Australian Synchrotron

LIGHTSPEED February 2011

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From the Acting Director - Building the future

With the New Year 2011 barely begun, major developments are already well underway at the Australian Synchrotron.

The area around the main synchrotron building is starting to resemble a series of construction sites as work commences in earnest on an extensive building program made possible by a grant from the federal government's Education Infrastructure Fund.

New facilities under construction include the National Centre for Synchrotron Science on the old gravel car park near Blackburn Road, a separate engineering building to house an uninterruptable power supply (UPS), a user accommodation block and a 'pod' extension for staff offices. Further information appears later in this Lightspeed, and as work progresses, we will post regular updates and photos on our website.

Also rapidly taking shape is the extended and upgraded imaging and medical beamline. This work involves construction of a near-beam surgery preparation area inside the main synchrotron building and a second storey for the satellite building that will house additional preparation and handling facilities for clinical research programs using the long beamline.

We have recently made new appointments to two key positions. We welcome Dr Andrew Peele as our new Head of Science and Dr Shirley Lanning as the new Head of External Relations. Andrew and Shirley have begun working with their teams and introducing themselves to key stakeholders.

We are looking forward to working closely with the new Victorian and Australian governments on implementing strategies to achieve the objectives outlined in the synchrotron business case submitted last year. This important document presents in detail the case for future operational funding as well as funding for the improvement and expansion of our current facilities, including the initial suite of nine beamlines (specialised experimental stations). The business case is complemented by 'science case II', which outlines a range of proposed developments, including new beamlines to meet the future needs of the research community.

We are delighted that Daniel Taylor, Consul-General/Trade Commissioner for New Zealand will be visiting the facility this month, helping us to consolidate links with the business community in New Zealand.

We recently invited the new Victorian Minister for Innovation, Services and Small Business, the Hon. Louise Asher, to visit the facility and we look forward to welcoming her on site in the near future.

George Borg

Chief Operating Officer, Australian Synchrotron

Up to speed: Andrew Peele

This month our short interview features Andrew Peele, the new head of science at the Australian Synchrotron.

Describe your job in 25 words or less.

Responsibility for the core activities of user and beamline operations as well as catalysing the best scientific results from users, including our own scientific staff.

Best aspect of your new position?

The opportunity to interact with a world-leading group of people dedicated to the notion of supporting the best scientific research in Australasia.

Worst aspect of your job?

The commute!

Biggest challenge facing you in your new position?

Getting across the enormous diversity in research that can be done at the Australian Synchrotron and convincing stakeholders, funders and the public of the value of that research.

Apart from the Australian Synchrotron, what's the coolest job you've ever had?

Cleaning the caramel spreader at the Mars Bar factory in Ballarat.

What's your history as a synchrotron user?

Eclectic. Since 1994 I have used synchrotrons in Europe, Asia, the USA and Australia. I think I have participated in experiments on more than a dozen beamlines and used almost as many techniques.

Best things about living in Melbourne and why?

In recent years the climate. That and the terrain make riding to work a pleasure.

Your favourite overseas destination and why?

Australia – it's easy to get to and has everything you could want in a travel destination.

A little-known fact about the Australian Synchrotron?

Australian Synchrotron is an anagram of 'only ran anarchist tours'.

What would you like to see more of at the AS?

Beamlines!

Designer drugs to treat HIV/AIDS

Designing drugs that can help 30 million adults and children living with HIV is an ongoing battle made worse by the virus's ability to develop resistance to some existing drugs.

Researchers are using x-ray crystallography at the Australian Synchrotron to help identify potential new drugs to address the resistance problem. For example, Jerome Wielens from St Vincent's Institute in Melbourne recently used the Australian Synchrotron to obtain valuable new clues about different kinds of chemical compounds that could potentially be more effective against HIV.

Infection with human immunodeficiency virus (HIV) leads to acquired immunodeficiency syndrome (AIDS). This debilitating disease attacks and eventually sabotages the immune system, ultimately resulting in death. Treatments are available for HIV that reduce viral loads and slow the progression of AIDS but none of these eradicate the virus or prevent the spread of infection. Moreover, these treatment regimes are being compromised by the emergence of drug-resistant strains of HIV.

Although the development of effective treatments has helped reduce the death rate, AIDS-related causes still account for about 1.8 million deaths a year. HIV/AIDS is the second most common cause of death for people aged 20 to 24, according to UK-based international HIV and AIDS charity AVERT.

