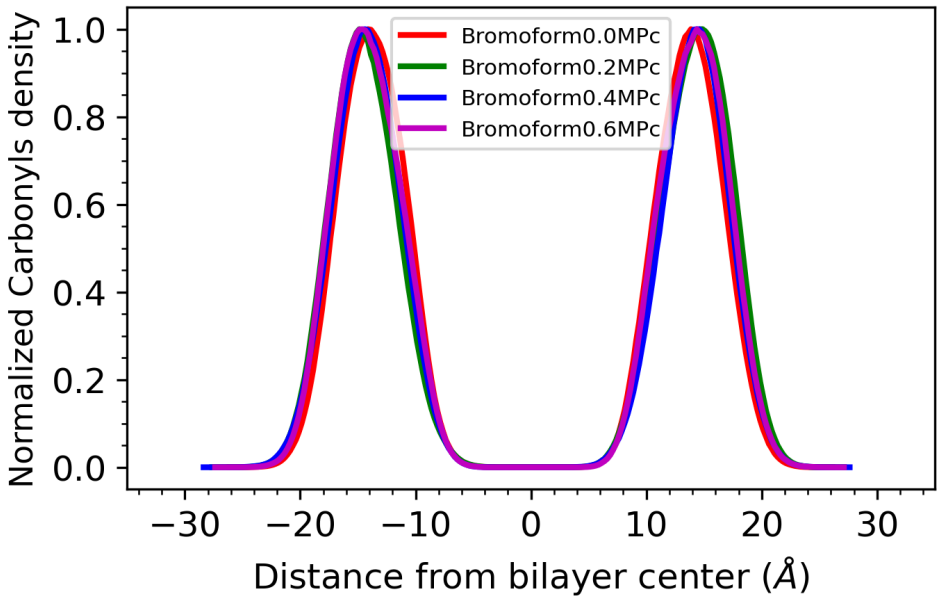
- Lipid membrane near the bromoform
- Bromoform concentration below a certain threshold

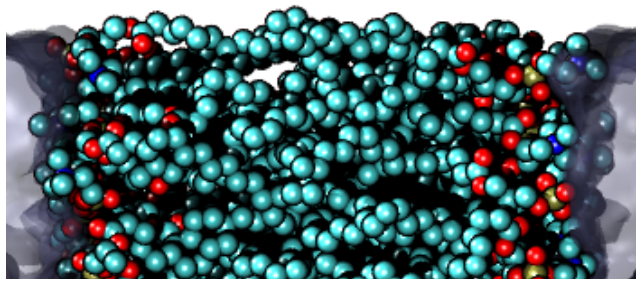
Solubility of bromoform in water at 303.15 K is 0.01 M.
Simulations at this bromoform concentration are currently running on supercomputers

