

ARC Centre of Excellence for Coherent X-ray Science



ANNUALREPORT 2006



CXS at a Glance

The Australian Research Council (ARC) Centre of Excellence for Coherent X-ray Science (CXS) brings together leading Australian researchers in the fields of X-ray physics, the design and use of synchrotron radiation sources, and the preparation, manipulation and characterisation of biological samples.

Its aim is to open a new frontier in biotechnology: the non-crystallographic structural determination of membrane proteins. These proteins mediate the activity of pharmaceuticals in human medical therapies. Their structures, however, are still mostly unknown because they do not form crystals suitable for analysis using the conventional crystallographic techniques that have driven almost all progress in structural biology. A breakthrough in this area would revolutionise rational drug design through the insight that would be gained into the function of membrane proteins. This would have far-reaching consequences for the pharmaceutical industry.

CXS's research is driven by its access to existing third-generation synchrotron light sources and to the Australian Synchrotron. We are also exploring the application to imaging problems of short wavelength high-harmonic generation sources and free-electron X-ray lasers that are under development worldwide. When combined with non-crystallographic diffractive imaging techniques, the brightness and intensity of these sources offers the possibility of taking snapshots of biomolecules. We are exploring fundamental issues in the use of these light sources, including the nature of the interaction between intense coherent X-rays and electronic matter, the efficiency of diffraction processes in these highly coupled light-matter systems, the detection of the scattered light, the preparation and handling of suitable biological samples, the management of radiation damage throughout the interaction, and the design of algorithms to extract structural information from diffraction data.

It is an ambitious interdisciplinary program of research.

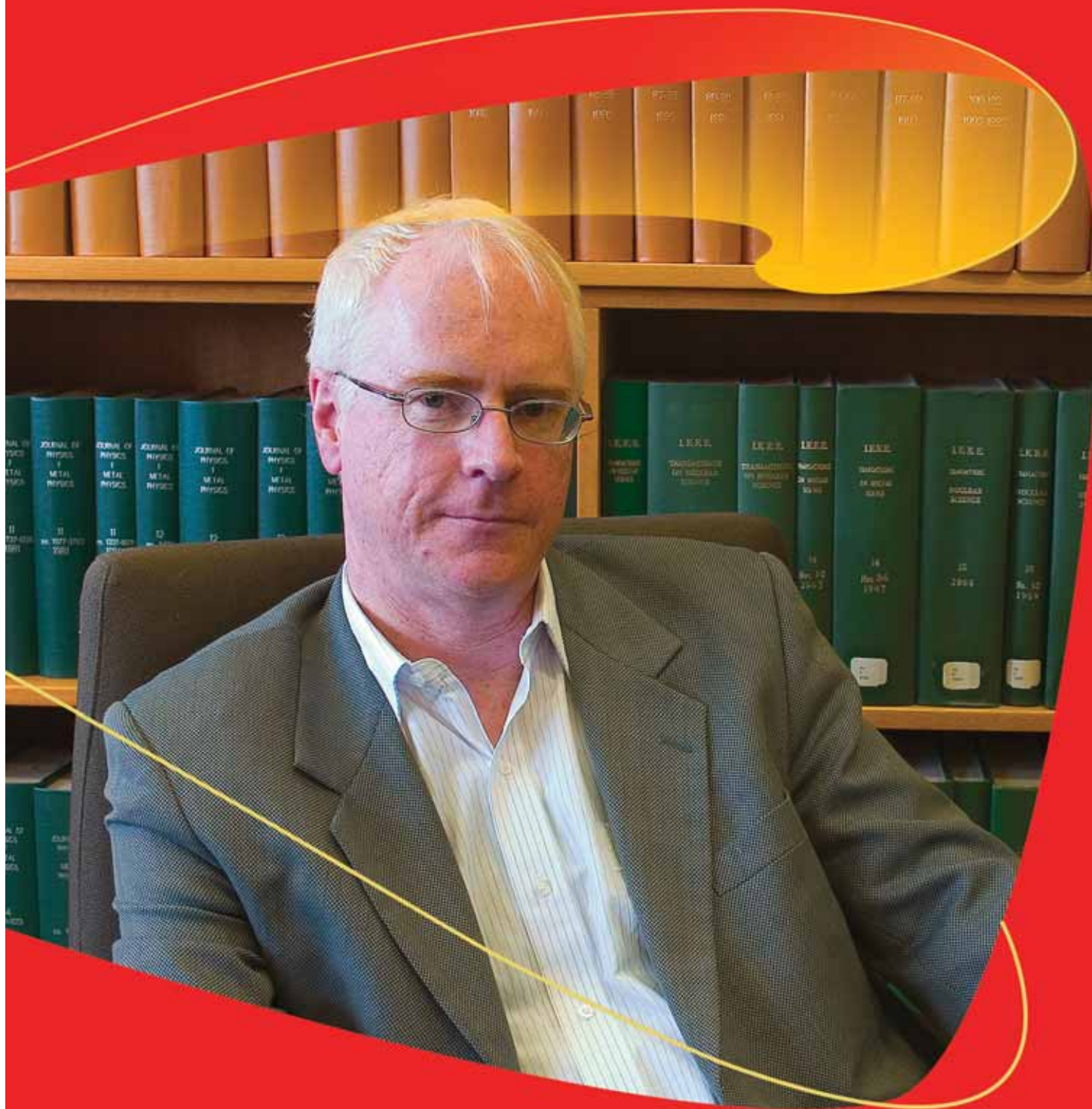
❖ CXS acknowledges the support of the Australian Research Council. We also acknowledge the financial and in-kind support provided by our collaborators – The University of Melbourne, La Trobe University, Monash University, Swinburne University of Technology and the Australian Commonwealth Scientific and Research Organisation (CSIRO). We are grateful for financial support provided by the State Government of Victoria through the Department of Innovation, Industry and Regional Development's Science, Technology and Innovation funding.

CXS would like to thank the School of Physics at the University of Melbourne, Dr John McDougall and Ms Norma Hayes of Monash University, and Ms Tatiana Tchernova of Swinburne University of Technology for their ongoing support.

Finally, CXS would like to thank the Australian Synchrotron and Bruce Smith Photography for the images contributed to this report.

Table of contents

Director's Report	4
Mission Statement	6
Research Programs	7
Biological Sciences	7
Detector and Beamline Development	8
Experimental Methods	8
Short Wavelength Laser Source	9
Theory and Modelling	10
Structure Determination Methods	11
Research Reports	13
Biological Sciences	13
Detector and Beamline Development	15
Experimental Methods	16
Short Wavelength Laser Source	18
Theory and Modelling	21
Structure Determination Methods	23
Outreach, Education & Training	28
Centre Connections	30
Taiwan	30
CXS Governance	33
Centre Management	33
Executive Committee	34
Advisory Boards	35
The 2006 CXS Team	36
Performance Indicators	40
Publications	42
Financial Statement	47



Director's Report

“Dedicated to bringing bright motivated people together to work on problems of major international importance regardless of the discipline to which they were trained.”

01

Director's Report

The ARC Centre of Excellence for Coherent X-ray Science (CXS) is dedicated to bringing bright, motivated people together to work on problems of major international importance, regardless of the discipline in which they are trained. CXS has a presence on six sites – the University of Melbourne, La Trobe University, Monash University, Swinburne University of Technology, CSIRO Manufacturing and Materials Technology, and CSIRO Molecular and Health Technologies. These sites are all located within the city of Melbourne, allowing CXS members readily to meet and discuss science.

CXS's priority is to help break down interdisciplinary barriers. Our aim is to nurture and mentor a generation of scientists for whom working across disciplines is not only natural but obvious. We must strive to ensure that scientists, irrespective of background and training, can contribute to our scientific program on an equal footing. This vision has been pursued through the organisation of numerous cross-disciplinary workshops. The quality of these workshops has been superb and it is a delight to see scientists communicating so effectively and sharing the excitement and challenge presented by fields other than their own. The workshop series began with the first CXS conference, held in April 2006, setting a high standard – one that has been maintained throughout the year in our smaller, more focused workshops. 2006 was the year of establishment for CXS. We have negotiated our agreements with partner institutions, we have been hiring staff and ordering the equipment needed to achieve our goals.

One of the delights in setting up a centre such as this is the ability to recruit young scientists, and we have been very fortunate in attracting an exceptionally talented group. We have also recruited the administrative staff for the Centre and we have built an excellent team that will ensure that CXS is managed with flair.

The Victorian state government has provided us with funding through the Science and Technology Initiative (STI) and this has enabled us to acquire a state-of-the-art laser facility that has now been installed and is ready for experiments. The Experimental Methods Group has led a successful bid for support from the ARC LIEF program for an experimental end-station to be located initially at the National Synchrotron Radiation Research Centre (NSRRC) in Taiwan, and we have negotiated a long-term agreement with NSRRC for this facility, one of a number of important developing international collaborations. The 2007–08 year is planned to be one of consolidation, in which we commission and install the major equipment and develop and prove our experimental techniques. The 2008–09 year will see CXS enter the phase of true interdisciplinarity.

The details of our achievements are presented in this report. We have essentially met all of our formal key performance indicators and I am delighted with the progress we have made. All members of the CXS team are delightful colleagues and I am very excited by the prospect of our future together.



Professor Keith Nugent
Director



Mission Statement

“CXS aims to be the world leader in the development of non-crystallographic techniques for the determination of membrane protein structures.”

02 Research Programs

Biological Sciences Program

The “holy grail” of structural biology is the determination of the molecular structure of a biomolecule without first obtaining a high-quality three-dimensional crystalline sample of the material for X-ray crystallographic analysis. X-ray crystallography, through the amplification of diffracted signal afforded by a periodic crystalline structure, has provided the basis for most of the advances in structural biology made during the past eighty years. While this form of structural analysis is now regarded as routine technology, the formation of suitable crystals of these biological molecules is what presents the greatest obstacle to sustained progress.

The most elusive of all crystalline samples – the membrane proteins – are also among the most significant from a pharmacological perspective. They tend to form either nanocrystals or two-dimensional quasi-periodic structures. These systems are of such biological significance that substantial investment of resources in the development of special structural characterisation techniques is warranted.

Apart from the production and handling of suitable membrane protein samples, CXS’s Biological Sciences Program is producing and processing contrast-enhanced samples for cellular imaging. Some progress has already been made in this direction by applying coherent diffractive imaging techniques to the imaging of malaria parasite-infected red blood cells.

The immediate aim is to obtain a more detailed picture of functionalities within cells by direct observation using X-ray diffractive imaging than is currently available from simple models. This is an essential step along the road to biomolecular imaging.

❖ *“The Biological Sciences Program are producing and processing contrast-enhanced samples for cellular imaging.”*



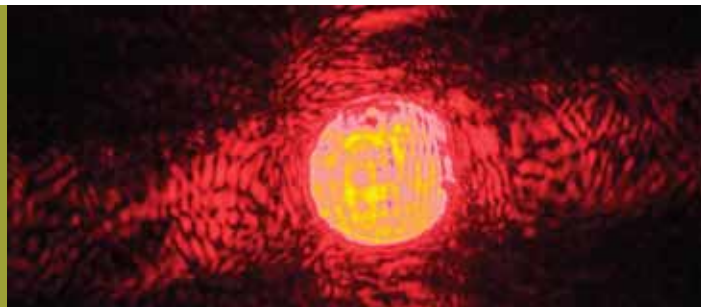
Detector and Beamline Development Program

The technical expertise of the members of the Detector and Beamline Development Program has been employed to develop experimental facilities at the Australian Synchrotron. These resources are essential to realising much of the research that is to be conducted by the other programs.

This program is developing detectors that are optimised to the experimental conditions prevailing in our X-ray diffraction experiments and will address issues such as sensitivity, response non-linearity, latent memory, and read-out fidelity.

In order to be able to complete the scientific goals of CXS, this program, in conjunction with the Experimental Methods Program, is designing and assembling the instrumentation for a vacuum beamline end-station at the Australian Synchrotron suitable for routine diffractive imaging of nano-scale particles.

❖ *“CXS has installed the Coherent Scattering Studies Laboratory at The University of Melbourne.”*



Experimental Methods Program

This program is developing the techniques to be used in X-ray imaging experiments, building on CXS's recent successes using curved beam illumination to aid image recovery. The fabrication of test samples within CXS forms an important part of this development work, since it will allow us to investigate critical aspects of the phase retrieval problem. These include the design of the experiment, the sensitivity of the phase recovery algorithms to noise, partial coherence, radiation damage and systematic effects such as internal translation of the beam or the various optical components.

Since the duty cycle for synchrotron experiments is so long, and because many of the features of diffractive imaging using X-rays can be simulated using visible sources, CXS has installed an experimental laser research laboratory known as the Coherent Scattering Studies Laboratory at the University of Melbourne. By a suitable scaling of the relevant variables and the careful selection of scattering targets, it is possible to simulate almost all of the features of an X-ray experiment using relatively inexpensive components and visible coherent light sources in this laboratory.