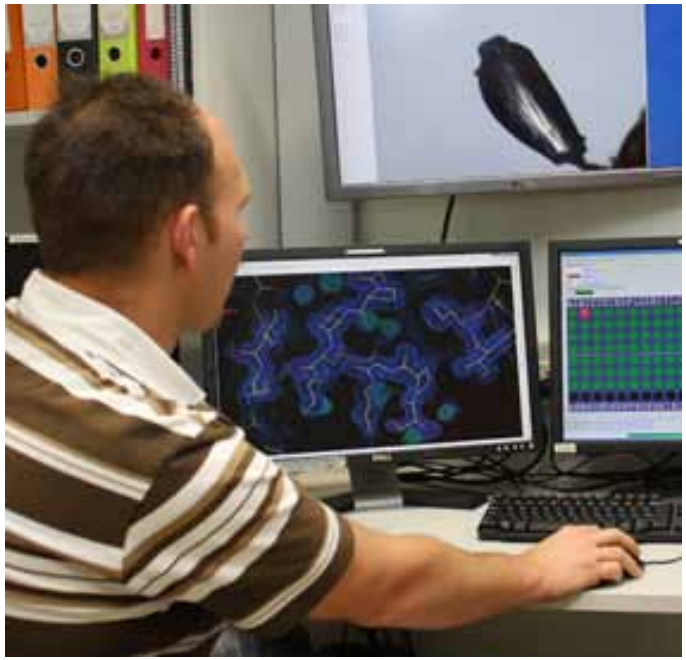
Drugs that block the action of an HIV protein called integrase are an important part of current treatments for HIV/AIDS. HIV-1 integrase is an essential protein for HIV replication and the development of AIDS. It catalyses the insertion of the viral DNA genome into the host DNA, which establishes the HIV infection in the host's body. Preventing integrase from performing this function stops the virus replicating and halts the progression to AIDS.

The first integrase inhibitor approved for clinical use is raltegravir. Several other inhibitors in advanced clinical development act via the same mechanism (i.e. they bind to the same site on integrase) as raltegravir. However, strains of HIV that are resistant to raltegravir are also resistant to some of these preclinical drug candidates. As a result, there is significant interest in identifying other potential drug-binding sites on integrase.

Structure-based drug design

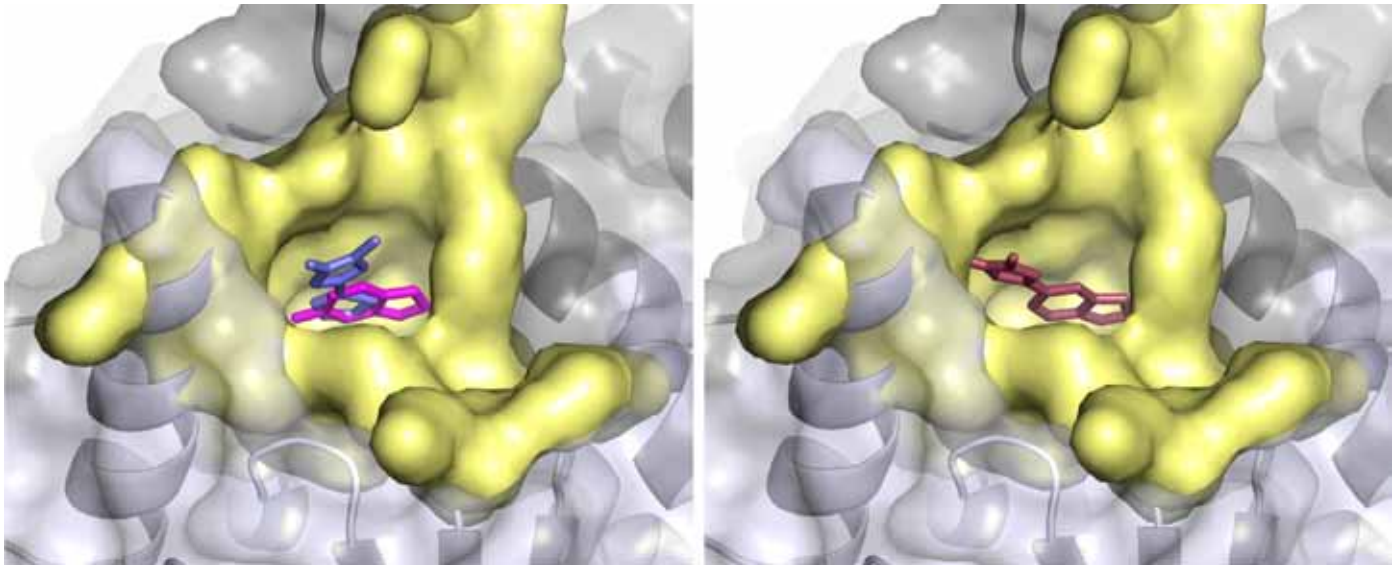
One of life's essential building blocks, proteins perform many tasks including acting as molecular machines, transporters, switches and catalysers, as well as contributing to the overall structure of an organism. X-ray crystallography allows researchers to determine the three-dimensional shape of a protein; they can then use this information to understand how the protein functions – and potentially modulate its activity. Because synchrotron x-rays are much more powerful than laboratory x-rays, they produce far more precise pictures of protein structures.

