
CXS
ARC Centre of Excellence for
COHERENT X-RAY SCIENCE
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2013
ANNUAL
REPORT
ARC CENTRE OF EXCELLENCE FOR
COHERENT X-RAY SCIENCE

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, Griffith University 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 and the National Australia Bank.

CXS would like to thank the School of Physics at the University of Melbourne, Tania Smith, Rosslyn Ball, Tania Carrubba and Nicole Anderson at the University of Melbourne, Fabienne Perani of La Trobe University, Tatiana Tchernova of Swinburne University of Technology and Elena Saj of Griffith University for their support.

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MISSION STATEMENT

"To be the world leader in the development of coherent X-ray diffraction for imaging biological structures"

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 characterisation of biological samples.

Its aim is to open a new frontier in biotechnology – the non-crystallographic structural determination of membrane proteins. These proteins mediate the activity of pharmaceuticals in human medical therapies. Their structures, however, are still mostly unknown because they do not form crystals suitable for analysis using the conventional crystallographic techniques that have driven almost all 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

As a biologist, I felt very privileged to be invited to take on the Directorship of the ARC Centre of Excellence for Coherent X-ray Science (CXS) in 2013. Our Centre uses the by-line, 'Physicists and Biologists Working Together', which encapsulates the ethos of CXS. We are working to bring together the physical and biological science disciplines to develop fundamentally new approaches to probing biological structures and processes.

In keeping with this sentiment, I have worked very closely in an executive partnership with physicist and Deputy Director, Associate Professor Harry Quiney, to lead the CXS in 2013. We are very grateful for the excellent work of our Chief Operating Officer, Tania Smith; and to the CXS Executive Committee. This dedicated team has worked with the Chief Investigators, the Partner Investigators and the Group Heads, with unfailing energy, enthusiasm and innovation, to ensure the successful management and operations of the Centre. I would also like to express my sincere gratitude to our International Scientific Advisory Committee: Professor John Helliwell; Professor Bonnie Wallace; and Professor Stephen Lane; for their unfailing support, sage advice and broad vision.

I would like to pay particular homage to Professor Keith Nugent, who directed the Centre during the first seven years of its operation. Under his leadership, the CXS received international acclaim for its cross-disciplinary and cross-institutional work and its contributions to the development of novel imaging techniques. It is an indication of the esteem in which Keith is held that he was persuaded to take on the role of interim Synchrotron Director in 2012, and then to take on the role of Deputy Vice-Chancellor, Research for La Trobe University in 2013. Keith has continued to contribute as a much-valued member of the CXS Executive Committee.

Another measure of the success of the centre and the high regard in which it is held is the fact that in 2012, Prof Andrew Peele, Head of the CXS Experimental Methods Program, was seconded to the position of Research Director of the Australian Synchrotron. Andrew took over from Keith as Interim Director in 2013, while an extensive international search was conducted to permanently fill the role. It is to Andrew's great credit that he was selected as the best candidate from a very distinguished field of applicants.

Andrew and Keith worked with Australian Synchrotron colleagues, members of the user community and other stakeholders to oversee a transition of the management of the Australian Synchrotron to the Australian Nuclear Science and Technology organisation (ANSTO) and the establishment of a new operating company, Synchrotron Light Source Australia (SLSA). Andrew and Keith drove funding efforts through the Special Research Initiative in Synchrotron Science – a large-scale cooperative initiative between the Australian Research Council (ARC), the National Health and Medical Research Council (NHMRC) and higher education organisations from across Australia. This initiative, in which I was very pleased to be involved, secures the operation of the Australian Synchrotron over the next four years.

I was also very pleased to be part of a group of colleagues who joined forces to establish the Victorian Microscopy Network (VMN). The VMN is a collaborative platform that pursues the advancement of microscopy and micro analytical infrastructure and capability. The group has put in place a Memorandum of Understanding between five Victorian Universities, stating a commitment to working together. CXS has thus contributed to driving a collaborative vision for imaging infrastructure in the Australian community.

We are delighted that a number of CXS members have been individually recognised in 2013 for their achievements. The list includes Rob Scholten who was promoted to Professor of Physics at the University of Melbourne; Harry Quiney who took up the position of Associate Professor in Physics at the University of Melbourne; and Professor Mike Ryan who was appointed President-elect of the Australian Society for Biochemistry and Molecular Biology.

The centre takes particular pleasure in seeing its early career researchers recognised for their achievements. Dr Jeff Davis took up an ARC Future Fellowship at Swinburne University, while Dr Diana Stojanovski took up a new Fellowship in the Department of Biochemistry and Molecular Biology at the Melbourne University. Diana was also the recipient of the Edman Award of Australian Society for Biochemistry and Molecular Biology. In the most recent round of fellowship funding, CXS members were awarded more than $2 million. Dr Brian Abbey received an ARC Future Fellowship and Dr David Stroud an NHMRC Early Career Fellowship to work at La Trobe University. Dr Andy Martin received an ARC DECRA Fellowship; Dr Ben Sparkes and Dr Yuning Hong, were awarded John McKenzie Melbourne University Fellowships; and Dr Marion Hliscs, a German Research Foundation Fellowship to work at Melbourne University.

As the funding period for the Centre draws to a close, members are exploring opportunities to secure cash resources from outside the centre, with 2013 proving particularly successful in these endeavours. CXS members were associated with research project grants totalling over $5 million through the ARC Discovery and Linkage, and NHMRC Project grant schemes. CXS members also participated in, or led bids to the ARC LIEF and NHMRC equipment schemes, including the successful linkage grant application by CXS commercial spin-off, MOGlabs Pty Ltd. Close to $1M of LIEF funds obtained in 2012 have been used to establish a cryo electron microscopy facility and a single molecule localisation super-resolution microscopy facility; as well as for the purchase of a Fast Soft X-ray Detector. In 2013, Jeff Davis led a successful bid to the ARC LIEF scheme to establish an Ultrafast Science Facility ($300,000).

We are very pleased to report that four members of CXS – Prof Keith Nugent, Dr Brian Abbey, Assoc Prof Harry Quiney and Prof Andrew Peele – contributed to a successful bid for a new ARC Centre of Excellence in Advanced Molecular Imaging based at Monash University, securing a grant for $28M. The new Centre will continue some of the work of CXS using high-resolution imaging technologies to explore the immune system.

During 2013, CXS published 95 refereed journal articles, more than doubling our KPI of 40 publications. More importantly, many of these appear in high impact journals, including Cell, Science, PNAS, and Nature. This exposure contributed to achieving an average impact factor of 5.92, an indicator that has been rising steadily over the life of the Centre. It is worth noting that many of the high profile publications involve successful Biology and Physics collaborations, demonstrating the commitment made to cross-disciplinary research made by CXS members.

At the core of CXS aspirations is the belief that answering the major medical and biotechnology questions of the 21st century will require convergence of the life and physical sciences and reliance on the use of advanced imaging techniques. We believe that the CXS has played an important leadership role in the exciting developments in this area.

In 2013, the centre made significant process in its long-term goal of making use of new X-ray Free Electron Lasers (X-FELs). X-FELs provide extremely intense pulses of femtosecond duration, which allow data collection from nanometre- to micrometre-sized crystals in a 'diffract-and-destroy' approach. CXS has established itself as one of the world leaders in the physics of coherent X-ray science and members have conducted the first Australian-led experiment using the X-ray Free Electron Laser (X-FEL) at the Linac Coherent Light Source at the SLAC National Accelerator Laboratory at Stanford, USA. Harry Quiney, Keith Nugent, Andrew Peele and Brian Abbey have led experiments that probe the reorganisation of C60 buckyballs upon exposure to the intense electron energies of the X-FEL, and with crystals of hemozoin from the malaria parasite, Plasmodium falciparum.

Associate Professors Trevor Smith and Lap van Dao are exploring the application of short wavelength high-harmonic generation sources to imaging problems and pursuing the development of high-resolution optical microscopy to complement the new x-ray imaging techniques. In particular, the centre made significant contributions to the development and use of 3D-Structured Illumination Microscopy. CXS has established a new area of investigation

in coherent electron diffraction and this year Professor Rob Scholten pushed the technology even further, demonstrating the production of ultra-short (picosecond) electron bunches.

CXS excellence continues over a range of biological science areas. I am particularly excited about a study from my own lab, providing insights into the mechanism of action and resistance to artemisinin, an antimalarial drug that saves the lives of millions of children every year. This work is the culmination of years of research using diffraction techniques, super-resolution optical microscopy, electron tomography and mathematical modelling – work that has involved close interactions between biologists and physicists. I find it very rewarding to think that the highly sophisticated work that we do as part of CXS is finding immediate applications in the field. This year it led me to visit health centres in a region of Cambodia where artemisinin resistance is developing, to discuss the implications of our findings.

An important achievement for the year was the physical installation and commissioning of the Soft X-Ray Imaging (SXRI) beamline and endstation at the Australian Synchrotron in a project led by Dr Grant van Riessen. Implementations of ptychographic coherent diffractive imaging have been successfully demonstrated on biological samples over a wide photon energy range at 40 nm spatial resolution. The endstation and research that it directly supports has attracted external funding exceeding $1.5M (2007-2013) and represents a major legacy of the CXS.

In addition to our significant scientific achievements, CXS has made important outreach achievements of which we are justly proud. Professor Mike Ryan and Associate Professor Trevor Smith worked with a dedicated group of CXS members to organise a workshop entitled "Frontiers of Light Microscopy – Physicists and Biologists Working Together". The title encapsulates the spirit of CXS, and reflects a statement made by Richard Feynman (Nobel Prize in physics) who suggested that physicists could make a major contribution to biology by making microscopes 100 times better. This workshop celebrated the fact that in recent years, our physical science colleagues have done just that. A convergence of the physical, biological and engineering sciences has led to the development of a number of revolutionary approaches to high resolution imaging. The symposium focused on some very exciting developments in light microscopy and showcased CXS contributions in this area. It also provided an opportunity to invite colleagues to visit the CXS-supported Super-Resolution Optical Microscopy Facilities at Bio21 Institute and the School of Chemistry at the University of Melbourne and at the La Trobe Institute for Molecular Sciences. The workshop attracted over 230 registrants and was hailed as a major success by participants.

CXS members have developed a number of important X-ray analysis algorithms that have been made available to the wider scientific community. The Theory and Modelling Program has created a standard software package (NADIA) that introduces users to the CXS image algorithms for X-ray diffraction data analysis in a user-friendly way. In 2013 T'Mir Julius and Harry Quiney ran two NADIA software workshops for beginners and more sophisticated users. Martin Scanlon also organised an NMR Workshop at Monash Institute for Pharmaceutical Science that sought to make a connection between 3D-NMR and Multi-Dimensional Spectroscopy. Additionally, CXS held a writing workshop aimed at helping early career CXS members improve their skills in writing research publications.

CXS Deputy Director, Harry Quiney, delivered a public lecture as part of the Physics July Lectures entitled "From Moseley's law to the molecular microscope: a century of X-ray physics, chemistry and biology". Despite the 8pm timeslot on a wintery Friday evening, the theatre was packed. I was also very pleased to deliver a public lecture entitled "Malaria Parasites: Blood, Sex and Drugs" as part of the Dean's Lecture series for the Faculty of Medicine, Dentistry and Health Science. It was another opportunity to promote the benefits of Biologists and Physicists working together.

We are very excited that CXS member, Robert Scholten was a member of a team that won the Eureka Prize for Excellence in Interdisciplinary Scientific Research for the development of quantum bio-probes that can detect individual atoms inside living cells.

It is pleasing to watch the continued success of the Growing Tall Poppies program – an initiative to increase the number of girls studying physics through partnerships with Universities. This is a pioneering student educational experience that was developed primarily as a partnership between Santa Maria College Northcote. The program was awarded a NAB Schools First Award in 2009. Program co-ordinator Eroia Nugent-Barone was nominated as

an Australian Museum 2012 Science or Mathematics Teaching Eureka Prize finalist for this program. CXS will continue to support the Growing Tall Poppies program in 2014 and we are very pleased to have been approached to be a partner of the Tall Poppies Campaign, a national program.

This 2013 Annual Report marks the scheduled conclusion of ARC funding of the CXS. The CXS will carry forward some funds to permit the continuation of selected research activities into 2014, however, we are taking this opportunity to review and consolidate our accomplishments over the life of the Centre, as well as reflect on its legacy. This process has seen us reflect on our achievements in X-ray science and in optics more broadly; consider how we have benefited from the ethos of biologists and physicists working together; and contemplate what's next for the exciting new approaches that CXS developed to probe biological structures.

As we look back over the years of operation of the centre it is clear that CXS has used the time and resources effectively. In particular, we can be proud of the collaborative relationships established, the technical infrastructure built and the national and international partnerships that have been developed. However, the main legacy of a centre like CXS is its people, and we are enormously proud to see senior CXS members taking up highly influential positions in Australian science management, while early career CXS members take their place as leaders of research programs. The CXS has created an outstanding multi-disciplinary environment for research, learning and outreach, and has achieved an impressive research output that is having an international impact and will leave a lasting legacy.

LEANN TILLEY
DIRECTOR

RESEARCH PROGRAMS

ATTOSECOND SCIENCES PROGRAM

The Attosecond Science Program, which began collaborating with CXS in June 2009, offers new opportunities for coherent X-ray science that are unique within Australia. The new and rapidly expanding field of attosecond science is based on recent revolutionary developments in ultrafast optics that resulted in the award of the Nobel Prize in 2005.

It is now possible to generate high-energy infrared light pulses consisting of only a few cycles of the electric field and to control the optical electric field waveform within the light pulses. Such optical pulses have been used to generate isolated soft X-ray bursts with durations below 100 attosecond (1 as = 10^{-18} s). They can also provide information on atomic and molecular dynamics on the attosecond timescale and have been used to map the electronic structure of molecules. The Australian Attosecond Science Facility (AASF) is the only one of its type in Australia and is therefore uniquely utilised for attosecond science investigations. The facility is directed by A/Prof Kielpinski, leader of the CXS Attosecond Science program since January 2010. The heart of the facility is a laser source providing 6 fs, 300 μJ, phase-stabilised laser pulses, commissioned in 2007 through an ARC LIEF grant.

In 2009, the AASF experimental group began a close collaboration with the CXS Theory and Modelling group on the response of atomic hydrogen to strong few-cycle laser pulses. Atomic and molecular dynamics in strong optical fields plays a crucial role in many CXS activities, from the Biological Sciences program's goal of molecular structure retrieval from single-molecule X-ray diffraction to the high-harmonic generation work of the Short Wavelength Laser Source program. However, theory and experiment in this area rarely give quantitative agreement. As the only attosecond science group with access to atomic hydrogen, the AASF group has a unique opportunity to benchmark strong-field theories with the help of the Theory and Modelling group.

Throughout the course of its collaboration with CXS, the AASF group has also pursued the generation of isolated attosecond X-ray pulses, which have proved useful as tools for probing electronic structure of atoms, molecules, and surfaces. Currently only four research groups in the world have this capability. Isolated attosecond pulses can help unravel the problem of nonlinear X-ray back-action on molecular diffraction imaging, a key step in realising CXS goals in biomolecular structure determination. Modelling of back-action during the long X-ray pulses from synchrotrons and free-electron lasers (FELs) requires simultaneous incorporation of several mutually interacting many-body effects, a highly challenging task. In contrast, attosecond pulses provide a window into the short-time dynamics, effectively decoupling the many-body effects. Attosecond interactions can also selectively incorporate or exclude particular processes. Although the total energy delivered in an attosecond pulse is much lower than that expected at a FEL, the peak X-ray intensity can be nearly as high because of the short pulse duration.

PHOTOIONISATION OF ATOMIC HYDROGEN

The Program has obtained data on the total photoionisation probability of atomic hydrogen over a wide range of intensities. By analysing the sources of uncertainty in this data, it was found that data achieved a measurement precision of 1% (see "case study"). This is the highest-precision data ever obtained for an attoscience experiment. Data were compared to the commonly used Ammosov-Delone-Krainer (ADK) model, which is often used for calibration of attosecond science experiments (Figure 1). It is clear that the ADK model is not

adequate for current experiments – in fact, it is wrong by a factor of two!

The data agree closely with the exact numerical calculations provided by CXS theoretical physics collaborators, showing that the data from our experiment is reliable at the 2% level. However, the exact calculations consume weeks of supercomputer time. Ironically, it now seems that theoretical simulations developed within our own program are the limit. The Attosecond Science Program is working with the Theory and Modelling Group to improve the theoretical calculation and achieve 1% agreement.

Using identical experimental conditions, data was obtained for the photoionisation yield of the hydrogen molecule and compared to theoretical calculations. As expected, even the best calculations are quite inadequate. However, we can use these calculations to derive an effective calibration for laser intensity by observation of H_2 alone. Hence, this accurate intensity calibration can now be transferred to attoscience laboratories around the world, without the need for the complex and delicate atomic hydrogen source.

The Program has also been investigating photoelectron spectra of atomic hydrogen as a function of the laser carrier-envelope phase. The low-energy spectra show peaks separated by the photon energy as expected. The phase dependence has been mapped over coarse (2 eV) energy bins. The phase effect passes through a null and reverses sign at energies somewhat above the ponderomotive energy, as predicted by numerical theory. We continue to analyse the CEP-dependent electron energy spectra for higher-order CEP oscillations. These seem to appear at characteristic atomic binding energies.

Experiments to date have been hampered by low signal from the hydrogen atomic beam. To address this, the atomic beamline has been shortened to increase the flux of H atoms and increase the signal The atomic beam apparatus has also been moved closer to the laser source. These improvements are expected to result in faster and more straightforward data collection.

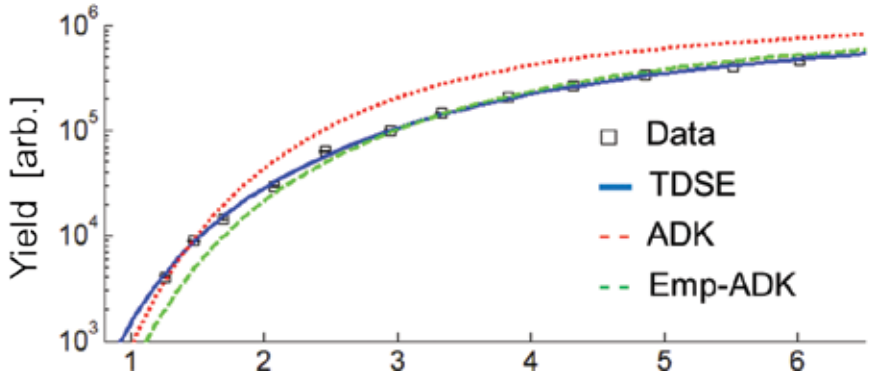
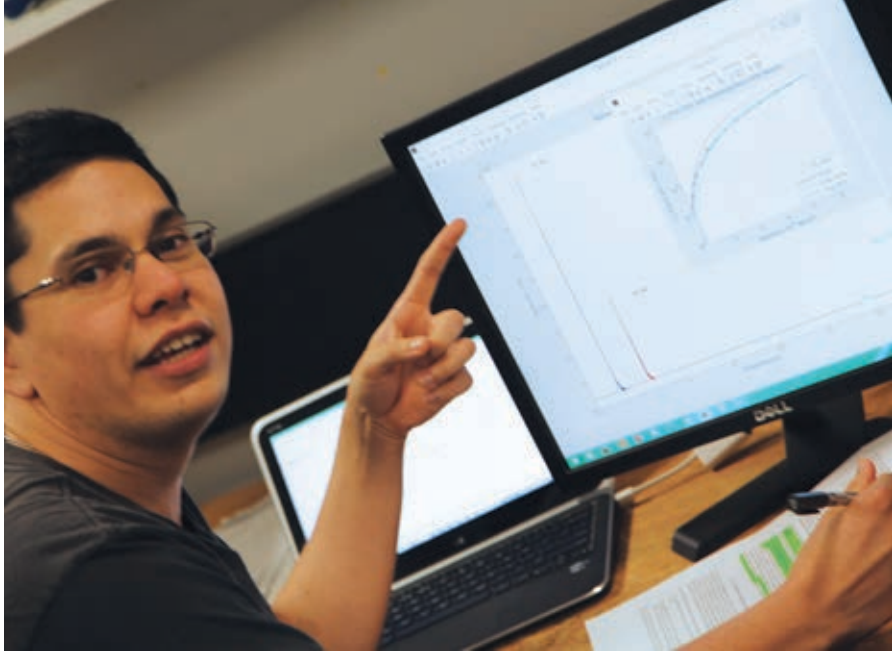


Figure 1: Comparison of our data for atomic hydrogen with several theoretical models. The exact numerical simulations (TDSE) follow the data to within 2%. The widely used ADK model is wrong by a factor of two, while the "empirically corrected" model (Emp-ADK) is still off by 15%.

ISOLATED ATTOSECOND PULSE GENERATION

The newly acquired extreme-ultraviolet spectrometer was used to measure photons with energy up to 100 eV, produced by high harmonic generation. Carrier-envelope phase effects consistent with isolated attosecond pulse generation at 95 eV were observed – this is the design wavelength for the attosecond streaking beamline. The yield of high harmonic generation (HHG) photons in this band was systematically optimised with respect to gas cell length, gas pressure, and laser focus position. Such optimisation data for attosecond beamlines have not been presented in the literature, and the results have been submitted for publication.

Construction of the attosecond beamline was completed during the reporting period, in line with last year's planning. Additionally, the time-of-flight electron spectrometer and the XUV-optical delay stage were successfully tested. The CXS gas jet source was found to influence the local electric field of the time-of-flight spectrometer, therefore the gas source was mounted on a precise positioning stage



William Wallace, a final-year PhD student in CXS, shows off the most accurate data ever obtained for matter in intense laser fields.

to remove this effect. The entire >2 metre beamline was put under high vacuum, as required for successful operation.

The electron energy spectrum was measured by XUV-induced photoemission from argon. Attempts were made to influence the spectrum with the infrared laser field, however the intensity was too high in experiments conducted thus far, leading to multi-photon ionisation that masked any signal. Control of the iris that determines this intensity was improved by adding a mechanical linkage between the iris movement and a micrometer stage outside the vacuum system.

ATTOSECOND SCIENCES PROGRAM CASE STUDY

Super-strong laser pulses are used to destroy matter placed within their field, for the purpose of examining the ions that remain once the laser pulse has passed by. It is important to be able to accurately measure the laser intensity in order to compare the real data to theoretical calculations. Accurate measurement of the intensity of super-strong laser pulses has historically been problematic. William Wallace, a final-year PhD student in CXS, obtained data on the ions being examined and has spent the last several months isolating the accuracy of the measurement. To do this, he had to consider not just the strength of the ion signal, but also the slow changes of the laser system over time, and even the electronic charging and discharging of the ion detection system. Using sophisticated statistical analysis, William showed that his measurements were precise to 1% – about 10 times more accurate than the previous record – and determined that slow changes of the laser intensity are the biggest factor in the remaining uncertainty. By carefully uncovering the sources of uncertainty in this kind of data, William's results will help future researchers avoid experimental pitfalls.

BIOLOGICAL SCIENCES PROGRAM

The Biological Sciences program involves research groups from La Trobe University, The University of Melbourne and Monash University.

Methods for imaging cellular architecture and ultimately macromolecular complexes and individual proteins, within a cellular environment, are an important goal 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. Program members collaborate closely with the Experimental Physics Program in the development and implementation of novel imaging techniques to provide insights into the structures of cells and cellular compartments. The Program also interacts with the Structure Determination Methods, and Theory and Modelling Programs to optimise techniques that determine the structures of membrane proteins and other components of biological interest. Program members additionally work with the Attosecond Science and Short Wavelength Laser Source Programs to develop non-linear spectroscopic methods to investigate the mechanisms of electron transport to understanding the structure and dynamics of oxidative protein folding.

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 (RBC) is effectively a floating sack comprising a membrane that encloses the oxygen-transporting protein, haemoglobin. Unlike other cells, RBCs have no nucleus 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. These membrane structures play an important role in the trafficking of virulence proteins to the host cell surface, however their ultrastructure is only partly defined and there is on-going debate regarding their origin, organisation and connectivity. Parasite endocytic processes are also poorly understood. The parasite consumes host haemoglobin in order to support its own growth. Packets of haemoglobin are transferred from the host cell cytoplasm to a parasite digestive vacuole for haemoglobin digestion and heme detoxification; however, the precise mechanism for uptake is debated. One of the aims of CXS is to image these compartments and develop an understanding of their function and the way in which they are formed. Such research can lead to new avenues for drug and vaccine design to combat the serious problem of malaria.

MITOCHONDRIA: UNDERSTANDING THE POWERHOUSE AND THE POISON CUPBOARD

Mitochondria are the generators within our cells, synthesising chemical energy in the form of the molecule ATP. They also act as 'poison cupboards', where upon opening

of the mitochondrial outer membrane, 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 and Alzheimer's disease. In addition, efforts to activate the machinery involved in mitochondrial permeabilisation can act as anti-cancer agents. Work has been undertaken by CXS 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. Work has been completed in parallel to provide insights into the structure of mitochondrial membrane proteins and their complexes.

PROTEIN-SMALL MOLECULE INTERACTIONS FOR DRUG DESIGN

This project has focused on understanding the interaction of proteins with small molecules. The information gained facilitates understanding of how drugs work and the design of new drugs that target disease-causing proteins. A family of bacterial proteins that are catalysts of oxidative protein folding have been shown to be important in virulence, antibiotic sensitivity and infection. Consequently, these proteins are potential targets for the development of an entirely new class of antibiotics. The project has been occupied in the structure determination of these proteins using coherent X-ray imaging methods. Members of this research group have also been working with members of the Attosecond Science, and Short Wavelength Laser Source Programs to develop non-linear spectroscopic methods that will enable them to investigate the mechanisms of electron transport in this system. Understanding the structure and dynamics of the oxidative protein folding system will provide us with key information for the design of potent and specific antibiotics.

GOALS:

- Prepare and optimise 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 and novel X-ray-based approaches.
- Undertake studies on protein dynamics using conventional and non-linear spectroscopic methods.

UNDERSTANDING HOW MITOCHONDRIA UNDERGO DIVISION

Mitochondria are dynamic organelles that undergo fission and fusion events that are critical for well-being. Direct defects in mitochondrial fusion, fission and distribution processes have been identified in various diseases with symptoms such as peripheral neuropathy, optic and muscle atrophies and general mitochondrial dysfunction. Defects in mitochondrial morphology have also been implicated in a number of common disorders including hypergylcemia, Alzheimer's, Parkinson's and Huntington's disease. Fission has also been seen as a precursor to apoptosis following insults such as oxidative stress and viral infection. How fission and fusion is regulated is not well understood. We have recently identified two mitochondrial outer membrane proteins that we termed MiD49 and MiD51 (mitochondrial dynamics proteins of 49 and 51 kDa), that induce morphological changes to the mitochondrial network following their overexpression or knockdown. Characterisation of these proteins revealed that they mediate mitochondrial fission by participating in the recruitment and action of Drp1 at the mitochondrial surface. However, different reports have ascribed opposing roles in fission and fusion. We showed that MiD49 or MiD51 overexpression blocked fission by acting in a dominant-negative manner by sequestering Drp1 specifically at mitochondria, causing unopposed fusion events at mitochondria along with elongation of peroxisomes. Mitochondrial elongation caused by MiD49/51 overexpression required the action of fusion mediators mitofusins 1 and 2. Furthermore, at low-level overexpression when MiD49 and MiD51 form discrete foci at mitochondria, mitochondrial fission events still occurred. Unlike Fis1 and Mff, MiD49 and MiD51 were not targeted to the peroxisomal surface, suggesting that they specifically act to facilitate Drp1-directed fission at mitochondria. The Drp1 recruitment activity of MiD49/51 appeared stronger than that of Mff or Fis1 indicating that MiD49 and MiD51 can act independently of Mff and Fis1 in Drp1 recruitment and provide specificity to the division of mitochondria. In collaboration with Prof Carolyn Larabell (UCSF), Dr Kirsty Elgass was able to image mitochondrial morphologies in a set of cells using correlative fluorescence microscopy

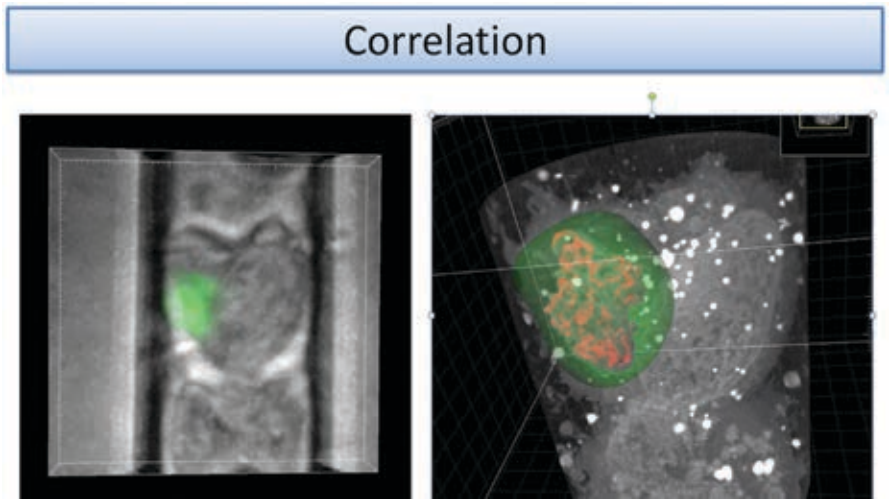


Figure 2: Left panel shows the fluorescence of mouse B cells expressing mitochondrial localised MiD49 inside a glass capillary. The right panel is a composite image of the x-ray tomogram and the reconstructed mitochondrial network (red) overlaid with the fluorescence image.

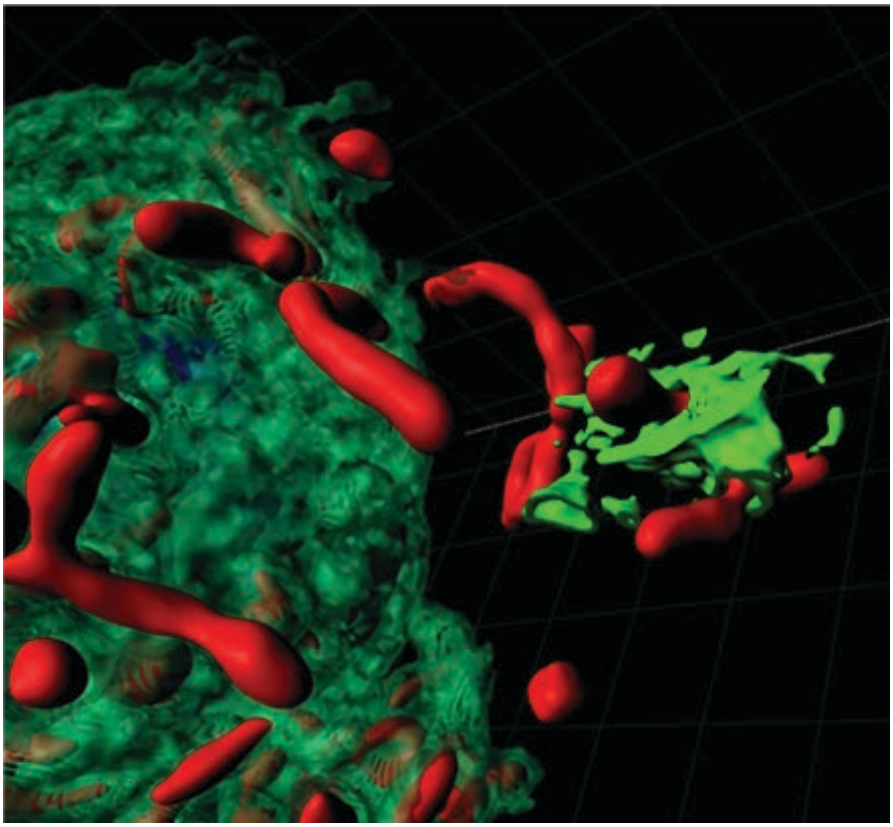


Figure 3: The mitochondrial network (green) can be seen closely associated with the endoplasmic reticulum. This is a rendered image reconstructed from tomographic x-ray imaging of a mouse B cell.

and x-ray tomography at the Advance Light Source (Berkeley). Data analysis including segmentation and correlation of the images as well as statistical analysis of the linear absorption coefficient (LAC) values of mitochondria and ER was conducted. It was found that MiD49 induces mitochondrial condensation at the nuclear periphery. Furthermore, we were able to identify areas of the endoplasmic reticulum closely aligned with mitochondrial constriction sites. This is consistent with the role of the endoplasmic reticulum in mitochondrial fission.

THE MALARIA PARASITE: FROM HIGH RESOLUTION IMAGING TO FIGHTING DRUG RESISTANCE

Malaria kills close to one million children every year. Mortality and morbidity due to infections with the most virulent malaria parasite (falciparum) are associated with growth of the parasite inside the red blood cells of its human host, and most antimalarial drugs target this phase. Malaria endemic countries have adopted the World Health Organisation-recommended Artemisinin-based Combination Therapies (ACTs) for treating malaria. Therefore, recent reports that parasites are becoming resistant to artemisinins are extremely concerning.

The Biological Sciences Program at CXS has applied a range of approaches to try to understand the molecular basis of the action of artemisinins and to determine how parasites can evade the drug's activity. In collaboration with colleagues from the Experimental Methods Program, cryo-X-ray microscopy, coherent diffraction imaging and electron tomography were used to image malaria parasites. These techniques use computational strategies to build a 3D picture of the insides of the parasite at the highest possible resolution, demonstrating how malaria parasites digest hemoglobin using a stomach-like organelle referred to as the digestive vacuole.

Working with the CXS Theory and Modelling Program, the Biological Sciences Program identified the structure of a crystalline material that accumulates inside the parasite. These haemozoin crystals represent the waste disposal mechanism for the breakdown products of haemoglobin digestion. This gave us insights into the way the parasite deals with the toxic side-effects of its blood meal. We found that artemisinin subverts the haemoglobin breakdown pathway, using it to unleash its killing properties.

