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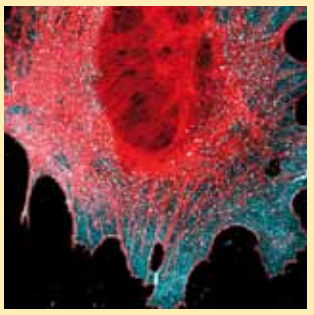
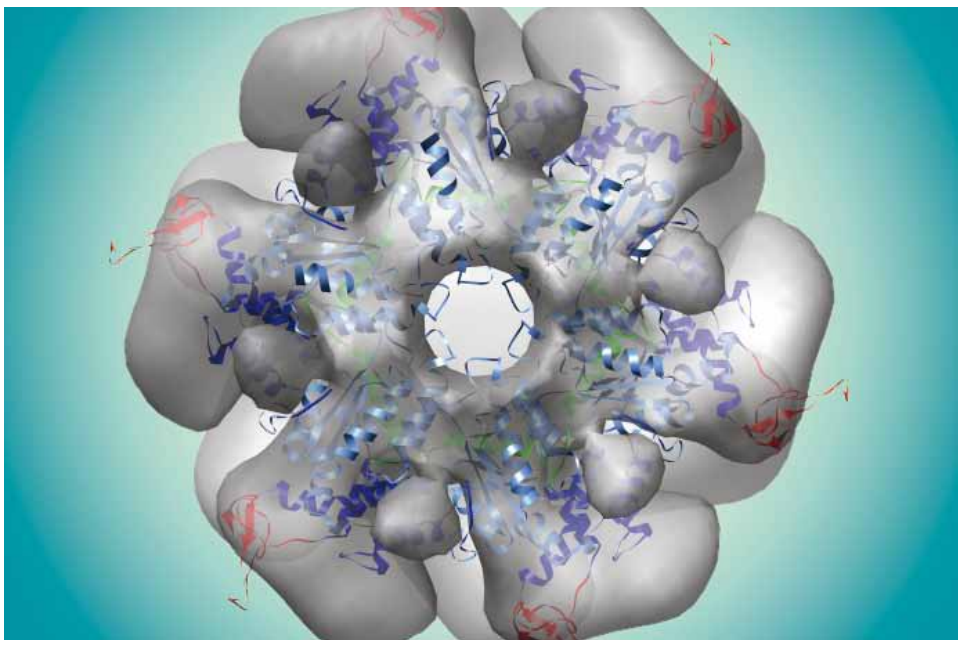
AUSTRALIAN MICROSCOPY & MICROANALYSIS RESEARCH FACILITY



RESEARCH



The structure of the Vps4 protein as determined by cryo-TEM. It has six-fold rotational symmetry, and is 14 nanometres in diameter. Important regions of the protein backbone are highlighted in the form of a ribbon, superimposed on the single-particle density map.

Lightening the impact of HIV and Ebola

AMMRF @ UQ

Understanding protein structure is hugely important if we are to design specific drugs to alter a protein's function. This is exactly what Dr Michael Landsberg and colleagues have been doing at the high-throughput cryo-TEM facility at the University of Queensland.

Dr Landsberg – in conjunction with A/Prof. Ben Hankamer, Rosalba Rothnagel, Dr Parimala Vajjhala from the University of Queensland's Institute for Molecular Bioscience (IMB) and Griffith University's Dr Alan Munn – has taken an important step in the characterisation of a viral infection pathway that may potentially lead to the development of new drugs targeting a broad range of viruses including human immunodeficiency virus (HIV) and Ebola. They have recently solved the 3-D structure of a key control enzyme in the pathway of enveloped virus infection. This is where viruses become wrapped in envelopes of cell membrane and bud off the cell. The potential of this important research has been recognised through its publication in the international journal *Structure* in March 2009.

The enzyme, Vps4, normally controls the budding of small, lipid-enclosed vesicles from cell membranes; these vesicles transport proteins and other important molecules to different destinations. Importantly, a number of viruses, including HIV, Ebola, hepatitis and herpes simplex, appear to hijack this budding pathway to facilitate their own spread.

