Application Notes

Measuring solubility curve and metastable zone width

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A successful industrial crystallization first requires development of a robust process in the laboratory. Knowledge of the solubility curve and stability of the solution in the vicinity of the equilibrium point as indicated by the metastable zone width (MSZW) is essential to successful development, optimization, and scale up.

This study demonstrates the use of Lasentec® FBRM® technology to detect the point of "disappearance" during dissolution trials and the point of nucleation during successive cooling experiments on aqueous potash alum and D-Mannitol solutions. Several process parameters that affect the MSZW are also investigated.

Experimental setup

A crystallizer with a minimum agitatible volume of 1 L and maximum working volume of 2 L is used. Two instruments: a Lasentec® M400L (with FBRM® technology) and PVM700 (with PVM® technology) are installed in the crystallizer to characterize the nucleation and dissolution behavior of the material under investigation.

METTLER TOLEDO

Solids (potash alum or D-Mannitol) and solvent (water) are charged to the vessel. A variety of heating profiles ranging from 0.1°C to 1.0°C per minute are applied to the solution. FBRM® is used to track the nucleation and dissolution of the material during this temperature cycling. Concentration adjustment is made by diluting the system with a fixed mass of solvent.

Experimental data

FBRM® provides an *in situ* measurement that is a function of the number and dimension of particles under investigation. The trended FBRM® count data in Figure 1 shows a cooling/heating cycle from the experiment. Because growth of approximately 10 µm / 10 sec is expected at the supersaturation levels encountered, counts in the region of 0-20 µm are used to detect the point of nucleation.

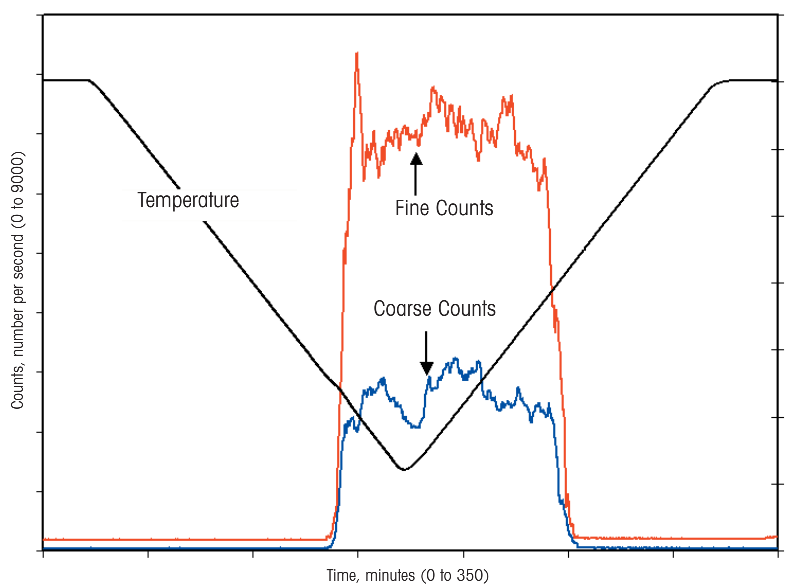

Figure 1: FBRM® detects the point of nucleation during the cooling/heating cycle

This data, which is also used to detect the subsequent point of disappearance, is validated using images from the PVM700. During a dissolution process, fine particles dissolve at a faster rate than coarse particles due to their higher surface-area-to-volume ratio. Figure 2 shows that toward the end of the dissolution period only large particles remain.

