Small molecule interactions with lipid bilayers by neutron diffraction

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While well established for studying the internal structure of bilayers and orientation of peptides and proteins with respect to bilayers, neutron lamellar diffraction is also a powerful tool for studying the average locus of solubilisation of small molecules in stacks of lipid bilayers. The approach has provided unique insights into important issues in anhydrobiology and cryobiology, where previously only molecular dynamics simulations (MD) had been able to provide molecular scale insights. Currently we use the methodology to understand the interaction of cryo-protectants with bilayers, with the aim of providing important validation of MD parameters to further enhance the utility of the method. Here we discuss the experimental approach, both in terms of the use of contrast variation and the use of selective deuteration to simplify the extraction of scattering length density profiles within the bilayer.