

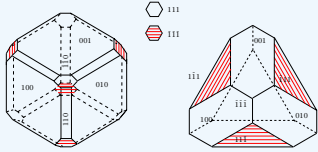
On-line Monitoring and Control of Crystal Morphology

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1 Prototypical shape control problem

- High value-added products in the chemical industry are becoming increasingly complicated in structure. Pharmaceutical compounds almost always exhibit multiple polymorphs and typically the desired polymorph is not easily obtainable because of unmeasured disturbances during processing.
- Unlike popular techniques such as light scattering and XRD, image analysis can measure on-line size and shape characteristics, however, in-situ image analysis probes and data analysis is a challenge.
- The 110, 111 and $\bar{1}\bar{1}\bar{1}$ faces of sodium chlorate (NaClO_3) grow fast under relatively high supersaturation and "grow out" leaving only the 100 faces visible under microscopy, seen as **cubes**.

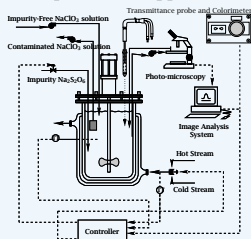


(Ristic, R. et al., *J.Phys.Chem.* 1993)

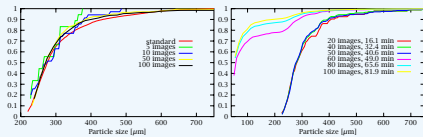
- The 100, 110, and 111 faces grow fast in the presence of sodium dithionate ($\text{Na}_2\text{S}_2\text{O}_6$) and "grow out" leaving only the $\bar{1}\bar{1}\bar{1}$ faces visible, seen as **tetrahedra**.

2 Experimental Studies

Experimental apparatus



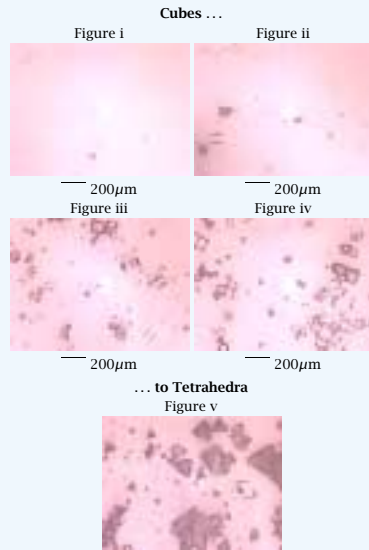
- Image analysis is tested with glass beads manufactured by the National Institute of Standards and Technology.



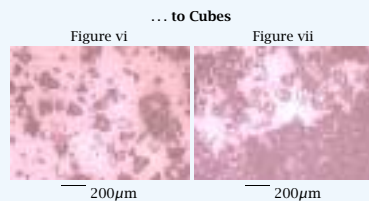
- Cumulative distribution data show particle size and transient changes can be monitored accurately.

Nucleation and growth of NaClO_3 at 22.5°C

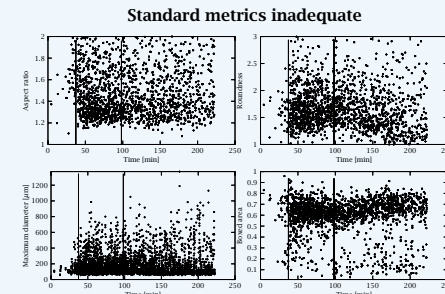
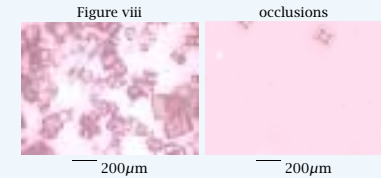
- NaClO_3 nucleates as cubes. After Figure i, 50 ppm $\text{Na}_2\text{S}_2\text{O}_6$ is injected and the crystals continue to grow and evolve towards a tetrahedral morphology.



- Manipulate crystal habit from one morphology (hexahedra) to another morphology (tetrahedra) and return to the original morphology in a batch crystallizer.
- Monitor and control crystal shape by adjusting the impurity level to maintain a tetrahedral morphology.



- Impurity free solution fed to and solids free solutions removed from the crystallizer at equal rates after Figure v. Once the impurity has been flushed out, the crystals continue to grow back to cubes.



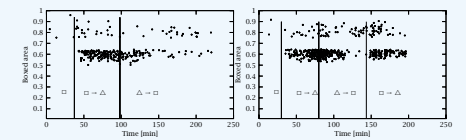
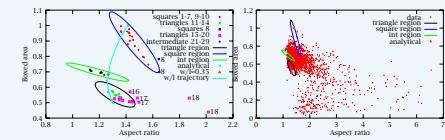
- Boxed area as a function of time shows trends in the correct direction.

Classifying shapes

- Saw tooth waves of increasing amplitude are added to the boundaries of a square, an equilateral triangle and an intermediate shape with $w/l = 0.35$ sitting on the $\bar{1}\bar{1}\bar{1}$ face. The objects are sized to assess the reliability of the sensor for detecting cubes, tetrahedra and intermediate shapes.

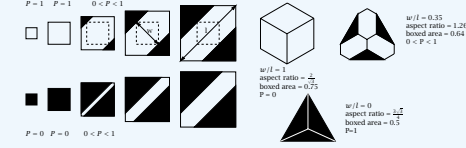


	square	triangle
aspect ratio	$\frac{l_{max}}{l_{min}} = \sqrt{2}$	$\frac{3\sqrt{3}}{4}$
roundness	$\frac{perimeter^2}{4\pi \cdot object\ area}$	$\frac{4}{\pi}$
boxed area	$\frac{object\ area}{bounding\ box\ area} = 1.0$	0.5



Modeling and controlling the crystal population

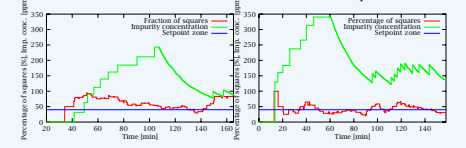
Particle resting on 100 face Particle resting on $\bar{1}\bar{1}\bar{1}$ face



The 2D population balance equation incorporates information about particle shape.

$$\frac{\partial f(l, w, t)}{\partial t} = -G_l \frac{\partial f(l, w, t)}{\partial l} - G_w \frac{\partial f(l, w, t)}{\partial w}$$

- $f(l, w, t)$ is the time varying particle size density.
- $0 < G_w = G_l = \text{const}$, $0 \leq C_{imp} < C_{crit}$
- $0 < G_w = \text{const} \ll G_l = \text{const}$, $C_{imp} \geq C_{crit}$



3 Conclusions and Future Work

Conclusions

- The morphology of sodium chlorate can be transformed back and forth between cubes and tetrahedra.
- Photo-microscopy and image analysis provide excellent on-line measurements of particle size and morphology for simple geometric shaped particles within 50 to 600 µm based on boxed area and aspect ratio classification.
- Particle shape can be controlled by maintaining the habit modifier near the critical concentration that maintains the presence of 111 faces on the crystal during growth.

Future Work

- Implement an in-situ image analysis probe using strobing for rapid sampling.
- Explore pharmaceutical applications.
- Develop extended Kalman filter to provide an optimal estimate of $f(l, w, t)$ and use this state estimate to implement predictive control to grow crystals in a prescribed manner using a minimal quantity of habit modifier.