Rigorous microscopy work demonstrated that in the early stage of parasite growth

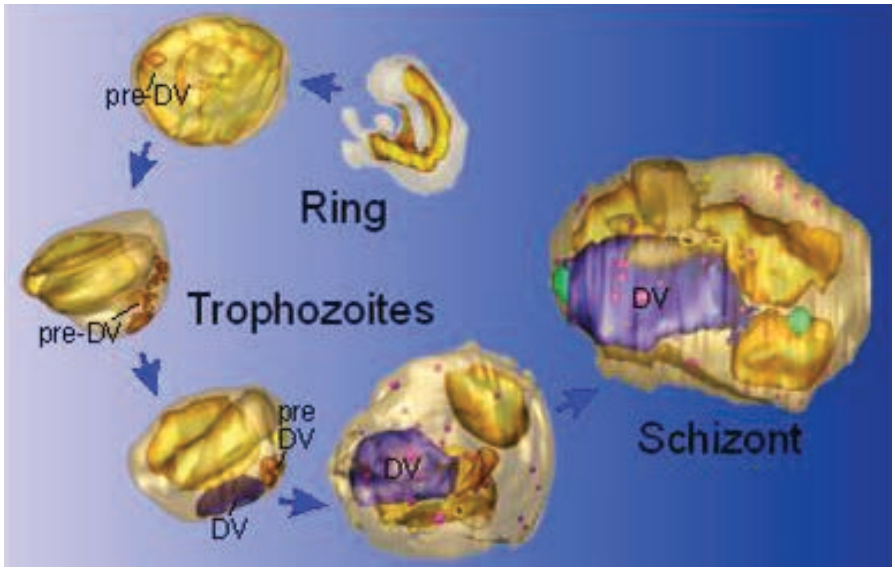


Figure 4: Immature malaria parasites (front) have a much less developed digestive system than mature parasites (back) and as a consequence are much less sensitive to artemisinin. Model generated from two electron tomograms by Dr Eric Hanssen, Advanced Microscopy Facility, Bio21 Institute, University of Melbourne.

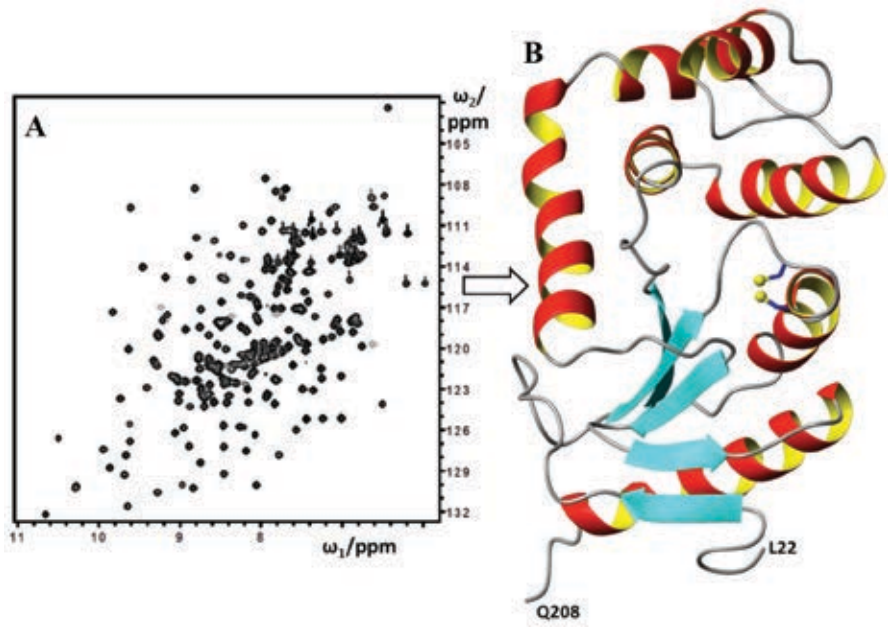


Figure 5 (A) & (B): (A) [15N,1H]-HSQC of NmDsbA2. Highly dispersed backbone amide peaks indicate that the protein is well folded. (B) Solution NMR structure of NmDsbA2. Active-site cysteines are indicated in ball and stick representation.

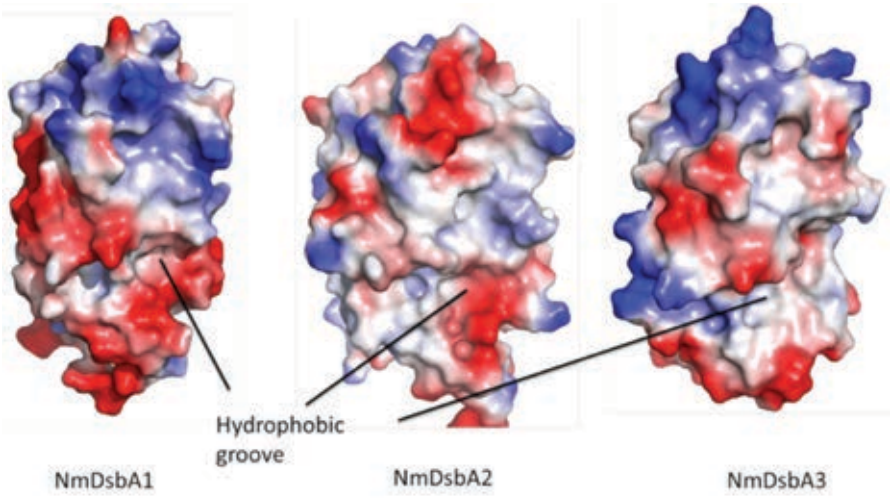
inside the red blood cell, before haemoglobin digestion starts, it is effectively resistant to artemisinin. A number of different strategies were then designed to inhibit or slow hemoglobin digestion in mature stage parasites. This showed that parasite are resistant to artemisinins if they can stop digesting hemoglobin. Even a short period of "refraining from eating haemoglobin" is sufficient to enable them to survive until this very labile drug disappears from the bloodstream. This helps explain how parasites are becoming resistant in the field.

The findings from this program are providing a guide for changing the timing of the treatment regime with artemisinins and for developing longer lasting drugs. This will enable more efficient killing of the parasites and will circumvent the development of drug resistance.

NEW STRUCTURES TO UNDERSTAND ENZYME DYNAMICS AND UNCOVER NOVEL ANTIBIOTICS

Protein oxidation pathways in Neisseria meningitidis and N. gonnorhoeae – two obligate human pathogens and causative agents of fatal meningitis and sexually transmitted gonnorhoea – have been studied over the life of CXS. These oxidation pathways are essential for bacterial virulence. We are seeking to clarify structural and functional aspects of the enzymes involved in protein oxidation (called Dsb) in efforts to design novel, narrow spectrum inhibitors of their activity. A key aspect of the work is to develop a structural understanding of the substrate specificity that is observed in the system. Previously

Figure 6: Electrostatic surface potential of three NmDsbA proteins.



NmDsbA2 present significantly different surfaces around their active sites (Figure 6) which is likely to underpin the apparent differences in substrate specificity. NmDsbA3, which has lower sequence identity retains a similar DsbA fold, but is significantly different to both NmDsbA1 and NmDsbA2 in the regions around the active site (Figure 7).

FRAGMENT SCREENING AGAINST THREE NMDSBAS TO INVESTIGATE SPECIFICITY

To investigate the differences in substrate specificity of the three DsbA enzymes, a primary STD-NMR screen of the CXS fragment library has been completed against three NmDsbAs. To validate the hits and to investigate their binding location and affinities using 15N-HSQC-NMR, the backbone amide resonances were assigned in each case. So far ~ 97% backbone assignments for NmDsbA1, 98% for NmDsbA2 and 80 % for NmDsbA3 have been completed.

DESIGN OF DSBB CHIMERA AND ATTEMPTS TO REFOLD IT IN NANODISCS

It was demonstrated that DsbB expressed and purified from Escherichia coli is functional when reconstituted in detergent micelles. Whilst E. coli DsbB is capable of re-oxidising neisserial DsbA enzymes, it does so much more slowly than the cognate neisserial DsbB. This is thought to be due to differences in the redox potentials of the respective enzymes. An understanding of the mechanistic basis for the differences in redox activity is limited by a lack of structural knowledge of different DsbB enzymes. Previous studies with

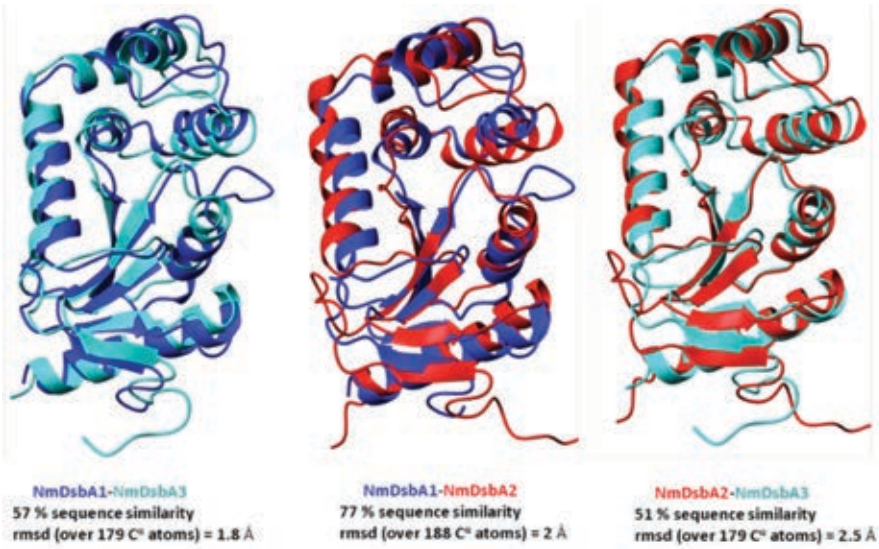


Figure 7 Structure comparisons between three NmDsbA homologs.

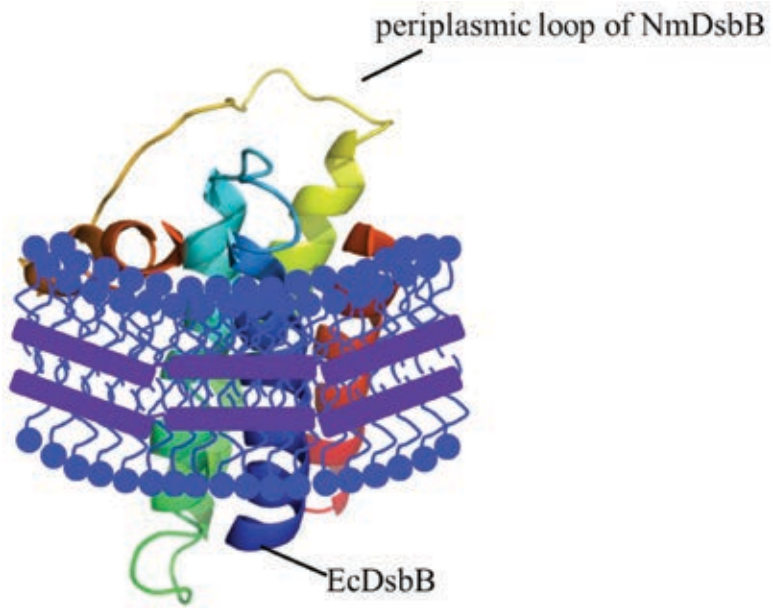
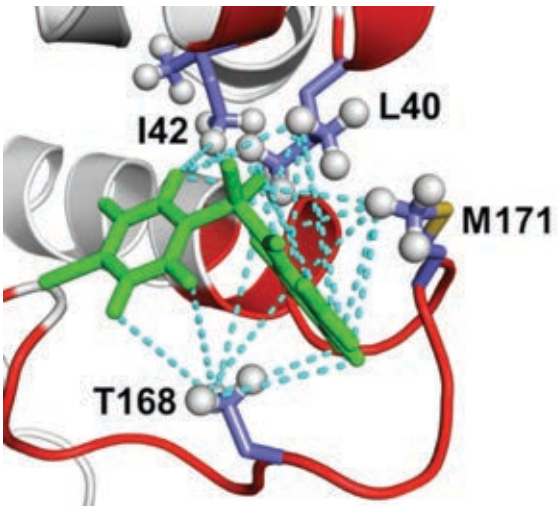


Figure 8: A chimeric DsbB in which the periplasmic loops of NmDsbB have been fused into the sequence of EcDsbB. Five helices of EcDsbB are shown as cylinders embedded in the nanodisc.

Figure 9: The structure of protein-ligand complex. The protein is shown as a cartoon, with methyl containing residues at the binding site coloured blue. The ligand is shown in green sticks. Experimental NOEs observed for the complex are shown as blue dotted lines.



EcDsbB have been undertaken in detergent micelles. Structural, dynamic and functional studies have demonstrated that the protein is sensitive to the detergent composition. Investigation of the activity of DsbB proteins in a more membrane-like environment in currently being undertaken by purifying DsbB in nanodiscs (Fig. 8) and testing its ability to catalyse DsbA oxidation.

DEVELOPING A FAST NMR-BASED METHOD TO GENERATE STRUCTURAL DATA FOR PROTEIN-LIGAND COMPLEXES THAT ARE NOT AMENABLE TO X-RAY CRYSTALLOGRAPHY

In fragment based drug discovery, structural data are generally needed to develop weakly-binding hits into high-affinity lead compounds. CXS has developed a fast NMR-based method for structure determination of low-affinity protein-ligand complexes that are not able to be crystallised.

A procedure was utilised that results in selective isotope labelling of all methyl groups in protein. The methyl resonances for each of these methyl groups can be assigned to specific groups in the protein. Acquisition of the NMR data using a non-uniform sampling schedule allows data to be acquired with very high resolution, without requiring long data acquisition times. Finally, intermolecular NOEs and ambiguous interaction constraints derived from chemical shift perturbations are used to generate the structures using computational approaches.

Using the protocol developed by Biological Sciences Program, data acquisition, analysis and determination of the structure of the complex can be achieved quickly enough to inform programs of structure-based drug design. To illustrate the approach, CXS has solved structures of small molecules in complex with bacterial enzymes that are potentially targets for the development of antimicrobial agents.

NMR SOLUTION STRUCTURE OF NEISSERIA MENINGITIDIS DSBA2

Neisseria meningitidis express three disulfide-dithiol oxidoreductase enzymes that are key regulators of bacterial virulence. The goal is to understand the mechanism, substrate specificity and role in virulence of these three enzymes. The structures of NmDsbA1 and NmDsbA3 were solved previously (both by CXS and others) using X-ray crystallography. However, the third enzyme was not able to be crystallised. Therefore the solution structure of NmDsbA2 was determined using NMR spectroscopy. Despite a high level of sequence identity, comparison of the structures reveals that NmDsbA1 and NmDsbA2 present significantly different surfaces around their active sites, which is likely to underpin predicted differences in their substrate specificity. NmDsbA3, which has lower sequence identity, retains a similar DsbA fold but is significantly different to both NmDsbA1 and NmDsbA2 in the region around the active site.

FRAGMENT SCREENING AGAINST THREE NMDSBAS TO INVESTIGATE SPECIFICITY

To investigate the differences in substrate specificity of the three DsbA enzymes, the team completed a primary STD-NMR screen of the CXS small molecule fragment library against each of the three NmDsbAs. To validate the hits and to investigate their binding location and affinities using 15N-HSQC-NMR, the backbone amide resonances were assigned in each case. So far ~97% of the backbone assignments have been completed for NmDsbA1, 98% for NmDsbA2 and 80% for NmDsbA3.

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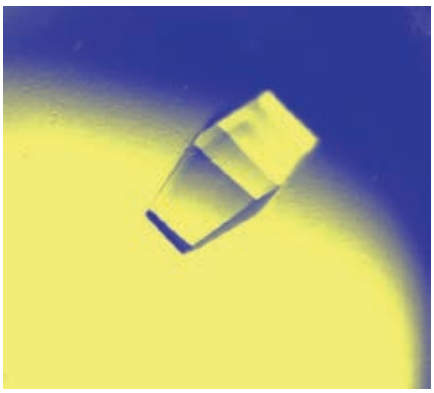
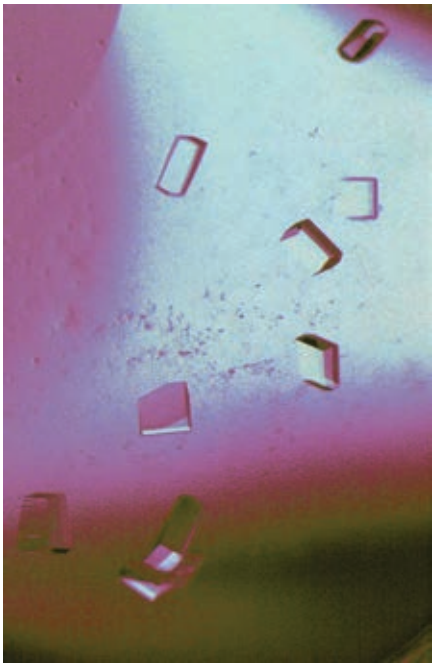
DEVELOPING A FAST NMR-BASED METHOD TO GENERATE STRUCTURAL DATA FOR PROTEIN-LIGAND

(Left) Figure 10: MiD51 protein crystal

(Right) Figure 11: MiD51 protein crystal





COMPLEXES THAT ARE NOT AMENABLE TO X-RAY CRYSTALLOGRAPHY

In fragment based drug discovery, structural data are generally needed to develop smaller hits into high-affinity lead compounds. CXS has developed a fast NMR-based method for structure determination of low-affinity protein-ligand complexes rapidly enough to support a program of medicinal chemistry.

Selective isotope labelling of isoleucine, leucine and valine (ILV) methyl groups is well established as a means of obtaining information about large protein-ligand complexes. CXS has utilised an alternative procedure, which provides methyl assignments for alanine, methionine and threonine in addition to those of ILV. This requires two protein samples for completion of the necessary chemical shift assignments: (i) a triple-labelled sample is employed to obtain the backbone and methyl resonance assignments using non-uniform sampling (NUS) and requiring only low protein concentrations (0.3 – 0.4 mM); (ii) a 10% 13C-labelled protein is used for stereospecific assignments using CT-[13C,1H]-HSQC. Once the resonance assignments are obtained, a uniformly [13C,15N]-labelled sample is needed for 3D ω1-13C,15N-filtered, ω3-13Cali (methyl) edited [1H,1H]-NOESY experiment, using similarly low protein concentrations to generate intermolecular NOEs for protein-ligand complexes of interest. It was noted that methionine assignments from 3D 13Cali edited [1H,1H]-NOESY data are only possible if the protein structure is available. Finally, sparse intermolecular NOEs and ambiguous interaction constraints derived from chemical shift perturbations are used to generate the structures using a constrained docking approach to structure calculation that have been implemented by CXS.

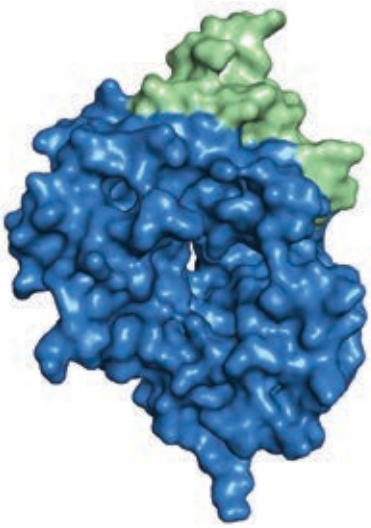
Using the CXS protocol, data acquisition, analysis and determination of the structure of the complex can be achieved within 2-3 weeks where the resonance assignments are unknown and in under one week once the protein has been assigned. To illustrate the approach, the team solved structures of Escherichia coli DsbA (EcDsbA) and Vibrio cholerae DsbA (VcDsbA) in complex with small molecules, both of which were not amenable to characterisation by X-ray crystallography. Broader analysis of structural data for a range of protein-protein and protein-ligand complexes that are not amenable to crystallography indicates the widespread applicability of this approach.

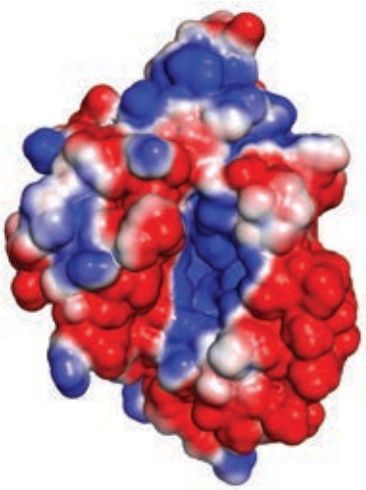
MONASH GROUP'S WORK INTO THE FUTURE

Many cellular processes are regulated by the interaction between biological molecules. The affinity of such interactions – as measured by the equilibrium dissociation constant (KD) for the complex – spans a wide range of values, which can vary by > 10 orders of magnitude. Much understanding of these interactions is derived by visualisation of structures of the complexes using X-ray crystallography. However, for this reason the vast majority of complexes that have been studied are considered to be strongly-interacting (KD ≤ 10-6 M) and stable. It is becoming increasingly clear that many important biological processes are regulated by transient and weak interactions between molecules. Such complexes do not often form crystalline structures and are therefore not amenable to X-ray crystallography. The Biological Sciences Program at CXS is developing solution-based NMR techniques based on NMR spectroscopy and quantum chemistry to generate an approach to visualisation of these weakly interacting complexes.

BIOLOGICAL SCIENCE PROGRAM CASE STUDY 1

Mitochondrial fission is important for organelle transport, inheritance and turnover. Alterations in fission are seen in neurological disease. In mammals, mitochondrial fission is executed by dynamin related protein 1 (Drp1), a cytosolic GTPase that polymerises and constricts the organelle. Recruitment of Drp1 to mitochondria involves receptors including Mff, MiD49 and MiD51. MiD49/51 form foci at mitochondrial constriction sites and co-assemble with Drp1 to drive fission. In order to understand how MiD51 functions at a molecular level, PhD student Viviane Richter solved the crystal structure of the cytosolic domain of human MiD51. Xenon derivatisation of native crystals was performed using a xenon chamber at the Australian Synchrotron. Native and derivative data were collected at the Australian Synchrotron, Beamline MX2, at 100 K and wavelengths of 0.9537 and 1.4586 Å, respectively. MiD51 was found to adopt a nucelotidyltransferase fold. It was subsequently found that MiD51 lacks catalytic residues for transferase activity but nevertheless binds GDP and ADP. MiD51 mutants unable to bind nucleotides were still able to recruit Drp1. Disruption of an additional region in MiD51 not part of the nucleotidyltransferase fold blocked





(Left) Figure 12: MiD51 structure (surface rendered) showing the large cleft for nucleotide binding and the Drp1 recruitment domain (in green)

(Right) Figure 13: MiD51 structure (surface rendered) showing the large cleft for nucleotide binding

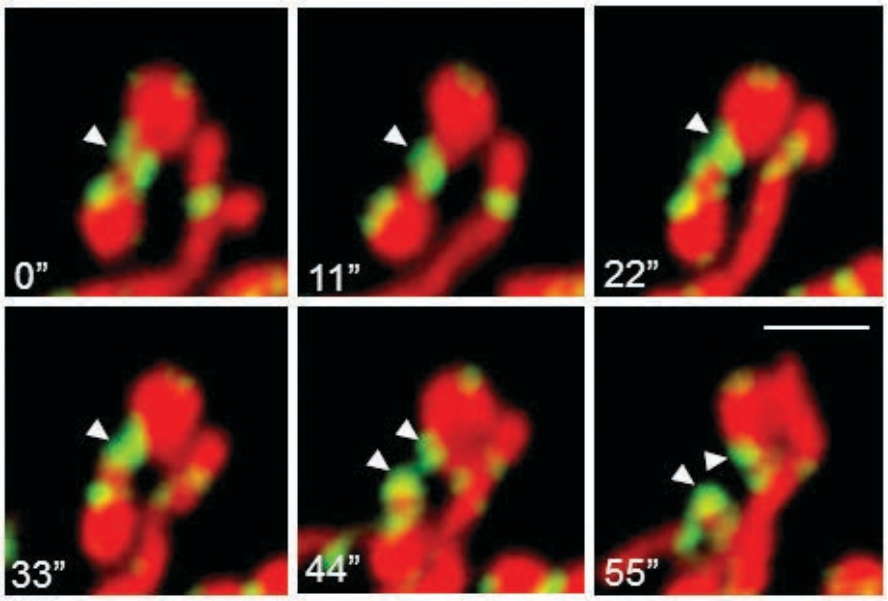


Figure 14 Time lapse imaging of mitochondria (red) undergoing a fission event at the site where MiD51 foci (green) are located

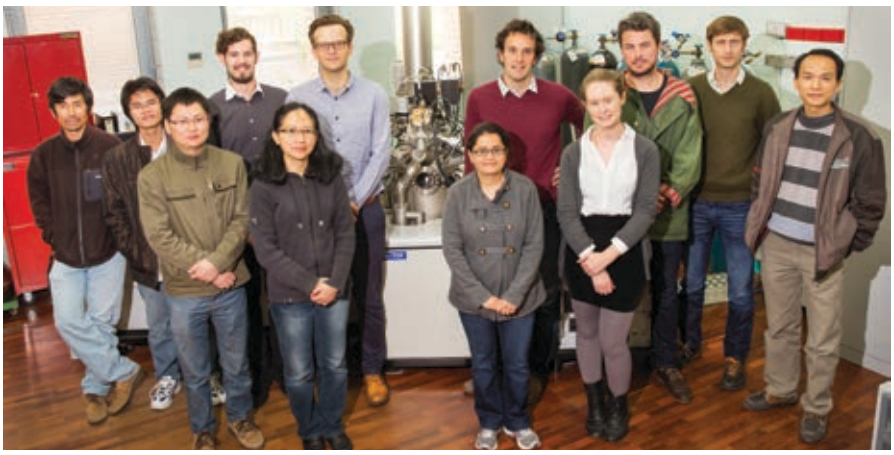
Drp1 recruitment and assembly of MiD51 into foci. MiD51 foci are also dependent on the presence of Drp1 and following scission, they are distributed to daughter organelles supporting the involvement of MiD51 in the fission apparatus.

BIOLOGICAL SCIENCE PROGRAM CASE STUDY 2

One of the Program's goals of studying NmDsbA enzymes is to understand the structural basis of the observed substrate specificity of the three enzymes. In order to complement the structural data on the proteins, a fluorescence-based assay has been developed to monitor enzymatic activity. The assay makes use of the disulfide oxidase activity of the DsbA enzymes to catalyse disulfide formation in a substrate peptide, which brings together a fluorescence donor and acceptor to stimulate sensitised emission from a bound lanthanide. The peptide substrate is prepared with a 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) group amide-coupled to the N-terminus to which a lanthanide is coordinated, and a methylcoumarin amide-coupled to the Ð-amino group of the C-terminus. Oxidation of the two cysteines in the peptide to form an intramolecular disulfide-bond results in a large increase in fluorescence as the coumarin is brought into closer proximity to the lanthanide. This increase in fluorescence can be used to monitor the oxidation of the peptide and catalysis of this reaction by DsbA.

The oxidation assay can be used both with different peptides to probe the substrate specificity of the three enzymes and as a reported assay to monitor the activity of fragments identified in the FBDD screening.

Some members of the EMP group gathered at La Trobe University (left to right): Thanh Bao Pham, Giang Tran-Nhan, Bo Chen, Nicholas Phillips, Benedicta Arhatari, Grant van Riessen, Chandni Doshi, Michael Jones, Hannah Coughlan, Henry Kirkwood, Mark Junker and Mac Luu.



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 nanofabrication techniques; tomographic imaging of three-dimensional objects; the detailed characterisation of radiation sources; and the development of novel imaging methodologies using diffraction data. In 2013 The EMP group had members based at La Trobe University, the University of Melbourne and the Australian Synchrotron.

Through its broad spectrum of members and activities, the EMP interacts strongly with most of the other programs of CXS. A unifying theme of the work in this program is the utilisation of synchrotron radiation and ultra-bright free-electron lasers to develop new experimental methods for revealing biological and materials phenomenon at the nanoscale. This work involves a particularly strong connection to the Centre's Theory and Modelling program, particularly in the area of understanding partially coherent light sources. The EMP designs and performs novel experiments to explore key ideas from this area and their extension to surprisingly distant problems of imaging sample structure and dynamics.

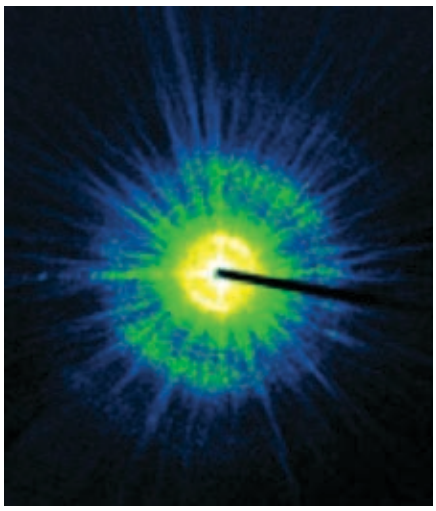
The program also works closely with the centre's Biological Sciences and Structure Determination Methods Programs to develop distinctive approaches to X-ray imaging and nanocrystallography for biological studies. Researchers from EMP and BSP regularly work together to prepare samples; undertake synchrotron experiments; and interpret experimental results. These interactions are fundamental to the mission of CXS and provide unique opportunities for the mutual translation of physics and biology.

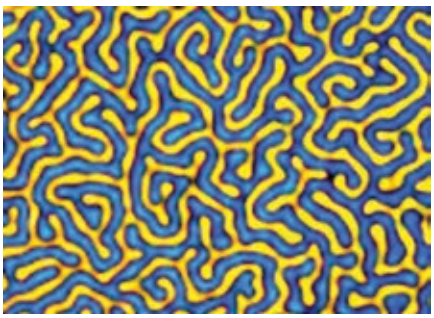
In 2013 the EMP continued to explore new methods in imaging and coherence using some of the most advanced and most intense light sources available. The group has pushed the boundaries of imaging with partially coherent light sources, explored very low X-ray energy biological imaging, and found new opportunities for probing materials properties using X-ray microbeam diffraction techniques. The EMP team has also continued to make a distinctive contribution toward the challenge of non-crystallographic structural determination of membrane proteins using X-ray free electron lasers, which is central to the goals of CXS. Concurrently, the program has developed a unique soft X-ray microscopy facility at the Australian Synchrotron, cementing a place for future studies of imaging and coherence. Some of the key achievements for 2013 are described in more detail below.

COHERENT DIFFRACTION MICROSCOPY USING SYNCHROTRON RADIATION

Coherent diffraction imaging (CDI) is a rapidly developing microscopy technique that can provide two- and three-dimensional images of the internal structure of materials and biological samples with the advantages of quantitative amplitude and phase information, and spatial resolution that is effectively limited only by the numerical aperture of the detector. During 2013 the EMP continued to drive the development of novel implementations of CDI, including Fresnel CDI (FCDI), which takes advantage of the divergent illumination such as that which emerges from the focal plane of a Fresnel zone plate. The role of the image-forming lens of a traditional microscope is replaced in all forms of coherent diffractive imaging by iterative reconstruction algorithms that are used to recover real-space images from oversampled far-field diffraction intensities.

The application of CDI to biological samples is made challenging due to the effects of radiation damage on the specimen. Much of the work of the program has therefore been focused on optimising the sensitivity and dose efficiency of the technique. Extensions of FCDI using methods of ptychography, phase diversity and tomography allow particularly sensitive imaging a substantially lower X-ray dose than is typically required by other forms of X-ray microscopy. Ptychography is a scanning diffraction





(Left) Figure 15: Coherent X-ray diffraction pattern from a magnetic microstructure.

(Right) Figure 16: Magnetic domain structure in a multilayer thin film reconstructed from coherent diffraction data obtained at the SXRI beamline of the Australian Synchrotron. (credit: A. Tripathi)

technique that dispenses with the need for isolated specimens by moving the specimen through a coherent illuminating beam to create on the specimen a sequential array of overlapping illuminated areas.

It has previously been shown by this program that including knowledge of the spatial and temporal coherence properties of the illumination in the image reconstruction process makes it possible to perform CDI with dramatically relaxed coherence requirements. This means that more of the light produced by synchrotron undulator sources can be used for very fast imaging. However, until recently, CDI with partially coherent illumination had been demonstrated only for model samples. During 2013 the EMP turned its attention to demonstrating through simulation and experimentation that partially coherent CDI can be applied to complex, real-world samples. Despite added computational challenges, it was shown that considerable benefits can be realised in ptychography with partially coherent illumination. A 'universal' limit on the degree of partial coherence that can be tolerated without any loss of information was also established.

The unique strengths of x-ray microscopy include high penetration depth and energy- and polarisation-dependent resonances that can be exploited to provide chemical and magnetic state information. In 2013 various forms of resonant coherent diffractive imaging were demonstrated to obtain quantitative maps of materials and biological specimen properties at high spatial resolution. One example used ptychography with X-rays resonant with the absorption edges of magnetic microstructures that exhibit circular or linear magnetic dichroism (Figure 15) to obtain high resolution maps of magnetic domain structures (Figure 16).

ULTRABRIGHT AND ULTRAFAST X-RAY LASERS

X-ray free electron lasers – or X-FELS – are the brightest sources of X-ray light on the planet, delivering an increase in the coherent X-ray flux available from synchrotron light sources by ten orders of magnitude. Anticipating the arrival of hard X-ray free electron lasers, CXS embraced the ambitious goal of opening a new frontier in biotechnology through the non-crystallographic structural determination of membrane proteins. Early X-FEL experiments at the world's first hard X-FEL were undertaken by the EMP in collaboration with the CXS Theory and Modelling Program to explore how the interpretation of the structure of nanocrystals from diffraction of extremely intense and extremely fast femtosecond X-FEL pulses can be affected by sudden photoionisation. These experiments showed that the electronic structure of fullerene molecular crystals is modified by the X-FEL pulse in femtoseconds without change to the translational symmetry of the crystal. In other words, a new, transient phase of the fullerene crystal was found. This work, which was recently submitted to the journal Science[1], opens a new research frontier and strikingly demonstrates the importance of understanding the interaction of matter with ultra-bright, ultrafast X-ray pulses.

Subsequent to the initial X-FEL experiments with relatively simple, highly symmetric molecules, the program directed its attention to understanding the role of ultrafast electron dynamics in the formation of X-ray diffraction patterns from single nano-crystals of β-Hematin illuminated by a an X-FEL pulse. This work, undertaken in collaboration with CXS Theory and Modelling and Biological Sciences Programs, has broad implications for X-FEL nanocrystallography and may eventually allow new insights into how β-Hematin formation can be inhibited by antimalarial drugs.

Early success in exploiting the availability of X-ray Free Electron Lasers (X-FEL) created new opportunities for international collaboration in 2013. Dr Brian Abbey took part in a collaborative X-FEL experiment led by Prof. Ian Robinson (London Centre for Nanotechnology) by which the first nanoscale 'movies' of shockwaves propagating through gold nanocrystals were created. The experiment used a picosecond optical laser pulse to initiate the shockwave after which a femtosecond X-ray pulse was used to 'image' the resulting modifications to the nanocrystals refractive index as a result of phonon propagation through the sample. The results from this experiment could shed light on how nanocrystalline materials respond to shock and increase our fundamental understanding of the physics of phonon propagation in confined systems. The lead author of this study, which appeared in the prestigious journal Science, was Dr Jesse Clark, who is a former CXS PhD student supervised by Prof. Andrew Peele (La Trobe).

