General Applicability and Quantitative Predictability of Complex Population-based Crystallization Models

What is the PhD Project About?

This project performed in collaboration with Bayer AG (Leverkusen, Germany) will address key challenges in developing experimentally validated process models to aid in the production of crystalline pharmaceuticals and agrochemicals at different scales (lab-pilot-plant). Modeling of crystallization processes offer several advantages. Accurate and predictive mathematical models have been and can be used for understanding the underlying physics, for process design, optimization, and control. Within the domain of crystallization, these models are composed of population balance equations (PBE) for the solid phase and the mass conservation constraint for the liquid phase. The former enables one to model the evolution of the particle size and shape distribution of ensembles of crystals. The latter enables one to model the evolution of the liquid phase concentration/supersaturation. Often, these models are developed in an academic setting at scales and conditions that are far from a realistic industrial scenario. Additionally, even though all the models developed in the literature account for the evolution of "size", majority of them do not account for the evolution of the shape of crystals (e.g., needles, plates, etc.). These factors can have potential implications on the general applicability and *quantitative* predictability of crystallization process models across different scales (lab to industrial scale).

The overarching goal of the proposed collaborative project between Bayer and the University of Manchester is two-fold. These are

1. To *quantitatively* evaluate the limits of the predictive capability of lab-scale models.
2. To propose a sound experimentally validated framework that facilitates developing predictive crystallization process models applicable over different scales.

It is anticipated that this project will help Bayer and the broader crystallization community to *judge whether pursuing significant efforts in developing models for process design and operation is worthwhile in terms of its predictability at different scales and the time and resources invested.*

How Will this Challenge be Addressed?

To address the goals of the project we will develop an innovative research campaign, capitalizing on the state-of-the-art experimental (microscopic and multiprojection imaging devices) and computational tools (process models and parameter estimators), readily available at the University of Manchester. We will develop generic multidimensional population balance equation solvers in an open-source language to simulate batch and semi-batch processes under different conditions (nucleation, growth, and dissolution) and scales (100 mL to 20 L). Subsequently, we will perform *in silico* studies to identify resources required in terms of number of experiments, number of solid and liquid phase sampling points, and choice of operating conditions (heating/cooling rates, temperatures, seed loading, etc.), to ensure satisfactory model identifiability to describe crystal growth, dissolution, and nucleation. The outcome from the *in silico* studies will guide in identifying process models, through a targeted experimental campaign using non-proprietary and proprietary (from Bayer) compounds. The predictability of the experimentally obtained models will be evaluated at different scales and if needed, they will be fine-tuned. Finally, best practices surrounding model development, parameter estimation, design of experiments, size and shape characterization of crystalline products will be provided to the broader crystallization community.

Supervisory Arrangements for the PhD Student and the Environment

The PhD student will be supervised by Dr. Ashwin Kumar Rajagopalan, Lecturer in the Department of Chemical Engineering at the University of Manchester. The project is an industrial CASE studentship; hence the student

will also work closely with our industrial project, Bayer. The student will spend 6 months at the company site in Leverkusen, Germany to get exposed to industrial research. The student will have access to the laboratory facilities of the group in the newly opened Engineering Building (part of the MECD program) at the University of Manchester. The student will also have access to the computational shared facility, a 10000 node cluster and one of the best in the world, to tackle the computational aspects of this project.

What can the PhD Student Expect?

- Disseminate results obtained over the course of the PhD program through prestigious peer-reviewed journals (e.g. Chemical Engineering Science, Chemical Engineering Journal, Crystal Growth & Design, etc.,)
- Attend national (British Associate of Crystal Growth) and international (International Symposium on Industrial Crystallization, American Institute of Chemical Engineering Annual Meeting etc.,) scientific conferences and workshops (EFCE summer schools on crystallization) across the globe to present research findings and network with peers from academia and industry
- Work with a young and growing research group at the birthplace of chemical engineering
- Can collaborate with other research groups working on relevant topics at the University of Manchester
- Have access to several one-of-a-kind experimental and computational tools in the UK, that has the potential to be transferred to an industrial setting soon
- Get direct exposure to industrial partners through this project and indirect exposure through projects of other PhD students in the research group
- Obtain a PhD degree on solving classical chemical engineering problems and learn and hone 21st century experimental and computational skills that can be readily transferable to both an academic and an industrial setting

Ideal Candidate

Applicants should have or expect to achieve a first-class honours degree in Chemical Engineering or Process Engineering. Under exceptional circumstances, high 2.1 applicants will be considered. The applicant should qualify for the home tuition fees.