

conditions, and different types of crystallizers that fundamentally offer more opportunities for process actuation comparable to batch crystallization (*e.g.*, plug-flow crystallizers). Second, crystal quality attributes are shaped by a number of physical phenomena such as crystal growth, nucleation, agglomeration, and breakage, which cannot be well manipulated independently in conventional continuous crystallizers, but only at best collectively *via* bulk variables.⁶ Therefore, trade-offs often have to be made, which limit the range of attainable product qualities.⁷ The development of novel actuators that selectively target specific crystallization phenomena is a promising area to improve the flexibility and predictability of crystallization process control as well as the development of dynamic process models. Third, due to the nature of continuous processing, material has to be further processed immediately to benefit from integrated continuous manufacturing, which calls for a need to measure crystal quality attributes in an on-line fashion. The spectacular advancement of process analytical technologies (PAT) is highly encouraging in that regard.⁸ Furthermore, since continuous crystallization is usually embedded within a larger continuous process, control objectives at the level of a unit operation have to be aligned with so-called plant-wide control objectives, which for example have been studied in detail for continuous pharmaceutical processes involving crystallization steps.^{3,9,10} Fourth, scale-up of crystallization processes is complicated due to scale-dependency of mixing, which is particularly a challenge for open-loop control strategies. Finally, crystallization processes typically exhibit highly non-linear behaviour, which complicates tuning of conventional PID controllers and limits standard model-based control strategies using model linearization. The great advancements in nonlinear dynamic modelling of crystallization processes and associated numerical methods nowadays offer many opportunities for the development and feasible implementation of model-based control strategies in practice.

When developing a control strategy for continuous crystallization, the definition of the control objectives is one of the first questions that arise. As discussed above, typical control objectives for continuous crystallization may be related to various types of product quality control, process stabilization (*e.g.*, in case of oscillatory or unstable open-loop behaviour), the economic performance of the process (*e.g.*, related to the use of utilities or transient behaviour) or environmental criteria such as an E-factor.¹¹ Just as for any unit operation of a chemical process, the basic questions to be answered to design a control strategy for crystallization processes for a given control objective are:

- What variables do we wish to control?
- What variables can (or should) be measured?
- What manipulated variables are available?
- How do we pair them in automated control loops (structurally and mathematically)?