

ABSTRACT

Industrial crystallization plays a critical role in determining product quality attributes such as crystal size distribution, morphology, purity, and yield in pharmaceutical, agrochemical, and specialty chemical manufacturing. However, predictive design and scale-up of crystallization processes remain challenging due to the strong coupling between thermodynamics, kinetics, and spatially heterogeneous transport phenomena. This work presents a physics-inspired multiscale modeling and digital design framework for industrial crystallization that systematically integrates population balance modeling, compartmentalization, and model-based experimental design. Mechanistic population balance models are developed to describe nucleation, growth, dissolution, and agglomeration phenomena, with both moment-based and high-resolution finite volume formulations employed to balance physical fidelity and computational efficiency. Spatial heterogeneities arising from non-ideal mixing and heat transfer are incorporated through a physics-informed multi-compartment framework derived from computational fluid dynamics, enabling efficient representation of hydrodynamic and thermal non-uniformities without the prohibitive cost of fully coupled CFD–PBE simulations. An iterative model-based experimental design strategy is implemented to support systematic model discrimination, parameter estimation, and progressive refinement under data-limited conditions. The proposed framework is demonstrated through in-silico and experimental case studies, revealing how process parameters and spatial heterogeneities govern crystal size distribution, agglomeration behavior, and attainable design spaces. Overall, this work establishes a unified digital design methodology that supports in-silico-first process development, reduces experimental burden, and provides a scalable pathway toward physics-based digital twins for industrial crystallization processes.