Interleaflet Coupling and Domain Registry in Phase-Separated Lipid Bilayers

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Abstract: There is clear evidence of an interleaflet coupling in model lipid/cholesterol membranes exhibiting liquid-liquid phase separation. The strength of this coupling is quantified by the mismatch free energyγ. We calculate it using a molecular mean-field model of a phase-separated lipid/cholesterol bilayer, and obtain values that increase as the concentration of saturated lipids in the coexisting phases is increased. These values lie in the range 0.01 - 0.03 k_BT/nm^2. We clarify the relationship between the interleaflet coupling and the extent of interleaflet alignment of liquid domains by analyzing a statistical mechanical model of coupled fluctuating domain interfaces. The model is solved exactly using the correspondence between statistical mechanics and quantum mechanics, yielding an expression for the characteristic size of fluctuations out of domain registry. This length scale depends only weakly on the strength of the interleaflet coupling and inevitably is only of the order of nanometers, which explains the experimental result that fluctuations out of domain registry have not been observed by optical microscopy.