Introducing uncertainty analysis of nucleation and crystal growth models in Process Analytical Technology (PAT) system design of crystallization processes - DTU Orbit (17/12/2018)

**Introducing uncertainty analysis of nucleation and crystal growth models in Process Analytical Technology (PAT) system design of crystallization processes**

This paper presents the application of uncertainty and sensitivity analysis as part of a systematic model-based process monitoring and control (PAT) system design framework for crystallization processes. For the uncertainty analysis, the Monte Carlo procedure is used to propagate input uncertainty, while for sensitivity analysis, global methods including the standardized regression coefficients (SRC) and Morris screening are used to identify the most significant parameters. The potassium dihydrogen phosphate (KDP) crystallization process is used as a case study, both in open-loop and closed-loop operation. In the uncertainty analysis, the impact on the predicted output of uncertain parameters related to the nucleation and the crystal growth model has been investigated for both a one- and two-dimensional crystal size distribution (CSD). The open-loop results show that the input uncertainties lead to significant uncertainties on the CSD, with appearance of a secondary peak due to secondary nucleation for both cases. The sensitivity analysis indicated that the most important parameters affecting the CSDs are nucleation order and growth order constants. In the proposed PAT system design (closed-loop), the target CSD variability was successfully reduced compared to the open-loop case, also when considering uncertainty in nucleation and crystal growth model parameters. The latter forms a strong indication of the robustness of the proposed PAT system design in achieving the target CSD and encourages its transfer to full-scale implementation.

**General information**

State: Published
Organisations: Department of Chemical and Biochemical Engineering, Computer Aided Process Engineering Center, Center for Process Engineering and Technology
Contributors: Abdul Samad, N. A. F. B., Sin, G., Gernaey, K., Gani, R.
Pages: 911-929
Publication date: 2013
Peer-reviewed: Yes

**Publication information**

Journal: European Journal of Pharmaceutics and Biopharmaceutics
Volume: 85
Issue number: 3
ISSN (Print): 0939-6411
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 4.67 SJR 1.342 SNIP 1.378
Web of Science (2017): Impact factor 4.491
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.49 SJR 1.411 SNIP 1.416
Web of Science (2016): Impact factor 4.159
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 4.37 SJR 1.437 SNIP 1.471
Web of Science (2015): Impact factor 3.975
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 4.44 SJR 1.481 SNIP 1.583
Web of Science (2014): Impact factor 3.85
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 4.64 SJR 1.566 SNIP 1.696
Web of Science (2013): Impact factor 4.245
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes