Particle-Shape Monitoring and Control in Crystallization Processes

Daniel B. Patience and James B. Rawlings
Dept. of Chemical Engineering, University of Wisconsin, Madison, WI 53706

Limitations of sensors for the on-line measurement of solid-phase properties have restricted the development and implementation of improved design, monitoring, and control methods for crystallizers and other particulate processes. Image analysis has recently become a popular technique to monitor crystal size and shape in crystallization processes. Plummer and Kausch (1995) used image analysis to measure the real-time crystal size density (CSD) of polyoxymethylene as it crystallizes on a static stage under a microscope. Monnier et al. (1997) use image analysis to measure the final CSDs of adipic acid in water crystallization. Puel et al. (1997) use image analysis to measure two characteristic lengths of hydroquinone crystals as a function of time. The technique is not yet fully automated, however, and the crystal slurry is manually sampled and placed under the microscope. In addition, imaging requires an operator to occasionally interrupt automatic sizing and discard measurements before taking more samples. In their review, Braatz and Hasebe (2001) discuss the recently available *in situ* Lasentec particle and vision measurement (PVM) system. This sensor provides two-dimensional images of crystals in random orientation, however, the authors state that the quality of the images limits the ability of imaging software to automatically identify individual particles but is suitable for qualitative troubleshooting. Image analysis has not yet been demonstrated to automatically monitor in real time the size and shape characteristics of crystals in a suspension crystallizer. The strong advantage of image analysis in the preceding applications, however, is that it requires almost no assumptions about particle size or shape and does not require inversion of a signal and inference of the resultant particle size or shape density. Although image analysis is a direct observation technique, it is a two-dimensional measurement and care must be taken if one is to infer a three-dimensional shape.

Limited information regarding shape can be extracted from two-dimensional binarized images of objects given adequate sampling. Podczeck (2000) reviews the history of the range of methods used to assess the shape of particles from a two-dimensional image. Podczeck (1997) motivates the need to define new shape factors that are simple to calculate and incorporate commonly used measurements such as aspect ratio. She also defines one shape factor based on a combination of the object's elongation and other shape factors that describe an object's deviation from a square, circle, and triangle. Bernard-Michel et al. (1997) use Fourier descriptors of an object contour to classify more than 10 distinctly different shapes. These shape descriptors are not available with commercial image analysis software routines. The particles used in these studies are not broken and are not agglomerated. The particles are carefully arranged under the microscope without touching other particles, making it easy to digitize correctly all particles in the image. If commercial packages are implemented on-line, the user is often limited with software-designer-supplied functions. Typically, only simple measurements are available with commercial image-analysis packages, such as aspect ratio, roundness (the deviation of the object's shape from a circle), and boxed area. It can be difficult to extract meaningful shape information from aspect ratio and roundness measurements, let alone using more detailed shape descriptors for an image of particles sampled from a particulate process. Particles sampled from a suspension crystallizer, for example, can contain broken, agglomerated, aggregated, and irregularly grown crystals besides the correctly grown crystals, and in all cases, the shape measurements are replete with bad data and contain significant noise. Bharati and MacGregor (1998) use multiway principal-component analysis to decompose highly correlated data present in images obtained from a LANDSAT satellite as it passes over geographical regions of the earth. These techniques are useful to determine the most informative software-designer-supplied measurements for shape in commercial image-analysis software packages.

The habit of a crystal is determined by the various growth rates of the different faces of the crystal under different internal and external conditions. Internal conditions that affect the habit of a crystal include factors such as impurity content and liquid occlusions, while external factors include temperature and solution flow around a crystal. Some pharmaceuticals potentially exhibit multiple polymorphs because of their typical complex chemical structure, and these polymorphs often have different shapes. Shape may be an important characteristic to monitor in pharmaceuticals in order to detect

Correspondence concerning this article should be addressed to J. B. Rawlings.

morphology changes. However, it should be noted that polymorph assessment based on shape must be verified with X-ray diffraction. Because of these characteristics, shape is becoming an increasingly important variable to monitor in crystallization processes. Given the just-mentioned limitations in on-line measuring of crystal size with light scattering or image analysis, on-line measurement of shape is even more challenging.

