"NMR Crystallization": New In-Situ NMR Techniques for Time-Resolved Monitoring of Crystallization Processes

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The development of in-situ techniques for exploring details of crystallization processes from solution promises to yield significant new insights on fundamental aspects of such processes. With this motivation, we have developed new in-situ solid-state NMR techniques [1-6] that exploit the ability of NMR to selectively detect the solid phase in heterogeneous solid/liquid systems (of the type that exist during crystallization from solution), with the liquid phase “invisible” to the measurement. The technique allows the first solid particles produced during crystallization to be observed and identified, and allows the evolution of different solid phases (e.g. polymorphs) to be monitored as a function of time. This in-situ NMR strategy has been shown to be a powerful approach for establishing the sequence of solid phases produced during crystallization and for the discovery of new polymorphs.

A recent development of this in-situ NMR technique [4] exploits the fact that NMR can study both the liquid phase and the solid phase in heterogeneous solid/liquid systems using the same instrument, simply by changing the pulse sequence. By alternating between two different pulse sequences during an in-situ NMR study of crystallization, alternate solid-state NMR and liquid-state NMR spectra are recorded, yielding essentially simultaneous information on the time-evolution of both the solid phase and the liquid phase. This new strategy is called CLASSIC NMR (Combined Liquid- And Solid-State In-situ Crystallization NMR). We have shown that the CLASSIC NMR strategy significantly extends the scope and capability of in-situ NMR monitoring of crystallization processes, particularly by providing complementary information on the changes occurring in both the solid and liquid phases as a function of time.

The lecture will give an overview of in-situ solid-state NMR techniques for the study of crystallization processes, and the current state-of-the-art in the application of these techniques will be demonstrated by wide-ranging examples from our recent research in this field. In addition to highlighting the successes achieved in the application of the "NMR Crystallization" approach, challenges in extending the future scope of the methodology [5] will also be discussed.

References