Probing Nanomedicine Structures with Analytical Ultracentrifugation: Lipid Based Nanoparticles and Liposomes

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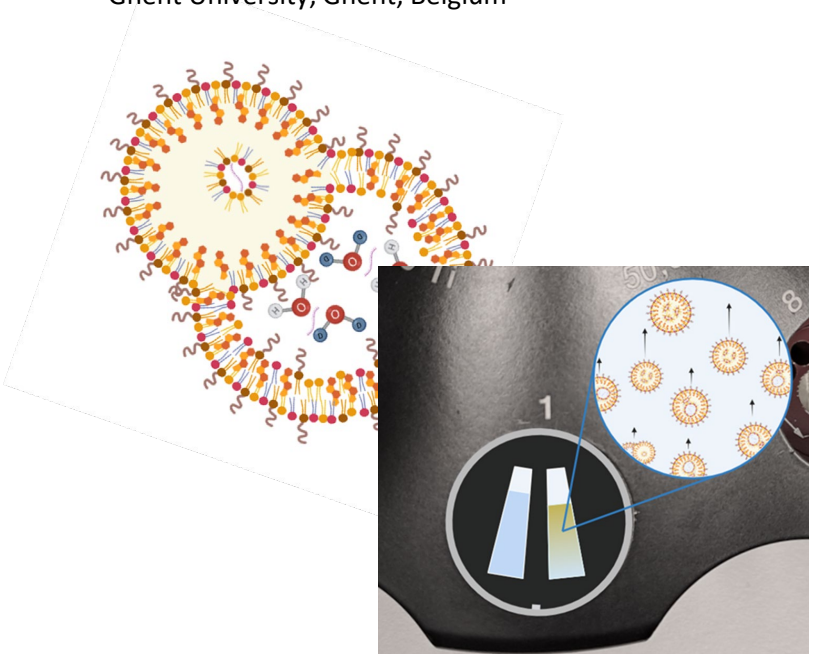
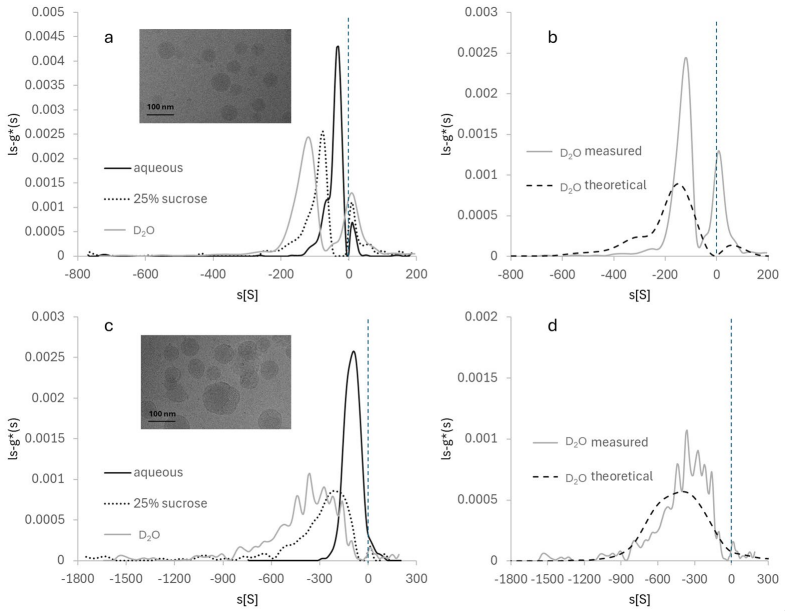
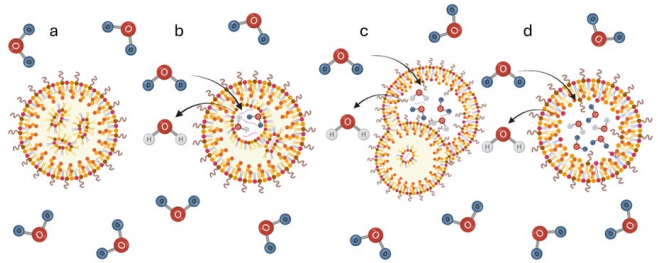




Sedimentation behavior of a) intact and compact mRNA LNPs and c) mRNA LNPs with blebs (solid, black line – PBS, grey line – D_2O/PBS, dotted line – 25% sucrose in PBS); b) and d) show the corresponding theoretically expected sedimentation coefficient distributions (dashed lines) compared to the measured ones (grey lines) in D_2O based solvent.

Density of soft nanoparticles is a rarely accessed but precious quality descriptor.[4] Our studies demonstrate the potential of AUC not only in determining density of liposomes and LNPs, but also in detecting particle non-homogeneity and morphological differences in lipid-based nanomedicines. We show that sucrose solutions are preferable to D_2O-based buffers in multiple velocity sedimentation experiments as sucrose doesn't permeate lipid bilayers.



Schematic drawing of D_2O and H_2O exchange between solvent and water loaded cavities in lipid-based particles when a) no detectable solvent exchange occurs in compact mRNA-LNPs, while D_2O enters water loaded cavities in b) and c) phase-separated mRNA-LNPs and d) liposomes. Created in BioRender. Mehn, D. (2026) https://BioRender.com/cmynnhs