In this note, we present a simple technique that can identify suitable data from a noisy signal produced on-line by commercially available image-analysis software. A controller successfully uses this signal to regulate the flow rate of a habit modifier stream to maintain a desired crystal habit. We demonstrate these methods on a simple chemical system: sodium chlorate ($NaClO_3$) crystallization using sodium dithionate ($Na_2S_2O_6$) as a habit modifier.

Chemical System and Experimental Apparatus

Ristić et al. (1993) found that sodium chlorate crystallized in impurity-free solutions forms predominantly the 100 faces responsible for the cubic shape, shown in the top left of Figure 1. In the presence of at least 50-ppm sodium dithionate, growth of the $\bar{1}\bar{1}\bar{1}$ faces are slowed and the 100, 110 and 111 faces grow out (top right of Figure 1), resulting in a tetrahedral shape with $\bar{1}\bar{1}\bar{1}$ faces. If sodium dithionate is no longer present in the solution phase, and provided enough supersaturation is remaining in solution, the tetrahedral sodium chlorate crystal will grow back to the natural cubic shape (Ristić et al., 1994).

The experimental apparatus used in this study is similar to that described by Matthews and Rawlings (1998) shown in bottom of Figure 1. The crystallizer is a 2.2-L, glass, jacketed vessel. The temperature of the crystallizer is controlled by a model-predictive controller. For a crystallization experiment, 1 600 g sodium chlorate is dissolved in 1 600 g H_2O (T^{sat} = 24.4°C) at a temperature of 33°C. The solution is held at this temperature for 30 min, then rapidly cooled at $16°C \cdot h^{-1}$ to 25°C and held for 30 min. Then the solution is cooled at $0.25°C \cdot h^{-1}$ until completion of the experiment. Two mL of sodium dithionate solution (18 g $Na_2S_2O_6$ in 100 g H_2O) is injected into the crystallizer when cubic crystals form, resulting in an impurity concentration of 225 ppm. When the crystals grow to the tetrahedral shape, an impurity-free solution of sodium chlorate (T^{sat} = 23.5°C) is fed to the reactor and a solids-free solution is removed from the reactor at equal rates of $80\ mL \cdot min^{-1}$. The crystals grow back to their original cubic shape during this semibatch phase once the sodium dithionate concentration is low enough to no longer slow the growth of the $\bar{1}\bar{1}\bar{1}$ faces. The flow streams to and from the crystallizer are stopped once the cubic shape is seen under the microscope, and then another 225 ppm of sodium dithionate is injected into the crystallizer.

Photomicroscopy and digital image analysis are used to monitor growth kinetics and particle size and shape characteristics of crystals in the size range of 50 μm to 1 000 μm using an Olympus BX60 microscope, a Hitachi HV-C20 charged-coupled device (CCD) camera, and a PC with frame grabber and Image Pro Plus image analysis software. The microscope uses a nonpolarized reflected halogen light source with a total magnification of 8×. The crystal slurry is pumped

