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Rapid online calibration for ATR-FTIR spectroscopy during batch crystallization of ammonium sulphate in a semi-industrial scale crystallizer

Somnath S. Kadam[a,*], Ali Mesbah[a,b], Eric van der Windt[c], Herman J.M. Kramer[a]

[a] Process and Energy Laboratory, Delft University of Technology, Leeghwaterstraat 44, 2628 CA, Delft, The Netherlands
[b] Delft Center for Systems and Control, Delft University of Technology, Mekelweg 2, 2628 CD, Delft, The Netherlands
[c] Bruker Optics B.V., Oostsingel 209, 2612 HL, Delft, The Netherlands

ABSTRACT

The knowledge of solute concentration throughout a batch crystallization process is essential from process control perspective. Despite the progress in process analytical technology (PAT), there still exist several challenges for online measurement of solute concentration at industrial scale. In this study, concentration monitoring was realized using attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy at lab as well as semi-industrial scale. Applications of the calibration model developed at lab scale for the measurements at the semi-industrial scale however resulted into strongly biased concentration predictions, caused by the differences in the curvature of fiber optics and the uneven thermal expansion of the probe. Therefore an alternative rapid online calibration method was developed during the start-up phase of the process. With this method, the time required for developing a working calibration model for concentration monitoring during crystallization of ammonium sulphate in a semi-industrial scale draft tube crystallizer has been reduced approximately by 90%. With the help of simultaneous concentration and crystal size distribution measurements at semi-industrial scale, the descriptive capability of the model was improved due to better kinetic parameters.

Keywords: Batch crystallization; Semi-industrial scale; Concentration monitoring; ATR-FTIR spectroscopy; Calibration; Parameter estimation

1. Introduction

Crystallization is an important unit operation which determines the product quality in the pharmaceutical, specialty, fine and agrochemicals industry. Generally, the crystal quality is defined in terms of the purity, size and shape distribution, polymorphic fraction, etc. (Mersmann, 2001). These properties are highly dependent on the operating conditions in the crystallizer. A small variation in these properties may affect the efficiency of the downstream processing units and the product performance (Braatz, 2002; Wibowo et al., 2001). Hence, an effective control over these properties and in turn the crystallization process is essential.

In recent years, with the developments in the computing power and the in situ monitoring of the process variables like crystal size distribution (CSD) and concentration, two distinct control approaches have evolved. One of these approaches (model-free) requires determination of a supersaturation profile (generally experimental) which seeks a trade-off between crystal quality and process productivity. The supersaturation profile determined in this way is always near-optimal. Once the supersaturation profile has been determined, a control strategy is devised which maintains the desired relation between the system states, viz. concentration and temperature, along the predefined supersaturation profile (Fujiwara et al., 2005; Nagy et al., 2008; Zhou et al., 2006). The other approach (model-based) relies on the model developed with the population balance (Hulburt and Katz, 1964), conservation laws and kinetic expressions (Braatz, 2002; Mesbah et al., 2010; Nagy, 2009). This model is used in an optimization framework

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[*] *Corresponding author*. Tel.: +31 015 2786628; fax: +31 015 2782460.
E-mail address: s.s.kadam@tudelft.nl (S.S. Kadam).

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wherein the objective function, generally related to the CSD, is used to obtain a desired supersaturation profile (Rawlings et al., 1993). The performance of the model based controller depends on the model structure and the precise determination of the kinetic parameters which in turn is dependent on the CSD and the concentration profile.

Accurate measurement of the process variables is a prerequisite for employing advanced control strategies. Several techniques exist for monitoring of concentration and CSD during a crystallization process. Their relative merits and demerits are summarized in the literature (Kadam et al., 2010; Neumann and Kramer, 2002). In recent years, techniques based on imaging are finding increased applications in monitoring process conditions during crystallization. The real-time images of the crystal slurry provide not only quantitative information like CSD for spherical (Darakis et al., 2010) and non spherical particles (Darakis et al., 2010; Larsen and Rawlings, 2009) but also qualitative information like change in morphological form during crystal growth (Calderon De Anda et al., 2005) and onset of nucleation (Simon et al., 2009a,b,c). The information obtained by imaging can also be integrated in the supersaturation control strategies to obtain better product quality(Simon et al., 2010).

