**Application of multiscale modelling and deep learning tools for flash nanoprecipitation and reactive crystallization**

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**Highlights**

* Multiscale modelling is applied to the simulation of crystallization processes
* Multiscale modelling is augmented by artificial intelligence and deep learning tools
* Experimental data is used for model validation
* Two examples are discussed: flash nanoprecipitation and reactive crystallization

**1. Introduction**

Crystallization and precipitation are very important in chemical engineering as numerous particulate products are manufactured by relying on these processes. Examples span from the pharmaceutical industry to the materials industry, including catalysis and batteries. The final products properties are characterized in terms of distributions, notably the size distribution. In turn the particle size distribution (PSD), or crystal size distribution (CSD), is strongly affected by the operating conditions under which the process is carried out and in order to design, scale up and down and optimize the process, computational models are extremely useful. In fact, they can answer the complex question: under what operating conditions a specific PSD or CSD can be obtained? In this contribution the main computational modelling techniques are presented and discussed.

**2. Methods**

As the main emphasis is on the prediction of the PSD/CSD the most popular computational models are based on the solution of the population balance equations (PBE), that dictates the evolution of the PSD/CSD. However, since the PBE is strongly connected with the fluid dynamics of the crystallizer, very often the PBE is tightly coupled with a computational fluid dynamics (CFD) model. The coupling is often realized with quadrature-based moments methods (QBMM) such as the quadrature method of moments (QMOM) or the conditional quadrature method of moments (CQMOM) [1].

Moreover, as the rates with which particles and crystals are formed are governed by molecular processes, very often these models are coupled also with atomistic and molecular models. Among the different modelling choices full atom molecular dynamics (MD) and coarse-grained molecular dynamics (CGMD) are mostly employed.

A plethora of codes is used to run these simulations, to couple the different models and to orchestrate the workflows, ranging from Ansys Fluent, OpenFOAM, code\_saturne, LAMMPS, GROMACS, Salome, etc.

All the above-mentioned models, being based on first principles and physical laws are labelled as physics-based models. However, recently the simulation of these processes also relies on the use of artificial intelligence and deep learning tools to build data-driven models, which is contrast to the previous ones, are not based on first principles. An interesting idea is that since very often the amount of experimental data is often not enough to build a data-driven model, validated physics-based models can be used to augment and enrich a limited experimental data set and to build the data-driven model, following the digital twin concept.

**3. Results and discussion**

Two examples will be discussed in this presentation. The first one focuses on flash-nanoprecipitation via solvent-displacement for the production of amorphous polymer nanoparticles for controlled drug delivery applications, whereas the second focuses on the precipitation of inorganic crystals via reactive crystallization or precipitation. In the first example it will be shown how multiscale modelling can be used to simulate the polymer particle formation process, starting from molecules up to the actual crystallizer and to successfully predict the effect of the choice of the good solvent, of paramount important in these processes [2,3]. In the second example the use of these computational tools will be discussed for a different application process involving inorganic crystals.

**References**

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