

1. Motivation

- A Population Balance Model (PBM) is developed by considering growth and dissolution, as well as primary and secondary nucleation kinetics.
- The mathematical model was validated against data from batch cooling and dired nucleation control (DNC) experiments, then used to optimize the number of MSMPR stages, design parameters and operating conditions (e.g. stage temperatures).
- Extension of model to multi-stage continuous systems with multiple decision variables.

2. Parameter estimation and model validation

- Parameter estimation of the batch cooling crystallisation system: MA/2-butanol
- Model validation against DNC experiments: Predicted $D_{50}$ and concentration agree well with measured data

3. Model-based optimization of a batch system

Model-based optimization and validation were done through T-cycling operations and compared with a model-free DNC system

- Objective function: Maximise $D_{50}$ or Minimise Span
- Decision variables: $T_{11}-T_{12}$; Seed mass
- Constraints: $20 \leq T_{11}-T_{12} \leq 60^\circ C$
- $5\% \leq$ seed mass $\leq 20\%$
- $0.95 \leq$ yield $\leq 1$

4. Multistage continuous MSMPRs optimization

- Objective function: Max $D_{50}$ or Min Span
- Decision variables (n = 5): $T_{11}-T_{12}$; Seed mass
- Constraints: $20 \leq T_{11}-T_{12} \leq 60^\circ C$
- $5\% \leq$ seed mass $\leq 20\%$
- $0.95 \leq$ yield $\leq 1$

5. Conclusions

- Digital workflows were developed to design experiments, collect batch data, identify mechanisms, estimate kinetic parameters
- Models were then validated using more complex batch operation, e.g. temperature cycling
- Multi-stage continuous crystallization Digital Twin were built with in silico optimization of steady-state operations of a MicroFactory, with many decision variables
- Sensitivity analysis was employed to determine the most influential model parameters, Critical Process Parameters and Critical Material Attributes
- Future work involves the validation of MicroFactory operation and integration with upstream and downstream process operations

Acknowledgement: The authors would like to acknowledge support from EPSRC Future Continuous Manufacturing and Advanced Crystallisation Research Hub Grant EP/P006965/1