

High-Throughput Small Angle X-ray Scattering (HT-SAXS) Pipeline for Lipid Nanoparticle (LNP) Development at the SIBYLS Beamline

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Lipid nanoparticles (LNPs) have been used as carriers for the effective delivery of oligonucleotide therapeutics, resulting in development and approval of the two mRNA vaccines in response to the recent COVID-19 pandemic. While many LNP formulations have been extensively studied, their highly variable structures resulting from slight changes in experimental parameters, such as lipid composition and formulation method, make the full design space of LNPs challenging to characterize comprehensively. Additionally, automation of LNP formulation has resulted in the efficient production of LNPs at a speed that is unmatched by most characterization methods such as cryogenic transmission electron microscopy (cryo-TEM). Here, we introduce a high-throughput small angle X-ray scattering (HT-SAXS) platform for screening LNP structures that enables data collection from 96 samples in only 1.5 hours. This system can be used complementarily with cryo-TEM to identify and validate structural features in bulk samples at an unparalleled rate. We have also been working on a pipeline for analysis to be conducted at the scale of data collection. Through this workflow, we can better understand how various composition and formulation conditions are linked to changes in structure and, ultimately, their function.