Beamline specifications

High-throughput protein crystallography (PX1)

Source	3BM1 dipole
Energy range	5-20 keV
Optimal energy range	5-19 keV
Resolution *delta*E/E	within 15% of theoretical
Nominal beam size at sample (horizontal x vertical)	150 x 100 µm
Flux at 12.6 keV	1.4 x 10^{11} photons/sec
Harmonic content at 5-20 keV	< 0.1%
Techniques available	• MAD • high resolution single wavelength

Protein micro-crystal and small molecule x-ray diffraction (PX2)

Source	3ID in-vacuum undulator
Energy range	5.5-28 keV
Optimal energy range	5.5-27 keV
Resolution *delta*E/E	within 15% of theoretical
Nominal beam size at sample (horizontal x vertical)	20 x10 µm – 100 x 100 µm (FWHM)
Flux at 12.6 keV	1 x 10^{12} phot/sec
Harmonic content at 5-28 keV	< 0.1%
Techniques available	• MAD • high resolution single wavelength • large cell unit • micro-crystals • chemical crystallography

Contact info

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Image: Sandra Morrow

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PX1 – Protein Crystallography

The high-throughput protein crystallography beamline is a dedicated facility for determining the structure of protein crystals and undertaking initial assessment of more complex crystals. Single crystals are analysed using multiple wavelength anomalous dispersion (MAD). Expert technical assistance is available to help users who are not specialist crystallographers.

Features

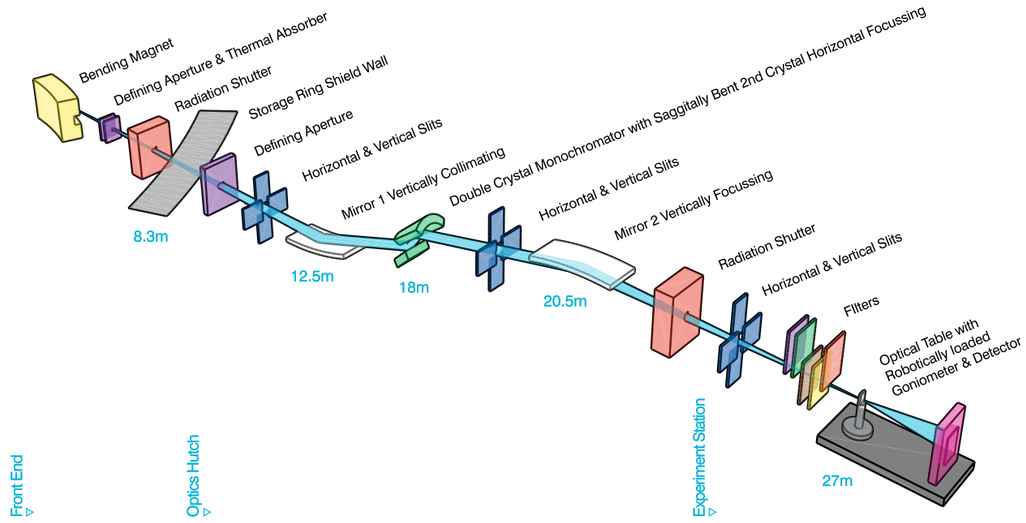
- high-throughput, high-resolution structure determination
- rapid, automatic data collection and interpretation to provide detailed crystal structure information in real time
- robotic loading and centring of crystals
- remote operation.

Applications

The rapid determination of large numbers of protein structures is now essential in many fields of science, including molecular biology, rational drug design and proteomics.

For example, protein crystallography provides primary structural information on complex macromolecules that drive biological processes. Proteomics involves systematic characterisation of the full set of an organism's gene products, with a key component being structural genomics—the elucidation of three-dimensional protein structures.

X-ray diffraction is the most widely-used method for protein structure determination, providing information for a wide range of applications, including drug development, food technology, agriculture, manufacturing and chemical processing.



PX2 – Protein Crystallography

The protein micro-crystal and small molecule x-ray diffraction beamline uses multiple wavelength anomalous dispersion (MAD) to determine crystal structures and derive electron density maps.
It is ideal for weakly-diffracting, hard-to-crystallise proteins, viruses, protein assemblies and nucleic acids as well as smaller molecules such as inorganic catalysts and organic drug molecules.