"There is growing evidence that therapeutic strategies that target Vps4 are able to elicit a protective response against infection by at least some of these viruses," Dr Landsberg said. This process was recently demonstrated by a team of scientists in the USA. They observed that 70% of laboratory mice deficient in Vps4 were able to survive injection with an otherwise lethal dose of Ebola virus. Conversely, a survival rate of less than 20% was observed in normal mice, comparable to human survival rates following outbreaks of the most lethal forms of the virus.

"In order to develop new therapeutics that target Vps4, it is critical that we first know the 3-D structure of the biologically-active form of the enzyme," Dr Landsberg said. "Our study gives some insights into this structure and, in so doing, has identified important regions of the enzyme that are required for it to assemble into its fully functional, biologically active form."

The team used a technique known as single particle analysis to determine the 3-D structure of what they believe is the biologically active form of Vps4. This involves using a transmission electron microscope to record tens of thousands of images of individual protein molecules in different molecular orientations, at high magnification. The images are then combined by computational techniques to obtain a structure of the protein in 3-D.

"The next step now is to build on this research and identify parts of Vps4 that can potentially be targeted by drugs, and in so doing block virus infection. This would be a crucial step in preventing the spread of viruses throughout the body and lessening the impact of diseases such as Ebola and HIV on human populations around the world."

The researchers used instruments at the University of Queensland's Centre for Microscopy and Microanalysis (CMM) extensively throughout the project, including the AMMRF flagship high-throughput cryo-TEM facility.

"The state-of-the-art electron microscopy instrumentation accessible to us through the AMMRF certainly means that we have been able to accomplish research outcomes, such as solving the Vps4 3-D structure, on a far more rapid timescale than would be otherwise possible," Dr Landsberg said.

"Drug discovery is a lengthy process, and any technology that can speed up the research stage is welcome." ■

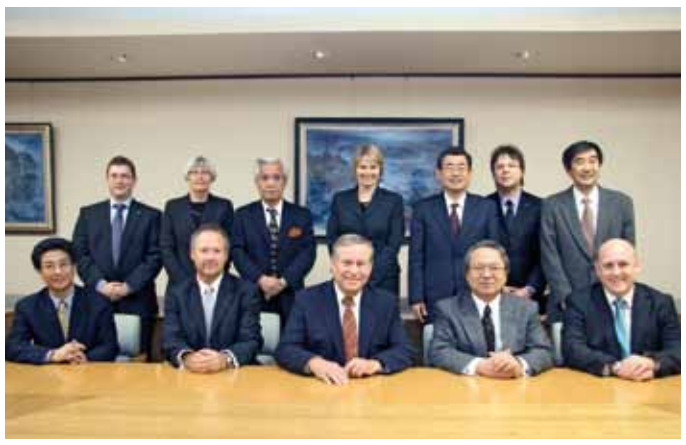
Dr Michael Landsberg at the high-throughput cryo-TEM facility at the CMM, which was used to solve the structure of Vps4.

COMMUNITY

AMMRF and WA Premier talk science in Japan

AMMRF @ UWA

Earlier this year, University of Western Australia Node Director Prof. David Sampson accompanied the Hon. Colin Barnett, MLA, Premier of WA, on his first foray to Japan. A trilateral collaboration exists between the states of WA, Hyogo in Japan and Zhejiang in China, which extends to their major universities. This visit continued to strengthen the collaboration, and the delegation took the opportunity to see first-hand the science and technology infrastructure in the Kobe region. Prof. Sampson was able to advise Premier Barnett as he toured Kobe's impressive Port Island Precinct, dedicated to the biomedical sciences and technology. It houses the Riken Centre for Developmental Biology (CDB) and the Kobe Medical Industry Development Project. The Riken CDB has over 400 staff and extensive microscopy infrastructure centred on live-cell and embryo imaging, which Prof. Sampson took the opportunity to explore in depth. At Kobe University, he briefed the delegation on progress under the Trilateral Collaboration and presented the AMMRF's unique flagship capability in ion microprobes, emphasising the central role played by the State Government in funding core microscopy infrastructure in WA. ■



The Hon. Colin Barnett, MLA, Premier of WA (centre front) and to his right Prof. David Sampson with the WA State Government delegation and officials from Kobe University, including Toshiyuki Nogami, President, Kobe University (to the premier's left).

RESEARCH

Iron teeth capture media attention and the scientific imagination

AMMRF @ UWA

Work emerging from the biomineralisation research group at the Centre for Microscopy, Characterisation and Analysis (CMCA) at the University of Western Australia has appeared in the research spotlight several times this year, particularly in relation to Dr Jeremy Shaw's work on the iron-mineralised teeth of chitons. These fascinating marine animals scrape algae from rocks in tide pools and other coastal habitats, with teeth that are hardened with a range of iron-oxide- and calcium-based minerals. Dr Shaw and the team have made significant progress as a result of access to the CMCA's facilities and the cutting-edge instrumentation made available through the AMMRF Travel and Access Program.

Dr Jeremy Shaw collecting chitons from their natural habitat. (Photo: Colin Murty/Newspix).

Chitons have a number of strings to their bow when it comes to research applications. Their ability to mineralise iron has inspired researchers who think that new biomimetic materials and technologies could be developed based on biomineral formation. Dr Shaw is also investigating the potential for chitons to act as indicators of environmental contamination by studying the uptake of heavy metals in their teeth. In the latest development, these iron-mineralised teeth may hold clues to understanding the cycling of iron in ancient oceans and therefore add to our understanding of climate change.

This research was revealed to the public earlier this year when Dr Shaw and his chitons appeared in *The Australian* newspaper and on *Channel 10 News*. The team's TEM images were recently featured on the cover of *Microscopy & Microanalysis*, and they have been invited to contribute an article to *Microscopy Today* on using FIB to produce TEM sections of biomineralised tissue. In April, Dr Shaw was awarded the Robert P. Apkarian Memorial Scholarship to attend the Microscopy & Microanalysis 2009 Meeting in Richmond, Virginia, where he will speak on electron microscopy techniques for investigating biomineralisation. ■

GOVERNANCE

Welcome to the Board – Professor Jill Trewhella

Prof. Jill Trewhella is no stranger to characterisation – her whole career has revolved around it. Prof. Trewhella, who grew up and did her PhD in Sydney, worked for 20 years at Los Alamos where she developed techniques for the application of neutron scattering to the determination of structure in proteins that could not be crystallised. During this time, she gained a wealth of valuable data on various proteins' roles in health and disease.

Prof. Trewhella returned to Australia in 2005 as a Federation Fellow, with joint appointments at the University of Sydney and the Bragg Institute at ANSTO, where she was able to continue answering the questions that have always fascinated her – how do the structures of proteins affect their biological functions?

Earlier this year, Prof. Trewhella took up the role of Deputy Vice-Chancellor (Research) at the University of Sydney, and it is in this capacity that she becomes a member of the AMMRF Board. We are extremely lucky to have the benefit of her amazing experiences and expertise in helping to guide the AMMRF into the future and to continue strengthening links with our colleagues at ANSTO. We wholeheartedly welcome Prof. Trewhella to the Board and hope she finds working with us an interesting and fulfilling experience. ■

LAB NEWS

Microscope booking in an iWorld

AMMRF @ UNSW

Dong Ming Zheng of the AMMRF's UNSW node continues to develop and expand the capabilities of the online booking and data-access system known as the AC Lab System. This system is now used, well beyond the Electron Microscope Unit and the UNSW Analytical Centre, in many other Australian and international institutions. This online application already allows staff to register and manage profiles and bookings, enables automatic backup and remote access, and tracks actual instrument usage.

Recently, features have been added that allow staff to check and modify users' logged instrument hours, to grant and restrict user access to instrument bookings according to their level of training and expertise, to automatically broadcast emails to users, and to register and track the progress of samples.

Ongoing enhancements will improve the convenience of the system by interfacing with such systems as Blackberry and iPhone handsets. This facility will allow users to monitor current facility status, view and make bookings, and download image and data files anytime, anywhere, from their own mobile device. Full-scale implementation is planned for 2010. ■

EXECUTIVE DIRECTOR'S COLUMN

Recently, I met with government and academic officials of the German-Jordanian University in Amman, Jordan, at the inaugural Jordanian International Conference on Materials. I was invited to present our vision for a national facility in materials characterisation, based around microscopy and microanalysis. The need for better structures for the organisation of user-focused core facilities is clearly a topic on the minds of scientific policy makers everywhere. I particularly noticed their enthusiasm and emphasis on the need to establish national *research facilities* and national *research centres* of excellence to advance scientific and technological questions of national significance. It is noteworthy that directors of the AMMRF nodes have been invited to explain how the AMMRF works to interested parties in South Africa, New Zealand, the USA, Sweden, Japan, China and now Jordan.