VISUALISING THE STRESS OF IMPERFECTION

Another major breakthrough by the EMP in 2013 was the first ever X-ray measurements of the long-range stresses in a crystal due to single dislocations using X-ray microbeam diffraction. This work was the result of a collaboration between the EMP, La Trobe University and Oxford University Engineering Science. By using a micron-sized X-ray beam probe, the team was able to directly measure the stresses and lattice rotations due to a single edge dislocation in a InGaAs/GaAs heterostructure. This work, published in the high-impact journal Nature Communications, has important

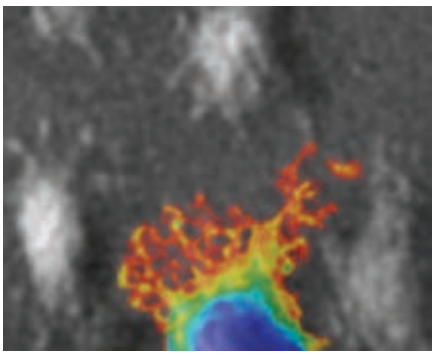


Figure 17 : Phase-diverse coherent diffraction imaging in the water window is used to obtain high-contrast, quantitative images cells (colour overlay). An exceptionally low X-ray allows flexible correlative imaging strategies with, for example, confocal fluorescence microscopy (greyscale). (credit: M. Jones, La Trobe University)

implications for the in-situ study of dislocation structure formation, self-organisation and evolution in the bulk. This work was led by Dr Brian Abbey (La Trobe University) and Dr Felix Hofmann (Oxford), who was the lead author of the publication. The unique heterostructures were fabricated through a collaboration with Dr Eugeniu Balaur (La Trobe University).

CASE STUDY: CELLULAR PTYCHOGRAPHY

Cell imaging often relies on the contrast provided by genetic or synthetic fluorescent labels that render the cell quite different to its in vivo state. Label-free imaging techniques are increasingly valuable in biological research and drug discovery programs where minimising cellular manipulation and the interruption of cell culture conditions to preserve normal cell function is critical. The availability of a bright, highly coherent source of low energy X-rays at the Australian Synchrotron allowed rapid progress in cell imaging during 2013. The EMP successfully extended the biological application of Fresnel coherent diffraction imaging (FCDI) for label-free, high contrast X-ray cell imaging at nanoscale resolution.

Using the Centre's flagship X-ray imaging facility at the Australian Synchrotron the team demonstrated that FCDI can be used to reveal the structure and composition of biological specimens at nanoscale resolution in a way that is complementary to conventional imaging techniques. Coherent X-rays were used in the 'water-window' energy range that lies between the carbon and oxygen K-shell absorption edges. In this range, the difference in the X-ray interaction strength between protein based biological materials and water is increased. In a study led by Dr Michael Jones in collaboration with the Biological Sciences Program, FCDI was used to image mitochrondrial networks within mouse embryo fibroblasts (Figure 17). Mitochondria are dynamic organelles that fuse and divide to form constantly changing tubular networks. Understanding the mechanisms that control fusion and division has important consequences for managing disease and genetic disorders. The EMP showed that FCDI can be used to directly identify mitochondrial fission sites inside fibroblasts despite the weak intrinsic material contrast between cellular components. Furthermore, the team has demonstrated that the combination of the specimen phase and magnitude distributions that are simultaneously recovered in techniques used within the program can be used to isolate these subtle compositional variations from the thickness and density variations across the specimen. It is particularly significant that the FCDI technique is able to provide this rich information across length-scales from tens of microns to tens of nanometres.

LOOKING FORWARD

As 2013 drew to a close, the EMP started planning the wind-up of some of its projects and the continuation of others with new sources of funding. The successes of the CXS, particularly those of the EMP, have given rise to a number of new funding opportunities that will enable particular aspects of coherence and imaging to be pursued beyond the life of the centre. Some of the research activities will be absorbed into a new Disciplinary Research Program at La Trobe University, which was established in 2013, due in part to the research outcomes of members of the program. Some of the key methods and much of the deep expertise developed by the EMP will be carried to new projects through recently awarded funding for Centres of Excellence, fellowships and postgraduate scholarships.

The endstation project will be supported principally by La Trobe University with support from the Australian Synchrotron and collaborating institutions. An Australian Research Linkage and Equipment Funding grant continues to support a critical detector upgrade.

The most important legacy of the EMP will be its students and research staff who will carry their experience to exciting new positions around the world. Present EMP members can look forward to following in the footsteps of former members who hold positions as academics, group leaders, and beamline scientists at the Argonne National Laboratory; European X-FEL; Linac Coherent Light Source; and several leading universities around the world. In 2013 there were several awards and appointments of EMP members that recognise their outstanding contributions to our field: Prof. Andrew Peele was appointed Director of the Australian Synchrotron; Dr Brian Abbey was awarded an Australian Research Council Future Fellowship and Melbourne Centre for Nanofabrication Technology fellowship; and Prof. Keith Nugent commenced as Deputy Vice Chancellor and Vice President (Research) at La Trobe University.

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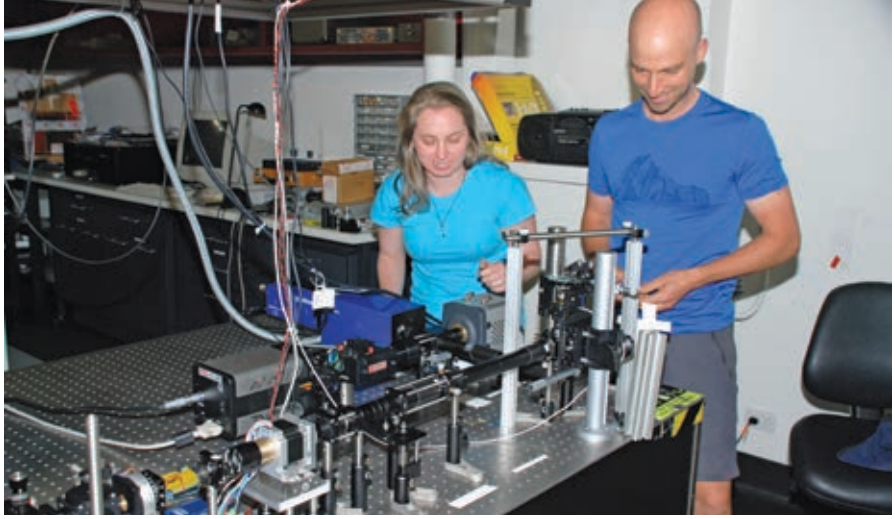


Developmental Structured Illumination Microscope in Chemistry at the University of Melbourne. This microscope can be reconfigured for multiple modes. Shown here is the SIM coupled to a picosecond intensified CCD camera

SHORT WAVELENGTH LASER SOURCE PROGRAM

The Short Wavelength Laser Source Program has investigated the generation of extreme ultraviolet (XUV) and soft X-ray pulses by high harmonic generation (HHG) and applied these sources in atomic and molecular spectroscopy; condensed matter physics; and imaging on the micron- and submicron-scale. These compact (table-top) femtosecond pulsed sources will complement imaging studies using X-ray free-electron laser (X-FEL) sources currently under development at large international facilities.

By their nature, HHG sources produce a laser-like beam that consists of a number of harmonic orders. Therefore, a harmonic source with just a few intense orders (ideally a single harmonic order) may be advantageous for many applications because they can be used directly without additional spectral selection optics.

The high harmonic generation process can be explained in terms of a semi-classical three-step model. In this model, under interaction of a strong laser field the active electrons first tunnel through the potential barrier, are then accelerated in the first half of the optical cycle of the laser field, and then are pulled back and finally recombine with parent ions to emit high-energy photons in the second half of the cycle. The electronic acceleration processes and the variation of the molecular or atomic ground state throughout the interaction with the driving laser field play important roles in quantum systems and need to be studied in more detail.

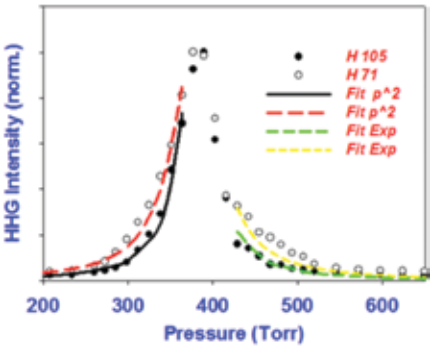
Unlike atoms, molecules are not spatially isotropic systems. For randomly aligned molecules, their HHG spectrum has been shown to have characteristics similar to that produced by atoms, but for aligned molecules, which can be realised by using another laser field, the HHG is influenced by the angle between the molecular frame and the polarisation vector of the femtosecond laser field. An investigation to clarify the roles of intramolecular quantum processes in field-free aligned molecules is highly desirable, in order to obtain an improved understanding of the underlying physics which is the basis of future applications.

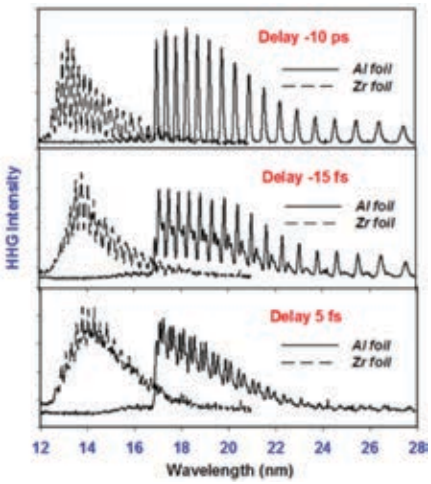
Due to the low efficiency of the HHG process, phase-matched propagation of the fundamental and harmonic radiation throughout a macroscopic sample is required to obtain a measurable signal. The degree of phase-matching depends on the harmonic order and several experimental parameters, including the focusing characteristics of the laser beam, the absorption coefficient of the target gas at the harmonic frequencies, the ionisation fraction of the gas and the difference in the refractive index at the fundamental and harmonic wavelengths. We have been investigating ways of optimising the phase matching.

The high harmonic spectrum and intensity contains information about the electronic structure of the atom or molecule and other quantum processes involving the free and bound electrons. Studies of the process of high harmonic generation provide a better understanding of the microscopic and macroscopic process and may lead to additional information about the electronic structure of the atom or molecule.

PHASE-MATCHED GENERATION OF HIGH ORDER HARMONIC WITH INFRARED LASER FIELD

To obtain a high order harmonic source at high photon energy an infrared laser field at ~1400 nm has been used. The conditions for the phase-matched generation are studied in a semi-infinite gas cell configuration. Figure 18 shows the dependence of the total intensity on pressure for the 105th (H105) and 71st (H71) harmonics for the case when the focal point position is set at the exit pinhole of the gas cell. The optimised value for the pressure is found to be pAr = 370 Torr. For pAr < 370 Torr the harmonic intensity increases quadratically with pressure





(Left) Figure 18: Intensity of 105th (H 105) and 71st (H71) harmonics from argon gas versus gas pressure when a pulse at 1400 nm is used for HHG. The p2 scale indicates that the generation of harmonics is phase-matched.

(Right) Figure 19: High harmonic spectra from argon gas for different delay times between the two laser fields. Laser pulses at 1400 nm and 800 nm are used for generation and control of the HHG process, respectively.

(p2) and thus indicates that the harmonic emission is phase-matched for this spectral band-width. For pAr > 450 Torr the variation of the harmonic emission intensity is dominated by re-absorption of the generating gas and an exponential decay curve can be fitted in this region (Figure 18). Also, larger values of pressure appear to optimise the phase-matching conditions for higher harmonic orders and allow a larger number of atoms to contribute to the coherent build-up of a higher harmonic order.

CONTROL OF THE HIGH ORDER HARMONIC GENERATION WITH TWO LASER FIELDS

To obtain a high order harmonic source at high photon energy an infrared laser field at ~1400 nm has been used. The conditions for the phase-matched generation are studied in a semi-infinite gas cell configuration. Figure 18 shows the dependence of the total intensity on pressure for the 105th (H105) and 71st (H71) harmonics for the case when the focal point position is set at the exit pinhole of the gas cell. The optimised value for the pressure is found to be pAr = 370 Torr. For pAr < 370 Torr the harmonic intensity increases quadratically with pressure (p2) and thus indicates that the harmonic emission is phase-matched for this spectral band-width. For pAr > 450 Torr the variation of the harmonic emission intensity is dominated by re-absorption of the generating gas and an exponential decay curve can be fitted in this region (Figure 18). Also, larger values of pressure appear to optimise the phase-matching conditions for higher harmonic orders and allow a larger number of atoms to contribute to the coherent build-up of a higher harmonic order.

TRANSVERSE PHASE VARIATION IN HHG PROCESS

The atomic phase plays an important role in the phase-matched generation of high order harmonics, especially in determining the coherence properties of HHG source. The gradient of the atomic phase will create an effective wave-vector $K_t(r,z) = \nabla\varphi_{at}(r,z)$ which is proportional to the spatial derivative of the action. In a simple case this phase varies linearly with the laser intensity I: $\varphi_{at} = -\alpha_q I$ [23], where $\alpha_q \approx 1 \times 10^{-14}$ cm^2 W^{-1} and $\approx 25 \times 10^{-14}$ cm^2 W^{-1} for the short and long quantum trajectories, respectively. Using an off-axis pulse to modify the phase-matched harmonic intensity and the spatial distribution, the contribution of different electron trajectories can be revealed.

The insets in Figure 20 show the beam profile of H21 and H17 for oxygen at around 10 fs where the phase-mismatch is large and the harmonic intensity is low. Within one optical cycle a shifting of the maximum can be observed with delay time away from the axis (for delay ~ - 108 fs) to an asymmetrical annular beam (for delay ~ - 109 fs) and then an abrupt change back to on-axis (for delay ~ - 110 fs). When the divergence is a maximum contributions from both off-axis and on-axis radiation are observed. An asymmetrical annular beam may result when the two fields are aligned off-axis. The momentum gain of a free electron, $\delta P_{elec} = \hbar K_t$, is transferred to the harmonic photon, and is taken into account in the phase-matching condition. Based on momentum conservation of the wave-vector, $K_q = qK_0 + K_t$, the $|K_t|$ for

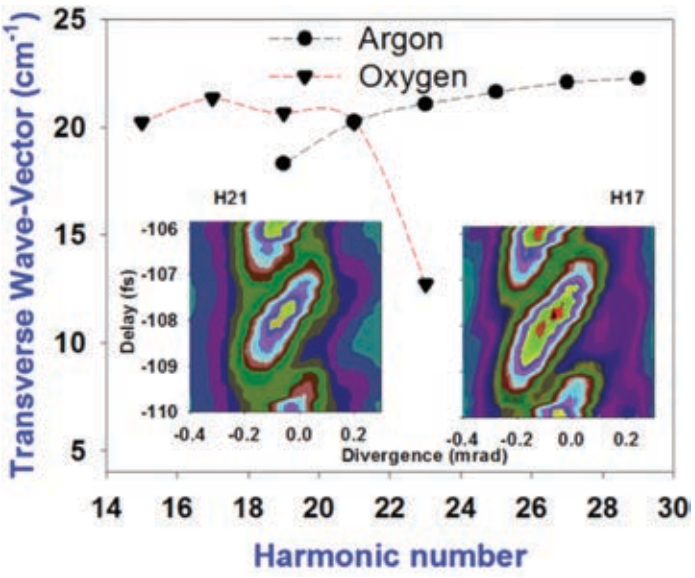


Figure 20: Maximum of the transverse wave-vector measured by the second beam. The insets show the beam profiles of H21 and H17 for oxygen at around -110 fs.

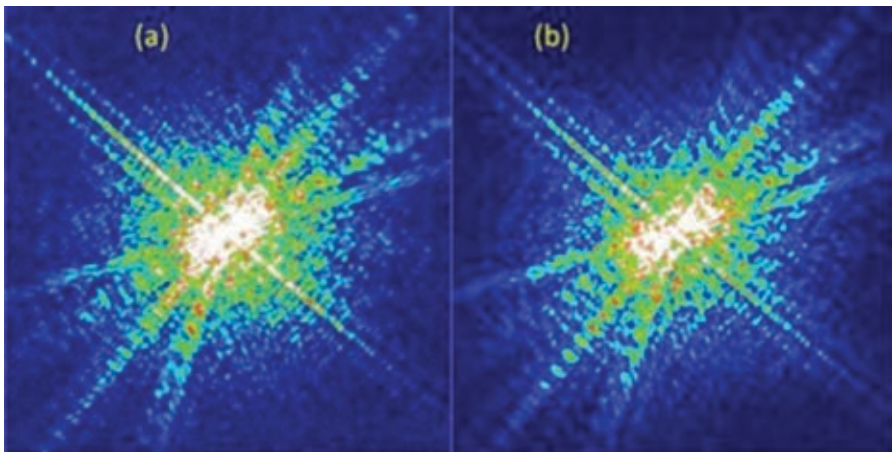


Figure 21: Diffraction images from a 3 μm x 3μm sample at distances of (a) 1.5 mm and (b) 1 mm from the focus.

Figure 22: Transmission electron microscope and reconstruction image of the 3 μm x 3 μm sample. The distance between sample and CCD is 1.5 mm from the focus. A plan-wave field code is applied for reconstruction.

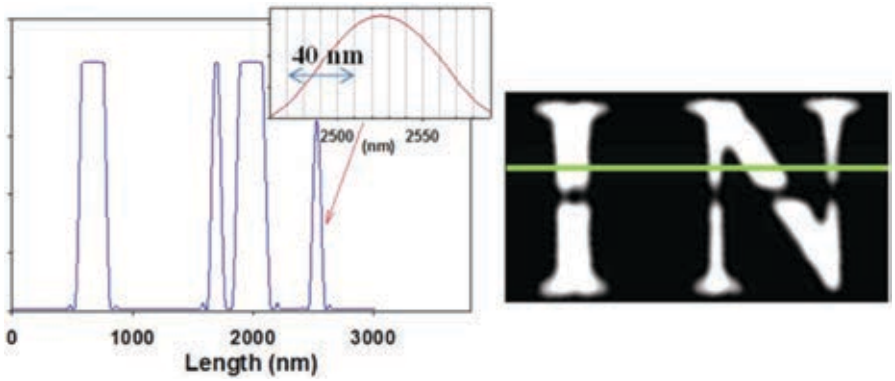


Figure 23: Knife-edge test to determine the resolution of the reconstructed image of test sample.

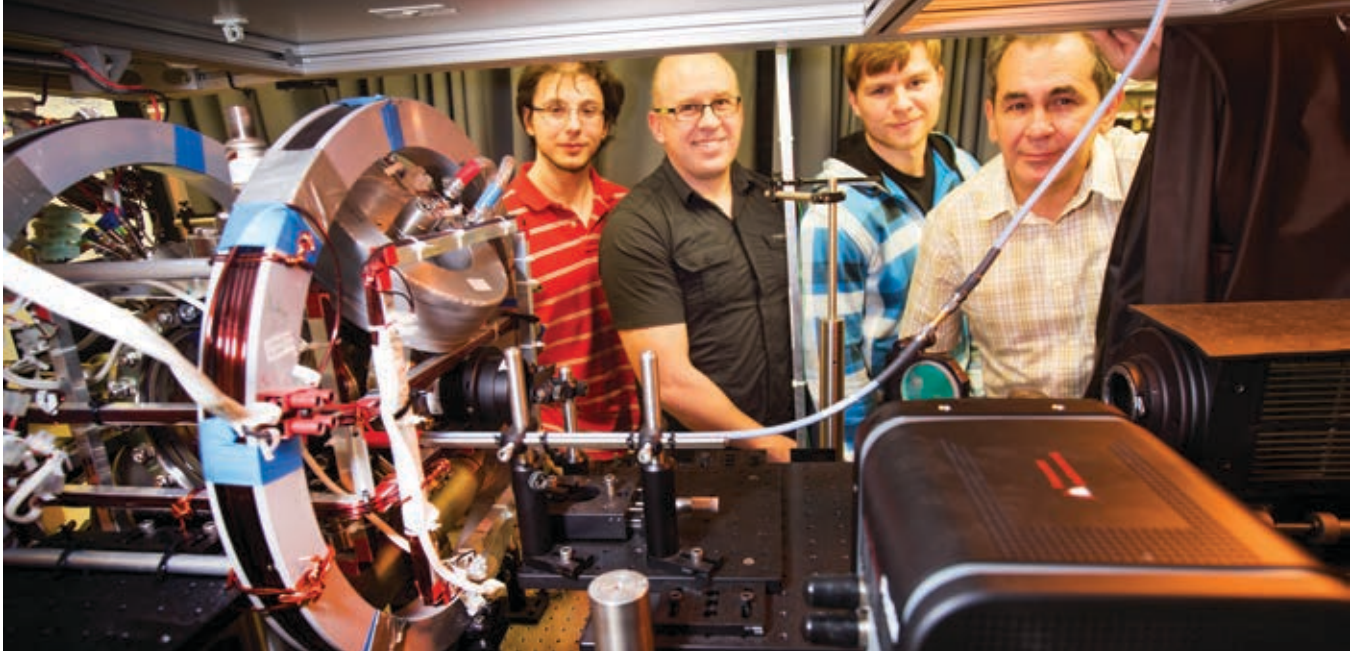
different harmonic orders can be determined. While the transverse effective wave-vector and hence the transverse phase exhibits a slight monotonic increase with harmonic order for argon, the phase for molecular oxygen changes abruptly for the harmonic at the cut-off as shown in Figure 20. The changing of the return time (τs) involving the second pulse alters the phase front of the harmonic field, which is reflected in the far-field spatial profile. We can expect that the variation of the spatial profile depends on the atomic and molecular structures.

HIGH SPATIAL RESOLUTION DIFFRACTION IMAGING WITH 30 NM HHG SOURCE

The program has demonstrated that a high resolution image (< 50 nm resolution) can be reconstructed from a CDI diffraction pattern generated by a table-top high-harmonic source at a wavelength of around 30 nm. By using a focussing mirror, a single harmonic can be selected and focussed to illuminate the sample. As a result, the quality of the diffraction pattern is improved and the required exposure time is significantly reduced (< 5s for a 3 μm x 3 μm sample size) as shown in Figure 21. The reconstruction with a plane-wave field code shows a spatial resolution of 45 nm (Figure 22). In order to increase the quality of the reconstructed image, the object needs to be placed at an optimum distance from the focus point to ensure the object is illuminated by an approximate plane wave.

SUPER-RESOLUTION OPTICAL IMAGING

Super-resolution optical microscopy provides imaging resolution beyond the



typical diffraction limit of optical systems, and can provide resolution comparable to that achieved with other methods, including CDI. Correlating optical images with CDI reconstructions on the tens of nanometres scale will provide additional information to that provided by one technique alone. The program has concentrated its efforts on the technique of structured illumination microscopy (SIM), but has also been developing other methods including Stimulated Emission Depletion (STED) and localisation microscopy techniques using an ultrashort pulsed laser to implement multi-photon-induced photoactivation coupled with temporal focussing.

We have been developing software for the reconstruction of structured illumination microscopy (SIM) images. The aim is to make such reconstruction software openly available along the lines of the CDI software project. Brendan Allman has developed the code to produce and analyse simulated data and Clare Henderson is furthering this to look at real data collected from our developmental SIM. Along with this work, we are incorporating code with which to "denoise" the raw component SIM images prior to image reconstruction. Our developmental system has undergone significant changes to exploit the unique advantages of this system over commercial instruments. We have added a polarisation image splitting to enable the simultaneous collection on the same camera of two images of orthogonal emission polarisation. We have also added a picosecond intensified CCD camera to the system to enable, for the first time, time-gated SIM images to be collected with ~200ps gate widths.

The Shortwave Laser Source Program has also undertaken to produce self-assembled

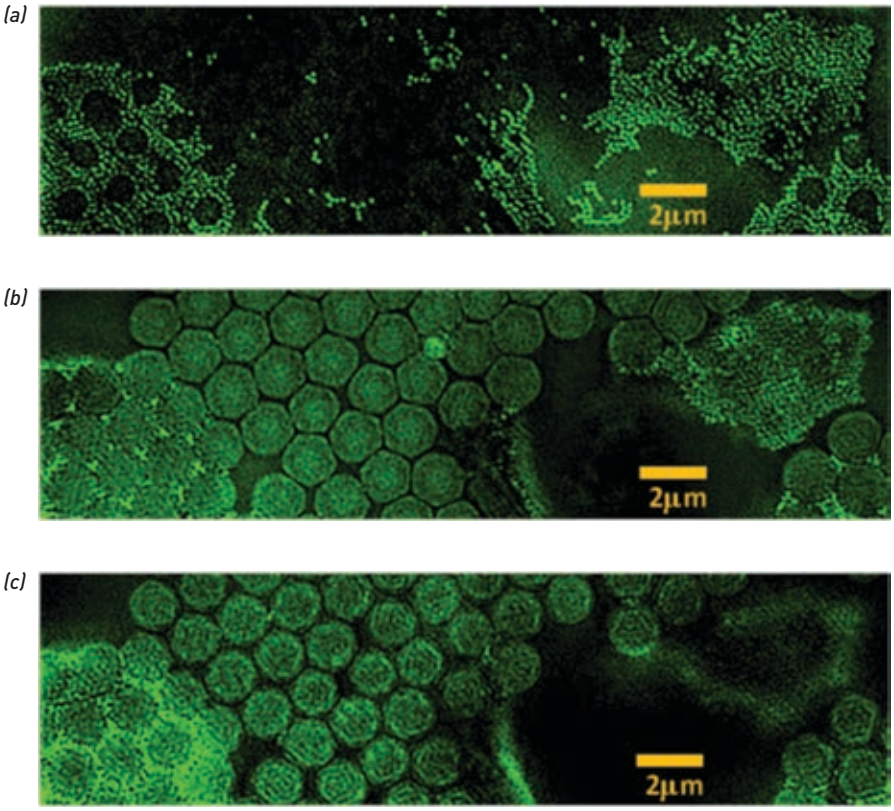
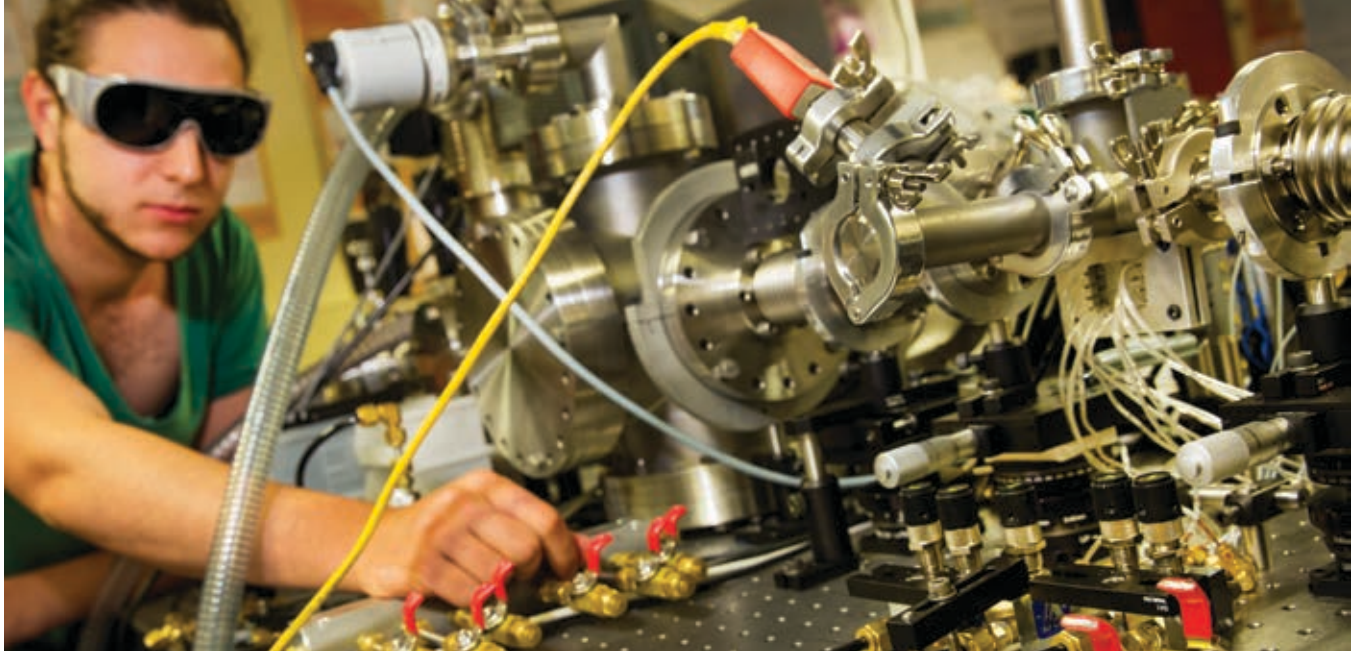


Figure 24: Z-slices from a single 3D-SIM reconstruction of a 1.5µm/200 nm binary colloidal assembly of fluorescent spheres at (a) the coverslip and (b) mid-way through the large spheres and (c) near the top of the large spheres. 2D and 3D packing of mono- and binary assemblies are seen.



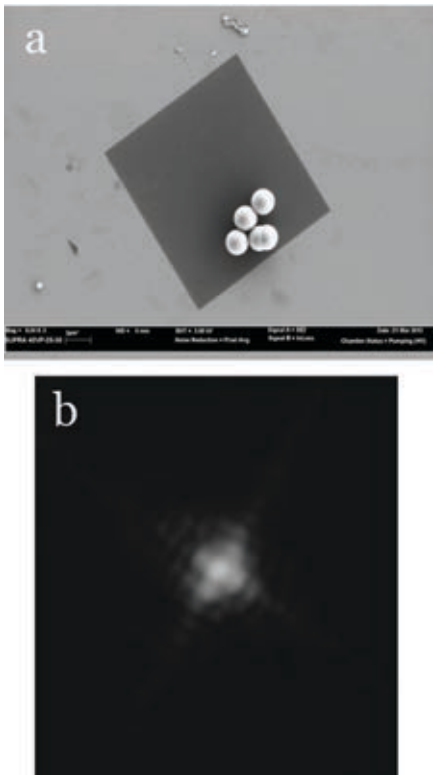


Figure 25: (a) SEM image and (b) diffraction pattern of 2 µm silica spheres on a silicon nitride substrate.

nano/micro-structures as test samples that can be used for both fluorescence-based super-resolution optical microscopy as well as coherent diffractive imaging. The ideal test sample is: fluorescent in the visible region, has structure on the tens of nanometre to micrometre scales, readily and reproducibly synthesised, provides contrast in the XUV/soft X-ray regime, can withstand irradiation in this wavelength range, and has some scientific interest. The team has produced self-assembled binary polymer colloid structures by varying the proportions of two sizes of spherical polymer particles, at least one of which can be fluorescent (Figure 24). Diffraction data has also been successfully obtained from these self-assembled colloidal structures using the HHG (Figure 25), for reconstructions similar to the SWIN sample mentioned above. Additionally, well-defined structures have been produced from conjugated polymers.

SUPER-RESOLUTION MICROSCOPY CASE STUDY

Since the seminal work of Ernst Abbe in 1873, Lord Rayleigh in 1896 and others, the achievable resolution of optical microscopy techniques has been limited by diffraction to approximately half the wavelength of the light used to illuminate the sample. In recent years a number of approaches have been developed that overcome some of the limitations in optical resolution, which has spawned the term 'super-resolution' optical microscopy. The fundamental laws of optical physics are not broken, but rather circumvented, by a range of relatively simple strategies. In 1998, it was suggested that a fine sinusoidal grating pattern could be used to improve lateral resolution[1] and this was first demonstrated in 2000[2]. This 'structured illumination' technique has now been commercialised and forms the basis of the some of the super-resolution facilities used in CXS to complement coherent diffractive imaging. Ben Morrison, Dr Clare Henderson and Adabelle Ong – all members of this CXS program – are developing the technique further through improved image reconstruction software and by adding other detection modes, and applying these to study a range of both biological and materials science related samples.

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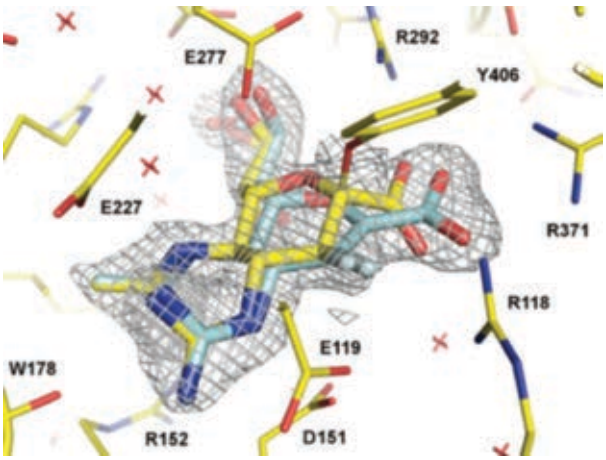


Figure 26: X-ray crystallographic structure of the active site of the enzyme trapped as its 3-fluoro(eq)-4-guanidino-sialyl-enzyme intermediate (elimination product is in pale cyan) overlaid with the electron density map shown as a graymesh contoured at 1s within 1.6 Å of ligands. The electron density extends from the ligand molecule to Y406, suggesting a covalent link between the inhibitor's C-2 atom and the OH of Y406.

STRUCTURE DETERMINATION METHODS PROGRAM

The Structure Determination Methods Program 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, crystallisation 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. A collaboration within CXS 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 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 spanning coherent diffractive imaging and 3-D crystallography and is 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.

INFLUENZA

Influenza (Flu) antiviral agents play important roles in modulating disease severity and in controlling pandemics while vaccines are prepared, but the development of resistance to agents like the commonly used neuraminidase (NA) inhibitor oseltamivir may limit their future utility. The Structure Determination Methods Program solved structure of Flu virus NA (neuraminidase) with new inhibitors (Figure 26) in collaboration with the Flu group at CSIRO and chemists from UBC (Canada) and University of Bath (UK) in development of new class of anti-flu drags. The paper has published in the prestigious Science magazine.

ALZHEIMER'S DISEASE

Alzheimer's disease (AD) accounts for ~70% of all dementias and is currently Australia's 3rd overall leading cause of death, after heart disease and stroke. Amyloid-β (Aβ) is the major constituent of the senile plaques in the AD brain. During 2013, the team finalised analysis of the protein crystallography synchrotron data on the complex of anti-amyloid-β antibody (WO2) with amyloid-beta peptide fused with immunoprotein Im7. This paper was published in the well-regarded publication, Proteins.

MALARIA

Malaria, one of the top five leading infectious diseases in terms of mortality, causes almost one million deaths annually. Widespread resistance to quinoline (e.g. chloroquine), antifolate, and more recently endoperoxide (e.g. artimisinin) antimalarial compounds has prompted the search for new chemotherapeutics. Quinoline antimalarial compounds have been shown to target iron(III) protoporphyrin IX (Fe(III) PPIX), inhibiting its incorporation into haemozoin. The aim of this study is to use Extended X-ray Absorption Fine Structure (EXAFS) to elucidate structural information about a novel synthetic haemozoin species, as well as the Fe(III)PPIX complexes of antimalarial drugs, e.g. 4-aminoquinolines: chloroquine and amodiaquine, and quinoline methanols: quinine, quinidine and mefloquine. An understanding of drug-target interactions in solution may assist in the rational design of novel haemozoin inhibiting antimalarial compounds. EXAFS data for aqueous Fe(III) haem species and their complexes with antimalarial drugs collected data processing is in progress in close collaboration with Stellenbosch University and Cape Town University (Prof. T. Egan). PhD student Kaliefie Gildenhuys from Stellenbosch University (Universiteit Stellenbosch) visited CSIRO and participated in XAFS experiment.

