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Micro robotics enables non-contact, fully automated protein crystal harvesting

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Statement of the Problem: Most aspects of macromolecular structure determination, from synthesis and purification of materials, through crystallization, data collection and model building, are highly automated. But the recognition, harvesting and cryocooling of crystals reminds of a predominantly manual task. Several concepts, including *in situ* crystallography, are being developed to overcome these difficulties, but frequently impose other restrictions such as data collection strategies. We are developing hardware and software to support crystal harvesting using standard crystallization procedures, thus avoiding such limitations.

Methodology & Theoretical Orientation: We use a magnetically driven mobile, rolling micro robot, the RodBot, to locally move the liquid surrounding crystal. The crystal then passively follows the flow. Crystal position is monitored using low level UV-light. Transport is controlled using flexible algorithms that allow for error-recovery, following stochastic disturbances.

Findings: We demonstrated the effectiveness of the technique using crystals of different geometries and densities in a variety of buffers and cryoprotectants. Even at this developmental stage average harvesting time is reduced compared to manual operations.

Conclusion & Significance: This non-destructive, non-contact method allows crystals to be extracted reliably from the growth droplet in a completely automated process. Harvesting can take place remotely in climate-controlled chambers, ensuring optimal conditions throughout the process with respect to temperature, humidity and composition of the environment. Damage to valuable crystals due to operator jitter or fatigue is eliminated. Incorporation into existing robotics setup for sample handling will also allow increased reproducibility of flash-cooling. Fully automated structure determination pipelines using well-established techniques are now possible and can yield improved data quality at reduced cost.

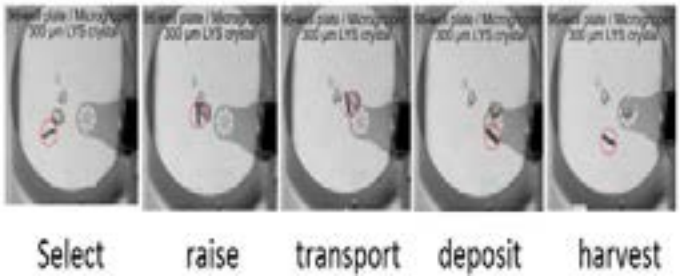

Figure1: *Crystal harvesting using the RodBot micro robot (in red circle). From left: Selecting one of several crystals in a droplet of a 96-well plate; fluid flow from the approaching RodBot raises the crystal off the bottom of the droplet and transports the crystal towards the micro-mount; the crystal is deposited on the micromount, where upon the crystal can be harvested, flash-cooled and stored using a robotic arm.*

Biography

David F Sargent has obtained his PhD in Biophysics from the University of Western Ontario, Canada, followed by Postdoctoral studies at the ETH Zurich and the University of Sydney (Australia). He has extensive experience in macromolecular crystallography at the ETH Zurich, and recently has also been associated with the Multiscale Robotics Laboratory (ETH Zurich) of Bradley J Nelson. He is one of the founders of MagnebotiX, a spinoff of the ETH, which provides tools for magnetic propulsion and guidance at the microscopic scale. The work reported above uses this technology to streamline and accelerate the process of macromolecular crystal structure determination.

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