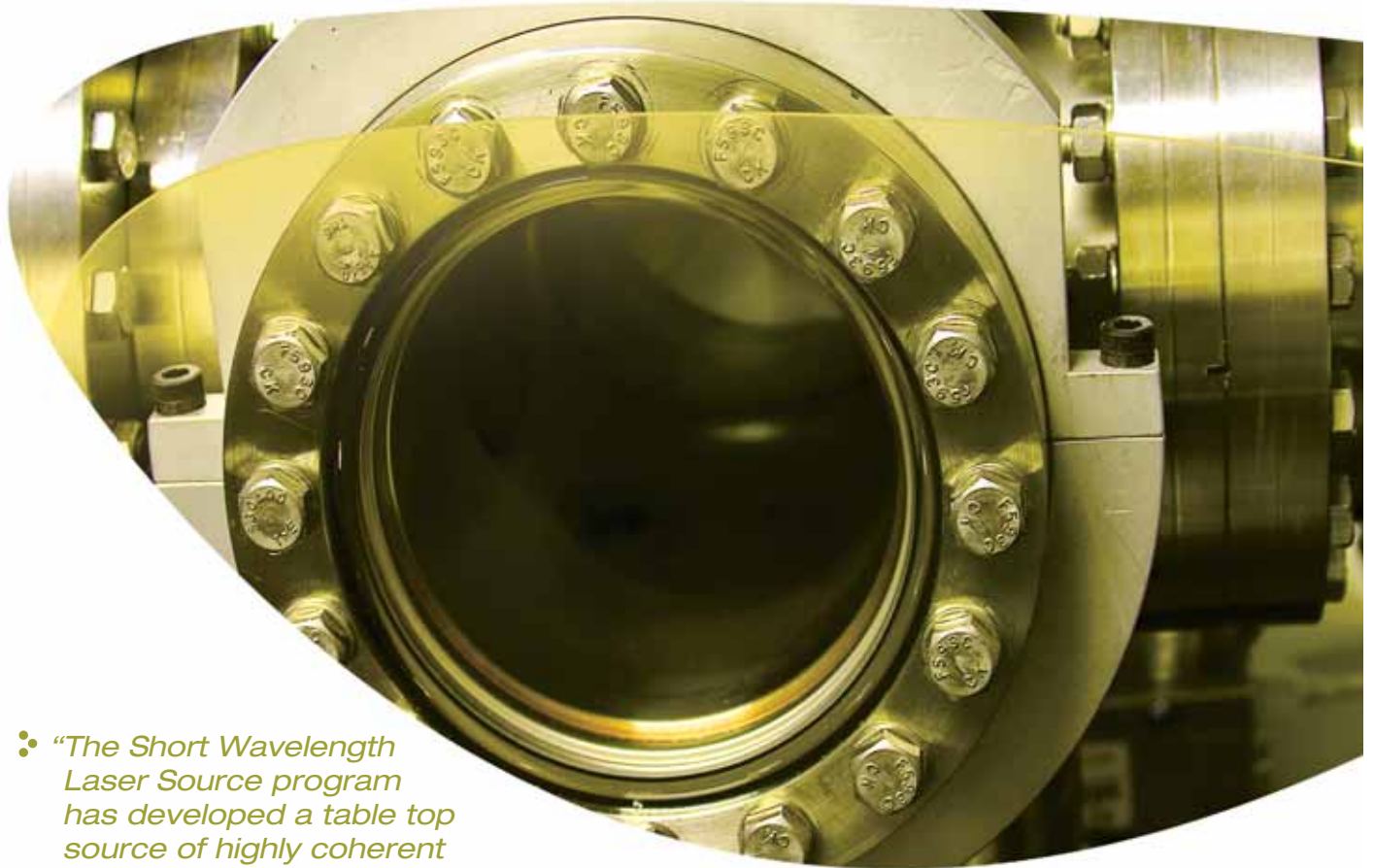
The Experimental Methods Program is working closely with the Theory and Modelling Program to put in place effective methods of image recovery for use at the Australian Synchrotron.

Short Wavelength Laser Source Program

One of the long-term possibilities being investigated by CXS is the use of X-ray free-electron laser sources in imaging applications. Such facilities are under development in both Germany and the USA. While we expect to be able to gain at least limited access to XFEL sources when they become available, there are currently no plans for similar resources to be built in Australia. They are hugely expensive facilities involving the construction of linear accelerators more than one kilometre in length.

In the meantime, the Short Wavelength Laser Source Group, based at Swinburne University of Technology and the University of Melbourne, has developed a tabletop source of highly coherent vacuum-ultraviolet or soft X-rays using high-harmonic generation techniques. An intense pulse of visible or UV wavelength light is allowed to interact with an atomic gas to form a highly coupled radiation-matter system. In the de-excitation process, pulses are created corresponding to multi-photon absorption by the atoms, followed by the coherent emission of a photon whose wavelength may be up to 1000 times shorter than that of the incident laser.

CXS is engaged in the development of these compact short wavelength sources to investigate alternatives to the use of XFELs in coherent diffractive imaging. The significance of this research goes far beyond the mere production of the source, since the use of XFELs in any process involving the interaction of the highly coherent intense pulse produced by high-harmonic generation raises fundamental issues concerning the modelling of the electronic processes. Investigation of the nature of these non-linear physical processes in laser-molecule interactions forms an integral part of the activities of the Short Wavelength Laser Source Program.



- ❖ *“The Short Wavelength Laser Source program has developed a table top source of highly coherent vacuum-ultra-violet or soft X-rays using high harmonic generation techniques.”*

Theory and Modelling Program

The imaging methods being developed by the Theory and Modelling Program team depend on the existence of a unique relationship between a diffraction pattern and an over-sampled periodic diffracting object. The program has found success in the past year in developing techniques adapted to imaging using beams of X-rays focused by zone-plates as well as iterative phase retrieval algorithms derived from Fresnel propagators.

on the basis of models of the diffracting object and the sources of error. This second line of attack will involve the detailed modelling of the experiment, including treatments of the partial coherence of the source, the detector response function, the characteristics of the focusing zone-plate optics and the influence of scatter from intermediate apertures in the system.



❖ *“The possibility exists that it will be possible to extract structural information from the diffracted intensities resulting from these encounters.”*

As well as these physical effects, detailed electronic models of the scattering materials are to be used to formulate tests against which to measure the likely accuracy of the reconstruction to the experimental data.

All methods of this type use whatever a priori information is available about the diffracting object to assist in obtaining a representation of its image from diffracted intensity data. Such information includes its spatial extent (support), its material composition, the phase and intensity structure of the illuminating source, and the geometrical parameters of the experiment. Also needing to be handled are sources of systematic and random error (such as sources of noise), detector response functions and errors in determining the geometrical parameters on which the reconstruction algorithms critically depend.

Two general approaches are being explored in this program. The first is based on numerical propagation of the electromagnetic information between planes that are subject to known constraints. To this is currently being added a second layer of statistical methods, in which Bayesian hypothesis testing is used to assess the information content in the reconstruction

In preparation for the availability of highly coherent X-ray sources from high-harmonic generation or free-electron lasers, preliminary work has begun on modelling the interaction between molecules and intense electromagnetic fields. This is very much frontier territory in theoretical research because of the need to obtain a detailed description of the time-dependent response of a complex system to a rapidly varying external perturbation that is sufficiently strong to cause secondary effects such as ionization and the cleavage of bonds. Since it is envisaged that the interaction between a molecule and such a source will occur over the lifetime of a pulse of the order of a femto-second, it will be possible to extract structural information from the diffracted intensities resulting from these encounters. Success in this part of the program will require a fundamental reappraisal of methods currently used in coherent diffractive imaging because of the target's non-linear response to the illumination.

Structure Determination Methods Program

One of the main aims of the Structure Determination Methods Program is the development of novel experimental techniques and data analysis methods for extracting structural information from two-dimensional crystals, especially relating to the determination of the structure of integral membrane proteins (IMPs).

The program includes the fabrication of 2D arrays by novel methods. It also includes the exploitation of grazing incidence X-ray diffraction (GIXD) methods to obtain high-sensitivity structural information for thin samples. A powerful aid to the development of these techniques is simulation software being developed in order to help better understand the likely nature of diffraction data on such systems, including the influence of structural disorder. Methods of data analysis proposed for implementation include Bayesian and MaxEnt methods that seek to incorporate both data and a priori information.

The initial system being studied is the purple membrane, a naturally occurring two-dimensional crystal. This is a classical membrane protein system that has been much studied by high-resolution cryoelectron-microscopy and so valuable comparisons can be made about the efficacy of both electron and X-ray methods.

A long-term aim of the program is to develop novel instruments and techniques for the structure determination of integral membrane proteins, which might be implemented at the Australian Synchrotron.



❖ *“This program includes the fabrication of 2-D arrays by novel methods.”*



Coherent diffractive X-ray imaging and electron tomography

Non-crystallographic methods for imaging cellular architecture – and ultimately macromolecular complexes and individual proteins, particularly membrane proteins, within a cellular environment – is a crucial pursuit of cell and molecular biology.

We are developing methods to use X-ray coherent diffractive imaging (CDI) to obtain information about the architecture of cells and biological macromolecules. Soft X-rays have wavelengths of about 1–10 nm, allowing imaging of cellular and intracellular structures at high spatial resolution. Our test system for cellular imaging is the malaria parasite-infected erythrocyte. The parasite establishes a system of membranes within the host cell cytosol and induces changes in the host cell membrane. Because of the limitations of the available techniques, there is ongoing debate regarding the origin and organisation of the different membranous structures in the host cell cytoplasm.

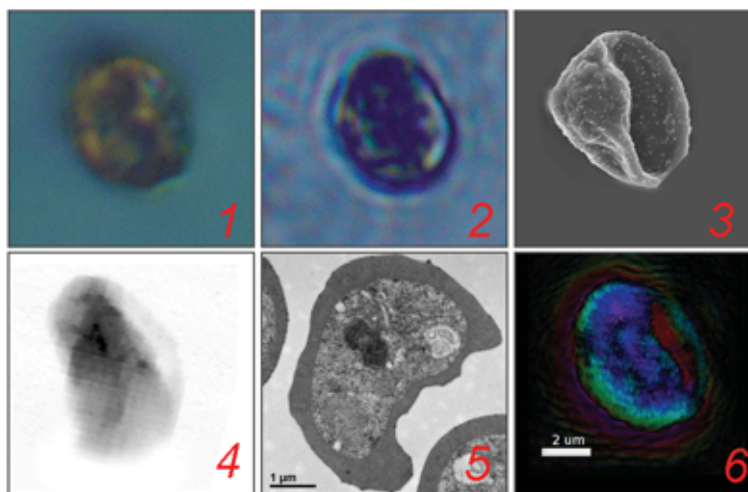
Research Fellow Eric Hanssen and Research Assistant Sam Deed prepared chemically fixed, dehydrated infected erythrocyte samples, which were labelled with different metals

or left unstained. The cells were imaged at the Advanced Photon Source, Chicago, in collaboration with Andrew Peele and Garth Williams. The diffraction signal was collected and integrated from data sets comprising 400 collections (1.5 keV, 8.2 \AA). The phase and intensity profiles of the cells have been successfully reconstructed revealing the major features of the cells. The CDI images were compared with X-ray fluorescence micrographs of the distribution of different metals in the cells. The cells were also imaged by phase X-ray microscopy in collaboration with members of Steve Wilkins' group and by fluorescence microscopy in collaboration with Nick Klonis.

The data suggest that the ultimate goal of obtaining 3D structural information from non-crystalline biological samples at a resolution of 10–40 nm is achievable. This work is made possible by a stimulating collaboration between theoretical and experimental physicists and cell and molecular biologists. Reconstructions were generated from images of a tilt series between -75 and $+75$ degrees. Novel methods for immunogold labelling of intracellular components have been developed to characterise the cell's molecular topography.

TECHNIQUES FOR IMAGING MALARIA-INFECTED RED BLOOD CELLS:

1. Optical microscopy: reflection
2. Optical microscopy: transmission
3. Scanning EM
4. Scanning Transmission X-Ray Microscopy
5. Transmission EM
6. Coherent Diffraction Imaging



Detector and Beamline Development Program

The task of CXS's Detector and Beamline Development Program has become clearer, with the CXS team meeting to review and revise its high-level plans throughout the year. Given the skill set within the program team, it was decided to seek a commercial solution to the immediate need for a low-energy X-ray detector, aimed at the end-station for the Taiwan synchrotron, the NSRRC. In the longer term, the options for the Australian Synchrotron station are still open. One potential solution is to use a development within another project and adapt this for use with CXDI.

Modelling of the detection process for various detector types remains a major theme of the work within the Detector and Beamline Development Program. Components for a complete source through to derived data model are being developed. This year great progress was made on the source models and the Monte-Carlo transport of the photons through various configurations of detector. Two members of the program are now fully conversant with the GEANT Monte-Carlo system and are in the process of training the first PhD student, Guido Cadenazzi.

❖ *“The Monash University GDAQ data acquisition card in-situ on a PC mother board.”*



A medical imaging detector based on pixel technology is currently being built within the Detector and Beamline Development Program. Although this is aimed at much higher energy photons, we believe the design could be adapted for X-rays suitable for use with CXDI. Alternative solid state and gas phase detectors have not been ruled out. The modelling and experimental research work in this area continues.

Guido Cadenazzi was recruited in 2006 and is a promising young researcher interested in modelling the details of the detection system and its impact on the synchrotron CXDI.

Also, a fully working data acquisition system was demonstrated during this period. The GDAQ electronics are fabricated on a PCI card and controlled using an in-house graphical user interface under a standard operating system software.



❖ *“The GDAQ data acquisition card showing the three dual input daughter cards carrying the 6x12 bit 210 MSPS ADCs.”*

Experimental Methods Program

THE MAJOR EXPERIMENTAL PROGRAMS FOR 2006 WERE:

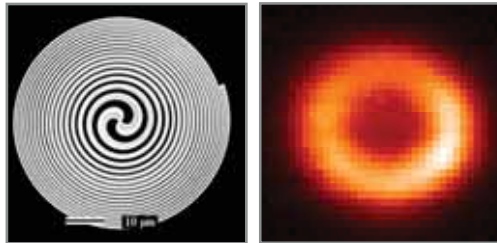
- Fabrication
- Coherent diffractive imaging experiments
- Tomography
- Partial coherence methods

Fabrication

CXS goals in this area are to establish a fabrication capability to allow for construction of test samples and to allow manipulation, arrangement and alignment of existing samples.

