Abstract
Lipid nanoparticles (LNPs) are intricate multicomponent systems widely recognized for their efficient delivery of oligonucleotide cargo to host cells. Gaining insights into the molecular properties of LNPs is crucial for their effective design and characterization. However, analysis of their internal structure at the molecular level presents a significant challenge. This study introduces 31P nuclear magnetic resonance (NMR) methods to acquire structural and dynamic information about the phospholipid envelope of LNPs. Specifically, we demonstrate that the 31P chemical shift anisotropy (CSA) parameters serve as a sensitive indicator of the molecular assembly of distearoylphosphatidylcholine (DSPC) lipids within the particles. An analytical protocol for measuring 31P CSA is developed, which can be implemented using either solution NMR or solid-state NMR, offering wide accessibility and adaptability. The capability of this method is demonstrated using both model DSPC liposomes and real-world pharmaceutical LNP formulations. Furthermore, our method can be employed to investigate the impact of formulation processes and composition on the assembly of specifically LNP particles or, more generally, phospholipid-based delivery systems. This makes it an indispensable tool for evaluating critical pharmaceutical properties such as structural homogeneity, batch-to-batch reproducibility, and the stability of the particles.

Connection Information
This will be a virtual meeting hosted via Microsoft Teams. A direct link to the meeting is located HERE.

Further information can be found on the NMR Topical Group website.

Please reach out to Christine Jorge (christine.jorge@bms.com) or Rongfeng Zheng (rongfeng.zheng@bms.com) with any questions.