



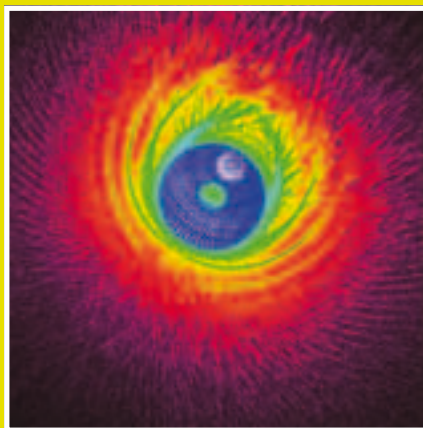
2008 ANNUAL REPORT

ARC CENTRE OF EXCELLENCE FOR
COHERENT X-RAY SCIENCE



ARC Centre of Excellence for
COHERENT X-RAY SCIENCE

www.coecxs.org



The image is a diffraction pattern measured using the CXS endstation (FResnel Imaging ENDstation – FRIEND). The test object is a 30 micron diameter radial spoke test pattern with smallest features of 40 nanometers. For comparison, a human hair with a diameter of 20 microns – 40 nanometers is 500 times smaller than this.

← If the diameter of this arc was the same as that of a human hair

• ← this dot would be the actual size of the image on our cover.

CXS would like to acknowledge the support of the Australian Research Council. We would also like to acknowledge the financial and in-kind support provided by our collaborators –University of Melbourne, La Trobe University, Monash University, Swinburne University of Technology, and the Australian Commonwealth Scientific and Industrial Research Organisation (CSIRO). We are grateful for the financial support received from the Science, Technology and Innovation (STI) Initiative coordinated by the Office of Science and Technology within the State Government of Victoria.

CXS would like to thank the School of Physics at the University of Melbourne, Ms Norma Hayes of Monash University, Ms Fabienne Perani of La Trobe University and Ms Tatiana Tchernova of Swinburne University of Technology for their support, and David Cohen for the use of the Australia Synchrotron photograph.

CXS

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CONTENTS

ABOUT CXS	2
DIRECTOR'S REPORT	3
MISSION STATEMENT	5
THE ARC REVIEW	6
RESEARCH PROGRAMS AND CASE STUDIES	7
BIOLOGICAL SCIENCES	8
DETECTOR AND BEAMLINE DEVELOPMENT	12
EXPERIMENTAL METHODS	15
SHORT WAVELENGTH LASER SOURCE	18
STRUCTURE DETERMINATION METHODS	22
THEORY AND MODELLING	25
ULTRA-COLD PLASMA SOURCE	28
STUDENTS LIFE @ CXS	31
LYNN LIANG, CSIRO	32
MICHAEL BAKER, LA TROBE UNIVERSITY	33
ANDY McCULLOCH, UNIVERSITY OF MELBOURNE	33
JESSE CLARK, LA TROBE UNIVERSITY	33
SVEN TEICHMANN, SWINBURNE UNIVERSITY	34
CXS MANAGEMENT AND GOVERNANCE	35
CENTRE MANAGEMENT	36
EXECUTIVE COMMITTEE	37
ADVISORY BOARD	37
SCIENTIFIC ADVISORY BOARD	37
PROFESSIONAL STAFF	37
RESEARCH TEAMS	38
MEMBER DEPARTURES	40
ORGANISATIONAL CHART AS AT 30 JUNE 2008	41
PRESENTATIONS, CONFERENCES & LABORATORY VISITS	42
AWARDS AND HONOURS	46
SCHOLARSHIPS AND STUDENTSHIPS	47
RESEARCH, TRAINING AND PROFESSIONAL EDUCATION	48
WORKSHOPS	49
VISITORS TO CXS	50
SCIENTIFIC LINKAGES	52
COMMERCIALISATION	54
OUTREACH	55
MEDIA COMMENTARIES	56
PUBLICATIONS	57
BOOK CHAPTERS	58
REFERRED JOURNAL PUBLICATIONS	58
REFERRED CONFERENCE PROCEEDINGS	62
IMPACT FACTOR STATISTICS	62
COVERS	63
GRANTS	64
CXS LOCATIONS	66
FINANCIAL STATEMENT	68

ABOUT CXs



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 characterization 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 the progress in structural biology. A breakthrough in this area would revolutionise rational drug design through the insight 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 gives us the opportunity to take snapshots of biomolecules. We are exploring the 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 is also under exploration.

It is an ambitious interdisciplinary program of research.

DIRECTOR'S REPORT

The Australian Research Council Centre of Excellence for Coherent X-ray Science (CXS) continues to be a beacon for interdisciplinary science in Australia. 2008 has been an excellent year with many exciting outcomes, as illustrated in this Annual Report.

2008 saw two major events. With support from the Australian Academy of Technological Sciences & Engineering, we organized and hosted a major international workshop that was a truly excellent event with outstanding speakers and a wonderful sense of shared purpose and common goals. The organization of these events is a major enterprise, falling on the shoulders of many CXS members, but none less than CXS Deputy Director, Leann Tilley. Leann and her team did yet another fantastic job, as is reported here.

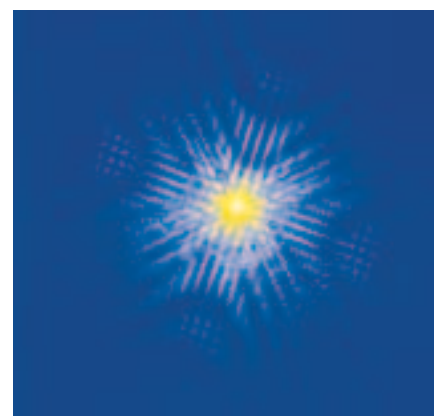
The second major event was the major review of our activities by our major funding body, the Australian Research Council. This process, which we now know to have been very successful, is also reported in some detail here. However I would like to take this opportunity to thank all who contributed to the preparation of the report document – something which took a great deal of the time of CXS members – but also to the truly fantastic support provided by our international collaborators. To see our colleagues from around Australia and around the world rally to support our cause was humbling, and very pleasing.

The case we made for renewal was substantially helped by the excellent science outcomes that we have achieved this year. These will be reported in the various sections of this report, but there can be no question that the fact that we could point to nine cases where our work has been featured on the cover of a journal helped with our argument for international impact. In fact, two further journal covers featuring CXS work were published in the couple of months after the review submission. Our work has also been featured in a number of commentaries and continues to be published in the highest impact journals in our respective fields.

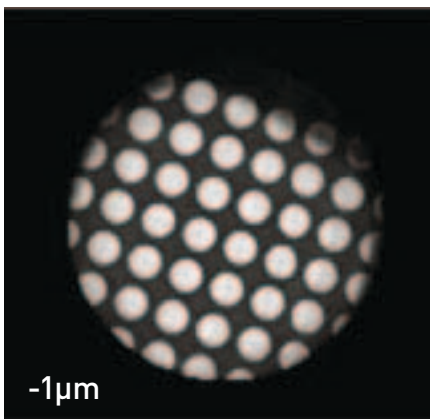
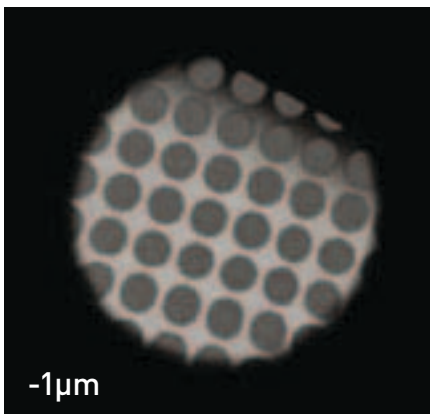
One important example of the collaborative nature of CXS is the work on imaging using high-harmonic generation sources, a collaborative effort across three CXS programs (Short-Wavelength Laser Source, Theory & Modelling, and Experimental Methods) and three CXS institutions (Swinburne, Melbourne, and La Trobe). This work was reported in *Physical Review A*, and the beautiful data (see figure) we obtained was highlighted in the Physical Review "Kaleidoscope" publicity section (<http://pra.aps.org/node/2478>). This work illustrates the power of the combined efforts of CXS scientists and has the potential to lead to an important new form of high-resolution microscopy using laser-based X-ray sources.

Another exciting demonstration of CXS-inspired collaboration is described in the section from the biological sciences program where we report the determination of the structure of parasite hemozoin using X-ray powder diffraction data via a collaborative effort between La Trobe and CSIRO members of CXS.

A further interdisciplinary example at the core of CXS goals is the application of coherent diffractive imaging to a malaria-infected red blood cell (work that is featured on the cover of the journal *Cytometry Part A*), a collaborative effort between La Trobe, Melbourne and



High-harmonic diffraction data obtained using the CXS facilities based at Swinburne. This image was highlighted in the Kaleidoscope section of the Physical Review website.



The top image shows an electron microscope image of the sample used to generate the data in the image above.

The bottom image is the reconstruction from that data using methods developed by the Theory & Modelling Program.

Monash Universities, also reported in the section describing the biological sciences.

As illustrated by the previous paragraphs, CXS continues to be a harmonious and collaborative organization with a continued program of workshops for the purpose of discussing collaborative activities. Of particular note is the Theory workshop organized by the Theory & Modelling Program to which we also invite members of the ARC CoE in Anti-matter Matter Studies (CAMS), as well as other scientists working in cognate areas. We are certainly planning that this should continue as part of our overall outreach program.

CXS has committed to the establishment of a state-of-the-art synchrotron-based X-ray imaging facility. At the start of 2008 it was our intention that the CXS-funded facility should be based at the National Synchrotron Radiation Research Centre in Taiwan, and we were delighted with the superb nature of the collaboration that was developing. In the meantime, a slot opened up at the Advanced Photon Source (APS) in Chicago, which offered significant technical advantages at a third-generation source. It was with considerable soul-searching, and regret, that we felt that we had a responsibility to withdraw from the NSRRC collaboration in favour of the APS collaboration. I would like to take this opportunity to express our appreciation of the excellence of the collaboration with Taiwan. The interaction with the Advanced Photon Source (APS), however, is built on an existing long-term relationship and is working better than ever, enhanced through its award to a CXS-led collaboration of a Partner User Proposal (PUP), guaranteeing the Australian community ongoing beamtime at the APS for four years. The collaboration with Ian McNulty of the APS is highly valued by CXS

and the opportunity to deepen and extend the relationship is much appreciated.

The collaboration underpinning the PUP consists of a number of CXS members, but others as well, and has been awarded a major ARC Linkage Infrastructure, Equipment & Facilities grant, with fantastic support from the partner universities, to a total of over \$1.2M. The development of this collaboration is a major priority for 2009.

CXS is continuing its strong industrial relationships via the Cooperative Research Centre for Biomedical Imaging Development, the research Director's ongoing relationship with IATIA Ltd, and it is very pleasing to see that Moglabs Pty Ltd, a spin-off from the Ultra-Cold Plasma program, is growing very strongly.

CXS is exceeding its key performance indicators and leading collaborations from around Australia; its members are publishing in high-profile journals and continuing to attract additional research funding. There are areas that need to be further nurtured and we need to keep our eye on our interdisciplinary goals, but the CXS team is a fantastically talented one and 2009 is sure to be even better.

PROFESSOR KEITH NUGENT
DIRECTOR



MISSION STATEMENT

TO BE THE WORLD LEADER IN
THE DEVELOPMENT OF COHERENT
X-RAY DIFFRACTION FOR IMAGING
BIOLOGICAL STRUCTURES

THE ARC REVIEW



A review team led by Professor Mark Wainwright visited CXS on October 1, 2008. The team was sent a 92 page document prepared by CXS outlining our achievements and spent the day talking with CXS members, including staff and students, and holding discussions with external stakeholders, Advisory Board members of representatives of the administering institution, the University of Melbourne.

The day went very smoothly and all of those interviewed reporting that the process seemed to be going well. The day concluded with an interview with the Research Director in which he and the Deputy Director were commended for the quality of their leadership. This augured well for a good outcome.

Much of the material presented to the review team will also appear in this report. The Executive Summary of CXS achievements is shown in the next column.

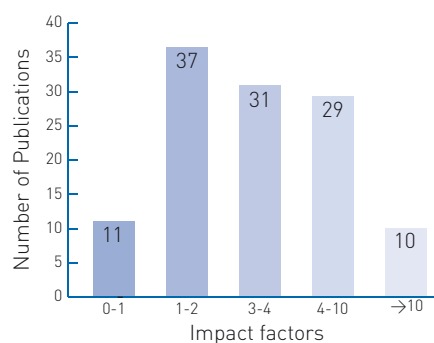


Figure 1: Number of papers as a function of impact factor.

EXECUTIVE SUMMARY OF CXS ACHIEVEMENTS

- CXS has met or exceeded all of its formal Key Performance Indicators
- Met all of its scientific goals
- Attained membership of approximately 80 staff and students
- Created a start-up company – Moglabs Pty Ltd
- Published 123 papers. We have made a concerted effort to direct our work to the highest possible impact factor journals and our success is displayed in Figure 1. We have achieved an average impact factor ~4.1
- Had work featured in nine journal front covers, including two in *Nature Physics*
- Established world-class femtosecond laser and X-ray imaging infrastructure
- Attracted \$2.5M support for the development of Physical Biosciences from a charitable foundation
- Generated a range of in-kind support, including a Partner User Proposal with the Advanced Photon Source worth in excess of \$600K per annum
- Established pathways to commercial markets through: Moglabs, the company we have created; latia Ltd, a company with which we have a long-standing relationship; and through our formal relationship with the Cooperative Research Centre for Biomedical Imaging Development
- Signed four Memoranda of Understanding with national and international research institutions
- Led a major national collaboration for the development of scanning X-ray microscopy for Australia
- Subject of 13 commentary and media pieces

We were also able to point to the fact that we had raised nearly \$10.5M in additional external support that could be directly attributable to the existence of CXS.

The outcome of the review was announced in early 2009 and the details and our responses to the recommendations will be a matter for reporting in the *2009 CXS Annual Report*. However, CXS was renewed and extended until the end of 2013 with increased funding. All CXS members should be congratulated on that achievement.

The review team did make comments to us at the conclusion of the review and an important one was that we were a little too modest in our reporting practices. The ARC wishes to know all of the outcomes from all CXS associated staff. The *2008 CXS Annual Report* incorporates such changes to reporting practice. This will result in an increase in the number of papers reported as CXS outputs and will include outputs on topics that are not CXS projects or directly CXS funded. We will also report on fundraising that is beyond the aegis of CXS. An example of this is that the fundraising reported to the review and quoted above \$10.5M would be revised to a figure of over \$33.7M. This underlines the success of CXS members, and also the impact of the requested widening the reporting ambit.



RESEARCH PROGRAMS & CASE STUDIES

RESEARCH PROGRAMS & CASE STUDIES

BIOLOGICAL SCIENCES PROGRAM

Methods for imaging cellular architecture and, ultimately, macromolecular complexes and individual proteins within a cellular environment, represent important goals for cell and molecular biology.

The Biological Sciences Program involves the participation of biochemists, structural biologists and cell biologists who are undertaking specific research in the biomedical area. As part of work undertaken within CXS, Biological Sciences Program members collaborate closely with members of the Experimental Methods Program (EMP) in the development and implementation of novel imaging techniques to provide new insights into the structures of membrane-enclosed compartments within cells. Members of this program also interact with members of the Structural Determination Methods Program to optimize techniques in determining the structures of membrane proteins and membrane protein complexes.

The groups within this program conduct world-class research in the following areas:

MALARIA AND REMODELLING OF THE RED BLOOD CELL

The most deadly of the human malaria parasites, *Plasmodium falciparum*, invades red blood cells and initiates a remarkable series of morphological rearrangements. The mature red blood cell is effectively a floating sack comprising a membrane that encloses the oxygen-transporting protein haemoglobin. Unlike other cells, red blood cells have no DNA and cannot make or traffic proteins. In order to colonise and remodel the red blood cell, the parasite generates a series of novel structures that are involved in the export of virulence proteins to the surface of the host cell. These include extensions of the parasite's vacuolar membrane, known as the tubulovesicular network, and structures referred to as Maurer's clefts. Maurer's clefts are convoluted collections of distorted discs that are tethered to the red blood cell membrane by structures with stalk-like profiles. One of the aims of CXS is to image these compartments and to develop an understanding into their function and the way in which they are formed. Such research can lead to new avenues for drug and vaccine design to inhibit the growth of malaria in red blood cells.

MITOCHONDRIAL BIOLOGY

Mitochondria are the generators within our cells, synthesizing chemical energy in the form of the molecule ATP. They also act as poison cupboards; when the mitochondrial outer membrane is opened, certain proteins become released that kill cells as part of programmed cell death. Defects in mitochondria cause energy-generation disorders and are implicated in other diseases including Parkinson's disease, Alzheimer's disease and cancer. Work within the CXS aims to understand some of the events involved in remodelling mitochondrial membranes during disease and to provide potential new insights into the formation of pores that lead to cell death. In addition, work is being undertaken to provide insights into the structure of mitochondrial membrane proteins and their complexes.

The goals of the program are:

- Prepare and optimize cellular samples for use as test-beds for X-ray coherent diffraction imaging and for other pioneering imaging techniques
- Use X-ray imaging and other imaging modalities to gain novel insights into cellular architecture and function
- Prepare samples of soluble and membrane proteins and determine their structural characteristics using both conventional X-ray crystallography techniques and novel X-ray-based approaches

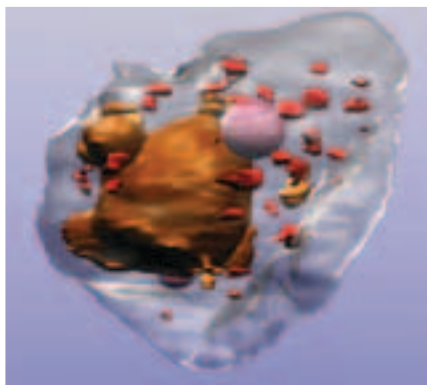


Figure 1: Rendering of the segmentation of a malaria parasite within the red blood cell using X-ray tomography. The red blood cell membrane is transparent, the parasite is shown in brown, haemoglobin within a vacuole is in purple, and Maurer's clefts are shown in red.

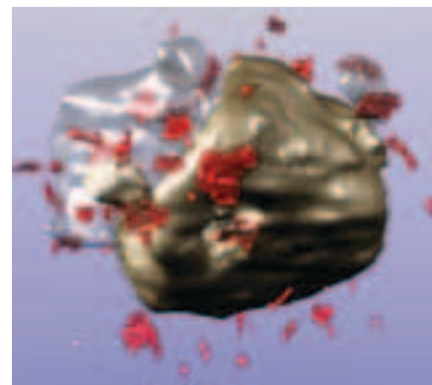


Figure 2: Rendering of the segmentation of a malaria parasite after electron tomography of serial sections. The parasite is coloured grey, the parasitophorous vacuole is transparent and Maurer's clefts are in red.

ACHIEVEMENTS

The malaria parasite *Plasmodium falciparum* has been used as a test system for X-ray coherent diffraction imaging (CDI), and the data have been correlated with other imaging modalities, including light and electron microscopy, and scanning and transmission X-ray microscopy. In particular, the group has performed pioneering efforts in the development of electron tomographic imaging, X-ray tomographic imaging and fluorescence imaging.

IMAGING OF THE MALARIA PARASITE USING CDI AND COMPARISON WITH OTHER TECHNIQUES

As a test system for cellular imaging, we have applied coherent diffraction imaging to the malaria parasite, *Plasmodium falciparum*. We employed a novel CDI approach, known as Fresnel CDI, which uses illumination with a curved incident wavefront, to image red blood cells infected with malaria parasites. We have examined the intrinsic X-ray absorption contrast of these cells and compared them with cells contrasted with heavy metal stains or immunogold labelling. We compared CDI images with data obtained from the same cells using scanning electron microscopy, light microscopy, and scanning X-ray fluorescence microscopy. We showed that CDI can offer new information both within and at the surface of complex biological specimens at a spatial resolution of better than 40 nm and we demonstrated an imaging modality that conveniently combines scanning X-ray fluorescence microscopy with CDI. The data provide independent confirmation of the validity of the coherent diffractive image and demonstrate that CDI offers the potential to become an important and reliable new high-resolution imaging modality for cell biology. CDI can detect features at high resolution within un-sectioned cells.

IMAGING OF CELL ARCHITECTURE AND FUNCTION

Three-dimensional structured illumination microscopy permits high resolution analysis of cells that are specifically labelled with fluorescent probes. Transmission X-ray cryo-microscopy can be performed in a tomographic format on whole hydrated cells and can be combined with immunospecific labelling with gold/silver aggregates to probe particular cellular compartments; and immunoelectron tomography can be combined with serial sectioning and immunogold labelling to permit precise mapping of the cellular architecture of entire cells.

During intraerythrocytic development, the human malaria parasite, *Plasmodium falciparum*, establishes membrane-bound compartments, known as Maurer's clefts, outside the confines of its own plasma membrane. The Maurer's clefts are thought to be

a crucial component of the machinery for protein sorting and trafficking; however, their ultrastructure is only partly defined. We have used high resolution imaging techniques to image Maurer's clefts of malaria parasites. The compartments are revealed as flattened structures with a translucent lumen and a more electron-dense coat. Individual 25 nm and 80 nm vesicle-like structures are also observed in the erythrocyte cytoplasm and are associated with the red blood cell membrane. The Maurer's clefts are connected to the red blood cell membrane by regions with extended stalk-like profiles. Immunogold labelling with specific antibodies confirmed differential labelling of the Maurer's clefts and the parasitophorous vacuole and erythrocyte membranes.

With colleagues, we disrupted the gene for the membrane-associated histidine-rich protein 1 (MAHRP1) and found that Maurer's clefts become disorganized. Trafficking of the virulence determinant, PfEMP1, accumulates within the parasite and is not presented at the red blood cell surface. We also analysed a protein with sequence similarity to a Golgi tethering protein, referred to as ring-exported protein-1 (REX1), which is associated with Maurer's clefts. A REX1-GFP chimera was trafficked to the Maurer's clefts and preferentially associated with the edges of these structures, as well as with vesicle-like structures and with stalk-like extensions that are involved in tethering the Maurer's clefts to other membranes. Electron



Biological Sciences Program team at La Trobe University (from left: Nick Klonis, Micky Baker, Abhishek Awasthi, Sam Deed, Jeff Yeoman, Matt Dixon, Leann Tilley, Shannon Kenny, Tasha Abu-Bakar, Paul McMillan, Lina Rozano, Tim Brown, Megan Dearnley, Eric Hanssen, Laura Osellame, Alex Maier, Mike Ryan, Ved Mooga, Diana Stojanovski).



Figure 3: Virtual section through an X-ray tomogram of three infected red blood cells.

microscopy revealed that the Maurer's clefts of REX1 truncation mutants have stacked cisternae, while normal parasites have unstacked Maurer's clefts. These studies revealed the importance of the REX1 protein in determining the ultrastructure of the Maurer's cleft system.