As a first step towards better product quality, it is essential to monitor concentration accurately at industrial scale. Many researchers have already confirmed that the attenuated total reflectance (ATR) Fourier transform infrared (FTIR) spectroscopy is well suited for concentration monitoring during crystallization (Borissova et al., 2008; Dunuwila and Berglund, 1997; Hojjati and Rohani, 2006; Kadam et al., 2010; Togkalidou et al., 2001). However, its proper implementation requires time consuming calibration work (Feudale et al., 2002; Honorato et al., 2005).

Calibration of ATR-FTIR for concentration monitoring during crystallization process is generally performed by collecting several spectra methodically at different concentrations and temperatures. The spectra are collected either by varying temperatures while keeping the concentration constant (Cornel et al., 2008) or vice versa (Borissova et al., 2008). Based on these spectra, a partial least square (PLS) (Wold, 1985) calibration model is developed that can predict concentration. As the spectra collection is usually done at lab scale, it would be of great interest for the industrial community to verify if the PLS model developed in the lab performs as expected at the industrial scale.

In this contribution we examine the feasibility of the ATR-FTIR spectroscopy for concentration monitoring at semi-industrial scale. In Sections 4.1–4.3, we first present the feasibility of ATR-FTIR spectroscopy for concentration monitoring at lab scale during the batch crystallization process of ammonium sulphate from its aqueous solution. A part of this result is published earlier (Kadam et al., 2010) but it is important to restate it for proper comparison with semi-industrial scale. Having done that, we discuss the problems associated with the use of the PLS model developed at the laboratory scale on a semi-industrial scale set-up for the same instrument in Section 4.4 and then present a method for rapid online calibration which avoids these problems in Section 4.5. To the best of our knowledge, the attempt was made for the first time to demonstrate this technique on a semi-industrial scale crystallizer. Finally in Section 4.6, we demonstrate the solute concentration monitoring at pilot plant with ATR-FTIR and show that this process information together with the on-line CSD measurements can lead to better kinetic parameter estimates and enhanced process understanding.

2. Experimental details

2.1. Experimental set-ups

Experiments were performed both on lab and semi-industrial scales.

2.1.1. Lab scale

The set-up at lab scale was used to carry out the calibration of ATR-FTIR, the subsequent validation of the developed calibration model in the presence of crystals and the batch cooling crystallization experiments. It consisted of a 1L jacketed glass crystallizer as shown in Fig. 1a, connected to a Lauda RK8KP thermostatic bath which maintained and controlled the temperature inside the crystallizer with the help of an external platinum resistance thermocouple Pt-100. The crystallizer was maintained well mixed by an IKA RET basic C magnetic stirrer. The gold plated hastelloy ATR probe with diamond internal reflection element (IN 350 T) connected to MATRIX-MF spectrometer from Bruker Optics GmbH was inserted from the lid. The spectrometer has tightly controlled environment with very minimal effect of water vapour in the path length of the beam. Hence, nitrogen flushing of the spectrometer was not performed.

2.1.2. Semi-industrial scale

The experiments at semi-industrial scale were carried out isothermally at 50 °C in a 75L seeded fed-batch evaporative draft tube crystallizer shown in Fig. 1b. The fed-batch operation was implemented to compensate for the losses of the crystallization volume by evaporation of the solvent and sampling of the slurry. Hence the crystallizer was continuously fed with the crystal free feed stream containing saturated ammonium sulphate solution at 50 °C. The crystallizer was equipped with an on-line laser diffraction instrument (HELOS-Vario, Sympatec) to measure evolution of the product CSD during the batch. A small product flow was withdrawn from the crystallizer at regular time intervals and was diluted with saturated feed solution to facilitate the CSD measurements. The in situ concentration monitoring was done simultaneously by an ultrasonic (US) probe (LiquiSonic 20, SensoTech) and the same ATR-FTIR instrument used during the lab experiments. The US probe can monitor the concentration till the seeding point only as it cannot work in the presence of crystals.

2.2. Experimental procedures

2.2.1. Lab scale calibration

Two common calibration approaches are described in the literature. In one of the approaches the temperature is kept constant while the concentration is changed by dilution with known amount of solvent (Borissova et al., 2008). In the other approach, the concentration is kept constant while the temperature is changed till nucleation is detected (Cornel et al., 2008). The constant concentration approach allows collection of the spectra in undersaturated as well as supersaturated regions. But care must be exercised in using this approach as it might be difficult to apply for the crystallizing systems which have narrow metastable zone widths and for systems