THE XCHEM PLATFORM AT DIAMOND

Patrick Collins
Diamond Light Source, Harwell Science and Innovation Campus, Didcot, OX11 0QX

X-ray crystallography is an exquisitely sensitive method for screening small molecule fragments against protein targets, providing binding modes, interactions, and chemical matter for drug discovery projects. Traditionally however, the logistical overhead for large scale X-ray fragment screening has been prohibitively high. The XChem platform at Diamond addresses these logistics by providing a streamlined crystal-to-model workflow with capacity for over 1000 crystals per week. We transfer fragments (over 2000 fragments available, or BYO library) to crystals using acoustic droplet ejection, which allows rapid crystal soaking, and mount them using the shifter, an in-house developed device for assisted crystal harvesting. X-ray diffraction data are automatically collected in an unattended mode at beamline i04-1 and processed using Diamond's automatic processing pipeline. A novel algorithm, PanDDA, which harnesses the power of many dataset to extract clear and interpretable electron density, is used to detect and model bound fragments, while further data analysis and final model refinement are handled by our bulk data processing software package XChemExplorer. XChem has been operating since mid-2015, providing both proprietary and peer-reviewed academic access modes. In that time over 26,000 crystals have been processed, providing an average of 40 fragment hits per project.