Crystallization in Microfluidic Systems

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Microfluidic systems offer a unique toolset for discovering new crystal polymorphs and for studying the growth kinetics of crystal systems because of well-defined laminar flow profiles and online optical access for measurements. Traditionally, crystallization has been achieved in batch processes that suffer from non-uniform process conditions across the reactors and chaotic, poorly controlled mixing of the reactants, resulting in polydisperse crystal size distributions (CSD) and impure polymorphs. This reduces reproducibility and manufactures products with inhomogeneous properties. The short length scale in microfluidic devices allows for better control over the process parameters, such as the temperature and the contact mode of the reactants, creating uniform process conditions. Thus, these devices have the potential to produce crystals with a single morphology and a more uniform size distribution. In addition, microfluidic systems decrease waste, provide safety advantages, and require only minute amounts of reactants, which is most important when dealing with expensive materials such as pharmaceutical drugs.

Figure 1 shows a microfluidic device used for crystallization and Figure 2 shows optical images of different shapes and sizes of glycine crystals produced in reactor channels. A key issue for achieving continuous crystallization in microsystems is to eliminate heterogeneous crystallization – irregular and uncontrolled formation and growth of crystals at the channel surface, which ultimately clogs the reactor channel. We have developed a sheath flow microcrystallizer using microfabrication and hot embossing of poly(dimethylsiloxane) (PDMS) and cyclic olefin copolymer (COC) to prevent heterogeneous crystallization. We are currently working on integrating an online spectroscopy tool for in situ polymorph detection. Our ultimate goal is to develop an integrated microfluidic system for continuous crystallization with the ability to control polymorphism and online detection.

▲ Figure 1: Microfluidic reactor used for crystallization.
▲ Figure 2: Different sizes and shapes of glycine crystals produced in reactor channel.