In Coherence

Autumn 2013 Newsletter for ARC Centre of Excellence for Coherent X-Ray Science

Nuclear Magnetic Resonance Symposium

The inaugural CXS Nuclear Magnetic Resonance (NMR) Symposium took place at Monash Institute of Pharmaceutical Sciences (MIPS) on the afternoon of Wednesday, 19th June. The aim was to provide an accessible introduction to several aspects of solution NMR theory and practice, ranging from spin system fundamentals to relaxation processes and isotopic labelling approaches. A dozen interested students and researchers affiliated with CXS were addressed by A/Prof Martin Scanlon and two postdoctoral members of his research group at MIPS.

The afternoon kicked off with Martin Scanlon's comprehensive introduction to the theory of NMR. Using the vector model of nuclear spin, illustrated by the use of "arm-waving" arguments, Martin outlined the fundamental processes of excitation and relaxation in strong magnetic fields. Thus he explained key concepts such as chemical shifts, scalar coupling and the nuclear Overhauser effect in terms easily comprehensible to the mix of structural biologists and physicists in the audience.

MIPS is located at Monash University's Parkville campus

A/Prof Scanlon introduced the symposium

The next talk was presented by Biswaranjan Mohanty, who eloquently explained the difficult concepts of T1 and T2 spin relaxation with particular emphasis on their relationship with molecular size. Biswaranjan extended his discussion to applications of relaxation to biomolecular NMR, particularly studies of intramolecular dynamics and intermolecular interactions.

The day ended with a comprehensive review of isotopic labelling methods, presented by Martin Williams.

Focusing on issues of spectral sensitivity, resolution and peak overlap, Martin discussed the benefits of deuteration and a range of approaches to the selective incorporation of 13C- and 15N-labelled amino acids, particularly into larger protein systems. Martin finished with a brief introduction to the preparation of membrane proteins for NMR and other research applications, bringing the discussion back towards the main theme of CXS, and rounding off a successful NMR Symposium.

Participants in the symposium including members or the CXS Biology team located at MIPS

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Coming Events

Intermediate NADIA Workshop

18th July, 2013

10am - 1pm

Laby Ideas Centre

David Caro Building

University of Melbourne

An Intermediate session on the NADIA software package.

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OPPORTUNITIES WORKSHOP

18 - 19 November 2013

University of Melbourne

MICROSCOPY WORKSHOP

21 - 22 November 2013

La Trobe University

Put these dates in your diary now!

Further details to come.

In Brief

Publications:

A selection of publications for the first half of 2013 include:

Martin, A.V., Loh, N-T. D.,*"X-ray free-electron laser: Illuminating a new path to single particle imaging"* Synchrotron Radiation News, 26:11-19 (2013)

Woodcroft, B. J., McMillan, P. J., et al., *"Determination of protein subcellular localization in Apicomplexan parasites."* Trends in Parasitology, 28(12):546-54 (2012)

Dorin-Semblat, D., McMillan, P.,J., Tilley, L., et al, *"An Atypical cyclin-dependent kinase controls Plasmodium falciparum proliferation rate."* Kinome, Feb (2013)

Arhatari, B., D., van Riessen, G., Peele, A.. *"Polychromatic X-ray tomography: direct quantitative phase reconstruction."* Optics Express, 20,(21), 23361-23366 (2012)

Dinh, K., B., Dao, L., V., *"Phase-matched high order harmonic generation and application " Book*, ISBN: 978-1-62618-1280-1m Nova Science Publishers, Inc. N.Y. USA. (2013)

Hao, X., Hirvonen, L., M., and Smith, T., A.,*"Nanomorphology of polythiophene-fullerene bulk-heterojunction films investigated by structured illumination optical imaging and time-resolved confocal microscopy. "* Meth. Appli. Fluor., 1, 015004/1-8 (2013)

Nisbet, N., R., Nuttall, S., D., Streltsov, V., A., *"Structural studies of the tethered N-terminus of the Alzheimer's disease AB peptide."* Proteins: Structure, Function, and Bioinformatics, Prot-00031-2013.R2 (2013)

McCulloch, A., J., Sheludko, D. V., Junker, M., Scholten, R., E., *"High-coherence picosecond electron bunches from cold atoms."* Nature Communications, 2699 DOI: 10.1038/nmcomms2699 (2013)

Wallace, W., C., Pullen, M., G., Kielpinski, D., et al., *"Carrier-envelope phase effects in above-threshold ionization of atomic hydrogen. "* New Journal of Physics, 15, 033002 (2013)

Xu, H., MacLean, J-P., Sang, R., T., et al, *"Carrier-envelope-phase dependent dissociation of hydrogen."* New Journal of Physics, 15, 023034 (2013)

CXS Visitors:

Clare Dumont visted the Biological Science Program at La Trobe University to work with Coralie Millet, April 2013.