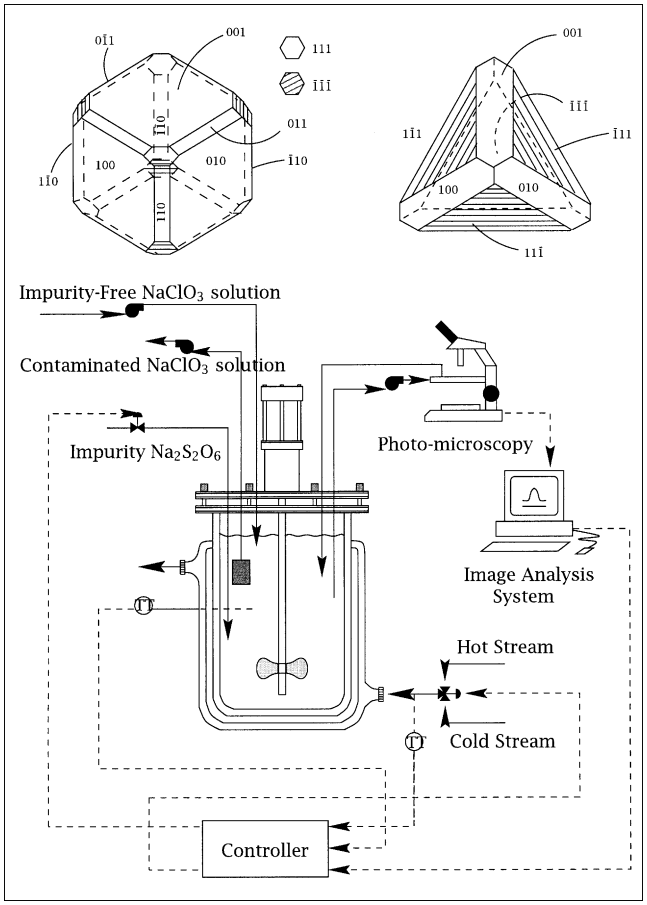

Figure 1. Typical cubic shape of sodium chlorate ($NaClO_3$) (top left); growth toward a tetrahedral shape in the presence of sodium dithionate ($Na_2S_2O_6$) (top right); experimental apparatus (bottom).

continuously from the crystallizer through a circulation loop. Periodically, the flow is automatically stopped and an image of the settled particles at the bottom of a 10 mm × 10 mm × 100 mm rectangular glass flow cell is captured and digitized. The CCD camera captures images of 585 × 700 pixels with 256 grayness levels. A Sobel filter, an Image Pro Plus supplied function, is applied to the image to enhance transparent crystals and increase the probability of detecting a cube. A red/green/blue threshold of 000/084/002 is applied. Any pixel darker than this color is considered to be background and any pixel lighter is part of an object. The brightness, contrast, and gamma corrections are set to their default values of 50%, 50%, and 1.0. The particles are then sized according to a pixel calibration using an image of a stage micrometer at the same magnification. Upon completion of image capture and digitization, the flow loop is restarted and the sample returns to the crystallizer. During image capture, 20–30 s are required to stop the flow, let the particles settle, digitize the image, size the particles, and restart the flow. The stop-flow cell is used for two reasons: first, the CCD camera is not able to capture quality images of the slurry as the particles are moving. Second, we obtain a preferred orientation of the

