Using sound pulses to solve the crystal harvesting bottleneck

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Crystal harvesting remains the bottleneck in protein crystallography experiments and is the rate-limiting step for many structure determination, high-throughput screening and femtosecond crystallography studies. Huge progress has been made towards the automation of high-throughput crystallization, even for membrane proteins. Moreover, free electron lasers and fourth generation synchrotrons support extraordinarily rapid rates of data acquisitions and put further pressure on the crystal-harvesting step. Here [1], a simple solution is reported in which crystals can be acoustically harvested from slightly modified MiTeGen In Situ-1 crystallization plates. Acoustic harvesting uses the automated and keyboard driven acoustic droplet ejection (ADE) technology, in which an acoustic pulse ejects each crystal out of its crystallization well, through a short air column and directly onto a micro-mesh. Crystals can be individually harvested or can be serially combined with a chemical library such as a fragment library.

As crystallization plates are used in most automated high-throughput crystallization robots, ejecting crystals directly from their crystallization wells eliminates the laborious and time-consuming manual harvesting of fragile protein crystals. We here made it possible with a very simple modification of the MiTeGen In Situ-1 crystallization plate, that consists in a light sanding of their edge pedestal (Figure 1a). This is enough to make the plate acoustically compatible with the Echo 550 liquid handler (Labcyte Inc.) and would not be needed if the plates were designed with acoustically compatible plastic. An acoustic compatible plate enables multiple acoustic harvests of crystals from different wells, directly to the X-ray diffraction data collection media (micro-meshes), (Figure 1b). Each harvested aliquot can then be combined with distinct chemicals, making combinatorial crystallography an obvious application. Our results demonstrate that acoustic harvesting is not merely a viable and gentle crystal harvesting technique, but it also makes protein crystal harvesting remarkably more efficient.

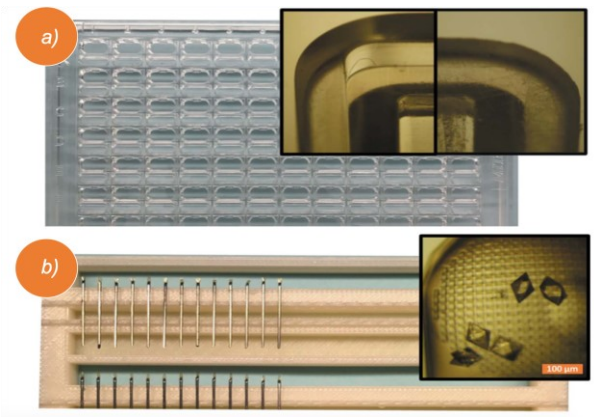

Figure 1. a) Intact MiTeGen plates with the edge pedestal lightly sanded down (inset). (b) Crystals were successfully acoustically harvested onto the micro-meshes (inset) in a pin platform.

[1] Samara, Yasmin N., et al. *Acta Crystallographica Section D:* Structural *Biology* 74.10 : 986-999, 2018

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