We have also undertaken techniques to image mitochondria and their remodelling within cells. This has been performed using electron microscopy and novel confocal techniques that utilise photo-conversion of specific fluorescent proteins to track intracellular movements. Work was also undertaken to determine the suitability of the pore forming protein equinatoxin to make cellular membranes selectively permeable, allow the entry of fluorescently labelled molecules into live cells.

STRUCTURAL STUDIES

The Tim9-Tim10 complex plays an essential role into the biogenesis of mitochondria by trafficking hydrophobic membrane proteins across the mitochondrial intermembrane space. How the complex interacts with these proteins is not clear, although it has been proposed that Tim10 acts in substrate recognition, whereas Tim9 acts in complex stabilization. We determined the structure of the yeast Tim9-Tim10 hexameric assembly determined to 2.5 Å resolution and performed mutational analysis in yeast to evaluate the specific roles of Tim9 and Tim10. Each Tim9 and Tim10 subunit contains a central loop flanked by disulfide bonds that separate two extended N- and C-terminal tentacle-like helices. Buried salt-bridges between highly conserved lysine and glutamate residues connect alternating subunits. Mutation of these residues destabilized the complex, causing defective import of membrane proteins and cell growth defects. Truncation analysis revealed that in the absence of the N-terminal region of Tim9, the hexameric complex no longer trapped incoming substrates. Our results demonstrated that Tim9 plays an important functional role that includes facilitating the initial steps in translocating precursor substrates into the intermembrane space.

We have also successfully isolated the large membrane protein complexes of the mitochondrial respiratory chain and novel Complex I assembly proteins for their structural analysis. Efforts are commencing to undertake 2-dimensional crystallization of these and other membrane proteins for conventional analysis and as test-beds in collaboration with the Structural Determination Methods program.

In conjunction with the Structure Determination Methods Program (SDP), we solved the structure of parasite hemozoin using X-ray powder diffraction data. The structure reveals the presence of two previously undescribed modes of hemozoin self-association involving π - π interactions. These π -bonding interactions may initiate crystal formation and stabilize the extended structure. This work has provided insight into the nature of haemozoin formation, which has implications for the inhibition of this process by quinoline antimalarials.

Students, Ved Mooga and Laura Osellame,
preparing samples for structural and
cellular imaging



BIOLOGICAL SCIENCE PROGRAM CASE STUDY

CHARACTERIZING THE ARCHITECTURE INSIDE THE MALARIA PARASITE

In order to understand the architecture of *Plasmodium falciparum* infected erythrocytes and the modifications that the parasite make within its host we used whole cell imaging techniques. So far, studies of the *de novo* trafficking machinery within the cytoplasm of the red blood cell have been performed either by electron microscopy using serial sections, leading to a good resolution but to a maximum depth of 500 nm, or by fluorescence that leads to a whole cell image but at a low resolution.

In order to improve the analysis, we used two main techniques, X-ray and electron tomography. Both techniques lead up to whole cell imaging with X-ray tomography affording easy sample preparation but with resolution limited to 50 nm. Electron tomography requires extensive sample preparation but with currently an unmatched resolution. The X-ray tomography was performed on Beamline 2.1 at the Advanced Light Source in Berkeley. The electron tomography of serially cut 300 nm sections was performed at the Bio21 Institute. For both techniques, the tomograms were reconstructed using IMOD and for the ET the serial sections were realigned and stacked using the same package.

Both techniques lead to the conclusion that the exporting machinery is made of independent entities known as Maurer's cleft that bud of the parasitophorous vacuole, migrate to the red blood cell membrane individually or in group depending of the strain.



George Jung, Kathryn Spiers, Chris Hall, Wilfred Fullagar

DETECTOR AND BEAMLINE DEVELOPMENT PROGRAM

The Detector and Beamline Development team (DBD) at Monash University are striving to design and build the optimal detector for X-ray coherent diffractive imaging. We are also partially responsible for the delivery of a high technology end station, which will control the Coherent X-ray Diffraction Imaging (CXDI) optics, sample, and detector positioning.

The CXS DBD project team are addressing the limitations of current couple-charged device (CCD) based X-ray imaging devices for CXDI. CCDs are well-established detectors for this area of research. They are integrating devices, which accumulate information about the X-ray field during an exposure period. The signal read out is related to the total charge released in a pixel as each X-ray photon interacts with the silicon. This method is a simple and reliable means to measure the X-ray intensity that falls on the detector. However, there are penalties to be paid for this simplicity. The signal-to-noise ratio and the dynamic range in integrating detectors are sub-optimal for a technique as demanding as CXDI. For successful CXDI image reconstruction the precise number of photons that hit a pixel should be recorded. Errors in this value should be less than 1% in order to allow the reconstruction algorithms to converge in reasonable time. The estimate provided by

an integrating detector is usually not good enough for imaging applications. Readout noise and other detector artefacts increase the measurement error especially when only a few photons being measured. This is always the case in the high scattering angle regions of the CXDI image.

A better alternative is to count individual X-ray photons as they arrive at the detection plane. Given full quantum efficiency, the measurement of flux in this case is accurate with almost no noise. An important limitation to the counting technique arises when the flux is high. In this case the electronic circuits can struggle to keep up with the rate of arrival of the photons. The rate limit can be increased if the area for which the counting is taking place is very small. Using very large scale integrated circuit (VLSI) technology, the readout circuitry for a given pixel can be made very small. Using modern integrated circuit processes it is now feasible to place all the readout circuitry for an individual X-ray detector in an area of less than 100 microns square. It is also possible to reproduce this circuitry many times and devise a means to multiplex the outputs into just a few electronic channels. Using this technique a matrix of readout nodes can be fabricated covering the whole of the sensitive area required. Placing an X-ray sensitive material above this matrix circuit and connecting to it electrically, or even optically, produces a versatile and accurate X-ray detector. The general name given to such a device is a hybrid pixel detector (HPD), or simply 'pixel detector'. The particular demands of CXDI are highest in the specification of sensitivity and dynamic range. High sensitivity is required to detect the faint scattered X-ray flux at high angles from the sample. The difference in flux between the central region of the image and the diffraction region is many orders of magnitude, therefore requiring a large dynamic range in the detector. For both sensitivity and dynamic range the HPD has the potential to provide superior performance to CCDs; this is the device of choice for a future CXDI detector.

ACHIEVEMENTS

DETECTOR TEST APPARATUS DEVELOPMENT

An instrument has been designed and is currently being assembled to allow the testing of detectors in the X-ray energy regime down to 200 eV. At these energies, air attenuation is significant so the detector and the path from the X-ray source needs to be evacuated. Our apparatus is designed to enable precise testing of soft X-ray detectors using both conventional and synchrotron sources. Masks and other test object can be positioned accurately in front of the detection plane and manipulated within the evacuated volume. Soft X-rays from a variety of sources illuminate the detector with a path through an extensible evacuated flight tube. The facility incorporates a double valve isolator with one valve including a thin X-ray transparent window. This will ensure UHV compatibility with external equipment such as a synchrotron soft X-ray beam line. The window can be

LEFT: Wilfred Fullagar – Assembling a thin film evaporator. This apparatus is used for coating substrates with materials suitable for soft x-ray detection using optical readout.

RIGHT: Kathryn Spiers – Analysing data from the CXS Medipix2 detector.



removed if required for use with conventional x-ray sources. The port which interfaces to the detector has been designed for the current Princeton Instruments CXS detector, but will easily provide mechanical and vacuum compatibility with interfaces to the Medipix2 and other detectors for future testing.

MEDIPIX2 CHARACTERIZATION

A promising candidate for a CXDI hybrid pixel detector is the Medipix2 hybrid pixel device from CERN. It is of particular interest since the design and development work on the chip is now complete. A fully functioning detector is available to purchase through a semi-academic route and CXS has taken out such a license. DBD have purchased this device on behalf of CXS and have been characterizing it during the year. The Medipix2 detector consists of a 256 x 256 pixel CMOS readout chip which is bump-bonded to a segmented silicon sensor 300 microns thick. Each pixel measures 55 x 55 μm . Underneath each pixel is identical readout circuitry. The analogue section comprises a charge pre-amplifier that feeds a pair of comparators. The threshold levels for the comparators can be accurately set using a 12-bit digital-to-analogue converter (DAC). The last three bits are individually adjustable for each pixel to compensate for fabrication tolerances. An internally generated test pulse can be fed into the charge amp through a fixed capacitor.

FIELD AND CHARGE TRANSPORT MODELLING

Some of the DBD work in 2008 focussed on background research into modelling potential X-ray detector configurations. Our PhD student (Evan Curwood) embarked on building a Monte Carlo model of two layers of a realistic HPD. He used a tried-and-trusted code developed at CERN for modelling photon and charged particle transport. The GEANT4 code is complex, but comprehensive. It has the potential to allow the DBD group to model the movement of charges generated by X-rays in the detection layer, subsequently providing a prediction of the size and shape of signals from electrodes placed on surfaces. This is crucial information to feed forward to an electronic design team, who would use this information to design the front-end amplification.

OPTICAL DETECTION MATERIALS

Radiation-induced colour centres in materials are the detection mechanism by which X-rays were first discovered. This method has a pedigree in the broader context of photography. Historically, photographic materials offered the mechanism through which semiconductor detectors first came to be studied for use as electronic photon detectors. Optical and X-ray fluorescence also permits detection and imaging, these being among the relaxation processes associated with colour centres. It is interesting to note that there is a strong overlap involving this research and the development of solar cells, with which our group is seeking synergy.

In principle, the creation of colour centres can offer single photon detection. In condensed materials, the optically detectable events will diffuse significantly, sometimes with a small time constant. The rate depends on the material in question. In photographic film, the material chemistry effectively traps the colour centres for long periods. The locally altered chemistry is amplified using developing procedures to make the photon-induced events easily visible. However, such trapping and amplification is not necessary if brief laser pulses are used to optically probe the colour centres. The pulsed time structure of laser pulses is easily capable of probing events on timescales that are very short compared to the diffusion and dissolution times. Furthermore, the large number of optical photons in the interrogating laser pulse obviates the need for chemical amplification. The kinetics and chemistry of the excitation in particular materials determines whether the optically detectable disturbance needs to be probed on timescales of picoseconds or whether it may be read out at a more leisurely pace using a CW laser or spectrometer. Both approaches have been demonstrated in the past and are now being assessed by the CXS DBD team for their suitability in CXDI experiments. The object of this work is to determine suitable materials, establish feasibility, and create prototype variable latency transient gratings for CXDI applications.



DETECTOR AND BEAMLINE DEVELOPMENT PROGRAM CASE STUDY

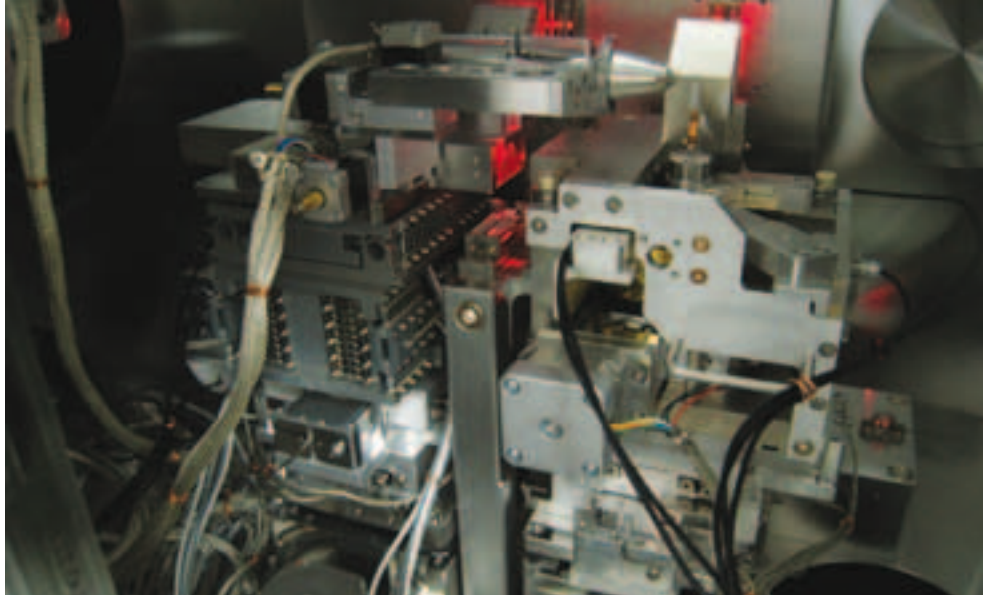
OPTICALLY-BASED DETECTION AND RECONSTRUCTION OF SHORT WAVELENGTH HOLOGRAMS

The sub-picosecond pulsed nature of future radiation sources means that a different approach needs to be taken to the detection of scattered fields in CXDI using these facilities. Pulse repetition rates can be low, with 1 kHz being a common benchmark for moderate intensity ($\sim 10^{18}$ W cm⁻²) ultrafast laser systems. This provides a large window for detector readout despite the high flux. Instantaneous photon rates generally preclude the use of counting-based detectors. Integrating detectors are, therefore, desirable in this context. In particular, we are studying the potential for the optical readout of colour centres in appropriate X-ray sensitive materials.

Interference fringes formed by the overlap of numerous scattered photons lead to a potential for X-ray holography read out using an optical laser. With appropriate geometric design, the fringe spacing can be arranged to match optical wavelengths. One can then use visible laser light to re-convert the holographic interference fringes to an image of the scattering object. The difference in the forming wavelength (X-ray) and readout wavelength (optical) provides a large effective magnification. In such holographic reconstructions, the sample resolution is ultimately limited by the X-ray wavelength. The interference fringes captured by colour centre formation in suitable materials constitute a complex optical grating. The gratings are usually transient with a latency can be varied by tuning the chemistry of the material. The advantages of variable latency transient gratings over conventional CCD/semiconductor detection approaches include:

- large dynamic range, ultimately limited only by the number of atoms in the gauge volume of the material
- the detection of fringes can involve either direct imaging of fringes or even individual events and subsequent analysis. Alternatively, a longer wavelength laser light can be used directly to optically transform the fringe information to a visible image of the object
- transient gratings can be cheap and disposable
- they can be tailored to suit specific radiation types and energies, also laser wavelengths

Detail of the central chamber stages in FRIEND. The conical mount holds the order sorting aperture next to a zone plate. The gold stage is the sample rotation stage and reflections from the LDDM can be seen.



EXPERIMENTAL METHODS PROGRAM

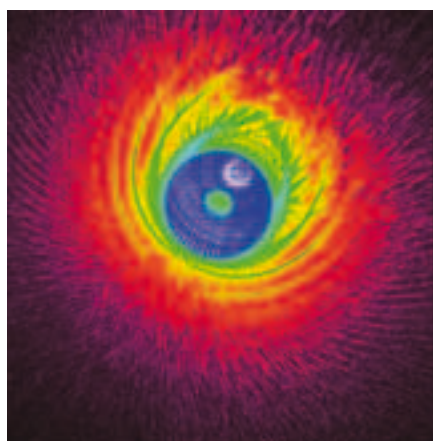
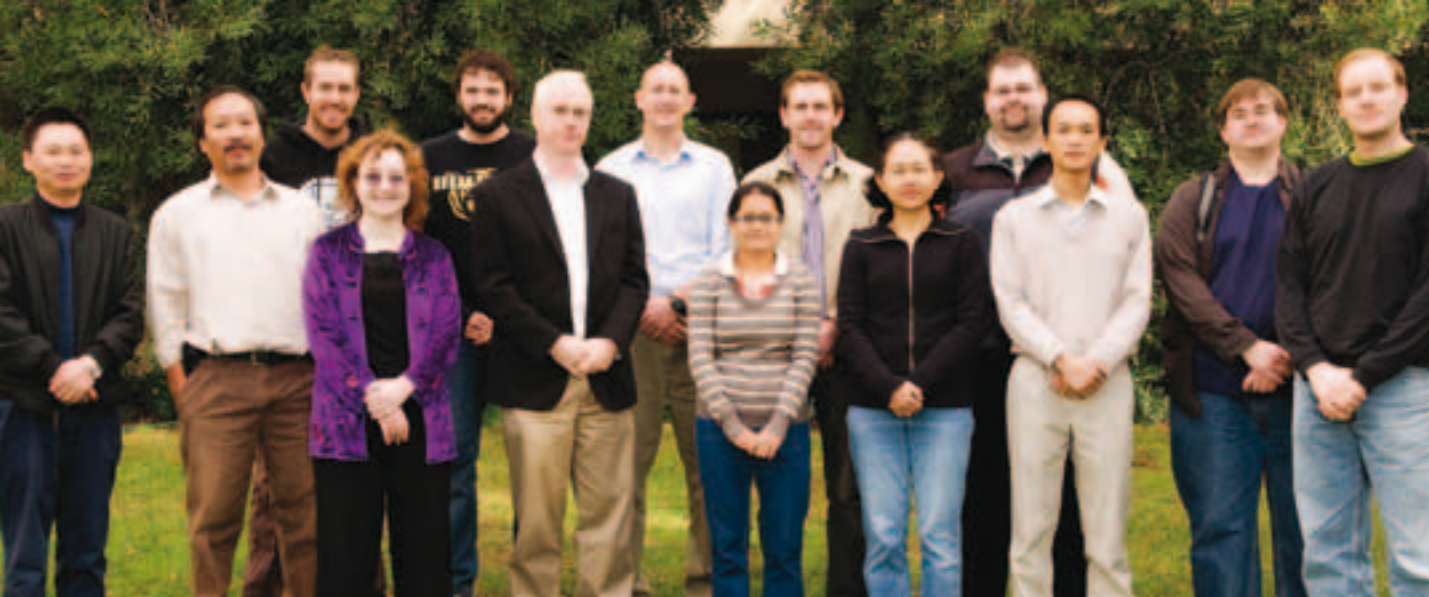
The Experimental Methods Program (EMP) develops imaging methods using coherent and partially coherent light sources. The research profile of EMP includes the design of experimental systems, sample handling and nano-fabrication techniques, tomographic imaging of three-dimensional objects, the detailed characterization of radiation sources and the development of novel imaging methodologies using diffraction data.

These are the key experimental techniques required to undertake the CXS mission. In particular, the EMP has developed a dedicated endstation that will greatly facilitate the investigation of biological samples. It is the first instrument of its type that provides sufficient stability to apply the imaging methods developed for CXS.

The EMP group has members based at La Trobe University, the University of Melbourne and Monash University. Through its broad spectrum of members and activities, the EMP is ideally suited for interaction with the other programs of CXS. Through regular interaction with the Theory and Modelling Program, the EMP has established standing research activities with most of the other programs in CXS:

- Biological Sciences Program (BSP) – this is a fundamental CXS interaction. The work of the EMP is to image biological samples in three-dimensions. This basic work is assisted by both groups and by the Theory and Modelling Program in analyzing imaging data obtained from biological samples. With the bulk of their membership based at La Trobe University, EMP and BSP staff regularly meet to develop imaging methods. To further facilitate the mutual translation of physics and biology BSP staff attend EMP experiments at overseas facilities, which has led to the exploration by BSP of access to other imaging techniques and facilities around the world. EMP and BSP also hold seminars and meetings designed to encourage interaction between students and staff from the two groups.
- Theory and Modelling Program (TMP) – TMP and EMP regularly cross-fertilize. EMP provides experimental data that TMP can apply new methods of analysis to and TMP provides new directions for the experimental work. Members of TMP are co-located at the University of Melbourne with several of the EMP group so that interaction is frequent.
- Short Wavelength Laser Source Program (SWLP) – the SWLP provides a novel source of coherent photons at wavelengths approaching X-ray. Again, with strong interaction from TMP, the EMP and SWLP have a standing experimental activity based around pursuing the limits of imaging with these sources.
- Ultra-Cold Plasma Source Program (UCP) – the UCP was formed within CXS to exploit techniques developed by EMP and TMP to demonstrate imaging using a bright coherent source of high-energy electrons. Again with membership based at the University of Melbourne UCP and EMP have a high degree of interaction.
- Detector and Beamline Development Program (DBD) – the DBD has significant interaction with EMP in the development of experimental facilities. In particular, the endstation developed for CXS experiments was a joint activity and budget share for the DBD and EMP.

The Experimental Methods Program undertook an ambitious sequence of experiments and infrastructure development in 2008 against the goals that had been stated in the 2007 annual report. In meeting these goals, EMP conducted 11 overseas experiments involving more than 200 researcher days at synchrotron facilities. We continued experiments with the SWLP at Swinburne University of Technology, supported the CXS developed laboratories at the University of Melbourne (Optics Laboratory) and La Trobe University (Fabrication Laboratory and Tomography Laboratory). We established a Partner User Program to host FRIEND (FResnel Imaging ENDstation) at the Advanced Photon Source in Chicago, completed the construction and commissioning of FRIEND at the Advanced Photon Source, formed the Beamline Advisory Panel and obtained an ARC Linkage Infrastructure and Equipment Funding grant to assist in the eventual relocation of FRIEND to the Australian Synchrotron.



Scattering data measured using FRIEND from a spoke test pattern.

The specific goals were:

- Proof of principle imaging using the coherent source developed by the Short Wavelength Laser Source Program (SWLP);

In conjunction with the SWLP and TMP, the EMP effort, led by Bo Chen, towards imaging using a High Harmonic Generation laser source was rewarded with publications on source spectrum characterization and on imaging. Throughout 2008, further imaging improvements have been demonstrated.

- Developing the CXS technique of imaging known as Fresnel Coherent Diffractive Imaging (FCDI) at overseas facilities such as the Swiss Light Source and the Centre for Nanomaterials and Fabrication at the Advanced Photon Source;

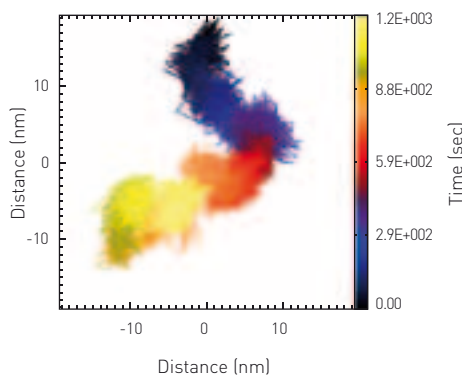
EMP personnel, Mark Pfeifer and Garth Williams, have pursued this work at the Swiss Light Source and at the Centre for Nanomaterials and Fabrication at the Advanced Photon Source. The application of the FCDI technique to the data acquisition process has been demonstrated.

Detail of the central chamber stages in FRIEND. The conical mount holds the order sorting aperture next to a zone plate. The gold stage is the sample rotation stage and reflections from the LDDM can be seen.

