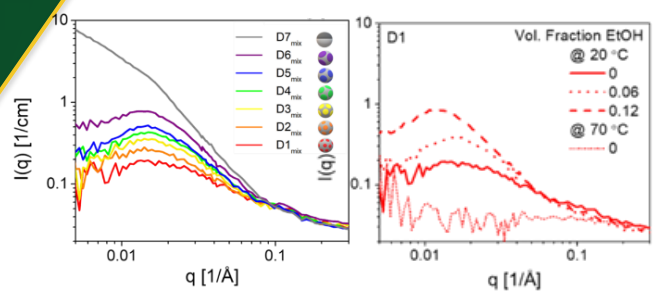
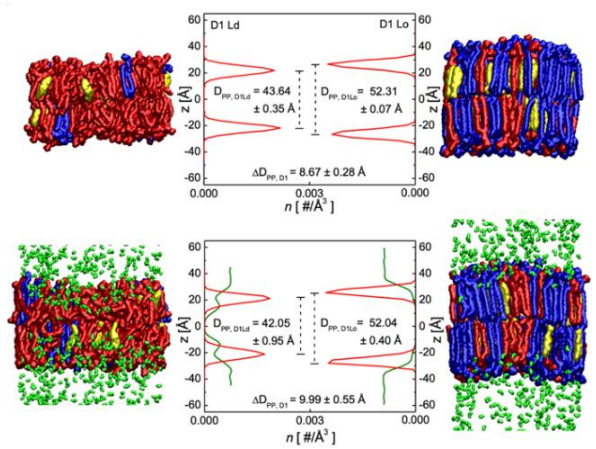
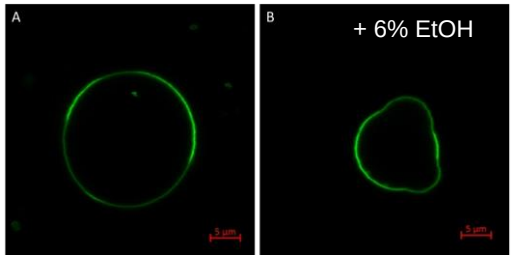
Amphiphilic co-solvents modulate structure of membrane domains



Small-angle neutron scattering (SANS) reveals the presence of nanoscopic lipid domains at different lipid mixtures (left) and shows how EtOH alters their structure (right for the $D1_{mix}$). SANS also measures bilayer thickness and solvent partitioning, showing that EtOH partitions unequally between phases, inducing differential thinning and softening of co-existing regions of the membrane – this drives an increase in line tension.



All-atom MD simulations also showed different solvent partitioning, bilayer thinning and other effects between the co-existing lipid phases.



Confocal fluorescence microscopy reveals the presence of co-existing lipid domains in bilayer lipid vesicle models and illustrates the EtOH induced changes in size, curvature and bending properties.

Scientific Achievement

We have demonstrated that ethanol drives a coarsening or disruption of lateral lipid domains and elucidate the mechanism of action. We show that unequal partitioning of EtOH between the co-existing phases leads to an increase hydrophobic mismatch of the thickness of these phases and a corresponding increase in the domain line tension. This is a driver to minimize the domain interface to domain area ratio. This represents the physical basis for a novel mode of co-solvent induced cell stress due to domain disruption.

Significance and Impact

Biofuels are an increasing part of the sustainable energy picture, making it a societal and economic imperative to optimize biofuel production. Biofuels poison fermenting microbes by increasing membrane fluidity and passive proton flux, eventually compromising the integrity of the membrane and leading to a loss of the electrochemical gradient - cell death. Mitigating the toxic effects of biofuels is one way to improve the efficiency of biofuel production.

Research Details

In this work, we present the hypothesis that membrane lateral organization is disrupted by biofuels and amphiphilic co-solvents at concentrations lower than those which lead to full membrane destabilization. Lateral membrane organization is increasingly recognized as a critical feature of cell membrane architecture due to its role in protein sorting and oligomerization. The alteration or disruption of lateral membrane domains has deleterious effects on many cellular processes.

We show precisely this type of disruption in model membranes and elucidate the mechanism by which it is occurring. This represents an unrecognized mode of solvent-induced stress in biofuel production – and in cells of the gastrointestinal tract impacted by dietary alcohol. These findings establish new targets for intervention to improve fermentation yields.

L. Tan, H.L. Scott, M.D. Smith, S.V. Pingali, H.M. O'Neill, J.L. Morrell-Falvey, J. Katsaras, J.C. Smith, B.H. Davison, J.G. Elkins, and J.D. Nickels, "Amphiphilic co-solvents modulate structure of membrane domains" *ACS Sust Chem Eng,* 2023. DOI: 10.1021/acssuschemeng.2c06876

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