minimum resolvable domain size of 40 nm for the achievable contrast in this preliminary work.

86-Plat
A Fundamental Force that Regulates Nano-Clustering of Proteins in Biological Membranes
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Using coarse-grained molecular dynamics simulations, we demonstrate the nature of the membranophobic effect – a proposed phenomenon that governs self-assembly of inclusions within a lipid bilayer, inspired by the statistical mechanics of the hydrophobic effect. We study the nature of this effect on membrane inclusions of various chemistries and sizes. We identify the range of hydrophobic thicknesses over which this phenomenon occurs and characterize the effects of the proposed phenomenon on small inclusions such as cholesterol versus larger, multidomain transmembrane proteins. Our results show that this effect can provide a force for assembly and reorganization in a lipid bilayer based on the in-plane size and hydrophobic thickness of the inclusion, and the melting temperature of the surrounding lipids. We propose that this effect provides a physical framework that can explain lipid raft formation.

87-Plat
Theory of Registered and Antiregistered Phase Separation in Mixed Amphiphilic Bilayers
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Wide interest in the phase behaviour of amphiphilic bilayers has arisen since the realisation that it can be exploited by nature, and engineers, to design-in function via membrane domains. A key confounding feature is the presence of two separate, yet coupled, leaflets within the bilayer. The question of inter-leaflet domain alignment (registration) or otherwise is central to proposed cellular roles such as protein localisation and, more fundamentally, creates a zoo of phase behaviour that can only be captured by properly considering the coupled leaflets. Experiment and simulation yield intriguingly disparate observations, but a full theoretical picture is lacking; existing phenomenological theories provide insight but do not link large-scale behaviour to small-scale features. We introduce a theory for phase separation in coupled leaflets by explicitly coarse-graining a lattice model that includes molecule-level structuring and interactions. We show that accounting for hydrophobic mismatch between the mixed species leads to a complex competition of inter-leaflet coupling energies. The free energy obtained helps unify some prima facie contradictory observations by showing that domain antiregistration typically occurs as a metastable state, but can be kinetically preferred during the initial demixing of a bilayer. The role of kinetics in governing registration/antiregistration is explored, and we find that a bilayer in the usual ''spinodal region'' may in fact require a nucleation process to equilibrate. Our results provide a tractable coarse-grained model that explicitly depends on simplified molecular interactions, providing novel insight and encouraging important future work in which the intra- and inter-leaflet behaviour of mixed bilayers is carefully investigated.
Reference: J. J. Williamson and P. D. Olmsted, arXiv:1408.2744 (in preparation).

88-Plat
How GM1 Affects the Phase State and Mechanical Properties of Phospholipid Membranes
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Even though glycolipids are present at increased concentrations in the outer leaflet of eukaryotic biomembranes, their influence on the mechanical properties of the membrane has not been studied in much detail. In this work, we investigate the effect of GM1, a prominent example among glycolipids, on the physical characteristics such as phase state and bending rigidity of membranes. Both giant vesicles and large unilamellar vesicles made of palmitoyloleoylphosphatidylcholine (POPC) are explored. We find that for GM1 fractions above ~5 mol%, the membranes are phase separated at room temperature and exhibit GM1-rich microdomains with gel-like nature as observed by fluorescent microscopy. However, cholera toxin B, which is conventionally used as a GM1 marker, is found to be excluded from these domains. So is the fluorescently labelled conjugate Bodipy-GM1. We also explore the influence of GM1 on the membrane bending rigidity, which determines how pliable the membrane to deformations is. Results obtained from fluctuation analysis of giant vesicles and from the method of vesicle electrodeformation show a significant decrease in the membrane bending rigidity with increasing GM1 fractions when approaching the 5 mol% region. Micropipette aspiration measurements show that GM1 also leads to a decrease in the stretching elasticity modulus suggesting stronger coupling of the two leaflets of the membrane and probably also thickening of the bilayer. Our results are relevant to understanding the plasticity of neurons and their protrusions.

89-Plat
Examining the Effects of Cholesterol: Laurdan and Patman see it Differently
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The liquid-ordered phase induced by cholesterol in phosphatidylcholine bilayers can be detected with Laurdan fluorescence by an increase in the associated Generalized Polarization (GP) value. This increase in GP is usually interpreted as a reduction in the access of water molecules to the bilayer at depths approaching the phospholipid glycerol backbones. Comparisons of Laurdan fluorescence over a broad range of temperatures with various saturated and unsaturated phosphatidylcholines demonstrated that cholesterol has little effect on GP at temperatures below the melting point of the pure lipid (t_m). However, above t_m, increasing cholesterol concentrations monotonically raised the value of GP. The resulting GP increments generally did not vary with temperature above t_m. In contrast, the observations were more complex with Patman, a charged derivative of Laurdan. First, cholesterol raised the value of Patman GP at temperatures below t_m, and its effect as a function of concentration was bimodal. Second, although cholesterol increased Patman GP above t_m (similar to Laurdan), the effect size was smaller and was bimodal as a function of cholesterol concentration. Finally, the GP values at high versus low cholesterol concentration converged as temperature was raised well beyond t_m. In some cases, such as with unsaturated lipids $\geq 54°C$ above t_m, this convergence of Patman GP values reached a cross-over point; Patman GP was reduced by the presence of cholesterol beyond this point. These results suggest that the charge associated with Patman, or possibly the slightly deeper location of the probe in the bilayer, provides a means for identifying additional effects of cholesterol on the membrane that are not visible with Laurdan.

90-Plat
Orientational Texture of Membrane Domains: Effect of Lipid Composition and Binding of a Bacterial Toxin
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The principles governing the in-plane organization of biomembranes remains enigmatic more than 20 years after the proposition of the raft hypothesis.
The recent discovery of orientational texture of membrane gel domains represents a previously hidden level of membrane complexity[1]. Using polarized two-photon fluorescence imaging we have shown that gel domains in phospholipid membranes may contain long-ranged orientational texture patterns originating from the projection of the tilted acyl chains on the bilayer plane. Fourier analysis of the signal variations with respect to polarization angle enables the lipid orientation to be resolved spatially. We find that the texture of gel domains can exhibit topological defects including a vortex, pairs of half-integer vortices, and line defects[2]. Membrane texture resembles texture found in liquid crystals and Langmuir monolayers and have also been associated with hexatic positional order of the lipids.
The texture pattern in membranes is closely linked to the lipid composition as demonstrated by the occurrence of uniformly aligned domains for some compositions. Specifically, a close correlation has been found between the hydrophobic (thickness) mismatch at the border of domains and the texture pattern[3].
Recently we have explored the possibility that the Shiga toxin protein from the bacteria Shigella dysenteriae may remodel texture patterns in membranes. A