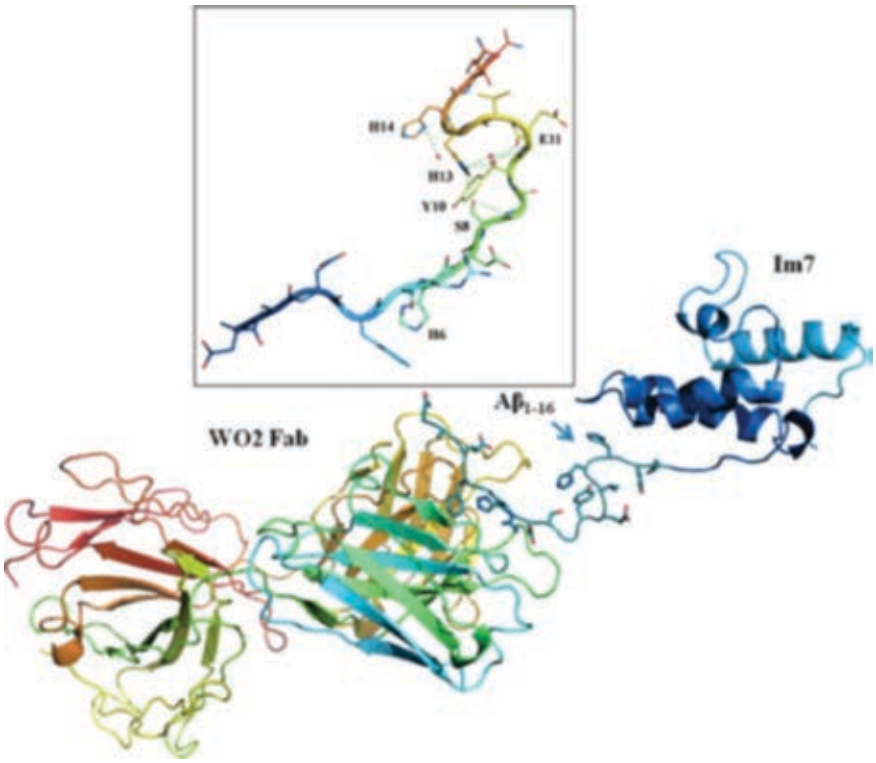


Figure 27: Structure of the Aβ1–16Im7–WO2 Fab crystal complex (a) and Aβ1–16 fragment of this structure (b).

CASE STUDY

THE CHARACTERISATION OF THE STRUCTURAL PROPERTIES OF β-HEMATIN AT EARLY STAGES OF THE FORMATION OF CRYSTALS.

Diffraction pattern obtained from submicron β-Hematin crystals using XFEL microfocus source at LCLS indicates significant difference from the one previously obtained from large crystals using the synchrotron sources. The possibility that very small crystals may have some structural differences compared to large crystals may be the key to understanding the chemical functions of anti-malarial drugs. During the last two months, several sets of powder diffraction

patterns from β -Hematin crystals of different sizes have been collected using the synchrotron X-ray source. The data was collected at two beamlines, MX1 and MX2, with nominal beam size 103x90 and 37x32 micron respectively. Obtained powder diffraction patterns were analysed by Rietveld refinement and the maximum entropy method. Preliminary analysis shows that the crystallite size and the real structure of β-Hematin affect the diffraction pattern, Figure 28.

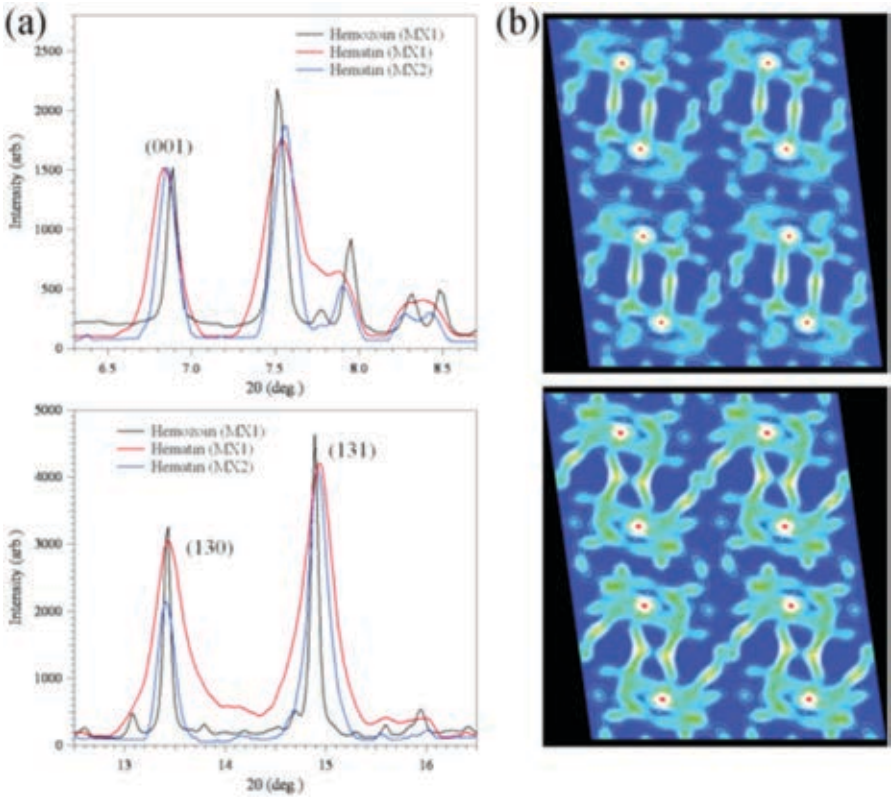


Figure 28: (a) Sections of powder diffraction patterns from β -Hematin crystals; (red) data collected at the MX1 beamline, (blue) data collected at the MX2 beamline. The diffraction pattern from the Haemozoin large crystals (black line, data collected at the MX1 beamline) is also shown for comparison. (b) The projection of the electron density of Haemozoin (top, MX1 beamline) and β -Hematin (bottom, MX2 beamline) crystals on the (ab) crystallographic plane obtained using the MEM approach.

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.

Its interests involve:

1. The solution of inverse problems.
2. The characterisation of partial spatial and temporal coherence in short wavelength light sources.
3. The relativistic formulation of molecular electronic structure and quantum electrodynamics.
4. The dynamical description of non-linear interactions between molecules and strong coherent fields.
5. Coherent energy transfer processes in biomolecules and (vi) the design of efficient computational algorithms.

The Theory and Modelling Program collaborates closely with all of 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.

ACHIEVEMENTS

X-RAY LASER IMAGING TECHNIQUES

RADIATION DAMAGE IN NANOCRYSTALLOGRAPHY

In March 2013, an experiment was performed at the LCLS, a hard X-ray free-electron laser (X-FEL), to look for damage effects in beta-haematin nanocrystals. Following the remarkable observation of a new electron state of crystalline C_{60} induced by an X-ray laser, theory suggests that other small molecules like haematin are likely candidates for similar effects. The TMP group contributed theoretical modelling, data analysis and design elements of the experiment. Differences with the expected structure of beta-haematin were observed and, after comparisons to synchrotron data, early indications are that nanocrystalline beta-haematin exhibits a surprising level of structural variability that is not evident in larger crystals.

MOLECULAR ORIENTATIONS

The ambitious goal of imaging single molecules with X-ray lasers in 3D requires many diffraction measurements of identical molecular copies to be combined together. This is impossible without knowing the molecular orientation, which cannot be measured in the experiment. The TMP team has been studying outstanding issues in this pivotal aspect of single molecule imaging, including the impact of radiation damage. New statistical theories are providing a general and expedient alternative to cumbersome large-scale simulations.

Dr Andrew Martin was awarded a DECRA for his work in this area and will continue working within the Theory and Modelling group in Melbourne.

X-RAY HOLOGRAPHY

X-ray holography is currently the most promising technique for imaging magnetic

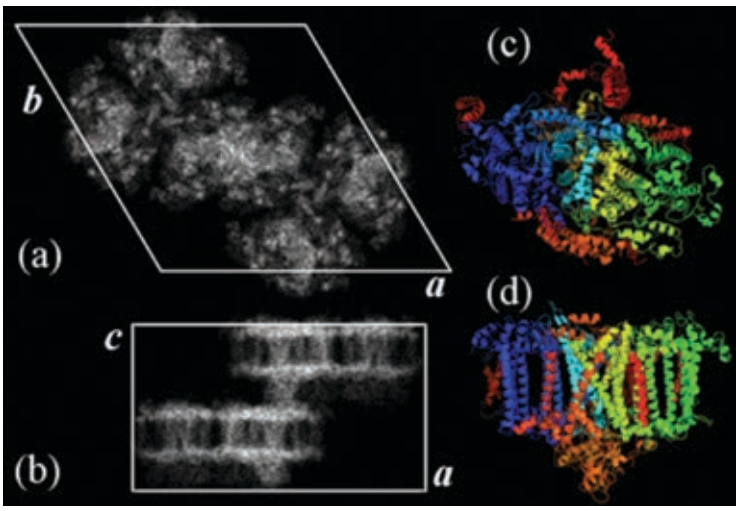


Figure 29: The projections of the electron density of the Photosystem I molecular cluster, reconstructed with resolution of 4.1 Å by incorporating models of the structural imperfections: (a) (ab) crystallographic plane, (b) (ac) crystallographic plane, (c) and (d) the models of the Photosystem I molecule, (ab) and (ac) projections respectively.

structures with X-ray free-electron lasers. It can potentially be applied to study magnetic nanostructures and magnetic dynamics. In collaboration with the Theoretical Condensed Matter Physics (TCMP) group at the University of Melbourne, the CXS TMP team has been developing new X-ray holographic methods which permit an almost unrestricted choice of experimental geometry, avoiding the strict limitations of existing techniques. It has perhaps the first X-ray holography technique that can handle missing data, a ubiquitous problem with imaging with high-brightness sources. We have demonstrated the technique on data taken at the FERMI, a seeded soft X-ray free-electron laser.

A holographically inspired theory was developed to deconstruct a diffraction measurement of multiple particles into the diffraction of each individual particle. The method generates more data for 3D single particle imaging experiments from experimentally unavoidable and otherwise useless diffraction measurements.

NANOCRYSTAL DIFFRACTION THEORY

Unlike diffraction from an almost infinite crystal, diffraction from nanocrystals is sensitive to the specific molecular configuration used to define the lattice, particularly at the nanocrystal's edge. Averaging over multiple nanocrystals of varying size and edge configuration leads to a loss of contrast in the diffraction signal, analogous to the effects of partial coherence. The TMP group is developing theory to describe these effects, which is essential for the success of new *ab initio* methods of structure determination.

PROTEIN CRYSTALLOGRAPHY

The recent development of the extremely bright X-ray free-electron laser (X-FEL) sources has created an opportunity for the structure analysis of proteins which only form crystals less than 1 micron in size. However, the fact that proteins form crystals of the nanoscale size indicates that their crystal structures are far from ideal. Structural imperfections play a significant role in formation of the diffraction pattern and should be taken into account during the structure analysis. The interference phenomenon caused by such defects was analysed by the TMP group and it was found that the structural imperfections can be described in terms of a partial coherency of adjacent molecular clusters. This allows application of the modal expansion Coherent Diffraction Imaging (CDI) approach for the structure analysis of the protein nanocrystals. The Photosystem I protein molecule was used as a target for the structure reconstruction. The resulting images, Figure 29, clearly show structure details, including envelopes

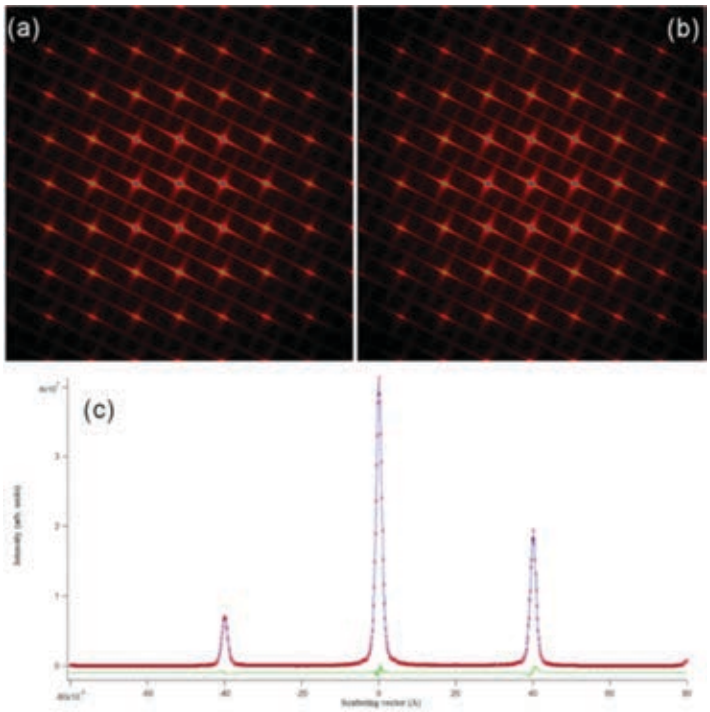


Figure 30: (a) 2D interference patterns, (hk0) crystallographic plane for the accumulated distribution of 1000 crystallites with unit cell dimensions a = b = 100A (a); (b) the fitted distribution using a continuous 2D pseudo-Voigt distribution. Fitting achieved with an R_p factor of 0.02. (c) Cross-sections of the distributions are shown in linear scale. Simulated distribution, fitted distribution and the residual are shown in red, blue and green respectively.

of Photosystem I protein molecules and transmembrane α-helixes.

Given that X-FEL protein nanocrystal diffraction patterns are accumulated from large numbers of X-FEL "snapshots", accommodation for the variation in protein crystal size and disorder is necessary, with the averaged result of these factors being represented in the accumulated diffraction patterns which are very similar to powder diffraction patterns. The averaged intensity distributions from X-FEL sources contain non-negligible X-ray scattering between Bragg peaks. The method presented aims to extract integrated intensities from XFEL diffraction data using continuous descriptions of the diffractive field. The proposed continuous fitting method is a two-dimensional extension of that used in powder diffraction, such as Le Bail analysis, in the extraction of structure factor amplitudes. This involves treating the intensity distribution as a continuous one, and fitting with analytic profile functions, such as a pseudo-Voigt. Interference patterns were simulated for 1000 needle-like crystals with tetragonal symmetry and with their dimensions taken from Poisson distributions. The accumulated result is shown in the (hk0) crystallographic plane to 12.50A resolution. Two-dimensional continuous distributions of profile peakshape functions were fitted to the distribution with close agreement.

OPTICAL MULTIDIMENSIONAL SPECTROSCOPY

Work continues in collaboration with Dr Jeff Davis (Swinburne) on developing analytical tools for multi-dimensional Fourier transform spectroscopy. Rather than rely on interferometry to determine the phase information contained in a four-wave mixing experiment, a scheme has been developed by the TMP group that utilises ideas borrowed from the phase retrieval techniques used to recover images using diffraction patterns. These ideas have led to the development of a range of methods to examine what role, if any, quantum coherence phenomena may play in the efficient transport of energy in naturally occurring light harvesting complexes. These techniques have recently been applied to carotenoids and to complexes extracted from marine algae.

ATTOSECOND PHYSICS

The TMP group is committed to supporting Griffith University's experimental research on attosecond physics and few-cycle interactions with electronic media. The strong-field modelling project has been undertaken by Daniel Wells in his PhD studies. Daniel performed detailed calculations of the photoionisation yield of atomic hydrogen subjected to an intense pulse and has developed a complete three-dimensional model within the velocity form of the electronic dipole approximation. This scheme employs a novel approach to the solution of the propagation equations that promises increased efficiency and generality; it is planned to extend the treatment to include non-dipole and spin-dependent effects using a relativistic formalism based on the Dirac equation and quantum electrodynamics.

STRUCTURED ILLUMINATION MICROSCOPY

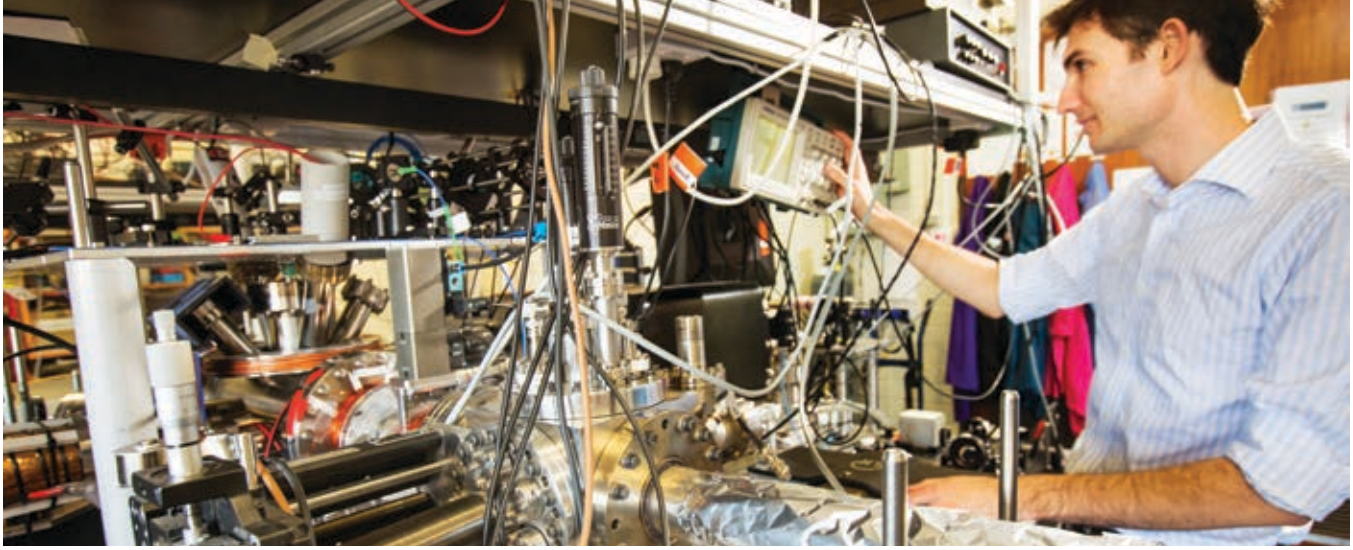
Work on simulation software was initiated by Dr Brendan Allman to support the development of Structured Illumination Microscope (SIM) by Trevor Smith and his team in the Short Wavelength Laser program. This development has been undertaken in IDL and has been continued by Dr Clare Henderson. The code currently exists in two versions:

- A code to fully simulate a SIM microscope, generating a theoretical SIM result and Moiré images from a given input image, in this case modelled on the UML microscope in Chemistry.
- A code to take in theoretical or experimentally generated Moiré images and produce a SIM result.

These codes are now operational and ready to be fully-formatted and documented into the CXS Software Interface. This now also includes documentation of Phase Diverse CDI code within the program.

SOFTWARE

The efforts of CXS, both theoretical and experimental, in developing practical approaches to diffractive X-ray imaging have been collected into a software package, which is now known as NADIA. The acronym is derived from Nadia's Algorithms for Diffractive Imaging Applications and includes a recursive reference to Nadia Davidson, who designed and developed the package using an inhomogeneous collection of software that had been circulating in CXS for some time. This package now includes most of the iterative algorithms that are widely used in diffractive imaging community, including the Fresnel coherent diffractive imaging approach developed by CXS a few years ago. This software is under continuing development and, it is hoped, will be taken up as a standard at facilities that perform diffractive imaging experiments. This work has been continued throughout 2013 by T'Mir Julius.



ULTRA-COLD PLASMA SOURCE PROGRAM

Formed within CXS in 2007, the Ultra-Cold Plasma Source Program (UCP), has been developing an ultra-bright, coherent source of electrons for imaging of biologically relevant targets. By applying technical developments taken from the ultracold atom community, and the theoretical algorithms developed in the TMP program, the UCP group will enable a new approach to electron imaging. 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 most significant aspect of 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 ultracold 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 ultracold atoms can be accelerated and focused with unprecedented resolution. The comparison is like that of a conventional light bulb and a laser: we need laser-like coherence and brightness to image molecular structure with atomic resolution.

The UCP team has strong expertise with ultracold atom technology; conventional optical imaging; and with electron optics. The team is 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. The teams have jointly published work based on the centre's imaging approaches for applications in characterising the cold atom cloud. The UCP team is now collaborating with the TMP group to employ their expertise on partially coherent x-ray sources for modelling a recently operational electron source. The theoretical formalism of partial coherence has not previously been applied to electron imaging, but the development of new sources has made partial coherence highly relevant. Modelling undertaken within CXS will be used to design the imaging component of the system, firstly to enable verification that the electron source is indeed coherent and bright, and secondly to enable imaging applications. In the longer term, collaboration with TMP will be essential to unravel electron-molecule interactions so that target structural information can be separated from the complexity of the diffraction data. 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. Our initial collaboration with the Biological Sciences group has established two-dimensional crystals of bacteriorhodopsin as a promising target for the first experiments. Such inter-program collaborations, the envy of our colleagues at Eindhoven, are simply not available to other groups around the world and will allow the UCP team to rapidly achieve high-impact results across disciplines.

NATURE COMMUNICATIONS PAPER AND FIRST SINGLE-SHOT ELECTRON DIFFRACTION IMAGES

Electron microscopy has revolutionised science by showing us the structure at micro and even nanometre scales, but is far too slow to show us critical dynamic processes, for example the folding of a protein molecule which requires time resolution of picoseconds. The UCP group is developing a novel high-coherence electron source which has the potential to enable ultrafast nanoscale imaging. In 2011, the group demonstrated some of the key performance characteristics of their innovative cold-atom electron source (CAES),

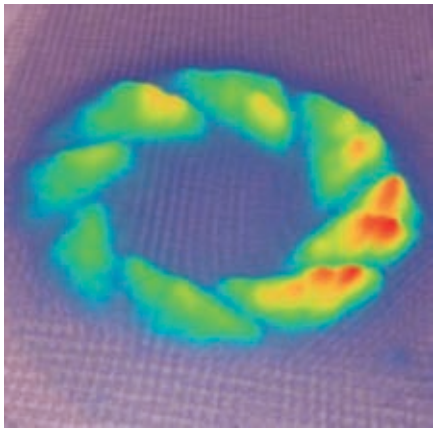


Figure 31: False-colour three-dimensional rendering of electron density for a bunch of ultrafast electrons created in a pattern similar to the iris shutter of a photographic camera, invoking the concept of a time-resolved snapshot.

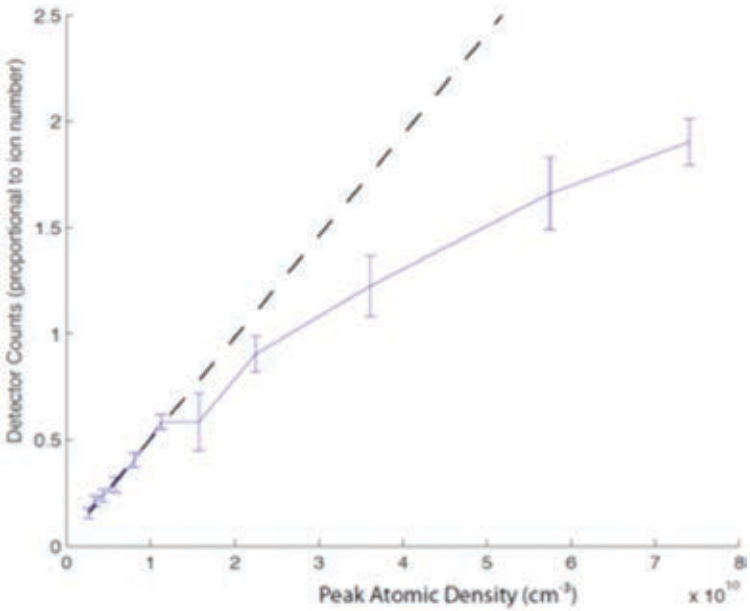


Figure 32: Variation in ion number with atomic density for ions produced by field-ionisation of Rydberg atoms created by continuous two-step excitation with 780nm and 480nm lasers. The saturation of ionisation fraction indicates Rydberg blockade which prevents Rydberg excitation of closely spaced atoms.

including high intrinsic spatial coherence and unique three-dimensional bunch shaping capability (*Nature Physics* **7** p785, 2011). The UCP group has now demonstrated another major milestone, showing that the source can produce ultra-short (picosecond) electron bunches without sacrificing the low electron temperatures and high spatial coherence (*Nature Communications* **4** 1692, 2013). Figure 31 above shows a shaped bunch of ultrafast electrons, in a pattern similar to the iris shutter of a photographic camera, invoking the concept of a time-resolved snapshot.

The cold electrons at the heart of the CAES derive from atoms laser-cooled to below 100μK, but heating effects increase the bunch temperature to around 10K. Spatial ordering of the atoms prior to ionisation has been investigated, to see if it will be possible to reduce those heating effects and achieve even lower electron temperatures with higher spatial coherence. In particular, *Rydberg blockade* has been demonstrated, which was expected to increase the spatial ordering of the cold atoms. Two continuous laser beams at 780nm and 480nm are used to excite cold atoms to Rydberg levels; that is, excited states with high principal quantum number. The atoms become very susceptible to perturbation by neighbouring atoms. If one atom is excited, the energy levels of a nearby atom will be affected so that the same laser frequencies can no longer excite the second atom. Thus only atoms with large spatial separation can be excited, reducing the number of electrons created with small separations and thus reducing the variation in potential energies and consequently the electron temperature.

Figure 32 above shows variation in the number of ions against initial atomic density. Without blockade, a linear increase in counts with density is expected, but there is clear evidence that as the density increases, the ionisation efficiency is decreasing due to blockade. Future work will measure the corresponding effect on electron and ion temperatures.

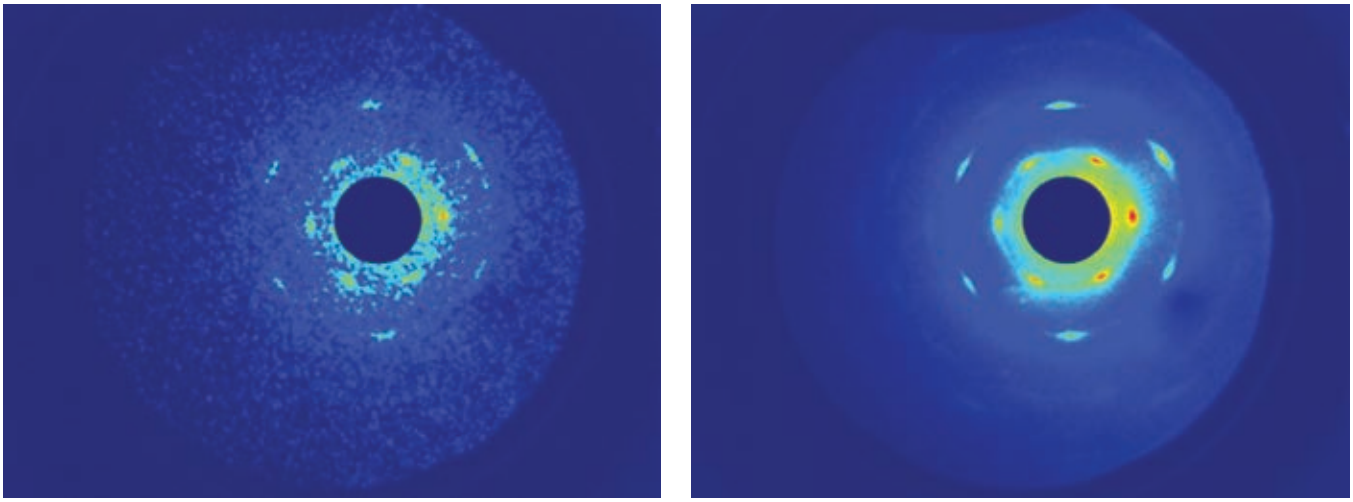


Figure 33: False-colour electron density images for ultracold electron diffraction from graphene. The images were acquired with 5ns duration electron bunches. Left image shows a single exposure; right image shows average of 100 exposures. The six-fold symmetry of graphene is clearly apparent.

DIFFRACTION FROM POLYCRYSTALLINE GRAPHENE CASE STUDY

The group has achieved diffraction from polycrystalline graphene, including single shot diffraction images. The images below show a diffraction pattern acquired in just five nanoseconds (left) and a 100-shot average (right). The six-fold symmetry of graphene is clear from the six short arcs at characteristic angles.

REVERSAL OF THE COULOMB EXPLOSION BY SHAPING COLD ELECTRON AND ION BUNCHES INTO THREE DIMENSIONAL UNIFORM DENSITY ELLIPSOIDS.

Electron imaging is limited by Coulomb repulsion, which causes electron bunches to rapidly expand thus reducing the brightness of electron sources and reducing either the speed or resolution that can be obtained. The cold atom electron source has a unique ability to shape the electron bunches in three dimensions. With the appropriate shape, it will be possible to recompress the Coulomb-expanded bunches and recover the high brightness of the source.

COHERENT DIFFRACTION IMAGING OF 2D CRYSTALS, FOR EXAMPLE BACTERIORHODOPSIN, USING THE COLD ATOM ELECTRON SOURCE.

The team has demonstrated diffraction from graphene crystals but the high coherence of the cold electron source will eventually allow coherent diffractive imaging from single molecules. In the near term, the high coherence for two dimensional crystals of biologically interesting targets, (for example bacteriorhodopsin (BR)), will be used initially. BR readily forms 2D crystals which are thin enough for transmission electron diffraction.

COMBINATION OF A NEW HIGH-FLUX COLD ELECTRON SOURCE WITH A COMMERCIAL ELECTRON MICROSCOPE COLUMN TO ACHIEVE PRACTICAL NANOSCALE IMAGING.

A new compact and efficient cold atom source will be constructed, based on a thermal atom beam rather than a cloud of laser-cooled atoms. The source will be much simpler and also provide much higher density electron bunches to improve resolution and speed. Rather than designing our own electron optical system we will take advantage of commercial quality electron optics in readily available and low-cost second-hand microscope columns.

These projects will rely on our recent success in obtaining three years of ARC funding through the Discovery Projects scheme, and award of a McKenzie Fellowship to our postdoctoral research leader, Ben McKenzie.

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FACILITIES @ CXS

FEMTOSECOND HIGH POWER LASER FACILITY AT SWINBURNE UNIVERSITY

The Femtosecond High Power Laser Facility was established in 2007 through the Victorian Government Science, Technology and Innovation (STI) Initiative funding. At that time, the laser system provided femtosecond laser pulses with a pulse energy of 5 mJ and pulse duration of 30 fs at a wavelength of 800 nm. In 2009 the laser system was upgraded to a pulse energy of 10 mJ. In 2010, the wavelength of the laser pulses was extended to 1400 nm with the addition of a home-built high power optical parametric amplifier. The system was equipped with a hollow fibre compressor and carrier envelope phase stabilisation through an ARC LIEF grant in 2011 and 2012. The laser pulse duration is now ~10 femtosecond.

Using this laser system the Short Wavelength Laser Source Program has investigated the generation of high fluxes of extreme ultraviolet (XUV) and soft X-ray pulses by high harmonic generation (HHG) and applied this source to atomic and molecular spectroscopy, condensed matter physics, and imaging on the micron- and submicron-scale. These compact (table-top) femtosecond pulse sources will complement larger installations such as X-ray free-electron lasers (XFELS) and third generation synchrotrons by means of generating coherent soft X-Rays.

KEY OUTCOMES

The Ultra Cold Plasma Source Program has been able to generate XUV beams through HHG by focussing the femtosecond laser beam in a long gas cell of various noble gases – argon (Ar), neon (Ne) and helium (He). With ionisation energies of 15.8 eV (Ar), 21.6 eV (Ne) and 24.6 eV (He), and with 800 nm pulses, a photon flux of ~ 109-1011 photons/cm2 is obtained in the wavelength range 9-35 nm. Control over the characteristics of the output is essential in the study of generation process – particularly the brightness or flux; the spatial and temporal coherence properties; and the spectral range of the harmonic orders – and depends strongly on the interaction geometry. Therefore, consideration has been given to different configurations for HHG, such as a long gas cell and multiple gas jet arrays.

The aim of the program is the generation of a small bandwidth HHG source. The high order harmonic emission is confined to just a few orders because of a small phase-mismatch in the harmonic cut-off region that allows macroscopic phase-matching to be satisfied. The spatial degree of coherence is >0.9. The group's technique for HHG obtains the same benefits of homogeneous phase matching as in hollow-core fibres and shows that the generation process can be controlled effectively.

The group has established that, using a combination of 1400 nm and 800 nm laser pulses with pulses at 1400 nm HHG in the water window as successfully achieved at 3 nm – 4.4 nm, a broadband HHG spectrum (with a bandwidth >30 eV) is generated. This opens up a new way to generate attosecond pulses and increases the efficiency of HHG by some orders of magnitude.

Due to its coherent nature, HHG emission can be used for coherent diffractive imaging (CDI). The UCP team has performed multiple-wavelength CDI by using several phase-matched harmonics from an argon and helium gas cell in the wavelength ranges 26 – 43 nm and 13 nm, respectively. It has demonstrated high quality imaging with 30 nm and 13 nm wavelength light. The team has also shown that it is possible to use multiple wavelengths to obtain high-resolution imaging. Most recently, the group achieved a spatial resolution of ~50 nm with a 30 nm wavelength source. Biological samples do not show intrinsic contrast at these wavelengths, although a staining mechanism is being sought that will allow useful contrast.

Using a second pulse to modify the phase-matched harmonic intensity and the spatial distribution, the contribution of different electron trajectories and molecular orbitals can be revealed. The group has demonstrated that information on atomic

and molecular structural dynamics can be obtained from the high-order harmonic generation process. This offers the possibility of studying the dynamics of the phase matching of an atom and the molecular structural dynamics with high time and spatial resolution.

Collaboration within CXS nodes and with other groups at international institutions – such as Gwangju institute of Science and Technology (Korea); Ecole Polytechnique-ParisTech (France); and the Imperial College London (UK) – on generation and application of HHG sources has been well established.

