Journal of
Synchrotron Radiation
ISSN 0909-0495

current events

This section carries events of interest to the synchrotron radiation community. Works intended for this section should be sent direct to the Current-Events Editor (s.s.hasnain@liverpool.ac.uk).

Another Nobel prize for synchrotron radiation protein crystallography

Brian Kobilka, MD, professor and chair of molecular and cellular physiology at the Stanford University School of Medicine, has won the 2012 Nobel Prize in Chemistry for his work on G-protein-coupled receptors, or GPCRs. Over the course of the last three decades, Kobilka, who is 57, and his former mentor and colleague Robert Lefkowitz, MD, who is 69, who share the prize, have played an important role in discovering and understanding GPCRs. Last year, Kobilka was the first to crystallize and analyze one of the receptors bound to its signaling molecule, which is a critical step toward understanding how to control them.

Brian Kobilka received his MD from Yale University in 1981. In 1984 he joined the Lefkowitz laboratory. Early in his career, Lefkowitz used radioactivity to understand the receptors' function and their shape in the cell wall. Lefkowitz said at a news conference at Duke University today that his life's work had been dedicated to defining these receptors, beginning with a fellowship at the NIH in 1968. 'When I started there was a lot of skepticism about whether such receptors even existed, and there was no way to study them', he said. Lefkowitz's research dispelled such doubts, and he credited Kobilka with advancing the understanding to a new level. 'What Kobilka has done is to carry this to atomic resolution', he said, explaining that it was now possible to see the protein 'literally atom by atom'.

A critical development, which enabled the crystallographic work on this very challenging system, was the microcrystallography [*Acta Cryst.* (2008). D**64**, 425–435; *J. Synchrotron Rad.* (2009). **16**, 217–225; *Acta Cryst.* (2011). A**67**, C158]. This enabled data collection strategies to be developed that outran the radiation damage, reduced scattered background and matched the intense X-ray beam to the diffracting volume. This Nobel prize is a special occasion for the synchrotron radiation community as it marks the fifth Nobel prize that is associated with synchrotron radiation, the first being awarded to John Walker in 1997 on the structure-mechanism of F1-ATPase, a moment that was marked by a special celebratory issue of the *Journal of Synchrotron Radiation* [(1999). **6**, 809–945]. It is also a special occasion for the Advanced Photon Source that becomes the first synchrotron to be associated with two Nobel prizes, the last one awarded three years ago. We note that ESRF played an important role in the early stages contributing to the structure solution of the second GPCR structure after rhodopsin as reported in *Nature* in 2007.

Brian, commenting on the importance of the microcrystallography facility at the Advanced Photon Source, said 'My lab has been very fortunate to have access to the GM/CA-CAT beamlines. The high-quality minibeam has been essential for our work on GPCR crystals, and the specialized software developed by the beamline staff makes it possible to find and collect data from very small crystals. The beamline staff are very helpful and always interested in what they can do to make data collection easier and more efficient.' Janet Smith, who is scientific director of the beamline, said 'We were delighted in early 2007 when Brian contacted us about beam time for his GPCR project, delighted because Bob (Fischetti) had just tested the first collimator to produce a 10 μm minibeam and proven its success. Here was an important project that required a hot, stable, small beam, a project that greatly accelerated our development of the mini-beam apparatus and the software to use it. Everyone at GM/CA congratulates Brian and Bob Lefkowitz on their Nobel prize. We are thrilled to have provided the right technology at the right time to help this project succeed.' Bob Fischetti commented 'it has been such an honor to work with Brian to drive the development of new micro-crystallography tools that enabled the structural determination of such an important class of molecules. Brian is a dedicated, hard-working scientist and is truly deserving of the Nobel prize.'

In the 1980s, Brian Kobilka and Bob Lefkowitz began to work together to learn more about the epinephrine receptor, also known as the β-adrenergic receptor. Brian was able to isolate the gene for the receptor (no small feat at the time) to learn more about its composition. When he studied the sequence, he realised that it was very similar to that of another, seemingly unrelated, receptor called rhodopsin that detects light in the retina of the eye. This research helped the scientists realise that GPCRs are a large family, with many different examples throughout the body. In 2011, Kobilka and his team were the first to obtain a three-dimensional image of the same G-protein-coupled receptor bound to its signaling molecule, an extremely difficult technical endeavor due to the protein's size and complexity. Knowing the structure is important in order to be able to design better drugs to activate or inhibit the receptors. 'It was so exciting to see this three-dimensional structure and finally know how these trans-membrane regions interact during signaling', said Kobilka. 'I hope my discovery leads to better and less expensive drugs for patients.'

He and his wife Tong Sun, a practicing physician and research scientist herself, moved with their two sons to Stanford in 1989 when Brian was recruited by Richard (Dick) Tsien, founder and chair of the Department of Molecular and Cellular Physiology. Professor

From left to right, Brian Kobilka, Andrew Kruse, Brian DeVree, Soren Rasmussen and Roger Sunahara. Roger was dropping the team off at Chicago airport after they had finished collecting the final data for the b2AR-Gs complex.

