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Batch Crystallisation Control Optimisation Using In-Line Monitoring and External Dynamic Nucleation Control

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Batch production remains widely used in the manufacture of fine chemicals and active pharmaceutical ingredients, mainly due to relatively small production scales and the diversity of target compounds. Crystallisation plays a decisive role, as it directly determines the properties of the final product.

This work presents the development and experimental validation of a prototype system designed to enhance crystallisation control through active nucleation control. The proposed solution integrates a modified crystalliser design with an external dissolution unit, enabling real-time control of the crystal population during operation.

A central feature of the system is continuous monitoring using in-line microscopy, combined with advanced image processing techniques supported by machine learning. This setup provides real-time information on crystal size distribution and process dynamics, forming the basis for closed-loop control.

The control strategy relies on process analytical technology (PAT), employing an advanced algorithm to adjust operating parameters in response to the current system state. This allows rapid corrective actions, resulting in improved product consistency and a reduced risk of off-specification material.

An experimental setup was assembled by adapting an existing internal DNC system with readily available and cost-effective components. A linear cooling experiment was first conducted to establish a reference case and define the expected particle count range. Subsequent experiments focused on increasing crystal size, demonstrating that process optimisation could be achieved within only a few experimental runs.