Naylan Gaffney using the Femtosecond Laser

SUPER-RESOLUTION OPTICAL MICROSCOPY IN CHEMISTRY AT THE UNIVERSITY OF MELBOURNE

Super-resolution optical microscopy is a maturing field of (largely) fluorescence-based imaging that provides optical resolution beyond the physical limits imposed by the laws of diffraction. Super-resolution optical methods with resolution typically below 100 nm are of direct relevance to the interests of CXS as they provide comparable resolution to the X-ray techniques being developed, including coherent diffractive imaging (CDI), but with standard sample preparation protocols. They can therefore provide complementary and supporting information to CDI measurements.

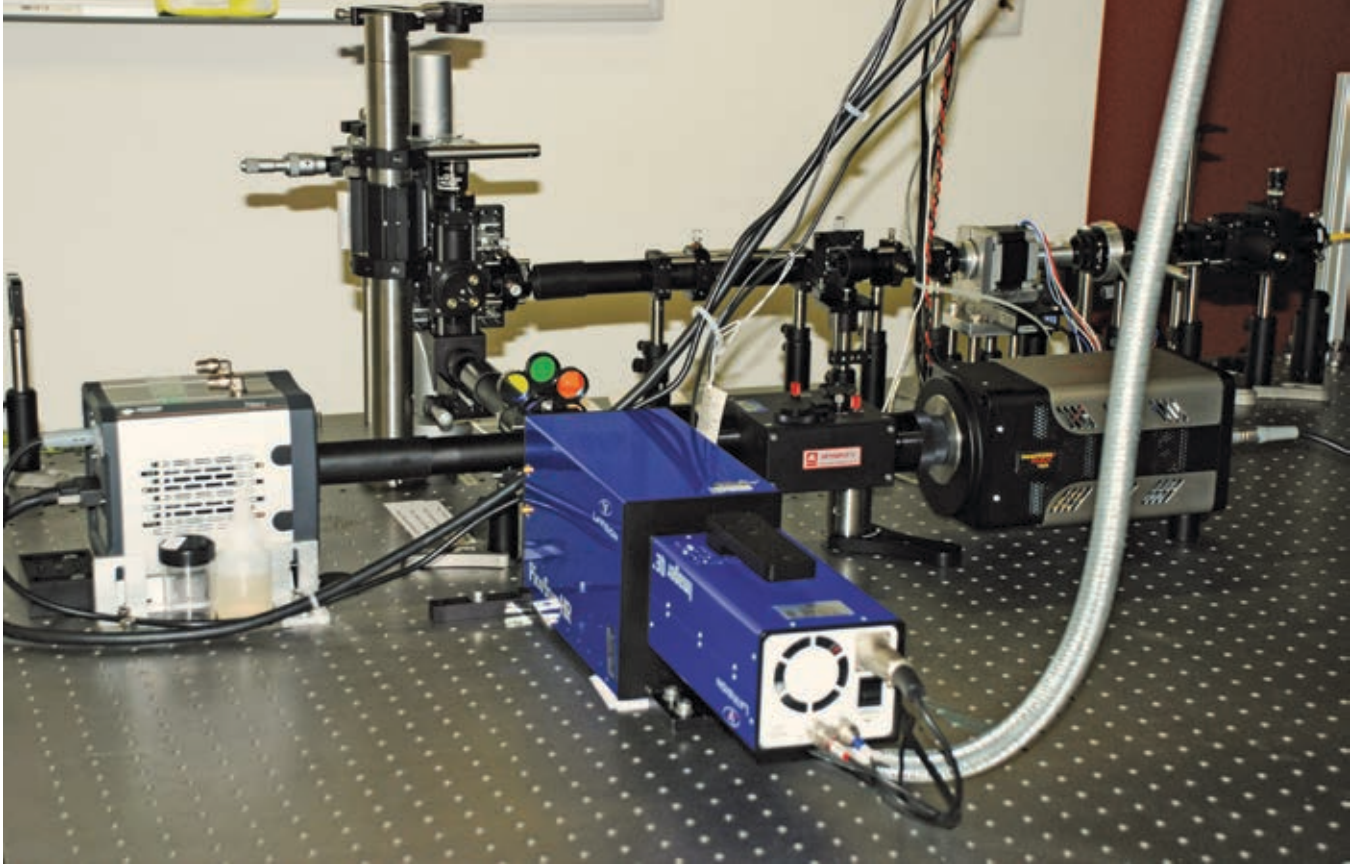
Super-resolution optical microscopy gained momentum in the early 1990s with the introduction of structured illumination microscopy (SIM) by Rainer Heinztmann and Matts Gustaffson. Since then a range of relatively simple strategies have been implemented to provide ways around the diffraction limit, leading to Stimulated Emission Depletion (STED) microscopy, and single molecule localisation methods such as Stochastic Optical Reconstruction Microscopy (STORM) and Photoactivated Localisation Microscopy (PALM). Each of these methods affords advantages and disadvantages over other techniques for a specific sample in terms of sample preparation, light exposure, required resolution, speed of acquisition, data processing, etc.

Interest in the various super-resolution optical microscopy techniques is escalating, as highlighted by the large numbers of attendees drawn to a series of workshops organised by CXS, which concentrated on such methods. The rapidly growing interest in super-resolution optical microscopy has encouraged members of CXS to initiate the formation of the Cellular Nano-Imaging Consortium (http://www.coecxs.org/cnic/); a forum through which specific requirements and capabilities in this area can be discussed and facilities highlighted. These activities have lead the way to the installation of several commercial instruments in the region. Commercial instruments are expensive, and the high costs have thus far impeded the establishment of a single facility at which the most appropriate super-resolution optical microscopy technique can be trialled and assessed for a given sample type.

Despite their undoubted attractiveness for immediate use, the commercial instruments cannot be modified readily, resulting in the implementation of new advances in the field being largely reliant upon their commercial release. Whilst still in its infancy, this field is developing rapidly.

Super-resolution optical microscopy techniques rely on understanding and controlling the photophysics/photochemistry of the fluorophore, rather than any new optical physics. Furthermore, many of these techniques require, or can benefit from the use of ultrashort pulse lasers. The Ultrafast and Microspectroscopy Laboratories at the University of Melbourne (http://uml.chemistry.unimelb.edu.au) are uniquely placed to exploit these requirements using the extensive laser and microscopy facilities established by CXS. The approach taken has been to develop instruments in-house in order to assemble a relatively complete set of techniques and allow modification and adaptation of the apparatus as new developments emerge.

Within the group, there is a well-established expertise in, and a comprehensive facility for, time-resolved fluorescence microscopy, with access to excitation wavelengths from the deep ultraviolet to infrared (single and multi-photon excitation), any pulse repetition rate, with picosecond temporal resolution. Through its CXS activities, the team has added to this capability high spatial resolution proficiency. A unique 3D SIM system has been constructed that can complement the commercial 3DSIM instrument at Bio21, whilst being highly adaptable. By coupling the 2D system to the picosecond and femtosecond mode-



locked lasers and a specialist ultrafast CCD camera the instrument can be configured for time-resolved (~200 picosecond) imaging. In collaboration with one of the pioneers of SIM, Prof, Rainer Heinztmann, the team is also developing computer programs for the reconstruction of SIM images by implementing faster and more robust algorithms and providing more control over the parameters involved in the reconstruction. Such a program is not currently freely available elsewhere and the CXS development will be open source and freely available to external SIM researchers, analogous to the development of the coherent diffractive imaging NADIA code also produced by CXS. The group has also developed a STED microscope based on a picosecond super-continuum laser. This can be configured with the centre's extensive fluorescence lifetime imaging capabilities to provide time-resolved STED imaging (<100 nm spatial and <100 ps temporal resolution). In addition, the ULP program is constructing a new localisation microscope, based on multi-photon-induced photoactivation of the fluorescent probes coupled with temporal focussing (using a 15fs, ~800 nm laser source) to provide high resolution imaging in three dimensions.

The CXS Ultra Cold Plasma Source Program has pioneered the adoption of these high temporal and spatial resolution techniques to materials science, (self-assembled binary colloidal crystals; conjugated polymer films for photovoltaic devices; and polymer inclusion membranes), in addition to the biological and botanical samples of our colleagues. These facilities are used by CXS post-doctoral students and research assistants and is also open for collaborations with local, national and international colleagues. Our development of configurable imaging systems provides not only a unique resource for scientists from various disciplines, but also creates a platform for interdisciplinary research, which is unique in the world.

Paul McMillan operating the OMX-BLAZE Super-Resolution Microscope installed in the Bio21 Microscopy Facility

SUPER-RESOLUTION MICROSCOPY CAPABILITY AT BIO21 INSTITUTE

CXS members, Prof Leann Tilley, Prof Mike Ryan, and Prof Keith Nugent, along with colleagues from the Universities of Melbourne, Monash and La Trobe, and the Walter and Eliza Hall Institute were successful in obtaining ARC LIEF grant funding, and an NHMRC Equipment grant to set up a Super-Resolution Microscopy Facility at the University of Melbourne. As a result one of the first OMX-BLAZE 3D-SIM instruments in the world was purchased at a cost of over $1M, and has been installed at the Bio21 Institute. This instrument enables super-resolution microscopy at a sufficiently high speed to image live cells.

The Super Resolution Microscopy Facility is managed as part of the Biological Optical Microscopy Facility, managed by Dr Paul McMillan and is part of the Bio21 Advanced Microscopy Facility managed by Dr Eric Hanssen – both of whom are CXS members. The facility is open to researchers nationally and is coupled to a 3D Cryo Electron Microscopy capability (purchased at a cost of $3M). This combined capability represents a fantastic resource for cell biologists and is unique in the world.

HELPING CURRENT AND FUTURE RESEARCH

Conventional light microscopy cannot image details smaller than 250 nanometers. Because many biological structures are smaller than this, current microscopes effectively blur different structures together. This makes it problematic to see very small organisms such as viruses and bacteria, and the inner workings of cells in the detail that is required by life scientists. In 2012 the BLAZE-OMX microscope was installed with 3D-structured illumination microscopy (3D-SIM) capability. In 2013 the system was expanded with the inclusion of TIRF optics and a MONET localisation microscopy capability for PALM/STORM imaging. These imaging methods are providing images of tiny pathogens and cellular nanostructures at a level of detail never before possible.

EFFECTS ON AUSTRALIAN SCIENCE RESEARCH POTENTIAL

Australian researchers, including CXS members, such as Trevor Smith are pioneering the development of new super-resolution microscopy techniques. CXS Biological Sciences Program members, such as Leann Tilley, Paul McMillan and Matt Dixon, are pioneering the application of these techniques to studies of important human pathogens such the malaria parasite, while other colleagues are using the techniques to understand cancer and neurodegenerative diseases. Access to these new techniques is critical to maintaining the international competitiveness of Australian researchers.

A number of major scientific achievements, such as the elucidation of the structure of DNA, have resulted from collaborations between biologists, chemists and physicists. Answering many of today's important medical and biotechnological questions requires similar cross-disciplinary co-operation. This is particularly evident in the area of super-resolution microscopy. A unique collaboration of biologists and physicists developed the BLAZE-OMX 3D-SIM and PALM/STORM systems, providing a tool that will change the way we do cell biology.

WHAT IS SPECIAL ABOUT OMX BLAZE?

The Applied Precision OMX Blaze™ is a major development, specifically optimised for live cell imaging. The OMX BLAZE's faster super-resolution capability is made possible through high-speed acquisition electronics and reconstruction algorithms; complete control of the operational environment; and new sCMOS cameras. Fast 3D-SIM (a 1 micron image stack can be collected in approx 1 second) makes live cell imaging a reality, important for applications

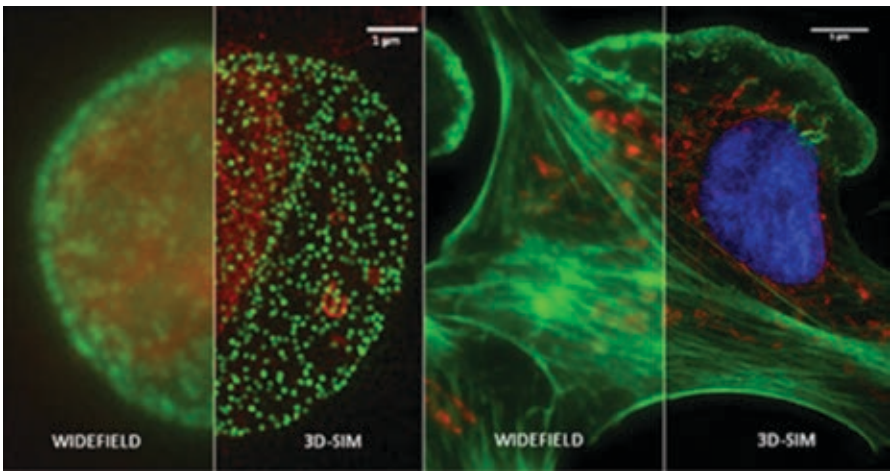


Figure 34 Left Panels: Malaria parasite-infected erythrocyte expressing a GFP fusion of the knob protein (green), co-labelled with a lipid probe (red).

Right Panels: Cultured human cell line showing actin (green), tubulin (red) and DNA (blue).

In each case a comparison is shown between samples imaged using conventional widefield microscopy and the new OMX-BLAZE Super-Resolution microscopy.

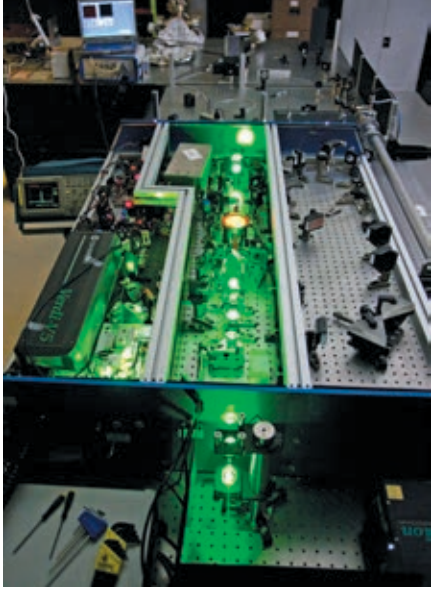
where cell signalling and dynamic events need to be observed.

OMX BLAZE offers an XY resolution between 80-120 nm, and Z resolution between 250-350 nm (depending on wavelength) with 30 micron depth of optical sectioning (z-depth). The newly implemented OMX-MONET offers up to 20 nm XY resolution.

WHAT IS EXCITING OR INTERESTING ABOUT THIS RESEARCH?

As Richard Feynman (Nobel Prize in Physics) once said, "It is very easy to answer many fundamental biological questions; you just look at the thing". He went on to suggest that what physicists should do to help biologists is to make better microscopes. And indeed in the last few years optical microscopy methods have undergone breathtaking developments. Professor John Sedat, Professor of Biochemistry at the University of California, San Francisco, was a leader of the consortium that developed the OMX microscope, which can image cellular components at a volume resolution up to an order of magnitude well beyond the current limits. He opened the new Super-Resolution Facility at the University of Melbourne.

As John Sedat says, the OMX microscope is "part of a revolution in light microscopy", a revolution that he says will "bring new understanding of how all living things function". New microscopy techniques, predicts Sedat, will allow scientists to delve deeper into "how we develop from embryos into whole organisms, from the aesthetics of trying to understand how we're built, or what goes wrong in disease." It's extraordinarily exciting to be able to see images of live cells at a greater level of detail than ever seen before.



The main laser system of the Australian Attosecond Science Facility, providing the shortest laser pulses in the country.

AUSTRALIAN ATTOSECOND SCIENCE FACILITY AT GRIFFITH UNIVERSITY

The Australian Attosecond Science Facility (AASF) could be described as Australia's fastest camera. The goal of the AASF is to observe chemical and molecular processes as they happen. By measuring how atoms and electrons move and interact, it is hoped to learn how atoms bind together to make molecules and how those molecules gain their particular chemical properties.

The heart of the AASF is a specialised laser system that produces ultrashort, high-power laser pulses. Just as a camera flash can take a freeze-frame image of a fast-moving object, a pulse from the AASF can take a snapshot of electrons as they move inside molecules, with a time resolution of about 200 attoseconds. An attosecond is equal to approximately 10^{-15} of asecond, so taking 200 attoseconds out of 1 second is like taking 1 second out of the time since dinosaurs walked the earth. At the peak of each pulse, the optical power briefly reaches 100 gigawatts, much more than the output of the entire Australian power grid. However, since each pulse is so short, the overall power consumption of the laser is only a few hundred watts.

The AASF was established in 2007 by a collaboration led by Prof David Kielpinski of Griffith University and partners from Macquarie University, University of Western Australia, and University of Queensland. It is the first and only attosecond research platform in the Southern Hemisphere. Funding for the $800,000 facility was provided by a Linkage, Infrastructure, Equipment, and Facilities grant from the Australian Research Council as well as matching funds from the university partners.

Within CXS, the AASF has enabled fundamental research on the processes that happen in intense laser pulses. Presently, intense X-ray laser pulses are the cutting-edge technology for determining the structure of nanoscopic protein crystals. Molecules deform and shatter under these extreme conditions, so it's essential to understand the effects of the laser, but the basic physics of these effects is not entirely clear. The research done with the AASF has provided the first quantitative agreement between theory and experiment for these processes.

ULTRACOLD PLASMA COLD ATOM ELECTRON SOURCE FACILITY (CAES) AT THE UNIVERSITY OF MELBOURNE

The source is based on near-threshold photoionisation of atoms which have been laser-cooled to micro-Kelvin temperatures, to create an ultra-cold plasma (UCP). The UCP provides a very large electron charge in a very small volume at a very low temperature. In combination, these provide much lower transverse emittance, which leads to much higher transverse brightness than is possible with conventional pulsed electron sources. The cold electrons are then accelerated to produce a beam of electron bunches with extremely high spatial coherence, sufficient to enable diffractive determination of structures the size of a protein molecule (up to 10nm) with sub-nm resolution.

In addition, an inherent bunch compression effect arising from the potential gradient across the plasma may ultimately enable femtosecond single-shot diffractive imaging of biomolecules, with unprecedented spatial and temporal resolution, and allow us to observe the sequential processes of a chemical reaction, or the folding of a protein molecule, in real time.

The crucial element underlying these ambitious goals is the brightness of the electron source. Even with the inherent advantages of the ultracold origin of the electrons, space-charge repulsion of the electrons within the beam would normally degrade the spatial coherence. This problem is addressed by shaping the charge cloud into elliptical uniform density

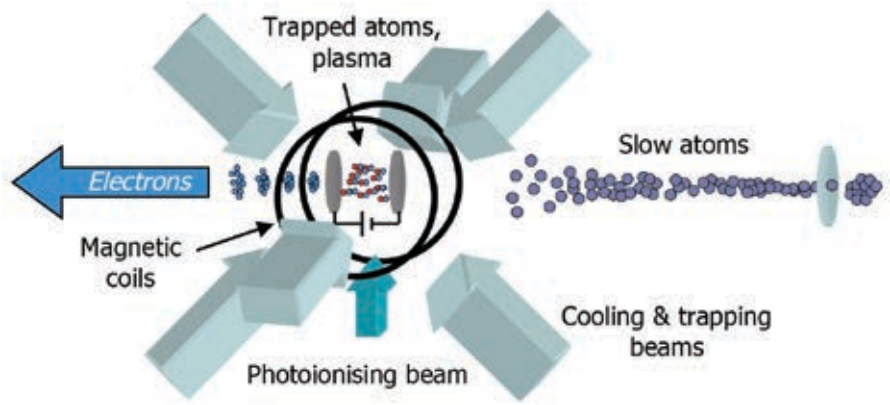
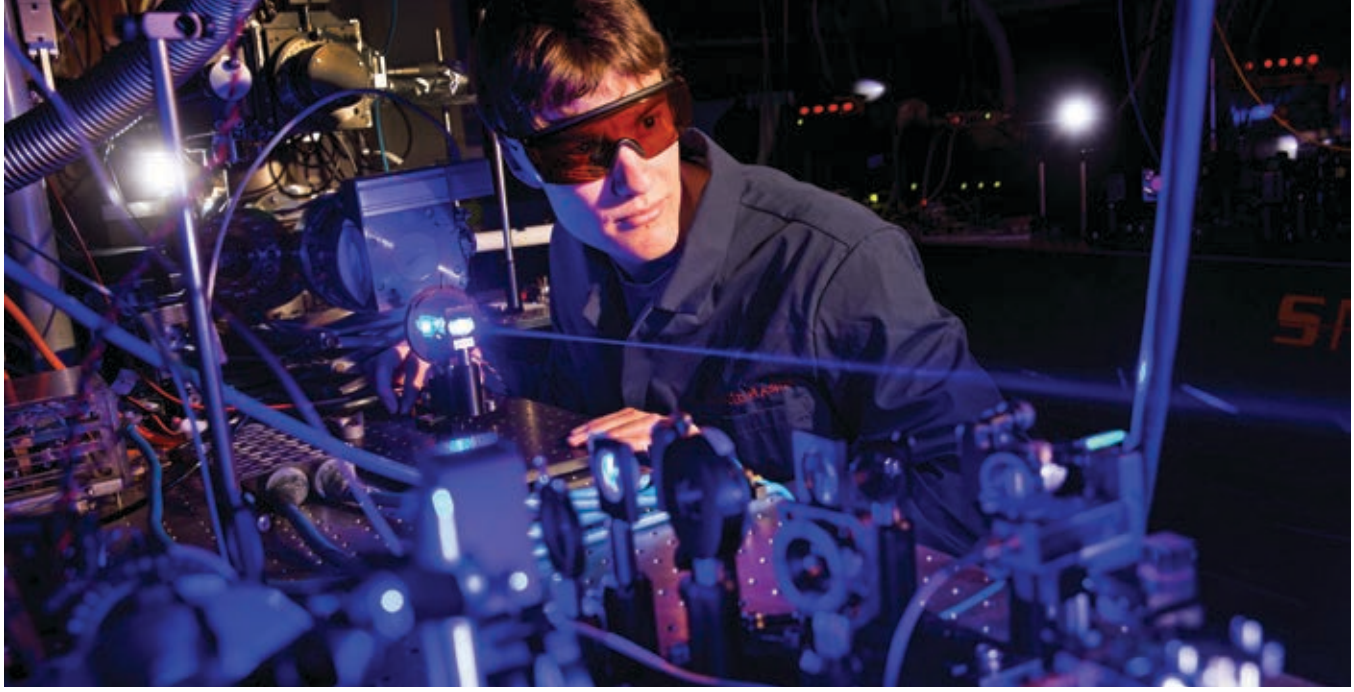


Figure 35: Atoms are cooled and trapped, and then photoionised to produce a very cold electron bunch, which can be accelerated to form an ultrabright beam.



bunches using the excitation and photo-ionisation lasers. Such elliptical bunches intrinsically preserve their brightness, and can be refocused with conventional accelerator techniques.

Figure 36 is a schematic of the combined cold atom electron source and electron diffraction target chamber. The facility allows investigation of key physical processes including space charge effects, Rydberg blockade, and electron diffraction. The facility also includes a number of laser systems, including high power frequency stabilised external cavity diode lasers at 780nm; a tunable pulsed 480nm laser for photoionisation; a tunable CW 480nm laser for Rydberg excitation; and an amplified femtosecond laser for generation of ultrashort electron bunches.

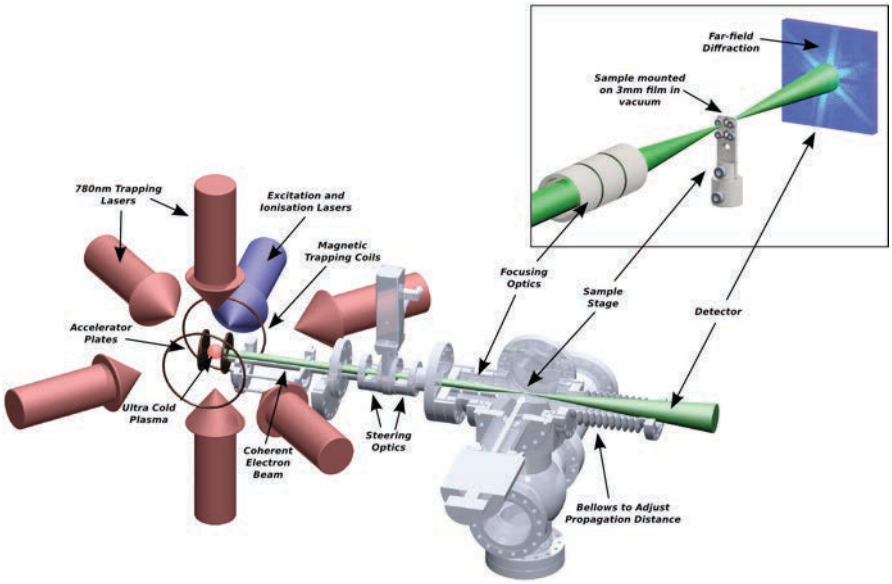
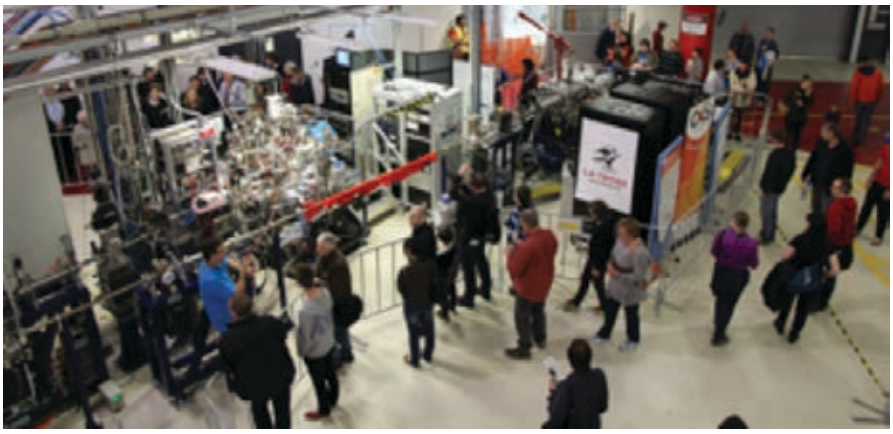
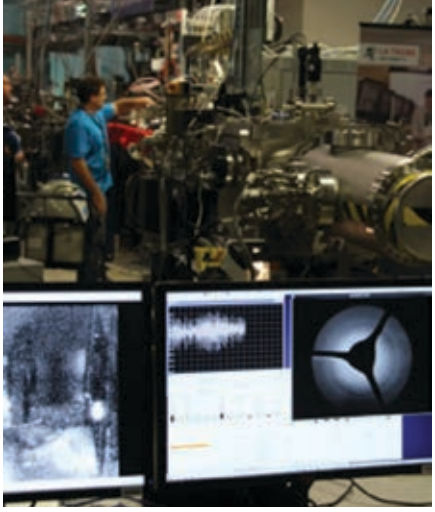


Figure 36: Cold atom electron source, combined with electron diffraction target chamber. Inset shows detail of electron optics and sample holder.



Visitors to the Australian Synchrotron Open Day at the Soft X-ray Spectroscopy and Imaging Beamlines.



An operator's view of the soft X-ray imaging beamline at the Australian Synchrotron.

THE SOFT X-RAY IMAGING BEAMLINE AT THE AUSTRALIAN SYNCHROTRON

Since its inception, CXS has aimed to be the world leader in the development of coherent X-ray diffraction for imaging biological structures. An early step toward achieving this was the development of the Frensel Imaging Endstation (FRIEND), in partnership with the Advanced Photon Source.

FRIEND is an X-ray microscope that was designed to excel in a range of coherent imaging techniques. It supported a productive period for CXS in which a number of important contributions to coherent X-ray science and its applications in biological imaging were made. Meanwhile, a dedicated branch of the Australian Synchrotron's Soft X-ray (SXR) beamline was designed and constructed to accommodate the microscope. Early in 2013, the microscope was brought to Melbourne where it was adapted for use with the new beamline branch. The result was a highly versatile imaging facility called SXRI that can uniquely address the growing need to explore the detailed structural properties of materials and biological specimens at the nanoscale.

The Experimental Methods Program leads the SXRI development project. Support from a team of scientists, technical specialists and engineers from La Trobe University and the Australian Synchrotron has allowed rapid progress through the early commissioning phase and subsequent refurbishment of core components. In late 2013 the team started to shift its attention to the tasks of optimising imaging performance and building up a research capability that can support existing CXS projects and new collaborations.

The source of photons at SXRI is an elliptical polarised undulator that can deliver X-rays with variable polarisation over the the energy range 0.2-2 keV. A fixed planar grating monochromator is used to select and/or scan the energy of the X-ray beam. The monochromatic beam can be focused to a probe of as little as 30 nm using Fresnel zone plates fabricated by CXS in partnership with the Melbourne Centre for Nanofabrication. Samples are aligned at or near the focal plane of the zone plate and raster scanned to perform ptychography. With full circular polarisation it is possible to operate the monochromator in zero order to deliver a first harmonic beam with roughly a 4% band pass for fast "broadband" ptychography, i.e. with longitudinal partial coherence.

The X-ray microscope can be operated over the energy range 0.2-2 keV thus giving access to the K-edges of C to Si, together with the L-edges of many elements, including the technologically important transition metals. The high coherent flux in the "water window" between the O and K absorption edges makes the microscope particularly attractive for biological imaging.

The wide spectral operating range of the microscope is attractive for spectro-microscopy. The microscope allows taking multiple images of a single sample region at different incident energies. It also offers the possibility to perform highly spatially resolved X-ray absorption spectroscopy on small regions of the sample.

The microscope underwent a major refurbishment during 2013 to incorporate a system of accurate positioning and dynamic stabilising of the position of the sample with respect to the zone plate optics. This is essential for large-area imaging and the acquisition of very high dynamic range data that is required to achieve nanoscale spatial resolution.

Further upgrades are planned to ensure that the SXRI beamline can support world-class research for years to come. Concurrently there are collaborative projects, supported by the Australian Research Council, the Australian Synchrotron and several leading laboratories to upgrade the main detector; and produce high resolution X-ray optics, in situ sample environment control, and protocols for biological sample preparation.

In the 12 months since "first light", coherent diffractive imaging of biological cells in the water window was demonstrated, with sensitivity and image quality superior to that previously reported. Resonant coherent diffractive imaging using linearly and circularly polarised X-rays has also been demonstrated for mapping magnetic distributions in thin films. Already, tens of scientists from more than five institutions, including several CXS students, were involved in experiments at SXRI. If this is any indication, it seems we can look forward to a bright future for coherent X-ray science in Australia with the SXRI facility at its heart.

CXS MANAGEMENT & GOVERNANCE

CXS is a collaborative research program between the University of Melbourne, La Trobe University, Monash University, Swinburne University of Technology, Griffith University and CSIRO. It is 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 signed agreements. These agreements cover CXS management, collaboration and intellectual property arrangements.

All collaborating organisations are represented within the CXS boards. Commercial expertise is present on the CXS Intellectual Property Committee and Sub Committee, and the International Advisory Board. The Scientific Advisory Board and the International Advisory Board 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 LEANN TILLEY
Director of Research

ASSOCIATE PROFESSOR HARRY QUINEY
Deputy Director of Research

MS TANIA SMITH
Chief Operating Officer

EXECUTIVE COMMITTEE

During 2013, the administration of CXS was overseen by the Executive Committee, which comprises:

MS KATHY ALLEBLAS
Executive Officer to Committee

ASSOCIATE PROFESSOR DAVID KIELPINSKI
Attosecond Science Group Leader

PROFESSOR KEITH NUGENT
Associate

DR ANDREW PEELE
Australian Synchrotron

ASSOCIATE PROFESSOR HARRY QUINEY
Deputy Director Research and Theory and Modelling Group Leader

PROFESSOR MIKE RYAN
Biological Sciences Group Leader

DR MARTIN SCANLON
Biological Sciences Monash University Representative

PROFESSOR ROBERT SCHOLTEN
Ultra Cold Plasma Source Group Leader

MS TANIA SMITH
CXS Chief Operating Officer

ASSOCIATE PROFESSOR TREVOR SMITH
Short Wavelength Laser Source Group Member

DR VICTOR STRELTSOV
Structure Determination Methods Group Leader

PROFESSOR LEANNE TILLEY
Research Director (Chair)

PROFESSOR LAP VAN DAO
Short Wavelength Laser Source Group Leader

DR GRANT VAN RIESSEN
Experimental Methods Group Leader

ADVISORY BOARD

The CXS Advisory Board met in October 2013 at the University of Melbourne CXS office. The meeting focussed on the recommendations of the CXS Scientific Advisory Board and discussed matters relating to the long-term future of CXS, industry and community outreach, and the leadership of the Centre leading into its windup phase.

CXS would like to thank the International Advisory Board Chair, David Krenus, and its international members, John Helliwell, Bonnie Wallace and Stephen Lane for their service to the Board over the life of the Centre.