During 2006 the main effort was in the continuance of investigations into X-ray lithography via the PhD research of Kaushal Vora. This work has successfully pursued methods into modelling high aspect ratio structures and resulted in one refereed and one unrefereed conference publication, with a further four refereed publications accepted during 2006. This work has established our capability in high aspect ratio structures, which will be used in sample handling.

In 2006, planning for an in-house fabrication facility, based on a prototyping e-beam facility, culminated in the commissioning of the e-beam system, the appointment of a post-doctoral fellow (Eugeniu Balaur) and the specification of equipment. The last equipment will be delivered mid-2007, which will see the fabrication laboratory operational. The operation of the e-beam saw the production of coherent X-ray optics in the form of spiral zone plates. This has furthered our collaboration into X-ray singular optics with Dr Ian McNulty at the Advanced Photon Source.



❖ *“Spiral Zone Plate made using the La Trobe University e-beam facility (scale bar is 10 μm). The donut pattern shows an x-ray beam produced using a Spiral Zone Plate at the Advance Photon Source.”*

Coherent Diffractive Imaging Experiments

Our goals in this area are to establish and improve experimental methods in coherent diffractive imaging (CDI), specifically in Fresnel CDI. The mainstay of this work is our synchrotron beamtime. Work continued in 2006 with experiments in June and December at beamline 2-ID-B at the Advanced Photon Source. Experiments in 2006 concentrated on nanofabricated test samples and our biological test sample – malaria-infected red blood cells.



Significant progress was made in work led by Garth Williams with the publication of the first demonstration of reconstruction of a sample using Fresnel CDI. Work in quantifying the quality of the reconstruction forms part of the PhD project of Jesse Clark and work investigating experimental configurations forms part of the PhD project of Lachlan Whitehead.

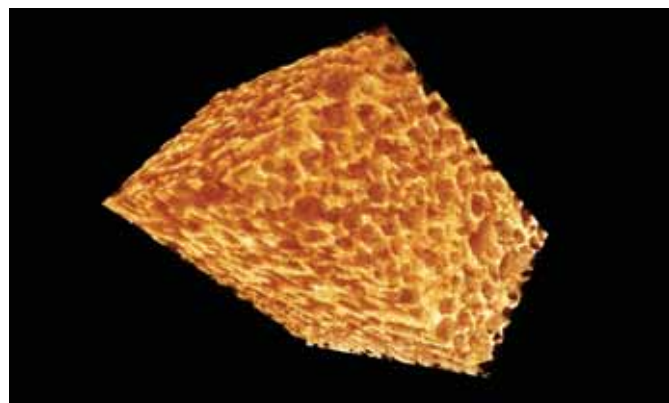
❖ *Left: Reconstruction of a 8 μm wide nanofabricated gold test pattern.
Right: preliminary reconstruction of a malaria infected red blood cell.*

Additional progress is being made in understanding the experimental issues via programs in an optical test-bed laboratory established by G Williams and in the appointment of B Abbey as a post-doctoral fellow. A computational effort involving a post-doctoral appointment (R Norman) is underway to simulate experimental effects.

This work also demonstrated the need for improved X-ray experimental facilities. An extensive design study has specified the requirements for an experimental facility and led to the appointment, at the end of 2006, of M Pfeifer as a post-doctoral fellow. The endstation project will see the installation of a high-stability system at the Taiwan synchrotron – currently scheduled for early 2008.

Tomography

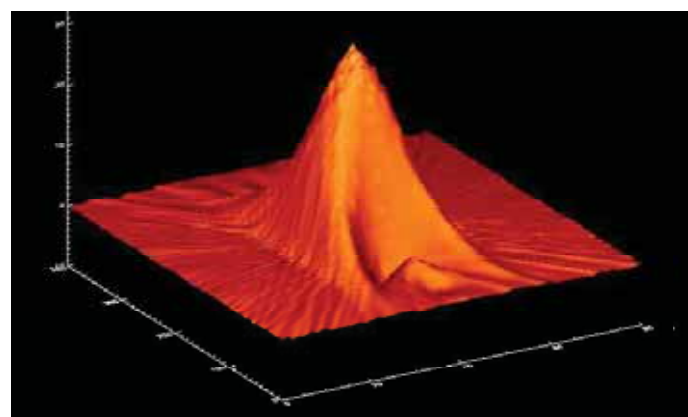
This work seeks to develop the computational methods and data visualisation required when three-dimensional data sets start to be produced using coherent diffractive imaging. The work is based on extending standard methods using the Micro X-ray Tomography facility at La Trobe University. The facility has been successfully commissioned in work led by post-doctoral fellow B Arhatari. Use of the facility forms part of the PhD project of K Hannah.



❖ *“Rendering of a porous TiNi sample.”*

Partial Coherence Methods

An important goal of CXS is to understand the role of partial coherence in the image formation process. To come to grips with this issue, full knowledge of the four-dimensional coherence function describing two dimensional wave fields is required. In 2006 the research towards complete recovery of partially coherent wave fields using phase-space tomography made major steps forward. In work led by C Tran the program team successfully demonstrated the possibility of using refractive lenses as an extra degree of freedom required for the full reconstruction of four-dimensional coherence functions. An alternative simplified approach based on the generalised Schell model was also proposed. This is one of a few approaches that have been significantly exploited towards the development of a full and practical technique which is capable of full reconstruction of partially coherent wave fields.



❖ *“Depiction of the coherence properties in a one-dimensional beam.”*

Short Wavelength Laser Source Program

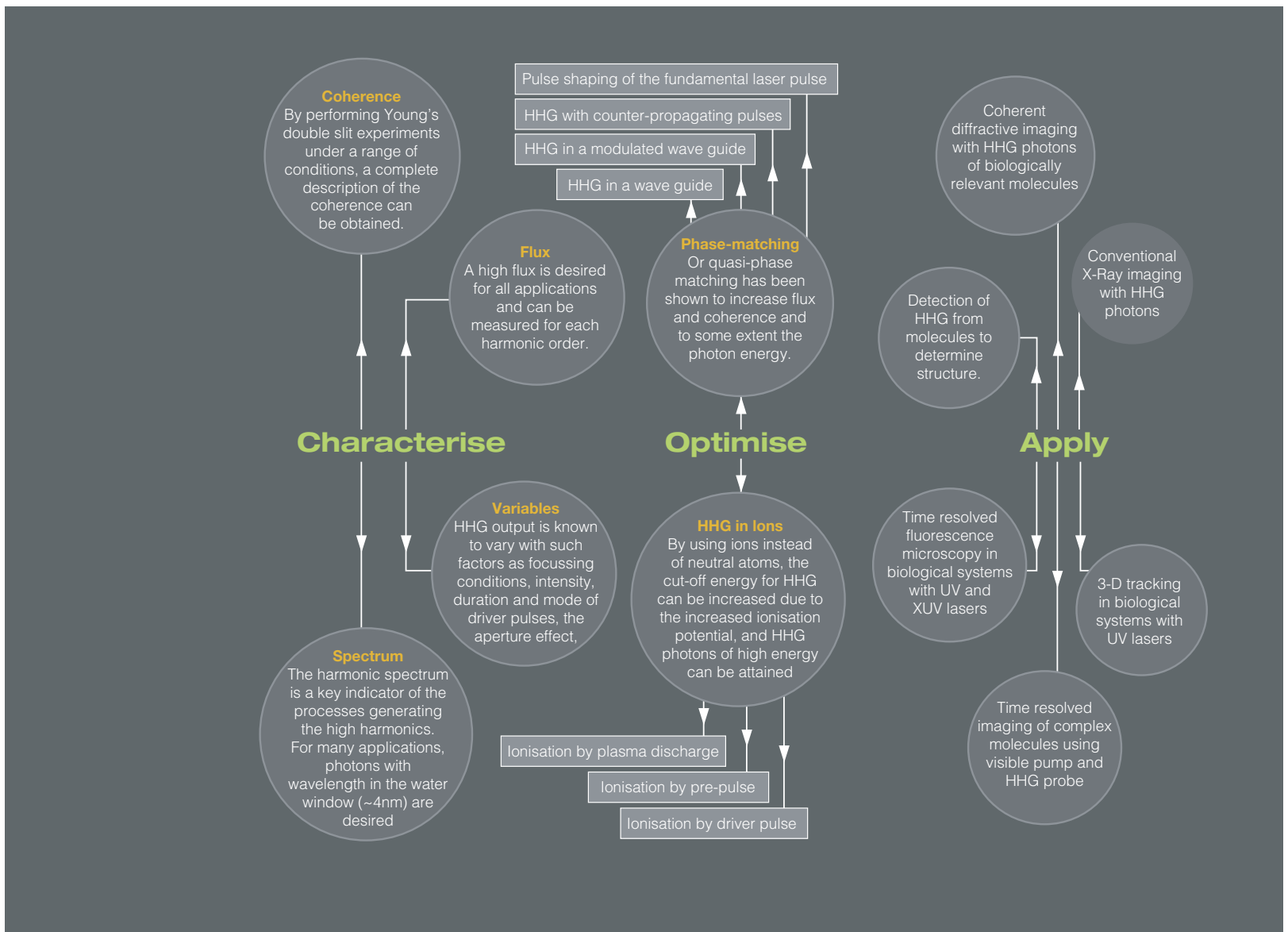
The Short Wavelength Laser Source Program, based at Swinburne University of Technology and the University of Melbourne, is developing a tabletop source of ultrashort, highly coherent pulses of extreme-ultraviolet and soft X-ray radiation using high-harmonic generation techniques.

The basic idea is that an intense pulse of visible light is allowed to interact with an atomic gas or ionic plasma to form a highly coupled radiation-matter system. In the de-excitation process, pulses are created corresponding to multi-photon absorption by the atom or plasma followed by the coherent emission of a photon whose wavelength may be up to 1000 times shorter than that of the incident laser.

Project Milestone and Scientific Goals

Generation, through the high-order harmonic generation process, of ultrashort-pulse high-flux coherent beam with energy in the water window (~ 4.2 nm) for use as a source for coherent diffractive imaging of biologically important molecules.

Project Structure





Femtosecond Laser Oscillator (Femtolasers):

Mode-locked titanium sapphire laser (< 20 fs)

Femtosecond Amplifiers (Quantronix):

Multi-stage titanium sapphire amplifiers with diode pumped pump lasers

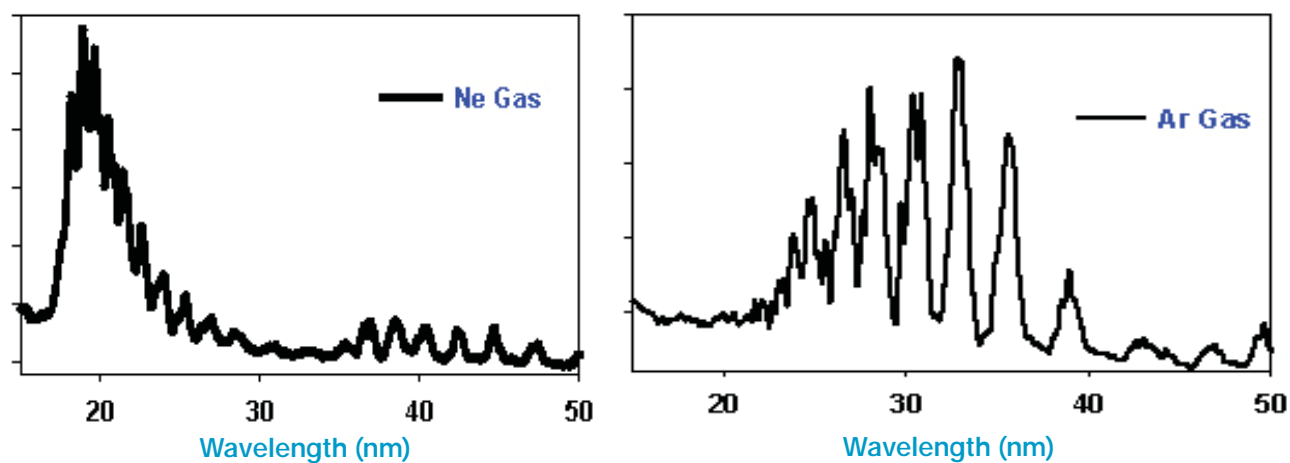
Pulse energy 5 mJ

Pulse duration ~ 30 fs

Pulse repetition rate 1 kHz

Beam quality $m^2 \sim 1.6$

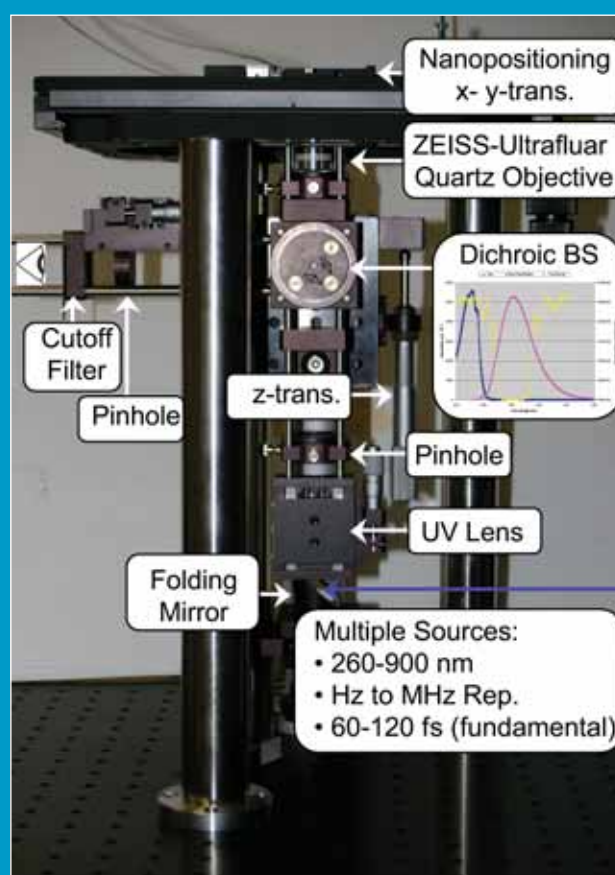
HHG Spectrum from Ar and Ne Gas (with Al-Foil Filter)



Deep-UV Confocal Microscope

TIME-RESOLVED FLUORESCENCE IMAGING:

- following direct (UV) excitation of tryptophans
- detection by time-resolved single photon counting



Theory and Modelling

The Theory and Modelling Program provides support to the experimental programs of both the Experimental Methods Program and the Short Wavelength Laser Source Program. It also seeks to gain insights into fundamental aspects of mathematical inverse problems in imaging systems, as well as the physics of the interaction of atoms and molecules with intense laser fields.