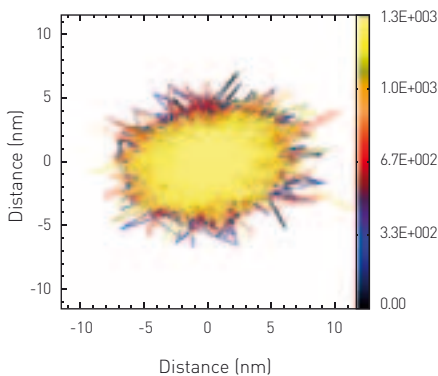
- Commissioning a dedicated endstation for FCDI (FResnel Imaging ENDstation, or FRIEND). This involved a planned home at the Taiwanese National Synchrotron Radiation Research Centre, creating a Beamline Advisory Panel for the soft X-ray branchline at the Australian Synchrotron and an associated funding bid to obtain funds to relocate FRIEND, and demonstrating improved quality in FCDI.

In early 2008, an opportunity from the Advanced Photon Source arose to locate FRIEND at beamline 2-ID-B. With the understanding and support of our Taiwanese colleagues (with whom we had planned to locate FRIEND in Taiwan), a Partner User Proposal to develop FCDI at the Advanced Photon Source was initiated. The proposal (also supported by the Australian Synchrotron and a wide range of the soft X-ray community in Australia) was accepted and the installation plans for FRIEND amended accordingly. In an associated development, a proposal to the ARC for Linkage Infrastructure and Equipment Funding was submitted to eventually relocate FRIEND to the Australian Synchrotron as well as upgrade its capability to allow for nano-probe measurements.

This proposal was also successful and the Chief Investigators, who largely form the membership of the associated Beamline Advisory Panel for the branch line at the soft X-ray beamline at the Australian Synchrotron, now also constitute the oversight committee for the relocation program. In parallel with these developments, FRIEND was constructed and commissioning runs undertaken at 2-ID-B at the Advanced Photon Source in July, October and December. These tests have demonstrated improved capability for FCDI imaging. FRIEND has also now been used to obtain data for CXS student PhD projects (Jesse Clark, Corey Putkunz, Lachlan Whitehead and Angela Torrance) as well as having been used in a number of external user experiments.



LDDM readout information: 1334 seconds, x vs y position (quiet conditions).



LDDM readout information: 1334 seconds, x vs y position (quiet conditions). Closed loop showing tracking of sample with respect to optics.



Reconstruction of an Xradia "X" pattern from X-ray data measured using FRIEND.

ACHIEVEMENTS

In addition to its stated program goals, EMP continued with its overall mandate – to explore new methods in imaging and coherence. Some of the results in 2008 are as follows:

- An experimental study (forming part of Lachlan Whitehead's PhD) showing the benefits of curved beam illumination for Coherent Diffractive Imaging with partially coherent wavefields;
- A study (led by Keith Nugent) on the effect on imaging of partial coherence in an X-ray microscope arrangement, that study was used to explain earlier observations (taken by Benedicta Arhatari);
- An experimental study into fitting coherent modes to partially coherent x-ray light (forming part of Sam Flewett's PhD) was successfully conducted at the Advanced Photon Source;
- The work commenced in 2007 into extending FCDI into a full field imaging method (known as Keyhole FCDI) was extended in 2008. Work performed and accepted in 2007 appeared in *Nature Physics* and a further study (led by Brian Abbey) into the imaging of part of an integrated circuit at high resolution appeared on the front cover of *Applied Physics Letters*;
- A review paper and a book chapter were written by EMP members (Andrew Peele and Keith Nugent);
- The existing laboratories in EMP have been used as input into experiments and into student projects. The optics laboratory developed by Garth Williams has been used for optical data for student projects (Claire Henderson, Angela Torrance, Corey Putkunz). The tomography laboratory developed by Benedicta Arhatari has been used for X-ray data for student projects (Kevin Hannah) and the fabrication laboratory developed by Eugeniu Balaur and Kaushal Vora has produced samples for many of the EMP experiments during the year;
- Studies into processes in X-ray lithography which form part of the EMP investigation into sample holders and fabrication (forming part of Kaushal Vora's PhD) were published and one was selected by IOP Publishing as a highlight publication for the *Journal of Micromechanics and Microengineering*; and
- Kaushal Vora became the first CXS PhD student to graduate (his thesis attracted high praise from the examiners).

EXPERIMENTAL METHODS PROGRAM CASE STUDY

The FResnel Imaging ENDstation (FRIEND) is a custom designed experimental facility. It comprises a vacuum-housed Charge-Coupled Device imaging detector with water cooling and three axis of translation, including a long "z-axis" travel of 700 mm. The main chamber, constructed by Xradia Inc., contains another 15 computer controlled stages, 4 axes of which are monitored using a laser Doppler displacement measurement (LDDM) system that provides position information to better than 1 nm. The optic stages hold mounts and positioning for a zone plate and an order-sorting aperture, while the sample stage, which includes three axes of translation, uses a precision measurement system to track motions of the rotation stage for tomography measurements. The system is designed to maintain the position between sample and optic stages to approximately 3 nm root mean square.

FRIEND has passed its initial commissioning tests and has been used to produce data showing the relative trajectory of the sample and optics stages. With the feedback mechanism turned on, it is now possible to produce data where the limiting factor becomes beam instabilities rather than the stages used in the measurement system. In one of the first trials of FRIEND, EMP PhD student Jesse Clark has obtained data that is now in preparation for publication showing these results.

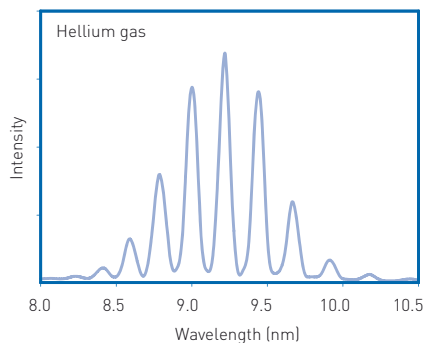
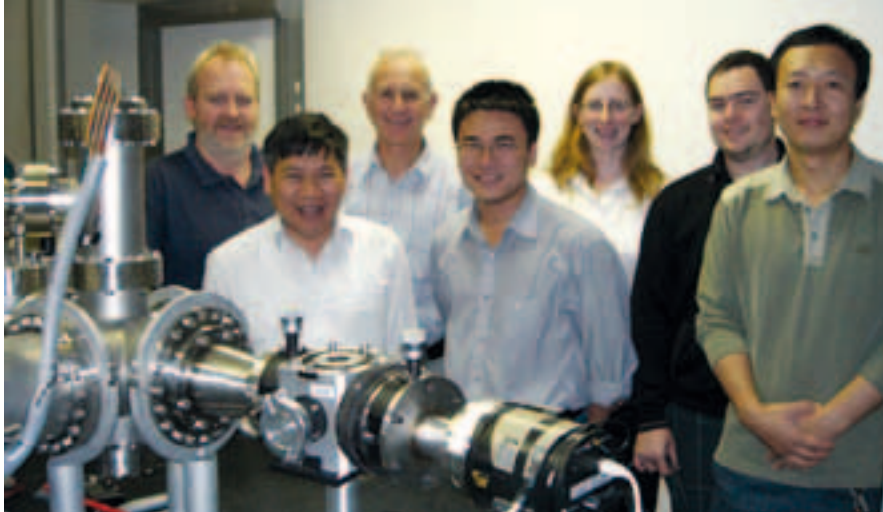


Figure 1: Small bandwidth spectra emitted from a helium gas cell at 800 Torr.



SHORT WAVELENGTH LASER SOURCE PROGRAM

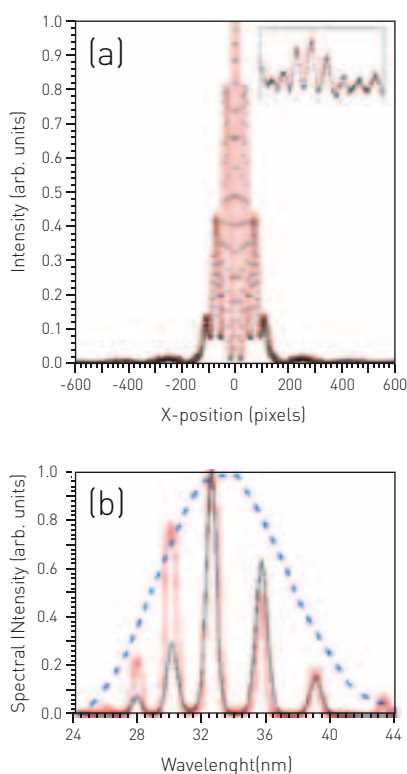


Figure 2: (a) Experimental (dotted curve) and calculated (solid curve) interference pattern. (b) HHG spectrum obtained from a spectrometer (solid curve + circles) and from the maximum entropy method-based reconstruction (solid curve). The dashed line is the spectrum recovered from the Fourier transform technique.

The Short Wavelength Laser Source Program (SWLP) has two concurrent main objectives. The primary responsibility is to undertake research into the high harmonic generation (HHG) of extreme ultraviolet (XUV) and soft X-ray pulses. A secondary program is the development of advanced imaging techniques, including time-resolved imaging, and high resolution imaging using harmonics of ultrashort pulse lasers.

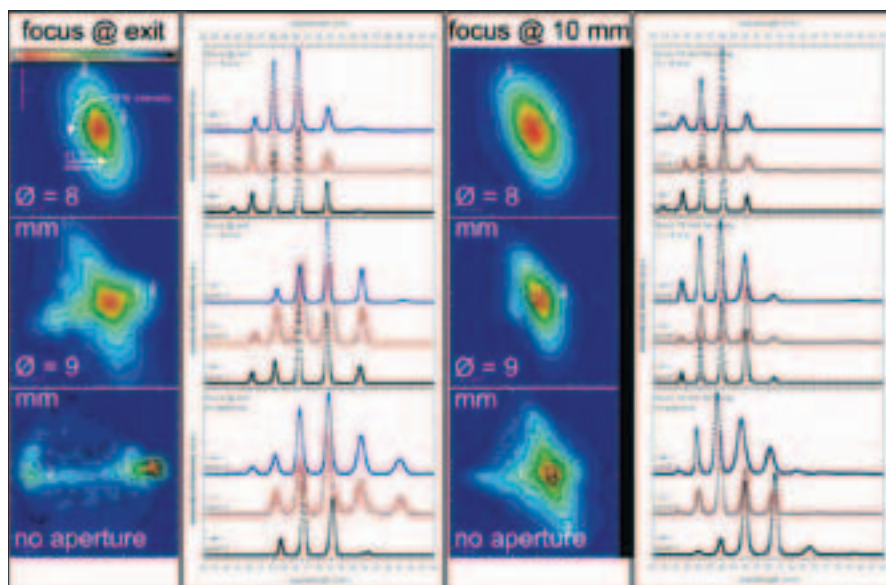
Control over the characteristics of the output, which, in particular, include the brightness or flux, the spatial and temporal coherence properties and the spectral range of the harmonic orders, is essential for the study of HHG processes and depends strongly on the interaction geometry. For enhancement of the HHG efficiency, the problem of phase matching the generated harmonics needs to be investigated in more detail, and the best way to do this is still an open and debated topic.

For many applications using HHG sources, including coherent diffractive imaging, a monochromatic beam or a beam with a narrow and well-characterized bandwidth is an important requirement. The generation of just a few harmonics, and especially a single harmonic, will provide a suitable source.

The highest photon energy produced in the HHG process is obtained from the cutoff rule: $h\nu_{\text{max}} = U_i + 3.17 U_p$, where U_i is the ionization potential of the gas and U_p is the laser ponderomotive potential. Higher HHG photon energies can be achieved by using higher laser intensities or a gas with a higher ionization potential. It can also be advantageous to ionize the gas for HHG at wavelengths approaching the water window between 2 and 5 nm, a region of great interest for biological applications.

We have also been actively developing imaging methods based on more conventional methods, primarily emission-based detection. Confocal fluorescence microscopy has developed into a mature and reasonably common mode of microscopy, particularly for the study of biological systems. New methods of optical microscopy are also being developed, such as structured illumination microscopy, which can provide high spatial resolution. The use of all these methods is currently dependent on artificially labelling the system with an extrinsic (visible) fluorophore, which can be difficult to achieve and may affect the properties of the system whose purpose it is to probe. We are therefore extending these methods into the ultraviolet regime to enable unlabelled imaging.

Figure 3: Spatial beam profile of the harmonic beam with the laser focus in the exit plane (left) and 10 mm (right) inside the gas cell for different aperture diameters. The reconstructed spectrum of the HHG beam when the YDS is positioned at different points: 1 (black line), 2 (red line) and 3 (blue line).



ACHIEVEMENTS

We have been able to generate XUV beams through HHG by focusing the femtosecond laser beam into an infinite gas cell of various noble gases argon (Ar), neon (Ne) and helium (He) with ionization energies of 15.8 eV (Ar), 21.6 eV (Ne) and 24.6 eV (He), respectively. The high order harmonic emission is confined to just a few orders because of a small phase-mismatch in the cut-off region that allows macroscopic phase-matching to be satisfied. Our technique for HHG achieves the same benefits of homogeneous phase matching as in hollow-core fibres and we have shown that we can control the generation process effectively. HHG spectra in the 10 nm region for He are shown in Fig.1 in which only about six harmonic orders are generated.

To study the spatial coherence properties of the HHG radiation, interference fringes from a Young double slit (YDS) experiment were measured, from which the degree of spatial coherence of the HHG radiation in an argon gas cell is determined to be about 0.95. The spectrum of the HHG source is obtained by using maximum entropy analysis of the YDS interference pattern (Fig. 2). This approach provides a new tool for the study of the HHG process by allowing us to study the spectral characteristics of the sources in more detail than has previously been possible (Fig. 3).

Due to its high spatial coherence, HHG radiation is increasingly being used for coherent diffractive imaging (CDI). We have performed multiple-wavelength CDI by using several phase-matched harmonics from an argon gas cell in the wavelength range 26 nm – 43 nm (Fig. 3, 4 and 5). We

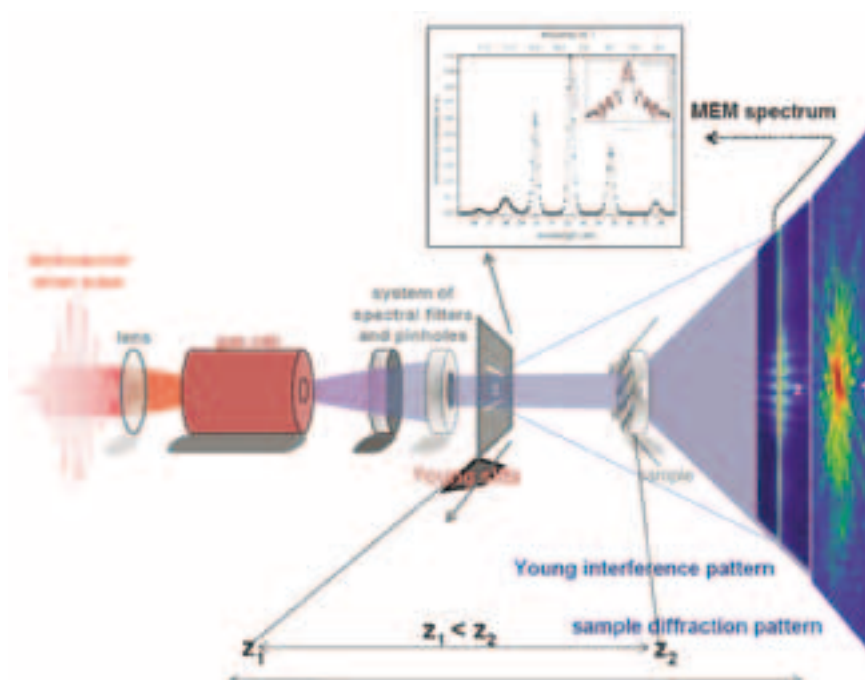


Figure 4: Experimental setup for coherent diffraction imaging using multiple harmonics

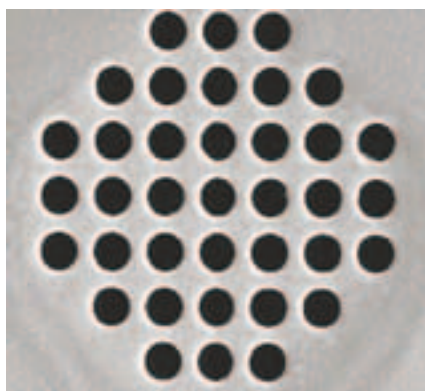


Figure 5: Scanning electron microscope (SEM) image of the sample used in the diffraction experiment.

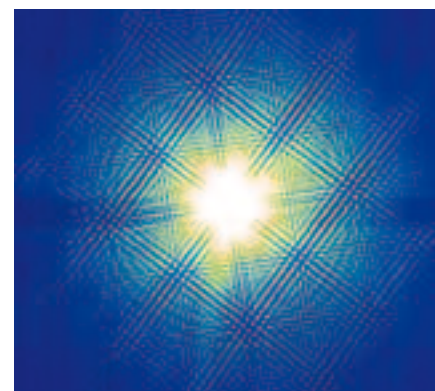


Figure 6: Diffraction data acquired from the sample of Figure 5. This consists of the combination of data, which were taken with and without a beam-stop to allow measurement of the very intense low angle scatter and the relatively low intensity high angle scatter.

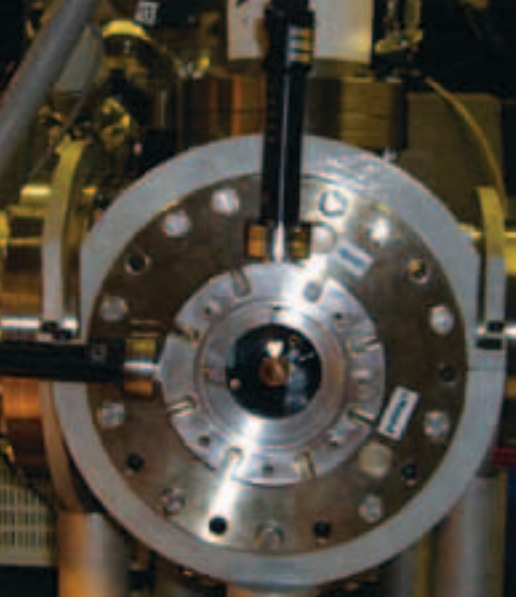


Figure 7: Construction of the beam stop for enhancement of the dynamic range of the CCD by a few orders of magnitude.



Figure 8: Semi-infinite gas cell for generation of high order harmonics.

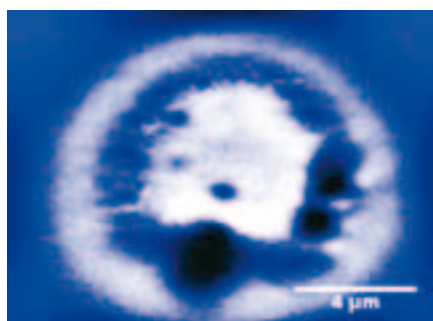


Figure 9a

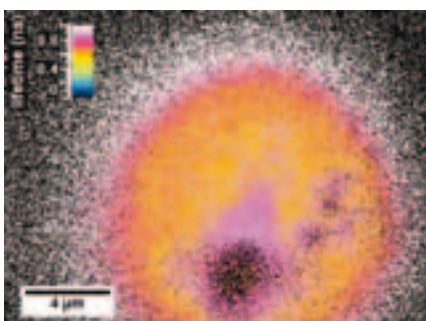


Figure 9b

Figure 9: (a) Fluorescence intensity and (b) fluorescence lifetime images of fluorescent protein-labelled RBC recorded using UV time-resolved confocal fluorescence microscopy and (c) fluorescence lifetime distribution corresponding to (b).

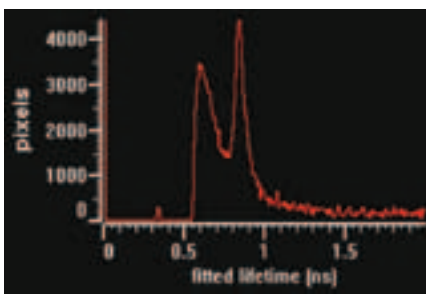
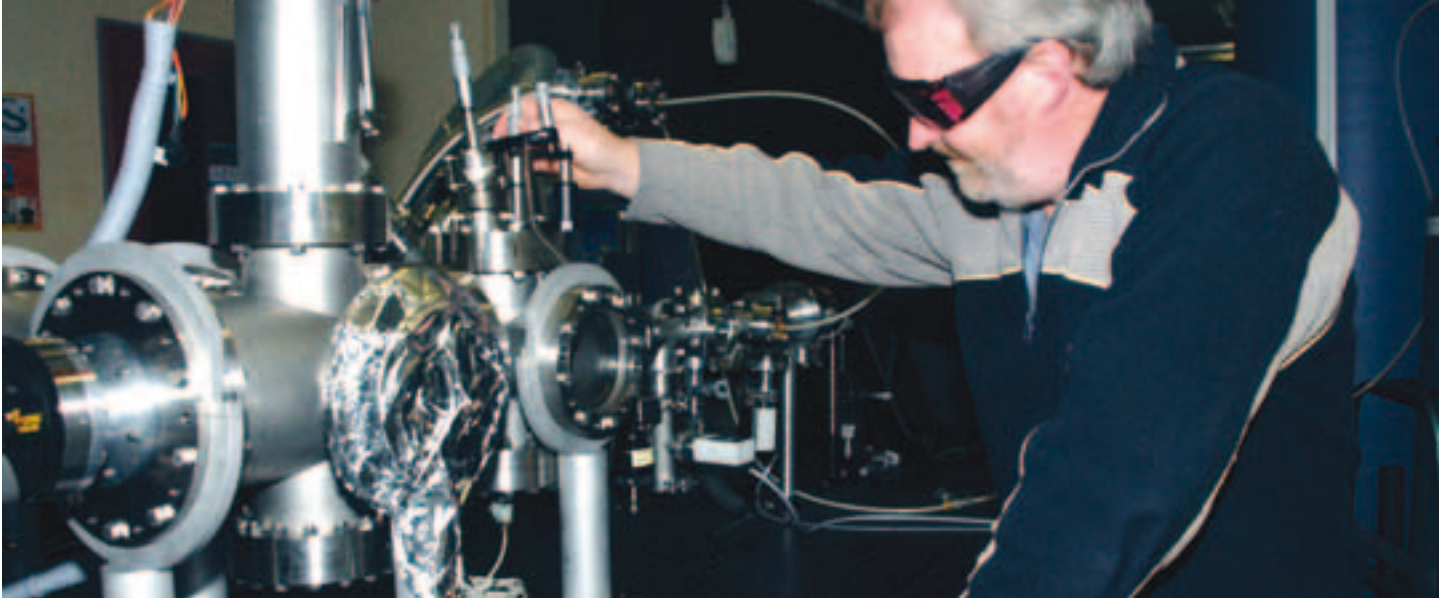


Figure 9c

have demonstrated high quality imaging with 32 nm radiation. We have also shown that it is possible to use multiple wavelengths to obtain high-resolution imaging. Biological samples do not show intrinsic contrast at these wavelengths, although we are seeking a staining mechanism that will allow useful contrast.