Structure-based drug design is a method of designing drugs that uses the three-dimensional shape of a protein target to develop compounds that modulate (usually inhibit) the activity of the protein to obtain a desired response. For example, a compound may prevent the protein from performing an essential function for the propagation or survival of a virus, a cancer cell or bacterium, and therefore have the potential to be developed into a treatment for that particular virus, cancer or bacterium.



Jerome Wielens (St Vincent's Institute) prepares to use the MX2 beamline at the Australian Synchrotron.

Designer drugs to treat HIV/AIDS (cont.)



LEFT: Fragment-based drug design involves finding small molecules or 'fragments' (two shown here in magenta/blue) that bind to a key protein (in this case HIV-1 integrase from the AIDS virus).

RIGHT: Researchers then designed a molecule (shown here in raspberry) that combines the characteristics of these fragments and binds more tightly to the protein. Images: Jerome Wielens. Figures prepared with PyMOL http://www.pymol.org

Fragment-based drug discovery (FBDD) is an approach for identifying which different types of molecules can bind to target proteins and then determining which part of the target protein they actually bind to (usually called a binding site or pocket). 'Fragments' are small compounds of relatively low complexity that bind to sub-pockets within a binding site on the protein. X-ray crystallography is used to visualise these fragments bound to the protein of interest so that chemists can develop more-complex compounds that combine different fragments or 'grow' them; the aim is that some of these more-complex compounds will bind the protein strongly enough to block its action and ultimately lead to the development of new medicines based on these compounds.

Small steps with big potential

Jerome Wielens from St Vincent's Institute in Melbourne and his colleagues and collaborators are working to identify fragment molecules that bind to HIV-1 integrase and determine the three-dimensional structure of these fragments in complex with integrase. They are using a structure-guided approach to design and build more complex molecules with improved binding power.

The researchers initially used nuclear magnetic resonance (NMR) spectroscopy to investigate a library of 500 molecules and identify a series of fragment compounds that bind to integrase. They then used the crystallography beamlines at the Australian Synchrotron to determine the crystal structures of some of these compounds in complex with integrase. The synchrotron information helped the group to elaborate their initial hits and produce compounds with much stronger affinity for integrase (in the micromolar range). In the process, they also identified a previously unknown binding pocket on integrase that has the potential to be a valuable drug target.

The group's synchrotron results provide a useful basis for designing more potent compounds that bind to integrase and disrupt its functioning.

The work was partly funded by an ARC Linkage grant and done in collaboration with Professor Michael Parker of St Vincent's Institute, Drs David Rhodes and John Deadman of Avexa Ltd and Dr Stephen Headey, Dr David Chalmers and A/Professor Martin Scanlon of Monash Institute of Pharmaceutical Sciences.

Click here to go to a recent research paper authored by Jerome and his colleagues.

Synchrotrons in the news February 2011

What ammonites ate

Ancient cousins of squid, octopus and cuttlefish, the ammonites died out at the same time as the dinosaurs. French and American researchers used synchrotron x-ray microtomography at the ESRF to obtain 3D images of fossilised ammonite mouthparts that provide new insights into ammonite feeding habits and their position in the Mesozoic marine food web.
http://www.bbc.co.uk/news/science-environment-12127790
http://www.sciencemag.org/content/331/6013/70.abstract

Study reveals clear view of asthma

The Monash Institute of Medical Research is using a synchrotron in Japan to create video images of how air moves through a mouse's lungs when a breath is taken. This capability will be used to help improve the effectiveness of asthma treatments. The researchers plan to do similar work on the extended Australian Synchrotron medical and imaging beamline when construction is complete.
http://www.theage.com.au/victoria/study-reveals-clear-view-of-asthma-20110102-19d32.html