PROFESSOR EDWINA CORNISH
Deputy Vice Chancellor (Research) Monash University, or nominee

DR CAL DRUMMOND
Chief of CSIRO Materials Science and Engineering

PROFESSOR JOHN HELLIWELL
Professor of Structural Chemistry University of Manchester

MR DAVID KRENUS (CHAIR)
Chief Executive Officer Cyclotek

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

PROFESSOR KEITH NUGENT
Deputy Vice-Chancellor (Research) La Trobe University of Technology, or nominee

ASSOCIATE PROFESSOR HARRY QUINEY
CXS Deputy Director, University of Melbourne

TANIA SMITH
CXS Chief Operating Officer, University of Melbourne

PROFESSOR LEANN TILLEY
CXS Director of Research, University of Melbourne

PROFESSOR BONNIE WALLACE
Professor of Crystallography
Birkbeck College

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

SCIENTIFIC ADVISORY BOARD

PROFESSOR JOHN HELLIWELL (CHAIR)
Professor of Structural Chemistry
University of Manchester

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

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CXS Deputy Director of Research
La Trobe University

PROFESSOR LEANN TILLEY
CXS Director of Research
University of Melbourne

PROFESSOR BONNIE WALLACE
Professor of Crystallography
Birkbeck College

PROFESSIONAL STAFF

KATHY ALLEBLAS
CXS Administrative Officer, University of Melbourne

SAMANTHA DEED
Bio21 Administrative Officer to CXS, University of Melbourne

KATHY PALMER
Finance Officer, University of Melbourne

FABIENNE PERANI
CXS Administrative Officer, La Trobe University

TANIA SMITH
CXS Chief Operating Officer, University of Melbourne

TATIANA TCHERNOVA
Administrative Officer, Swinburne University

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JAMES CALVERT
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DR XIAOHONG HAN
Research Fellow

MALCOLM KELSON
Technical Officer, Griffith University

DR CHAMPAK KHURMI
Post Doc, Griffith University

DANE LABAN
PhD Student, Griffith University

PROFESSOR DAVE KIELPINSKI
Program Leader, Griffith University

ASSOCIATE PROFESSOR ROBERT SANG
Research Fellow, Griffith University

WILLIAM WALLACE
PhD Student, Griffith University

DR HAN XU
Post Doc, Griffith University

AMNA ZAHID
PhD Student, Griffith University

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MEGAN DEARNLEY
PhD Student, University of Melbourne

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Research Fellow, University of Melbourne

DR CON DOGOVSKI
Research Fellow, University of Melbourne

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Research Fellow, La Trobe University

LUKE FORMOSA
PhD Student, La Trobe University

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PI, WEHI

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Affiliate Researcher, La Trobe University

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PhD Student, University of Melbourne

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PhD Student, University of Melbourne

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Research Fellow, University of Melbourne

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Research Fellow, Monash University

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THANH NGOC NGUYEN
PhD Student, La Trobe University

BORIS RELJIC
PhD Student, La Trobe University

VIVIANE RICHTER
PhD Student, La Trobe University

PROFESSOR MIKE RYAN
Program Leader, La Trobe University

ASSOCIATE PROFESSOR MARTIN SCANLON
Research Fellow, Monash University

ABEER SINGH
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CXS Director, University of Melbourne

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EXPERIMENTAL METHODS PROGRAM

DR BRIAN ABBEY
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Research Fellow, La Trobe University

DR EUGENIU BALAUR
Research Fellow, La Trobe University

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PhD Student, La Trobe University

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EVAN CURWOOD
PhD Student, University of Melbourne

CHANDNI DOSHI
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Research Fellow, La Trobe University

DR MARK JUNKER
Research Fellow, La Trobe University

HENRY KIRKWOOD
MSc Student, La Trobe University

DR MAC BA LUU
Post Doc, La Trobe University

PROF KEITH NUGENT
Federation Fellow, La Trobe University

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STEPHANIE PRADIER
PhD Student, La Trobe University

REBECCA RYAN
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Research Fellow, La Trobe University

GIANG TRAN-NHAN
PhD Student, La Trobe University

DR ASHISH TRIPATHI
Research Fellow, La Trobe University

DR GRANT VAN RIESSEN
Research Fellow, La Trobe University

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DAVID WOOD
MSc Student, University of Melbourne

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EVELYN CANNON
PhD Student, Swinburne University

PROFESSOR LAP VAN DAO
Program Leader, Swinburne University

DR JEFFREY DAVIS
Research Associate, Swinburne University

DR GARETH DICKENSON
Post Doc, University of Melbourne

BA KHONG DINH
PhD Student, Swinburne University

NAYLYN GAFFNEY
PhD Student, Swinburne University

PROFESSOR PETER HANNAFORD
CAOUS, Swinburne University

DR CLARE HENDERSON
Research Fellow, University of Melbourne

VU HOANG LE
PhD Student, Swinburne University

GRANT MCKENZIE
Student, University of Melbourne

BEN MORRISON
PhD Student, University of Melbourne

ADABELLE ONG
Research Assistant, University of Melbourne

MICHAEL PULLEN
Research Fellow, Swinburne University

ASSOCIATE PROFESSOR TREVOR SMITH
Chemistry, University of Melbourne

STRUCTURE DETERMINATION METHODS PROGRAM

HANNAH COUGHLAN
PhD Student, La Trobe University

DR CONNIE DARMANIN
CSIRO, Parkville

PROFESSOR CAL DRUMMOND
Membrane Chemistry, CSIRO, Parkville

DR VICTOR STRELTSOV
Group Leader – CSIRO, Clayton

THEORY AND MODELLING PROGRAM

DR RUBEN DILANIYAN
Research Fellow, University of Melbourne

DR SHAN SHAN KOU
Research Fellow, University of Melbourne

DR ANDREW MARTIN
Research Fellow, University of Melbourne

ASSOCIATE PROFESSOR HARRY QUINEY
Program Leader, University of Melbourne

DANIEL WELLS
MSc Student, University of Melbourne

ULTRACOLD PLASMA SOURCE PROGRAM

DENE MURPHY
PhD Student, University of Melbourne

PROFESSOR ROB SCHOLTEN
Program Leader, University of Melbourne

DR BEN SPARKES
Post Doc, University of Melbourne

RORY SPIERS
PhD Student, University of Melbourne

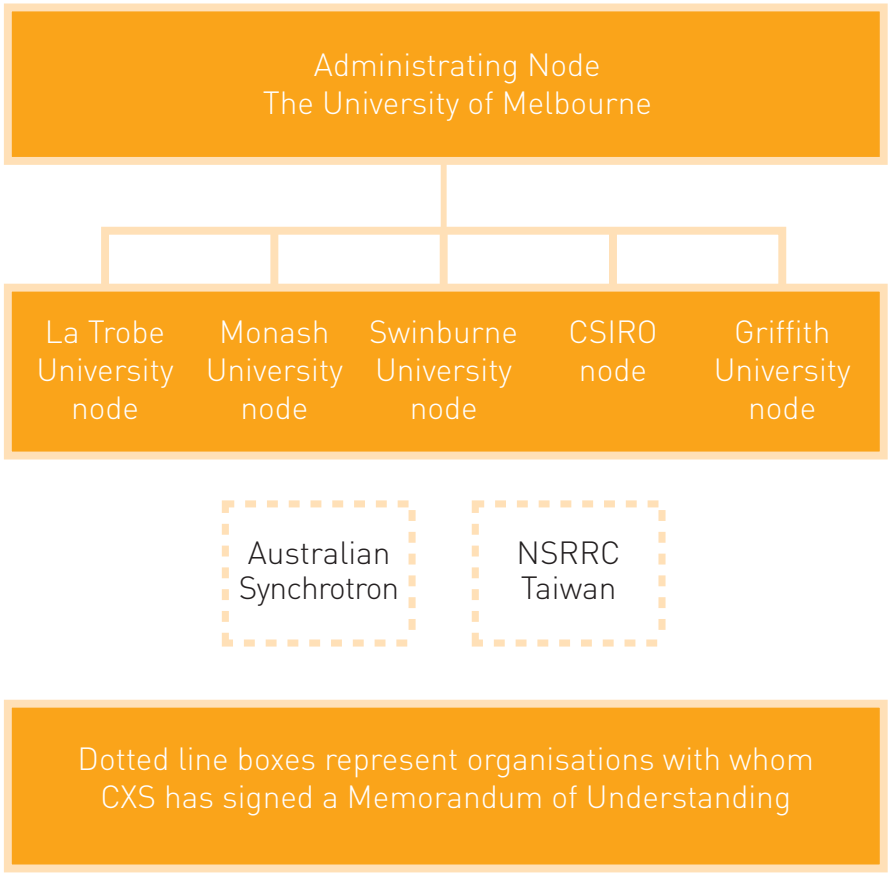
RICHARD TAYLOR
MSc Student, University of Melbourne

DANIEL THOMPSON
PhD Student, University of Melbourne

JOSHUA TORRANCE
PhD Student, University of Melbourne

ORGANISATIONAL CHART AS OF JUNE 2013

Designers to design from the information provided.



VALE STEVE WILKINS

FEBRUARY 15, 1946 – MARCH 25, 2013

by Andrew Stevenson

Steve Wilkins was a widely-respected and internationally-renowned X-ray scientist. As a CSIRO scientist for more than 35 years he made pioneering contributions in many areas of X-ray science and optics. In 1975 Steve joined the CSIRO Division of Chemical Physics as a Research Scientist and was quickly promoted through the ranks, becoming a Chief Research Scientist in 1998. I recall Steve relating to me his first meeting with the Chief of Division, Lloyd Rees, when he started at Clayton. Lloyd told Steve not to worry too much about what he did, "as long as it was brilliant"! Steve certainly adhered to Lloyd's advice.

Steve joined the X-ray Diffraction group, whose leader was Sandy Mathieson, the "father of X-ray crystallography in Australia" and a role model for many, including Steve. Sandy inspired Steve to undertake a number of ground-breaking studies of the fundamental interaction between X-rays and crystals. These included furthering our understanding of the way in which atoms vibrate; the phenomenon of "extinction" and its impact in crystal-structure determination; and developing novel approaches to handling the so-called "phase problem" in crystallography.

In the early 1980's Steve became convinced of the extraordinary possibilities for using synchrotron radiation in cutting-edge research. His determination and dedication to this cause has in no small way contributed to the establishment of the Australian Synchrotron at Clayton. This followed a natural development of Australia's involvement in international synchrotron science, with Steve being a key proponent at each step. One of these steps was the establishment of the Australian National Beamline Facility in Japan, with a multi-purpose X-ray diffractometer ("BIGDIFF"), conceived by Steve, as its centrepiece. After close to 20 years of dedicated service, BIGDIFF recently returned to Australia and will go on display at the Australian Synchrotron.

Steve was one of the pioneers of phase-contrast X-ray imaging and was the lead author on a seminal publication in the prestigious journal *Nature*, with one of our X-ray images displayed in false-colour on the cover. Phase-contrast imaging is one of the key aspects of the Australian Synchrotron's 140m-long Imaging and Medical Beamline, to which Steve has been an enthusiastic contributor from the very beginning of its planning and development.

He received many awards and honours, too numerous to mention here, but I would like to briefly relate three activities which were the focus of Steve's attention in the period prior to his passing. In December, 2012 the Bragg Symposium, celebrating 100 years of X-ray crystallography, was held in Adelaide. Steve put an enormous effort into the organisation of this meeting and its resounding success will forever be one of his legacies. Secondly; in February, 2013 Steve was the keynote speaker at a special meeting entitled "Taking X-ray Phase Contrast Imaging into Mainstream Applications", held at The Royal Society in London. A special issue of *Phil. Trans. R. Soc.* has just been published containing papers from this meeting, with Steve's last paper leading off the issue [Wilkins, S.W., Nesterets, Ya.I., Gureyev, T.E., Mayo, S.C., Pogany, A. & Stevenson, A.W. (2014), On the Evolution and Relative Merits of Hard X-ray Phase-contrast Imaging Methods. *Phil. Trans. R. Soc. A* 372: 20130021]. Finally; Steve always had an infectious passion for science and he loved to enthusiastically share this with others. As an Adjunct Professor at Monash University at the time of his tragic death, he was at Monash to give his first lecture of a course on X-ray science to eager Monash students. It is of some comfort to know that he was doing something that he loved at the end. He will be dearly missed.

WHERE ARE THEY NOW?

	CXS Node	Where are they now
Brian Abbey	University of Melbourne	Future Fellow, School of Physics, La Trobe University, Australia
Reem Al Amoudi	La Trobe University	Education Sector, Australia
Amanda Aloia	La Trobe University	Australian Nanotechnology Network, Australia
Nicole Anderson	University of Melbourne	Medical Administration, IECHS, Australia
Abhishek Awasthi	La Trobe University	Transition and Student Engagement Officer, La Trobe University, Australia
Michael Baker	La Trobe University	Cologne, Germany
Rosslyn Ball	University of Melbourne	PA to DVCR, La Trobe University, Australia
Simon Bell	University of Melbourne	Postdoc Research Fellow, Tubingen, Germany
Andy Berry	Monash University	Monash Centre for Synchrotron Science, Australia
Tim Brown	La Trove University	Parenthood
Jenny Carmichael	La Trobe University	Self employed, JC Protein Modelling, Melbourne, Australia
Stefania Castelletto	University of Melbourne	Senior Lecturer, RMIT, Australia
Alberto Cereser	CSIRO	Accepted Scholarship for the Technical University of Denmark
Jihun Cha	Griffith University	Working in Korea
Cherrine Chan	La Trobe University	Research Assistant, NCRIS Biologics, Australian Institute of Bioengineering and Nanotechnology, Australia
Jesse Clark	La Trobe University	Centre for Nanotechnology, Imperial College, London, UK
Maria Crespo	La Trobe University	Lecturer, University of Cali, Colombia
Tania Currubba	University of Melbourne	Research Management, Swinburne University, Australia
Nadia Davidson	University of Melbourne	Children's Hospital, Melbourne, Australia
Megan Dearnley	University of Melbourne	CSIRO, Geelong, Australia
Emma Duglas	La Trobe University	Development Manager, Research Focus Area, La Trobe University, Australia
Sam Flewett	University of Melbourne	Technical University, Berlin, Germany
Sarah Frankland	La Trobe University	Research Fellow, Faculty of Veterinary Science, University of Melbourne, Australia
Wilfred Fullagar	Monash University	Faculty of Science, Monash University, Australia
Omair Ghafur	Griffith University	PhD, Griffith University, Australia
James Gibbons	Monash University	Research Accounts Manager, Monash University, Australia
Chris Hall	Monash University	Beamline Scientist, Australian Synchrotron, Australia
Chris Hall	Swinburne University	Post Doc, Faculty of Engineering and Industrial Science, Swinburne University, Australia
Eric Hanssen	La Trobe University	Bio21 Institute, University of Melbourne, Australia
Clare Henderson	University of Melbourne	Post Doc, School of Chemistry, University of Melbourne, Australia
Liisa Hirvonen	University of Melbourne	Post Doc, King's College, London, UK
Stephen Holmes-Brown	La Trobe University	Research Assistant, La Trobe University, Australia
Martijn Jasperse	University of Melbourne	Bose-Einstein Condensation Research Group, Monash University, Australia
Dansha Jiang	University of Melbourne	Parenthood, USA
George Jung	Monash University	Monash Centre for Synchrotron Science, Australia
Lisa Lansfield	University of Melbourne	Royal Melbourne Hospital, Australia
Robert Lewis	Monash University	Monash Centre for Synchrotron Science, Australia
Craig Lincoln	University of Melbourne	Postdoc Research Fellow, Imperial College, London, UK
Alex Maier	La Trobe University	Research Fellow, Australian National University, ACT, Australia
Paul McMillan	La Tobe University	Bio21 Institute, Australia
Bohumil Maco	La Trobe University	Postdoc Research Fellow, EPSL, Lausanna, Switzerland
Adrian Mancuso	University of Melbourne	Group Leader, Instrument – SPB, European XFEL, Germany
Lachlan McKimmie	University of Melbourne	Technician, Coherent Scientific, Australia
Paul McMillan	University of Melbourne	BOMP Platform Manager, Bio21 Institute, Melbourne, Australia
Ted McMurchie	CSIRO	Fuels from Food Waste, University of Adelaide, Australia
Ved Mooga	La Trobe University	Post-Doc, University of Alabama, USA
Stephen Mudie	CSIRO	Beamline Scientist, Australian Synchrotron, Australia
Keith Nugent	University of Melbourne	Deputy Vice Chancellor – Research, La Trobe University, Australia
Adam Palmer	Griffith University	Scientific Officer, Griffith University, Australia
Catherine Palmer	La Trobe University	Research officer, La Trobe University, Australia
Andrew Peele	La Trobe University	Acting Director, Australian Synchrotron, Australia
Mark Pfeifer	La Trobe University	Cornell University, New York, USA
Olena Ponomarenko	University of Melbourne	Teaching Assistant, University of Saskatchewan, Canada
Michael Pullen	Griffith University	Research Fellow, Griffith University, Australia
Corey Putkunz	La Trove University	Postdoc Research Fellow, University of Melbourne, Australia
Alin Rai	La Trobe University	Technical Assistant, La Trobe University, Australia
Jesse Rudd-Schmid	La Trobe University	Research Assistant, Peter MacCallum Cancer Institute, Australia
Sebastian Saliba	University of Melbourne	Moglabs, Australia
David Sheludko	University of Melbourne	Research Associate, University of Melbourne, Australia
Danielle Smith	La Trobe University	Postdoc Research Fellow, UK
Che Stafford	La Trobe University	Honours Student, WEHI, Australia
Diana Stojanovski	La Trobe University	Bio21 Institute, University of Melbourne, Australia
Sven Teichmann	Swinburne University	Financial Risk Consultant and Engineer, Germany
Angela Torrance	University of Melbourne	Radiology, Albury Wodonga, Australia
Jose Varghese	CSIRO	Retired
David Vine	University of Melbourne	Advanced Photon Source, Chicago, USA
Kaushal Vora	La Trobe University	Processing Engineer, Australian National University, Australia
Lachlan Whitehead	University of Melbourne	Technical Assistant, Phillips Ormonde Fitzpatrick, Melbourne, Australia
Steve Wilkins	Monash University	Deceased
Garth Williams	University of Melbourne	National Accelerator Laboratory, Stanford University, USA
Jeff Yeoman	La Trobe University	Associate Lecturer, Molecular Sciences, La Trobe University, Australia
Rotha Yu	University of Melbourne	School of Physics, Monash University, Australia

PRESENTATIONS, CONFERENCES & LABORATORY VISITS

BRIAN ABBEY
- Invited Keynote Speaker – TMS 2013 Linking Science and Technology for Global Solutions, San Antonio, USA, March 2013
- Seminar – CSIRO, Melbourne Australia, April 2013
- Invited Speaker – Australasian Corrosion Association 2013, Queensland, Australia, August 2013
- Invited Seminar – Los Alamos National laboratory, USA, August 2013
- Lecture – La Trobe University, Melbourne, Australia, August 2013
- Speaker – The Australian Synchrotron Users Meeting, Melbourne Australia, November 2013
- Invited Speaker – 6th Annual Workshop of XFEL Science, Taiwan, November 2013

BENEADICTA ARHATARI
- Poster Presentation – The Australian Synchrotron Users Meeting, Melbourne, Australia, November 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

STEVEN BATINOVIC
- Poster Presentation – Early Career Victorian Infection and Immunity Conference, WEHI, Melbourne, Australia, September 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

JAMES CALVERT
- Attended – ISWAMP-2: Intense Field, Short Wavelength Atomic and Molecular Processes-2, Xi'an, China, July 2013
- Poster Presentation – ICPEAC XXVIII International Conference on Photonic, Electronic and Atomic Collisions, Lanzhou, China, July 2013

BO CHEN
- Speaker – SPIE 2013 X-ray Nanoimaging: Instruments and Methods, Dan Diego, USA, August 2013
- Poster Presentation – The Australian Synchrotron Users Meeting, Melbourne Australia, November 2013

HANNAH COUGHLAN
- Attended – MASSIVE Fifth Workshop on Massive Data Algorithmics, France, September 2013
- Attended – 12th Melbourne Protein Group Student Symposium, Melbourne, Australia, July 2013

SAM CROUCH
- Attended – KOALA Conference, University of Sydney, Australia, February 2013

RUBEN DILANIAN
- Attended – Linac Coherent Light Source. California, USA, March 2013

MATT DIXON
- Chair – 2013 Malaria in Melbourne Meeting, Australia, October 2013
- Invited Speaker – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

KRISTIN ELGASS
- Invited Speaker – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

LUKE FORMOSA
- Poster Presentation – Lorne Conference on Protein Structure and Function, Australia, February 2013
- Attended – US Protein Society Meeting, Boston USA, July 2013
- Presented – DynaMito 2013, Okinawa, Japan, October 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

XIAOHONG HAN
- Poster Presentation – ICPEAC XXVIII International Conference on Photonic, Electronic and Atomic Collisions, Lanzhou, China, July 2013

MARTIN JI
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

MICHAEL JONES
- Speaker – IXCOM22 International Congress on X-ray Optics and Microanalysis, Hamburg, Germany, September 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

T'MIR JULIUS
- Attended – ANZCOP – Australian and New Zealand Conference on Optics and Photonics – Fremantle, Western Australia, December 2013

MARK JUNKER
- Poster Presentation – The Australian Synchrotron Users Meeting, Melbourne Australia, November 2013

SHANNON KENNY

- Poster Presentation – Early Career Victorian Infection and Immunity Conference, WEHI, Melbourne, Australia, September 2013

CAROLINE LINDAU

- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

MAURO MAIORCA

- Visited – The University of Basel, Switzerland, May 2013
- Visited – Professor Joachim Weichert's lab at Saarland University, Germany, May 2013
- Poster Presentation – European Molecular Imaging Meeting, Torino, Italy, May 2013
- Attended – ImagO Scientific Conference, Utrecht University, Netherlands, May 2013
- Speaker – Saarland University, Germany, May 2013

ANDREW MARTIN

- Attended – Royal Society Conference X-ray Lasers in Biology, London, UK, October 2013
- Attended – Royal Society Conference X-ray in Biology Workshop, Chicheley, UK, October 2013
- Attended – Linac Coherent Light Source. California, USA, March 2013

BISWARANJAN MOHANTY

- Invited Speaker – 5th Asia-Pacific NMR Meeting, Brisbane, October 2013

DENE MURPHY

- Poster Presentation – 21st International Conference on Laser Spectroscopy, Berkeley, USA, June 2013
- Poster Presentation – 44th Annual DAMOP Meeting, Quebec, Canada, June 2013

THANH NGOC NGUYEN

- Presented – DynaMito 2013, Okinawa, Japan, October 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

ANDREW PEELE

- Attended – The Australian Synchrotron Users Meeting, Melbourne Australia, November 2013

NICK PHILLIPS

- Attended – MASSIVE Fifth Workshop on Massive Data Algorithmics, France, September 2013
- Attended – CXS Writer's Workshop, Melbourne, Australia, August 2013
- Presented – Euromat2013, Seville, Spain, September 2013

HARRY QUINEY

- Invited Speaker – Royal Society Workshop, Kavil Centre, UK, February 2013
- Invited Speaker – Max Planck Workshop, Schloss Ringberg, Germany, February 2013
- Attended – School of Physics Retreat, Daylesford, Australia, June 2013.
- Public Lecture – School of Physics Public Lecture Series, The University of Melbourne, Australia, July 2013
- Attended – Royal Society Conference X-ray Lasers in Biology, London, UK, October 2013
- Attended – Royal Society Conference X-ray in Biology Workshop, Chicheley, UK, October 2013

BORIS RELJIC

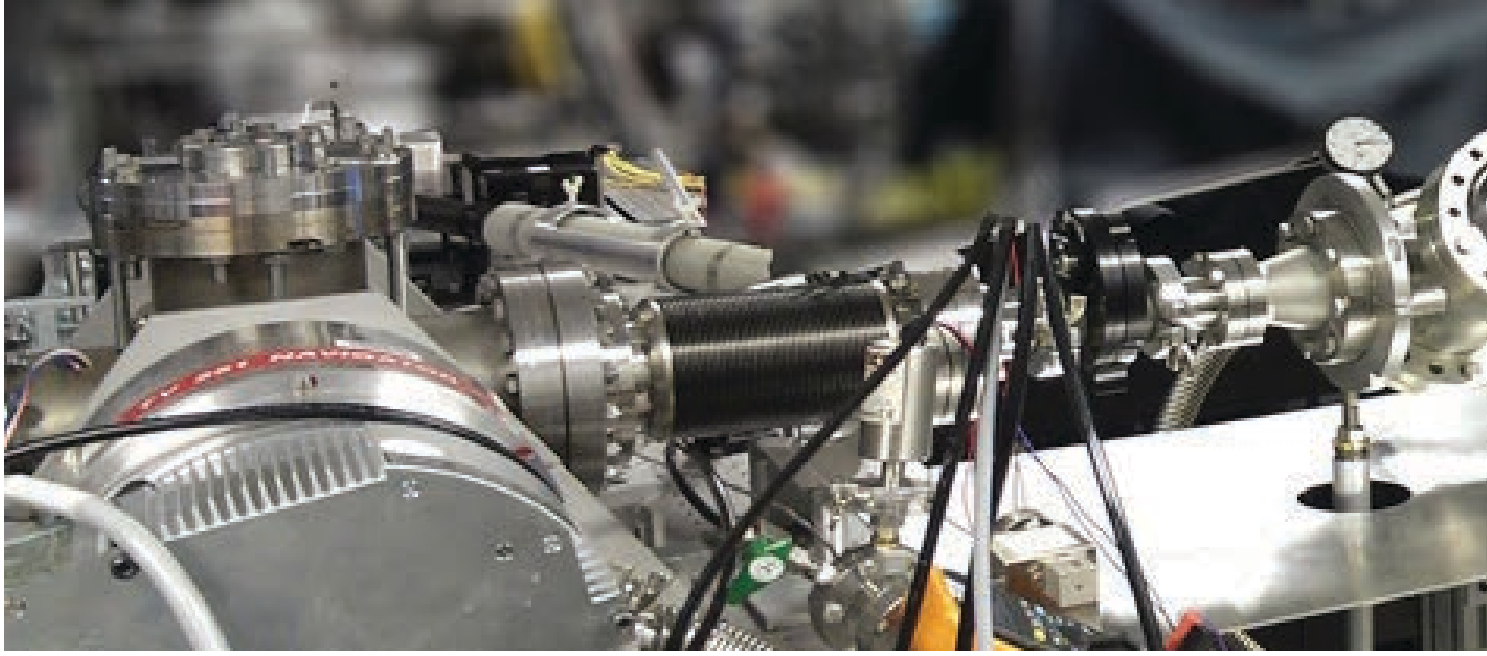
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

VIVIANE RICHTER

- Poster Presentation – Lorne Conference on Protein Structure and Function, Australia, February 2013
- Presented – ESF-EMBO Symposium, Poland, May 2013
- Invited Speaker – DynaMito 2013, Okinawa, Japan, October 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

MIKE RYAN

- Speaker – Opening ceremony of the LIMS Building, La Trobe University, Australia, February 2013
- Chair – Lorne Conference on Protein Structure and Function, Australia, February 2013
- Invited Speaker – US Protien Society Meeting, Boston USA, July 2013
- Co-Chair – Synthetic Biology Symposium on Organelles, ComBio2013, Perth, Australia, October 2013
- Speaker – Synthetic Biology Symposium, ComBio2013, Perth, Australia, October 2013



- Attended – DynaMito 2013, Okinawa, Japan, October 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

ROBERT SANG
- Invited Speaker – ICPEAC XXVIII International Conference on Photonic, Electronic and Atomic Collisions, Lanzhou, China, July 2013
- Speaker – ISWAMP-2: Intense Field, Short Wavelength Atomic and Molecular Processes-2, Xi'an, China, July 2013

MARTIN SCANLON
- Invited Speaker – NMRS2013 National Magnetic Resonance Society Symposium, Mumbai, India, February 2013
- Invited Speaker – ComBio2013, Perth, Australia, October 2013

ROBERT SCHOLTEN
- Invited Speaker – 3rd Banff Meeting on Structural Dynamics, Banff, Canada, February 2013
- Poster Presentation – 21st International Conference on Laser Spectroscopy, Berkeley, USA, June 2013
- Invited Review – ICPEAC XXVIII International Conference on Photonic, Electronic and Atomic Collisions, Lanzhou, China, July 2013

ABEER SINGH
- Presented – DynaMito 2013, Okinawa, Japan, October 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

TANIA SMITH
- Attended – Roadmap for Business Intelligence Strategy and Reporting, The University of Melbourne, Australia, February 2013
- Attended – Faculty of Science Training – HERDC Research Income Essentials, The University of Melbourne, Australia, February 2013
- Attended – School of Physics Retreat, Daylesford, Australia, June 2013.
- Chaired – Growing Tall Poppies Strategic Planning meeting, The University of Melbourne, Australia, July 2013
- Attended – Mental health Essentials Training, The University of Melbourne, Australia, July 2013
- Attended – Faculty of Science Business Improvement Planning Meeting, The University of Melbourne, Australia, July 2013

TREVOR SMITH
- Invited Speaker – 6th Conference on Advanced Materials and Nanotechnology, Auckland, New Zealand, February 2013
- Speaker – 26th International Conference on Photochemistry, Leuven, Belgium, July 2013
- Speaker – 13th Conference on Methods and Applications of Fluorescence: Spectroscopy, Imaging and Probes, Genoa Italy, September 2013
- Visited – COSMIC, Physics and Chemistry, University of Edinburgh, Scotland, October 2013

RORY SPEIRS
- Attended – KOALA Conference, University of Sydney, Australia, February 2013

VICTOR STRELTSOV
- Presented – The 8th Pacific Rim International Congress on advanced Materials and Processing, August 2013
- Attended – Frontiers of Light Microscopy Conference, November 2013

DAVID STROUD
- Visited – The lab of Bettina Warscheid, Freiburg, Germany. August 2013
- Presented – DynaMito 2013, Okinawa, Japan, October 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

RICHARD TAYLOR
- Attended – KOALA Conference, University of Sydney, Australia, February 2013

SILVIA TEGUH
- Attended – Frontiers in Medicinal Chemistry Conference, UCSF, San Francisco, USA, June 2013

LEANN TILLEY
- Speaker – Monash Institute of Pharmaceutical Sciences, Melbourne, Australia, May 2013
- Visited – Pasteur Institute of Cambodia, Phnom Penh, Cambodia, May 2013
- Speaker – Pasteur Institute of Cambodia, Phnom Penh, Cambodia, May 2013
- Chair and Advisory Board Member – 4th International Symposium on Diffraction Structural Biology 2013, Nagoya, Japan, May 2013
- Visited – Nagoya University, Japan, May 2013

- Public Lecture – MDHS Dean's Public Lecture, The University of Melbourne, Australia, June 2013
- Speaker – Pasteur Institute, Paris, France, September 2013
- Visited – Pasteur Institute, Paris, France, September 2013
- Speaker – Phillipps University Marburg, Germany, September 2013
- Visited – Phillipps University Marburg, Germany, September 2013
- Invited Speaker – Biology in Synchrotron Radiation Conference, Hamburg, Germany, September 2013
- Visited – Justus-Liebig University, Giessen, Germany, September 2013
- Invited Speaker – ComBio2013, Perth, Australia, September 2013
- Invited Speaker – Annual Meeting of the Biophysical Society of Japan, Kyoto, Japan, October 2013
- Invited Speaker – American Society of Tropical Medicine and Hygiene, Washington, USA, November 2013
- Invited Speaker – Department of Medicine and Molecular Microbiology, Howard Hughs Medical Institute, Washington University, St Louis, USA, November 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013
- Visited – Washington University Centre for Microscopy, Characterisation and Analysis, St Louis, USA, November 2013

JOSHUA TORRANCE

- Attended – KOALA Conference, University of Sydney, Australia, February 2013
- Attended – ANZCOP – Australian and New Zealand Conference on Optics and Photonics – Fremantle, Western Australia, December 2013

GIANG TRAN

- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013
- Attended – KOALA Conference, University of Sydney, Australia, February 2013

LAP VAN DAO

- Invited Speaker – COST MP2013 Advanced Spatial and Temporal X-ray Metrology, Paris, France, April 2013
- Invited Speaker – International Conference on Laser Optics and Photonic, San Antonio, USA, October 2013

GRANT VAN RIESSEN

- Visited – National Institute for Materials Sciences, Tsukuba, Japan, January 2013
- Visited – National Institute of Advanced Industrial Science and Technology, Tsukuba, Japan, January 2013
- Attended – Nanotech 2013, Nanotechnology Conference and Expo, Tokyo, Japan, February 2013
- Invited Speaker – International Materials Research Congress, Cancun, August 2013
- Speaker – SPIE 2013 X-ray Nanoimaging: Instruments and Methods, Dan Diego, USA, August 2013
- Speaker – The Australian Synchrotron Users Meeting, Melbourne Australia, November 2013
- Poster Presentation – The Australian Synchrotron Users Meeting, Melbourne Australia, November 2013
- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013
- Attended – 2013 ANFF Annual Research Showcase, Melbourne, Australia, November 2013
- Presented – Australian Synchrotron Scientific Advisory Committee, Melbourne Australia, November 2013

SHANNON WILLIAMS

- Attended – CXS Symposium: Frontiers of Light Microscopy, Melbourne, Australia, November 2013

DANIEL WELLS

- Attended – KOALA Conference, University of Sydney, Australia, February 2013

DAVID WOOD

- Attended – KOALA Conference, University of Sydney, Australia, February 2013

STANLEY XIE

- Speaker – Malaria Program Grant Seminar, WEHI, Melbourne, Australia, May 2013
- Poster Presentation – Early Career Victorian Infection and Immunity Conference, WEHI, Melbourne, Australia, September 2013

AMNA ZAHID

- Attended – ICPEAC XXVIII International Conference on Photonic, Electronic and Atomic Collisions, Lanzhou, China, July 2013

AWARDS, HONOURS AND SCHOLARSHIPS

2013 EUREKA PRIZE FOR EXCELLENCE IN INTERDISCIPLINARY SCIENTIFIC RESEARCH

Nano-scale diamond sensors that light up the insides of cells have been created by University of Melbourne researchers Professor Lloyd Hollenberg, Associate Professor Robert Scholten, Dr Alastair Stacey and Dr Yan Yan. The Quantum Bio-probes team showed they could detect individual atoms inside a living cell.

From their innovative combination of quantum physics, biology, chemistry and nanotechnology, the team has won the 2013 Australian Museum University of New South Wales Eureka Prize for Excellence in Interdisciplinary Scientific Research. Their work opens possibilities for improving the delivery of medicines by tracking molecules moving inside living cells.

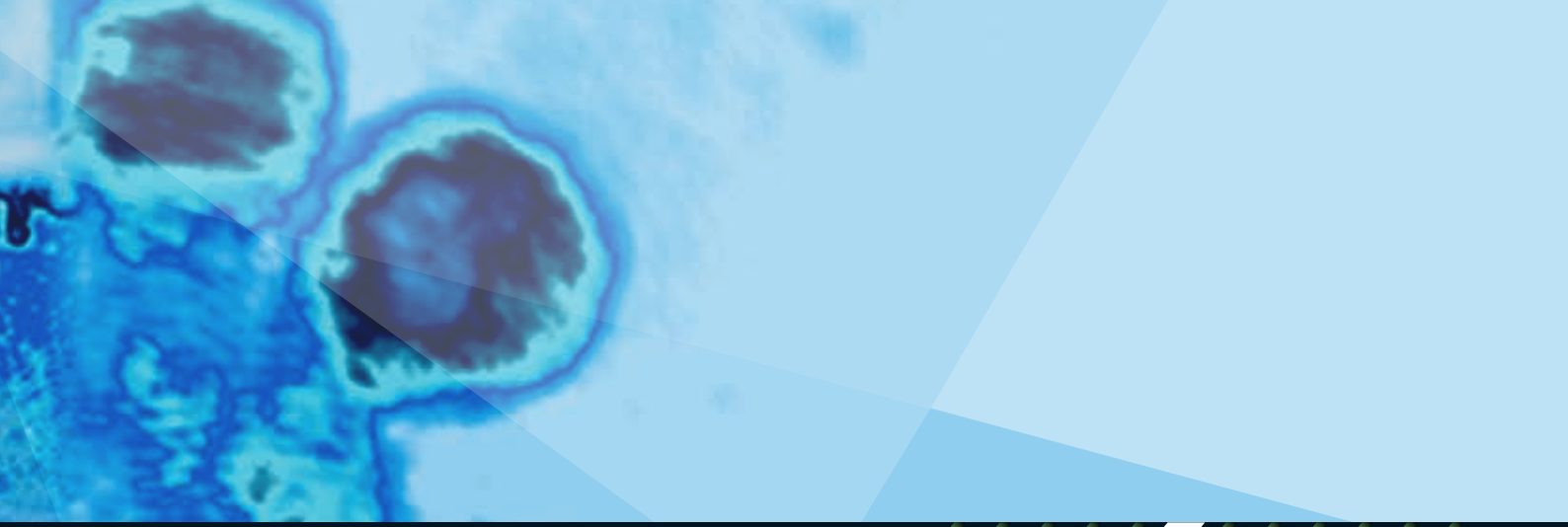
"This exciting combination of nano-engineering and biology will allow us to explore what's going on inside a living cell in more detail than has ever been possible in the past," said Frank Howarth, Director of the Australian Museum. "Existing medical imaging technologies have delivered huge benefits for human health. This invention opens the door to a new revolution in imaging".