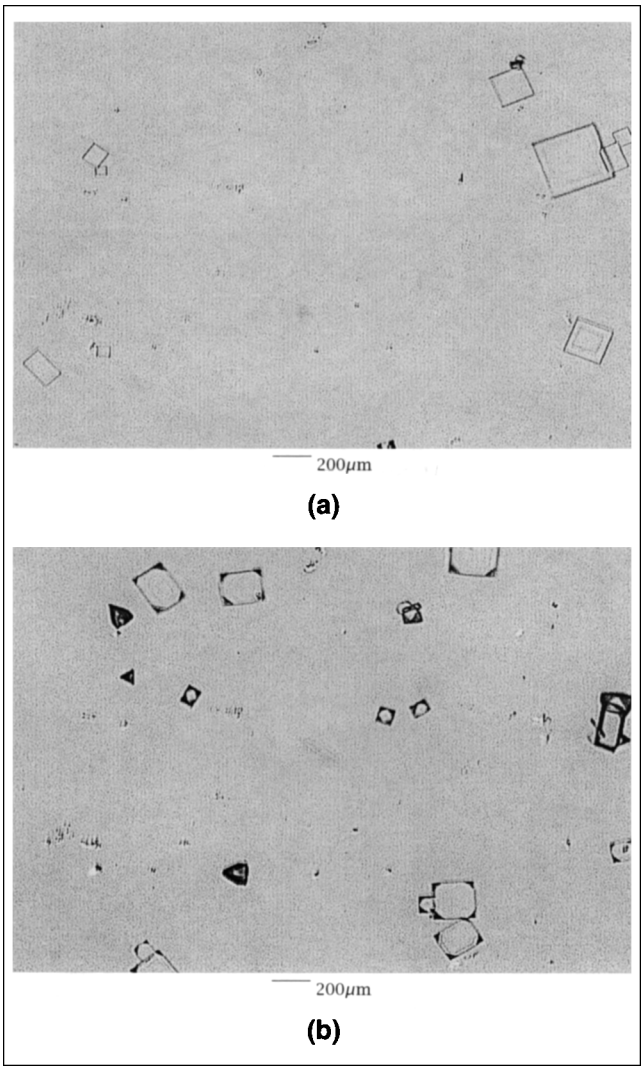

Figure 2. Nucleation and growth of sodium chlorate at 23.5°C.

$Na_2S_2O_6$ impurity is injected at 30 min. (a) 15 min; (b) 49 min.

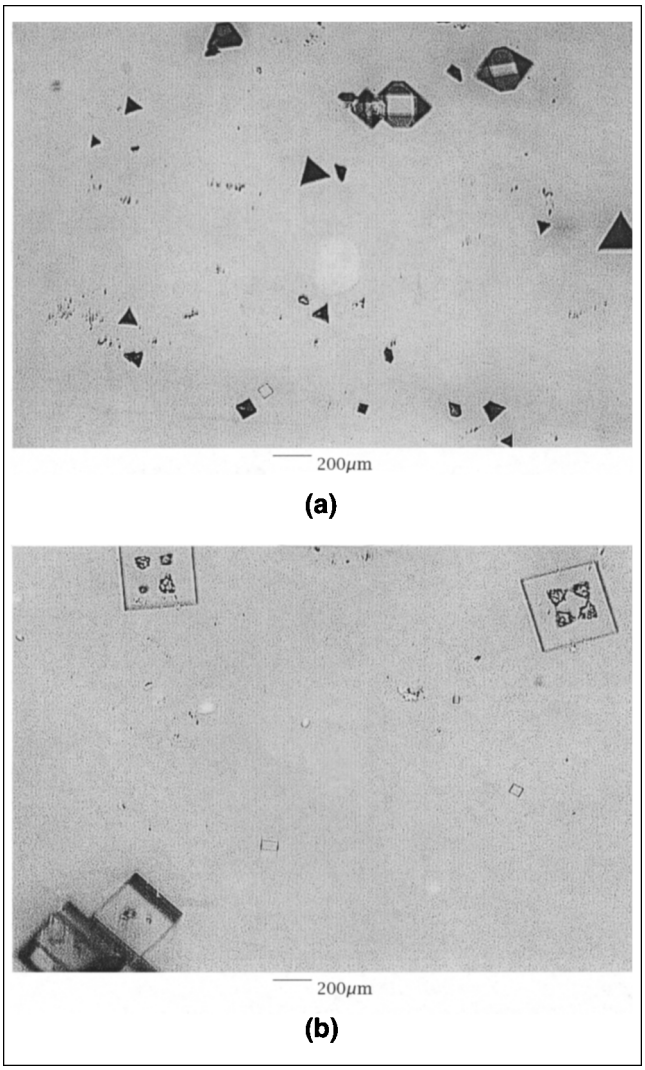

Figure 3. Nucleation and growth of sodium chlorate at 23.5°C.

Contaminated solution flush started at 80 min. (a) 70 min; (b) 135 min.

crystals on the 100 and $\overline{1}\overline{1}\overline{1}$ faces instead of a random orientation. Obtaining shape information from a moving, randomly oriented object requires further analysis.

