# CFD-DEM simulation study on thermodynamic and mechanical effects in spray drying of mRNA-LNP formulations

Jiqian Guo[1,*], Silas Wolf[1], Jan Henrik Finke[1] , Carsten Schilde[1]
[1] *Institute for Particle Technology, Technical University Braunschweig, Braunschweig, Germany*

Spray drying is gaining attention as a potential route for producing dry powder formulations of mRNA lipid nanoparticles (mRNA-LNPs), motivated by the need for improved storage stability, reduced cold-chain dependence, and flexible downstream processing of vaccine products. However, successful process design requires predictive models that can resolve how droplets exchange heat, mass, and momentum with a hot, humid, particle-laden gas environment, while capturing the strong coupling between evaporation, internal cooling, and dispersed solids.

In this work, we present a CFD–DEM modeling framework for spray drying that combines volume-of-fluid (VOF) interface tracking with coupled temperature and water-vapor transport, together with two-way coupling to dispersed particles. The liquid–gas interface is advanced consistently with evaporation, ensuring synchronized prediction of droplet shrinkage, latent-heat removal, and vapor release into the surrounding gas phase. Carrier-phase hydrodynamics are solved using a segregated pressure–velocity algorithm, while local micro-iterations between temperature, humidity, and interfacial source terms enforce thermo-mass consistency without case-specific parameter tuning. On the particulate side, the DEM formulation accounts for momentum exchange with the fluid, optional thermal coupling, and porosity effects relevant to dense spray regions and particle-rich droplets.

To improve robustness for chemically and thermally sensitive systems, the framework incorporates algorithmic stabilization measures, including interface compression, volume-conserving corrections within the VOF band, bounded interfacial source terms, and regularized transport properties. Demonstration cases in hot crossflow show physically consistent droplet evaporation, stable humidity evolution, and the expected approach of droplet temperature toward wet-bulb conditions.

The model is intended as a building block for process-scale chemical engineering questions in spray drying, including the influence of inlet conditions, gas humidity, residence time and droplet–particle interactions. In the longer term, such a framework can support the rational design of spray-drying strategies for mRNA-LNP-based pharmaceutical formulations, where controlling the local drying environment is essential for preserving product quality.