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Tentative topic of the invited talk

From Model to Digital Twin Manufacturing: Mechanistic Insights for mRNA-Lipid Nanoparticle Vaccine Formulation.

Abstract of the invited talk

Digital twins promise faster development, de-risked scale-up, and real-time decision support in bioprocessing. For manufacturing mRNA-loaded lipid nanoparticles (LNPs), particle-size distribution (PSD) is a key critical quality attribute. We develop a structure-aware rheology model motivated by cryo-TEM showing lopsided, sometimes interpenetrating nanodumbbells with the smaller bead often carrying the payload [Brader et al., Biophys. J. 120, 2766 (2021)]. Combining rigid-dumbbell orientation theory with an elastic-dumbbell extension including connector stretching, we derive closed-form expressions for relaxation time, rotational diffusivity, zero-shear viscosity, stress- relaxation, steady-shear viscosity, and the viscous part and (minus) elastic part of the complex viscosity. Parameters obtained from small-amplitude oscillatory shear experiments confirm departures from Newtonian behavior and show how particle shape and mechanics govern the measured viscosity and elasticity. We then validate against a representative time-resolved PSD dataset with a single calibration. The model predicts the full PSD time course and the Z-average trajectory. These relations supply the physics to close population-balance and mixing models, improving PSD prediction and enabling more predictive, trustworthy digital twins for LNP manufacturing.

Keywords: Digital twin; population balance model; particle-size distribution; dumbbell rheology (rigid & elastic); rotational diffusivity; complex viscosity; viscoelasticity; orientation distribution.