Automated crystallography pipelines for small-molecule screening and membrane proteins

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Abstract

The evolution of automation in structural biology over the last decade has facilitated the study of challenging targets and extended the use of protein crystallography in drug discovery. However, manual crystal mounting and processing are time-consuming and resource-intensive, thus limiting the efficiency and productivity of small molecule screening in the context of drug design. We have developed an approach called CrystalDirect™, enabling automated crystal soaking, harvesting, and cryo-cooling. This technology offers a remarkable level of control during sample processing, making crystal mounting a more reliable and systematic operation that can easily deal with problematic crystal morphologies and sizes. It also provides higher tolerance to organic solvents during soaking experiments. Thanks to the CrystalDirect™ technology, we are providing access to an integrated pipeline including high-throughput crystallization, crystal soaking and mounting, and synchrotron data collection into a fully automated and continuous workflow. This pipeline can support very-fast analysis of small molecule-target complexes as well as easy and efficient large-scale fragment screening. All the experimental information and results are tracked in real-time through CRIMS (the Crystallization Information Management System). The capabilities of this technology and the experience gained from the use of these automated pipelines for ligand screening and challenging membrane protein targets will be discussed.

References:

1) Zander et al. Automated harvesting and processing of protein crystals through laser photoablation. Acta Cryst. D72, 2016, 454-466 .

2) Robert et al. An automated platform for structural analysis of membrane proteins through serial crystallography. bioRxiv 2021.06.03.446146.