Determining the Location of Encapsulated Peptides, Proteins, and Other Biomolecules in Contrast-Matched Lipid Bicontinuous Cubic Phases using SANS

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To evolve biological and biomedical applications of hybrid biomolecule?lipid materials, including in meso protein crystallization and drug delivery, an understanding of the location of the biomolecules within the bicontinuous cubic phases is crucial. Theoretical modeling has indicated that proteins and additive lipids might phase separate locally and adopt a preferred location in the cubic phase, but this has never been experimentally confirmed. We have shown that perfectly contrast-matched cubic phases in D2O can be studied using SANS by mixing fully deuterated and hydrogenated lipid. The model transmembrane peptide WALP21 showed no preferential location in the membrane ofthe diamond and gyroid cubic phases of phytanoyl monoethanolamide [L. van ‘t Hag *et al*, *J. Phys. Chem. Lett.* 2016, 7(14), 2862-2866]. In addition, this result opens up the possibility of studying the conformation (and hence function) of amphiphilic proteins and peptides within a lipid bilayer environment. The effect of deuteration on the cubic phase forming lipid was also investigated to advance the use of neutron scattering techniques to study soft matter systems. Additionally, we have performed extensive characterizations of the cubic phase nanostructure subsequent to protein and peptide incorporation using synchrotron SAXS, as well as the protein and peptide secondary structures using synchrotron circular dichroism spectroscopy [L. van ‘t Hag *et al*, *Langmuir*, 2016, 32(27), 6882-6894].