Application Example: Online Monitoring of DCPD Precipitation

Motivation

Due to their role in the formation of bones and teeth and use in biomaterials, calcium phosphates have been studied extensively. The reaction kinetics of Dicalcium Phosphate Dihydrate (DCPD) precipitation is known to be strongly dependent on conditions such as pH and reactant concentration. With a Pixact Crystallization Monitoring (PCM) system it is possible to analyze these kinds of complex crystallization processes in real time. High-quality live image from inside the reactor enables the online monitoring of the initial nucleation point, crystal growth and final crystal size distribution. In the image data it is also possible to detect the presence of other solids, such as intermediates, during the process.

Application

Pixact has developed a PCM probe that can be fitted inside small reactors, pilot crystallizers and other small laboratory scale vessels to study chemical reactions and final product size distribution. A PCM system was installed in a 2000 ml lab reactor together with a Raman spectrometer. In the reactor, $CaCl_2$ solution is fed into KH_2PO_4 solution.

Images produced by the probe are analyzed with an optimized algorithm to recognize the DCPD crystals. In these conditions, HAP (hydroxyapatite) forms before DCPD starts to precipitate. This makes the detection of the first DCPD crystals challenging compared to some other precipitation processes in which no solid phase intermediate forms before the final product. Some HAP is detected as crystals before the actual DCPD crystallization begins. This forms the “basic/background level” for the size and number of crystals in the PCM data. However, PCM can also be used to monitor the solid formation similarly to a Raman spectrometer.

Results

Examples of the image data are shown in Figures 1A-D and trend curves for crystal size and number of crystals per image are plotted in Figure 2. In Figure 1A, HAP is dominating the solution and only a few stick-like DCPD structures can be found. The mean crystal size is increasing, which indicates that DCPD has started to form. Figure 1B illustrates the growth phase of DCPD. Between points B and C, the number of DCPD crystals per image is strongly increasing. HAP has disappeared from the images by point C, and crystal size is not growing remarkably between points C and D. Some DCPD flake agglomeration can be observed in Figure D.

The simultaneously measured Raman spectra plotted in Figure 3 shows how the peak of HAP is first growing and then decreasing at Raman shift 958 cm^{-1} while the peak of DCPD starts to increase at 986 cm^{-1} around 1600s. The increase of the number of crystals per image (Fig. 2) is concurrent with the increase of DCPD in the Raman spectra (Fig. 3) and is steepest from 1700s to 2250s. The Raman intensity at 986 cm^{-1} does not grow from 2500s onwards, which indicates that the concentration of DCPD remains stable.

Size distribution and other key statistics are displayed on the GUI in real time throughout the measurement.

Benefits

Being able to see inside the reactor is useful when the kinetics and outcome of the reaction strongly depend on the prevailing conditions. With PCM the formation of solid intermediates, polyforms and agglomerates can be detected. PCM also enables the measuring of crystal size during the precipitation process, which means less work steps for the lab personnel.

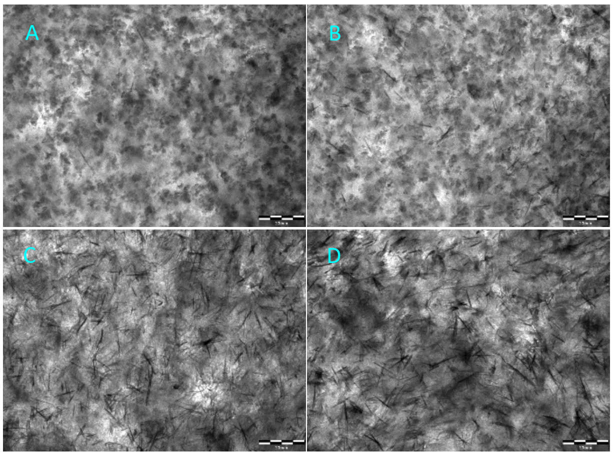

Figure 1. Images taken during DCPD precipitation. A=first stick-like DCPD crystals among HAP; B=Growth phase, C=HAP has disappeared, D=final crystals. The pictures are taken at the points indicated in Fig. 2. 200 µm scale bar.

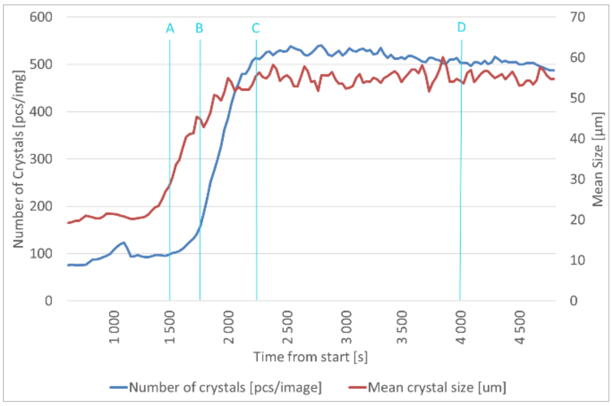

Figure 2. DCPD precipitation trends for the size and number of crystals

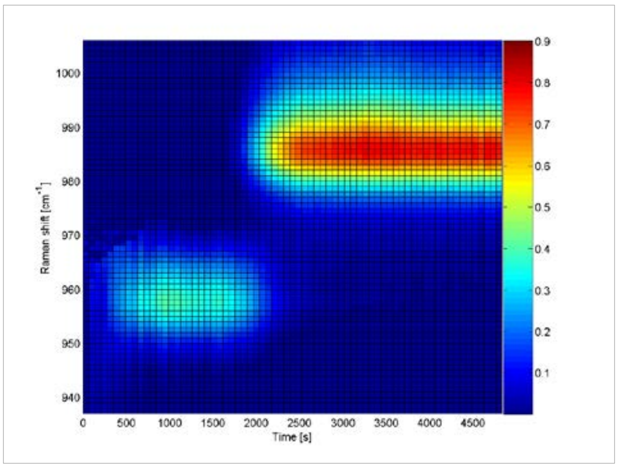

Figure 3. Raman spectra of DCPD and HAP

Technical implementation

The Pixact Crystalization Monitoring system utilizes a small dimension probe, which can be fitted into a lab reactor (Fig. 4). The analysis software is installed on a laptop. The whole measurement system can be packed inside a 40cm-by-50cm case for transportation and storage. A summary of the specifications of the measurement system is presented in the table below.

Probe diameter	45 mm
Material	Stainless steel AISI316L
Setup	Direct optical imaging, Pixstrobe illumination unit
Process interface	Sapphire window
Sealing	FPM

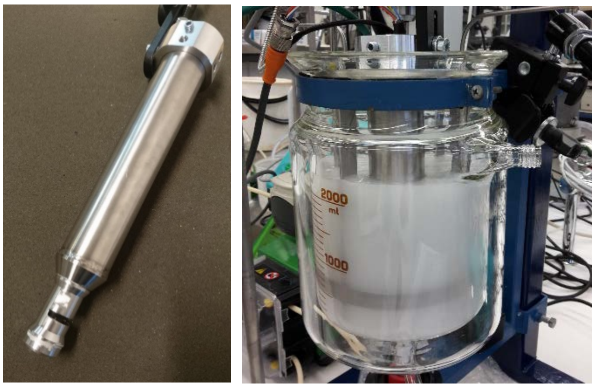

Figure 4. PCM probe for laboratory-scale reactors

More information on the Pixact Crystallization Monitoring technology and configuration options can be found in [the Pixact Crystallization Monitoring brochure].

Acknowledgement

Pixact would like to thank the Separations Technology research group at Lappeenranta University of Technology for the measurement data used in this application note.