Though still a young facility, we have had many successes and there are now quantitative and qualitative metrics available that indicate how we are tracking. Last November, the Characterisation Survey was conducted for the NCRIS National Characterisation Council (NCC) and the key findings are particularly interesting. Of the 912 respondents, 74% ranked advanced microscopy and microanalysis as the most important characterisation capability for their work now, and 25% consider there is under capacity in advanced microscopy and microanalysis. Although 68% said they were aware of the AMMRF, 76% said there was a great need for characterisation facilities to communicate their capabilities. This is a critical finding and underlines the need to communicate more details of our actual capability. As a result, it was proposed that a 'characterisation roadshow' could raise awareness and promote capability across the research sector.

The Australian Synchrotron, ANSTO's National Deuteration Facility, and the National Imaging Facility will join the AMMRF and work together to operate the 'National Characterisation Roadshow' that will provide an opportunity for the research community to understand what we can all do for them. The first Roadshow will be held in Perth on 4 August 2009, and the second in Adelaide on 6 August 2009. Details will appear shortly on the AMMRF and Characterisation websites (see yellow box on page 3). There will be seminars on the capabilities, user testimonies and, importantly, a consultation session. Here, staff will make themselves available for informal discussions with would-be users on how we can help them to solve their research questions. We will evaluate the success of these meetings and proceed from there. ■

Regards,
Simon Ringer, Executive Director & CEO

COMMUNITY

During three days in April, the University of Sydney's Australian Key Centre for Microscopy and Microanalysis was abuzz with members of the Australian light and optical microscopy community.

Sydney Advanced Light & Optical Microscopy Meeting

AMMRF @ USYD

Around 90 researchers from universities and research institutes around Sydney attended the inaugural Sydney Advanced Light and Optical Meeting held at the Australian Key Centre for Microscopy and Microanalysis, the University of Sydney, from 1–3 April 2009.

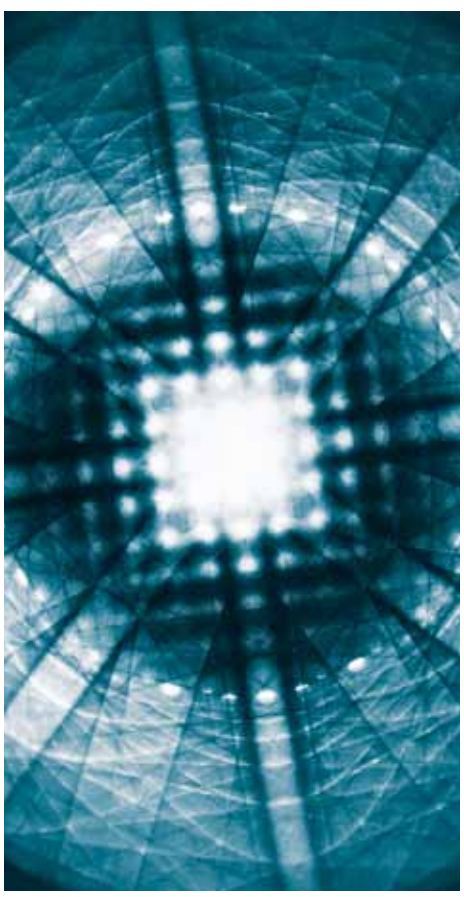
During the three-day program, 29 speakers shared their results from the numerous light and optical imaging techniques that they are using to solve a diversity of biological problems. One of many fascinating discussions was on how the lateral resolution barrier has been smashed by new techniques like STORM and PALM. All the techniques and ongoing improvements allow the light and optical community to collect ever more superior data, more quickly and with relative ease. However, the resulting large data sets, ensure that mathematicians, computer scientists and physicists will play a significant role in the future of biological light and optical microscopy.

Olympus Australia sponsored the meeting, providing fantastic food and drinks, and showcasing some of their latest equipment. Furthermore, they awarded several travel and encouragement prizes to young researchers.

The meeting was a major success, thanks to the participation and enthusiasm of the speakers and the audience, and to the sponsorship from Olympus.