Bromoform Affects Transverse Mass Density Distributions





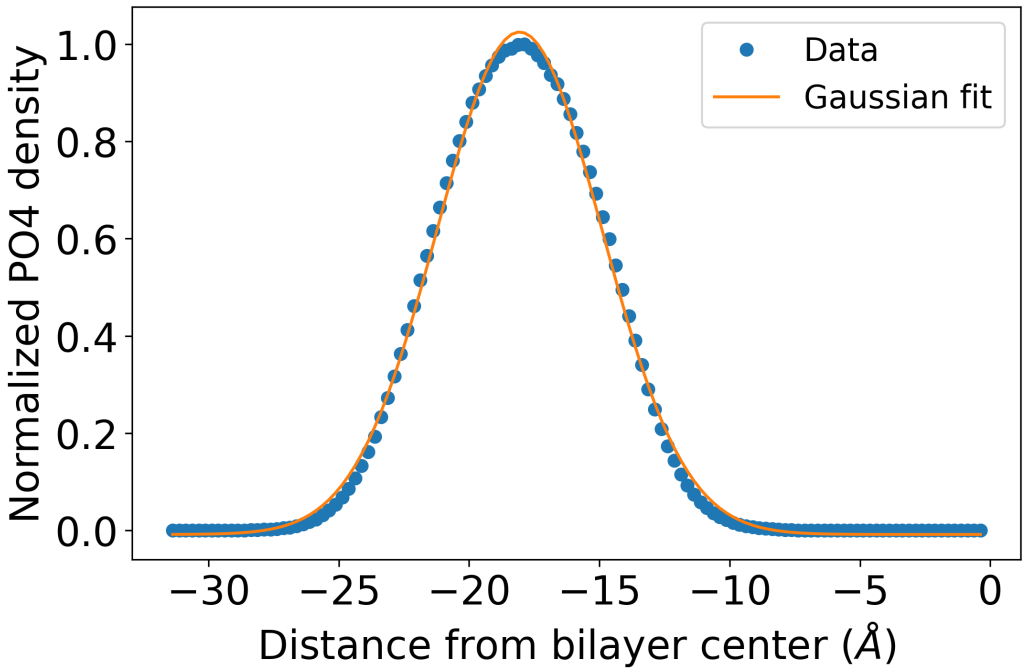




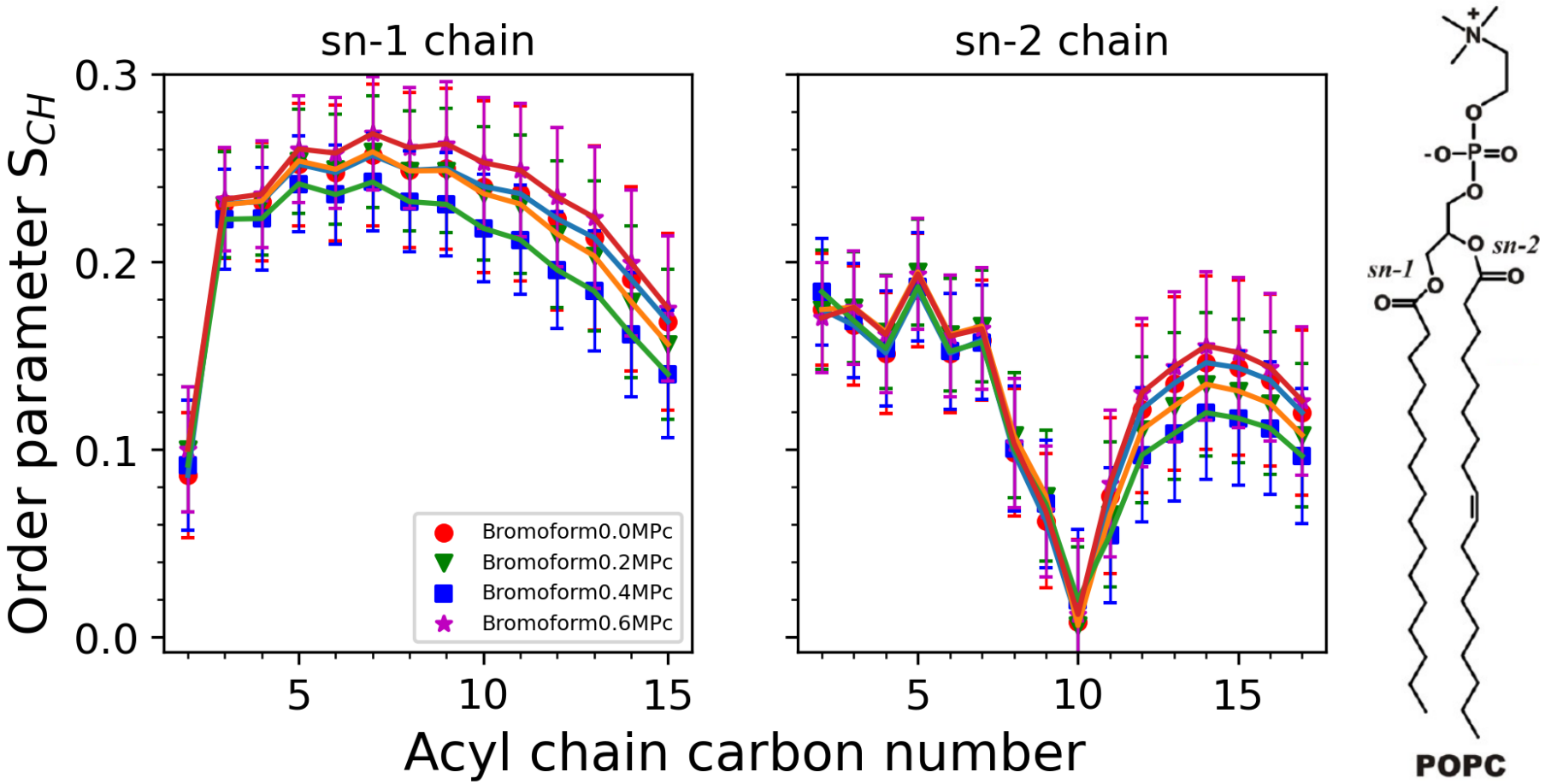
Bromoform Affects Transverse Mass Density Distributions

Bromoform Concentration	Phosphate-Phosphate (Å)	Carbonyl-Carbonyl (Å)
0.0 M*	36.14 ± 0.02	27.66 ± 0.03
0.2 M	37.68 ± 0.03	29.15 ± 0.03
0.4 M	37.12 ± 0.01	28.60 ± 0.01
0.6 M	37.04 ± 0.04	28.52 ± 0.04

*: in good agreement with previous study (See *Norbert Kucerka, etc, J. of Membrane Biol, 2005)*



Bromoform Has Negligible Effect on Membrane Internal Ordering



Effect of Bromoform on POPC Lipid Bilayers

- Increase in bilayers thickness with the existence of bromoform
- Bromoform penetrating the membrane further makes the membrane thicker
- Bromoform doesn't induce significant internal ordering change in membrane

Bromoform Diffusion Coefficient Across the Membrane

- Transmembrane diffusion coefficient (D_z) via Einstein relation:

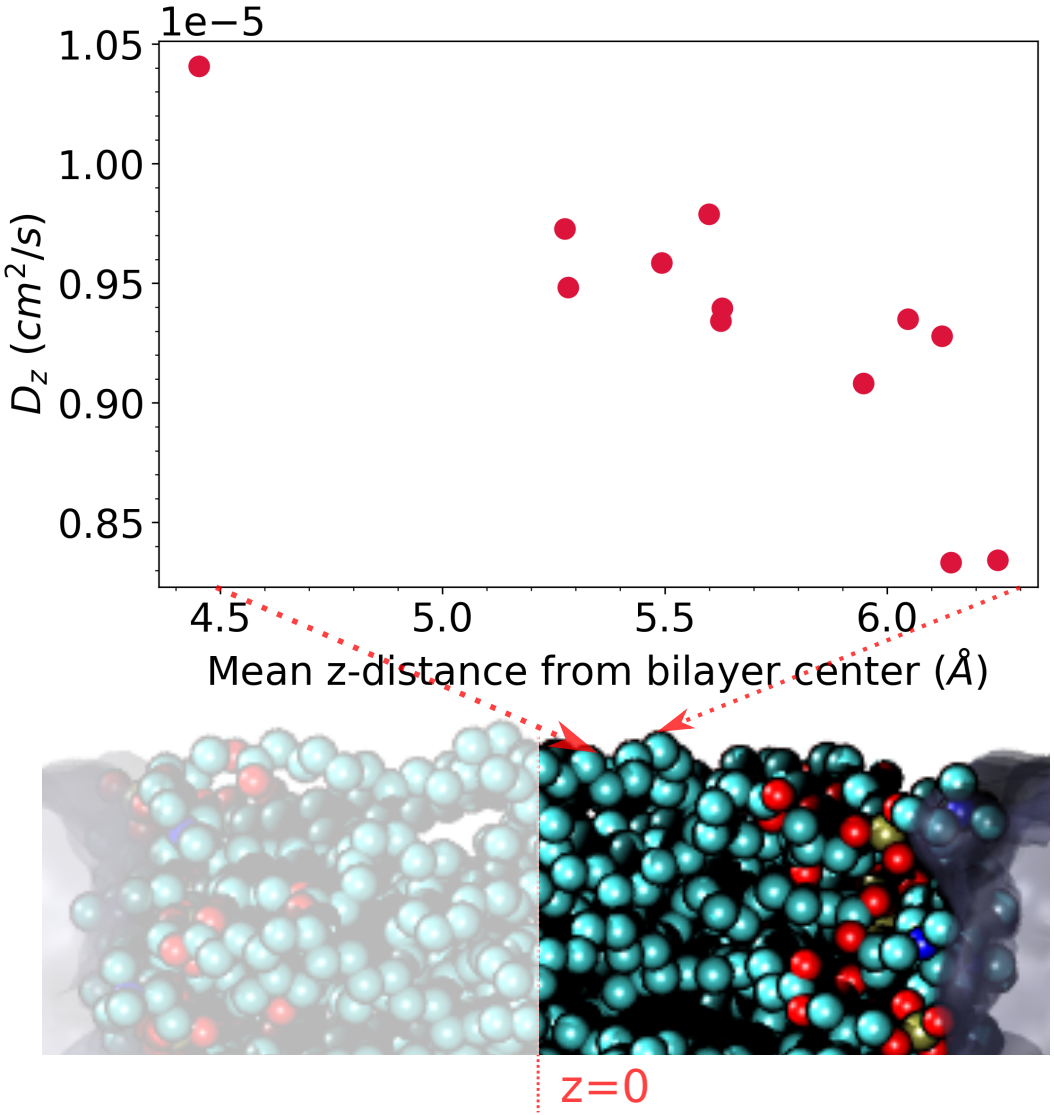
$$MSD_z(\tau) = \langle \left| r_z(t_0 + \tau) - r_z(t_0) \right|^2 \rangle_{t_0}$$
$$D_z = \frac{1}{2} \frac{d}{d\tau} MSD_z(\tau)$$

- D_z of bromoform: **9.34** $\pm$ **0.58** $\times$ **10**$^{-6}$ (cm^2/s)
  Cf. 3.47$\times$ 10^{-5} (cm^2/s) in pure bromoform solvent

- Within the reasonable range of D_z for common small organic molecules:
  ethane $>$ **bromoform** $>$ acetamide, benzene, methanol
  (*Mario Orsi, etc, J. Phys. Chem. B, 2009)*

Bromoform D_z is Lipid Region Dependent

D_z of fastest bromoform is 25% greater than the slowest



Take Home Messages

Simulation of bromoform in aqueous solution both with and without membranes found:

- Bromoform tends to aggregate under aqueous condition
- May passively traverse lipid membrane without aggregation if below a certain concentration threshold
- Bromoform can increase membrane traverse mass density ("thicker")
- Bromoform doesn't have significant effect on the lipid chain ordering
- D_z of bromoform inside the POPC membrane: 9.34×10^{-6} (cm^2/s)
- There is a correlation between D_z and z-coordinate

Acknowledgments

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Thank you!

Any questions or comments are appreciated!

Email address: *shijie@ibm.com*