Tsien, who had taught Brian at Yale, said 'That is just amazing news, fantastic!'. Tsien recalled 'I first taught Brian when he was a medical student at Yale, a skinny kid from Minnesota who was very conscientious, keen to know everything he could possibly know about being a good doctor and a good scientist. I remember him being particularly gaunt and definitely an ectomorph. He asked lots of questions after lectures, even though I didn't have the feeling he was going to become an electrophysiologist. Fast forward a few years to my time starting the Department of Molecular and Cellular Physiology at Stanford, when I had the opportunity to collaborate with the Department of Medicine in recruiting someone interested in doing research at the borderline of clinical work and basic science. I learned that Brian was on the job market, and he stood out for his spectacular work done with his wife Tong Sun, all in the Lefkowitz lab, where they fearlessly took on the cloning of various β-adrenergic receptors. I was really impressed by how helpful and thoughtful and enterprising he was in going after big problems.'

Roughly 800 different GPCRs have been identified to date, making them one of the largest families of human proteins. These proteins regulate the beating of our hearts, the workings of our brains and nearly every other physiological process. About 40% of all medications target these receptors, including Zyprexa, which is used to treat schizophrenia; the antihistamine Clarinex; and Zantac, which is used for stomach ulcers and gastro-esophageal reflux disease.

Friends and family pay tribute to Dame Louise Johnson

A day prior to her 72nd birthday on 25 September 2012, Louise Johnson, one of the pioneers of crystallography, passed away after a short illness. Louise Johnson will be very fondly remembered by the IUCr and synchrotron radiation communities for her generosity, thoughtfulness and care she took in nurturing so many careers while opening new areas of research. Her classic book on protein crystallography with Sir Tom Blundell, published in 1976, became a regular reference book for investigators, postdoctoral fellows and students from far and wide. We learn from the obituary by Sir Tom Blundell [*Acta Cryst.* (2012). D**68**, 1588–1590] how this book came about and Louise's total grasp of the subject.

Louise Johnson on the occasion of the opening of the Barkla Laboratory of Biophysics in Liverpool on 21 July 2011.

Louise Johnson graduated in physics from University College, London, in 1962 when she joined David C. Phillips at the Royal Institution for a PhD. Her PhD thesis, entitled 'The structure of *N*-acetyl-glucosamine and its relation to lysozyme', resulted in several papers in 1965/1966 [*Nature* (1965). **206**, 757; *Acta Cryst.* (1966). **21**, 885; *Sci. Progr.* (1966). **54**, 367]. Max Perutz emphasized the extraordinary significance of this work in these pages [*J. Synchrotron Rad.* (1999). **6**, 945–946] while writing an obituary for David Phillips, "Certain moments are deeply engraved in my memory. One is the Monday morning in March 1953 when Crick called me into his room to show me his and Jim Watson's double helical model of DNA which immediately revealed the molecular basis of heredity. Another is the moment when David Phillips, Louise Johnson and Charles Vernon made me understand how an enzyme works." In 1990 she became the first David Phillips Professor in Molecular Biophysics at Oxford, a position she held for 17 years. In 2003 she concurrently held the position of Life Science Director of the Diamond Light Source from which she retired in 2008.

In addition to crystallography and molecular enzymology, she had a special interest in promoting science in developing countries and several of her lecture engagements reflected this interest. She was particularly pleased when she was elected as an Associate Member of the Third World Academy of Sciences in 2000. She chaired the TWAS selection panel for elections in the fields of cell, structural and molecular biology. She also worked hard in her quiet manner in promoting projects such as SESAME, which aims to bring nations together, and made visits to Jordan and many of the member countries of this challenging project. She never shied from big challenges. We finish with a statement from Professor Jenny Martin, one of Louise's students, 'Louise touched many lives. And her impact on our field of science is immeasurable. She helped lead the way in crystallography and in synchrotron life science. She also trained a generation of crystallographers in Oxford who themselves now train future leaders across all four corners of the world. That is an amazing legacy.'

Soichi Wakatsuki to join Stanford in early 2013

Soichi Wakatsuki will be moving to Stanford in the new year and take a position at SLAC jointly with the Stanford School of Medicine. Soichi received his PhD in chemistry from Stanford in 1991, working in biophysics and small-angle X-ray scattering studies of protein structure and function. He then joined the late Dame Louise Johnson as a research assistant in Oxford's Laboratory of Molecular Biophysics prior to moving to the European Synchrotron Radiation Facility in 1994, initially as a beamline scientist, becoming a group leader of macromolecular crystallography in 1999. In 2000 he moved to Japan as professor of structural biology becoming the Director of the Photon Factory in 2006 at KEK, the High Energy Accelerator Research Organization in Japan. During the last decade he played a transformative role in enhancing the capabilities of the Photon Factory, establishing a major structural biology centre in KEK, and extending the life of now the 30-year-old storage ring facility significantly; it remains a highly desirable destination for many structural biologists in Japan despite the emergence of SPring-8 in 1997. We wish Soichi continued success with his latest move and look forward to hearing of the latest development in synchrotron-enabled structural biology from his new laboratory.