We are developing confocal and structured illumination methods of fluorescence microscopy based on the second and third harmonics of a femtosecond titanium:sapphire laser whereby we directly excite the inherent fluorophores of biological systems, such as tryptophan. Since most fluorophores absorb in the ultraviolet region, we can also excite the typically used fluorophores, such as fluorescent proteins. Since the excitation is sourced from a repetitively-pulsed femtosecond laser, we have the added capability to temporally resolve the emission on picosecond timescales. The following figures show the first results of UV confocal fluorescence microscopy of a parasite-infected red blood cell (RBC). The fluorophore, in this case a fluorescent protein, was excited with ultraviolet light and its visible fluorescence monitored by time-resolved confocal microscopy. The regions of the RBC where the malaria parasite is situated are dark (non-fluorescent). Two prevalent fluorescence lifetimes (~0.6 ns and ~0.85 ns) are seen with the species corresponding to the longer fluorescence lifetime more prevalent around the parasite region.

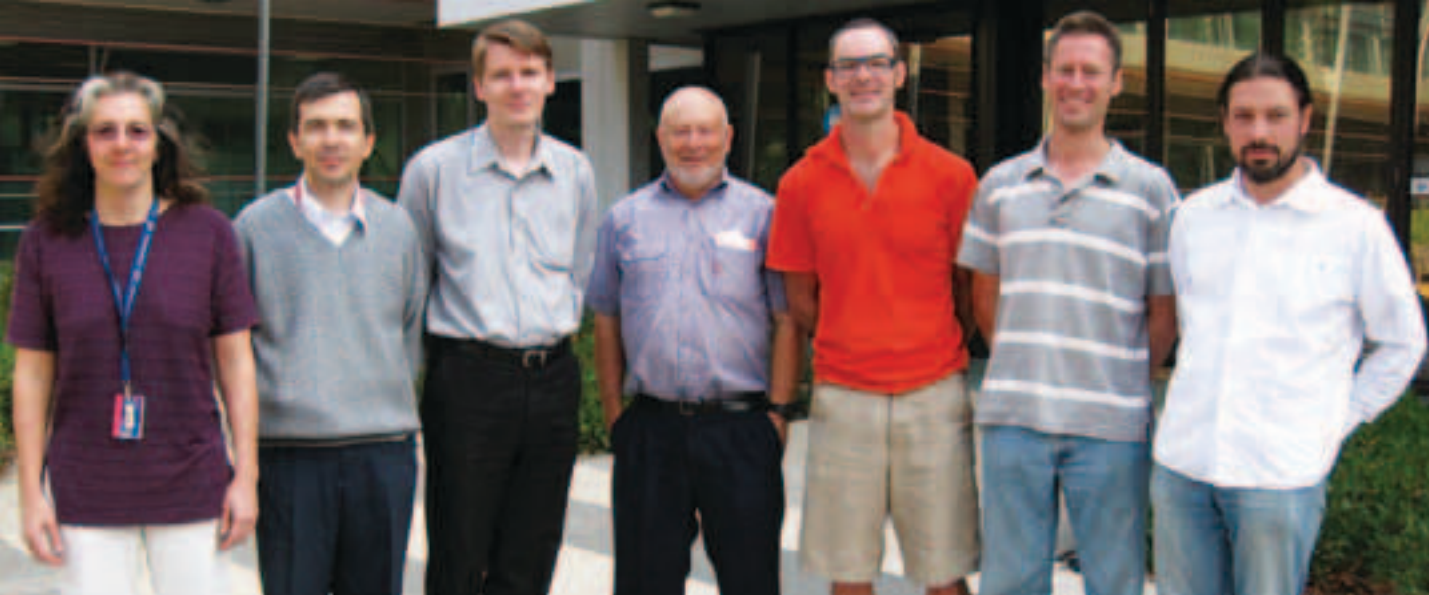


SHORT WAVELENGTH LASER SOURCE PROGRAM CASE STUDY

GENERATION OF FEW HARMONIC ORDERS FOR COHERENT DIFFRACTION IMAGING

The Short Wavelength Laser Source Program has established a facility for the study of high-harmonic generation light, producing a unique source for different applications such as coherent diffraction imaging. For many applications a monochromatic beam or a beam with a narrow bandwidth is an important requirement of the extreme ultraviolet source. The generation of just a few harmonics, and especially a single harmonic, that can be used directly without any additional optical components would be advantageous for such applications. Using a semi-infinite gas cell configuration we are able to generate just a few harmonic orders, ~ 30 nm in argon and ~ 9 nm in helium gas [1,2,3]. The high-order harmonic emission is confined to just a few orders because of a small phase-mismatch in the cut-off region that allows macroscopic phase-matching to be satisfied for just a few harmonics in this region. In collaboration with the Experimental Methods Program, this source has been used to acquire very high quality diffraction data [4].

1. L. Van Dao, S. Teichmann, J. Davis, and P. Hannaford, *J. Appl. Phys.* **104**, 023105 (2008).
2. L. Van Dao, S. Teichmann, and P. Hannaford, *Phys. Lett. A* **372**, 5254-5257 (2008).
3. S. Teichmann, P. Hannaford, L. Van Dao, *App. Phys. Lett.* (submitted)
4. B. Chen, R. D. Dilanian, S. Teichmann, B. Abbey, A. G. Peele, G. J. Williams, P. Hannaford, L. Van Dao, H. M. Quiney, and K. A. Nugent, *Phys. Rev. A* **79**, 023809 (2009).



STRUCTURE DETERMINATION METHODS PROGRAM

The Structure Determination Methods Program (SDP) consists of CSIRO researchers working broadly within the fields of X-ray and electron crystallography in collaboration with other CXS Centre members. Its main aim is to develop novel experimental techniques and data analysis methods for extracting structural information from 2-D crystals and 3-D nanocrystals, especially relating to the determination of the structure of the pharmaceutically very important class of proteins known as integral membrane proteins. This program brings with it internationally recognised expertise in the preparation, purification, crystallization and handling of these samples.

The ongoing study of *Purple Membrane*, a naturally occurring 2-D crystal of the membrane protein *Bacteriorhodopsin*, serves as a useful test case because there is high-resolution structural information available from 3-D X-ray crystallography and 2-D cryo-electron microscopy that can be used for comparison. Collaboration under CXS centre has helped link into expertise in developing and applying computer programs for deconvoluting data for diffraction from 2-D crystal powders and led to alternative ways to explore the use of 2-D crystal samples in the context of different X-ray diffraction techniques.

Development has begun of novel experimental and related theoretical methods for the preparation and analysis of powder samples for integral membrane proteins. These techniques include preparation of and data collection from various 2-D crystal powders, a little explored line of approach. They offer the exciting possibility of providing alternative and easier paths to the X-ray structure determination of this very important class of proteins that have mostly resisted efforts based on conventional 3-D single-crystal methods.

On the CSIRO Molecular & Health Technologies (CMHT) side, work has progressed on the preparation of a number of different types of powder samples of integral membrane proteins consisting of preferentially and randomly oriented 2-D crystal layers.

Work at CSIRO Materials Science and Engineering (CMSE) has been continuing on the development of analytical methods for structure determination using X-ray diffraction with two-dimensional 2-D protein crystals in powder samples. The research can broadly be divided into three areas. The first is concerned with fitting 2-D powder diffraction data using a non-empirical approach based on a physical model of the scattering process. The second and third areas are closely linked: phase retrieval and refinement, and structure determination. While these are separate problems, they are generally best treated together. Structure determination in the 2-D crystal powder diffraction context amounts to reconstruction of a 2-D projection map of the electron density in the crystal. This can be viewed as a technique between coherent diffractive imaging and 3-D crystallography aimed at high-resolution 3-D structure determination. The advantage of the technique being developed here is that it does not require 3-D crystals, nor does it require 2-D crystals of the size needed for structure determination by electron diffraction.

ACHIEVEMENTS

SAMPLE PREPARATION

Preparation of 2-D crystals have allowed us to collect higher resolution (up to 4 Å) data using the protein crystallography beamline at the Australian synchrotron, compared to previous attempts (7 Å). Further work is continuing in the sample preparation area to push further the resolution of the data. We will continue to optimise the sample preparation and try different beam lines, including the SAXS/WAXS and the micro-focus beamline which has just become available at the Australian Synchrotron in order to obtain higher resolution data.

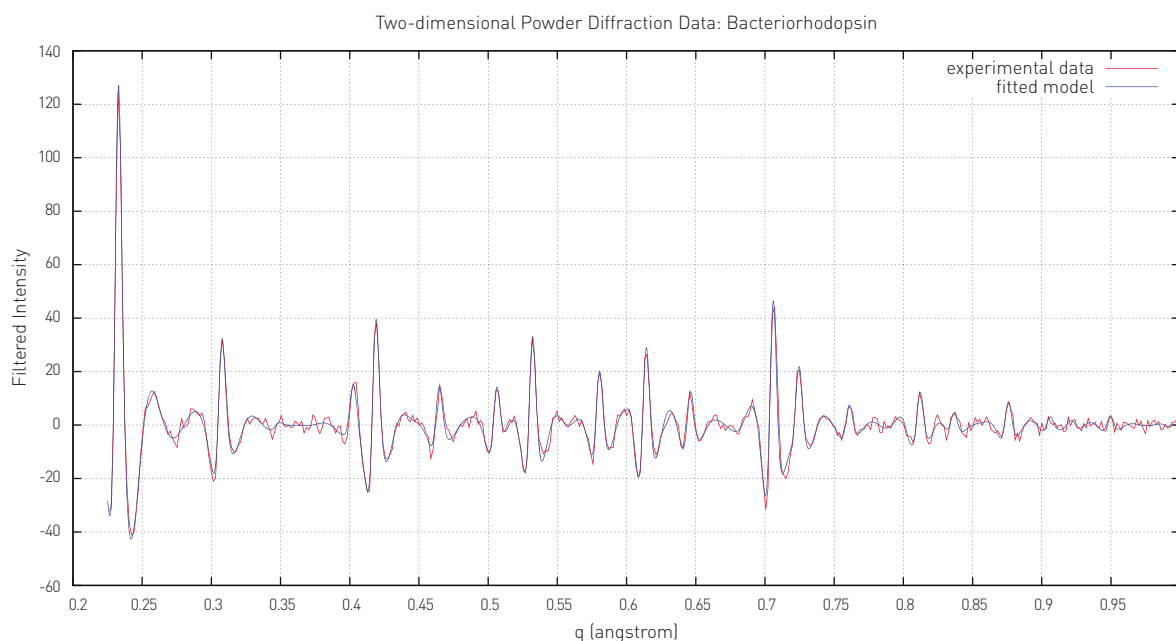


Figure 1: Integrated 2-D powder diffraction profile for *Bacteriorhodopsin* with experimental data and least-squares fit of theoretical model developed at CSIRO.

FITTING 2-D POWDER DIFFRACTION DATA

A method for fitting experimental 2-D powder diffraction data has been developed using a model based on a physical description of the scattering process. The model explicitly takes into account known physical properties of the sample, such as the 2-D nature of the crystallites, unit cell parameters, characteristic crystallite size, and the non-uniform randomly distributed orientations of the crystallites. The theoretical model has been incorporated in computer programs used for fitting the 2-D powder diffraction patterns.

The fitting scheme also includes strategies, analogous to the Rietveld method for 3-D crystal powder diffraction data, for resolving partially overlapping reflections in experimental 2-D powder diffraction data. A two-step process is involved. First, the plane group and the corresponding location of every reflection are specified by 2-D indexing of the data. Second, a parametrised model profile, based on physical properties of the sample, is assigned to each reflection, followed by a least squares fit for the unknown parameters, including Bragg peak intensities that contain structural information about the contents of the unit cell. All reflections except those that overlap exactly reflections may be resolved using this approach.

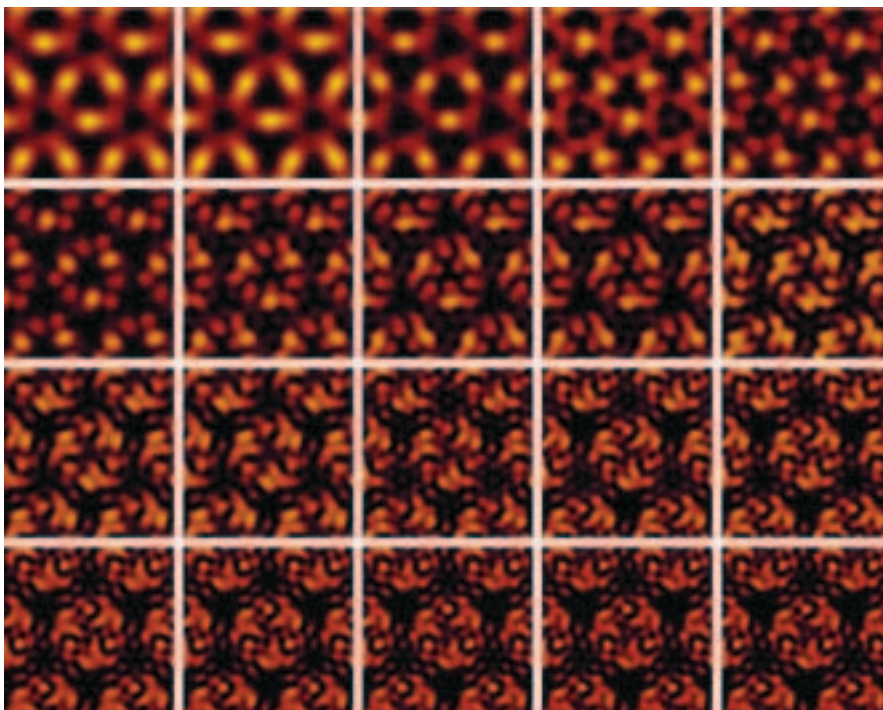
These analytical methods have been applied successfully to fitting 2-D powder diffraction data for *Bacteriorhodopsin*, obtained at the Advanced Photon Source, Chicago Synchrotron. (See Fig. 1.)

PHASING AND STRUCTURE DETERMINATION

Techniques for phasing of 2-D powder diffraction data as well as for the treatment of ambiguities in the data due to exactly overlapping non-equivalent reflections have been developed using an integrated approach, in conjunction with work on structure determination methods. To test the effectiveness of new methods, X-ray powder diffraction data were generated in simulations for model structures of 2-D crystalline *Bacteriorhodopsin*, based on the near atomic resolution molecular model (protein data base, PDB, entry 1BRD) and the more complete but lower resolution model for purple membrane (PDB entry 2BRD). Work in collaboration with fellow CXS Centre member, Ruben Dilanyan, at the University of Melbourne is ongoing, employing maximum entropy methods (MEM) for structure determination and phasing.

A number of methods have been explored for phasing and structure determination, including MEM, compressive sensing, electron density participation ratio minimisation, charge and solvent flipping, and solvent flattening. The latter of these has been found to be the most promising thus far for obtaining 2-D projections of the electron density in the unit cell.

Figure 2: Iterative refinement evolution of solvent-flattened electron density projection map for *Bacteriorhodopsin* reconstructed from 2-D powder diffraction data. The final map (bottom right) includes data to 6.8 Å resolution.

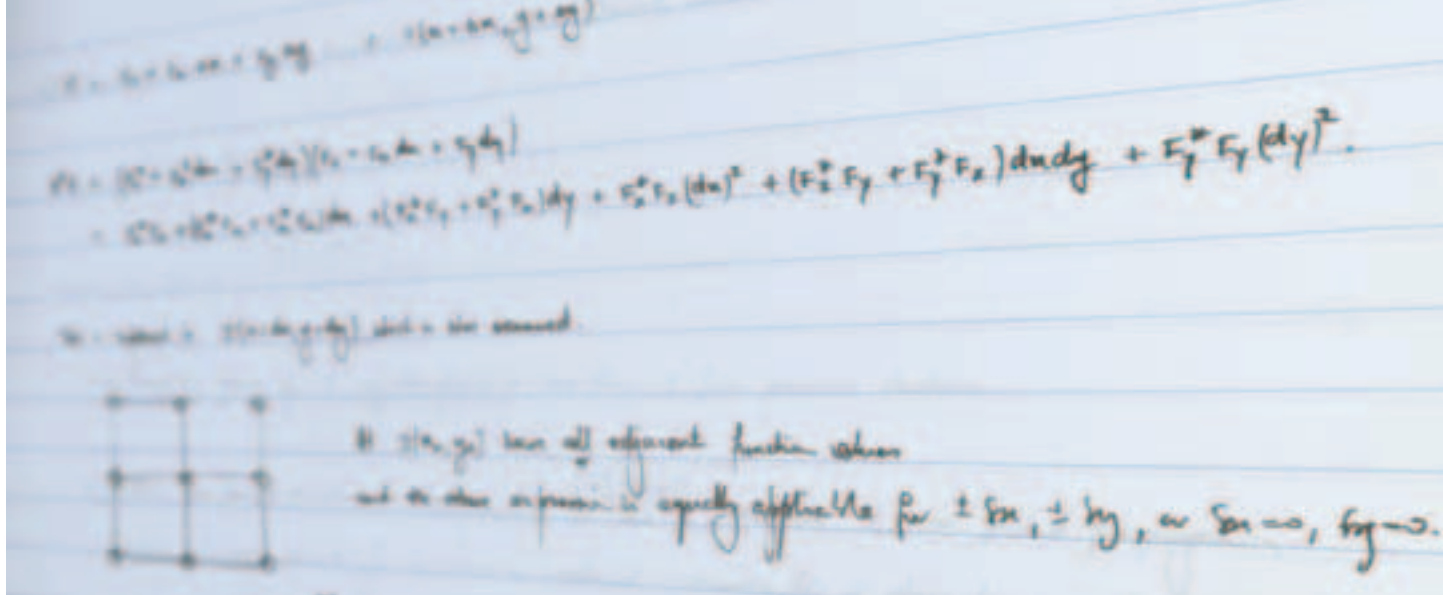


STRUCTURE DETERMINATION METHODS CASE STUDY

ELECTRON DENSITY RECONSTRUCTION USING SOLVENT FLATTENING IN 2-D

The solvent flattening method, which is commonly used in conventional 3-D protein crystallography for phase refinement, has been adapted here to 2-D powder diffraction data. A stepwise “one data point at a time” iterative scheme has been implemented and reconstructions performed from previously acquired synchrotron data. The algorithm incorporates a strategy for resolving exactly overlapping non-equivalent reflections by imposing constraints that ensure consistency with experimental data while allowing other parameters to evolve within the solvent flattening scheme. The algorithm requires a low-resolution initial guess for the electron density projection map, which may be obtained from theoretical considerations or alternative experimental methods such as electron microscopy or atomic force microscopy. The X-ray diffraction structure is solved by iterative refinement of the electron density map constrained by the experimental data and the flat solvent criterion.

An electron density map projection at 6.8 Å resolution has been obtained for *Bacteriorhodopsin* using this approach. Work continues on improving the robustness of the algorithm, especially with respect to sensitivity to the initial guess for the electron density, by incorporating a figure-of-merit weighting scheme for unknown phases, and by imposing additional constraints based on prior knowledge and information theoretical considerations, as expressed in the Maximum Entropy Principle.



THEORY AND MODELLING PROGRAM

The Theory and Modelling Program (TMP) is responsible for developing the theoretical and computational physics needed to support the experimental programs in CXS.

Our interests involve (i) the solution of inverse problems (ii) the characterization of partial spatial and temporal coherence in short wavelength light sources (iii) the relativistic formulation of molecular electronic structure and quantum electrodynamics (iv) the dynamical description of non-linear interactions between molecules and strong coherent fields (v) coherent energy transfer processes in biomolecules and (vi) the design of efficient computational algorithms.

Goals: The Theory and Modelling Program collaborates closely with the other programs in the Centre, especially in identifying fruitful directions for the experimental programs to pursue, and by supporting these activities with theoretical and computational tools. The key aims of TMP involve the development of:

- Image reconstruction algorithms for diffraction data obtained using sources exhibiting partial spatial or temporal coherence.
- Quantum electrodynamical models of high-harmonic generation in atomic systems using visible and infra-red light sources and of the interaction of molecules with strong-field high-frequency X-ray free-electron laser (XFEL) sources.
- Non-interferometric phase recovery techniques in photon echo spectroscopy.

Activities and outcomes: The Theory and Modelling Program collaborates closely with the physics-based experimental activities in CXS: the Experimental Methods Program (EMP), the Short Wavelength Laser Source Program (SWLP) and the Ultra-Cold Plasma Source Program (UCP).

Our collaboration with SWLP in 2008 was driven by a core aspect of the work of CXS, in which short wavelength light from a high-harmonic generation (HHG) source is used in diffractive imaging. This research originally required that the HHG light source be rendered monochromatic by the use of a monochromator, which would have been accompanied by an attendant loss of flux. We were able to devise a new algorithm for imaging using this spatially coherent VUV source, in which the raw power of the HHG source is used in the image reconstruction process, even though the illumination is highly polychromatic. This approach involves the detailed characterization of the polychromatic source by a Young's two-slit experiment, and the use of another innovative computational scheme to extract the power spectrum by a maximum entropy algorithm.

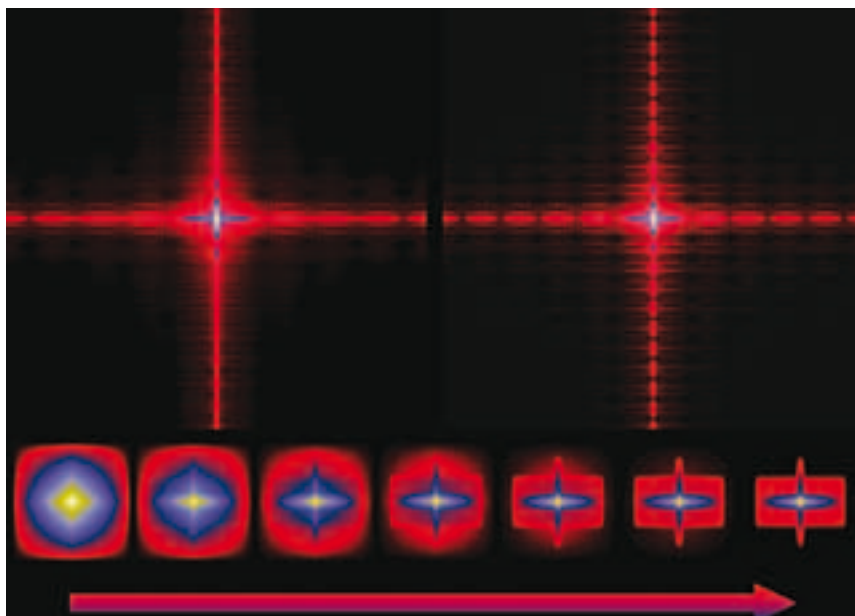
We also continued to develop phase retrieval techniques in Fourier transform spectroscopy, and the use of this technique in understanding energy transfer dynamics within chromophores. A partnership involving members of SWLP, TMP, EMP and a Japanese researcher were successful in attracting ARC Discovery Project funding to pursue the continued development of this approach.