Marta Tiburcio visited the Biological Science Program at La Trobe University to work with Matt Dixon, April 2013.

Prof Hai Ming and Douguo Zhang from the University of Science and Technology of China visited the Experimental Methods Program in December 2012.

Damien Hicks from Liverpool National Laboratory in the USA visited the Experimental Methods Program in January 2013.

Conferences & Workshops:

Mike Ryan chaired a session at the Lorne Confernce in February 2013.

Martin Scanlon was an invited speaker at NMRS2013 in India, February 2013.

Ved Mooga gave an oral presentation at the 2nd Annual Conference on Mitochondria in Health and Disease organised by the Society of Mitochondrial Research and Medicine in India, November 2012.

Brian Abbey was an invited Keynote Speaker at TMS 2013, USA, March 2013.

Benedicta Arhatari presented a poster at the Australian Synchrotron Users Meeting in Melbourne, November 2012.

Lap Van Dao was an invited speaker at the meeting of COST, Paris, April 2013.

Trevor Smith was an invited speaker at the Non-Linear Ultrafast Microscopy Techniques and Applications workshop at Swinburne University, December 2012.

Robert Scholten was an invited speaker at the Workshop on Ultrafast Electron Sources for Diffraction and Microscopy Applications at UCLA, December 2012.

David Kielpinski attended the Ultrafsat Laser-Matter Program Review held by the US Air Force in Potomac, USA, in December 2012.

Welcoming New Members:

CXS would like to welcome the following new members to the team:

Biological Science Program:
- Emma McHugh
- Steven Batinovic
- Con Dogovski

Short Wavelength Laser Source Program:
- Emma Hooley
- Khuong Ba Dinh

CSIRO:
- Hannah Coughlan

Ultracold Plasma Source Program:
- Ben Sparkes

Attosecond Science Program:
- Champak Khurmi

Outreach:

Leann Tilley gave a talk in the Chancellor's Scholars Program at the University of Melbourne.

The CXS 2012 Annual Report is now available for download from the CXS website:

http://www.coecxs.org/joomla/index.php/publications/annual-reports.html

Awards:

Congratulations to the following people for recieving CXS Awards:

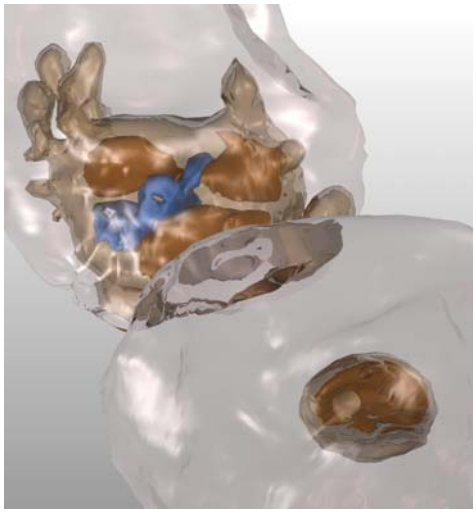
Hannah Coughlan, William Wallace, Rory Speirs, Megan Dearnley and Stanley Xie were awarded a CXS Top Up Scholarships.

Student Vacation Scholarships were awarded to Martin Ji and Daniel Rodgars-Pyor.

CXS Travel awards were presented to Viviane Richter to attend the ESF EMBO Symposium in Poland and Thanh Ngoc Nguyen to attend Dyna Mito 2013 in Japan in 2013.

Modern Microscopy Addressing an Age-old Problem

The Biological Science Program at the Bio21 Institute spend a lot of their time designing and playing with the latest and greatest microscopy 'super-toys' to produce a myriad of weird and wonderful images of very, very small living things. While obviously a lot of fun for this multidisciplinary group, the goal of this work is deadly serious; the power and information provided by these latest techniques in super-resolution optical microscopy and electron tomography are finally revealing some of the malaria parasite's long-held secrets.



Immature stage parasite (front) has a much less developed digestive system than the mature parasite (back) and as a consequence is much less sensitive to artemisinin. Model generated from two electron tomograms by Dr Eric Hanssen, Advanced Microscopy Facility, Bio21 Institute, University of Melbourne.

Looking at the changes of the malaria parasite as it undergoes a remarkable series of morphological transformations during its lifecycle through human and mosquito hosts will help decipher the mechanisms underlying the parasite's most intractable and problematic traits. In particular, its resistance to nearly all of the antimalarial drugs thrown at it over many years. To date, none of the antimalarial drugs that are currently used are 100% effective – indeed, combinations of agents are now used to optimise efficacy and slow the spread of resistance. A major stumbling block to improving existing drugs is that scientists don't really know how they work in the first place. The biological mechanisms of action for all the major players, on the whole, remain a mystery.

