MS39-2-1 Encapsulated Nanodroplet Crystallisation: Expanding Solution-Phase Crystallisation Methodologies for Polymorph Screening
#MS39-2-1

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Abstract
Polymorphism is a solid-state phenomenon where a chemical species may adopt different conformational or packing arrangements, therefore allowing for the formation of more than one distinct crystal structure. As a result of these different packing arrangements, crystal polymorphs can exhibit varying physical and chemical properties. These properties such as solubility, hardness, colour, and melting point can all be important in the design of a compound.[1]
In the pharmaceutical and crystal engineering fields, a thorough understanding of the polymorphic landscape of a chemical species is critical to reliably select and grow crystal forms with suitable properties for their intended functionality. For example, the bioavailability of an active pharmaceutical ingredient can be drastically altered by the crystal form in which it is formulated.[2] Whilst computational crystal structure prediction can be used to highlight likely crystal forms of a given chemical species[1], manual crystallisation screens remain the only way to effectively assess the impact of polymorphism on a compound. The techniques classically applied to grow high-quality single crystals are often time-consuming and require significant quantities of the sample compound.[3] In the pharmaceutical industry, this often leaves crystal form screening to a later stage of drug development when large quantities of material are available for such experiments. This has led to significant demand for rapid, small-scale crystallisation techniques that would permit crystal form screening at a much earlier phase of drug development.[3]
Herein, we describe how encapsulated nanodroplet crystallisation (ENaCt), a small-scale, high-throughput, robot-assisted crystallisation technique, can be applied to probe areas of the polymorphic landscape that were previously inaccessible to solution-phase crystallisation techniques. Polymorph screens of 5-methyl-2-[(2-nitrophenyl)amino]-3-thiophenecarbonitrile (ROY) and nicotinamide resulted in the growth of high-quality single crystals of polymorphs only previously known to crystallise from melt-based experiments, demonstrating the capability of ENaCt for probing a large area of the polymorphic landscape.[4-7]

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