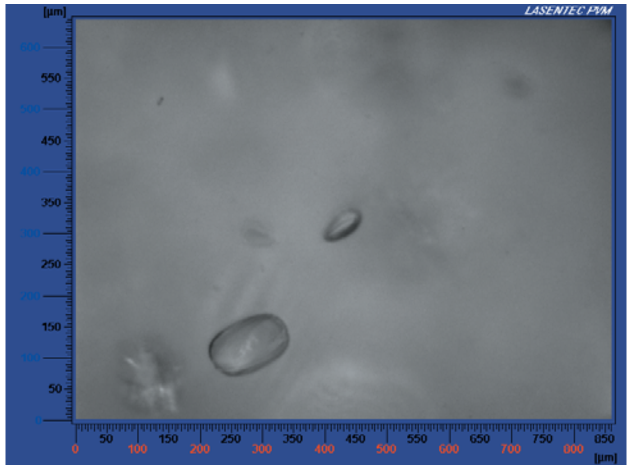

Figure 2: PVM® images show that fine particles dissolve faster than coarse particles

FBRM® counts in the region of 100-1000 μm are used to track the large crystals and hence the dissolution event. FBRM® distributions, which help quantify the change in number of fine particles during dissolution, emphasize that there is little change in the coarse population (see Figure 3).

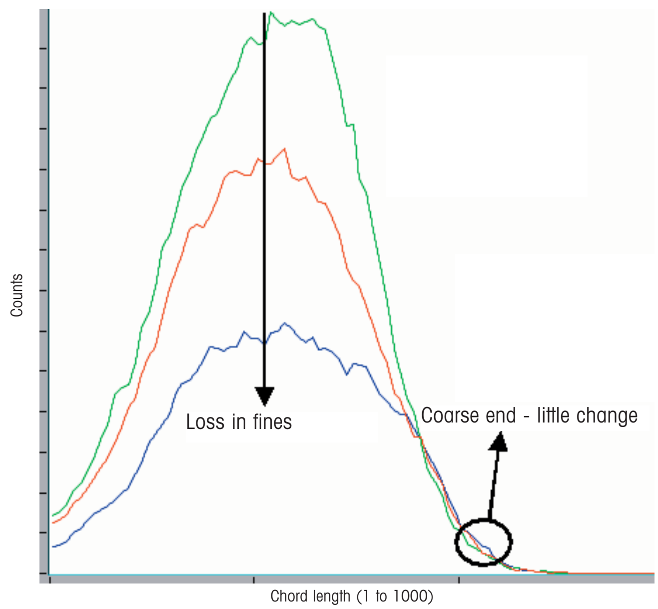

Figure 3: FBRM® data confirms the loss of fines while showing little change in the coarse end distribution

Determining solubility curve

The point of disappearance is measured at a variety of heating rates and the saturation temperature is estimated by extrapolating the data back to an infinitely slow heating rate. The measured solubility data is then compared with literature results. The MSZW data obtained can be used to help determine the optimum operating conditions for the crystallization and also to quantify the nucleation kinetics (see Figure 4).

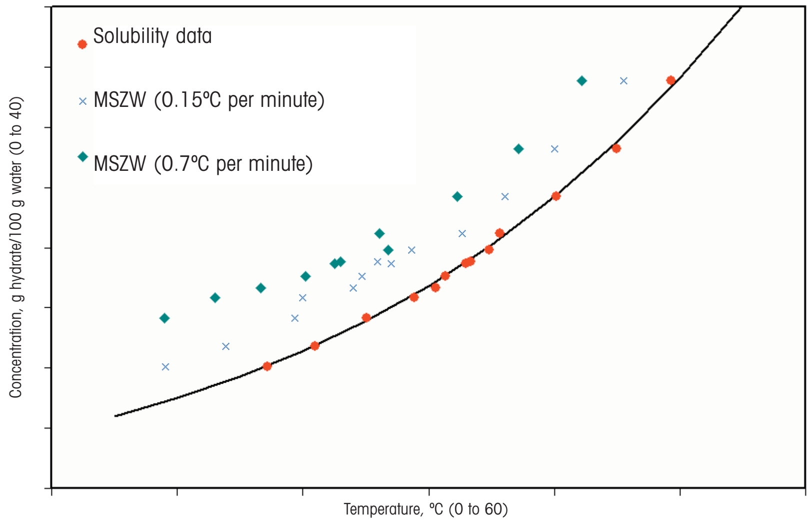

Figure 4: Solubility and MSZW data for potash alum water

Process parameters affecting the MSZW

Because a variety of parameters (impurity profile, solution history, mixing, etc.) are known to influence the MSZW, it is important to characterize these parameters, particularly if the MSZW data is to be used for scale up.