Phase Retrieval Algorithms

Throughout 2006 the Theory and Modelling Group and the Experimental Methods Group were engaged in developing the technique we have described in recent publications as Fresnel coherent diffractive imaging. Firstly the properties of an optical system comprising an X-ray zone plate, order-sorting aperture and detector are fully characterised using iterative phase retrieval methods and all of the a priori information that is available about the system, such as the geometry, the spatial extent of the zone plate, its focal length and the physical characteristics of the detector. Then electromagnetic theory is used to construct the X-ray wavefield in a plane containing a thin sample. The wavefield contains significant phase structure in this plane, which offers considerable advantages in the second stage of the procedure – the determination of the structure of the diffracting sample, given only an approximate knowledge of its spatial extent, which may be known either from a separate measurement or by using a low-resolution imaging technique such as holography. The successful reconstruction of a nanofabricated gold sample from a single diffraction pattern using this approach demonstrated two things: the accuracy of the reconstruction of the illumination that plays such a key role in the algorithm; and the feasibility of retrieving structural features with a resolution of the order of tens of nanometres using Fresnel CDI.

In parallel with this work, we investigated several alternative approaches to phase retrieval in an effort to identify the mathematical features of the problem that led to the well-known stagnation difficulties iterative methods. A number of remedies for these algorithmic pathologies have been suggested. Many of them claim a basis in some form of fundamental analysis but most rely wholly on empirical evidence obtained in particular cases that indicate that their effects are, at best, palliative. A rather obvious and well-understood strategy is to design a scheme that fits the diffraction data to the forward-propagated intensity of the reconstructed object in a least-square sense.

This procedure is subject to constraints dictated by the finite extent of the diffracting object and whatever other information is to hand. It is well known that the most elementary of the iterative methods, the “error reduction” algorithm devised by Fienup based on the work of Gerchberg and Saxton, is an algorithm of this

type. It is plagued by convergence problems in its search for a global error minimum to the extent that it usually stagnates unless the iteration is started at a configuration that is, in a well-defined mathematical sense, “close” to the exact solution. This led us to investigate the nature of the abstract multi-dimensional surface that is explored in any such error-minimising scheme.

In the case of Fraunhofer diffraction, the distribution of local minima is so dense that any of the commonly used strategies for following a path to a stationary point invariably led to a local minimum very far from the required solution. If one can traverse this rocky terrain, or start the iteration near the position of the global minimum, convergence is generally very rapid. For configurations corresponding to Fresnel diffractive imaging, however, determination of the correct structure at the global error minimum occurred with a probability that approached unity as the incident phase curvature was increased, as we had found previously using a variety of conventional phase retrieval algorithms. The modification of the multi-dimensional surface that defines the fitting error by the phase curvature evidently removes most of the troublesome local minima.

It is by no means obvious that this desirable behaviour occurs exclusively when the illumination is structured with a spherical phase or that this represents the optimal configuration. An outcome of this research has been ongoing investigation into the construction of error-minimising schemes that provide means to resolve stagnation when it occurs.

The orthodox mathematical approach to the solution of inverse problems is to cast them as integral equations. During 2006 we devised and implemented an algorithm to solve an integral equation derived from the autocorrelation of a finite object based in the Newton-Raphson scheme for the solution of the resulting non-linear equations. In common with numerical experience in this field, this approach offers the most powerful of all methods, provided that one begins the iterative procedure close enough to a solution, which one can sometimes contrive by seeding the procedure with one of the conventional iterative approaches. In such cases, convergence to the solution is achieved quadratically, reducing the fitting error of the

data by several orders of magnitude in just a few iterations. Unfortunately, the radius of convergence of this scheme proved to be quite small, but it does offer a potential “polishing method” to add to our arsenal of techniques.

The foundations of the phase retrieval problem were investigated by constructing a link between the transport of intensity equation, which is widely employed in phase contrast microscopy, and the iterative methods based on numerical Fresnel propagation of wavefields. This has led to a rather complete analysis of the phase retrieval problem as well as a practical method for obtaining, non-iteratively, approximate solutions to the imaging problem from a single dataset.

The outcome has shed considerable light on the analytical structure of the phase retrieval problem.

We continue to pursue methods to resolve the phase structure of optical vortices, in collaboration with experimental colleagues, using a combination of iterative methods in conjunction with astigmatic perturbations. The most satisfactory methods found so far, however, rely either on selecting a starting guess with the correct phase structure or providing a mechanism to filter out all incorrect components, corresponding to wave components with angular momenta differing from that of the vortex. A truly satisfactory solution to this problem, based only on analytical considerations of the diffraction data, remains an elusive challenge to the successful phase retrieval of these systems.

Coherence studies

In experimental studies it was observed that our formulation of the Fresnel CDI conveys the additional benefit that iterative phase retrieval algorithms are considerably more robust to the presence of partial coherence. Mathematical analysis of the problem using representative models led to the formulation of a relationship between the radius of curvature and the coherence length of the illumination that determines the circumstances under which reliable reconstructions may be obtained using partially coherent light. This has since led to a detailed study of this phenomenon as part of the Experimental Methods program.

New approaches to the characterisation of partial coherence of X-ray sources have been pursued in collaboration with members of the Experimental Methods Group. These include an iterative method based on numerical propagation of the mutual optical intensity between an aperture of known dimensions and multiple planes in which the intensity has been measured. The computational complexity of this approach led to the formulation of a new algorithm that utilises a set of coherent planar modes, propagating these two-dimensional quantities separately rather than the four-dimensional mutual optical intensity. A finite set of modes representing the mutual optical intensity in the plane of an aperture is determined in this scheme by propagation to the planes containing measured intensities, updating the parameters that define the modes iteratively. Additionally, a detailed study of the propagation of partially coherent beams was constructed, based on a generalised Gaussian model. This was undertaken to determine the relationship between coherence length and phase curvature in a beam of this type, in support of experiments that reported apparently anomalous resolution in images taken with bending magnet synchrotron sources.

Electronic structure and molecular physics

A short visit was made to the laboratory of the Centre for Computational Molecular Studies at the University of Perugia, where the group maintains a collaboration in the development of electronic structure methods based on the relativistic formulation of density functional theory and the theoretical study of the electric and magnetic properties of complex electronic systems. This project will feed into the activities of CXS in coming years, since the Theory and Modelling Group is becoming increasingly involved in its collaborative work with the Short Wavelength Laser Source Group at Swinburne. The latter group is developing short-wavelength coherent radiation sources through high-harmonic generation involving strong-field laser-atom interactions and the possibility of direct molecular imaging through analysis of laser-molecule interactions. This work was greatly enhanced by an extended visit to the Blackett Laboratory at Imperial College London, which houses one of the world's leading groups in strong-field laser physics. This visit catalysed the current research in Theory and Modelling which is developing the tools to model high-harmonic generation by time-dependent quantum theory, and the inversion of high-harmonic spectra of aligned molecular targets to obtain structural information.

Structure Determination Methods Program

Membrane Proteins and Novel Structure Determination Methods

The Structural Determination Methods Program based at CSIRO is taking a multi-faceted approach to tackling the problem of developing improved methods for the determination of the structure of integral membrane proteins (IMPs). This program has embraced new and improved methods for sample preparation as well as new and improved methods for structure determination, the latter being primarily based on X-ray diffraction and particularly relying on the very high brilliance and special properties of synchrotron radiation sources and related instruments.

Considerable progress has been achieved on a number of fronts in the CSIRO program of work aimed at novel and improved methods for the determination of the structure of IMPs and to new methods of sample preparation. This work has spanned CMHT (Parkville and Adelaide) and CMMT (Clayton).

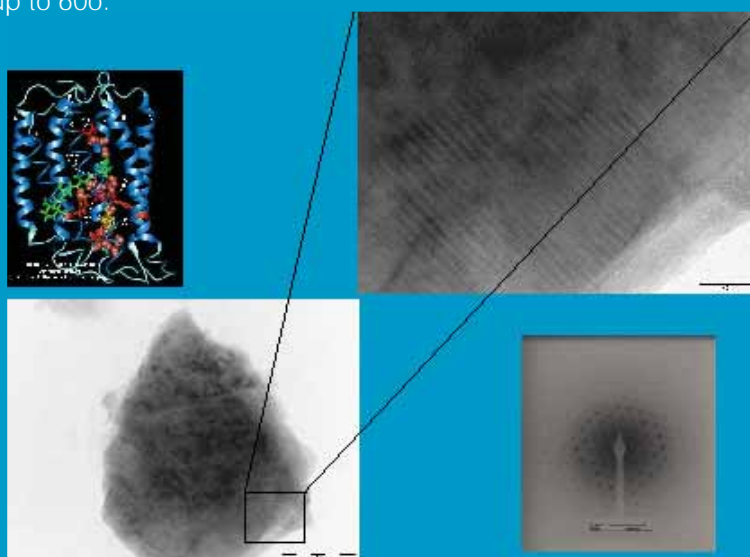
The Structural Determination Methods Group has concentrated a large part of its effort and resources on producing 2D membrane protein crystals (e.g. Bacteriorhodopsin) and in developing related methods for determining the

structure of these, and especially in treating the 2D diffraction problem for such samples. This is a comparatively undeveloped area of X-ray science and crystallography, which is opening up exciting new opportunities for structure determination of membrane proteins in or near their functional form. A key feature of the work is based on the fact that diffraction data for a given 2D crystal shows Bragg spots in 2D but has a continuous distribution of scattering in the third dimension. This in turn means, for example, that random distributions of such 2D crystals lead to 2D powder diffraction patterns that can be more easily indexed than for the usual case of 3D crystallites, since there are fewer Bragg peaks. These key aspects are being understood by detailed computer simulation and by mathematical analyses of the diffraction problem. The properties and quality of 2D crystals are being studied by HRTEM, small-angle X-ray scattering (SAXS – both on solid and solution form samples) and by grazing incidence X-ray diffraction (GIXD). Much of the X-ray data is being collected using the small-angle X-ray scattering station (15-ID-C) at ChemMatCARS at the Advanced Photon Source (APS) within Argonne National Laboratory in Chicago.

Assessment of Quality of Crystals by X-ray and TEM Methods

Below are electron micrographs of single bacteriorhodopsin 2D crystals. The crystallinity is confirmed by an electron diffraction image (bottom right hand corner) of a heavy metal stained 2D crystal. Electron diffraction data on the native crystals has been collected on the Technai 120keV Electron Microscope with tilt angles up to 60°.

This data has been processed and Fourier amplitudes and phases have been extracted to produce a 2D projection density. X-ray diffraction data on multilayer specimens both in solid form and in solution have been collected from both laboratory sources and synchrotron sources, indicating good quality powder diffraction from 2D crystals. The data has been processed to yield a 2D projection image of bR using phases from electron diffraction.