Results and Discussion

Raw measurement and standard image analysis

Figures 2 and 3 show the results of an experiment in which sodium chlorate crystals nucleate heterogeneously and grow in impurity-free solution. Once impurity is injected (occurs between Figures 2a and 2b) the crystals continue to grow and evolve to the tetrahedral shape (Figures 2b to 3a). Once the crystals are tetrahedrons, the impurity is flushed from the system and the crystals continue to grow and return to the original cubic shape (Figure 3b).

The image analysis algorithm by Image Pro is similar to the algorithm presented by Pons (1990). Objects that are in contact with the border are eliminated and objects that have holes are filled. An *autosplit* split option analyzes all existing outlines and attempts to automatically split clustered objects. Two clustered objects are separated if their intersection can be identified by two concave points. If the resulting split results in convex objects, then the split is considered; otherwise, the object remains unsplit. Autosplitting has the advantage of separating touching crystals, but can split agglomerated crystals or crystals with irregular protrusions unnecessarily. The sensor has been tested with glass beads manufactured by the National Institute of Standards and Technology (NIST) and found to give particle-size densities agreeing with those measured by NIST. Measurements such as an aspect ratio and a boxed area provide a description of particle shape. The aspect ratio used in this study is defined as the ratio between the major and minor characteristic lengths of an object. The boxed area is defined as the ratio of the area of an

object to the area of the minimum-size bounding box of the object. For an equilateral triangle, the values for aspect ratio and boxed area are $3\sqrt{3}/4$ and 0.5, respectively. For a square, the values are $\sqrt{2}$ and 1.0, respectively. A roundness measurement also describes shape, though in this study, the measurement is correlated with the boxed area.

Unless the light thresholding and focusing are set manually and individually for each image, and particles in the image are chosen, split correctly, and sized manually and individually, then data from automated image analysis for sodium chlorate crystallization are going to contain many erroneous points. The raw measurement of the boxed area as a function of time in the top of Figure 4 shows no trends as the impurity is injected or when the impurity is flushed from the solution, even though images clearly show changes back and forth between the cubic and tetrahedral shapes as the impurity is injected and flushed from the system. The noise is caused by many factors: particles may be touching and are not split; particles may be broken or agglomerated; perfect transparent crystals may not be completely detected, and when the object is digitized, the boundary of the object may not be completely closed.

Refined image analysis

Sodium chlorate crystals can be produce a family of images ranging from squares to equilateral triangles when viewed from above after they settle on a flat surface. For simplicity we focus here on distinguishing squares and equilateral triangles. The top of Figure 5 shows squares and equilateral triangles that have sawtooth waves of increasing amplitude added to the boundaries of the shapes. Adding these waves to the boundaries of squares and triangles mimics the noise in determining the particle boundary of a sodium chlorate crystal under the microscope. The noise in the boundary of a square or equilateral triangle object is caused by the degree of camera focusing and the light threshold setting. These factors can change the object size and shape measurements by many pixels.

In the boxed area–aspect ratio plane (bottom of Figure 5), the region for detecting a square is based on squares 1–7, 9–10 in Figure 5 at two sizes. The region for detecting a triangle is based on triangles 11–14 at two sizes in Figure 5. The region $\boldsymbol{X}$, namely the aspect ratios and boxed areas for the shapes in Figure 5, is given by the ellipsoid

$$(\boldsymbol{X} - \bar{\boldsymbol{X}})^T \boldsymbol{V}_{XX}^{-1} (\boldsymbol{X} - \bar{\boldsymbol{X}}) \le s, \qquad (1)$$

in which $\boldsymbol{V}_{XX}$ is the covariance matrix of $\boldsymbol{X}$ for the objects in Figure 5, and s is a scaling factor. The values for s (25 for squares and 5 for triangles) are prechosen in preliminary shape experiments to get the desired trend in shape change, and then these values are used throughout the experiments in this study. As each image is analyzed by Image Pro Plus as a function of time, the routine then examines each object and if its aspect ratio and boxed area lie in either ellipse, then the data for that object is accepted, otherwise it is rejected. The middle of Figure 4 shows the raw data in the top of Figure 4 plotted in the boxed area–aspect ratio plane with the elliptical regions in the bottom of Figure 5. Clearly, most of the data are rejected because the objects are unclassifiable departures from a square (cube) or equilateral triangle (tetrahedron). The bottom of Figure 4 shows the final result of the boxed area as a function of time after the data (objects) have been classified as either squares or triangles. A sodium chlorate crystal with a shape intermediate between a cube and a tetrahedron can be viewed and sized as a square if the crystal