A non-iterative phase retrieval algorithm developed by TMP, which is based on functional analysis, was adopted by UCP in order to image cold atom clouds from a single optical measurement. The development of this technique provides a good example of how regular interactions between the groups can fortuitously lead to surprising solutions to problems. This project sprang out of student report by Sebastian Saliba, in which it became clear that the standard techniques were deficient. This has since been developed into a routine methodology within UCP for imaging the cold-atom clouds that are to be used as targets in their ultra-cold plasma research.

Of course, our well-established interactions with EMP continued and strengthened in 2008. The coherent mode description of partially coherent sources proposed by TMP has been developed by members of EMP as a powerful tool in the characterization of partially coherent sources and their practical use in high-resolution imaging applications. We have participated in the development of diffractive imaging methods as quantitative techniques in analyzing the compositions of nanoscale objects, the phase retrieval of vortical wavefields, and the role of phase curvature in ameliorating the effects of partial spatial coherence in diffractive imaging experiments.

We also continued a long-standing collaboration with the University of Perugia in the development of high-performance algorithms in relativistic density functional theory. These will feed into CXS programs through the development of 'real-time' methods for modelling the time-evolution of molecular systems subjected the light from fourth-generation XFEL sources.

Figure 1: Simulated diffraction data for a polychromatic source (the two-step CDI algorithm). The panel at the top left represents the polychromatic diffraction data while the panel at the right represents the diffraction that would be obtained using a perfectly coherent, monochromatic source with a frequency selected to be at the maximum value of the power spectrum. The panels at the bottom of the figure represent the refinement of the autocorrelation function of the monochromatic representation during the maximum entropy procedure used to isolate the single frequency component.



ACHIEVEMENTS

The primary focus of the group during 2008 was the support of the SWLP group in their efforts to develop an imaging technology using their HHG source. This collaboration was based on a proposal by TMP that an attempt be made to use the output power spectrum produced by the source without passing it through a monochromator, in order to maximize the flux available for imaging. This necessitated the development of new algorithms to recover images from the polychromatic diffraction data. We have identified two distinct approaches to overcome these difficulties. Two approaches were developed by Ruben Dilanyan to recover images from polychromatic data. In the first of these, the power spectrum of the source is used to extract a representation of the diffraction data corresponding to a single wavelength component of the polychromatic data, from which an imaging solution can be obtained directly; *the two-step CDI algorithm*.

In the second approach, an image is obtained by propagating independently the frequency components of the exit surface wave at the sample, which are combined in the detector plane to reproduce the polychromatic diffraction data as closely as possible; *the multi-wavelength CDI algorithm*. In both cases, the power spectrum must first be obtained by inverting the diffraction data obtained from a Young's two-slit experiment using the known analytical relationship between measure intensities, the degree of partial coherence of each frequency component and the geometrical parameters that define the experimental configuration.

Figure 1 represents an example of the *two-step CDI algorithm*. The left-hand panel represents a simulation of a diffraction pattern obtained using a polychromatic source. On the right is the diffraction pattern that would have been obtained if the illumination were monochromatic, in which case standard methods of analysis can be used to obtain an image of the diffracting object.

Maximum entropy methods were used in both approaches to refine the analysis of the diffraction data for the target object, and for the determination of the power spectrum of the source. The approach proved to be sufficiently powerful that our simulations were able to serve as a reliable diagnostic tool in the design of the experiments, which were exploring uncharted territory in the landscape of diffractive imaging. The collaboration between TMP, EMP and SWLP succeeded in performing diffractive imaging experiments using a laboratory-based HHG source with a median wavelength of 32 nm, and with power distributed across six harmonic of the 806 nm infra-red driving laser. Details of the experiment may be found in the contributions by EMP and SWLP.

A collaboration between TMP and SWLP also led to the award of an ARC Discovery Project grant for the further development of non-interferometric Fourier transform spectroscopy. This combines experimental expertise in time-resolved photon echo spectroscopy with a computational approach to obtaining the phase information that is lost in the act of measurement. This approach is able to identify energy pathways in light-harvesting molecules, and has already led to the identification of quantum coherence effects that lead to unusually long-lived excited in some naturally occurring chromophores. This is important information in piecing together an understanding of the remarkable efficiency of the energy transfer processes involved in photosynthesis, and find future application in the design of quantum information and solar energy harvesting nanoscale devices.

In our long-standing collaboration with our partners at the University of Perugia, we developed an algorithm to construct a detailed representation of the electronic state of complex molecules containing heavy elements, within the relativistic density functional formalism. So efficient is this scheme that it is now possible to proceed with the development of quantum dynamical models for the interaction of complex molecular systems and strong electromagnetic fields. This is of significance to one of the core research targets of CXS, which involves the study of the interaction between molecules and the spatially coherent high-frequency light produced by X-ray free-electron lasers. This fundamental research in the quantum electrodynamics of non-linear, electrodynamic interactions is vital if fourth-generation light sources are ever to be used in their intended role in diffractive imaging experiments on isolated biomolecules.

Some of our preliminary work in modelling non-linear interactions in molecule laser interactions is shown in Figure 2. Here, Olena Ponomarenko has investigated the simplest molecular system, H_2^+ , in the field of a strong infrared laser field using a one-centre finite

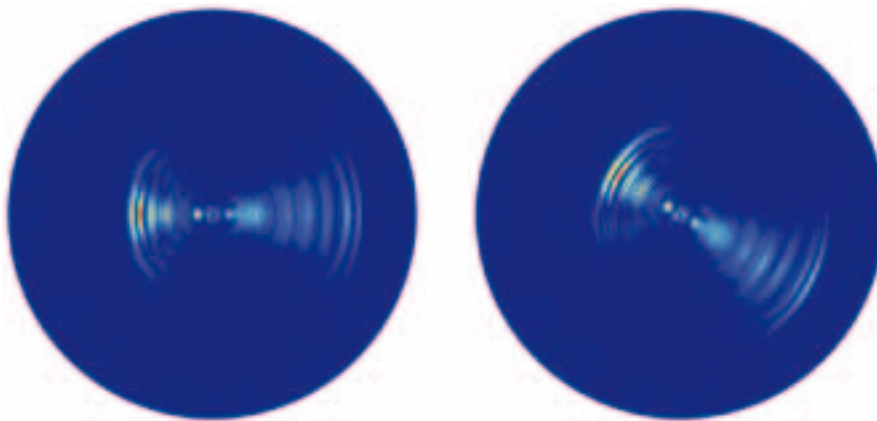


Figure 2: Electron density of an H_2^+ molecule ion subjected to a strong external laser field. In the left panel the molecular axis is aligned with the polarization axis of the laser field; the molecular axis is at an angle of 30 degrees to the polarization axis in the right-hand panel. The repeated scattering of the laser-driven electron by the Coulomb fields of the nuclei leads to pronounced diffraction of the electron density.

difference expansion of the three-dimensional molecular wavefunction. The development of these tools will enable us to investigate the possibility of extracting structural information directly from non-linear processes using infrared and visible light sources, where the non-linear response of the electronic structure to the field generates, in effect, a nanoscale electron diffraction experiment.

THEORY AND MODELLING PROGRAM CASE STUDY

This could be considered a 'Cold Case' study, and a reminder that successful collaborative science is essentially a social enterprise requiring good communication between participants. When the Ultra-Cold Plasma Source (UCP) group first joined CXS, it wasn't clear what support TMP could offer them, since their goals were already very clear but essentially experimental in nature. It turned out, however, that they had a need to image their cold plasmas using a single diffraction measurement, a fact that only became apparent to TMP in a student presentation by Sebastian Saliba. As luck would have it, TMP had recently published an imaging technique based on functional analysis rather than differential calculus, in which the phase structure of an optical wavefield could be determined, under certain conditions, from a single measurement of its Fresnel diffraction pattern. These 'certain conditions' are that the diffracting object should be finite and smooth, and that the illumination be well-approximated by a sum of Gaussian functions. It was an interesting formal development, but one without an obvious application. Saliba managed to mention all of these critical triggers in his talk, which meant that TMP and UCP were able to begin an immediate collaboration to solve this fundamental problem. Under the subsequent expert guidance of David Sheludko, the somewhat esoteric 'one-shot density functional' imaging scheme has been developed by UCP into a quantitative tool for characterizing the ultra-cold plasmas that will soon be used to generate ultra-bright coherent electron pulses for CXS imaging applications. A more detailed account may be found in the UCP Research Report. This offers a perfect example of the nodes CXS operating as they should.



UCP group and friends celebrate the establishment of the new UCP laboratory.

ULTRA-COLD PLASMA SOURCE PROGRAM

The Ultra-Cold Plasma Source Program (UCP), formed within CXS in 2007, is developing an ultra-bright, coherent source of electrons for imaging of biologically relevant molecules.

By applying technical developments taken from the ultra-cold atom community, and the theoretical algorithms developed in the TMP program, we hope to leapfrog current electron imaging modalities. The enhanced probe-molecule interaction strength that a coherent electron source offers, combined with an improvement of four orders of magnitude in brightness over existing electron sources, will enable high-resolution imaging of biological targets with atomic scale resolution.

The key to the UCP source and the basis of the dramatic enhancement in brightness that it promises is the origin of the electrons: they will be extracted from ultra-cold atoms, just a few millionths of a degree above absolute zero. The brightest conventional electron sources start with hot material, by blasting a target with a high-energy laser pulse. The hot electrons then expand like steam from a kettle, and are equally difficult to tame and control. Electrons extracted from ultra-cold atoms can be accelerated and focused with unprecedented resolution. The comparison is like the difference between a conventional light bulb and a laser: we need laser-like coherence to be able to image molecular structure with atomic resolution.

The UCP team has strong expertise with ultra-cold atom technology, with conventional optical imaging, and with electron optics. They are collaborating with the world-leading research group in this area, at the University of Eindhoven in the Netherlands. The project is strongly connected with the Centre's TMP program: firstly, to develop methods for characterizing the very high coherence of the electron beams and, secondly, to adapt the Centre's imaging approaches for applications in characterizing the cold atom cloud. In the longer term, we aim to unravel the electron-molecule interactions so that target structural information can be separated from the diffraction data. Once the source becomes operational, the UCP program will benefit from the imaging hardware, data capture and visualization technology developed by the Centre's EMP program. The ultimate goal, the high-impact demonstration of electron diffraction from molecules, will require close liaison with the Biological Sciences Program, to determine the optimum biological targets and the appropriate sample preparation strategies. These inter-program collaborations are simply not available to other groups around the world and will allow the UCP team to rapidly achieve high-impact results across disciplines.

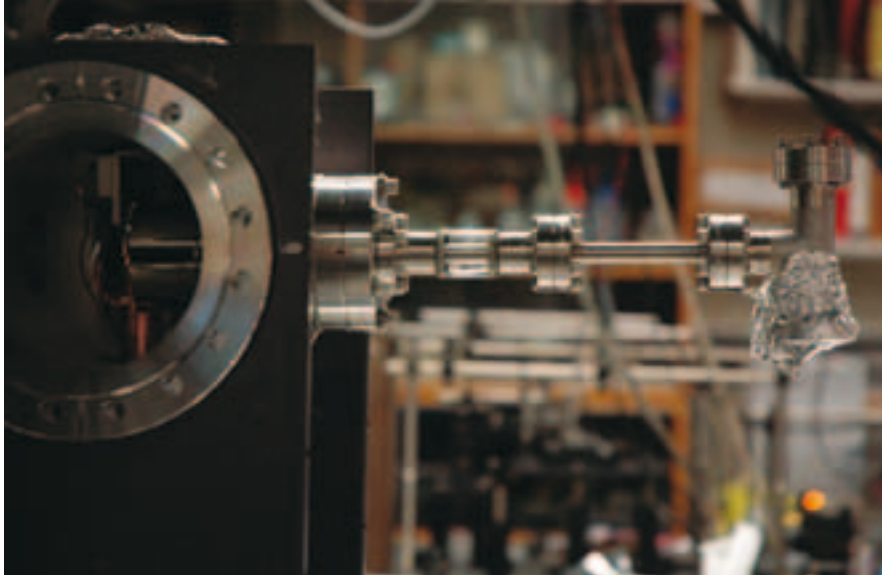


Figure 1: Rubidium oven during early stage of construction.

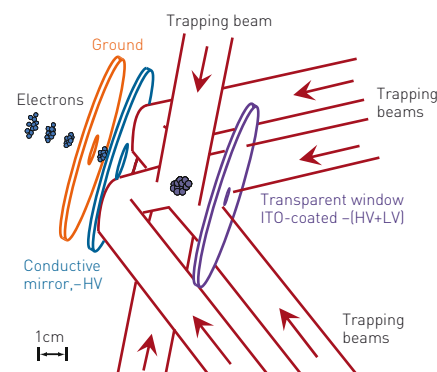


Figure 2: Combination mirror/electrode system, to cool and trap atoms, and accelerate electrons.

ACHIEVEMENTS

The first steps to achieving electron diffractive imaging of molecules using the proposed high-brightness source include:

- attaining a high-density cold atom cloud, inside an electrostatic accelerator
- ionization of the cold atoms, and acceleration to produce an intense bunch of cold electrons
- control of the shape of the electron bunches, to eliminate space-charge spreading.

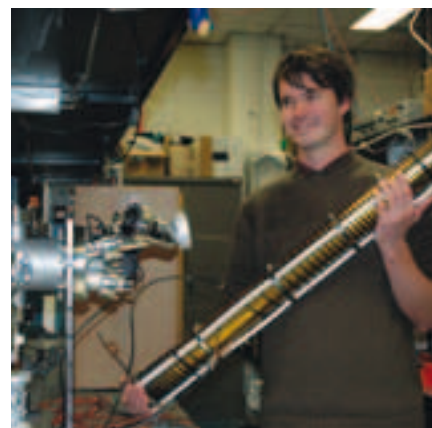
The group has created the first stage of the cold atom source: a rubidium oven followed by a Zeeman slower to reduce the atomic velocity from 350m/s down to a few tens of m/s. A novel design based on a single-layer coil has been successfully designed, constructed, and tested, and has attracted considerable interest from the cold-atom community.

In parallel, a new atom trap has been designed and constructed. The design includes three electrostatic accelerator electrodes: one is also a mirror, to reflect the laser light that cools and traps the atoms; another is transparent to allow the laser light to pass through, though still electrically conductive.

Once the atoms have been cooled and trapped at micro-Kelvin temperatures, they will be *ionized* with a nanosecond flash of blue light. The light will be produced with a pulsed, amplified dye laser, which has recently been acquired and installed using funding from the ARC Linkage-Equipment program.

Even though ultra-cold, the electron bunch will still expand, due to the electrostatic repulsion between the like-charged particles. The expansion can be *reversed*, provided the initial electron density distribution is uniform. In principle, the density distribution can be controlled by shaping the cold atom cloud, via the laser beams that trap the atoms. To shape the atom cloud, it is necessary to first image the cloud. In 2008, the UCP team demonstrated two new approaches to imaging cold atoms. Diffraction contrast imaging (DCI) uses the known ratio between the atomic cloud absorption and phase, to construct a column density distribution from a single diffraction image. The method was applied to selectively imaging atoms in an excited state [*Phys Rev A* **77**, 033401, 2008].

The second method is based on coherent diffractive imaging (CDI) concepts from the TMP group. The method is important across cold atom research areas, such as for Bose-Einstein Condensation experiments, because it allows for the first time a method to extract both the amplitude and phase of an atomic cloud, using only non-interferometric intensity images.



Simon Bell holding the innovative single layer tapered Zeeman slower coil, before final installation.



UCP student, David Sheludko (right), discusses the ultracold plasma project with Christoph Hofmann, a visitor from the ultra-cold plasma group at the University of Freiburg, Germany.

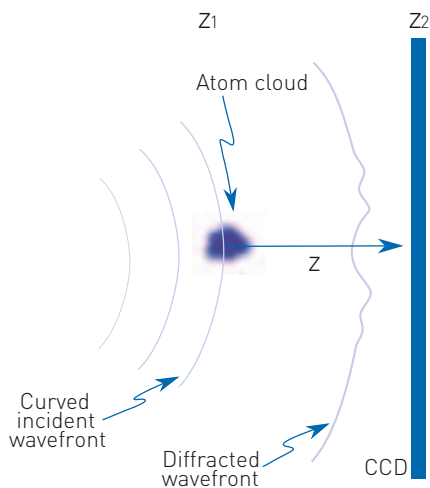
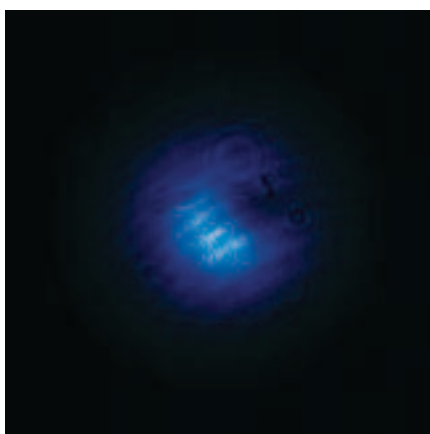
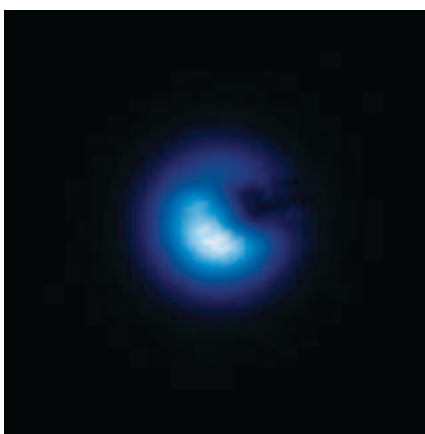


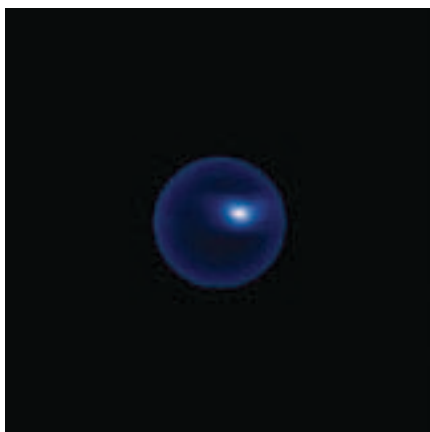
Figure 1: Coherent diffractive imaging of an ultra-cold rubidium cloud. A diverging laser, tuned close to the rubidium resonance wavelength, is diffracted by the atoms. The intensity of the diffracted wave is recorded on a CCD detector.



a



b



c

Figure 2: Coherent diffractive imaging of an ultra-cold rubidium cloud. (a) raw diffraction pattern; (b) simulation; (c) reconstructed image of cold atom cloud (bright blob slightly above and right of centre).

ULTRA-COLD PLASMA SOURCE PROGRAM CASE STUDY

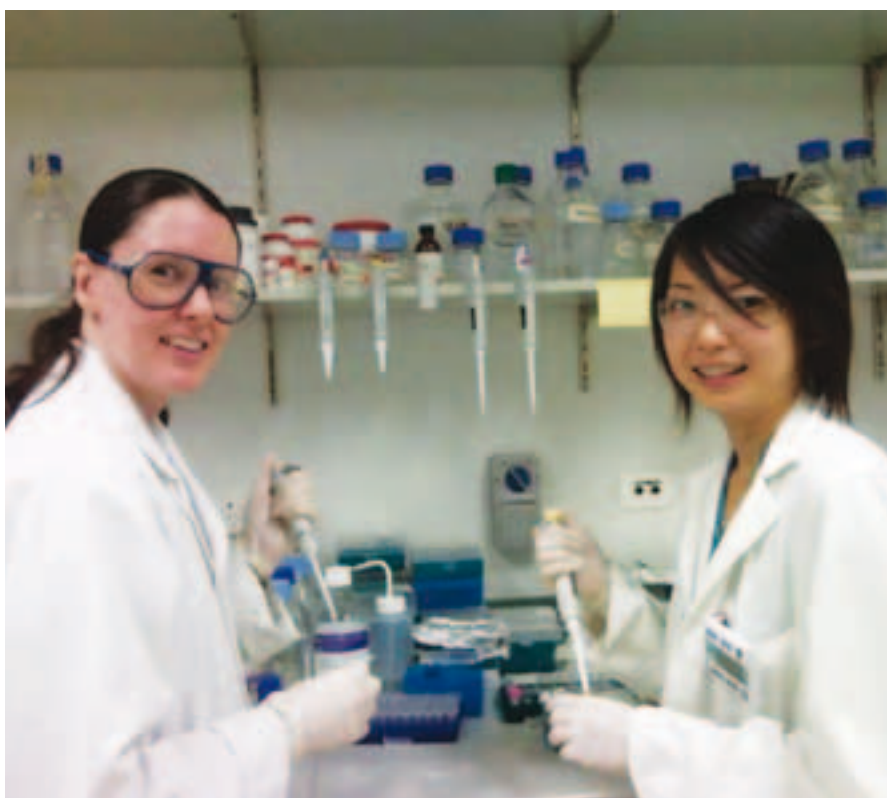
COHERENT DIFFRACTIVE IMAGING OF COLD ATOMS

In 2008, the UCP team demonstrated two new approaches to imaging cold atoms. Diffraction contrast imaging (DCI) uses the known ratio between the atomic cloud absorption and phase, to construct a column density distribution from a single diffraction image. The method was applied to selectively imaging atoms in an excited state [*Phys Rev A* **77**, 033401, 2008]. The second method is based on coherent diffractive imaging (CDI) concepts from the TMP group. The method is important across cold atom research areas, such as for Bose-Einstein Condensation experiments, because it allows, for the first time, a method to extract both the amplitude and phase of an atomic cloud, using only non-interferometric intensity images. The figures show the setup and results for a cloud of rubidium atoms at temperature below 100 μ K. A diverging laser, tuned close to the rubidium resonance wavelength, is diffracted by the atom cloud (Fig. 1). The intensity of the diffracted wave is recorded (Fig. 2a) and using the CXS algorithm, reconstructed to extract the density map of the cloud (Fig. 2c).



