diamond

Drug Discovery

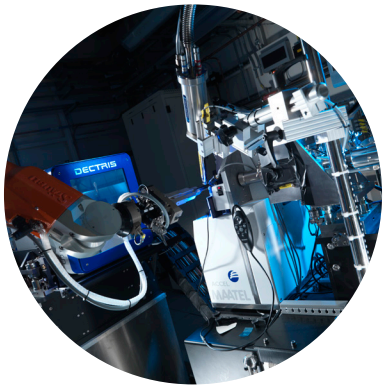
CASE STUDY

High throughput macromolecular crystallography

Macromolecular crystallography (MX) is a key asset in the development of new drugs via structure based drug discovery. This process is now widely used by the pharmaceutical industry to gain structural insights into drug targets and map interactions with ligands. However, isolating and optimising a new lead compound is a time consuming process which usually involves screening hundreds of samples.

Vernalis

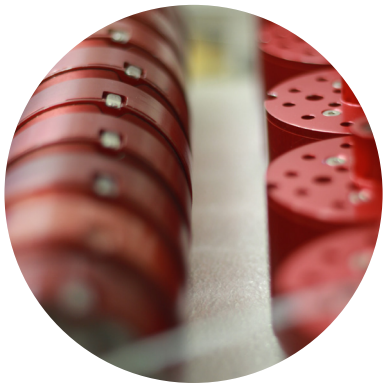
The Challenge



The average time taken to collect a complete dataset has been dramatically reduced in recent years by the use of intense synchrotron sources, especially compared to lab based sources, which has made it possible to screen hundreds of samples in less than a day.

Nonetheless, the rate of progress in screening projects is defined by the speed that results are achieved rather than samples measured and so a streamlined and efficient data collection, processing and analysis process is essential if researchers are to extract meaningful results on a realistic timescale.

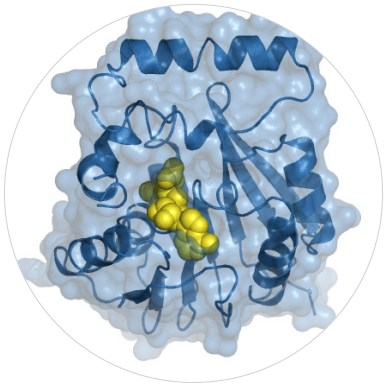
The Solution



The MX beamlines at Diamond employ highly brilliant X-ray beams and the latest detector technologies to reduce sample exposure times. Cutting edge robotics coupled with efficient on-axis microscopes offer a rapid and reliable system for handling a large number of crystals. All these components are seamlessly integrated and operated through an intuitive and flexible graphical user interface.

After the acquisition of a few images, each sample is automatically characterised and a collection strategy formulated to help users make quick and informed decisions. While sample anisotropy or decay can be isolated during data collection through per image analysis software, the Diamond high performance auto-processing pipeline provides immediate feedback about the diffraction experiment, typically within minutes. A detailed information management system tracks the crystal from dewar to electron density map, allowing users to view results only minutes after data collection.

The Benefits



This automated and high throughput MX environment is ideal for conducting structure based drug discovery projects. It not only speeds up the sample screening process, but it also requires minimal user input to characterise or process a sample. While reduced data are readily available for downstream applications, immediate structure analysis performed at the beamline streamlines the identification of ligands binding to a drug target. In addition, users can rely on real-time feedback to efficiently manage their beamtime by allowing them to focus only on the most relevant samples.

> "The high throughput high resolution data we achieve at Diamond cannot be replicated in the home laboratory. It is an essential tool in our Structure Based Drug Design efforts, guiding our chemists from initial mM hits to the final pM drug candidates." **Dr Pawel Dokurno, Vernalis**

For further information

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