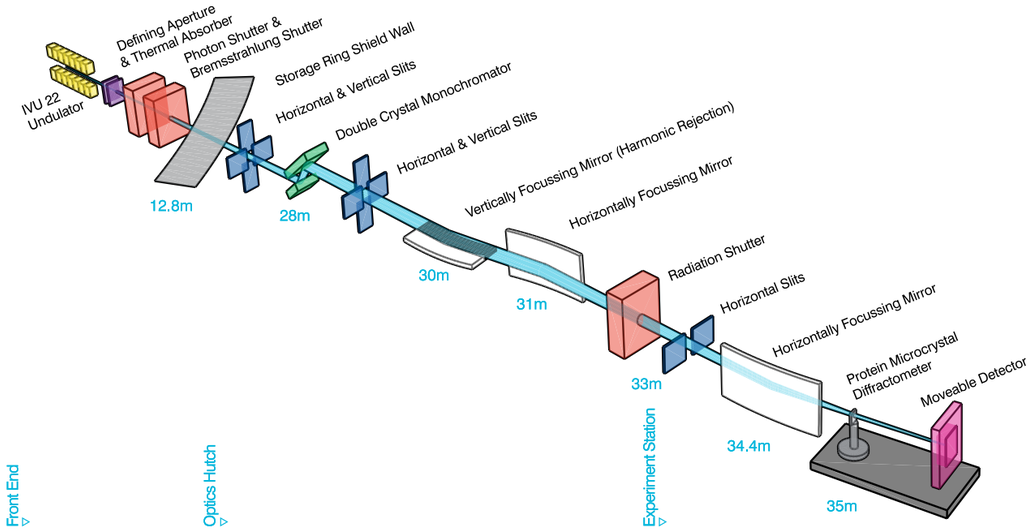
Features

- finely focussed x-ray beam (10-20 microns) for high-resolution structure determination from extremely small crystals (down to 10 microns)
- potential to add second end-station designed specifically for small molecules
- four-circle goniometer for full diffraction sphere coverage
- shorter wavelength x-rays to minimise absorption
- robotic loading and centring of crystals
- remote operation.

Applications

High-resolution crystal structures and electron density maps provide essential information for many fields of science, including molecular biology, rational drug design and proteomics. In addition to providing higher-resolution information to refine preliminary structures from high-throughput methods, the micro-crystallography beamline will enable structure determination for substances that are difficult to obtain in crystalline form, such as receptors.

Small-molecule structure elucidation will support a wide range of chemical, geochemical, material science and medical research and development activities.



Examples of synchrotron x-ray crystallography applications

- determination of the structures of protein complexes, providing valuable information for other synchrotron studies of mechanisms and ligand binding at atomic resolution
- structural studies of proteins critical to insect physiology to inform the development of new or improved insecticides
- structural studies of transport proteins in plant roots to improve knowledge of salt resistance mechanisms used by native plants and agricultural crops
- structural studies of malarial proteins to assist the development of drugs that block the malaria parasite's entry to red blood cells
- structural studies of growth factors to improve understanding of cancer growth and develop better treatments
- investigation of the global structures of large biological molecules, to complement information obtained from NMR and other studies, and investigate the regulation of key cellular processes that underpin healthy biological functioning or are implicated in disease states
- structural studies of antibodies, to assist the identification of bio-sensor platforms for cancer detection
- determination of the structure of the anthrax lethal factor, making it possible to pursue the development of anti-toxins.

Case study 1

Rational drug design—influenza

The ability of synchrotron x-rays to reveal the detailed structures of biological proteins and their interactions has enabled researchers to develop a new approach to drug discovery. Rational drug design identifies opportunities to block or modify molecular interactions. The anti-influenza drug Relenza™ is the world's first structure-based anti-viral drug and an early example of rationally based drug design methodologies. Relenza™ was developed in the mid-1990s by a CSIRO team led by Peter Colman and Jose Varghese. Colman and Varghese used synchrotron protein crystallography to create a high resolution picture of the neuraminidase protein on the virus surface.

Case study 2

Therapeutics for chronic inflammatory diseases

Chronic inflammatory diseases represent one of the greatest health problems in the developed world, and macrophages play a central role in the inflammation process. Researchers from the University of Queensland are investigating macrophage proteins from mice. They want to develop a better understanding of the inflammation process in arthritis and other chronic inflammatory diseases and to identify targets for the development of new anti-inflammatory therapeutics. Associate Professor Jenny Martin and her colleagues have established a bacterial expression system to screen hundreds of proteins to identify those that are suitable for structural studies. Proteins that express well in the small-scale bacterial system are then produced in large scale and evaluated further by structural techniques.