What is known is that for the malarial parasite to grow and prosper during its important proliferative stage inside the human host red blood cell (RBC), it needs a good source of amino acids and the best source is the host's own haemoglobin. It also needs to create a bit of growing room. Indeed, malaria parasites will 'eat' up to 75% of the host hemoglobin during an infection.

Work by the Biological Sciences Program at Bio21 showed that endoperoxide antimalarials, including the drug artemisinin, are activated by the haem released during the haemoglobin breakdown. This led to studies implicating the digestive vacuole as an important site of artemisinin activity, with the parasite's haemoglobin digestive process the target. More specifically, it was postulated that artemisinin is activated by interacting with the haem products, forming free radical species that react with material in the immediate vicinity of the parasite to induce cellular damage and, ultimately, cell death.

To investigate this the team started to use whole-cell electron tomography to look at the mechanics of haemoglobin digestion and to build a 3D picture of the structures inside the parasite at a maximum level of resolution. They found that this relatively new approach was fantastic for looking at the malaria parasite in human host cells. With the idea of the haemoglobin digestion and artemisinin mode of action in mind, they decided to look at it in more detail. They soon discovered that by just looking at the different immature stages by electron microscopy they could predict that the early stages of the parasite developing inside the RBC would be much less sensitive to artemisinin. In addition, when they biochemically stopped mature parasite stages from digesting haemoglobin, they found that they became resistant to the presence of artemisinin.

Next, they called on some mathematical colleagues to do some modeling studies of what would need to happen for these immature parasites to become resistant and confirmed that these immature parasites are the likely cause of artemisinin resistance. Research shows that the modeling data reflects the real situation – where it appears that the 'younger' parasites can survive the presence of artemisinin for the few hours that the drug remains stable in the patient's circulation.

The team is wasting no time translating their 'high-end' science into the real-life situation through collaboration with field colleagues. The next steps will involve using parasites from areas where drug resistance is known to be a problem; specifically from an area in Cambodia near the border with Thailand where there seems to be a cradle of antimalarial drug resistance.

These electron tomography findings on the parasite lifecycle and drug resistance could have immediate clinical applications for patients; one is in the area of drug dosing and another in drug development efforts to synthesise longer-lived forms of endoperoxide antimalarials like artemisinin.

For CXS it is exciting to see such high-end techniques like electron microscopy tomography used in a basic science context leading to a discovery that is potentially of immediate use for treating malaria in some of the world's poorest populations.

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The ARC Centre of Excellence for Coherent X-ray Science (CXS) is an Australian Government Initiative which began in July 2005 to explore what can be achieved with coherent X-ray optics; including an understanding of exotic phenomena such as X-ray phase discontinuities.

CXS headquarters is located at the University of Melbourne in Victoria, Australia, with participating nodes at La Trobe University, Monash University, Swinburne University of Technology, Griffith University and the CSIRO. Its mission is to be the world leader in the development of coherent X-ray diffraction for imaging biological structures.

“In Coherence” is produced quarterly (or there abouts) by CXS. Contributions are welcome and should be forwarded to Ms. Tania Smith, CXS Chief Operating Officer, University of Melbourne, Parkville, Vic, 3010, fax to +61 3 9347 8912, email: cxsenquiries@ph.unimelb.edu.au or Ms. Kathy Alleblas, Administration, email: kathy.alleblas@unimelb.edu.au

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Teeth Modelling for Students

Tooth decay is Australia’s most prevalent health problem with half of all children and almost all adults, or over eleven million Australians, affected each year. Such high statistics demonstrate the urgent need in Australia for a review of oral health care promotion to improve personal tooth care advice to the public and to end tooth decay.

One step towards achieving this has been the work of Dr Benedicta Arhatari from the Experimental Methods Program and Dr Maurice White from the Supertooth NDK Company. The pair have been working together at La Trobe University to map teeth using X-ray tomography to create large scale plastic models using 3D printers.

Dr White approached Benedicta as he was interested in gaining a better insight into the pits and fissures inside young teeth that are often filled with food when a child chews, trapping food particles inside and leading to decay and/or the demineralising of teeth.

Benedicta was provided with tooth samples to X-ray which showed decay starting inside the pits and fissures and the resulting images were sent to Rob Ross at La Trobe University’s Electronic Engineering Department and Thomas Baum at RMIT for 3D printing. The 3D printed models created realistically show grooves and fault lines in teeth which are often hard to see with the naked eye.

The 3D models are now being used as teaching and learning resources in the Oral Health Department at La Trobe University’s Bendigo campus. It is hoped that future collaborations will produce further models of healthy and diseased teeth specimens to teach oral health professionals about the affects of tooth decay and provide them with a better understanding of teeth anatomy.

3D model to tooth specimens

Members of the team working on the 3D tooth modeling (Dr Benedicta Arhatari and Dr Maurice White pictured centre)