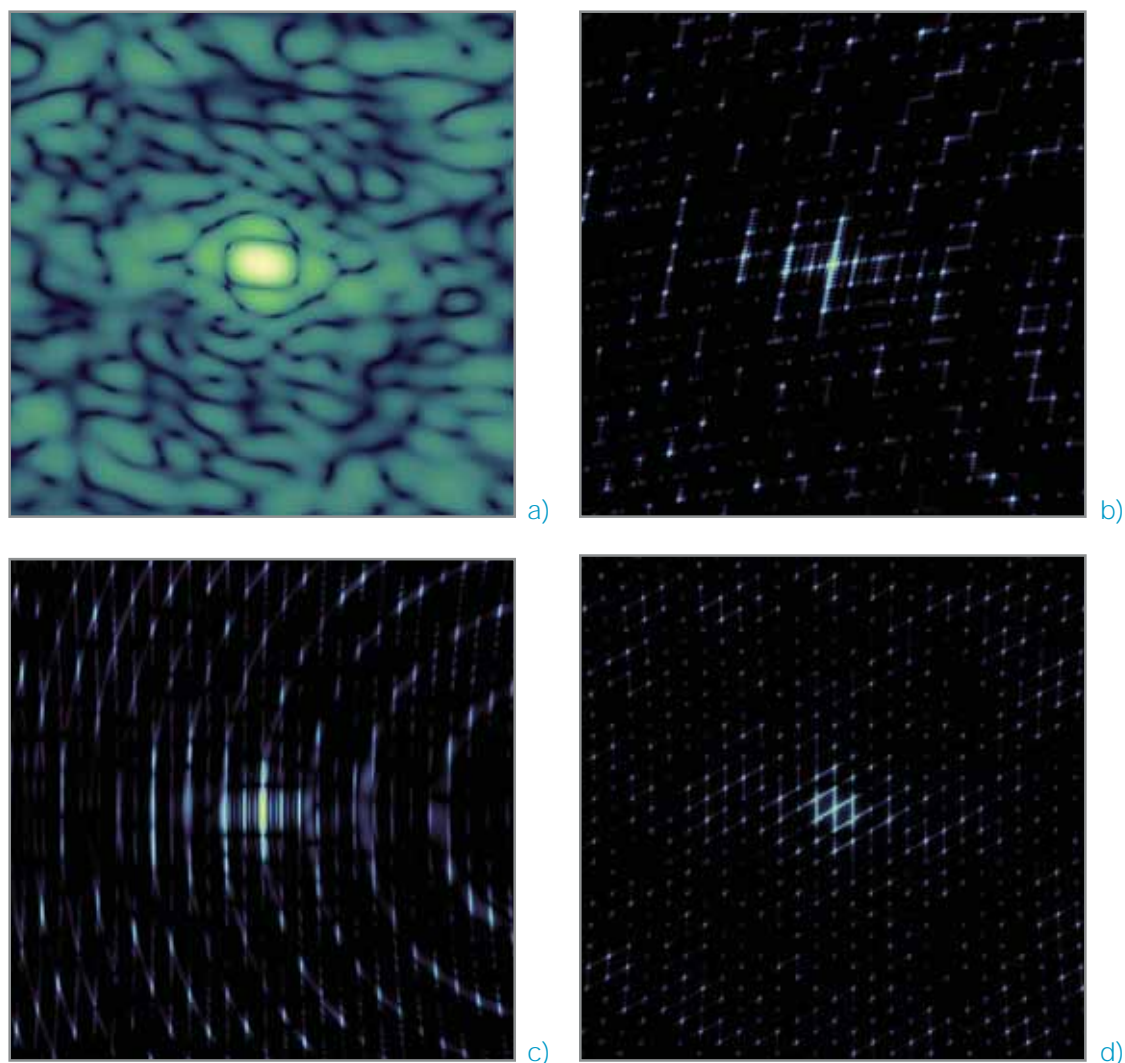


Scattering by Single Protein Molecules, 2D-Arrays and Crystallites

Atomic scattering theory-based computer simulations of X-ray diffraction have been carried out for a variety of samples, including single molecules, 2D micro-arrays and 3D crystals, as well as disordered assemblies of 2D crystals. Figure 3 shows examples of results for single molecules and crystals of Bacteriorhodopsin (bR).

SIMULATED THEORETICAL DIFFRACTION PATTERNS FROM

- (a) single molecule,
- (b) 3D nano-crystallite,
- (c) 2D micro-array with X-rays at grazing incidence,
- (d) 2D micro-array with X-rays at normal incidence, under monochromatic illumination with a wavelength of 1\AA .

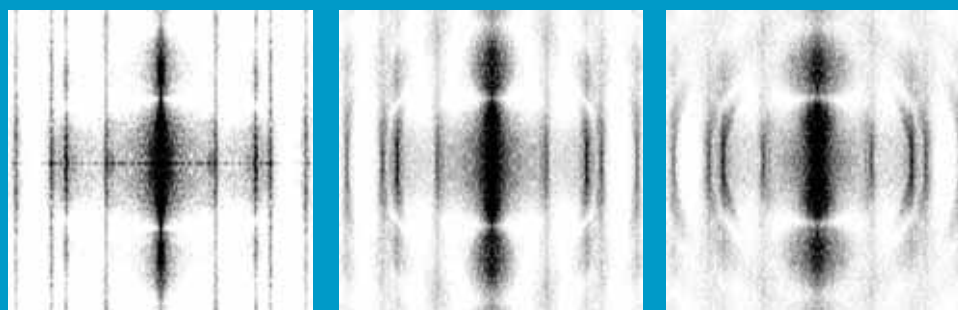


- ❖ *“Simulated theoretical diffraction patterns from (a) single molecule, (b) 3D nano-crystallite, (c) 2D micro-array with X-rays at grazing incidence, (d) 2D micro-array with X-rays at normal incidence, under monochromatic illumination with a wavelength of 1\AA .”*

Detailed Numerical Studies of Disorder in Composite 2D Samples

Detailed atom-by-atom modelling of diffraction from random ensembles of 2D micro-arrays of bR-exhibiting orientational disorder have been carried out using the supercomputing facilities of the High Performance Computing & Communications Centre (HPCCC) of the CSIRO and the Bureau of Meteorology. The simulations investigated the effect of the degree of disorder on the diffraction pattern. The results were compared with recently published experimental X-ray powder diffraction data for 2D micro-arrays of bR naturally occurring in the purple membrane (Oka et al., *Journal of Synchrotron Radiation* 13, 281–4 (2006)). Figure 5 shows grazing incidence small angle scattering (GISAXS) patterns for preferentially oriented powders with varying degrees of orientational disorder, as well as some experimental data obtained by Oka et al.

Results of this work were presented by Steven Homolya at the Workshop on Grazing Incidence X-ray Techniques for 2D Crystals on 6 July 2006 at the Centre of Excellence for Coherent X-ray Science, CSIRO Manufacturing and Infrastructure Technology, Clayton, Victoria, Australia.



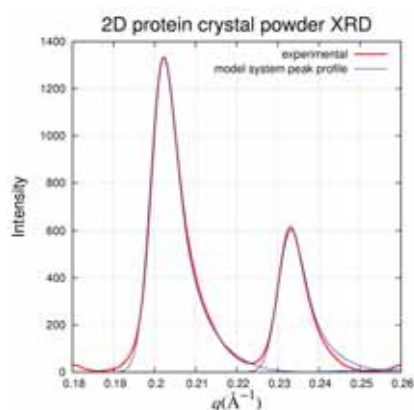
❖ *“Grazing incidence diffraction patterns from simulated bR 2D powder samples with varying degrees of orientational disorder.”*

Semi-analytical Models of Disorder

Even with the use of HPCCC supercomputing facilities, detailed studies of samples containing a realistic number of molecules are very time consuming and only feasible for a select few case studies. For a more efficient approach that can be applied routinely to most cases of interest, a mathematical description of the effect of disorder in 2D powders was developed. The results of this work have been written up as a CSIRO internal report, and the implementation of the analytical model in efficient computer simulation software is ongoing. This will allow very efficient modelling of diffraction by a wide variety of samples with varying degrees and types of orientational disorder, ranging from perfect powders through preferentially oriented powders to perfect stacks of micro-arrays of biomolecules.

Analysis of Experimental Diffraction Data for 2-D Protein Powder Samples

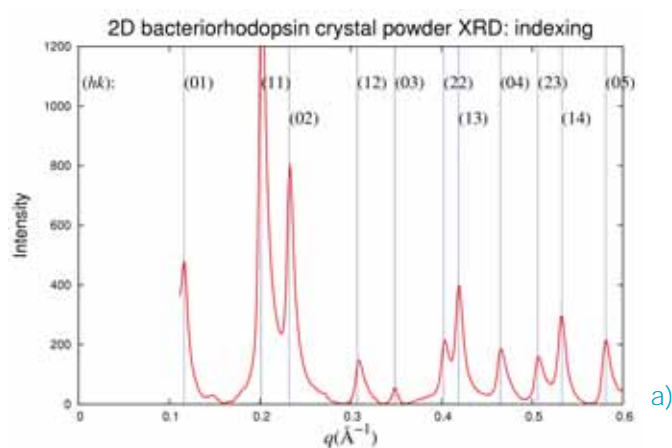
The analytical model for scattering by powders composed of 2D micro-arrays developed for more efficient computational modelling will also serve as the basis for analysis of experimental results, aiding indexing and profile fitting. The line-shape profiles of powders of 2D arrays are very unlike those for 3D crystals because of the non-crystalline nature of the components of the system along one of three dimensions. Analysis shows that this gives the line-shapes structure that is uniquely dependent on the structure of the molecules that make up the 2D arrays. No existing powder diffraction software is equipped to properly analyse powder diffraction data from 2D systems. Work on satisfactory models for line-shape functions that will allow largely automated fitting of powder diffraction profiles for 2D systems is ongoing.

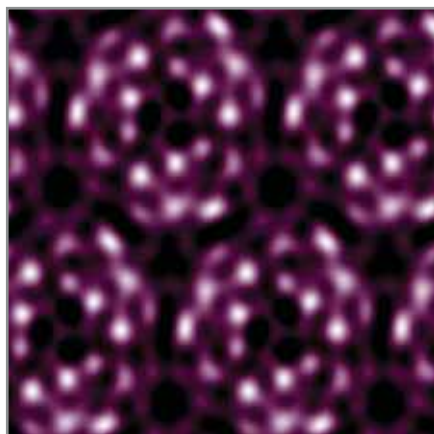


- “Experimental line-shapes and fitted asymmetrical profiles obtained from a ‘uniform density’ approximation of a 2D crystal.”

Electron Density Reconstruction from 2D Diffraction Data: Ongoing Work

Data recently obtained at the Advanced Photon Source (APS) for 2D bR powder samples and the projected electron density at 8 angstrom resolution reconstructed after indexing and manually fitting the data. Work on phase retrieval methods is ongoing, with low-resolution electron microscopy images serving as initial guesses for the inherently unknown phases. The phases are yet to be determined in an iterative procedure using a combination of Solvent Flattening and Maximum Entropy methods. The reconstruction shown below employed phases borrowed from previously published electron diffraction results (Henderson et al., Journal of Molecular Biology 213, 899–929 (1990)). Preliminary results from this work were presented by Connie Darmanin and Steven Homolya at the CXS 2nd Annual Workshop in April 2007 at the Bio21 Institute, Melbourne, Australia.



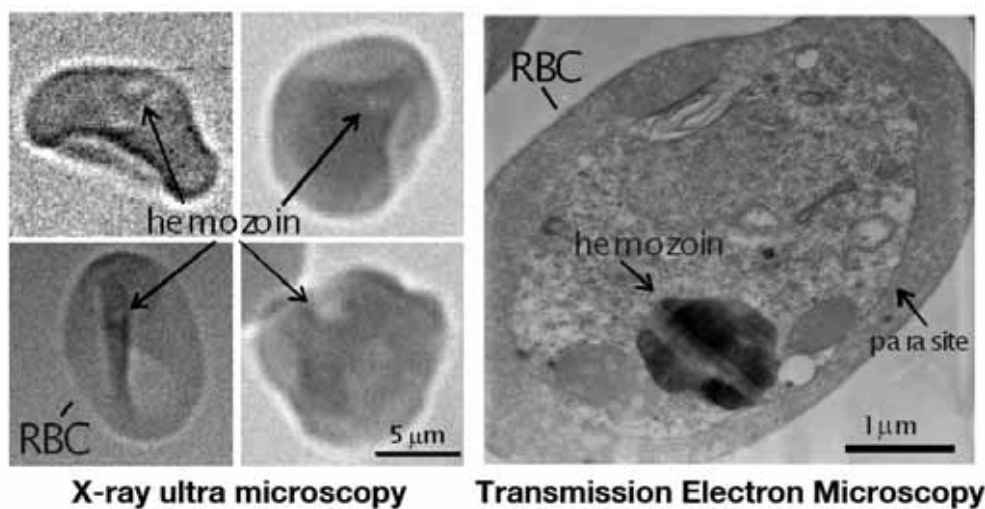


(a) Experimental 2-D powder diffraction data for bR shown indexed up to a spatial resolution of approximately 10Å, and
 (b) reconstructed electron density projection in 2D unit cell from indexed data to resolution of 7.5Å collected at ChemMatCARS in Chicago.

Intra-Cellular Studies

In addition to the above program of research aimed at molecular structure determination, work has also been carried out on structure determination at the sub-cellular level, in particular with Professor Leann Tilley and Dr Eric Hanssen at La Trobe University. This has involved use of the X-ray ultramicroscope (XuM) at CMMT and the development of improved techniques for studying biological samples using the XuM.

Some of this work has been incorporated in an ESI-related publication by D Gao et al. in Optics Express (see Publications). Collaborative work with CXS on determining the molecular structure of the Fe-rich hemozoin crystal is continuing.



X-ray ultra microscopy **Transmission Electron Microscopy**

Osmium tetroxide-stained infected red blood cells (RBCs) on 150 nm thick silicon nitride membrane. Type I ISC chamber fitted with a Ta (Ta L α characteristic line 8.145 keV) foil target inclined to the electron beam direction. The X-ray source size was approximately 100-200 nm. The SEM objective aperture size and spot size were kept fixed throughout and the accelerating voltage was at 15 kV. The X-ray camera uses a direct detection, deep depletion CCD with 1340 \times 1300 pixels each 20 μ m by 20 μ m in size and is fitted with a 250 μ m thick Be window. The target-detector distance, $R1+R2$, was fixed at 259 mm. The exposure time was 1 minute for each frame; 20 frames were collected. Each image is the average of 20 individual frames. Each frame in an image series has been aligned to the first frame to correct for any drift during the experiment and dark current correction has been applied.

