Effect of pH on hydration-driven phase transitions in lipids.

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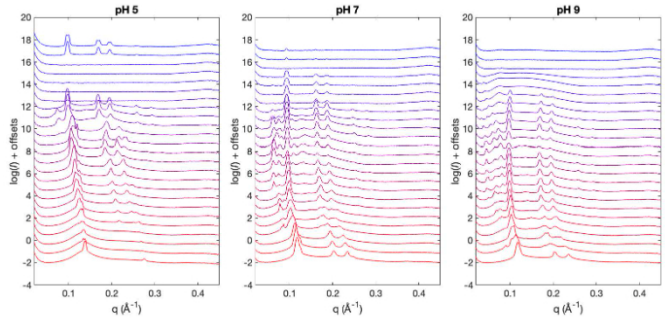
The role of pH is important to the effective design of drug delivery systems, particularly in biological environments where local pH gradients can strongly influence material behaviour. This is especially relevant for lipid-based formulations, where phospholipids are widely used due to their biocompatibility and although generally considered zwitterionic and insensitive to pH, may still exhibit pH-dependent effects. Previous works support this, demonstrating that hydration can drive lipid redistribution and the formation of different structural layers in lipid depots [1], as well as pH-dependent structural changes in lipid nanocarriers [2]. Here, we extend this concept to investigate how pH further affects hydration-driven lipid phase changes and transport processes.

In this study, small-angle X-ray scattering (SAXS) was used to probe hydration-driven structural transitions with spatial and temporal resolution. A capillary-based setup, in which lipids were at the bottom with excess buffers on top, created a hydration gradient, enabling spatially resolved measurements from the aqueous phase across the interface and into the lipid bulk, while measurements at defined hydration times captured the evolution of phase behaviour.

Our results show pH-dependent differences in hydration behaviour and structural reorganization across the lipid systems, characterized by the emergence and coexistence of multiple liquid crystalline phases, including hexagonal, several cubic, and intermediate structures. These observations highlight a complex, spatially heterogeneous phase behaviour that evolves over timescales of days and weeks along with hydration gradients. Together, these findings highlight the need to account for pH-dependent effects in phase distribution, lipid rearrangement, and transport processes in lipid-based delivery systems.

Keywords:
lipid phase behaviour, water diffusion, pH effect, hydration gradient, SAXS



SAXS profiles of SPC/Span80 50/50 weight ratio at different pH (5,7,9) after 1 week of hydration.

References:

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