STUDENTS LIFE
@ CXS

STUDENTS LIFE @ CXS



Janelle William and Lynn Liang

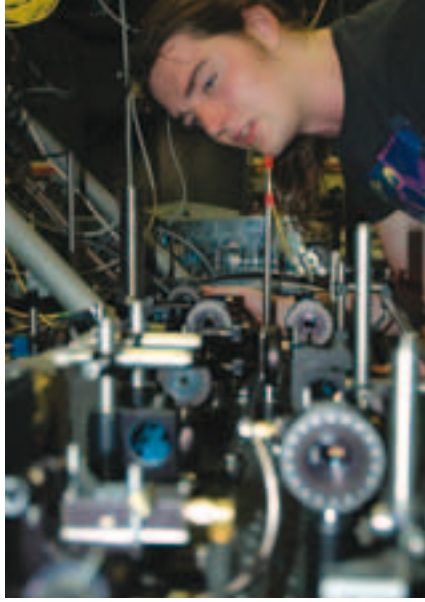
LYNN LIANG, STRUCTURE DETERMINATION METHODS PROGRAM

CSIRO PARKVILLE

My 12 months as a member of CXS has taught me what it is like to work in a group and I have valued the great support I have received from the Centre. As a member of CXS, I was given the opportunity to attend several workshops where great ideas were exchanged by interactions with other members of CXS. These workshops had speakers from all around the world, which expanded my knowledge with cutting-edge theories and techniques within and outside my fields of research. The opportunity to meet various scientists with different expertise has helped me consider my research question from new and different perspectives. Being a member of CXS has allowed me to obtain valuable experiences and knowledge that will help in achieving my research goals.



Mr Michael Baker preparing recombinant Tim9 and Tim10 proteins for structural studies in the Mitochondrial Biogenesis and Disease Ryan Laboratory



Andy McCulloch ensuring optical alignment



Jesse Clark

MICHAEL BAKER, BIOLOGICAL SCIENCES PROGRAM

LA TROBE UNIVERSITY

My PhD studies in Mike Ryan's laboratory have focused on analyzing the structure and function of the mitochondrial Tim9-Tim10 complex, which chaperones membrane proteins through the mitochondrial intermembrane space.

This has been in collaboration with the Gulbis group at WEHI.

In February of 2008, some of these findings were presented at the international Lorne Conference on Protein Structure and Function. In June, I visited the lab of Professor Thomas Langer in Cologne, Germany and presented some of my findings to his group, which were well-received. In addition, I attended the Mitochondrial Physiology and Pathology meeting in Bari and the Biochemistry of Cell Regulation conference in Athens, where aspects of my work were presented. I was also invited to speak at the annual Melbourne Protein Group meeting, where I was fortunate enough to win an oral presentation prize. Furthermore, I was invited to present some of my findings at the CXS annual meeting and also at the first 'AussieMit' meeting in Melbourne. Lastly, late last year my work was accepted for publication in *Molecular Biology of the Cell*.

ANDY MCCULLOCH, ULTRA-COLD PLASMA SOURCE PROGRAM

UNIVERSITY OF MELBOURNE

My first year with CXS was 2008, as an Honours student in the Ultra-Cold Plasma (UCP) group. My project was concerned with the production and focussing of an ultra-cold atom beam, which was not directly related to the UCP project. My project was concerned with the production and focussing of an ultra-cold beam, which although was not directly related to the UCP program's goals, nevertheless, provided valuable insight into the techniques used in UCP work, and formed the basis for the PhD project.

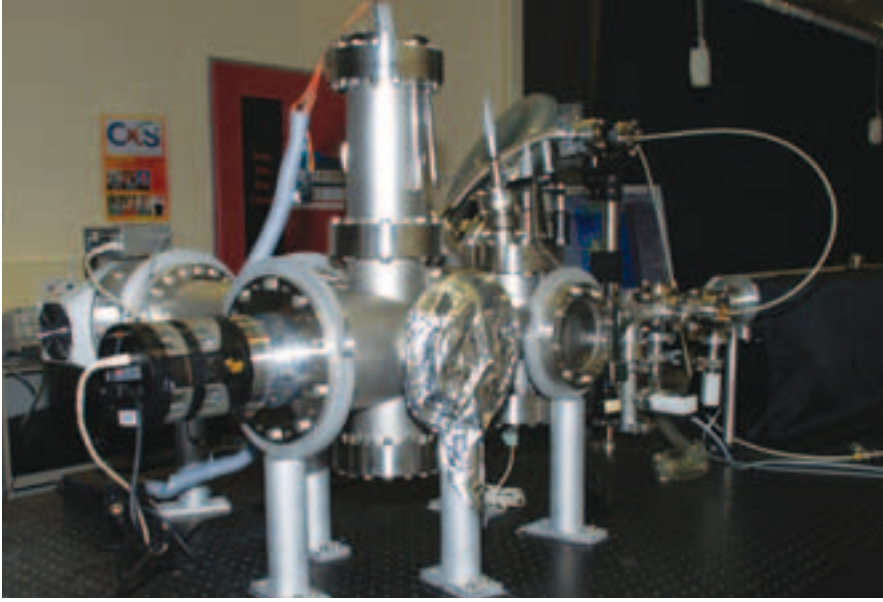
All members of both the UCP group and the CXS community were extremely welcoming, with the highlight of 2008 being the CXS workshop held in September. This provided an opportunity to hear about current research, as well as interact and collaborate with some of the world leaders in the field of biological imaging. I am grateful for the opportunity to work in the CXS, and look forward to continuing my research with the Centre.

JESSE CLARK, EXPERIMENTAL METHODS PROGRAM

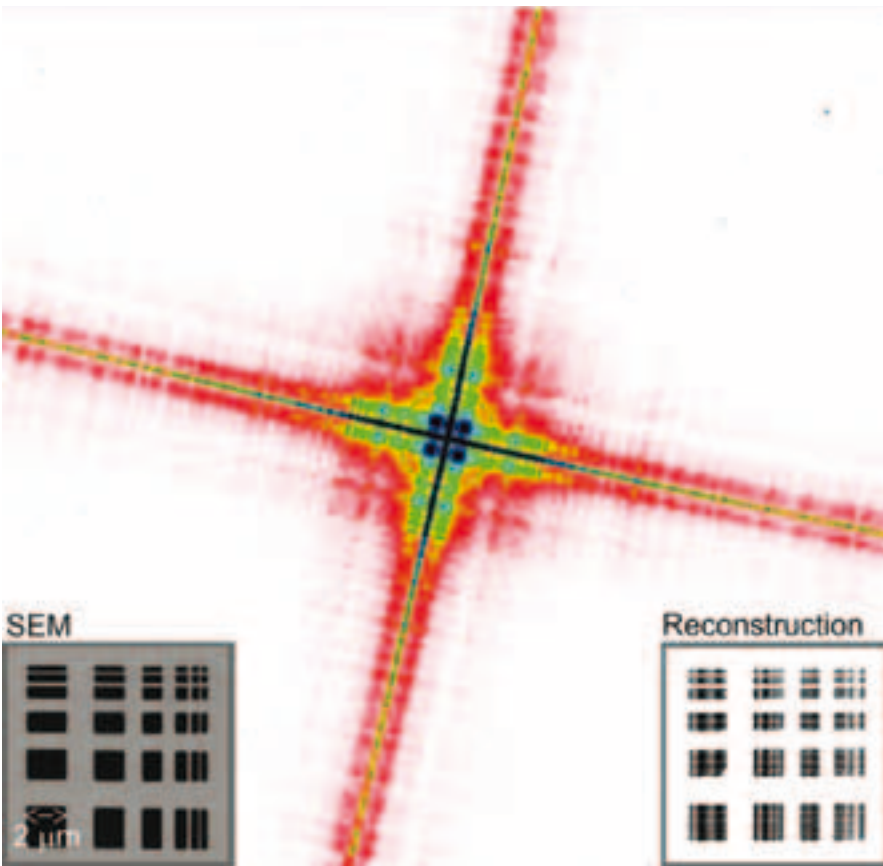
LA TROBE UNIVERSITY

Since joining the CXS at the start of 2006, to undertake a PhD in Fresnel Coherent Diffractive Imaging (FCDI) with the Experimental Methods Program, my experience has been very positive, and 2008 was no exception. The year was quite busy with four trips made to the Advanced Photon Source to conduct experiments. Each of these experiments was invaluable, providing me with a wealth of experience about experimental physics and FCDI. Another highlight was the opportunity to present recent work at the CXS workshop, 'Biologists and Physicists working together'. The workshop also provided the opportunity to meet and chat with high profile scientists in the field.

Being a part of CXS has allowed me to work on a number of different experiments and projects; and in 2008, several of these were published. Overall 2008 was a very enjoyable year.



The main part of the high-harmonic generation machine (femtosecond laser not in the picture).



A high-dynamic range multiple-harmonic orders diffraction pattern; the right inset shows the non-periodic binary sample; the left inset displays the object reconstructed from the diffraction pattern.

SVEN TEICHMANN, SHORT WAVELENGTH LASER SOURCE PROGRAM

SWINBURNE UNIVERSITY
OF TECHNOLOGY

The year 2008 has been the most important during my doctorate in the SWLP group of CXS. After the installation of the femtosecond laser system in March 2007 and refurbishment of our laboratory at Swinburne, preparing the HHG apparatus for CDI meant even more work on and constant improvement of the experimental setup for refining the conditioning of the HHG emission, sample control and positioning, and improving the quality of high-angle CDI. The work paid off and, in collaboration with the EMP and TMP groups, high-spatial resolution reconstruction of the acquired diffractive images was achieved. Another highlight was the opportunity to attend the conference Ultrafast Phenomena 2008 in Italy and learn from fellow academics that have been doing HHG for CDI for several years. In addition, the CXS annual workshop, and the seminars and joint group meetings provided an excellent opportunity for broadening horizons and for professional and social networking.



CXS
MANAGEMENT
& GOVERNANCE

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's Science, Technology and Innovation (STI) Initiative.

As Lead Administering node, the University of Melbourne manages the grants and distributes funds in accordance with the signed agreements. These agreements cover CXS management, collaboration and intellectual property arrangements.

All collaborating organisations are represented within CXS boards. Commercial expertise is represented on the CXS Intellectual Property Committee and Sub Committee. A Scientific Advisory Board and a General Advisory Board have been established and meet annually.

CENTRE MANAGEMENT

The CXS Management team and its Executive Committee are responsible for administration as it pertains to centre policy, performance, financial matters, research output, research training and professional education of members, partnerships, national and international liaison, commercialisation and outreach.

The management team is:

PROFESSOR KEITH NUGENT
Director of Research

PROFESSOR LEANN TILLEY
Deputy Director of Research

MS TANIA SMITH
Chief of Operations

From Left: Ms Tania Smith, Professor Keith Nugent, Professor Leann Tilley





EXECUTIVE COMMITTEE

During 2008, administration of CXS was overseen by the Executive Committee, which comprises:

MS ROSSLYN BALL

Executive Officer to Committee

DR CHRIS HALL

Detector and Beamline Development Group Member

PROFESSOR KEITH NUGENT

Research Director

ASSOCIATE PROFESSOR ANDREW PEELE

Experimental Methods Group Leader

DR HARRY QUINEY

Theory and Modelling Group Leader

ASSOCIATE PROFESSOR MIKE RYAN

Biological Sciences Group Leader

ASSOCIATE PROFESSOR ROBERT SCHOLTEN

Ultra-Cold Plasma Source Program Group Leader

MS TANIA SMITH

CXS Chief of Operations

ASSOCIATE PROFESSOR TREVOR SMITH

Short Wavelength Laser Source Group Member

PROFESSOR LEANN TILLEY

Deputy Research Director

PROFESSOR LAP VAN DAO

Short Wavelength Laser Source Group Leader

DR JOSE VARGHESE

Structure Determination Methods Co-Group Leader

DR STEVE WILKINS

Structure Determination Methods Group Leader

ADVISORY BOARD

The CXS Advisory Board met in September 2008 as part of the 3rd Annual CXS Workshop – *Physicists and Biologists Working Together*. The meeting focussed on key areas such as papers and articles, patent possibilities, linkages, the ARC review, management and outreach.

PROFESSOR MICHAEL BARBER

Vice Chancellor Flinders University, or nominee

PROFESSOR TIM BROWN

Deputy Vice Chancellor (Research) La Trobe University

PROFESSOR EDWINA CORNISH

Deputy Vice Chancellor (Research) Monash University, or nominee

PROFESSOR ANDREW FLITMAN

Pro Vice-Chancellor (Research) Swinburne University of Technology, or nominee

PROFESSOR JOHN HELLIWELL

Professor of Structural Chemistry University of Manchester

DAVID KRENUS

CEO, Cyclotek

DR STEPHEN LANE

Chief Science Officer NSF Centre for Biophotonic, Science & Technology, UC Davis

PROFESSOR PETER RATHJEN (CHAIR)

Deputy Vice Chancellor (Research) University of Melbourne

PROFESSOR BONNIE WALLACE

Professor of Crystallography Birkbeck College

BRUCE WHAN

Chairman of INNOVIC (Victorian Innovation Centre Ltd) & Director Swinburne Knowledge

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PROFESSOR LEANN TILLEY

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Professor of Crystallography Birkbeck College

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FABIENNE PERANI

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TATIANA TCHERNOVA

Administrator, Swinburne University

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BIOLOGICAL SCIENCES PROGRAM

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PhD Student, La Trobe University

TIM BROWN

Research Assistant, La Trobe University

DR JENNY CARMICHAEL

Research Fellow, La Trobe University

SAMANTHA DEED

Research Assistant, La Trobe University

DR MATT DIXON

Research Fellow, La Trobe University

LAHIRU GANGODA

MSc Student, La Trobe University

DR JACQUI GULBIS

Structural Biology Division, WEHI

DR ERIC HANSEN

Research Fellow, La Trobe University

DR NICK KLONIS

Associate Researcher, La Trobe University

LYNN LIANG

PhD Student, La Trobe University

DR ALEX MAIER

Research Fellow, La Trobe University

DR PAUL MCMILLAN

Research Fellow, La Trobe University

LAURA OSELLAME

PhD Student, La Trobe University

ASSOCIATE PROFESSOR MIKE RYAN

Program Leader, La Trobe University

PROFESSOR LEANN TILLEY

CXS Deputy Director, La Trobe University

JEFF YEOMAN

PhD Student, La Trobe University

DETECTOR AND BEAMLINE DEVELOPMENT PROGRAM

EVAN CURWOOD

PhD Student, Monash University

DR WILFRED FULLAGER

Research Fellow, Monash University

DR CHRIS HALL

Research Fellow, Monash University

DR GEORGE JUNG

Research Fellow, Monash University

PROFESSOR ROB LEWIS

Program Leader, Monash University

ADAM LYNCH

Technical Assistant, Monash University

EXPERIMENTAL METHODS PROGRAM

DR BRIAN ABBEY

Research Fellow, University of Melbourne

MAC BA LUU

MSc Student, La Trobe University

DR BENEDICTA ARHATARI

Research Fellow, La Trobe University

DR EUGENIU BALAU

Research Fellow, La Trobe University

GUIDO CADENAZZI

PhD Student, University of Melbourne

DR BO CHEN

Research Fellow, University of Melbourne

JESSE CLARK

PhD Student, La Trobe University

SAMUEL FLEWETT

PhD Student, University of Melbourne

KEVIN HANNAH

PhD Student, La Trobe University

CLARE HENDERSON

MSc Student, University of Melbourne

ASSOCIATE PROFESSOR ANDREI NIKULIN

Research Fellow, Monash University

DR ROBERT NORMAN

Research Fellow, La Trobe University

PROFESSOR KEITH NUGENT

CXS Director, University of Melbourne

ASSOCIATE PROFESSOR ANDREW PEELE

Program Leader, La Trobe University

DR MARK PFEIFER

Research Fellow, La Trobe University

COREY PUTKUNZ

PhD Student, La Trobe University

DR CHANH TRAN

Research Fellow, La Trobe University

ANGELA TORRANCE

Honours Student, University of Melbourne

KAUSHAL VORA

Research Fellow, La Trobe University



LACHLAN WHITEHEAD
PhD Student, La Trobe University

DR GARTH WILLIAMS
Research Fellow, University of Melbourne

SHORT WAVELENGTH LASER SOURCE PROGRAM

DR JEFFREY DAVIS
Research Associate, Swinburne University

PROFESSOR PETER HANNAFORD
ARC CAOUS, Swinburne University

DR CRAIG LINCOLN
Research Fellow, University of Melbourne

ASSOCIATE PROFESSOR TREVOR SMITH
Chemistry, University of Melbourne

SVEN TEICHMANN
PhD Student, Swinburne University

PROFESSOR LAP VAN DAO
Program Leader, Swinburne University

DR CHUNYU ZHANG
Research Fellow, Swinburne University

STRUCTURE DETERMINATION METHODS PROGRAM

AMANDA ALOIA
PhD Student, CSIRO - Parkville

DR MATTEO ALTISSIMO
CSIRO - Clayton

DR CONNIE DARMANIN
CSIRO - Parkville

PROFESSOR CAL DRUMMOND
Membrane Chemistry, CSIRO - Parkville

DACHAO GAO
CSIRO - Clayton

DR TIM GUREYEV
CSIRO - Clayton

DR STEVE HOMOLYA
CSIRO - Clayton

LYNN LIANG
PhD Student, CSIRO - Parkville

DR PETER LYNCH
CSIRO - Clayton

DR SHERRY MAYO
CSIRO - Clayton

DR DAMIAN E. MYERS
University of Melbourne

DR YAKOV NESTERETS
CSIRO - Clayton

DAVID PARRY
CSIRO - Clayton

DR ANDRE POGANY
CSIRO - Clayton

DR ANDREW STEVENSON
CSIRO - Clayton

DR VICTOR STRELTISOV
CSIRO - Clayton

DR JOSE VARGHESE
Group Leader, CSIRO - Parkville

DR STEVE WILKINS
Program Leader, CSIRO - Clayton

JANELLE WILLIAMS
Research Fellow, CSIRO - Parkville

THEORY AND MODELLING PROGRAM

DR RUBEN DILANIAN
Research Fellow, University of Melbourne

DR OLENA PONOMARENKO
Research Fellow, University of Melbourne

DR HARRY QUINEY
Program Leader, University of Melbourne

ULTRA-COLD PLASMA SOURCE PROGRAM

SIMON BELL
PhD Student, University of Melbourne

STEFANIA CASTELLETTO
Research Fellow, University of Melbourne

MARTIJN JASPERSE
Honours Student, University of Melbourne

DR MARK JUNKER
Research Fellow, University of Melbourne

LIAM MCGUINNESS
Honours Student, University of Melbourne

SEBASTIAN SALIBA
PhD Student, University of Melbourne

ASSOCIATE PROFESSOR ROB SCHOLTEN
Program Leader, University of Melbourne

DAVID SHELUDKO
PhD Student, University of Melbourne



MEMBER DEPARTURES

The following members departed CXS in 2008:

BRIAN ABBEY

Experimental Methods Program,
University of Melbourne

MARIO BELTRAN

Experimental Methods Program,
La Trobe University

ANDY BERRY

Detector and Beamline Development
Program, Monash University

CHERRINE CHAN

Biological Sciences Program,
La Trobe University

JAN DALHAUS

Theory and Modelling Program,
University of Melbourne

CHANDNI DOSHI

Experimental Methods Program,
La Trobe University

EMMA DUGLAS

Administrator for the La Trobe
University node

LAHIRU GANGODA

Biological Sciences Program,
La Trobe University

ROSS FERNLEY

Structure Determination Methods Program,
CSIRO

TOM LAKTYUSHIN

Biological Sciences Program,
La Trobe University

CRAIG LINCOLN

Short Wavelength Laser Source Program,
University of Melbourne

ROGER LOWDEN

Ultra-Cold Plasma Source Program,
University of Melbourne

JOHN MCKENZIE

Chair of CXS Advisory Board,
University of Melbourne

TED MCMURCHIE

Structure Determination Methods Program,
CSIRO

STEPHEN MUDIE

Structure Determination Methods Program,
CSIRO

SERGUEY PRIYMAK

Theory and Modelling Program,
University of Melbourne

LYNNE WADDINGTON

Structure Determination Methods Program,
CSIRO

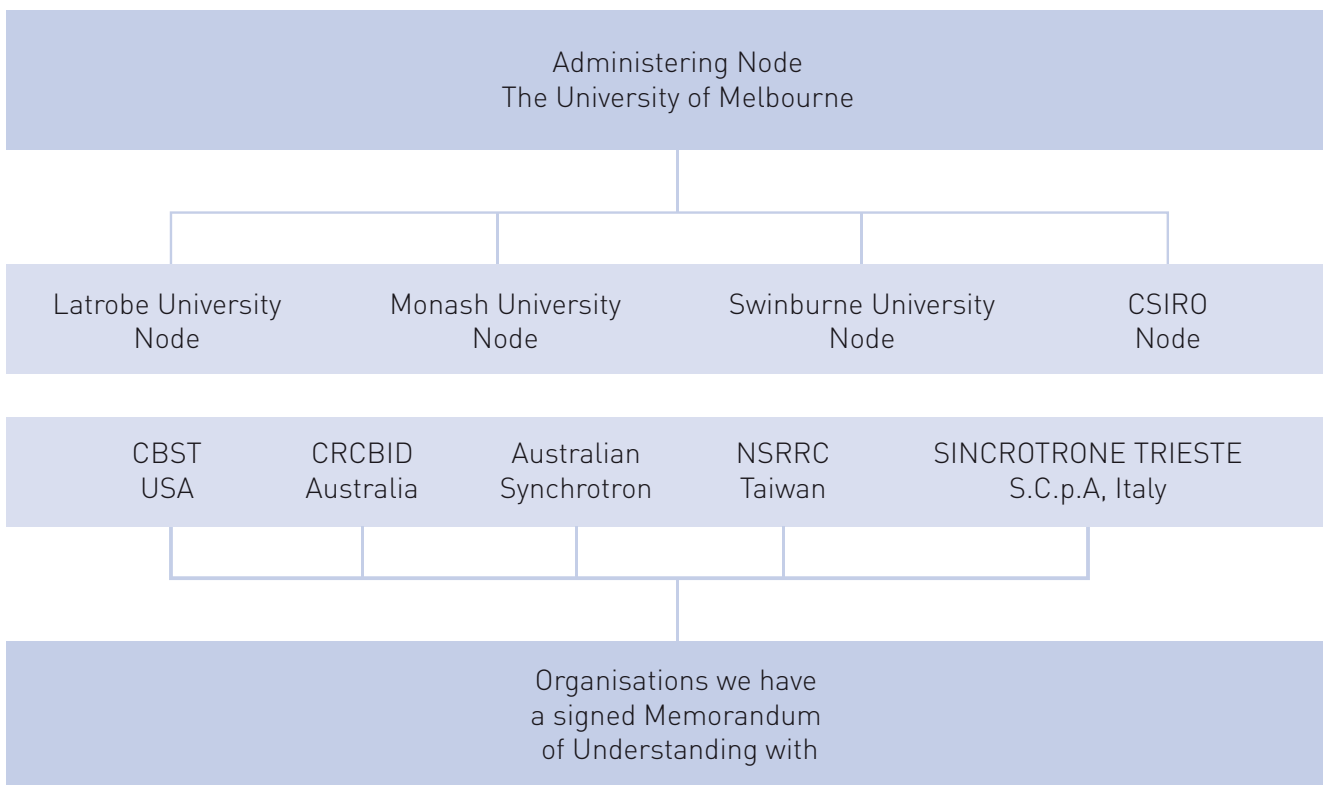
PETER WICHTA

Short Wavelength Laser Source Program,
University of Melbourne



Internal view of the Australian Synchrotron

ORGANISATIONAL CHART AS OF JUNE 2008



PRESENTATIONS, CONFERENCES & LABORATORY VISITS

DR BRIAN ABBEY

- Invited Speaker – Advanced Photon Source, Argonne, USA (February)
- Invited Speaker – CXS Workshop in Detectors for Coherent X-ray Diffractive Imaging, Monash University, Melbourne, Australia (May)
- Invited Speaker – CXS Biological Samples and Preparation Workshop, La Trobe University, Melbourne, Australia (May)
- Speaker – IC021 2008, Sydney, Australia (July)
- Invited Speaker – 3rd Annual CXS Workshop, Melbourne, Australia (September)