Cleavage reveals new electronic layer

French researchers cleaved a piece of strontium titanate, a transparent insulating material, to create a conductive layer just two nanometres thick. The two-dimensional metallic electron gas layer (which part of that did you not understand?) opens up new possibilities for microelectronic applications that combine properties such as superconductivity, magnetism and thermoelectricity.
http://www.azom.com/news.asp?newsID=27090
http://www.nature.com/nature/journal/v469/n7329/full/nature09720.html

Two-step enzyme clue to golden staph

Using a US synchrotron, researchers have revealed key details of an enzyme involved in creating the golden-coloured coating that helps 'golden staph' bacteria to resist antibiotics. The findings could lead to more-effective new drugs against this problem bacterium.
http://www.news.illinois.edu/news/11/0118staph_oldfield.html

Synchrotron aims to produce medical isotopes

Researchers at the University of Saskatchewan are planning to use the Canadian synchrotron to develop medical isotopes without a nuclear reactor.
http://www.lightsource.ca/media/media_release_20110124.php

Beamtime submissions for round 2011/2 (June-September 2011) open on 8 February 2011

Key dates for beamtime submissions are listed on the synchrotron website at: **http://www.synchrotron.org.au/index.php/features/applying-for-beamtime/proposal-deadlines**

If you would like to discuss your ideas for future beamline proposals with the beamline scientists at the Australian Synchrotron, please allow plenty of time.

For more information about applying for beamtime at the Australian Synchrotron, contact the User Office: **user.office@synchrotron.org.au**

Construction update

Watch those spaces!

Three of the new buildings being constructed around the Australian Synchrotron are now in use: the technical support laboratories building, the office extension pod and the switchroom extension. External construction of the user accommodation building is complete, and the building is being fitted with furniture in readiness for users.

The biggest construction project, the National Centre for Synchrotron Science building, is nearing completion, with installation of windows and Rodeca panelling on all exterior walls. Inside the building, auditorium seating and lighting are in place, and interior walls and office fittings are quickly taking shape.

Commenced in late 2010, these projects are an initiative of the Australian Government being financed from the Education Investment Fund.

Click here to download a map (pdf, 140kb) with information about new parking arrangements for visitors to the synchrotron.

National Centre for Synchrotron Science (NCSS)

- Two-storey building with a 400-seat auditorium, seminar rooms, exhibition space, User Office, staff offices, cafeteria and underground parking.
- Building construction is ahead of schedule. Installation of the translucent Rodeca panelling facade is almost complete and most of the exterior windows have been fitted. Kitchen equipment has been installed and joinery items are being fitted out throughout the building. Auditorium lighting comprises an impressive array of 120 circular fluorescent luminaries.
- The NCSS building has a five-star rating under the Green Star system, which is a comprehensive, national, voluntary environmental rating system that evaluates the environmental design and construction of buildings. To achieve this rating, the building includes features such as 20 kilolitre water tanks for recycling water, high-efficiency heating and cooling systems, and 100 photo-voltaic panels on the roof to offset the power needed for the facade lighting, which is a key feature of the building's exterior. Click here to read more about the NCSS building and its green credentials.
- Several elements of the NCSS building, such as landscaping, fittings, and audiovisual equipment, are being managed separately from the main construction works.
- Investigations into the operation of the cafeteria are continuing.
- Following several feasibility studies in late 2011, a detailed landscaping design is being developed from the landscaping masterplan to address aspects such as tree types and locations, irrigation pipes, concreted areas, parking, benches and seating. The design calls for many new trees to be planted, particularly around parking areas and the user accommodation building. A vegetable garden will be established near the existing barbecue area. The entrance roadway and lighting for the main synchrotron building will be redesigned. The landscaping work is expected to be put out for tender in March 2012.
- See overleaf for photos of construction work on NCSS building.

User accommodation building

- Two-storey building with 50 self-contained rooms, communal kitchens, lounges, laundry and reception. The ground floor includes disabled facilities.
- Construction is complete. Following successful assessment of the prototype bedroom, all bedrooms are being fitted out with furniture. The kitchen, laundry and lounge areas are also being equipped with furniture, fittings and equipment.
- "The user accommodation building is so nice, particularly the lounge area, that synchrotron staff are already joking about occupying the building themselves," says Alexis Kouts from the Synchrotron's Major Projects and Technical Services Group.
- "Provided the new furniture is delivered on schedule, we hope to begin making the accommodation available to users in April 2012."
- Processes are being developed for carrying out the necessary cleaning, scheduling, security, repair and maintenance tasks.