This workshop has lead to new relationships being formed and everyone is now looking forward to coming together again next year for the 2nd Sydney Advanced Light and Optical Microscopy Meeting. ■

Wine and crystallography forge new relationships



AMMRF @ SARF

In April, the Crystal 26 conference attracted 130 Australian and overseas delegates to the Barossa Valley for four days of stimulating crystallography presentations. The AMMRF was able to reach out to this important crystallography community and sponsored the poster session and wine tasting held on the Thursday evening. AMMRF Executive Director Prof. Simon Ringer was an invited speaker, and John Terlet, Director of Adelaide Microscopy, also attended to introduce the AMMRF to the assembled delegates during the sponsored event. The audience were very interested in the collaborative nature of the AMMRF. They also appreciated the fact that one of the world's leading microscopy and microanalysis facilities offers assistance through a Travel and Access Program.

The meeting also served to highlight the complementary nature of neutrons, X-rays, electrons and ion beams as tools for characterisation in the many excellent presentations throughout the four days. ■

TECHNOLOGY

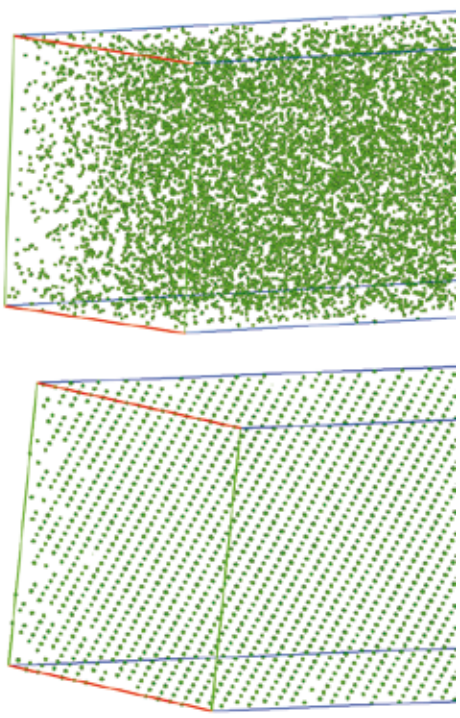
Advancing atom probe tomography

Atom probe tomography (APT) provides highly accurate chemical identity and 3-D positional information at the atomic level. In practice, however, the spatial resolution of current atom probe instruments falls short of the ideal of characterising and exactly locating every atom within a sample. Atoms in the APT reconstruction are offset slightly from their true positions and further, due to instrumental limitations, a fraction of the ions striking the detector are not registered. This results in structural and crystallographic characterisation of the specimen being incomplete. At the University of Sydney's AMMRF node, pioneering and novel techniques are being developed for recovering missing structural information from APT datasets.

The approach uses spatial distribution maps of atoms within the dataset, similar to radial distribution functions (RDF), to map out local atomic neighbourhoods and recover the limited structural information already existing in APT data across multiple crystallographic directions. Characterisation of the inherent crystal lattice in the reconstruction enables us to pinpoint, in real space, each atom's most likely true lattice site. This technique then systematically re-places every atom in the data back onto the perfect lattice, while maintaining the integrity of the local atomic distributions, as depicted in the figure.

Restoration of the lattice in the APT reconstructions will enable the detailed investigations of lattice-rectified data, with unrivalled 3-D spatial resolution, taking characterisation of nanoscale features to new levels of precision. Furthermore, it will enable us for the first time to input atom probe data directly into atomic-scale simulations of mechanical properties. The insight gained through these techniques has exciting implications for our understanding of nanostructure and its relationship to material properties and performance. ■

For more information contact:
Dr Michael Moody: m.moody@usyd.edu.au



The top panel shows a small sub-volume of an APT reconstruction of pure aluminium where there is no visual evidence of a crystalline structure. Below is the same volume after lattice rectification. The lattice structure has become readily apparent.

COMING UP

National Characterisation Roadshow

The Characterisation Survey held last year showed that it is vital that we expand our efforts in spreading the word about the capabilities we offer. In light of these findings, the AMMRF will be joining the other NCRIS Characterisation partners to do just that. We will visit different capital cities, starting with Perth and Adelaide, showing Australian researchers the extent of the exciting facilities and techniques available.