The Quantum Bio-probes team inserted tiny diamonds with single flaws into living human cells. The diamonds were able to measure the magnetic fields from individual atoms and molecules with far greater resolution than that achieved by current medical imaging.

To watch the YouTube video type in the following url into your favourite internet search engine: http://youtu.be/xljwkQ9FbLY

To read the journal article on this work published in Nature Nanotechnology go to: http://www.nature.com/nnano/journal/v6/n6/abs/nnano.2011.64.html

The Eureka Prize winning team from left: Alastair Stacey, Yan Yan, Lloyd Hollenberg and CXS's own Robert Scholten



2013 AWARDS AND HONOURS

CXS recognised a number of its members for their work in 2013. The centre extends its sincere congratulations to each of them for their efforts and awards in the following honours:

- Robert Scholten for being jointly awarded the Eureka Prize for Excellence in Interdisciplinary Research.
- Mike Ryan for appointment as President elect of the Australian Society for Biochemistry and Molecular Biology.
- Thanh Ngoc Nguyen for the prize of the most engaged student at DynaMito 2013.
- Stanley Xie for a University Travel Award to attend the ASTMH meeting in Thailand.
- Diana Stojanovski for receiving the 2013 ASBMB Edman award. This is awarded to a biochemist or molecular biologist with no more than seven years postdoctoral experiment, in recognition of their outstanding research work.
- Luke Formosa and David Stroud for being awarded a poster prize at AussieMit Conference.
- Catherine Palmer for winning an ASBMB fellowship as an annual or early career researcher in recognition of their outstanding work in an area of biochemistry or molecular biology.
- Catherine Palmer for the Fred Collins award which included $1000 in addition to Fellowship travel expenses.
- Simon Jones for receiving the Business Victoria Science, Technology and Innovation Victorian Fellowship.
- Victor Streltsov for receiving Office of the Chief Executive funding for a CSIRO Post Doctorate Fellow.
- Robert Scholten for his Special Studies Program sabbatical from 10 December 2012 to 12 March 2013.
- Marion Hliscs for receiving a DFG Fellowship to work on cytoskeleton Modulating proteins in the sexual stage parasite.
- Ben Sparkes for receiving a three year McKenzie Fellowship.

2013 SCHOLARSHIPS AND STUDENTSHIPS

We would like to congratulate the following students for their successful applications for **CXS Top-Up Scholarships in 2013**:

- Hannah Coughlan, La Trobe University
- Megan Dearnley, Bio21 Institute
- Mauro Maiorca, The University of Melbourne
- Isaac Peterson, The University of Melbourne
- Rory Spiers, The University of Melbourne
- William Wallace, Griffith University
- Stanley Xie, Bio21 Institute

CXS also congratulates the following students for their successful applications for **CXS Travel Awards Scholarships in 2013**:

- Luke Formosa, La Trobe University
- Xiaohong Han, Griffith University
- Dene Murphy, The University of Melbourne
- Thanh Ngoc Nguyen, La Trobe University
- Adabelle Ong, University of Melbourne
- Nick Phillips, La Trobe University
- Viviane Richter, La Trobe University
- Abeer Prakash Singh, La Trobe University
- Ben Sparkes, The University of Melbourne
- Rory Spiers, The University of Melbourne
- Joshua Torrance, The University of Melbourne
- Stanley Xie, Bio21 Institute

The centre extends its congratulations to the following students for their successful applications for **CXS Vacation Scholarships in 2013**:

- Robert De Gille, The University of Melbourne
- Martin Ji, Bio21 Institute
- Patrick Kennedy, The University of Melbourne
- Daniel Rodgars-Pyor, The University of Melbourne

CXS SPONSORED EVENTS

CXS sponsored the following events in 2013:

- BAMBII – Imaging Symposium, Melbourne, Australia, September 2013
- MIM – Malaria in Melbourne Conference, Melbourne, Australia, October 2013
- KOALA Conference on Optics, Atoms and Laser Applications, Sydney, Australia, November 2013
- ACMC – Asian Conference on Membrane Computing, Chengdu, China, November 2013
- ANZCOP – Australian and New Zealand Conference on Optics and Photonics – Fremantle, Western Australia, December 2013

THE FOLLOWING MAJOR AWARDS AND HONOURS HAVE BEEN RECEIVED BY CXS MEMBERS OVER THE LIFE OF THE CENTRE

Roche Molecular Biochemicals Medal 2006 – Michael Ryan
DAAD Fellowship 2007 – Claudia Leidhold
Australia Research Council Federation Fellowship 2007 – Keith Nugent
Deutscher Akademischer Dienst German Academic Exchange Fellowship 2007 – Michael Baker
Rio Tinto OTX Prize 2007 – Corey Putkunz
Inaugural Graeme Clarke Research Outcomes Forum Address 2008 – Keith Nugent
Knowledge Transfer Award 2009 – Keith Nugent
National Australia Bank School's First State Award 2009 – CXS & Santa Maria College
Under the Coverslip Scientific Photography Competition 2009 – Clare Henderson
Bancroft-Mackerras Medal 2010 – Leann Tilley
Alex von Humboldt Research Fellowship 2010 – Michael Baker
Tall Poppies Award 2010 – Marc Kvansakaul
Alan Walsh Medal 2010 – Robert Scholten
Eureka Prize – Sleek Geeks 2010 – CXS & St Helena College
CSIRO Payne Scott Award 2010 – Connie Darmanin
Caswell Grave Scholarship 2011 – Megan Dearnley
David Syme Research Prize 2011 – Harry Quiney
Network Researcher Exchange Training & Travel Scholarship 2011 – Megan Dearnley
LTU DVCR Excellence in Research Award for Mid Career Researcher 2011 – Alex Maier
Andres Travel Award 2011 – Megan Dearnley
Beckman Coulter Discovery Science Award 2011 – Leann Tilley
Bruce Stone Travel Award 2011 – Megan Dearnley
Highly Commended Certificate for Contribution to Science Education 2011 – Eroia Barone-Nugent
La Trobe University Dean's Award 2011 – Diana Stojanovski
Lorne Protein Conference Student Poster Prize 2011 – Catherine Palmer
APA PhD Scholarship 2011 – Aidan Carroll
LIMS Miller Travel Grant 2011 – Ved Mooga
Extreme Imaging Competition Second Place Winner 2012 – Ben Norton
ASBMB Vic Branch Poster Prize 2012 – Ved Mooga
Under The Coverslip Imaging Competition Prize 2013 – Megan Dearnley
ASBMB Edman Award 2013 – Diana Stojanovski
ASBMB Fellowship 2013 – Catherine Palmer
Fred Collins Award 2013 – Catherine Palmer
DFG Fellowship 2013 – Marion Hliscs
Deputy Vice-Chancellor Research La Trobe University 2013 – Keith Nugent
Eureka Prize for Excellence in Interdisciplinary Scientific Research 2013 – Robert Scholten (joint winner)
Discovery Early Career Research Award 2013 – Andrew Martin
ARC Future Fellowship 2013 – Brian Abbey
Elected President of the Australian Society of Biochemistry and Molecular Biology – Mike Ryan
Most Engaged Student Prize DynaMito 2013 – Thanh Ngoc Nguyen
ASTMH Travel Award 2013 – Stanley Xie
ASBMB Edman Award 2013 – Diana Stojanovski
ASBMB Fellowship 2013 – Catherine Palmer
Fred Collins Award 2013 – Catherine Palmer
AussieMit Conference Poster Prize 2013 – Luke Formosa and David Stroud
Business Victoria Science, Technology and Innovation Victorian Fellowship 2013 – Simon Jones
DFG Fellowship 2013 – Marion Hliscs
McKenzie Fellowship 2013 – Ben Sparkes

RESEARCH TRAINING & PROFESSIONAL EDUCATION

The Centre met all of its recruitment and professional education targets for 2013, and has exceeded expectations in the area of *Presentations to Schools and/or Teaching Communities.* As this is the final year of official CXS operations our *Postgraduate Recruitment* activity was decreased. Recruits are now formally a part of attached Schools or Departments of their respective universities.

WORKSHOPS

CXS conducted the following interdisciplinary workshops in 2013:

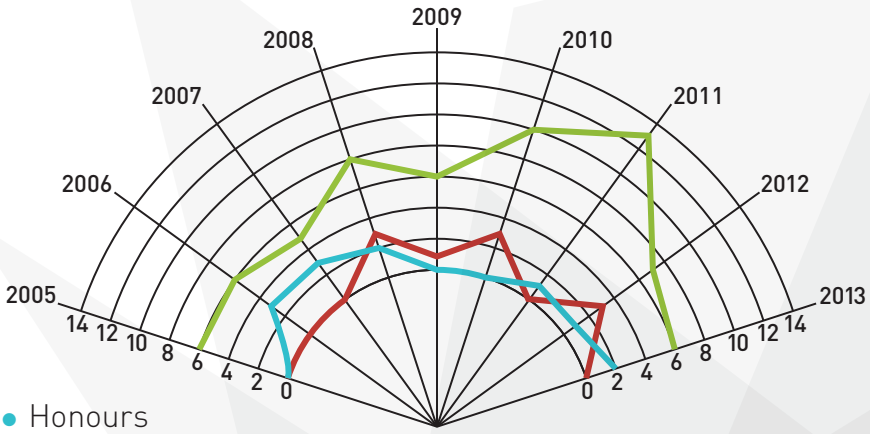
- NADIA Software Training Workshop for Beginners, held at the School of Physics, The University of Melbourne, on 17th June 2013
- NADIA Software Training Workshop for Beginners, held at the National Centre for Synchrotron Science at the Australian Synchrotron in Clayton on 11th July 2013
- NADIA Software Training Intermediate Workshop, held at the Laby Ideas Centre at the University of Melbourne on 18th July 2013
- CXS Writer's Workshop, La Trobe University on 26 August 2013
- CXS International Microscopy Workshop, University of Melbourne and Bio21 Institute on 18 and 19 November 2013
- Meeting of the Scientific Advisory Board, They University of Melbourne on 20 November 2013
- Meeting of the CXS International Advisory Board, The University of Melbourne on 20 November 2013
- CXS End of Year Review, The University of Melbourne on 13 December 2013

CXS STUDENT ENROLMENTS AND COMPLETIONS

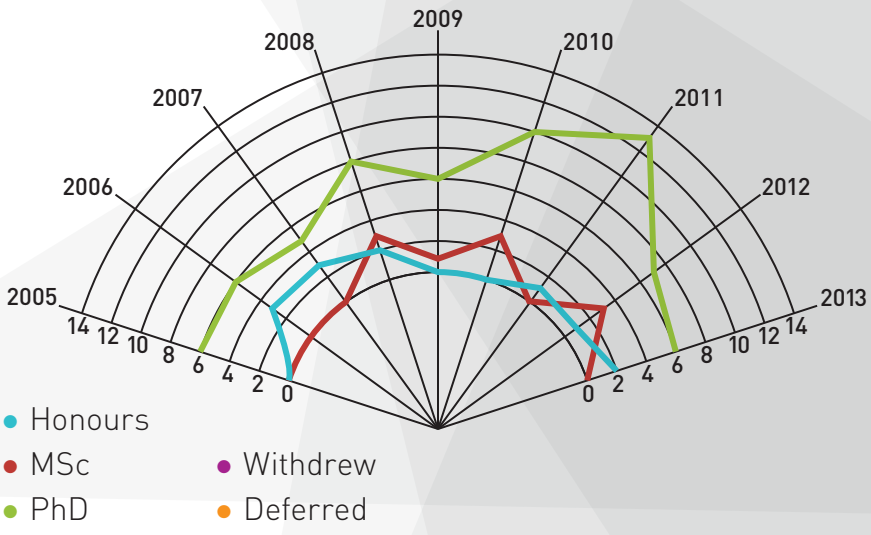
As 2013 was its final year of operation, CXS wound down its student intake during the reporting period. In 2013, two honours students and six PhD students enrolled as members of the Centre. The School or Department of which they are associated will source the financial support of these students in 2014 and beyond outside of the Centre.

As shown in the charts below The centre has had a solid intake and completion record with just seven withdrawals over the entire eight years of CXS operations.

CXS STUDENT ENROLMENTS 2005 – 2013



CXS STUDENT COMPLETIONS 2005 – 2013



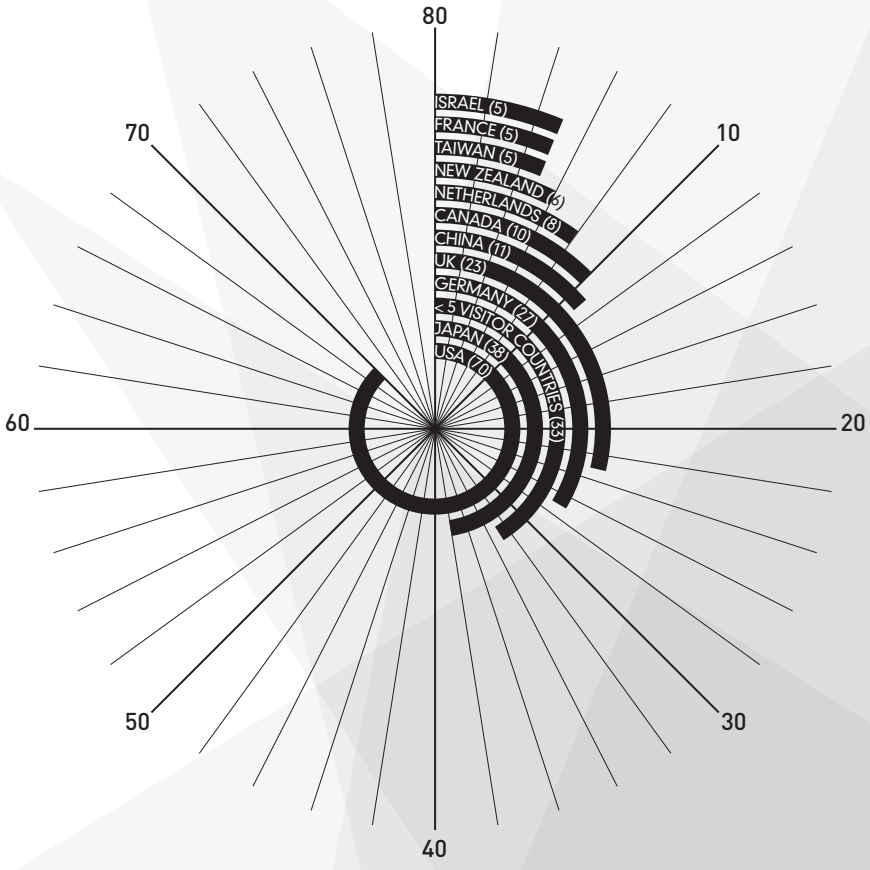
VISITORS TO CXS

Since its inception, CXS has invited 441 eminent professors, researchers and professionals from around the world to carry out joint research work; give seminars and lectures; take part in collaborative discussions; and conduct short courses. The following guest attended CXS during 2013:

1. Toby Bell, Monash University, Australia
2. Till Boecking, University of New South Wales, Australia
3. Nick Dixon, University of Wollongong, Australia
4. Ms Claire Dumont, University of Paris 7 Diderot, France
5. Schuyler van Engelenburg, NICHD, University of Colorado, Boulder, USA
6. Andres Figueiras, Spanish Research Student, Spain
7. Yann Gambin, Dept of Integrative Biology & Pharmacology, Texas, USA
8. Kat Gaus, University of New South Wales, Australia
9. Philipp Glock, Wurzburg, Germany, Germany
10. Enrico Gratton, Laboratory for Fluorescence Dynamics, USA
11. Klaus Hahn, Dept of Pharmacology & Lineberger Cancer Center, USA
12. Samir Hamdan, Division of Biological and Environmental Sciences, Saudi Arabia
13. Michael Hickey, Monash University, Australia
14. Dr Damien Hicks, Lawrence Liverpool National Laboratory, USA
15. Elizabeth Hinde,Laboratory for Fluorescence Dynamics, USA
16. Johan Hofkens, Katholieke Universiteit Leuven, Belgium
17. Dr Kristin Hoydalsvik, Norwegian University of Science & Technology, Norway
18. Angus Johnson, University of Melbourne, Australia
19. Carolyn Larabell, Department of Anatomy, University of California, USA
20. Jong-Bong Lee, Department of Physics, POSTECH, Korea
21. Vania Leite, Universidade Federal de Sao Paolo, Brazil
22. Caroline Lindau, University of Cologne, Germany
23. Prof Hai Ming, University of Science and Technology of China, China
24. Antoine van Oijen, Zernike Insittute for Advanced Materials, Netherlands
25. Ms Arisa Parameyong, Mahidol University, Thailand
26. Steve Petrou, The Florey Neuroscience Institute, Australia
27. Nicolas Plachta, Monash University, Australia
28. Anne Rios, WEHI, Australia
29. Michael Roberts, The University of Queensland, Australia
30. Sarah Russell, Swinburne University of Technology, Australia
31. Ethan Scott, The University of Queensland, Australia
32. Dr. Inga Sidnen-Kiamos, Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology – Hellas, Greece
33. Elizabeth A. Smith, Department of Anatomy, University of California, USA
34. Ms Nishita Srivastava, IIT Madras, India

35. Marta Tiburico, Radboud University, Nijimegen, Rome, Italy
36. Lynne Turnbull, University of Technology Sydney, Australia
37. Alvin van Niekerk, University of Queensland, Australia
38. Rajagopal Vijayaraghavan, MIT Alliance for Research and Technology, Singapore
39. Kyoko Yokomori, Dept of Biological Chemistry, Uni of California, USA
40. Prof Douguo Zhang, University of Science and Technology of China, China

INTERNATIONAL VISITORS TO CXS 2005 – 2013



< 5 VISITOR FROM THE FOLLOWING COUNTRIES:

- Belgium
- Brazil
- Greece
- India
- Italy
- Korea
- Malaysia
- Norway
- Russia
- Saudi Arabia
- Singapore
- South Africa
- Spain
- Sweden
- Switzerland
- Thailand

CXS COLLABORATIONS

A number of collaborations continued to develop with the following groups in 2013:

BETTINA WARSCHEID, GERMANY

- David Stroud went to Fielburg Germany for a co-operation with the lab of Bettina Warscheid from 1 August 2013 to 23 August 2013.

PROFESSOR YASHINORI FUJIOSHI

- Leann Tilley worked at Professor Yoshinori Fujiyoshi laboratory at Nagoya University in Japan in May 2013.

PROFESSOR KOENDERINK

- Mauro Maiorca visited Professor Jan J Koenderink in Belgium for collaborative work in May 2013.

ADRIENNE MENRICK

- Mauro Maiorca collaborated with Adrienne Mendrick at the Image Science Insititue in the Netherlands in May 2013.

ADVANCED PHOTON SOURCE BEAM TIME

- Nick Phillips, Hannah Coughlan, Brian Abbey and henry Kirkwood worked together on an experiment at the Advanced Photon Source 34-ID-C from 4 to the 10 December 2013.

JOINT INSTITUTE FOR LABORATORY ASTROPHYSICS

- Grant van Riessen and Bo Chen collaborated with the Kapteyn-Murnane group at JILA, USA in August 2013.

ALESSANDRA GIANONCELLI

- Grant van Riessen and Michael Jones developed a proposal for CDI at Fermi in collaboration with Alessandra Gianoncelli and submitted for spetromicroscopy with CDI at SXRI.

SLAC LINAC COHERENT LIGHT SOURCE

- Eugeniu Balaur, Mark Junker and Grant van Riessen had beam time at SXRI to test custom Zone plates and to explore methods of imaging the magnetisation distribution in patterned magnetic films.

AUSTRALIAN SYNCHROTRON

- Grant van Riessen was invited to report on progress on the status of the SXRI beamline to the Scientific Advisory Board of the Australian Synchrotron.

AUSTRIAN SCIENCE FUND

- Robert Scholten took part in a review of the FWF Austrian Science Fund review of Doctoral Program Complex Quantum Systems, Vienna, Austria from 27 October 2013 to 3 November 2013.

TALL POPPIES CAMPAIGN

- Tania Smith and Eoria Barone-Nugent meet with members of the National Tall Poppies Campaign to work on the securing the CXS Growing Tall Poppies Program future at a national level beyond the life of CXS.

SANTA MARIA COLLEGE

- Tania Smith continued discussion with the Principle of Santa Maria College Northcote, Deborah Baker, regarding the ongoing collaboration of Santa Maria as a feeder school for the Growing Tall Poppies Program.

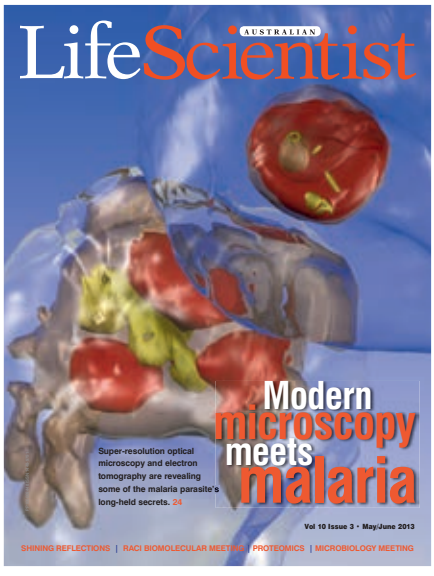
CXS OUTREACH 2013

9

CXS has exceeded all of its performance indictors in the area of outreach. Its focus on liaising with related research institutions to formulate collaborative arrangements and information sharing has been very successful, and community outreach and secondary school interactions via the Growing Tall Poppies program has achieved a quantifiable impact with Santa Maria College student numbers into physics increasing by 75% over the last 3 years.

As part of the CXS Outreach Program, a number of key initiatives took place in 2013:

- Paul McMillan was on the organising committee of the Imaging in Biology Symposium with more than 150 participants from across the University of Melbourne. The symposium was attended by the broader research community, including industry from across Melbourne. The event was conceptualised and organised by the BAMBII student group.
- Matt Dixon spent a day at Gisborne Secondary College talking to year 9-12 students about malaria research and life as a medical researcher. This was part of the ASMR Rural Schools Tour program.
- Australian Life Science May/June issue, page 24-28 (2013) "Modern microscopy addresses an age-old problem." The feature showcased the Electron Tomography and antimalarial drug work of Eric Hanssen and the Tilley Lab.
- Leann Tilley gave a talk in the Chancellor's Scholars Program at The University of Melbourne.
- Sharon Sim completed a BIOM30003 Project supervised by Megan Dearnley.
- Nick Phillips organised a synchrotron remote experiment for school groups at the Australia Synchrotron on MX1 in August 2013.
- Grant van Riessen, Michael Jones, Nick Phillips, Hannah Coughlan and Andrew Tait exhibited the SXRI endstation to over 3500 people that attended the Australian Synchrotron Open Day in October 2013.
- Harry Quiney gave a public lecture as part of the School of Physics Free Public Lecture Series titled, *"From Moseley's Law to the Molecular Microscope: A Century of X-ray Physics, Chemistry and Biology"* at the University of Melbourne in July 2013.
- Leann Tilley gave a public lecture as part of Biochemistry and Molecular Biology at the University of Melbourne titled, *"Malaria Parasites: Blood, Drugs and Sex"* in June 2013.
- The CXS Growing Tall Poppies program hosted project group for students at Santa Maria College Northcote, Mater Christi College, Charles La Trobe College and Star of the Sea College. The project ran for five weeks, with 40 students participating, The ARC Centre for Quantum Computation and Communication Technology hosted one of these programs.



Australian Life Science May/June issue, page 24 – 28 (2013) "Modern microscopy addresses an age-old problem."

Attendees of KOALA 2013 at the University of Sydney, November 25th-29th

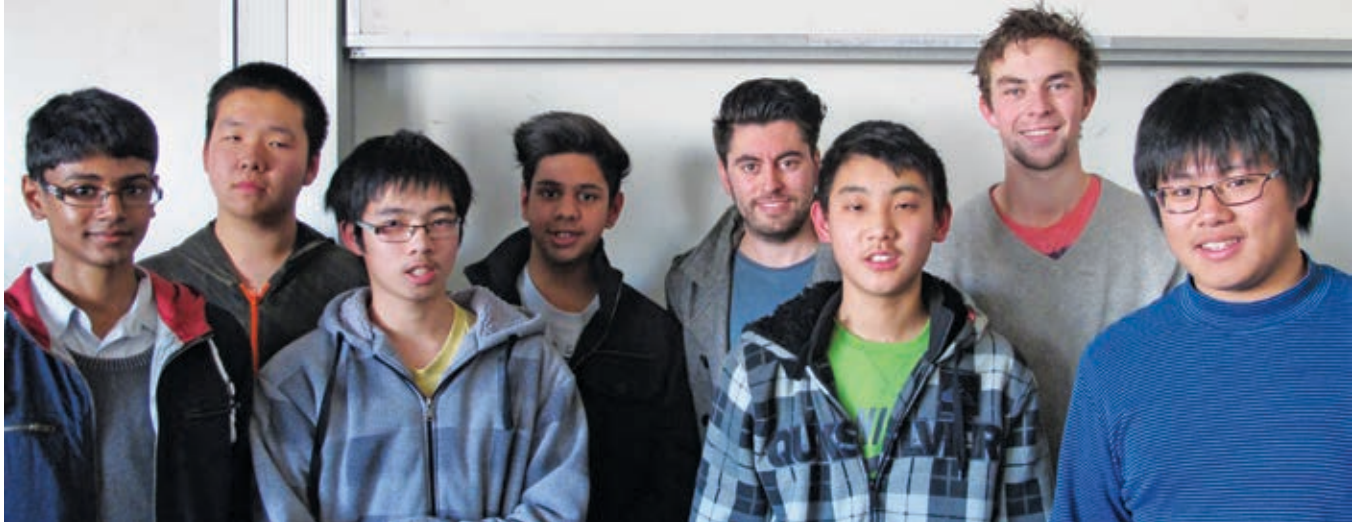
KOALA CONFERENCE 2013

KOALA (Conference on Optics, Atoms and Laser Applications) is an annual student-run conference targeted at postgraduate optics students from Australia, New Zealand and further afield.

CXS was proud to participate as a sponsor of the 2013 event, which was hosted at the University of Sydney and was organised by the local student chapter of the Optical Society of America. With 93 students attending from over 12 universities, the program covered a broad range of fields in optics. This included X-ray science, high harmonic generation, atom optics, biomedical optics, plasmonics, Bose-Einstein condensation, photonics, nonlinear optics, quantum optics and optical engineering. The showcasing of such a broad range allowed attendees to come into contact with current optics research outside of an isolated field and also to develop skills with communicating research to a broader audience.

The conference spanned five days with a broad program that included invited speakers; student talks; student-run tutorials; a poster session; and a social day. Plenary talks and technical workshops were given by Prof. Kishan Dholakia (University of St. Andrews), A. Prof. Michelle Povinelli (University of Southern California), Prof. Greg Forbes (University of Rochester) and Emertius Prof. Geoff Smith (University of Technology, Sydney). These talks were extended across a wide range of topics and were particularly informative, while the public lecture by Prof. Kishan Dholakia on the biological applications of optical manipulation was a genuine highlight of the week. The presence of the international speakers across the conference also provided further valuable discussions and networking opportunities.

The social day was held on a beautiful, sunny day at Manly beach and was a great opportunity to spend time in the company of fellow optics students and to make ties with students from different universities. Overall, KOALA 2013 provided great opportunities to present new research in a student-driven environment, learn about research currently underway in different research groups, and be a part of a wider young community in optical science.



McClelland College students worked on the Ultra Cold Plasma: How to Make it and What it is Good for at The University of Melbourne, School of Physics

THE GROWING TALL POPPIES IN SCIENCE PROGRAM IN 2013

This year has established the *Growing Tall Poppies Science Program* as the premier outreach program to promote the relevance, importance and impact of the physical sciences. The retention rate of girls in physics from years 11 to 12 at Santa Maria College in 2013 and 2014 has remained at a steady seventy per-cent, well over the retention rate prior to the program's implementation.

The goal in 2013 was to equitably increase the uptake of Growing Tall Poppies programs in schools. New schools that participated were Charles La Trobe Secondary College, Nossal High School and Mater Christ College Belgrave. The program now supports over twelve schools and more than ninety students per year to experience and explore the interdisciplinary science of world-class scientists. Students gained understanding of how physics advances scientific understanding and knowledge that changes outcomes for people, community and society.

During the year, University of Melbourne outreach funds have been raised alongside Dr Daniel Dias in order to expand the program into the plant molecular sciences. These efforts will come to fruition in June 2014. There have also been further developments with the Monash Biological Imaging Group, headed by Prof Gary Egan who hosted a group of students from Mater Christi Catholic College. Through this venture the intricacies of the Australian Synchrotron as a paradigm shifting mechanism for the biological sciences was a highlight.

Scientists Dr Victor Streltsov and Dr Tom Caradoc-Davies of the CSIRO and Australian Synchrotron respectively have supported Year 11 physics students from Santa Maria College to experience the elegant place physics holds in the interdisciplinary sciences by running experiments on world class robotic and synchrotron equipment. These groups have played a pivotal role to increase the retention of girls in physics at our feeder school Santa Maria College.

Throughout the year Eroia Barone-Nugent has presented at the Physics, Chemistry,

Santa Maria College Students on the X-ray Sudoku: Question of Public Health Meets Sudoku Project at The University of Melbourne, School of Physics

Charles La Trobe College students worked on the Green Fluorescent Protein Project at La Trobe University, School of Molecular Sciences

Mater Christi College Students who worked on the Biomedical Imaging Project at Monash University, School of Biomedical Imaging

Biology and Environmental Science VCE Teacher Conferences; the National Teacher Conference (CONASTA); and the Catholic Education Office of Melbourne's Wellbeing & Community Partnership Conference 2013. These presentations highlighted the benefits to the secondary students and the science community for paradigm shifting meaningful outreach that changes students' choices to follow the physical sciences.

There is continuing interest and support from the Australian Synchrotron, and further interest from ANSTO to develop Growing Tall Poppies programs that reach secondary students in states throughout Australia. However, the *coupe de résistance* for 2013 is the partnership established between the Growing Tall Poppies Program and the national Tall Poppies Campaign. This new liaison will see the establishment of the 'Growing Junior Tall Poppies' as an outgrowth of the CXS Growing Tall Poppies program where secondary students are elected as emerging *science wunderkind*. Six to eight students will be elected to participate from Victoria in 2014 with the same to occur throughout the six states to follow.

The Growing Tall Poppies Science Program has changed the face of science outreach in this country. It has asked questions about changing student choices, and has insisted on answers through ascertaining meaningful numbers that show we can increase science uptake by demonstrating how physics in an interdisciplinary landscape can be relevant, important and have an impact. Congratulations to each and everyone in the Centre of Excellence for Coherent X-Ray Science.

Star of the Sea College students worked on the Nano-Diamond Quantum Sensors in Living Cells Project at The University of Melbourne with the ARC Centre For Quantum Computation and Communication Technology

Santa Maria College students worked on The Scorpion Project at The University of Melbourne., School of Chemistry

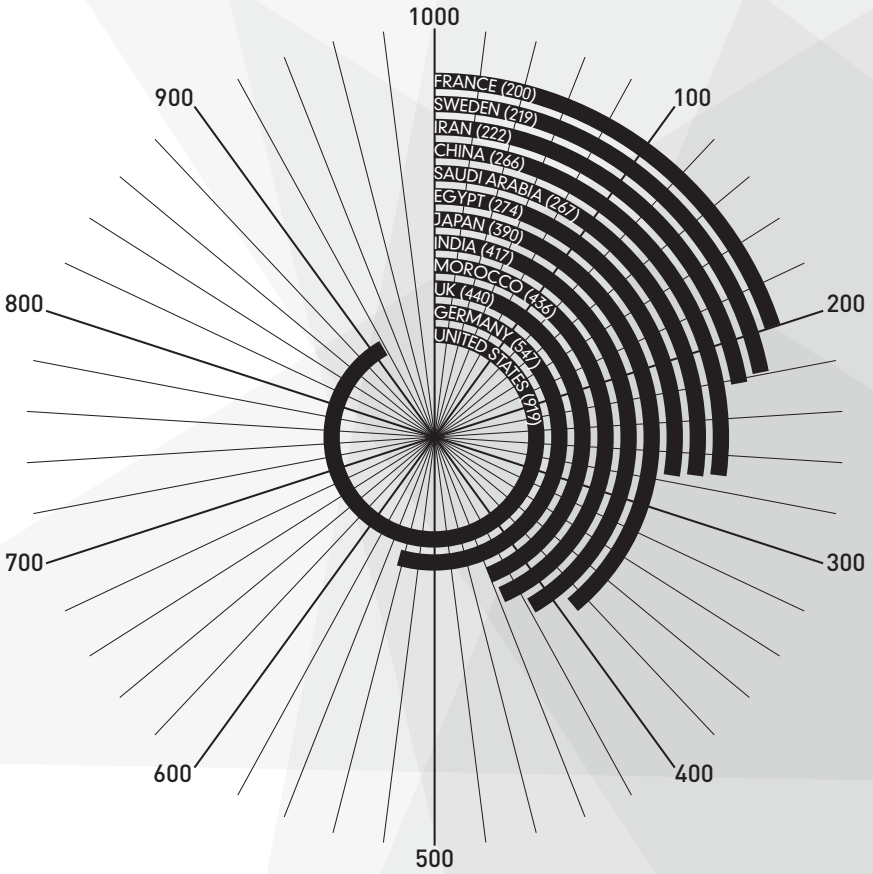
WEBSITE TRAFFIC

Collection of CXS website data commence in 2009. The following information is an analysis of the data currently available to date. The statistics suggest that the increased traffic during 2010 was due to the student recruitment drive undertaken at the time (with scholarships being a key factor); and the development of the CXS Facebook page (140 members). The majority of CXS website visitors are between the ages of 18 and 34, with about 10% more males than females.