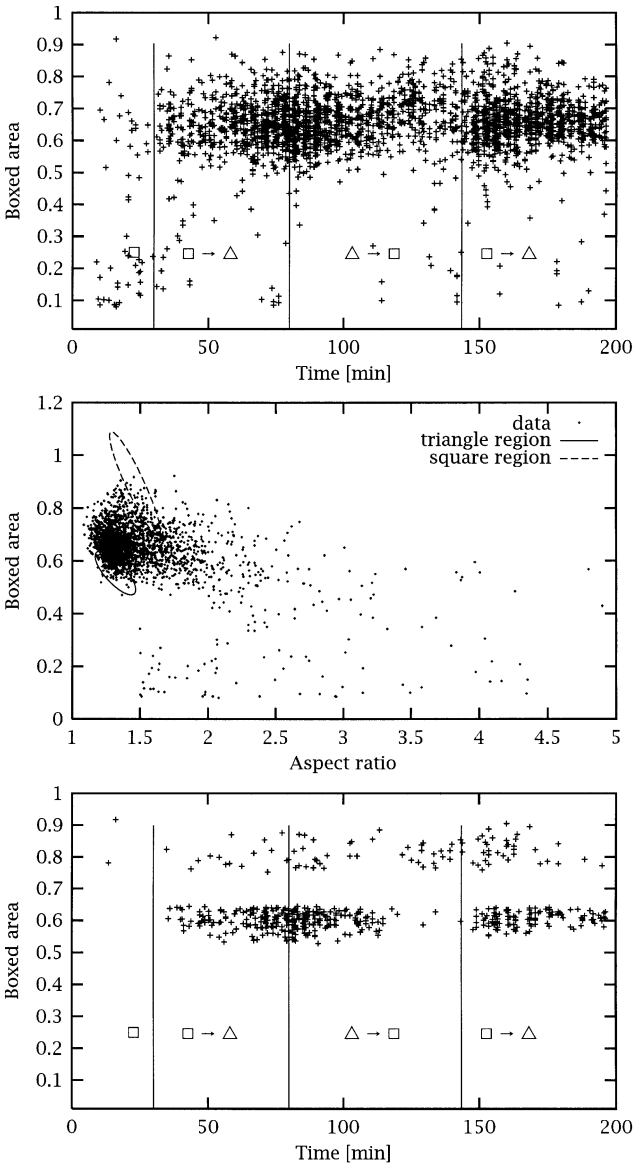

Figure 4. Raw-data boxed area as a function of time: (top) impurity injected at 30 min, contaminated solution flush started at 80 min and stopped at 144 min; a second dosage of impurity is injected at 144 min; raw data in boxed area–aspect ratio plane with regions indicating where an object is a square or triangle (middle); refined data boxed area as a function of time (bottom).