Researchers will hear talks from the four NCRIS Characterisation Capability members, the Australian Synchrotron, the AMMRF, the National Imaging Facility and the National Deuteration Facility, on the diverse ways that they support research. There will also be case studies from users of the facilities, and a consultation session where researchers have the chance to discuss their own specific experimental needs with experts from across all areas of characterisation. ■

Tuesday, 4 August 2009, 12–5 pm
Curtin Technology Park Function Centre
Thursday, 6 August 2009, 12–5 pm
The University of Adelaide, Union House
Registrations for both events open late June on www.characterisation.org.au

Materials Australia Microscopy Symposium

This symposium is being jointly organised by Materials Australia and the AMMRF to launch Materials Australia's special interest group in microscopy. Delegates from SMEs will hear about AMMRF facilities and how they add value to manufacturing processes and therefore help businesses to prosper. Case studies will provide effective examples of this process in action and a tour of the AKCMM will demonstrate the cutting-edge instruments on offer. ■

Friday, 18 September 2009
The University of Sydney, Australian Key Centre for Microscopy and Microanalysis (AKCMM)

For details on both events contact: Dr Jenny Whiting: jwhiting@usyd.edu.au

COMMUNITY

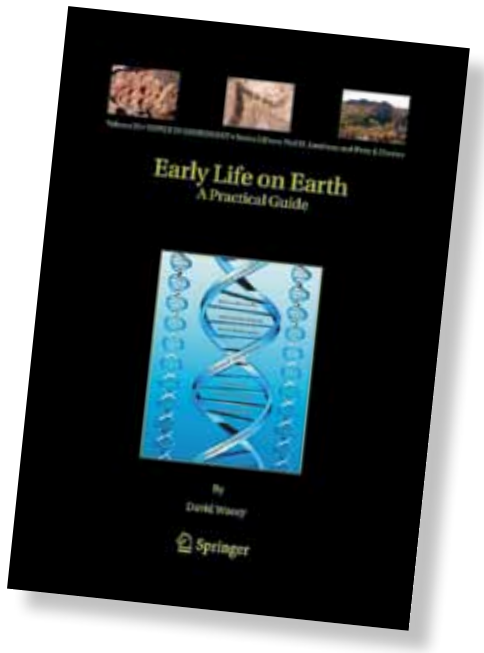
Early life on Earth – how to tell what's what

AMMRF @ UWA

Dr David Wacey, a University Postdoctoral Research Fellow based at the Centre for Microscopy, Characterisation and Analysis (CMCA) at UWA, has recently written the first textbook giving researchers and students a step-by-step guide to evaluating evidence for Earth's earliest life.

Early Life on Earth: A Practical Guide equips the reader with knowledge required to successfully analyse new potential biological signals in rocks more than three billion years old. David believes this will be a valuable resource for the growing number of courses and research groups in the fields of Precambrian palaeobiology and astrobiology. "The correct decoding of possible biological signals on Earth is critical to our interpretation of extraterrestrial material analysed, or even recovered from, future Mars missions. One key to this is figuring out which techniques and instrumentation are going to be most successful for the job". A major section of the book is devoted to this issue. Traditionally, palaeobiologists have concentrated on a morphological approach using optical microscopy. Over the last couple of decades, however, more and more high-resolution techniques have been applied, following the realisation that non-biological processes can mimic biological morphology. This new multi-technique approach depends on the types of instruments available through the AMMRF (SEM, microprobe, TEM and EELS, FIB, SIMS, NanoSIMS, X-ray tomography, AFM). Several illustrations consist of images taken by David and his colleagues at CMCA.

With 145 illustrations, another major emphasis is on showing the reader the places on Earth where the best preserved rocks can be found, and what types of morphology and chemical signals might be indicative of life. The book demonstrates robust examples of both life and the multitude of non-biological features that appear to mimic life, together with some of the ongoing controversies that exist in the field. ■



STAFF NEWS

The University of South Australia

Zophia Swierczek has recently joined the Ian Wark Research Institute at the University of South Australia and will be responsible for collecting and interpreting data using the Qemscan system. She will also develop species identification protocol databases and train Qemscan users on the instrument. Zophia was educated in the Department of Geology, Geophysics and Environmental Protection at the University of Science and Technology (AGH) in Krakow, Poland, from where she graduated in 2006. She is an enthusiastic mineralogist who wants to share a passion with geoscientists. Zophia does, however, also have experience in multiple disciplines, with her master's thesis covering aspects of mineralogy, medicine and archaeology. ■