DR BENEDICTA AHATARI

- Invited Speaker – CXS Biological Samples and Preparation Workshop, La Trobe University, Melbourne, Australia (May)
- Speaker – IC021 2008, Sydney, Australia (July)
- Poster Presentation – 3rd Annual CXS Workshop, Melbourne, Australia (September)

MICHAEL BAKER

- Invited Speaker – Department of Genetics, University of Cologne, Germany (June)
- Oral Presentation – Melbourne Protein Group Meeting, Melbourne, Australia (August)
- Invited Speaker – 3rd Annual CXS Workshop, Melbourne, Australia (September)

DR EUGENE BALAUR

- Poster Presentation – 3rd Annual CXS Workshop, Melbourne, Australia (September)

SIMON BELL

- Invited Speaker – KOALA Conference 08, Queensland, Australia (November)

ANDY BERRY

- Attended – IEEE Medical Imaging Conference, Dresden, Germany (October)

JESSE CLARK

- Poster Presentation – 3rd Annual CXS Workshop, Melbourne, Australia (September)

EVAN CURWOOD

- Attended – Position Sensitive Detector Conference 8, Glasgow, Scotland (October)

DR ROUBEN DILANIAN

- Invited Speaker – 3rd Annual CXS Workshop, Melbourne, Australia (September)

DR CONNIE DARMANIN

- Attended – HERCULES Workshop, Grenoble, France (February)
- Invited Speaker – 3rd Annual CXS Workshop, Melbourne, Australia (September)

DR JEFF DAVIS

- Attended – International Conference on Ultrafast Phenomena, Maggiore, Italy (June)

SAMUEL FLEWETT

- Poster Presentation – 3rd Annual CXS Workshop, Melbourne, Australia (September)
- Poster Presentation – IEEE 2008, Dresden, Germany (October)

DR JACQUELINE GULBIS

- Attended – UK Membrane Protein Structure Initiative Meeting, Maryland, USA (February)

DR CHRIS HALL

- Speaker – SSRF/AS Bilateral workshop, Australian Synchrotron, Melbourne, Australia (May)
- Speaker – CXDI Detector Workshop, Monash University, Melbourne, Australia (May)
- Attended – Position Sensitive Detector Conference 8, Glasgow, Scotland (October)

PROFESSOR PETER HANNAFORD

- Poster Presentation – 5th Asian Conference on Ultrafast Phenomena, National University, Singapore (January)

DR ERIC HANSSEN

- Invited Speaker – Annual Meeting of the NSF Centre for Biophotonic Science and Technology, California, USA (July)
- Visitor – laboratory of Professor Carolyn Larabel, University of California, California, USA (July)
- Visitor – Laboratory of Dr Joe DeRisi and Professor John Sadat, University of California, California, USA (July)

- Co-Chair session – Melbourne Protein Group Meeting, Melbourne, Australia (August)
- Invited Speaker – 3rd Annual CXS Workshop, Melbourne, Australia (September)

DR STEVEN HOMOLYA

- Poster Presentation – CAMS 2008, California, USA (February)

PROFESSOR ROB LEWIS

- Keynote Speaker – Annual Scientific Meeting of Medical and Imaging & Radiation Therapy, Melbourne, Australia (April)
- Speaker – CXDI Detector Workshop, Monash University, Melbourne, Australia (May)
- Invited Speaker – Pacific Rim International Conference on Protein and 4th Asian Ocean Human Proteome Organisation, Brisbane, Australia (June)
- Invited Speaker – RadAIM Conference, Gold Coast, Brisbane, Australia (July)
- Attended – Queensland Institute for Medical Research Seminar, Queensland, Australia (August)
- Visitor – Dandenong Development Board, Melbourne, Australia (August)
- Attended – Christie Hospital Seminar, Manchester, United Kingdom (September)
- Co-host – MCSS/CSIRO New Synchrotron Users Symposium, Melbourne, Australia (September)

- Invited Speaker – Ludwig Institute for Cancer Research, Melbourne, Australia (October)

DR CRAIG LINCOLN

- Attended – Advanced optical Imaging Workshop, University of Melbourne, Melbourne, Australia (January)
- Poster Presentation – 5th Asian Conference on Ultrafast Phenomena, National University, Singapore (January)
- Visited – Ultrafast laboratories, University of Toronto, Toronto, Canada (May)

PROFESSOR KEITH NUGENT

- Invited Speaker – NSLS-II Workshop, National Synchrotron Light Source, New York, USA (March)
- Invited Speaker – Wilhelm and Else Heraeus-Seminar, Physikzentrum Datteln, Germany (March)
- Keynote Speaker – ARC inaugural Graeme Clark Research Outcomes Forum, Canberra, Australia (April)
- Chair – BHP-Billiton Science Prizes Committee, Melbourne, Australia (April)
- Invited Speaker – Australian Synchrotron, Melbourne, Australia (May)
- Chair – Program Committee, Congress of the International Commission for Optics, Sydney, Australia (July)

- Invited Speaker – ICO21 2008, Sydney, Australia (July)
- Invited Speaker – Microscopy & Microanalysis 2008, Albuquerque, USA (August)
- Chair – Australian Synchrotron International Program Advisory Committee, Melbourne, Australia (September)
- Host – 3rd CXS Annual Workshop, Melbourne, Australia (September)
- Member – Program Committee, Synchrotron Radiation Instrumentation International Conference, Melbourne, Australia, September, 2009
- Invited Speaker – University of California Davis, California, USA (October)
- Member – X-ray Microscopy & Imaging Advisory Committee, Advanced Photon Source, Argonne National Laboratory, Illinois, USA (October)
- Invited Guest – Griffith University, Queensland, Australia (November)

LAURA OSELLAME

- Speaker – Harden Conference on Mitochondrial Physiology, Dublin, Ireland (July)
- Co-Chair session – Melbourne Protein Group Meeting, Melbourne, Australia (August)



CXS 3rd Annual Workshop Audience

ASSOCIATE PROFESSOR ANDREW PEELE

- Invited Guest – Ideas Factory on Tomographic Image Reconstruction and Analysis Workshop, Manchester, United Kingdom (January)
- Attended – X-ray Vision, Monash Centre for Synchrotron Science, Monash University, Melbourne, Australia (February)
- Invited Speaker – Second International Symposium on X-ray Phase Contrast Imaging, Anhui, China (March)
- Invited Speaker – Australian Synchrotron, Melbourne, Australia (May)
- Invited Speaker – ICO21 2008, Sydney, Australia (July)
- Invited Speaker – ALS User's Workshop 2008, Berkeley, California, USA (October)
- Invited Speaker – IEEE 2008, Dresden, Germany (October)

DR MARK PFEIFER

- Invited Speaker – Advanced Photon Source, Argonne, USA (February)
- Invited Speaker – CXS Biological Samples and Preparation Workshop, La Trobe University, Melbourne, Australia (May)
- Speaker – ICO21 2008, Sydney, Australia (July)
- Invited Speaker – 3rd Annual CXS Workshop, Melbourne, Australia (September)

DR OLENA POMOMARENKO

- Poster Presentation – International Conference On Nanoscience and Nanotechnology, Melbourne, Australia (February)
- Attended – MPI in parallel computational algorithms, Australian National University, Canberra, Australia (March)
- Attended – Gordon Conference, New Hampshire, USA (May)
- Presentation – The 2008 World Congress of The World Association of Theoretical and Computational Chemists, Sydney, Australia (September)
- Poster Presentation – 8th Biennial Australian Institute of Physics Congress, Adelaide, Australia (November)

COREY PUTKUNZ

- Invited Speaker – CXS Biological Samples and Preparation Workshop, La Trobe University, Melbourne, Australia (May)
- Poster Presentation – 3rd Annual CXS Workshop, Melbourne, Australia (September)

DR HARRY QUINEY

- Invited Speaker – University of Perugia, Italy (March)
- Invited Speaker – University of Auckland, New Zealand (August)

ASSOCIATE PROFESSOR MIKE RYAN

- Invited Speaker – AAS Australian Frontiers in Science, Canberra, Australia (February)
- Chair – Lorne Conference on Protein Structure and Function, Victoria, Australia (February)
- Seminar Presentation – Australian High Commission, Kuala Lumpur, Malaysia (February)
- Invited Speaker – Universiti Sains Malaysia, Malaysia (February)
- Invited Speaker – Universiti Patra Malaysia, Malaysia (February)
- Invited Speaker – Universiti Kebangsaan Malaysia, Malaysia (February)
- Invited Speaker – Universiti Sains Islam Malaysia, Malaysia (February)
- Invited Speaker – University of Malaya, Malaysia (February)
- Seminar Presentation – Department of Physiology, University of Melbourne, Melbourne, Australia (March)
- Invited Speaker – University of Freiburg, Germany (June)
- Seminar Presentation – Institute of Molecular Bioscience, University of Queensland, Australia (October)
- Seminar Presentation – IMB, Queensland, Australia (October)

ASSOCIATE PROFESSOR ROB SCHOLTEN

- Poster Presentation – OSA Conference, Wollongong, Australia (February)

DAVID SHELUDKO

- Invited Speaker – 3rd Annual CXS Workshop, Melbourne, Australia (September)

TANIA SMITH

- Invited Speaker – ARC Centre of Excellence for Quantum Computer Technology Annual Workshop, Melbourne, Australia (February)

ASSOCIATE PROFESSOR TREVOR SMITH

- Attended – Advanced optical Imaging Workshop, University of Melbourne, Melbourne, Australia (January)
- Poster Presentation – 5th Asian Conference on Ultrafast Phenomena, National University, Singapore (January)
- Invited Speaker – 5th Asian Conference on Ultrafast Phenomena, National University, Singapore (January)
- Invited Speaker – 3rd Advanced Optical Techniques Workshop, Shenzhen, China (May)
- Invited Speaker – 7th International Weber Symposium on Fluorescence Methodologies in Biochemistry and Medicine, Kauai, USA (June)
- Attended – IUPAC Symposium on Photochemistry, Gothenburg, Sweden (July)
- Attended – RACI Physical Chemistry Student Conference, McLaren Vale, South Australia (July)

PROFESSOR LEANN TILLEY

- Invited Speaker – Pasteur-WEHI Workshop, Melbourne, Australia (January)
- Invited Speaker – Molecular Approaches to Malaria, Lorne, Australia (February)
- Chair – Lorne Conference on Protein Structure and Function, Victoria, Australia (February)
- Invited Speaker – University of Technology, Sydney, Australia (March)
- Invited Speaker – Department of Microbiology, Monash University, Melbourne, Australia (May)
- Invited Speaker – Institut National de la Transfusion Sanguine, Paris France (July)
- Invited Speaker – Pasteur Institute, Paris France (July)
- Invited Speaker – Montpellier University, Montpellier, France (July)

SVEN TEICHMANN

- Poster Presentation – 5th Asian Conference on Ultrafast Phenomena, National University, Singapore (January)
- Attended – International Conference on Ultrafast Phenomena, Maggiore, Italy (June)
- Invited Speaker – 3rd Annual CXS Workshop, Melbourne, Australia (September)

DR CHANH TRAN

- Speaker – 21st X-ray conference on X-ray and Inner-Shell Processes, Paris, France (June)
- Speaker – ICO21 2008, Sydney, Australia (July)

PROFESSOR LAP VAN DAO

- Poster Presentation – 5th Asian Conference on Ultrafast Phenomena, National University, Singapore (January)
- Invited Speaker – 5th Asian Conference on Ultrafast Phenomena, National University, Singapore (January)
- Attended – National Institute of Advanced Industrial Science and Technology Seminar, Tsukuba, Japan (April)

DR JOSE VARGHESE

- Invited Speaker – AIP Council, University of Melbourne, Melbourne, Australia (February)
- Led workshop – CAMS 2008, California, USA (February)
- Invited Speaker – CXS Public Lecture Series, University of Melbourne, Melbourne, Australia (April)
- Invited Speaker – Accelerator Physics Workshop, University of Melbourne, Melbourne, Australia (April)
- Keynote Speaker – Adelaide, Protein Group Inaugural Meeting, Adelaide University, Adelaide, Australia (April)
- Invited Speaker – International Conference on Medicinal Chemistry, Vienna, Austria (August)
- Invited Speaker – Scientists in Schools Symposium, WEHI, Melbourne, Australia (October)

DR STEPHEN WILKINS

- Invited Speaker – European Synchrotron Radiation Facility, France (April)
- Visitor – European Synchrotron Radiation Facility, France (April)
- Visitor – KTH Royal Institute of Technology, Stockholm, Sweden (April)
- Invited Speaker – 2nd International Symposium on X-Ray Phase-Contrast Imaging, Anhui, China (April)
- Invited Speaker – SPIE Conference, Strasbourg, France (August)
- Invited Speaker – International Union of Crystallography, Osaka, Japan (December)

LACHLAN WHITEHEAD

- Speaker – ICO21 2008, Sydney, Australia (July)
- Poster Presentation – 3rd Annual CXS Workshop, Melbourne, Australia (September)
- Invited Speaker – Geoff Opat Seminar Series, University of Melbourne, Melbourne, Australia (October)
- Invited Speaker – KOALA Conference 08, Queensland, Australia (November)

DR GARTH WILLIAMS

- Invited Speaker – MCSS Seminar, Monash University, Melbourne, Australia (March)
- Invited Speaker – Swiss Light Source Seminary, Paul Scherrer Institute, Switzerland (May)
- Invited Speaker – XRM 2008, Zurich, Switzerland (July)
- Invited Speaker – IUCr 2008, Osaka, Japan (August)
- Invited Speaker – ALS User's Workshop 2008, Berkeley, California, USA (October)
- Invited Speaker – Linac Coherent Laser Source Users Workshop, Stanford University, USA (October)
- Invited Speaker – International Union of Crystallography, Osaka, Japan (December)

JANELLE WILLIAMS

- Invited Speaker – CSIRO/Bio21 Protein Expression Workshop, Melbourne, Australia (August)

AWARDS & HONOURS

CXS recognised a number of its members for their work in 2008. We extend our congratulations to each of them for their efforts and awards in the following honours:

- Professor Keith Nugent was chosen by the Australian Research Council to address the inaugural Graeme Clark Research Outcomes Forum in Canberra.
- Professor Leann Tilley was appointed Associate Dean Research at La Trobe University.
- Kaushal Vora's paper, SidewaMST using deep X-Ray lithography was chosen by Institute of Physics for a special collection of journal articles. This collection was chosen by the editors for papers that show substantial advances or significant breakthroughs, have a high degree of novelty and/or have a significant impact on future research.
- Laura Osellame was awarded best student poster at the Lorne conference on Protein Structure and Function, February.
- Michael Baker was awarded best oral presentation at the Melbourne Protein Group Meeting, Melbourne, August.
- Laura Osellame was awarded a poster prize at the Melbourne Protein Group Meeting, Melbourne, August.



Professor Keith Nugent speaking at the Graeme Clark Research Outcomes Forum in Canberra

SCHOLARSHIPS & STUDENTSHIPS



Abhishek Awasthi



Minh Tam



Mac Ba Luu



Khuong Ba Dinh

We would like to congratulate the following students for their successful applications in 2008:

ABHISHEK AWASTHI

CXS Vacation Scholarship – Biological Science Program, La Trobe University

MINH TAM

CXS Internship – Experimental Methods Program, La Trobe University

BRAD STRINGER

CXS Summer student placement – Experimental Methods Program, La Trobe University

MAC BA LUU

CXS Summer student placement – Experimental Methods Program, La Trobe University

KHUONG BA DINH

3rd year scholarship with Short Wavelength Laser Source Program, Swinburne University of Technology



RESEARCH TRAINING & PROFESSIONAL EDUCATION

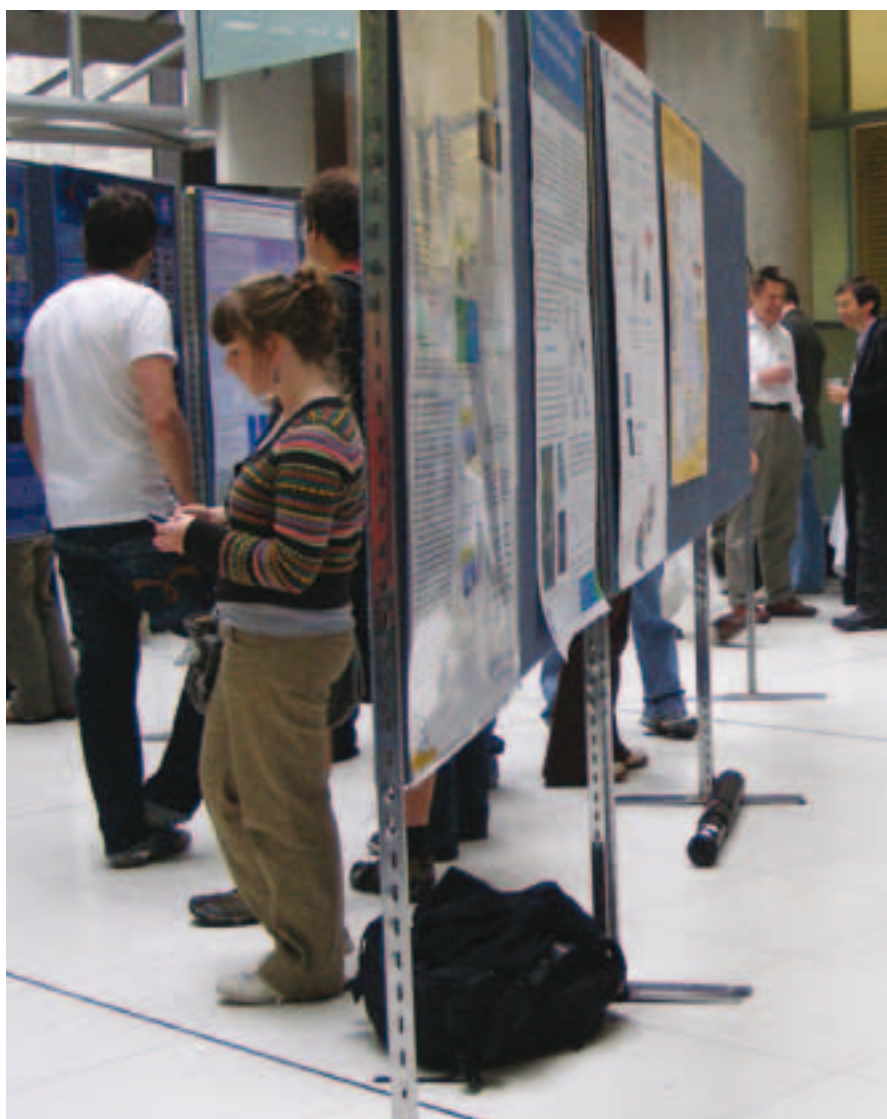
The Centre met all of its recruitment and professional education targets for 2008, and has exceeded expectations in the areas of *Postgraduate Recruitment* and *Presentations to Schools and/or Teaching Communities*. An increase in CXS member awareness was also a focus in 2008 with a number of media sources being utilised to educate members.

- Lahiru Gangoda completed a Masters degree by coursework after undertaking a CXS project on acid phosphatase as a cytochemical marker for microscopy applications.
- Summer student, Brad Stringer worked on tomography image processing. This resulted in a user macula for the rendering program and the demonstration of visualisation of some data sets.
- Sebastian Saliba of the Ultra-Cold Plasma Source program went to Freiburg, Germany to work on using EIT to probe frozen Rydberg gas.



Sam Flewett and Prof Keith Nugent at the CXS Member Overview 2008

WORKSHOPS



CXS 3rd Annual Workshop Poster Session

CXS conducted the following interdisciplinary workshops in 2008:

- 2nd Advanced Optical Imaging Workshop, University of Melbourne (January)
- CXS Biological Samples and Preparation Workshop, La Trobe University (May)
- CXS Workshop in Detectors for Coherent X-ray Diffractive Imaging, Monash University (May)
- *Ultra-Cold Matter and Scattering Workshop*, University of Melbourne (June)
- *3rd Annual CXS Workshop, Biologist and Physicists Working Together*, Melbourne (September)

VISITORS TO CXS



SHEILA AKINIRY
Emory University, USA

PROFESSOR BEN ADLER
ARC CoE Structural and Functional
Microbial Genomics, Australia

DR ALBERTO BRAVIN
European Synchrotron Radiation
Facility, France

PROFESSOR HENRY CHAPMAN
University of Hamburg, Germany

PROFESSOR ROSS COPPEL
ARC CoE Structural and Functional
Microbial Genomics, Australia

DR JOSEPH DERISI
University of California, USA

ASSOCIATE PROFESSOR JOANNE ETHERIDGE
Monash University, Australia

PROFESSOR JAMES FIENUP
University of Rochester, United Kingdom

DR ANN FRAZIER
La Trobe University, Australia

HIROSHI FUKUMURA
Sedai, Japan

AKIHIRO FURUBE
Tsukuba, Japan

DR RAINER HEINTZMANN
King's College of London, United Kingdom

DR LIZ HEWAT
Institut de Biologie Structurale Jean-Pierre
Ebel, France

DR CHRISTOPH HOFMANN
University of Freiburg, Germany

PROFESSOR SIMON HOOKER
Oxford University, United Kingdom

PROFESSOR SO IWATA
Imperial College, United Kingdom

ASSOCIATE PROFESSOR ANITA JONES
Edinburgh University, Scotland

DR URSULA KELLER
ETH Zurich, Switzerland

DR MARCUS KITCHEN
Monash University, Australia

DR D. KIELPINSKI
Griffith University, Australia

PROFESSOR Y. KOYAMA
Kwansei University, Japan

PROFESSOR WERNER KÜHLBRANDT
Max Plank Institute for Biophysics, Germany

PROFESSOR ROB LAMB
Australian Synchrotron, Australia

PROFESSOR CAROLYN LARABEL
University of California, USA

DR MARK LE GROS
University of California, USA

ASSOCIATE PROFESSOR TREVOR LITHGOW
Monash University, Australia

PROFESSOR JENNY MARTIN
University of Queensland, Australia

PROFESSOR RICK MILLANE
University of Canterbury, New Zealand

PROFESSOR JULIAN ROOD
ARC CoE Structural and Functional
Microbial Genomics, Australia

PROFESSOR VASSILIOS SARAFIS
Israel

PROFESSOR JOHN SEDAT
University of California, USA

DR KATE SOUSLOVA
Biological Faculty, Moscow State
University, Russia

PROFESSOR JOHN SPENCE
University of Arizona, USA

DR DANIELA STOCK
Victor Chang Cardiac Research
Institute, Australia

PROFESSOR LOTHAR STRÜDER
Max Plank Institute for Physics, Germany

DR BILL THOMLINSON
Canadian Light Source, Canada

ASSOCIATE PROFESSOR SCOTT TYO
University of Arizona, USA

**ASSOCIATE PROFESSOR EDGAR
VREDENBREGT**
Eindhoven University, Netherlands

**ASSOCIATE PROFESSOR CYNTHIA
WHITCHURCH**
University of Technology, Australia

PROFESSOR T WILSON
Oxford University, United Kingdom

PROFESSOR LISA XU
Shanghai Jiaotong University, China

DR WEN BING YUN
Xradia, USA



SCIENTIFIC LINKAGES

CXS is pleased to announce the signing of Memoranda of Understanding with:



Australian Synchrotron



National Synchrotron Radiation Research Center of Taiwan



ELETTRA



CRC for Biomedical Imaging Development



The Centre for Biophotonics Science and Technology



A number of ongoing collaborations continue to develop with the following groups:

CENTRE FOR HIGH PERFORMANCE COMPUTING, PERUGIA ITALY

Developing a scheme for the molecular dynamics of complex systems in strong radiation fields.