❖ **Figure 9. Comparison of X-ray microscopy results for malaria infected red blood cells with TEM showing haemozoin.**

Outreach, Education and Training

International Visitors to CXS

CXS program teams invited a number of eminent professors and researchers from around the world to carry out joint research work, to give seminars and to conduct short courses in 2006, as follows.

- Prof. Chris Jacobsen, Professor of Physics at Stony Brook University, New York, USA, and leader in coherent diffracting imaging, July to September 2006
- Prof. Peter Thorsness, Wyoming State University, Wyoming, USA, sabbatical visitor and Institute for Advanced Studies Fellow, August to December 2006
- Dr Nils Wiedemann, Freiburg, Germany, October 2006
- Prof. David Ferguson, Nuffield Department of Pathology, University of Oxford, John Radcliffe Hospital, Oxford, UK, 16 October – 4 November, 2006
- Enrico Gratton, Laboratory for Fluorescence Dynamics, UC Irvine, USA November 2006
- Ken Jacobsen, Cell & Developmental Biology, School of Medicine, Chapel Hill, U. North Carolina, USA, November 2006
- John A Burns, School of Medicine, University of Hawaii, Manoa, USA, November 2006
- Claudia Leidhold, Freiburg, Germany, October 2006
- Wenbing Yen, Xradia, San Francisco, USA
- Zhonghou Cai, APS, Chicago, USA
- Maik Frohlich, University of Applied Science, Jena, Germany

CXS Conducted Workshops

- Advanced Optical Imaging, The University of Melbourne
- Theory and Modelling Computational Workshop The University of Melbourne
- Coherent X-ray Imaging in Biology, La Trobe University
- Grazing Incidence X-ray Diffraction, CSIRO
- Annual Overview Workshop, The University of Melbourne

Outreach and Education Program

Fundamental to achieving one of CXS's prime objectives is the development of an Outreach and Education Program. In its first year of operation, CXS participated in a number of outreach activities, including:

- The Career Day VCE Lecture Series to Year 10 to 12 students at Mercy College, Camperdown, in August 2006
- Conducting the La Trobe University Postgraduate Seminar Series in March and April 2006
- The ComBio 2006 Career Development Forum in Brisbane, in September 2006
- The 2006 Einstein's Science Public Lecture at La Trobe University
- The Science with Synchrotron Lecture Series at the University of Melbourne 2006–2007
- CXS University of Melbourne tour to Yalourn North Primary School students, September 2006

The CXS Outreach and Education Program aims to increase the appreciation and understanding of X-ray science via the following objectives:

- to inspire the next generation of X-ray scientists
- to spread the knowledge of X-ray science and the exciting processes being developed at CXS and around the world.

These objectives will be achieved through the use of various media, including printed materials, the CXS website, community visits, multimedia, education programs and lecture series, exhibits, displays and contributing to curriculum development.

An outreach and education framework is being developed that will provide ideas and terms of reference in support of CXS planning. It is not meant to represent a particular institution's organisational approach to community outreach. The intended framework will help identify suitable elements of the CXS research program and help forge mutually beneficial connections with the community. The planned components as outlined.

CXS Outreach Highlights

- Career Development Forum, ComBio 2006, Brisbane
- Postgraduate Seminar, Walter and Eliza Hall Institute, Melbourne
- Postgraduate Seminar, Burnet Institute, Melbourne
- Year 10 and VCE Lectures, Mercy College, Camperdown
- Einstein's Science Public Lecture, La Trobe University
- Grade 5 and 6 CXS Tour, Yallourn North Primary School
- Synchrotron Seminar Series, University of Melbourne

Formal Education:

Formal education involves student and teacher learning in the formal education system; either classroom based or via the CXS website. Teacher workshops in our unique environment will be used to address multiple intelligence and educational standards. Areas considered will include curriculum, textbooks, teacher workshops, and introductory courses.

Public Outreach:

Public outreach will be used to address shorter term opportunities and will involve CXS members going out into the community. This could involve attending community events and participating in educational radio and television as a means of reaching a wider cross-section of the public. Our main aim will be to provide information in new and exciting ways to arouse the public's curiosity.

Informal Education:

The informal education aspect of the CXS program will involve CXS members travelling to unique settings such as the Australian Synchrotron, careers and science fairs and libraries and conducting science public awareness activities, hands-on workshops, field trips etc, to provide informal learning through motivation and encouraging interest in X-ray science. This may include entertainment and educational/interactive demonstrations.

❖ *“Developing mutually beneficial connections with the community.”*



Marketing and Media:

The marketing component of the framework will be tailored to our target audiences (such as teachers, industry, physicists, etc), and will consist of products and activities such as brochures, posters, displays and booths, and the like. Displays will be produced as a source of information and a resource in support of formal education efforts. Marketing products and souvenirs such as stickers, mugs, t-shirts, mouse pads and bookmarks will be used as giveaways to generate goodwill or as prizes or rewards for those attending CXS events.

The media component of the framework will deal primarily with providing information to the media via reporters and press releases. The specific media support will be considered case by case but may include press conferences, press kits for reporters, video clips for television news spots and media interviews.

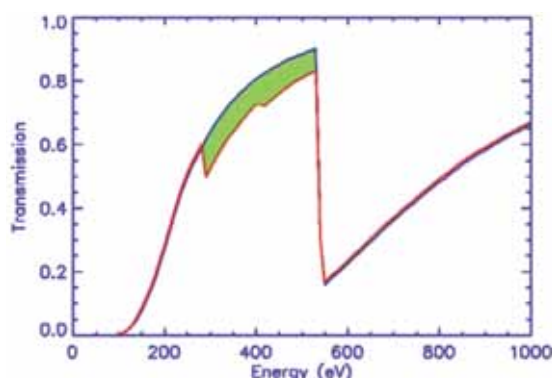
Centre Connections

A Taiwanese Connection

CXS has recently begun work towards establishing a dedicated end-station suitable for undertaking experiments in Fresnel CDI. The new end-station is to be commissioned and initially operated at Beamline 09A2 at the National Synchrotron Radiation Research Centre in Taiwan. The end-station will offer us significant improvements in a number of areas over the types of experiments we have been able to perform to date.

The Move to Vacuum I - The Water Window

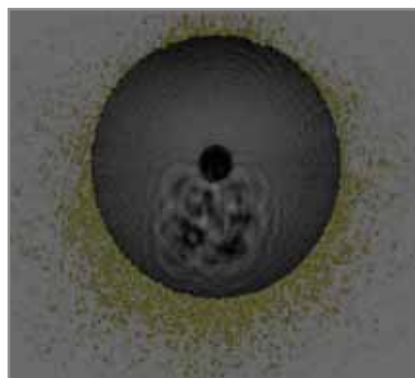
One of the most fruitful areas for X-ray microscopy of biological materials has been to image in the so-called "water window". The water window provides a natural contrast mechanism for two of the most plentiful materials in living matter – water and carbon. At energies above the carbon edge but below the oxygen edge (See Figure 1) water is relatively transparent, while carbon-based compounds such as proteins are strongly absorbing. This provides us with a way to see the carbon-rich areas of a sample such as a cell while rendering the bulk of the cell (the water) invisible. The difficulty with working in the water window is that the X-ray energies involved are low (from around 300 eV to 500 eV or wavelengths of 4–2.4 nm). At such low energy, X-rays are strongly absorbed in air and so the entire experiment is best conducted in a vacuum.



❖ *Figure 1: The red curve shows the X-ray transmission through a small amount of biological material as a function of energy. The blue curve shows the transmission through water. The green filled region is the water window where the transmission properties of the two materials are different.*

The Move to Vacuum II – Scattering

Other factors have also encouraged the move towards conducting our experiments in vacuum. CDI experiments rely on the collection of X-rays scattered from a sample and recorded on a position-sensitive detector. The further out from the centre of the image (See Figure 2) that flux can be recorded, the higher the resolution of the reconstructed image. However, the intensity of the flux falls away very quickly from the centre of the image and it is difficult to measure. Any source of spurious signal exacerbates this problem. One such source is scatter of the X-ray flux from air molecules in the path between the sample and the detector. If the experiment is conducted in a vacuum then this source of noise is removed.

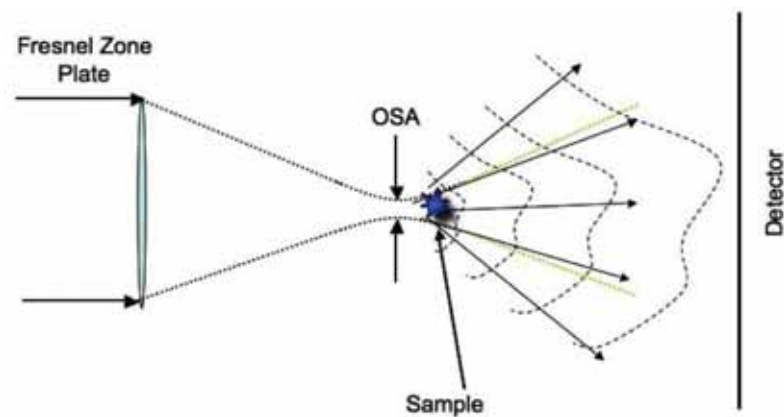


❖ *Figure 2: Detector image of the diffraction pattern produced in Fresnel Coherent Diffractive Imaging. The central area in grey is a known as an in-line hologram of the sample and represents the interference of the flux scattered by the sample with the illuminating beam. The scattered flux outside this region is orders of magnitude fainter and has been coloured here to render it visible.*

A Dedicated Endstation for Stability

Another reason for a dedicated endstation in the context of Fresnel CDI is stability. In the experiment (see Figure 3) a focusing optic is used to create an expanding beam of light which illuminates the sample. It is this curved illumination that produces the particular diffraction pattern seen in Figure 2 and which provides certain advantages when it comes to reconstructing an image from the diffraction pattern. However, the drawback is that, if the sample moves with respect to the beam, the diffraction pattern changes. Typically, we build up our data by adding together many diffraction patterns and only those where there has been no movement are suitable. To a first approximation, the resolution of an

image that is reconstructed from diffraction patterns where there has been movement is degraded by an amount that is similar to the scale of the movement. Consequently, if we want to image cells with a resolution of better than 10 nm, we need to keep motions in the system down below this level. Our approach to this is to build dedicated high-stability stages with a short mechanical distance between the sample and focusing optic and to do this in a vacuum. These factors will help minimise the relative motion. In a planned upgrade to the system we will introduce laser-based interferometric measurement of the sample and optic positions so that their relative positions can be controlled by active feedback.



❖ *Figure 3: Schematic of the Fresnel coherent diffractive imaging experiment. The Fresnel zone plate focuses the X-ray flux, which then provides an expanding beam illumination of the sample.*

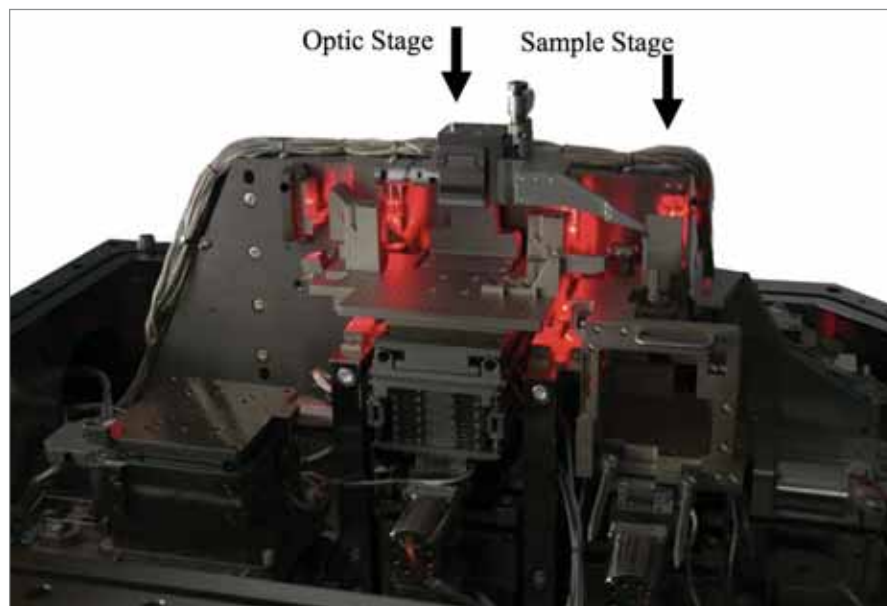
A Home for the Endstation

In order to operate in the water window and to be best able to commission and operate the end-station, significant amounts of time to be obtained on a beamline operating at the appropriate energy. We have recently formed an agreement with the director of the National Synchrotron Radiation Research Centre in Taiwan for 20% of the beamtime on the soft X-ray beamline 09A2 at that facility to be granted to CXS. This, coupled with support to modify the beamline as appropriate, provides us with an excellent location to undertake the commissioning and initial operation of the endstation. It will also allow us to define optimal beamline parameters for a longer term relocation to the Australian Synchrotron.

