MS34 Crystallization Techniques and chemical reactions driven by solid state interactions

MS34-02

Encapsulated nanodroplet crystallisation – unlocking structural resolution for sample-limited and complex molecular systems

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Abstract

The explosion of technologies, enabling the application of diffraction science to ever more complex materials, is truly staggering. With microfocus in-house X-ray sources through to the international XFEL facilities now being used to help resolve structural properties and molecular characteristics. However, all of these and their related instruments still have a common requirement, the prior preparation of a suitably crystalline sample for analysis.

Increasingly exotic molecular systems are now being prepared synthetically, or isolated from natural sources, as targets of interest. These targets suffer greatly from difficulties in structure elucidation outside the solid-state due to the complexities of data and information loss from spectroscopic methods. Therefore, the reliance on solid-state methods has increased for categoric materials characterisation. However, these increasingly complex molecular species have associated complications in determining suitable crystallisation conditions to provide samples of suitable quality for analysis.

Additionally, as both academia and industry strive to reduce the timescales for research projects bringing solid-state analysis earlier in the development pipeline is imperative. It has the advantage of reducing costs on projects that are less likely to come to fruition but has the major disadvantage that the quantity of material available is generally significantly reduced. The reduction in sample quantity available for analysis makes many classical crystallisation routes non-viable or extremely cost inefficient due to the sample recycling and additional processing required.

High throughput Encapsulated Nanodroplet Crystallisation[1] is a recently developed technique that has the capability to provide solutions to the problems outline. It has been successfully employed on a diverse range of structurally challenging compounds from small molecules through inorganic complexes to natural products and their synthetic analogues. The method has the major advantages of the limited amount of material required for crystallisation screening (<10 mg material gives >1000 crystallisations) and ease of polymorph screening across a wide range of chemical environments.

The methodologies employed in the technique will be discussed with case studies highlighting the structural diversity of the method's applicability, along with the mechanisms for easy access to the technique.

References

[1] Tyler ARM, Ragbirsingh R, McMonagle CJ, Waddell PG, Heaps SE, Steed JW, Thaw P, Hall MJ, Probert MR. Encapsulated Nanodroplet Crystallisation of Organic-Soluble Small Molecules. Chem 2020, (7), 1755-1765