Effect of mixing

Mixing conditions can influence the point of nucleation through a combination of diffusion effects and micro-/meso-mixing. This effect may be exacerbated during process scale up due to the different vessel and impeller configurations and typically less-optimal mixing environments of production vessels. Figure 5 plots the MSZW as a function of mixing speed for a D-Mannitol solution saturated at 45°C.

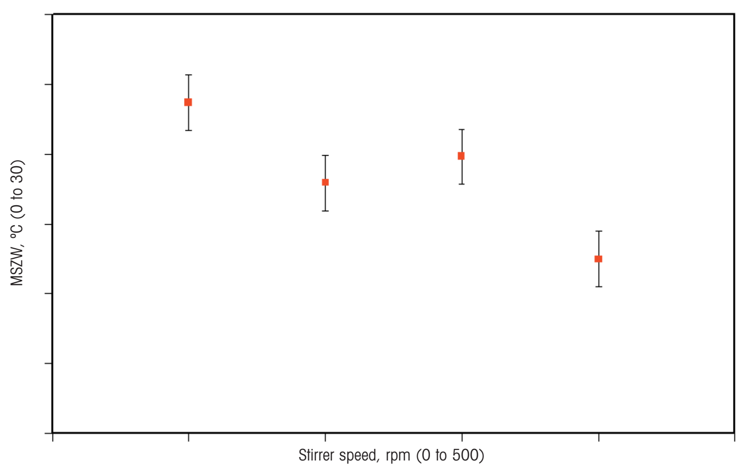

Figure 5: MSZW as a function of mixing speed

Effect of solids

The presence of even a tiny amount of solids (e.g., seeds) can influence the point of nucleation and result in a narrower MSZW. To avoid excessive secondary nucleation upon seeding, it is advisable to characterize this behavior before deciding on the seeding temperature. Figure 6 shows how a small amount of solids reduced the MSZW of D-Mannitol by 6°C-10°C.

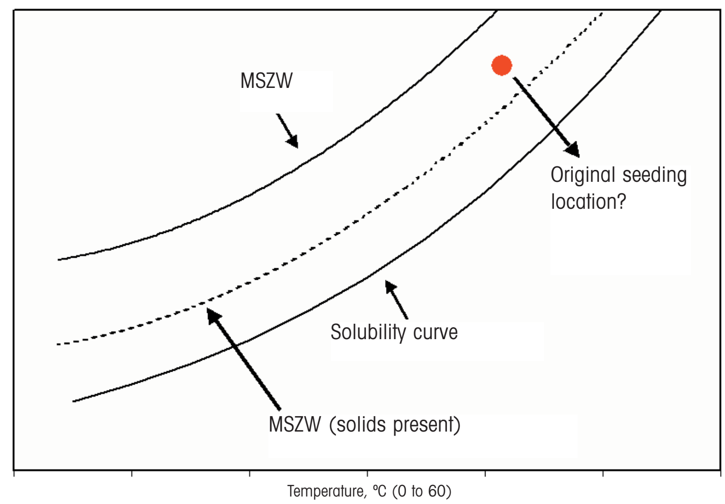

Figure 6: The presence of even a small amount of solids may narrow the MSZW

Conclusions

Lasentec® FBRM® and PVM® were successfully used to determine the solubility curve and metastable zone width for this experiment. Attention to the important process parameters (e.g., mixing, seed loading, etc.), will help ensure successful development and scale up of any crystallization process.

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