Status

THE STATUS OF THE PROJECT IS AS FOLLOWS:

1. Design philosophy – Professor Chris Jacobsen, Distinguished Fellow, La Trobe University Institute for Advanced Studies, during the period (August 2006) when the design approach to the end-station was planned. Initial drawings and specifications were prepared as a result.
2. Funding – Australian Research Council linkage infrastructure, equipment and facilities funding of \$449,680 (including institutional support) was obtained at the end of 2006.
3. Negotiations with Xradia Inc. to build and upgrade the system were conducted in the first half of 2007 and a purchase order has since been issued to build the initial system (See Figure 4) for delivery in the first part of 2008.
4. Upgrade funding – an application to obtain funding for the planned upgrade to interferometric feedback has been submitted.
5. Beamtime obtained – an agreement with the director of the National Synchrotron Radiation Research Centre in Taiwan has granted CXS 20% of the beamtime on the soft X-ray beamline 09A2 at that facility. In addition support will be provided to modify the beamline to optimise our experiment.
6. Operating funding – we have made an application for funding to support the significant amounts of travel to Taiwan.
7. Design – the design phase for complete specifications of the instrument has begun.
8. Preliminary tests – a second exploratory experiment testing coherence and stability on beamline 09A2 at NSRRC will be undertaken in July.



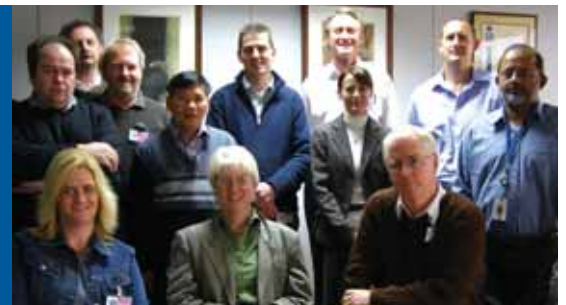
❖ *Figure 4: Initial version of the endstation delivered by Xradia Inc. to Argonne National laboratory. Our system will use the same vacuum chamber and central optic and sample stages.*

CXS Management & Governance

CXS is a collaborative research program between the University of Melbourne, La Trobe University, Monash University, Swinburne University of Technology and CSIRO, funded under the Australian Research Council (ARC) Centre of Excellence program and the Victorian government Science, Technology and Innovation (STI) program.

As chief administrator, the University of Melbourne manages the grants and distributes funds in accordance with the signed agreements. These agreements cover CXS management, collaborator agreements and intellectual property agreements.

❖ *Executive Committee Members*



Centre Management

DURING 2006 CXS ADMINISTRATION WAS OVERSEEN BY AN EXECUTIVE COMMITTEE AND CENTRE MANAGEMENT COMPRISING:

- Prof. Keith Nugent (Research Director)
- Prof. Leann Tilley (Deputy Research Director)
- Ms Tania Smith (Chief of Operations)
- Dr Harry Quiney (Theory and Modelling Team Leader)
- Assoc. Prof. Mike Ryan (Biological Sciences Team Leader)
- Assoc. Prof. Andrew Peele (Experimental Methods Team Leader)
- Dr Chris Hall (Detector and Beamline Development Team Member)
- Dr Lap Van Dao (Short Wavelength Laser Source Team Leader)
- Assoc. Prof. Trevor Smith (Short Wavelength Laser Source Team Member)
- Dr Steve Wilkins (CSIRO Team Leader)
- Dr Jose Varghese (CSIRO Team Member)
- Ms Rosslyn Ball (Executive Officer to Committee)
- Ms Emma Douglas (Administrative Officer)

Advisory Board

The CXS Advisory Board met in April 2006 as part of the CXS Annual Workshop. The meeting focused on key areas such as: Terms of Reference, The Centre's Overview, Progress Over 2006, Key Performance Indicators, Interactions with Other Organisations and End-users, Outreach and Commercialisation.

The Advisory Board

Professor John McKenzie

Deputy Vice Chancellor (Research)
The University of Melbourne (Chair)
johnam@unimelb.edu.au

Professor Edwina Cornish

Deputy Vice Chancellor (Research)
Monash University (or nominee)
diana.ferwerda@adm.monash.edu.au

Dr Michael Barber

Executive Director – Science Planning
CSIRO (or nominee)
Michael.Barber@csiro.au

Professor Bonnie Wallace

Professor of Crystallography
Birkbeck College
b.wallace@mail.cryst.bbk.ac.uk

Mr David Krenus

CEO, Cyclotek
david@berthold.com.au

Professor Erich Weigold

Deputy Vice Chancellor (Research)
La Trobe University (or nominee)
e.weigold@latrobe.edu.au

Professor Kerry Pratt

Deputy Vice Chancellor
(Research & Industry Liaison)
Swinburne University of Technology
(or nominee)
kpratt@swin.edu.au

Professor John Helliwell

Professor of Structural Chemistry
University of Manchester
hellsquash@yahoo.com

Dr Stephen Lane

Chief Science Officer
NSF Centre for Biophotonic
Science & Technology, UC Davis
slane@lnl.gov

Dr Bruce Whan

Chairman of INNOVIC (Victorian
Innovation Centre Ltd) and Director,
Swinburne Knowledge
bwhan@swin.edu.au

Scientific Advisory Board

Professor John Helliwell (Chair)

Professor of Structural Chemistry
University of Manchester
john.helliwell@manchester.ac.uk

Professor Leann Tilley

CXS Deputy Director
La Trobe University
l.tilley@latrobe.edu.au

Dr Stephen Lane

Chief Science Officer
NSF centre for Biophotonic,
Science & Technology UC Davis
slane@lnl.gov

Professor Bonnie Wallace

Professor of Crystallography
Birkbeck College
b.wallace@mail.cryst.bbk.ac.uk

Professor Keith Nugent

CXS Director
The University of Melbourne
k.nugent@physics.unimelb.edu.au

The 2006 CXS Team

Professional Staff

Ms Rosslyn Ball
CXS Administrator
The University of Melbourne
rball@ph.unimelb.edu.au

Ms Tania Smith
CXS Chief of Operations
The University of Melbourne
tnsmith@ph.unimelb.edu.au

Ms Emma Douglas
CXS Administrative Officer
La Trobe University
e.douglas@latrobe.edu.au

Biological Sciences Program Team

Assoc. Prof. Mike Ryan
Program Leader
La Trobe University
m.ryan@latrobe.edu.au

Ms Laura Osellame
PhD Student
La Trobe University
losellame@latrobe.edu.au

Ms Samantha Deed
Research Assistant
La Trobe University
s.deed@latrobe.edu.au

Mr Tom Laktyushin
PhD Student
La Trobe University
laktyushin@wehi.edu.au

Dr Eric Hanssen
Research Fellow
La Trobe University
e.hanssen@latrobe.edu.au

Professor Leann Tilley
CXS Deputy Director of Research
La Trobe University
l.tilley@latrobe.edu.au

Dr Jacqui Gulbis
Principal Investigator
WEHI
jgulbis@wehi.edu.au

Dr Danielle Smith
Research Fellow
La Trobe University

Dr Nick Klonis
Research Fellow
La Trobe University
n.klonis@latrobe.edu.au

Dr Stephen Holmes-Brown
Research Assistant
La Trobe University

Mr Michael Baker
PhD Student
La Trobe University
mj9baker@students.latrobe.edu.au

Detector and Beamline Development Program Team

Dr George Jung

Research Fellow
Monash University
george.jung@sync.monash.edu.au

Dr Andy Berry

Research Fellow
Monash University
andy.berry@sync.monash.edu.au

Dr Chris Hall

Research Fellow
Monash University
chris.hall@sync.monash.edu.au

Dr Stewart Midgley

Research Fellow
Monash University
stewart.midgley@sync.monash.edu.au

Professor Rob Lewis

Program Leader
Monash University
rob.lewis@sync.monash.edu.au

Experimental Methods Program Team

Assoc. Prof. Andrew Peele

Program Leader
La Trobe University
a.peele@latrobe.edu.au

Dr Mark Pfeifer

Research Fellow
La Trobe University
m.pfeifer@latrobe.edu.au

Dr Brian Abbey

Research Fellow
The University of Melbourne
babbey@physics.unimelb.edu.au

Dr Craig Lincoln

Research Fellow
The University of Melbourne
clincoln@unimelb.edu.au

Dr Chanh Tran

Research Fellow
La Trobe University
CQ.Tran@latrobe.edu.au

Dr Benedicta Arhatari

Research Fellow
La Trobe University
b.arhatari@latrobe.edu.au

Dr Garth Williams

Research Fellow
The University of Melbourne
g.williams@physics.unimelb.edu.au

Dr Eugeniu Balaur

Research Fellow
La Trobe University
e.balaur@latrobe.edu.au

Dr Robert Norman

Research Fellow
La Trobe University
r.norman@latrobe.edu.au

Ms Angela Torrance

Honours Student
The University of Melbourne
a.torrance@physics.unimelb.edu.au

Mr Jesse Clark

PhD Student
La Trobe University
J.Clark@latrobe.edu.au

Ms Clare Henderson

MSc Student
The University of Melbourne
c.henderson@pgrad.unimelb.edu.au

Dr Bipin Dhal

Research Fellow
The University of Melbourne
bdal@unimelb.edu.au

Mr Kaushal Vora

PhD Student
La Trobe University
kdvora@students.latrobe.edu.au

Prof. Keith Nugent

CXS Director of Research
The University of Melbourne
k.nugent@physics.unimelb.edu.au

Mr Corey Putkunz
PhD Student
La Trobe University
C.Putkunz@latrobe.edu.au

Mr Kevin Hannah
PhD Student
La Trobe University
kmhannah@students.latrobe.edu.au

Mr Darren King
Honours Student
The University of Melbourne

Mr Tom Rayne
Summer Cadetship
La Trobe University

Mr Sam Flewett
PhD Student
The University of Melbourne
s.flewett@pgrad.unimelb.edu.au

Mr Lachlan Whitehead
PhD Student
The University of Melbourne
l.whitehead@physics.unimelb.edu.au

Short Wave Length Laser Source Program Team

Professor Lap Van Dao
Program Leader
Swinburne University of Technology
dvlap@swin.edu.au

Professor Peter Hannaford
Principal Investigator
Swinburne University of Technology
phannaford@swin.edu.au

Dr Jeffrey Davis
Research Associate
Swinburne University of Technology
JDavis@swin.edu.au

Assoc. Prof. Trevor Smith
The University of Melbourne
trevoras@unimelb.edu.au

Mr Peter Wichta
Honours Student
The University of Melbourne
p.wichta@ugrad.unimelb.edu.au

Mr Sven Teichmann
PhD Student
Swinburne University of Technology
steichmann@groupwise.swin.edu.au

Theory and Modelling Program Team

Dr Harry Quiney
Program Leader
The University of Melbourne
quiney@unimelb.edu.au

Dr Rotha Yu
Research Fellow
The University of Melbourne
rpyu@unimelb.edu.au

Dr Rouben Dilanian
Research Fellow
Monash University
rouben.dilanian@sci.monash.edu.au

Structure Determination Methods Program Team

Professor Steve Wilkins

Program Leader
CSIRO – Clayton
steve.wilkins@csiro.au

Dr Steve Homolya

CSIRO – Clayton
steve.homolya@csiro.au

Dr Andrew Pogany

CSIRO – Clayton
andrew.pogany@csiro.au

Dr Matteo Altissimo

CSIRO – Clayton
matteo.altissimo@csiro.au

Dr Peter Lynch

CSIRO – Clayton
peter.lynch@csiro.au

Dr Andrew Stevenson

CSIRO – Clayton
andrew.stevenson@cmst.csiro.au

Dr Connie Darmanin

CSIRO – Parkville
connie.darmanin@csiro.au

Dr Sherry Mayo

CSIRO – Clayton
sherry.Mayo@csiro.au

Dr Jose Varghese

Group Leader
CSIRO – Parkville
jose.varghese@csiro.au

Professor Cal Drummond

PI – Membrane Chemistry
CSIRO – Parkville
calum.drummond@csiro.au

Asoc. Professor Ted McMurchie

Principal Investigator – GPCR Biology
CSIRO – Parkville
ted.mcmurchie@csiro.au

Dr Lynne Waddington

Research Associate
CSIRO – Parkville
lynne.waddington@csiro.au

Dr Ross Fernley

CSIRO – Parkville
ross.fernley@csiro.au

Dr Stephen Mudie

CSIRO – Clayton
stephen.mudie@csiro.au

Dr Janelle Williams

CSIRO – Parkville
janelle.williams@csiro.au

Mr Dachao Gao

CSIRO – Clayton
dachao.gao@csiro.au

Dr Yakov Nesterets

CSIRO – Clayton
yakov.nesterets@csiro.au

Dr Tim Gureyev

CSIRO – Clayton
tim.gureyev@csiro.au

Dr David Parry

CSIRO – Clayton
david.parry@csiro.au

Ms Amanda Aloia

PhD Student
CSIRO – Parkville
amanda.aloia@csiro.au

Performance Indicators

CXS intends to provide clear information relating to its performance across a range of key measures with the aim of creating greater opportunities in its research assessing the associated impact.

We continue to develop our interests and research requirements in order to fulfil the core function of our performance review, and our response continues a cycle of development reflecting those interests.

CXS is in the consolidation stage, with the majority of its projects operational and meeting the Centre's intermediate strategic goals.

It is necessary in projects of this complexity for intermediate goals to be attained according to the original schedule. Most groups have reported significant achievements in 2006, including the first observation of short wavelength high-harmonic generation light.

Research Training and Professional Education

CXS met all of its recruitment and professional education targets for 2006, and has exceeded expectations in the areas of postgraduate recruitment and presentations to schools and/or teaching communities.

