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Orchestrating Modelling & Simulation of Pharmaceutical Production Processes Via Large Language Models

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ABSTRACT

The digitalization of production processes necessitates the transition from siloed simulation tools to integrated, automated, and intelligent workflows. In the domain of particulate processes in pharmaceutical manufacturing, agitated drying is playing an important role. Predicting crystal attrition is critical to maintaining target particle size distributions (PSDs) and bioavailability. Traditionally, detailed 3D discrete element method (DEM) models and reduced-order process models have remained separate due to computational disparities. This work proposes an integrated approach to bridge these scales by leveraging physics-informed models and Large Language Models (LLMs) to orchestrate complex characterization and optimization loops. The first time Machine Learning was used to accelerate the characterization of powder properties for DEM was by Benvenuti et al. (2016) . Subsequent innovations introduced physics-informed reduced-order models, such as the two-dimensional population balance equation (2D-PBE) developed by Togni et al. (2025), which links attrition rates to impeller torque, particle aspect ratio, and residual solvent content.

While recent research has utilized Graph Neural Networks to further accelerate 3D granular simulations (Mayr et al, 2021 and 2021), the current challenge lies in the seamless integration of these heterogeneous models, material databases, and experimental data.We demonstrate an approach where an LLM assistant facilitates the re-combination and execution of python-based calculation elements—modular code units representing specific physical equations or ML methods—into executable workflows. Within our platform engicloud.ai, these calculators are derived both from expert knowledge and extracted from research literature, providing a verified foundation for cross-disciplinary collaboration. For the specific use case of predicting crystal attrition, the platform enables researchers to run a physics-based PBE model informed by 3D simulation data (Togni 2025) in an LLM-driven loop to optimize powder properties by dynamically adjusting process conditions based on material-dependent parameters calibrated from ring shear-cell and lab-scale experiments.

The role of the LLM can be manifold, such as complementing traditional optimization methods, e.g. to simulate scenarios in case of supply chain disruption (such as due to a war or pandemic) where the LLM agent would provide a list of materials available in a certain scenario, which in turn provides the material properties for the PBE model. By providing a low-entry-barrier, web-based environment for the exploration and the aility to interoperate with material models and databases via APIs and access to ~20,000 static (verified) models extracted from LLMs, engicloud.ai enhances the reproducibility and scalability of digital twins in materials science.

This work highlights how such modular software architectures foster FAIR initiatives and accelerate the transition from initial material conception to late-

stage process validation and optimization in real life scenarios.

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