OXFORD UNIVERSITY

Collaboration on fundamental relativistic quantum mechanics with Professor I.P Grant FRS.

GRIFFITH UNIVERSITY

Collaboration between the Kielpinski attosecond laser physics group and CXS Theory and Modelling Program and Short Wavelength Laser Source Program.

BLACKETT LABORATORY, IMPERIAL COLLEGE LONDON

Investigating relativistic methods in electron scattering.

TOHOKU UNIVERSITY OF JAPAN

Investigating X-ray generation from thin liquid films.

ARC CENTRE OF EXCELLENCE FOR ANTIMATTER-MATTER STUDIES (CAMS), CURTIN UNIVERSITY OF TECHNOLOGY

To work on non-linear atomic processes.

ARC CENTRE FOR QUANTUM COMPUTING AND THE THEORY

Developing computational tools for designing configurations of phosphorus donors in silicon.

CRC BIOMEDICAL IMAGING DEVELOPMENT

Collaboration to develop interaction with the Experimental Methods Program and CXS.

ELETTRA

Meeting with Burkhard Kaulich regarding science at the ELETTRA FEL project.

NATIONAL INSTITUTE OF ADVANCED INDUSTRIAL SCIENCE AND TECHNOLOGY

Collaboration developed with the Short Wavelength Laser Source Program.

MATTHIAS WEIDEMULLER OF FREIBURG, GERMANY

Established a collaboration proposal through the ARC Discovery program to work on ultra-cold plasma for high-brightness electron sources.

AUSTRALIAN SYNCHROTRON

CXS is leading discussions with other interested parties to form a Beamline Advisory Panel for the development of the branch line at the soft X-ray beamline at the Australian Synchrotron.

COMMERCIALISATION

Professor Keith Nugent continued to head the development team of IATIA Ltd. Using their globally patented QPI technology, IATIA has continued to expand into life sciences, nanotechnology, ophthalmology and defence markets, with customers including GE Healthcare, Columbia University, Oxford University, the Federal Bureau of Investigations (FBI) and the Australian Defence Force.

moglabs



The Ultra-Cold Plasma Source Program developed the MOGLab's range of external cavity diode laser (ECDL) controllers. Each MOG unit provides everything needed to run an ECDL and lock it to an atomic transition. Marketing material has been produced and a targeting marketing strategy was developed in 2008. All revenue derived from this activity will be the property of The University of Melbourne and one student inventor. There were been 50 sales in 2008.

Dr Chanh Tran obtained an Australian Provisional Patent, "Imaging Method and apparatus", No. 2008901157.

CXS and Melbourne Ventures have produced a DVD on the commercialisation of IP.

OUTREACH

As part of the CXS Outreach Program a number of key initiatives took place in 2008, expanding on current activities and implementing a number of new ones.

Presentations to schools and media exposure have also added to the public's awareness of CXS.

The CXS Free Public Lecture Series 2008 began in February, with international and local speakers giving excellent presentations to the general public. For the first time CXS video recorded a number of its public lectures and created podcasts which are available on the CXS website for free download and viewing. The lectures held in 2008 were:

- Professor Janos Hajdu, Uppsala University in Sweden and Stanford University USA presented a lecture titled, "*Structures in a Flash! X-Ray Lasers, Exploding Molecules and Biological Insights*".
- Dr Jose N Varghese, CSIRO Molecular and Health Technologies presented a lecture titled, "*Avian Influenza and the emergence of Influenza Pandemics*".
- Professor So Iwata, Imperial College, London presented a lecture titled, "*High-hanging fruit worth the risk – Seeing the atoms in human membrane proteins*".

National Science Week became a key feature of the CXS outreach program, with its novel approach of targeting Melbourne's senior citizens which gained much attention. CXS, in collaboration with the ARC Centre of Excellence of Free Radical and Biotechnology, and the ARC Centre of Excellence for Mathematics and Statistics conducted the National Science Week program, *The Science of Chocolate* at Rylands Retirement Villages in Hawthorn and Kew. This combined Centre of Excellence activity presented free radical and synchrotron science with the statistical data of a chocolate taste testing. The program proved so successful that CXS has received requests to host the program at other retirement villages in Victoria, and has been asked by the organisers of National Science Week to present the program at the Queen Victoria Market in 2009.

CXS sponsored the KOALA 08 Conference, a student- led conference on optics and laser application, which was held in Queensland, November 2008. This highly successful conference brought together students from all fields of optics and photonics from around the country to exchange ideas and network. CXS members Lachlan Whitehead and Simon Bell were invited speakers, and a number of CXS students attended the conference.

The AussieMit2008 Workshop on Mitochondrial Research was also sponsored by CXS. This was the first workshop devoted to mitochondria research in Australia and was held at the Institute of Advanced Study, La Trobe University. The program for the workshop included top mitochondrial researchers who were asked to chair sessions or make presentations. However, early career researchers and postgraduate students comprised well over half of the talks, as one of the aims of the meeting was to give them the opportunity to present their work.

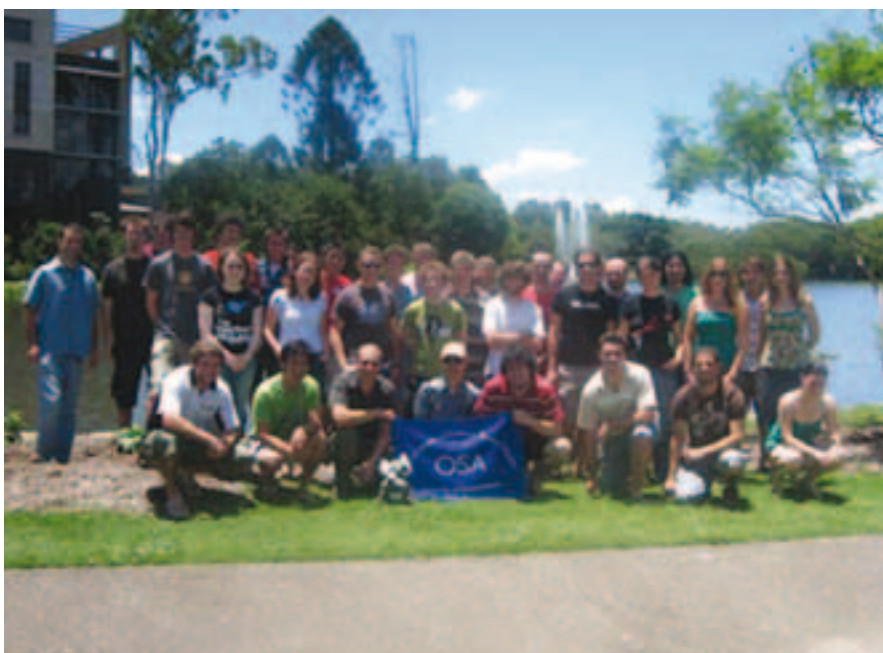
CXS is in the process of producing a Short Films Project to communicate to the wider community the relevance and importance of the cutting edge research being done by CXS. St Helena Secondary College, Kingswood College, Mill Park Secondary College and Craigieburn Secondary College are all participating in the project, in which the students will research, script, film and act in 3 five-minute documentaries. It is expected that the final products will be launched by CXS in mid 2009 and the films will be available to view on the CXS website.

MEDIA COMMENTARIES

The following articles relating to CXS were published or appeared in 2008:

- *X-ray Science in Australia*, International News, APS PHYSICS, Vol 16, No. 10, November 2007 (previously unreported)
- *Opening New Windows on the World*, Australian Research Council, OUTCOMES: RESULTS OF RESEARCH IN THE REAL WORLD, page 92.
- *Australian CXS and NSRRC signed MOU to affirm on collaborative research in science and technology*, News, NATIONAL SYNCHROTRON RADIATION RESEARCH CENTER, www.srrc.gov.tw, January 2008
- *New CXS Laser Facility*, Synchrotron Community News, LIGHTSPEED AUSTRALIAN SYNCHROTRON NEWS, Summer Edition, page 4
- *Shining a light on membrane proteins*, AUSTRALIAN LIFE SCIENTIST MAGAZINE, Vol 5, Issue 3 May/June 2008
- *Shining a light on membrane proteins*, AUSTRALIAN LIFE SCIENTIST ONLINE, www.biotechnews.com.au, June 2008
- *Disease Arms-Race Looks to Powerful New X-Ray Tools*, SWINBURNE NEWS, page 10
- *Disease Arms-Race Looks to Powerful New X-Ray Tools*, News, SCIENCE ALERT, www.sciencealert.com.au, June 2008
- *ARC Centre of Excellence for Coherent X-ray Science 3rd Annual Workshop Physicists and Biologists Working Together*, Events Daily, AUSTRALIAN SYNCHROTRON NEWS, August 2008
- *Chocolate – no longer a guilty pleasure*, ARC DISCOVERY NEWSLETTER, Summer edition, page 10.
- *The Science of Chocolate*, Community, Educational, FREE RADICAL CHEMISTRY AND BIOTECHNOLOGY, www.freeradical.org.au, October 2008
- *Coherent X-ray Science 3rd Annual Workshop*, AUSTRALIAN BIOCHEMIST, Vol 39, No. 3, Pages 38 39, December 2008
- *A sight unseen no more*, SUNDAY CANBERRA TIMES, 7 December 2008, page 17.

Delegates of the CXS sponsored KOALA Conference





PUBLICATIONS

PUBLICATIONS

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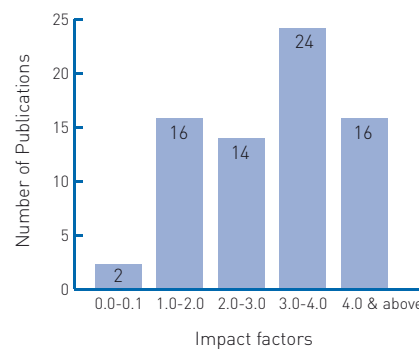
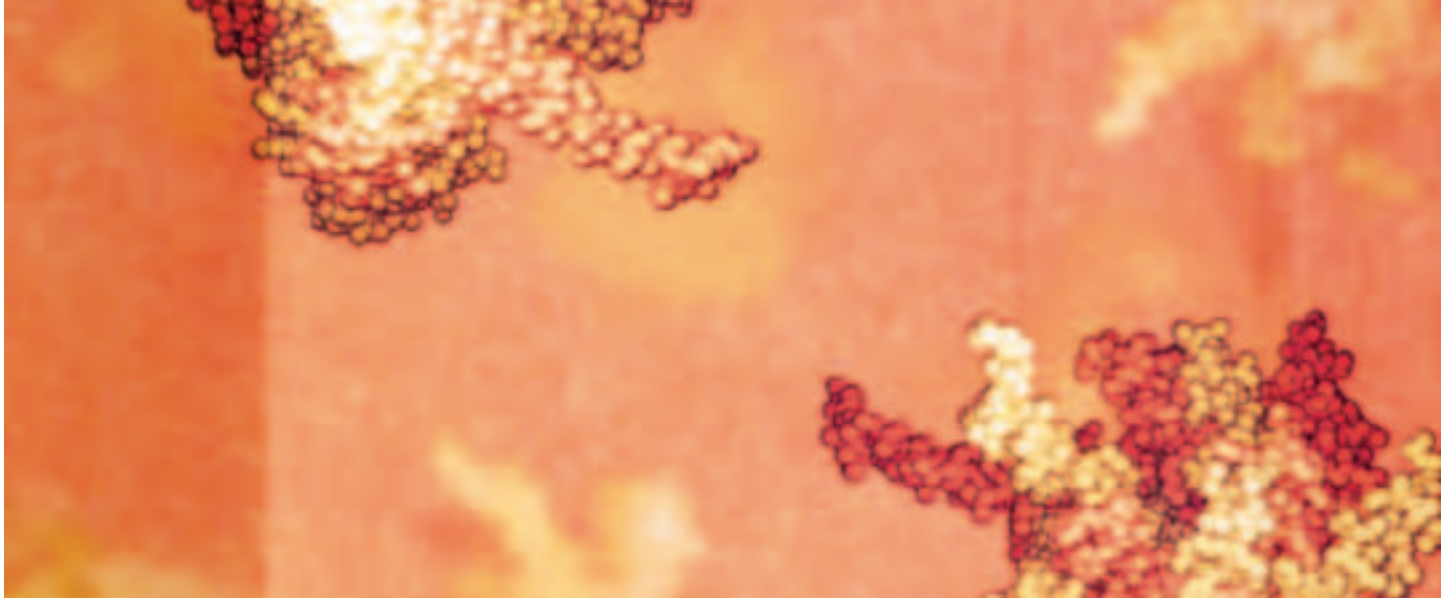
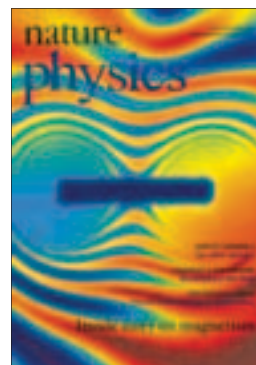
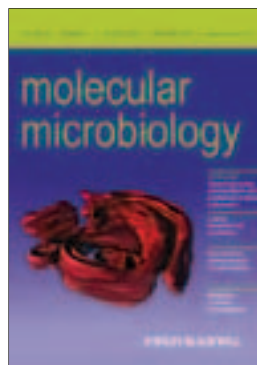
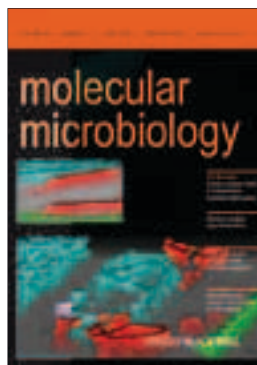
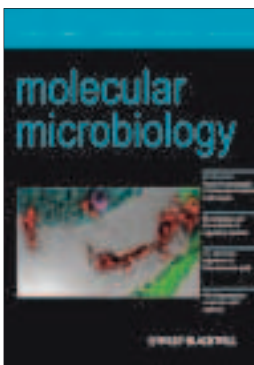
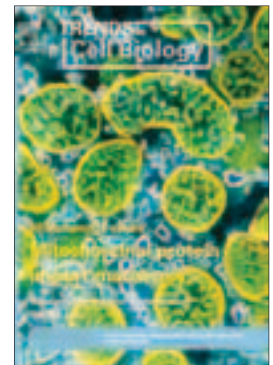
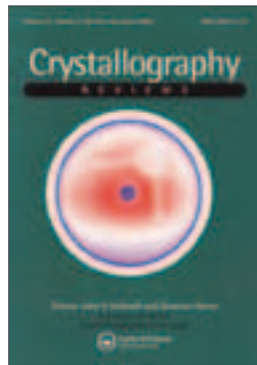
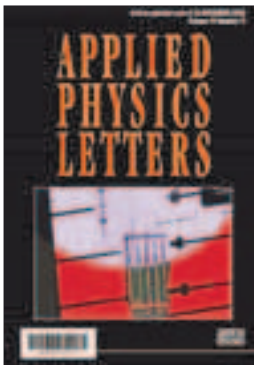


Figure 1: Impact Factor Statistics. Current as at December 2008



2008 COVERS



GRANTS

CXS members attracted \$4,403,214 in additional support in 2008:

AAS	
Image formation in partially coherent imaging	\$5,000
ARC	
Laser Facility for quantum optics, imaging and fabrication	\$400,000
A new window on Photosynthesis: Ultrafast coherence dynamics in biomolecules and semiconductor nanostructures	\$280,000
X-ray Biophotonics	\$210,000
Diffractive Imaging using soft X-rays & Electrons	\$34,226
ASRP	
Nanoscale determination of deformation fields in ion implanted crystals	\$10,701
ASRP/ANSTO	
Initial Installation and Commissioning of the Australian Research Council Centre of Excellence for Coherent X-ray Science Endstation: I	\$8,287
Initial Installation and Commissioning of the Australian Research Council Centre of Excellence for Coherent X-ray Science Endstation: II	\$13,020
Three dimensional Fresnel coherent diffractive imaging of internal structure in hard condensed matter samples	\$9,260
Investigation of the sensitivity of phase imaging in the near field region	\$10,000
Elemental mapping using coherent diffractive imaging	\$13,000
DEST	
Endeavour Executive Award 2008	\$25,000
LA TROBE UNIVERSITY IGS	
Fabrication of functional surfaces using ultra-violet nanoimprint lithography	\$7,850
Microstructure evaluation and quantification using 3D X-ray computed tomography	\$3,925
Developing 3D mounting for biological samples for FCDI experiments	\$3,925



NHMRC	
Researcher Exchange, Support a research visit to Light and X-ray Imaging Facilities in California	\$3,500
Research Exchange with the laboratory of A/Prof Mary Galinski, Emory University, Atlanta, USA to support visit of Sheila Akiny	\$2,707
Travel grant to employ novel red fluorescent proteins to study protein trafficking in malaria parasite-infected erythrocytes.	\$10,000
Network, Visualising the means by which the antimalarial drug, artemisinin, kills malaria parasites	\$886,250
Genetic Variation of Mitochondrial Complex I: its role in rare and common diseases	\$604,800
Regulation of Mitochondrial Fission, Fusion and Distribution	\$462,000
Assembly of Mitochondrial Respiratory Chain Complexes and Defects Associated with Disease	\$447,750
Identifying novel genes causing Complex IV deficiency	\$435,000
Phase contrast X-ray imaging of the lung at birth	\$508,646
SWISS TROPICAL INSTITUTE	
Researcher exchange with the Swiss Tropical Institute, Basel, Switzerland to support visit of Esther Pachlatko	\$8,367

CXS LOCATIONS



PARKVILLE CAMPUS

Corner Swanston Street and Tin Alley,
Parkville

PHYSICS BUILDING

CXS Head Office

The Experimental Methods Program
(also at La Trobe University)

The Theory and Modelling Program

The Ultra-Cold Plasma Source Program

PARKING

'Scratch & Display' car parking permits are available for the use of official visitors to the campus and nearby University parking areas. Upon notification, CXS staff can arrange permits in advance.



BUNDOORA CAMPUS

Kingsbury Drive, Bundoora

PHYSICAL SCIENCES BUILDINGS 1 AND 4

The Biological Sciences Program

The Experimental Methods Program
(also at University of Melbourne)

PARKING

Parking for visitors is on a fee-paying basis. Tickets can be purchased at car parks from the ticket machines. Upon notification, CXS staff and visitors can arrange daily temporary permits in advance.



CLAYTON CAMPUS

Wellington Road, Clayton

PHYSICS BUILDING

The Detector and Beamline
Development Program

PARKING

Parking permits are required during weekdays and short-term parking zones are also available.

Parking without a permit is available in the blue, red and yellow zones after 5pm on weekdays and all weekend.



HAWTHORN CAMPUS

John Street, Hawthorn

CENTRE FOR ATOMIC OPTICS AND ULTRAFAST SPECTROSCOPY

The Short Wavelength Source Program

PARKING

Parking in university car parks is on a fee-paying basis only. Tickets can be purchased in car parks from the ticket machines or from multi deck car park.

This campus is also situated a couple of minutes walk from the Glenferrie train station & tram stops.

CLAYTON

Gate 5, Normanby Road, Clayton

MANUFACTURING AND INFRASTRUCTURE TECHNOLOGIES

The Structure Determination
Methods Program

PARKVILLE

343 Royal Parade, Parkville

MOLECULAR AND HEALTH TECHNOLOGIES

The Structure Determination
Methods Program

FINANCIAL STATEMENT

CXS FINANCIAL REPORT JANUARY – DECEMBER 2008

	2008 REPORTING PERIOD (\$)		2009 REPORTING PERIOD (ESTIMATED) (\$)	
Carry Forward	\$	1,287,819	\$	991,825
STI Allocated Funds	\$	86,225	\$	0
Other Funds	\$	1,800,000	\$	1,800,000
	\$	980,000	\$	740,000
		ARC		ARC
		Node contribution		Node contribution
			\$	60,000
			\$	200,000
				Scholarships
				Fed Fellow Support
TOTAL INCOME	\$	4,154,044	\$	3,791,825
Expenditure	\$	5,500	\$	2,239,886
		Consultancies		Salaries
	\$	173,344	\$	589,909
		Consumables		Equipment
	\$	1,314,318	\$	282,600
		Equipment		Consumables
	\$	1,328,518	\$	222,200
		Salaries		Travel
	\$	12,036	\$	63,425
		Conferences		Scholarships
	\$	193,022	\$	241,277
		Travel		Laser repayment
	\$	9,968	\$	100,000
		Minor works		Outreach, Marketing, Sponsorships
	\$	53,307		Scholarships
	\$	4,110		Sponsorship
	\$	63,417		Outreach & Marketing
	\$	3,146		IT
	\$	1,227		Visitors Program
	\$	306		Training
	\$	3,162,219	\$	3,739,298
BALANCE	\$	991,825	\$	52,527

IN-KIND REPORT JANUARY – DECEMBER 2008

University of Melbourne	\$	3,277,818
La Trobe University	\$	2,372,136
Monash University	\$	1,041,754
Swinburne University of Technology	\$	597,804
TOTAL	\$	7,289,512

ARC CENTRE OF EXCELLENCE
FOR COHERENT X-RAY SCIENCE
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