2-years post-doctoral fellowship – Open position

"Scalabity of plasma-assisted crystallization of perovskite and APIs"

Context

Crystallization is a separation and purification process widely used in industry for drug synthesis, purification of battery-grade metals, food manufacturing, etc. Although the technique is mature, industrial crystallization still faces two main challenges: (1) controlling the crystal size distribution (CSD) to improve the efficiency of downstream processes (filtration, washing, drying), and (2) controlling the polymorphic phase in order to optimize the physico-chemical properties of the product –e.g. solubility of active pharmaceutical ingredient (API).

A better control of these features is hindered by undesired nucleation in the crystallization reactor. Nucleation is a stochastic phenomenon producing solid crystalline seeds from a supersaturated solution. In the development of crystallization processes, scale-up is often an issue because solution stirring (required for homogeneity) induces shear stress that strongly impacts the nucleation rate [1] and thus prevents accurate CSD control.

Industry circumvents the nucleation issue by seeding crystallizers with a specific amount of calibrated crystalline seeds at low supersaturation ratio in order to prevent undesired spontaneous nucleation event. Although this technique is satisfying, it can be constraining if crystallization is performed in a sterile environment, or if the seed material is not available in sufficient amount and quality.

Therefore, there is a need for *in situ*, on-demand and scalable seeding techniques allowing a high level of polymorph and crystal size distribution controls. Alternative techniques based on external fields are currently explored but their scalability is still an issue - e.g. sonocrystallization, laser-induced nucleation [2].

The INCRYS project (ANR PRC grant) aims to use **cold plasma** – a non-equilibrium ionized gas - for seeding crystallization reactors in a non-intrusive manner, *in situ,* and *on-demand*. Two main objectives will be addressed: (i) understanding the main nucleation mechanism using a plasma microfluidic reactor coupled with advanced diagnostics to capture plasma and nucleation dynamics, (ii) studying the scalability of plasma-induced nucleation in supersaturated flows typically encountered in batch stirred reactor.

Mission and objectives

We are looking for a post-doctoral associate highly motivated by interdisciplinary research to address the challenge of plasma-induced nucleation scale up.

First, the candidate will use a homemade temperature-controlled Couette cell in order to measure the nucleation frequency under controlled shear rate. The candidate will implement the optical diagnostics necessary to monitor the crystallization and use statistical analysis tools to infer the nucleation rate from the induction time. As a first step, the setup will be tested on the model API system glycine/water and the data will be compared with a reference paper [1].

Second, the candidate will evaluate the effect of plasma exposure on the measured nucleation frequency in different flow regimes in order to assess the possibility to use the cold plasma to control nucleation in stirred flows. Similar measurements will be performed on a perovskite system which is the model compound used to study the mechanism of cold plasma-induced nucleation in the framework of the INCRYS project.

Third, in collaboration with the LGPM CFD team, the candidate will design a stirred batch reactor with known shear stress. The post doc will develop a plasma-assisted crystallization process where the cold plasma is used to trigger the nucleation. Various characterization techniques (X-ray, Malvern MasterSizer,…) will be used to validate the effect of cold plasma on the crystallization features under different flow regime.

Laboratory framework

The candidate will work in the laboratory of chemical engineering (LGPM) located in CentraleSupélec on the campus of Paris Saclay university. The candidate will be involved in the INCRYS project and will thus work in close collaboration with the neighboring partners from CentraleSupélec (EM2C and SPMS laboratories) and ENS Paris Saclay (LuMin laboratory). Most of the experimental work will be performed at the LGPM laboratory. X-ray characterization of the crystal phase will be performed at SPMS laboratory.

Profile required.

The candidate must hold a PhD and have a solid experimental background in Chemical Engineering.
- Experience in the conception and validation of experimental setup
- Skills in programming (e.g. Python) for data treatment, automation of the acquisition, and implementation of population balance modelling (PBM)
- Knowledge of main characterization techniques of solid materials (PXRD, Raman, DSC,…) and process analytical tools would be ideal
- Highly motivated by multidisciplinary research
- Fluency in scientific and technical English
- Autonomy
- Good interpersonal skills for a rapid integration into the laboratory

Contract duration and remuneration

The duration of the postdoc is 24 months, with remuneration based on experience and the statutory salary scale.

Constraints and risks
Work in a chemistry laboratory with health and safety constraints (wearing PPE, etc.) and handling of Chemicals including perovskite compound and organic solvent;

Application: CV and covering letter citing a reference and/or letter of recommendation.

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[1] C. Forsyth et al., 2015, Cryst. Growth Des., 15, 94–102, https://doi.org/10.1021/cg5008878
[2] B. Clair et al., J. App. Cryst., 2014, 47: 1252. https://doi.org/10.1107/S160057671401098X