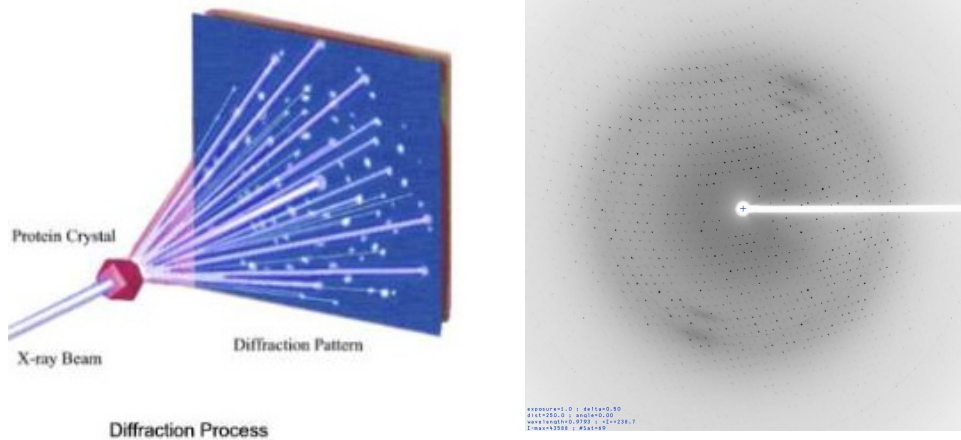


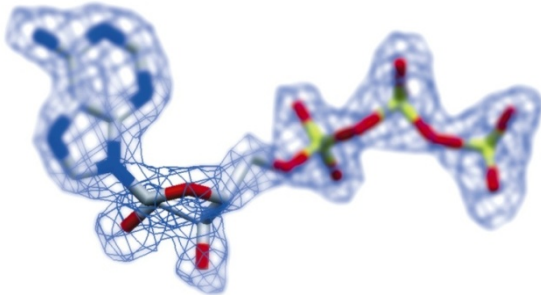
Canadian Macromolecular Crystallography Facility (CMCF)

Macromolecular crystallography is the use of X-ray diffraction to determine the structure of big ('macro') biological molecules, such as proteins and nucleic acids. This is the method that was used to discover the famous double-helix structure of DNA. A researcher that wishes to study the structure of a particular protein must first isolate it and then grow it into a crystal. A crystal of a macromolecule, made of thousands of identical molecules, is placed in a focused hard X-ray beam. As the x-rays pass through the crystalline structure, they are diffracted and the resulting diffraction pattern is recorded.



Modeled electron density and molecule structure (Image courtesy of Louis Delbaere)

A series of many diffraction images, collected while the crystal is rotated by a small amount from the previous image, leads to a three dimensional model of the electron density surrounding the molecule, which is then used to construct a model of the structure of the molecule, as seen above.



Diffraction image of a protein crystal (data provided by CMCF beamline staff).

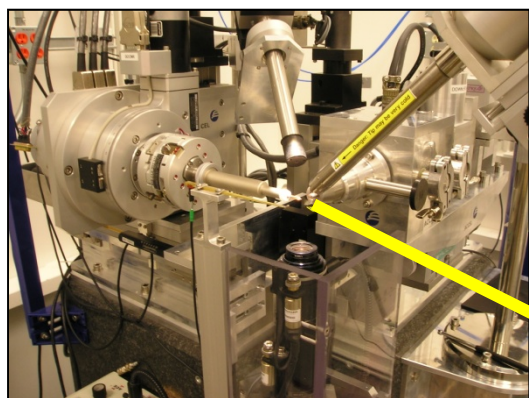
Synchrotron crystallography research has produced the detailed structures of tens of thousands of proteins and other macromolecules, such as the double helix of the DNA molecule. These structures have contributed to the understanding of fundamental processes in virtually all fields of biological and medical sciences, and are vital to drug design and protein engineering. A recent example of this is the discovery of the function of *Mycobacterium tuberculosis*, the bacterium

that causes tuberculosis, which will lead to new possibilities in treatment of the disease. The structure of KshA enzyme, which is crucial to the survival of this bacterium, was determined by Jenna Capyk, et al. (2009) using CMCF 1 beamline at CLS (top of the next page). This detailed structural information can now be used to develop a drug treatment that will inhibit this enzyme, allowing the body's immune system to conquer the bacteria.



Molecular model of the KshA enzyme from Mycobacterium tuberculosis, a new target for treating TB. From Capyk, et al. 2009, J. Biol. Chem 284: 9937-9946.

The CMCF consists of two beamlines. CMCF I, part of the Phase I beamlines, is capable of satisfying the requirements of the most challenging and diverse crystallographic experiments (physically small crystals with large unit cell dimensions) using single crystal X-ray diffraction (6500-18000 eV). CMCF II, part of the Phase II beamlines, is a fully automated, high throughput beamline within the energy range of 4000-18000 eV and will be accessible remotely using the Internet. Scientists will be able to send pre-frozen crystals to the facility and set up experimental parameters as well as inspect, evaluate, and download their data from their home laboratories. Pharmaceutical companies will find this beamline useful for analyzing bulk samples of one protein that is targeted for drug design expressed in many different environments.



Endstation within the Experimental Hutch showing the point at where the X-ray beam interacts with microscopic protein crystal (imaged below) held in the vapour of liquid nitrogen. Image courtesy of beamline staff.

