Data Fusion and Machine learning for the Particle sizing of Lipid nanoparticles

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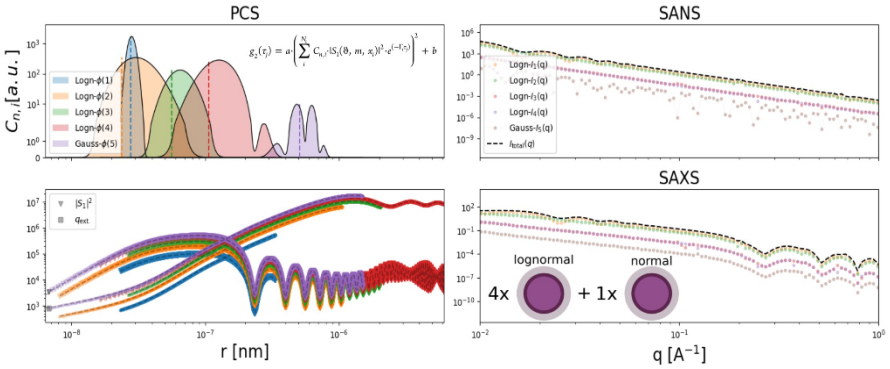
Lipid nanoparticles (LNPs) have established themselves as an essential drug delivery system, with widespread adoption during the SARS-CoV-2 pandemic. LNPs are versatile non-toxic carriers that offer efficient encapsulation of fragile polar cargos and its targeted delivery. LNPs self-assemble into a dispersion of Core multi-shell nanoparticles through liquid-liquid phase separation.[1,2]
Knowledge of the size distribution and the contributions of the individual components in the mesoscopic structure are crucial for a better understanding of environment dependent changes in structure and size. This leads to a better understanding of the release process and how to optimize it. Our group has developed a consistent method to determine the mesoscopic structure of LNPs by combining SAXS/SANS and PCS iteratively.[3] The method involves modeling multiple fractions of core dual shell particles that differ only in core radius, volume-fraction and system-dependent parameters. Small-angle scattering (SAS) data are fitted to derive a theoretical photon correlation spectroscopy (PCS) curve based on Mie theory (see Fig.). The particle fractions are adjusted and the fitting process is repeated until convergence with the experimental data has been reached. The complexity of the model makes it impractical to screen larger sample batches or to analyze environmental responses.
To address these limitations, recent advances in machine learning (ML) have achieved growing success in small-angle scattering (SAS) analysis.[4,5] These approaches provide new strategies to accelerate model convergence, improve parameter estimation, and enable automated interpretation of large and heterogeneous experimental datasets. Building on these developments, we integrate machine learning into our model-refinement workflow, using it both to guide parameter optimization and to reduce the computational burden of these high dimensional fits.

Keywords:
LNP, ML, SAXS, SANS, PCS, Data-Fusion



Indidual components and sum for SAS (left). Mie theory scattering amplitudes, extinction and PCS coefficients (right).

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