Click here to go to user accommodation building photo page.

Construction update (cont.)

Modular office extension (office extension pod)

The modular extension 'pod' connected to the main synchrotron building is complete. It has been fitted out with workstations and office furniture and is now occupied by staff from several groups, including Major Projects. The building provides a simple but functional open office area with plenty of natural light. Spare desks are available for visitors to use.

Click here to go to office extension 'pod' building photo page.

Technical support laboratories building

This building is occupied and fully operational with four laboratories, an open plan office, meeting rooms, mechanical workshop and stockroom. The large spaces within this building have enabled the engineering group to be consolidated into one area, supported by tools and equipment located downstairs.

Click here to go to technical support laboratories building photo page.

Switchroom extension

Extension to the existing low voltage switch room, which had reached capacity. The uninterrupted power supply (UPS) system is now operational. A cooling system is being installed for days of extreme heat.

Thanks to three brand-new 'uninterruptable power supply' (UPS) systems, the AS storage ring can continue operating for up to 15 seconds without any power, enabling synchrotron operators and users to continue working through any short-term power supply disruption.

Click here to go to switchroom extension building photo page.

We will post regular updates on our website to keep you informed of progress.

(18 January 2011): views of the excavation work in the gravel carpark near the synchrotron entrance gate on Blackburn Road.

(1 February 2011) L to R: excavation works for road relocation and NCSS building.

(15 February 2011): construction work for NCSS building.

MASSIVE progress

The new MASSIVE high performance computing facility at the Australian Synchrotron and Monash University is taking shape, with the installation of equipment, operating systems, software and a fibre optic cable linking the two sites.

One of a limited number of high performance computing facilities in Australia, MASSIVE (Multi-modal Australian Sciences Imaging and Visualisation Environment) will provide hardware, software and expertise to help scientists apply advanced imaging and visualisation techniques.

http://www.synchrotron.org.au/index.php/about-us/our-facilities/engineering/massive

Editor's note: An apology to the Australian National Data Service (ANDS)

In the 2010 December issue of Lightspeed, our publication highlighted the development of the TARDIS/My TARDIS system; a software solution, developed by Monash computer scientists to make data more accessible, easier to interpret, verify and report.

The software solution was developed to assist the Australian Nuclear Science and Technology Organisation (ANSTO) and Australian Synchrotron in their efforts to store and manage the large volumes of data generated by scientific experiments.

While the LightSpeed article talked about the purpose of the solution, the collaborating partners and the benefits of TARDIS, it failed to mention the funder of the project being the Australian National Data services (ANDS).

The Australian Synchrotron would like to formally apologise for this omission.

Tardis to store synchrotron data

The Australian Synchrotron and ANSTO have both selected an all-Australian software solution to assist with storing and managing the reams of scientific data generated by their experiments. They will use TARDIS/MyTARDIS, a software system developed by computer scientists at Monash University, to make data more accessible, easier to interpret and easier to verify and report.

The decision means scientists from the two organisations, which support some of Australia's most sophisticated scientific instruments, can cooperate more effectively, and better organise the information gathered from their experiments, ultimately making data easier to retrieve and use.

The TARDIS project is supported by the Australian National Data Service (ANDS). ANDS itself is supported by the Australian Government through the National Collaborative Research Infrastructure Strategy Program and the Education Investment Fund (EIF) Super Science Initiative.

Events diary

Synchrotron-related events in Australia and overseas.

Read more

Space for your event

To submit your synchrotron-related event for listing in Lightspeed and on the Australian Synchrotron website, click here.

Reader feedback

Lightspeed welcomes your comments and suggestions. Please send these to: info@synchrotron.org.au with 'Lightspeed comments' in the subject line.

Use of Lightspeed material

Careers at the Australian Synchrotron

The Australian Synchrotron offers a unique working environment for a wide range of specialists. For information on job postings, go to:

http://www.synchrotron.org.au/index.php/about-us/working-at-the-synchrotron/employment-opportunities

Staff list

http://www.synchrotron.org.au/index.php/about-us/working-at-the-synchrotron/staff-contact