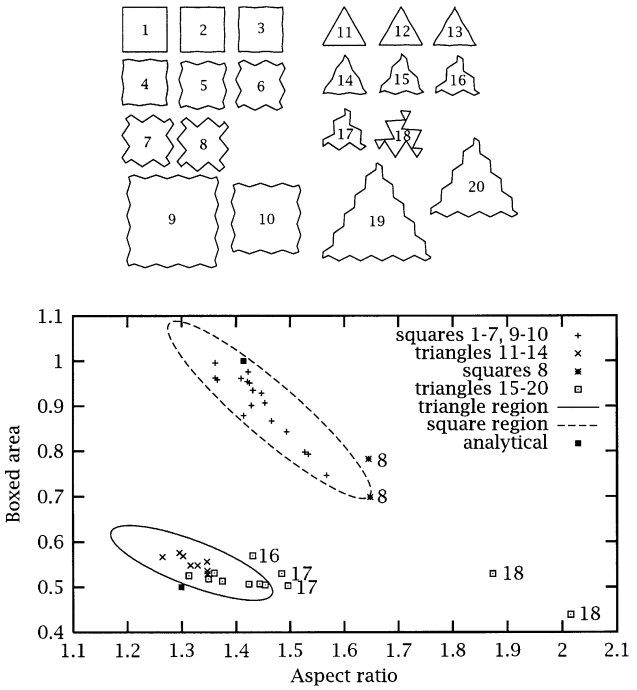

Figure 5. Possible sodium chlorate views in two dimensions when the crystal rests either on the 100 face (square) or $\bar{1}\bar{1}\bar{1}$ face (triangle) (top); likelihood regions in which Image Pro Plus will detect a square and equilateral triangle using boxed area and aspect ratio (bottom).

The ellipse for detecting a square is based on squares 1–7, 9–10 at two sizes. The ellipse for detecting a triangle is based on triangles 11–14 at two sizes.

rests on its 100 face. However, if the crystal with an intermediate shape between a cube and tetrahedron rests on its $\bar{1}\bar{1}\bar{1}$ face during image capture, it is likely that it is a rejected object.

The bottom of Figure 4 shows that as the impurity is injected, an increased number of tetrahedra are present in the crystallizer, and as the contaminated solution is flushed, the density of tetrahedra decreases, supported by images. With this algorithm, we are able to generate a signal that detects shape transition and particle size in a semibatch crystallizer, given on-line image analysis data from commercial software.

Feedback control

An impurity-free sodium chlorate solution stream is fed to the reactor and a solids-free solution is removed from the reactor at equal rates, of 80 $mL \cdot min^{-1}$. The impurity-free solution entering the reactor acts as a disturbance by flushing the habit modifier from the system and preventing the crystal from remaining in the tetrahedral shape.

For basic industrial control of shape, the percentage of cubes or tetrahedra may be all that is required to implement feedback control. The boxed area measurement is convenient for detecting the percentage of cubes or tetrahedra because of the discontinuity in the measurement. To remove the effects of low sampling of objects in one image, the percentage

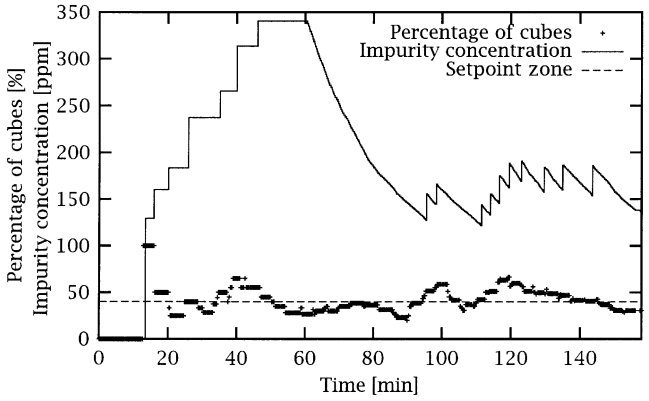

Figure 6. Feedback control of particle shape based on on-line measurements of percentage of cubes in the crystallizer.

After 60 min, an impurity-free solution of sodium chlorate is fed to the reactor and a solids-free solution removed at equal rates for the remainder of the experiment.

of cubes in the crystallizer at a point in time is based on the most recent 10 images. The sampling rate of 20–30 s is adequate to capture the system dynamics, shown at the bottom of Figure 4. A simple proportional-integral (PI) feedback controller uses the percentage-of-cubes signal to regulate the habit modifier concentration to maintain a desired shape.