CXS WEBSITE STATISTICS 2009 – 2013

Month	Visits	New Visitors	Return Visitors	Dominate Country other than AUST	Page Mainly Visited other than Home Page
2009	3948	47.5%	52.5%	Japan	Conference Page
2010	8715	60.7%	39.3%	USA	General Visit
2011	3464	63.3%	36.7%	USA	General Visit
2012	1391	79.9%	20.1%	USA	General Visit
2013	542	84.3%	15.7%	USA	General Visit
TOTAL	**18,060**	**60.5%**	**39.5%**		

TOP VISITORS TO THE CXS WEBSITE BY COUNTRY*



**Of the countries that do not appear on the chart there were 10,256 visitors from Australia and 120 other counties that had <200 visits.*

MEDIA COMMENTARIES

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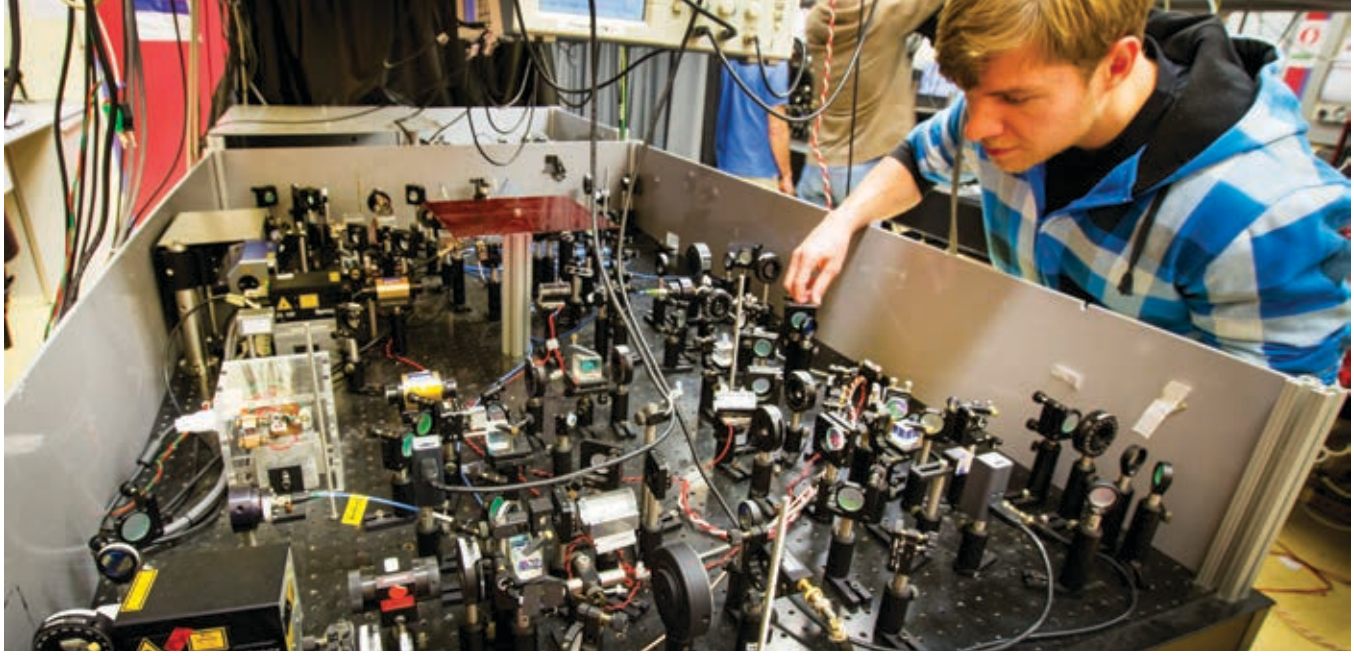

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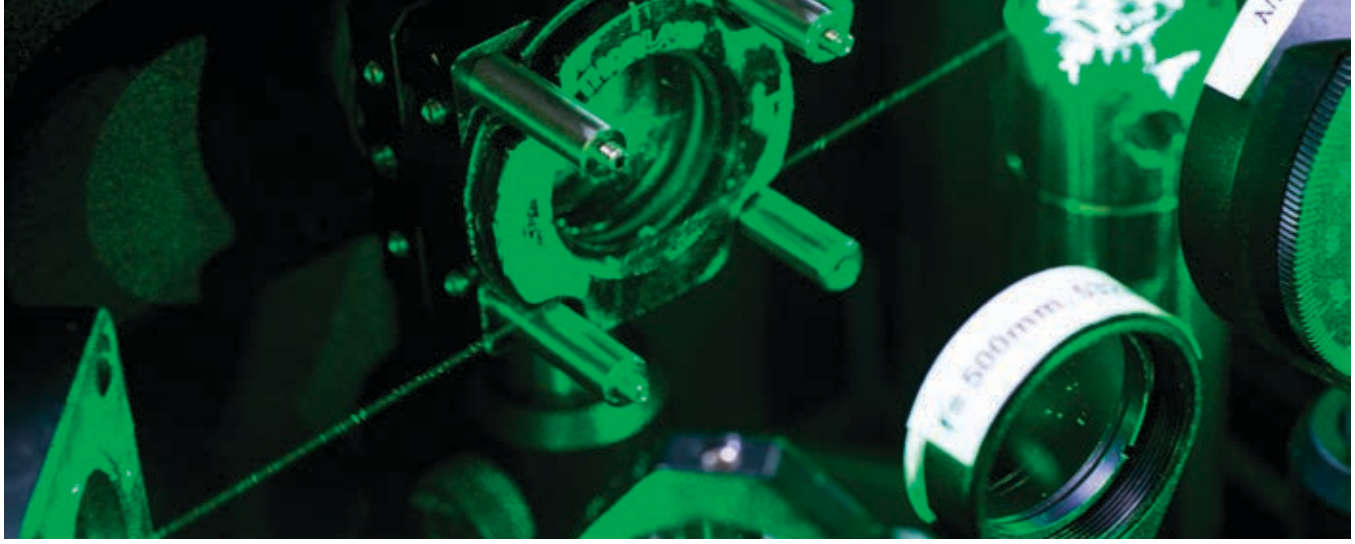
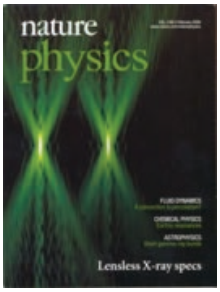
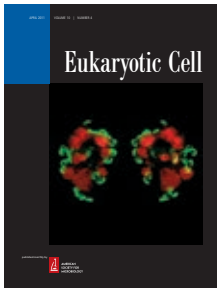
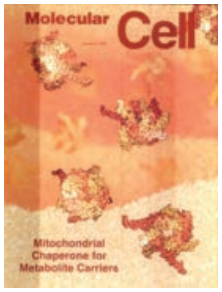
There has been a minimum of 844 media commentaries on CXS from the life of the centre with online media being dominant as per the worldwide trend. The most widely circulated articles during 2013 were by Robert Scholten, (Cold elections to aid better design of drugs and materials), Brian Abbey, (New technique shows molecular-sized objects with greater clarity), and articles relating to Keith Nugent's involvement with the Australian Synchrotron in 2011. There was also extensive worldwide coverage of the David Kielpinski article, First photo of atom's shadow; and the coverage of the Dearnley/Dixon article, Sex makes malaria parasite go "bananas".

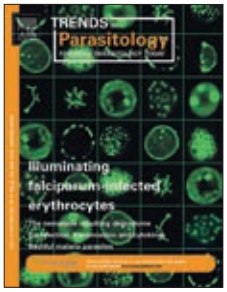


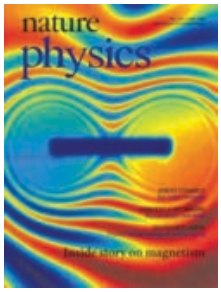
JOURNAL COVERS 2005 – 2013

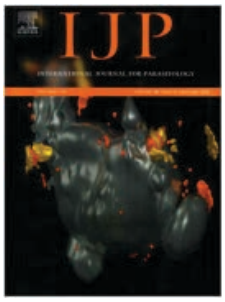


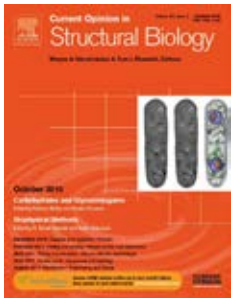


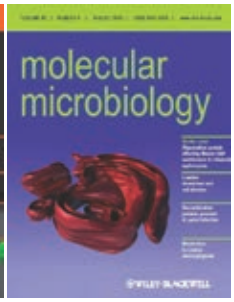


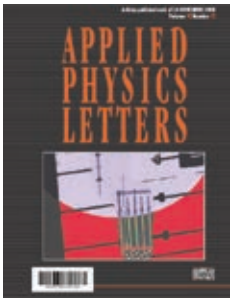


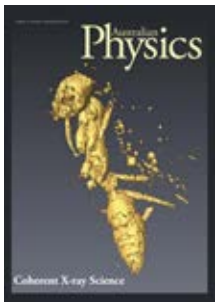


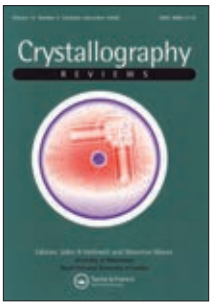


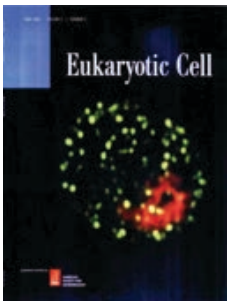


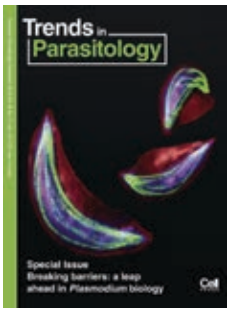


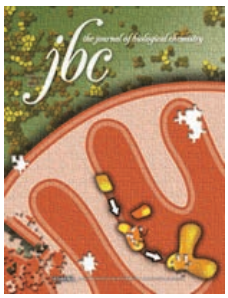












PUBLICATIONS

CXS published 94 papers in peer-reviewed journals in 2013 with an average impact factor of 5.92

BOOKS

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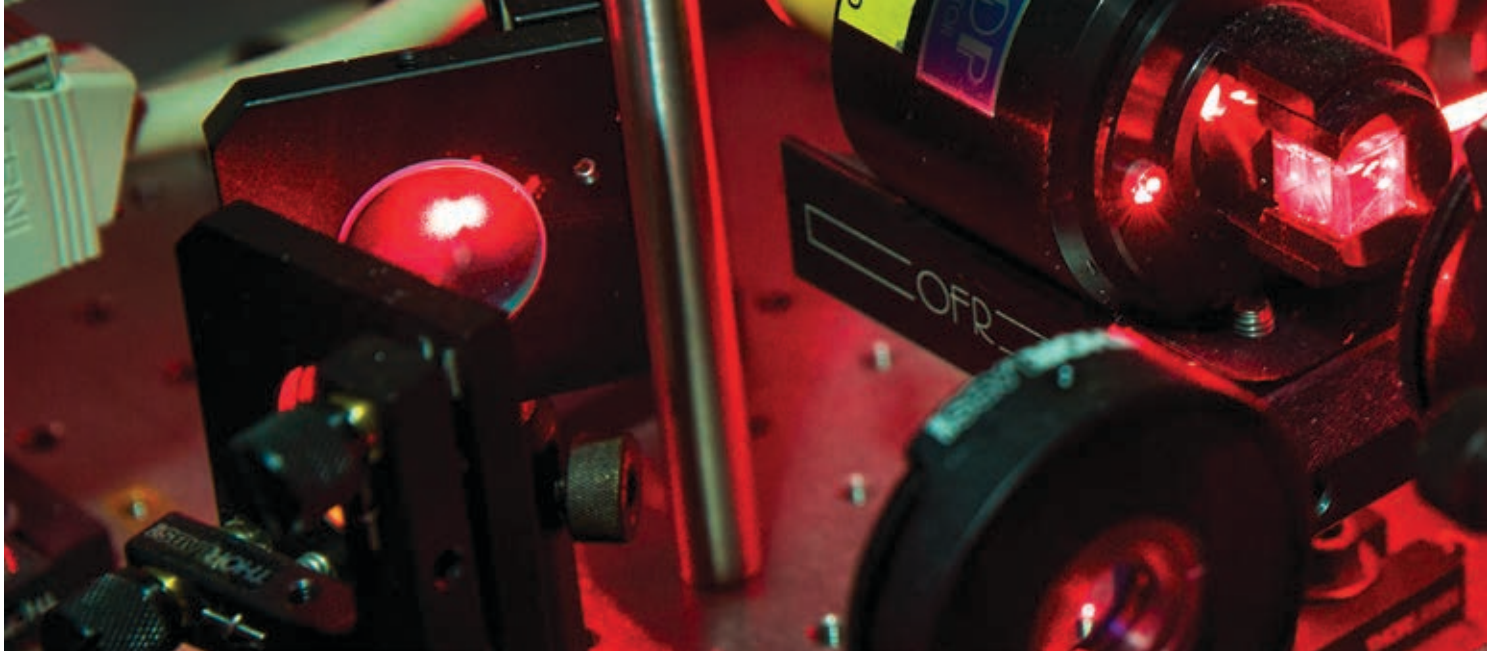

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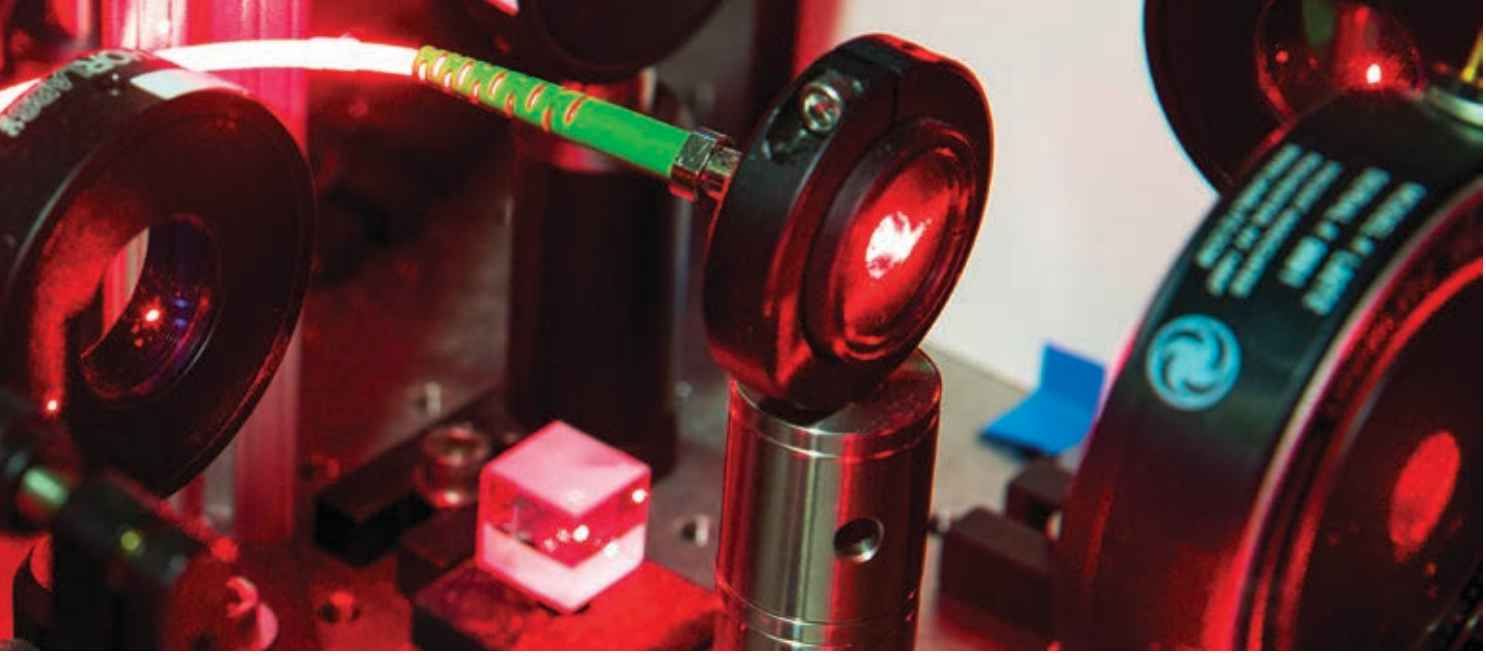

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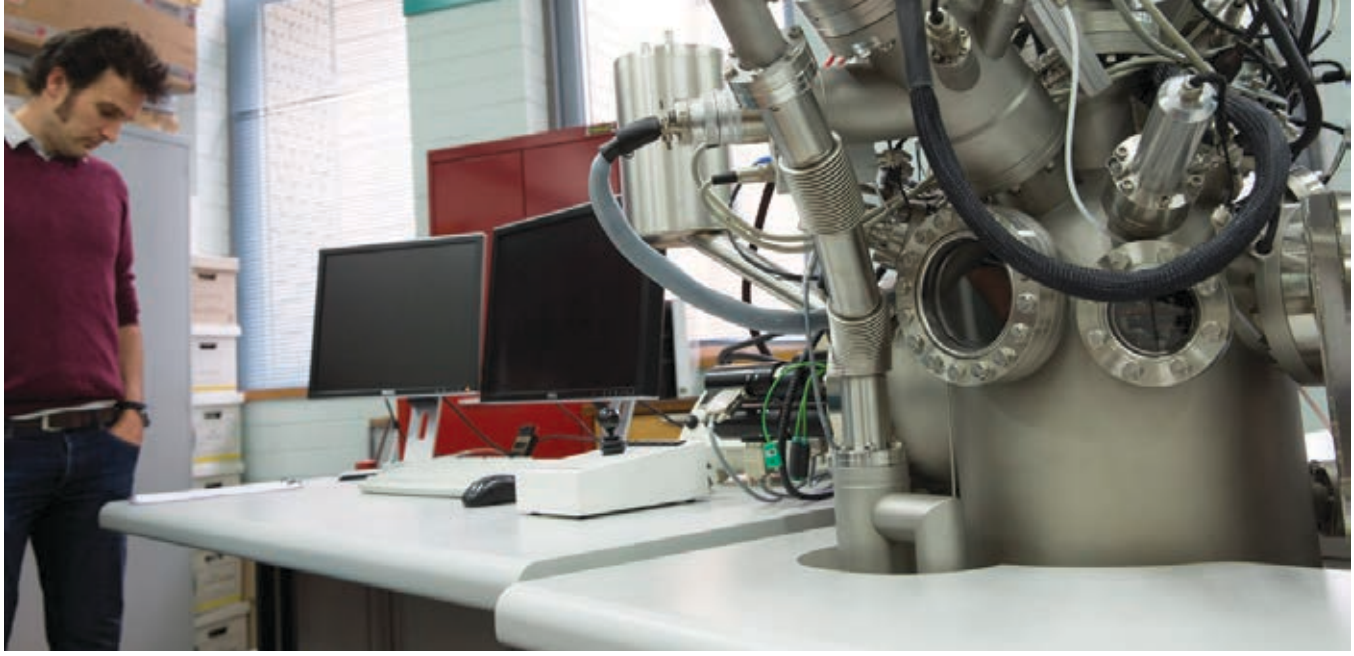
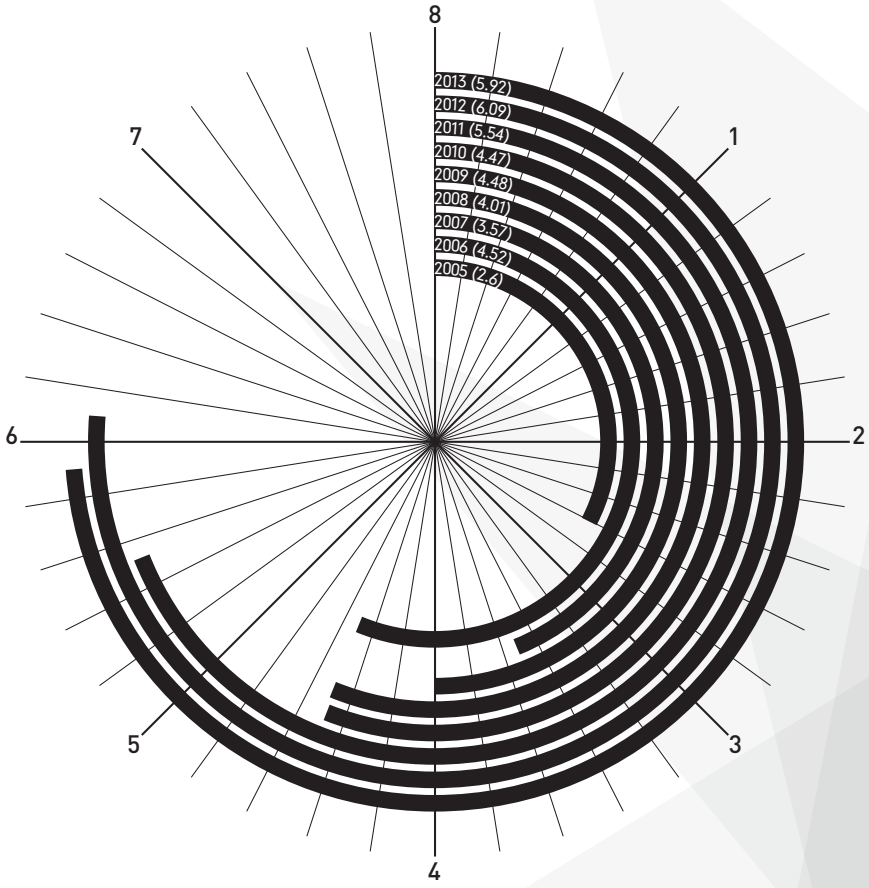
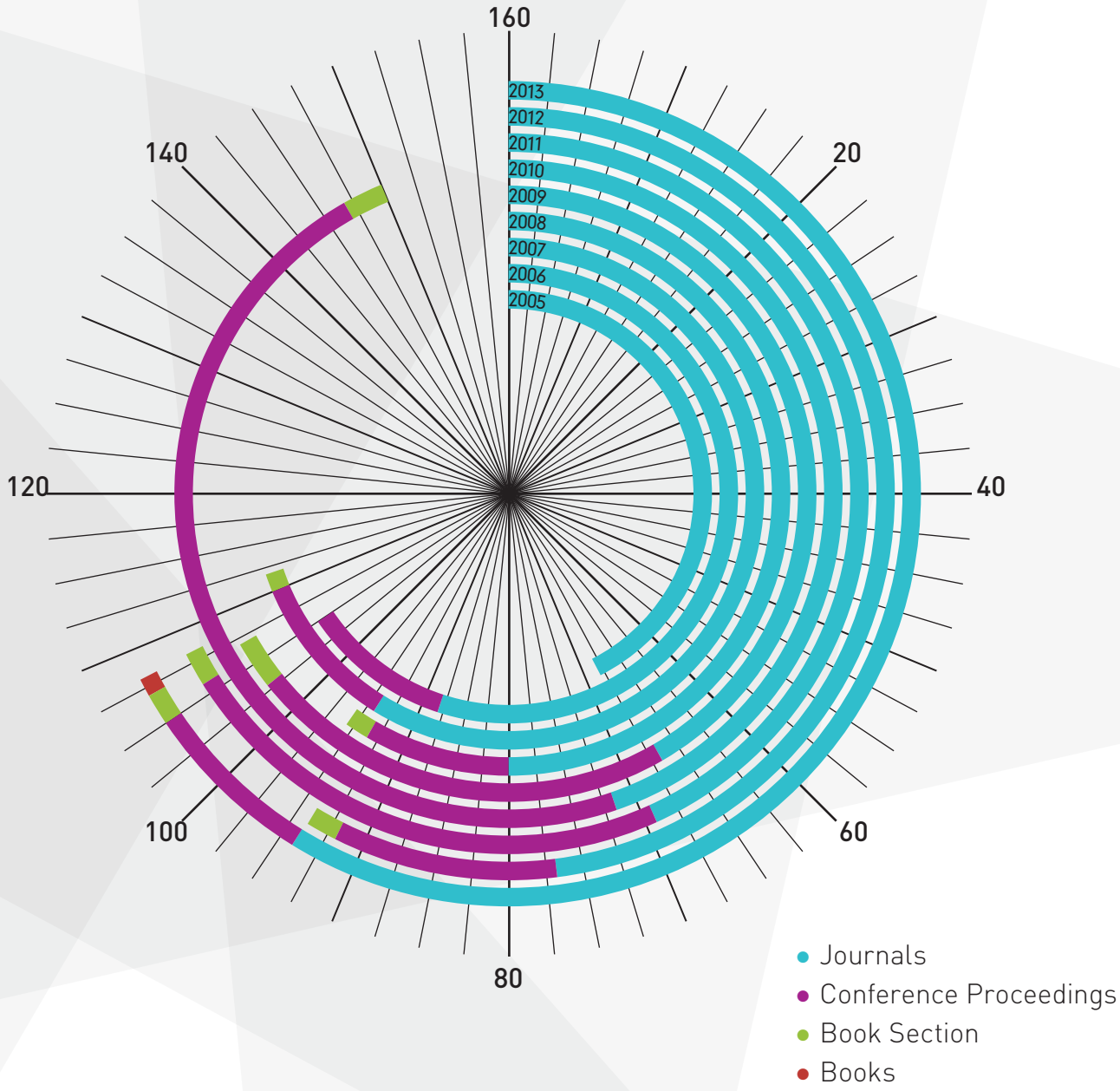


IMPACT FACTORS FOR LIFE OF CXS – 2005 – 2013

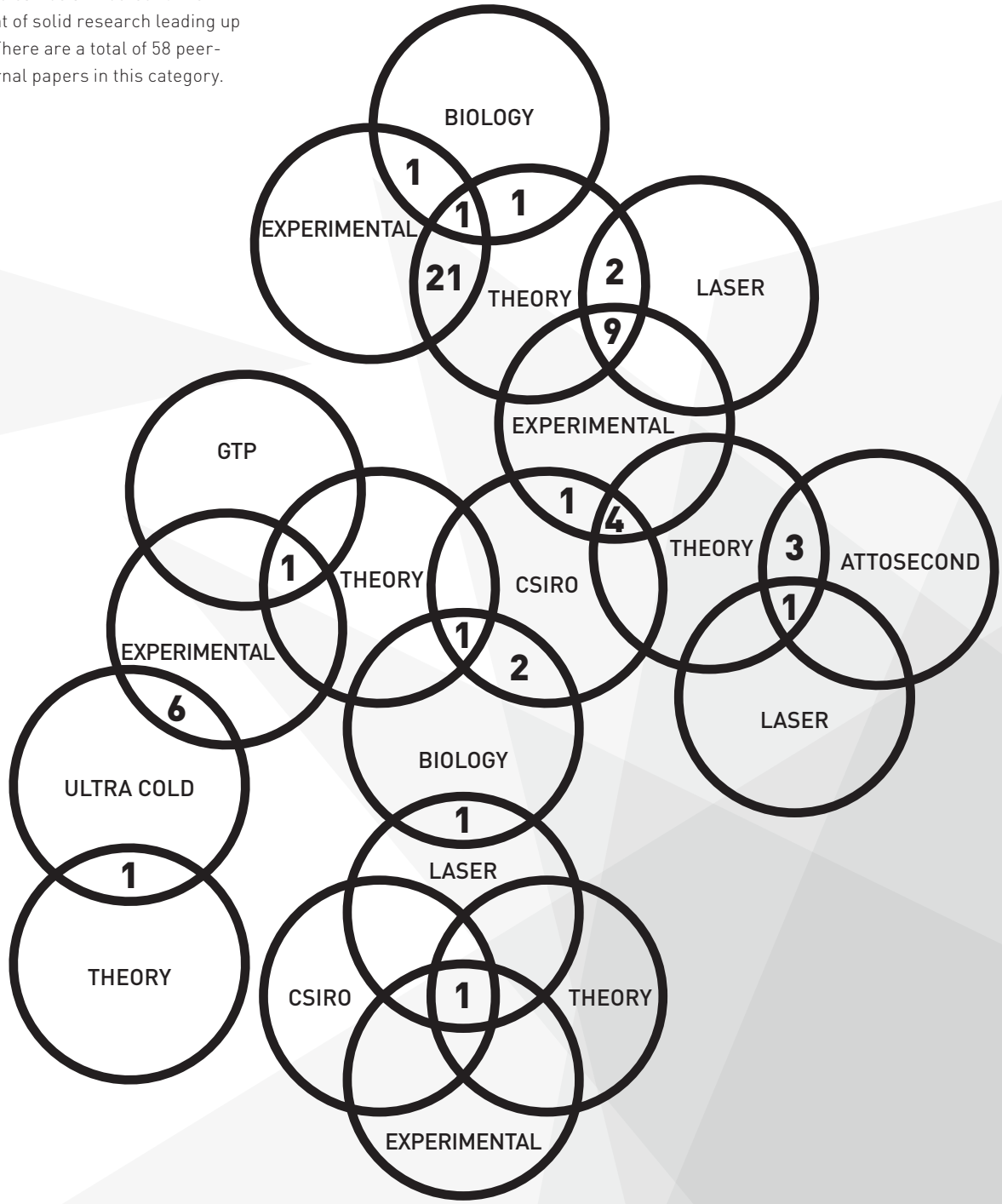


PUBLICATIONS OVER THE LIFE OF CXS – 2005 – 2013



CO-PRODUCED PAPERS BY PROGRAM TEAMS

CXS has taken various steps to ensure its members work in a cross-disciplinary, cross-collaborative and cohesive way. The diagram below demonstrates the results of this effort by outlining the links between programs when producing papers. A marked improvement in this output began from 2009 and can be attributed to the establishment of solid research leading up to this time. There are a total of 58 peer-reviewed journal papers in this category.



CELLULAR NANO-IMAGING CONSORTIUM

The Cellular Nano-Imaging Consortium (CNIC) is an affiliation of scientists with interests in Super-Resolution Optical Microscopy, managed under the auspice of CXS. Its inception is the direct result of a joint initiative undertaken by CXS Direct Professor Keith Nugent, Deputy Director Leann Tilley and CXS member Associate Professor Trevor Smith, School of Chemistry, University of Melbourne. The aim is to bring together institutions and research leaders with cross-disciplinary expertise and an interest in using and/or developing nano-imaging optical methods.

CNIC provides online access to information about conventional and super-resolution optical imaging techniques and what resources are currently (and potentially) available to interested parties. Through CNIC, workshops and conference sessions will be organised to inform Australian scientists about new high-resolution imaging modalities. CNIC aims to co-ordinate efforts to generate a super-resolution imaging capability in Victoria, providing information and access to the new techniques.

CNIC is working to ensure that all Victorian scientists have access to the Super-Resolution Microscopy format they need to be competitive as international research leaders.

The CNIC website can be visited at www.coecxs.org/cnic

CNIC
CELLULAR NANO-IMAGING CONSORTIUM

SCIENTIFIC LINKAGES

CXS is proud collaborate with the following partners:

Australian Synchrotron

National Synchrotron Radiation Research Center of Taiwan

ELETTRA

CRC for Biomedical Imaging Development

The Centre for Biophotonics Science and Technology

COMMERCIAL-ISATION

MOGLabs is a spin-off from the CXS ultracold plasma project. It began in 2007 with a single product, an electronics device developed to control the lasers required to cool, shape, excite and ionise the atoms at the heart of the ultracold plasma high-coherence electron source.

As 2013 draws to a close, MOGLabs has progressed since it inception. Now producing several products including laser systems at wavelengths from 370nm in the ultraviolet to 1092nm in the infrared, MOGlabs has customers in every corner of the globe, including the US, Canada, France, Germany, Spain, and China. Annual turnover is currently around AUD600,000. The business employs an electronics engineer and three PhD staff in Melbourne and an optics engineer in Berlin; runs dedicated MOGLabs-branded distributorships in the US and Germany; and partners with a major distributor in China. With several new products to offer early in 2014, MOGlabs has strong prospects for sustainable growth into the future.

moglabs

Prototype cateye laser (see DJ Thompson and RE Scholten, Narrow linewidth tunable ECDL using wide bandwidth filter Review of Scientific Instruments 83 023107, 2012).

GRANT INCOME

CXS members attracted $262,500 in additional support in 2013:

ARC	
Foundation technology for quantum measurement, sensing and computing	$222,500
Australian Synchrotron	
Special Research Initiative in Synchrotron Science	$40,000

GRANT INCOME FOR LIFE OF CXS 2005 – 2013

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 Ultracold 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 at there 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.

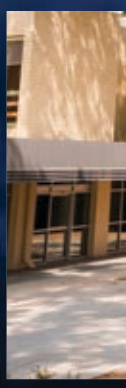
CLAYTON CAMPUS

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.

NATHAN CAMPUS

170 Kessels Road, Nathan QLD 4111

SCHOOL OF BIOMOLECULAR AND PHYSICAL SCIENCES

PARKING
Griffith University offers a variety of parking options on the Nathan campus. Casual visitors can choose from $5/day parking permits, metered parking or pay and display parking.

CLAYTON

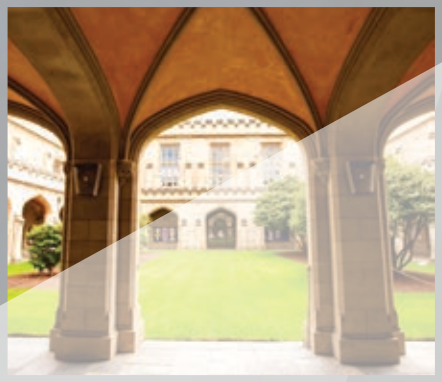
Gate 5, Normanby Road, Clayton

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 2013

	2013 REPORTING PERIOD ($)		2014 REPORTING PERIOD (ESTIMATED) ($)	
Carry Forward	$3,407,739		$2,742,635	
Other Funds	$2,200,000	ARC Income	$0	ARC Income
	$309,731	ARC Indexation	$10,560	Bio21 2013 Contribution made in 2014
	$966,458	Node Contributions		
Total Income	**$6,926,420**		**$2,753,195**	
Expenditure	$2,382,060	Salaries	$1,495,410	Salaries
	$323,794	Equipment	$313,342	Equipment
	$249,880	Travel, Accommodation and Conference	$85,730	Travel, Accommodation and Conference
	$68,939	Materials, Provisions and Services	$161,885	Materials, Provisions and Services
	$198,845	Scholarships	$37,348	Scholarships
	$157,118	Marketing, Outreach and Sponsorship	$44,239	Marketing, Outreach and Sponsorship
	$760,658	General & Clawback	$309,241	General
			$306,000	2014 Operations Admin Commitment
			$306,000	La Trobe Uni LIEF
	$ 4,141,294		**$2,753,195**	
	$2,742,635		**$0**	

IN-KIND REPORT JANUARY – DECEMBER 2013

University of Melbourne	$3,530,162
La Trobe University	$1,357,372
Monash University	$419,480
Swinburne University of Technology	$1,110,867
Griffith University	$883,838
CSIRO	$70,689
Total	**$7,372,408**

CXS

ARC CENTRE OF EXCELLENCE
FOR COHERENT X-RAY SCIENCE
SCHOOL OF PHYSICS

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THE UNIVERSITY OF MELBOURNE

LA TROBE UNIVERSITY

MONASH University

SWINBURNE UNIVERSITY OF TECHNOLOGY

Griffith UNIVERSITY

CSIRO

Australian Government
Australian Research Council

State Government Victoria AUSTRALIA