The University of New South Wales

Dr Aaron Dodd joined the UNSW's Electron Microscope Unit (EMU) in February as a research associate. He obtained his BSc and PhD in materials engineering from the University of Western Australia, and worked as a research scientist with Antaria Ltd before returning to academia at the University of Western Australia. Aaron's new role at the EMU will enable him to use his expertise in high-resolution and energy-filtered TEM imaging to provide support to advanced TEM users, and to pursue his research interests in nano-particulate materials synthesis and characterisation. ■

The EMU is also pleased to welcome **Mr Eugene White**, who took up the role of technical officer at the end of March. Eugene had been a user at the EMU during his honours year in 2007, so he certainly knew what he was getting himself into! His Honours work focused on super-hydrophobic thin film behaviour and morphology, with particular relevance to the self-cleaning properties of the films. Eugene is already being kept very busy with his role, providing technical support for a range of the EMU's SEMs and training their users. ■

AWARDS

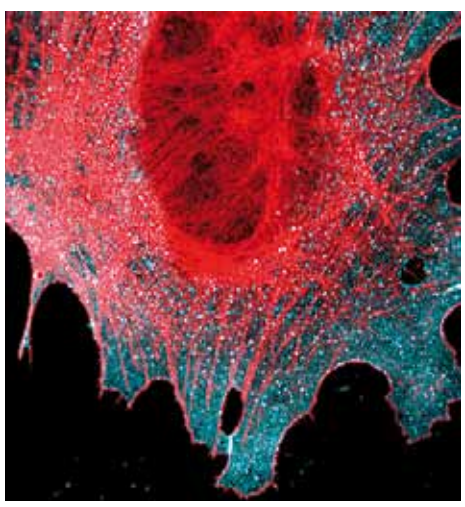
Congratulations to AMMRF team members

Prof. Rob Parton, Deputy Director of the AMMRF's University of Queensland node, has been awarded a prestigious Australia Fellowship from the NHMRC and, in addition, has recently been elected as a Fellow of the Australian Academy of Science. Rob is one of sixteen newly elected Fellows, chosen for their significant contributions to science in Australia and internationally.

Rob was elected for his work on the cell surface, which has a range of applications, including the potential to improve drug delivery and to better understand prostate cancer.

The Australia Fellowship was awarded earlier this year and is worth $4 million. It will fund research into tiny vesicles that bud off from the cell surface, and that could be engineered to deliver drugs directly to specific sites in the body. This would mean that healthy cells would not be targeted, greatly increasing the drug's effectiveness and minimising adverse reactions.

TEM and cryo-tomography with the AMMRF flagship instrument have enabled Rob to understand the structure and formation mechanisms of these membrane vesicles. ■



The blue stain labels the cell surface and allows visualisation of endocytic vesicles within the cell.

Assoc./Prof. Peta Clode, from the Centre for Microscopy, Characterisation and Analysis (CMCA) at the University of Western Australia (UWA), has been awarded an Australian Academy of Science Fellowship to visit Dr Kotaro Shirai at the Ocean Research Institute at the University of Tokyo. Peta, whose main interest lies in marine invertebrate biomineralisation, will visit Japan for four weeks in June 2009. Her fellowship will see her undertake experiments into the growth patterns of reef corals at Ishigaki Island, Okinawa, followed by the analysis of samples with the University of Tokyo's NanoSIMS. Corals form the structural foundation of reef ecosystems, and it is well recognised that their survival is under threat from environmental change. Understanding their growth mechanisms is of major importance in the context of coral reef preservation and management in the face of climate change. ■

Prof. Brendan Griffin, also based at the CMCA at UWA, has been awarded a prestigious Australian Academy of Science Fellowship to collaborate with Prof. David Joy at the Oak Ridge National Laboratory in August 2009. He intends to characterise the information content of images created by using the newly developed helium-ion scanning microscope. Through this research, the exciting sub-nanometre imaging capability and analytical potential of the new helium-based scanning-ion microscope will be explored. Brendan and David have already enabled the world's first measurements of relationships between the chemistry and morphology of the sample, the Rutherford backscattered ion yield and the helium-ion range. Brendan's fellowship will enable further development of this work. The results will provide evidence on fundamental helium-ion-scattering processes and, perhaps most importantly, will evaluate the future role of this technology alongside traditional electron-beam instruments in nanomaterial and device characterisation. ■

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