The Australian synchrotron and its impact on biology in Australia

Dr Jose Varghese

Chair, Protein Crystallography Beamlines
Advisory Panel of the
Australian Synchrotron
CSIRO Molecular and Health Technologies
Parkville VIC

The construction of the Australian synchrotron is proceeding on time and nearing completion, and the first suite of beamlines are expected to commence test experiments in April next year. The advent of this facility will be a big boost to the biological community, especially in the area of structural biology and protein characterisation.

Currently the protein crystallography community is dependent on the availability of beamtime at overseas facilities such as the Advanced Light Source in the USA and the Photon Factory in Japan, making it extremely difficult to remain competitive with overseas researchers and development in many areas of biochemistry.

Access to high brightness x-ray sources is an essential tool for understanding the complex chemistry of biological systems that require knowledge of the three dimensional molecular structure of biological macromolecules. Consensus is emerging that detailed atomic knowledge of the gene products of organisms and not the genes themselves are essential if we are going to understand and thereby control and modulate the chemistry of living organisms.

One of the first beamlines to be operational will be the high throughput MAD (multiple anomalous diffraction) beamline that is being built off a bending magnet synchrotron source. This will enable rapid collection of x-ray data near an absorption edge of a metal bound to the protein (or incorporated into the protein by replacing methionine with seleno-methionine) which allows the researcher to experimentally solve the 3-D structure of protein crystals.

Initially, data collection will be with a small 'off the shelf' detector that is found in many x-ray laboratories in Australia, but it is planned that, as funding becomes available, it will be replaced by a more sophisticated end-station that will be similar to the best end-stations overseas.

This beamline will be a big boost in areas of structure-based drug design and structural genomics where high throughput is essential. This beamline is being designed for the non-specialist user, as it will incorporate the latest robotics system that is capable of loading pre-frozen crystal samples onto the instrument from a standardised container that can store up to 96 frozen crystals mounted on regular Hampton-like pins.

These will be available to biochemistry and molecular biology laboratories throughout Australia. They will allow, for the first time, any Australian scientist who can crystallise biological macromolecules to obtain its atomic structure by bringing their samples to the Australian synchrotron. In the future, scientists will also be able to ship the samples to Clayton, collect the data and solve the structure through a web-based system that will operate from all major cities in Australia that are connected to a broadband node of the synchrotron.

The second protein crystallography beamline is a more specialist multi-purpose one that will come online in 2008. It will be a much brighter beam coming off an insertion device, and will be capable of collecting x-ray data from crystals as small as 10 microns as well as poorly diffracting crystals, and data from large protein complexes that have unit-cell sizes in the order of 1000Å.

This beamline will enable Australian users to be competitive internationally and come to the forefront of structural biology, and also enable a number of projects to proceed where there has traditionally been great difficulty obtaining large enough crystals for conventional data collection. This beamline will also be shared with small molecule crystallographers as its characteristics are suitable for many types of experiments that the small molecule community is pursuing.

In addition to the two protein crystallography beamlines, the biochemistry community will have access to: x-ray absorption spectroscopy (XAS) that will enable the unravelling of detailed interactions of metal ions with proteins; small angle scattering (SAX), which will be able to help determine the shape of proteins and protein complexes that cannot be crystallised; and, recently, inroads have been made in the area of protein structure determination using powder diffraction and grazing angle SAX.

There are also proposals for new beamlines in the area of circular dichroism which will enable secondary structure characterisation arising from spectral regions outside current laser methods and micro coherent sources for studying cellular organisation.

Many consortia around Australia are preparing for the advent of these beamlines by creating the infrastructure for high throughput protein expression, protein purification and crystallisation systems. Here in Parkville we have recently set up the C3 crystallisation facility that will service the Bio21 consortia in Melbourne. Other systems have been set up at the Universities of Queensland, Sydney, Monash and Auckland.

Currently, protein crystallography is at great disadvantage in space and time, being dependent on available time at foreign x-ray sources, the tyranny of distance and increasing difficulty in transporting biological samples in a paranoid world environment. This will change when the Australian synchrotron beamlines come online.