To illustrate a simple control example, it is desired that the percentage of cubes remains below 40%. If more than 40% of the particles are cubes, then the controller adjusts the habit-modifier level until the percentage is below 40%. The fresh feed reactant stream disturbance ($T^{sat} = 24°C$) is fed to the crystallizer and a solids-free stream is removed from the crystallizer at equal rates after 60 min. The exit stream is removing the added habit modifier, so the controller is required to maintain the level of habit modifier over the course of crystallization. Figure 6 shows that without any prior knowledge of the nucleation and growth kinetics of the sodium chlorate system, the controller is able to determine the critical concentration of 140–150 ppm sodium dithionate that is required to maintain the percentage of cubes at less than 40%.

Conclusions

This note has shown that a simple user-defined algorithm can be implemented with existing commercially available image analysis software to monitor transient crystal shape changes in a suspension crystallizer. The raw signal from image analysis is replete with bad data resulting in a noisy signal, but with prior knowledge of the crystal shape, a simple automated classification scheme can be used to determine which data result from correctly sized crystals. This signal can be used for basic control of crystal shape in a suspension crystallizer.

Acknowledgment

Financial support from The International Fine Particle Research Institute (IFPRI) is gratefully acknowledged. We also thank Professor John N. Sherwood at the University of Strathclyde in Glasgow for

stimulating this research through helpful discussions of sodium chlorate shape manipulation.

Literature Cited

Bernard-Michel, B., S. Rohani, M.-N. Pons, H. Vivier, and H. Hundal, "Classification of Crystal Shape Using Fourier Descriptors and Mathematical Morphology," *Part. Part. Syst. Charact.*, **14**, 193 (1997).

Bharati, M. H., and J. F. MacGregor, "Multivariate Image Analysis for Real-Time Process Monitoring and Control," *Ind. Eng. Chem. Res.*, **37**, 4715 (1998).

Braatz, R. D., and S. Hasebe, "Particle Size and Shape Control in Crystallization Processes," *Chemical Process Control—VI*, J. B. Rawlings, B. A. Ogunnaike, and J. W. Eaton, eds., AIChE Symposium Series, Vol. 97, No. 326 (2001).

Matthews, H. B., and J. B. Rawlings, "Batch Crystallization of a Photochemical: Modeling, Control and Filtration," *AIChE J.*, **44**, 1119 (1998).

Monnier, O., G. Fevotte, C. Hoff, and J. P. Klein, "Model Identification of Batch Cooling Crystallizations Through Calorimetry and Image Analysis," *Chem. Eng. Sci.*, **52**, 1125 (1997).

Plummer, C., and H. Kausch, "Real-Time Image Analysis and Numerical Simulation of Isothermal Spherulite Nucleation and Growth in Polyoxymethylene," *Colloid Polym. Sci.*, **273**, 719 (1995).

Podczeck, F., "A Shape Factor to Assess the Shape of Particles Using Image Analysis," *Powder Technol.*, **93**, 47 (1997).

Podczeck, F., "The Shape of Powder Particles and Its Influence on Powder Handling," *Proc. Int. Fine Particle Research Institute Conf.*, Den Haag, The Netherlands (2000).

Pons, M.-N., and H. Vivier, "Crystallization Monitoring by Quantitative Image Analysis," *Anal. Chim. Acta*, **238**, 243 (1990).

Puel, F., P. Marchal, and J. Klein, "Habit Transient Analysis in Industrial Crystallization Using Two Dimensional Crystal Sizing Technique," *Chem. Eng. Res. Des.*, **75**, 193 (1997).

Ristić, R., B. Y. Shekunov, and J. N. Sherwood, "Growth of the Tetrahedral Faces of Sodium Chlorate Crystals in the Presence of Dithionate Impurity," *J. Cryst. Growth*, **139**, 336 (1994).

Ristić, R., J. N. Sherwood, and K. Wojciechowski, "Morphology and Growth Kinetics of Large Sodium Chlorate Crystals Grown in the Presence and Absence of Sodium Dithionate Impurity," *J. Phys. Chem.*, **97**, 10774 (1993).

Manuscript received Oct. 17, 2000, and revision received Mar. 29, 2001.