

distribution was monitored using FBRM. The produced crystals were characterized offline using X-ray powder diffraction (XRPD) in order to determine their polymorphic form. Data from FTIR and XRPD were also used in the second part of the same work to estimate the kinetic parameters necessary to conduct dynamic simulations on the studied system and predict the process yield as a function of the operating conditions.

Preferential crystallization in MSMPR crystallizers has also been a subject of investigation. Galan and co-worker used on-line polarimetry to measure the optical rotation of the liquid phase and estimate the amount of each enantiomer in solution.²⁰ The clear solution from each vessel was circulated in an external loop where a polarimeter in series with a density meter was positioned. More recently FBRM and PVM have been used by Steendam and ter Horst to monitor the size and shape of chirally pure sodium bromate crystals.²¹ The chirality of the solid crystals produced was evaluated off-line using polarized microscopy.

9.7 Monitoring of Tubular Crystallizers

An alternative to MSMPR crystallizers for continuous processes are tubular crystallizers. In order to minimize attrition and improve mixing, slug flow²² and oscillatory operation *e.g.* the continuous oscillatory baffled crystallizers (COBC) have been investigated.²³⁻²⁵ Other alternatives are tubular crystallizers equipped with static mixers.²⁶

On-line chord length distribution monitoring of a tubular crystallizer equipped with a Kenics static mixer has been presented by Simon and Myerson using an FBRM probe,²⁷ which then was used for systematic on-line steady-state detection.¹⁷ Other monitoring methods are based on stereomicroscopes²⁸ and high speed cameras to monitor the size and number of crystals,^{12,13,25} aggregation,²⁹ mixing quality,³⁰ fouling³¹ as well as flow type.²³ Besenhard and co-workers²³ have used high speed imaging and on-line laser diffraction (a HELOS system equipped with a LIXELL flow cell installed on-line) to monitor the number of fines, the size of crystals produced and their polymorphic form in a segmented flow tubular crystallizer. The recorded images gave information about the quality of the mixing and the type of flow, gas bubbles and continuous liquid phase. Ferguson *et al.*¹⁰ used FBRM, PVM and ATR-FTIR to monitor crystals produced in a plug-flow anti-solvent crystallizer. In this case the instruments were positioned in a specifically designed flow cell situated outside the end section of the plug-flow crystallizer. Furthermore, Brown and Li used video imaging to study the crystallization of paracetamol in a COBC system. Image analysis algorithms have been developed to determine the metastable zone width, the mean particle size and the number density of crystals during the process.¹² The growth