Postgraduates recruited	11
Honours students recruited	6
Masters students recruited	4
Honours students graduated	5
Professional Course participation	4
Presentations to schools or the teaching community	6
Overseas visits by members	11

Partners, Supporters and Stakeholders

- Australian Research Council
- Australian Synchrotron Research Program
- Birkbeck College, Department of Crystallography, UK
- CSIRO Australia
- La Trobe University
- Lawrence Livermore National Laboratory, USA
- Monash University
- National Health and Medical Research Council
- Harima Institute, Riken - Spring8 Centre, Japan
- National University of Singapore, Singapore Synchrotron Light Source
- Stony Brook University, Department of Physics and Astronomy, USA
- Swinburne University of Technology
- University of London, School of Biological and Chemical Sciences, England
- University of Manchester, School of Chemistry, UK
- University of Melbourne

Key Results Area

Performance Measure	Outcome
CXS member as invited Speaker	25
International Visitors to CXS	11
CXS interdisciplinary workshops	5
Community presentations	8
Media Commentaries	3
Staff recruitment	9
Awards	2
Scholarships	2

Media Commentaries

The following articles relating to CXS were published in 2006.

A Pogany, 'A small step to higher resolution', Nature Physics 2 (10), 657–8

'New frontiers in imaging', La Trobe University Bulletin (Nov/Dec), 8–9

'Physicists collaborate for invisible worlds', La Trobe University Bulletin (Nov/Dec), 10

Infrastructure

The tender process for the ultra-fast laser system to be used for investigations into the nature of non-linear physical processes in laser-molecule interactions is complete. The laser system is housed at Swinburne University of Technology. Translation Stages and a CCD camera package was also purchased to accompany the ultra-fast laser system. The Short Wavelength Laser Source Program at Swinburne University of Technology has made a half pre-payment on a XUV monochromator.

The Experimental Methods Program at La Trobe University has established a new microfabrication facility including: basic labware and chemicals, water purification and convection oven, spin coater, ultrasonic bath and fume hoods, and computer controlled Dual Sputtering and RIE system to complement the existing electron-beam lithography system.

The new Coherent Scattering Studies Laboratory, located in room D013, School of Physics, at the University of Melbourne, is now operational, with the following equipment available: 3cm CCD detector that can move at a range of 30 x 30 cm, an optical table, and various operational equipment (DELL Dual core processor, testing and experiment equipment, workstation, tools, etc.).

A sample chamber, as part of the Experimental Methods Program, is currently in the design stages. Although it has not been fully costed, it is on track and will be partly funded by an ARC LIEF grant already secured.

Awards

The CXS membership would like to congratulate Professor Keith Nugent on his second ARC Federation Fellowship and Associate Professor Mike Ryan for receiving the Roche Molecular Biochemicals Medal (May 2006) from the Australian Society for Biochemistry and Molecular Biology.

Also congratulations and welcome to Ms Cherrine Chan on her CXS 2006 Summer Cadetship and Ms Claudia Leidhold of Freiburg (PhD student) for visiting the Biological Sciences Program Team on a DAAD Fellowship from October 2006 to January 2007.

Nature Physics



❖ "Nature Physics journal cover."

Eukaryotic Cell



❖ “Eukaryotic Cell journal cover.”

Molecular Cell



❖ “Molecular Cell journal cover.”

Publications

2006 publications by CXS members are as follows:

Abbey, B, JD Lipp, ZH Barber et al., 'Structure-film thickness relationship study of sputtered NiO/Ni bilayers using depth profiling and atomic force microscopy techniques', *Journal of Applied Physics*, Art. No. 124914, 99 (12)

Arhatari, BD, A Peele, K Nugent & F De Carlo, 'Quality of the reconstruction in X-ray phase contrast tomography', *Review of Scientific Instruments*, 37091-6, 77 (6)

Babankova, D, S Civis, L Juha et al., 'Optical and X-ray emission spectroscopy of high-power laser-induced dielectric breakdown in molecular gases and their mixtures', *Journal of Physical Chemistry*, 2113-20, A 110 (44) 1

Belpassi, L, F Tarantelli, A Sgamellotti et al., 'Electron density fitting for the Coulomb problem in relativistic density-functional theory', *Journal of Chemical Physics*, Art. No. 124104, 124 (12)

Bidault, JM, P Fonte, T Francke et al., 'A novel UV photon detector with resistive electrodes', *Nuclear Physics B - Proceedings Supplements* 158, 199-203, 158

Curl, CL, CJ Bellair, PJ Harris et al., 'Single cell volume measurement by quantitative phase microscopy (QPM): A case study of erythrocyte morphology', *Cellular Physiology and Biochemistry*, 193-200, 17 (5-6)

Dao, L, X Wen & P Hannaford, 'Time-resolved and time-integrated spectroscopy studies of the optical properties of silicon quantum dots', *International Society for Optical Engineering, Proceedings of the SPIE*, 231-5, 6118

LV Dao, MTTDo, P Hannaford, J Akahane, Y Koyama, 'Observation of coherent biexcitons in ZnO/ZnMgO multiple quantum wells at room temperature', *Applied Physics Letters*, Art. No. 182109, 89 (18)

Dhal, BB, AG Peele, PJ McMahon et al., 'Bending magnet source: A radiation source for X-ray phase contrast tomography', *Radiation Physics and Chemistry*, 2004-7, 75 (11)

Frankland, S, A Adisa, P Horrocks et al., 'Delivery of the malaria virulence protein PfEMP1 to the erythrocyte surface requires cholesterol-rich domains', *Eukaryotic Cell*, 849-60, 5 (5)

Frazier, AE, C Kiu, D Stojanovski, NJ Hoogenraad & MT Ryan, 'Mitochondrial morphology and distribution in mammalian cells', *Journal of Biological Chemistry*, 1551-8, 387

Frazier, AE, RD Taylor, DU Mick, B Warsheid, HE Stoepel, MT Ryan, B Guiard & P Rehling, 'Mdm38 interacts with ribosomes and is a component of the mitochondrial protein export machinery', *Journal of Cell Biology*, 553-64, 172

Gao, D, S Wilkins, D Parry, T Gureyev, P Miller & E Hanssen, 'X-ray ultramicroscopy using integrated sample cells', *Optics Express*, 7889-94, 14 (17)

Gureyev, TE, DM Paganin, GR Myers et al., 'Phase-and-amplitude computer tomography', *Applied Physics Letters*, Art. No. 034102, 89 (3)



- Gureyev, TE, YI Nesterets, DM Paganin et al., 'Effects of incident illumination on in-line phase-contrast imaging', *Journal of the Optical Society of America A – Optics Image Science and Vision*, 34–42, 23 (1)
- Gureyev, YL Nesterets, DM Paganin et al., 'Linear algorithms for phase retrieval in the Fresnel region. 2. Partially coherent illumination', *Optics Communications*, 569–80, 259 (2)
- Hoedlmoser, H, A Braem, G De Cataldo et al., 'Production technique and quality evaluation of CsI photocathodes for the ALICE/HMPID detector', *Nuclear Instruments & Methods In Physics Research Section A – Accelerators Spectrometers Detectors and Associated Equipment*, 338–50, 566 (2)
- Iacobaeus, C, T Francke, B Lund-Jensen et al., 'A high position resolution X-ray detector: An "Edge on" illuminated capillary plate combined with a gas amplification structure', *IEEE Transactions on Nuclear Science*, 554–61, 53 (2)
- Knuepfer, E, M Rug, N Klonis et al., 'Trafficking determinants for PfEMP3 export and assembly under the *Plasmodium falciparum*-infected red blood cell membrane', *Molecular Microbiology*, 722, 59 (2)
- McKenzie, M, M Lazarou, DR Thorburn & MT Ryan, 'Mitochondrial respiratory chain supercomplexes are destabilized in Barth syndrome patients', *Journal of Molecular Biology*, 462–9, 361
- Midgley, S, 'Angular width of a narrow beam for X-ray linear attenuation coefficient measurements', *Radiation Physics and Chemistry*, 945–53, 75 (9)
- Nesterets, YI & SW Wilkins, 'A flexible configuration for a high-energy phase-contrast imaging beamline involving in-line focusing crystal optics', *Radiation Physics and Chemistry*, 1981–5, 75 (11)
- Nesterets, YI, P Coan, TE Gureyev et al., 'On qualitative and quantitative analysis in analyser-based imaging', *ACTA Crystallographica Section A*, 296–308, Part 4, 62
- Nesterets, YI, TE Gureyev, KM Pavlov et al., 'Combined analyser-based and propagation-based phase-contrast imaging of weak objects', *Optics Communications*, 19–31, 259 (1)
- Nesterets, YI, TE Gureyev, SW Wilkins, 'Polychromaticity in the combined propagation-based/analyser-based phase-contrast imaging', *Journal of Physics D – Applied Physics*, 4259–71, 38 (24)
- O'Connor, KH, JP Banga, C Darmanin et al., 'Characterisation of an autoreactive conformational epitope on GAD65 recognised by the human monoclonal antibody b78 using a combination of phage display, in vitro mutagenesis and molecular modelling', *Journal of Autoimmunity*, 172–81, 26 (3)
- Peele, AG, HM Quiney, BB Dhal et al., 'New opportunities in X-ray tomography', *Radiation Physics and Chemistry*, 2067–71, 75 (11)
- Periale, L, V Peskov, C Iacobaeus et al., 'A study of the operation of especially designed photosensitive gaseous detectors at cryogenic temperatures', *Nuclear Instruments & Methods In Physics Research Section A – Accelerators Spectrometers Detectors and Associated Equipment*, 381–5, 567 (1)
- Pfeifer, M, G Williams, I Vartanyants, R Harder & I Robinson, 'Three-dimensional mapping of a deformation field inside a nanocrystal', *Nature*, 63–6, 44
- Pogany, A, 'A small step to higher resolution', *Nature Physics*, 657–8, 2 (10)
- Quiney, H, A Peele, Z Cai, D Paterson & K Nugent, 'Diffractive imaging of highly focused X-ray fields', *Nature Physics*, 101–200, 2

- Reinboth, B, J Thomas, E Hanssen et al., 'beta ig-h3 interacts directly with biglycan and decorin, promotes collagen VI aggregation, and participates in ternary complexing with these macromolecules', *Journal of Biological Chemistry*, 7816–24 281 (12)
- Smith, NC, L Tilley, RCA Thompson et al., 'An Australian network to support the understanding and control of parasite', *Trends in Parasitology*, 97–9, 22 (3)
- Spielmann, T, PL Hawthorne, MWA Dixon et al., 'A cluster of ring stage-specific genes linked to a locus implicated in cytoadherence in *Plasmodium falciparum* codes for PEXEL-negative and PEXEL-positive proteins exported into the host cell', *Molecular Biology of the Cell*, 3613–24, 17 (8)
- Spycher, C, M Rug, N Klonis, A Cowman, H Beck & L Tilley, 'Genesis of and trafficking to the Maurer's cleft secretory compartment of malaria parasite-infected erythrocytes', *Molecular and Cellular Biology*, 4074–85, 26 (11)
- Tilley, L., Davis, T. and Bray P. 'Prospects for treatment of drug-resistant malaria parasites'. *Future Microbiology*, 1 (1), 127-141
- Thornton, J., Arhatari, B.D., Peele, A.G., Nugent, K.A. 'Optimising visibility for the neutron radiography of titanium and nickel gas turbine components' *Physics B: Condensed Matter*, 385-386, pp. 917-920
- Tran, C.Q., Mancuso, A.P., Dhal, B.B., Nugent, K.A., Peele, A.G., Cai, Z., Paterson, D. 'Phase-space reconstruction of focused x-ray fields' *Journal of the Optical Society of America A: Optics and Image Science, and Vision*, 23 (7), pp. 1779-1786
- Tran, CQ & KA Nugent, 'Recovering the complete coherence function of a generalized Schell model field', *Optics Letters*, 3226–7, 31 (22)
- Vora, KD, B Lochel, EC Harvey et al., 'AFM-measured surface roughness of SU-8 structures produced by deep X-ray lithography', *Journal of Micromechanics and Microengineering*, 1975–83, 16 (10)
- Wiedemann, N, E Urzicam, B Guiard, H Muller, C Lohaus, HE Meyer, MT Ryan, C Meisinger, U Muhlenhoff, R Lill & N Pfanner, 'Essential role of Isd11 in mitochondrial iron-sulfur cluster synthesis on Isu scaffold proteins', *The EMBO Journal*, 184–95, 25
- Williams, G, M Pfeifer, I Vartanyants & I Robinson, 'Internal structure in small Au crystals resolved by three-dimensional inversion of coherent X-ray diffraction', *Physical Review B*, 41121–8, 73 (9)
- Williams, G, H Quiney, B Dhal, C Tran, K Nugent, A Peele, D Paterson & M de Jonge, 'Fresnel coherent diffractive imaging', *Physical Review Letters*, 55061–4, 97 (2)

Financial Statement

INCOME

Carry Forward	\$1,096,746
ARC Allocated Funds	\$1,872,718
STI Allocated Funds	\$1,200,000
Nodes Cash Contribution	\$1,020,000

TOTAL	\$5,189,464
--------------	--------------------

EXPENDITURE

Salaries	\$1,032,532
Equipment	\$1,148,456
Travel	\$82,575
IT	\$20,830
Scholarships	\$6,938
Marketing	\$28,370
Consultancies	\$51,429
Consumables	\$167,213

TOTAL	\$2,538,343
--------------	--------------------

IN-KIND

University of Melbourne	\$780,994
La Trobe University	\$700,746
Monash University	\$195,855
Swinburne University of Technology	\$523,321

TOTAL	\$2,200,916
--------------	--------------------



Contact Us

ARC Centre of Excellence for Coherent
X-ray Science
School of Physics

The University of Melbourne
Victoria, Australia 3010

ph: 561 (03) 8344 5444

email: cxsenquiries@ph.unimelb.edu.au



Australian Government
Australian Research Council



MONASH University

