

**Membrane thickness fluctuation amplitude measured by static and dynamic small angle scattering: Should SAS models include a dynamics term?**

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Cell membranes are composed of an intricate mixture of lipids, proteins, and sterols that self assemble into a flexible, dynamic bilayer. It has become increasingly apparent that the complex interplay between lipids and proteins within the membrane are essential to cell function. The implication of lipids in membrane mediated processes has motivated theoretical and experimental research interest to understand the functional significance of lipid chemical structure variations on the biomembrane structure and dynamics. In particular, hydrophobic mismatch between lipids with different acyl chain lengths is expected to play an important role in the local membrane structure and collective membrane dynamics. Herein we investigated these phenomena in large unilamellar vesicles of model membranes composed of binary mixtures of tail-mismatched lipids using a combination of small angle scattering and neutron spin echo spectroscopy. Using tail contrast matched samples highlights the bilayer structure and yields a clear determination of the structural parameters. NSE data shows an enhanced dynamics on the length scale of the bilayer thickness which is attributed to thickness fluctuations. The fluctuation amplitude increases with increasing temperature from  $\approx 0.4$  nm around the melting transition temperature to  $\approx 1$  nm at high temperature in the well mixed fluid phase while the time scale of the motion is almost constant in this temperature range. This leads to a very interesting question which we raise for discussion: to what extent are these nanosecond to microsecond dynamic reflected in the time averaged SAS data? And to the extent that they are, what is their implication on the interpretation of SAS data? In particular how is polydispersity different from fluctuations? Can the concepts in fact be decoupled? More fundamentally, to what extent does failure to consider dynamics in modeling SAS data lead to questionable conclusions and/or could SAS be used to reveal something about dynamics?