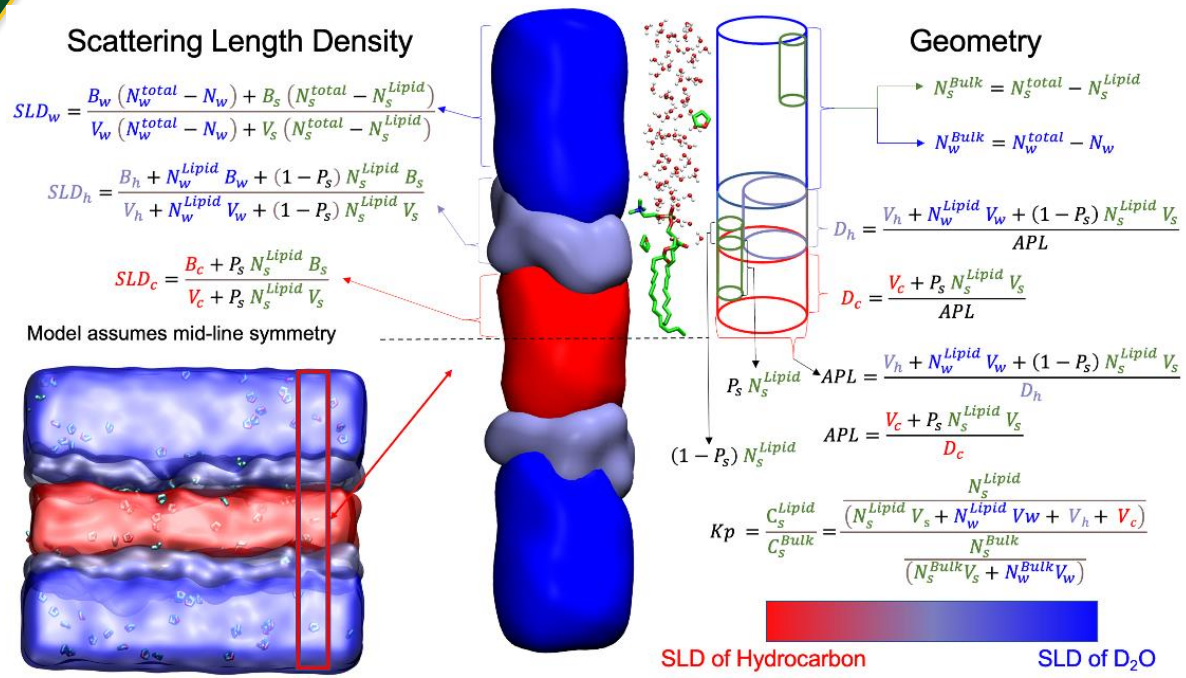
An improved model of partitioning of amphiphilic co-solvents in biomembranes for SANS fitting



The two-parameter partition constant model to describe the structure and partitioning of the co-solvents in a bilayer structure from neutron scattering data. The key parameter used include the area per lipid (APL), number of water molecules per lipid headgroup (N_w), the partition constant (K_p) and the co-solvent localization constant (P_s).

L. Tan et al. “Modelling the partitioning of amphiphilic molecules and co-solvents in biomembranes” *J. Appl. Crystal.* 55 (2022). doi.org/10.1107/S1600576722008998.

Scientific Achievement

We derive, implement and validate the two-parameter partition constant model for biomembranes — demonstrating its use for fitting scattering data for bilayer structures and partition coefficients.

Significance and Impact

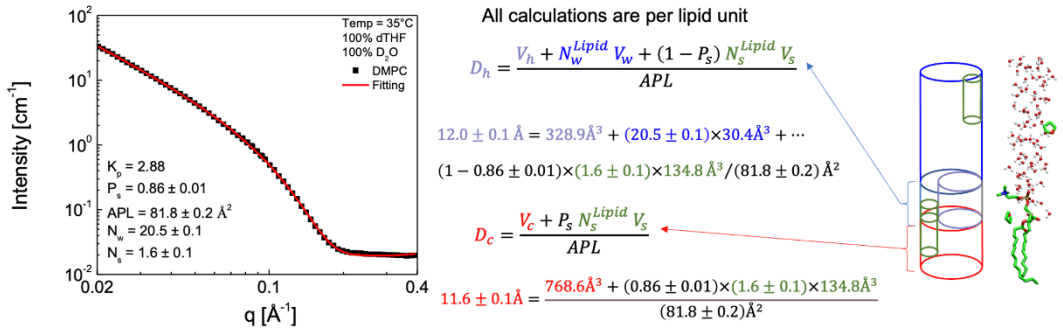
Solvent toxicity is a significant limitation in the total yield of biofuel and other fermentative production. Solvents interact with microbial membranes, thinning and disrupting the structure.

Small angle neutron scattering (SANS) is a powerful tool to probe membrane structure. The two-parameter partition constant model allows SANS data to be analyzed simultaneously for structure and co-solvent partitioning in lipid membranes; this leads to a more quantitative understanding of solvent toxicity. It led to a direct measure of solvent thinning of the biomembrane.

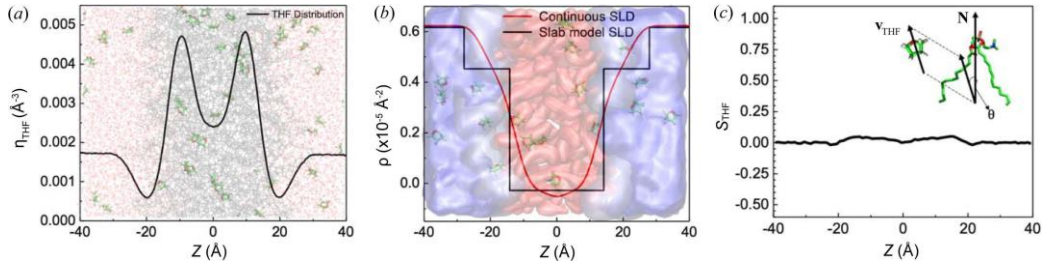
This model will also find application in biofuels research, anesthesia and pharmacokinetic modeling, and partitioning studies in lamellar block copolymer membranes.

This work was supported by the US Department of Energy (DOE), Office of Science, through the Genomic Science Program, Office of Biological and Environmental Research (contract no. FWP ERKP752). Neutron scattering research conducted at the Bio-SANS instrument, a DOE Office of Science, Office of Biological and Environmental Research resource (contract no. ERKP291), used resources at the High Flux Isotope Reactor, a DOE Office of Science Scientific User Facility operated by Oak Ridge National Laboratory (DEAC05- 00OR22725).

SANS can be a key method for studying membrane with amphiphilic co-solvent partitioning



The two-parameter partition constant model was validated against SANS data and MD simulations of THF partitioning into lipid bilayers – identifying bilayer structure, partition coefficients, and co-solvent localization.



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Research Details

The two-parameter partition constant model was implemented as a python script that can be directly used in the *SasView* suite.

SANS (Bio-SANS at ORNL) was used to directly measure structural information of model lipid (DMPC) membranes in the presence of the co-solvent tetrahydrofuran (THF).

This scattering data were well-described by two-parameter partition constant model.

SANS data were also measured under multiple neutron contrast conditions and a simultaneous fitting approach was demonstrated, leveraging the unique power of neutrons and biodeuteration to provide multiple scattering data sets for the same structure.

Atomistic MD simulations were performed in parallel to these validation experiments, providing a detailed structure in close agreement to the model output.

We demonstrated the use of MD simulation outputs as a constraint in the fitting of SANS data.