

Automated room temperature ligand screening on beamline FIP at the ESRF

J-L Ferrer, X Vernede, Y Sallaz-Damaz, M Pirocchi, C Berzin, P Jacquet, M. Spano, D. Cobessi, F Borel

Institut de Biologie Structurale, 71 Avenue des Martyrs, CS 10090, 38044 Grenoble Cedex 9 - France

FIP, an automated beamline at the ESRF for protein crystallography, is designed to host a large variety of experiments such as anomalous, on-line absorption spectroscopy coupled, humidity controlled, and *in situ* diffraction experiments. Several of these techniques are made possible by a robot based system, named G-Rob. It is a fully integrated, multi-purpose automated and remotely controlled system that integrates several functions: multi-standard sample changer for frozen crystals; goniometer for frozen samples or capillaries [1]; crystallization trays handling for *in situ* (in the plate) screening and data collection [2]; beam monitoring. Another, but important, feature of beamline FIP is a web-based user interface, named WIFIP. With this interface, several users can share the control of the experiment, from sample handling to data reduction, through a web browser, on the beamline or from the lab or home. WIFIP includes the CrystalListing capability, that makes possible the listing of series of crystals from a crystallization plate, in order to collect dataset in a row in an automated way. It makes *in situ* experiments much easier and automated.

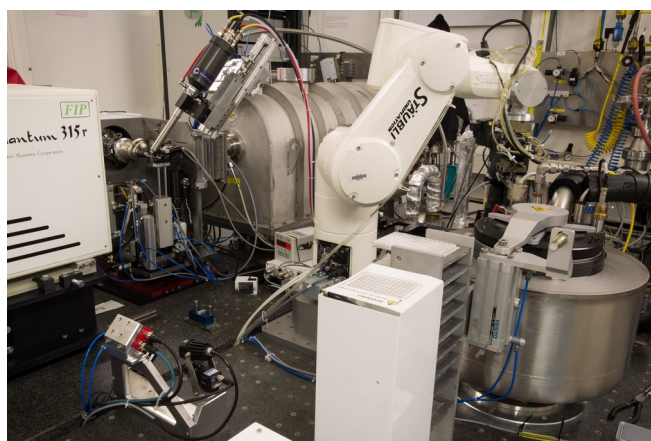
X-ray crystallography is an established technique for ligand screening in fragment-based drug-design projects, but the required manual handling steps – soaking crystals with ligand and the subsequent harvesting – are tedious and limit the throughput of the process. On FIP, an alternative approach is proposed: crystallization plates are pre-coated with potential binders from DMSO stock solutions [4], prior to protein crystallization, and X-ray diffraction is performed directly *in situ*. With these pre-coated plates, crystallographers can screen these libraries without any stock solution or crystal handling, and obtain the structure of complexes at room temperature.

In the future, pre-coated plates will be made available, either with generic libraries or with custom-made collections. The first one is prepared with a 3D 192-fragment library.

[1] Jacquamet et al., Acta Cryst. D 60, 2004, 888-894.

[2] Jacquamet et al., Structure 12, 2004, 1219-1225.

[4] Gelin et al., Acta Cryst. D 71, 2015, 1777-1787.



Overview of the robotized setup on beamline FIP at the ESRF.